CONFERENCE HANDBOOK

2011

APSA Annual Conference

Science Informing Practice
Practice Informing Science

UNIVERSITY OF SOUTH AUSTRALIA

11 – 14 December 2011

apsa

Welcome

On behalf of the Australasian Pharmaceutical Science Association (APSA), we welcome you to the 2011 APSA Annual Conference, being held in Adelaide at the University of South Australia, City East Campus.

The conference is the major gathering of pharmacy and pharmaceutical science academics and researchers from Australia and New Zealand. APSA members and conference delegates have a diverse range of expertise and have a commitment to teaching and research in the areas of pharmaceutical sciences, clinical sciences and pharmacy practice. This year's conference will continue to promote the research activities and achievements of honours and postgraduate students, and we expect them to have a strong presence at the conference.

Our conference program will address the theme 'Science Informing Practice, Practice Informing Science'. The highlight of the conference promises to be the presentations by Professor Edzard Ernst (Peninsula Medical School, Universities of Exeter and Plymouth), who is widely acknowledged as a world leader in the evidence basis of complementary medicines. Other highlights include Professor Ian Olver (CEO of Cancer Council Australia) and an address by Dr Jill Maxwell, a clinical leader with the National e-Health Transition Authority.

Our social program aims to showcase some South Australian food and wine icons and offers ample opportunity for conference delegates to network in a relaxed atmosphere.

The venue, University of South Australia, City East Campus, is conveniently located in the Adelaide CBD; numerous shops, cafés and restaurants are in close proximity, as are other attractions such as the Adelaide Zoo, Adelaide Oval and the National Wine Centre.

We hope you enjoy your time in Adelaide for APSA 2011.

Michael Sorich
and
Michael Wiese

Conference Organising Committee
Dr Michael Sorich (Co-Chair)
Dr Michael Wiese (Co-Chair)
Dr Timothy Barnes
Dr Elizabeth Elliot
Dr David Foster
Dr Libby Hotham
Dr Stephanie Reuter Lange
Dr Michael Ward
Dr Des Williams

Conference Secretariat
All Occasions Management
41 Anderson Street
Thebarton SA 5031
p: +61 8 8125 2200
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w: www.alloccasionsgroup.com

Sponsors

Major Sponsors

University of South Australia | Sansom Institute for Health Research

NAPE National Alliance for Pharmacy Education

The University Of Queensland AUSTRALIA | The University of Sydney | University of South Australia | Monash University

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PDL

University of South Australia | School of Pharmacy and Medical Sciences

Session Sponsors

University of South Australia | Australian Centre for Pharmacometrics

Quality Use of Medicines and Pharmacy Research Centre

SUNDAY 11 December 2011

12:30pm

3:00pm

4:30pm

5:00pm

5:30pm

6:00pm

6:30pm

7:00pm

7:30pm

8:00pm

WORKSHOPS

Workshops

REGISTRATION

Registration

Location: Foyer, Hetzel Building

PLENARY: Ian Olver

Conference Welcome

Ian Olver

Cancer in Australia Over the Next Decade

NAPE National Alliance for Pharmacy Education

The University Of Queensland | The University of Sydney | University of South Australia | Monash University

WELCOME RECEPTION

Welcome Reception

Location: City East Plaza

LOCATION LEGEND H2-02 P5-14 P5-15 P5-33 P5-34 PM-06 Brookman Hall

MONDAY 12 December 2011

8:30am

REGISTRATION

Registration

Location: Foyer, Hetzel Building

9:00am

PLENARY: Edzard Ernst

Edzard Ernst

Complementary and Alternative Medicines: Is Evidence Informing Practice or Practice Informing Evidence?

9:30am

University of South Australia | Sansom Institute for Health Research

10:00am

POSTERS

Poster Presentation Teasers

10:30am

MORNING TEA

Morning Tea

Location: City East Plaza

11:00am

CP01 Pharmaceutical Science: Analytical Techniques

Timothy Barnes
Biophysical characterisation informing the development of protein delivery systems

Clare Strachan
Rapid detection of adulterated herbal products using vibrational spectroscopy

11:30am

Qiang Huang
Development of a simple TLC method for the determination of aristolochic acids

Petra Priemel
Correlating recrystallisation with dissolution behaviour

12:00pm

Atul Awasthi
Separation and identification of degradation products in eprinomectin formulation using LC, FT-MS, H/D...

Madhur Shastri
Development of an effective ion chromatography technique for the separation of intact low-MW heparin

CP02 Pharmaceutical Science: Oncology

Vaughan Connell
Durability of low dose cisplatin-induced cell cycle arrest

Ashleigh De Marie
Cytotoxicity and chemo-sensitisation in malignant mesothelioma cells by small molecule Bcl-2 protein inhibitors

Ritu Jaiswal
Microparticle-associated nucleic acids mediate trait dominance in cancer

Victoria McLeod
Comparison of the pharmacokinetics and anti-tumour efficacy of a PEGylated doxorubicin-conjugated polylysine...

Joyce Gong
Microparticle-mediated resistance and vesicular drug sequestration in breast cancer

Lisa Kaminskas
Targeting methotrexate-conjugated dendrimers to the lymphatics enhances efficacy in a syngeneic rat model of...

CP03 Pharmacy Practice: Cardiovascular

Gina Gujral
Pharmacists reinforcing patients' beliefs about medications to improve adherence post myocardial infarction

Greg Kyle
Landmark studies impact on Australian antihypertensive usage trends from 1992 to 2010

Ashraf Eissa
Utilisation of thrombolysis in acute ischaemic stroke: A clinical audit

Janet Sluggett
Patterns of hospital separations after a transient ischaemic attack or ischaemic stroke

Alexandra Madden
International normalised ratio control in southern Tasmania

John Shaw
Anticoagulation management by New Zealand community pharmacists

CP04 Pharmacy Practice: Counselling

Shirin Hui Tan
Optimising pharmacists' counselling for patients with chronic pain

Krishneeta Kashyap
Assessment and counselling provided with over-the-counter sleep requests: A secret shopper study

Luma Alkhatib
An evaluation of the impact of down-scheduled ophthalmic chloramphenicol on the management of acute bacterial...

Lillian Huang
Commercial influences on community pharmacist recommendations of S2/S3 medicines

Parisa Aslani
The provision of an adherence support service by community pharmacists

Kylie Williams
Internet and community pharmacy provision of a children's cough and cold medicine

12:30pm

LUNCH

Lunch

Location: City East Plaza

1:00pm

1:30pm

LOCATION LEGEND H2-02 | P5-14 | P5-15 | P5-33 | P5-34 | PM-06 | Brookman Hall

MONDAY 12 December 2011

1:30pm

SYMPOSIUM 01: Complementary Medicines

Integrating Complementary and Alternative Medicines into Mainstream Medicine

Edzard Ernst
Michael James
Lisa Nissen

SYMPOSIUM 02: Formulation

Trends in Pharmaceutical Formulation: From Bench to the Clinic

Vânia Rodrigues Leite e Silva
Sanjay Garg
Hugo Albrecht
Graham Aldous

2:00pm

2:30pm

3:00pm

LUNCH

Afternoon Tea & Poster Presentations (Odd Numbered Presentations)

3:30pm

4:00pm

APSA LECTURE: Chris Porter

Chris Porter

Endogenous Transport Pathways as a Blueprint for Drug Delivery: Lessons Learnt from Lipid Absorption

4:30pm

5:00pm

APSA AGM

Annual General Meeting

Chair: Andrew McLachlan

5:30pm

6:00pm

7:00pm

DINNER

AAPS Student Dinner

Location: Ambassador's Hotel

11:00pm

LOCATION LEGEND H2-02 | P5-14 | P5-15 | P5-33 | P5-34 | PM-06 | Brookman Hall

TUESDAY 13 December 2011

8:30am

REGISTRATION

Registration

Location: Foyer, Hetzel Building

9:00am

PLENARY: Jill Maxwell

Jill Maxwell

The promise of e-health, and what barriers are there to realising its full potential?

9:30am

PLENARY: Bill Runciman

Bill Runciman

Systems to Improve Medication Safety: Can We Do Better?

10:00am

10:30am

MORNING TEA

Morning Tea

Location: City East Plaza

11:00am

CP05 Pharmaceutical Science: Formulation

Tri-Hung Nguyen
Nanostructured reverse hexagonal liquid crystals sustain plasma concentrations for a poorly water...

Sarah Hook
Thermoresponsive gels as sustained release vaccine delivery systems

11:30am

Nhung Dang
Polycaprolactone matrices for vaginal delivery of microbicides

Darren Svirskis
A drug delivery system based on intrinsically conducting polymers

12:00pm

Hywel Williams
Solidification of lipid-based formulations via adsorption onto an inorganic high surface-area carrier...

Angel Tan
Hybrid nanomaterials that mimic the food effect to enhance and control oral drug absorption

CP06 Pharmaceutical Science: Molecular Biology

Wei Chean Lee
The induction of P-gp and breast cancer resistance protein by xenobiotics in human carcinoma cell lines

George Li
Anti-inflammatory action of propolis extract: Inhibition of endothelial adhesion molecules and bioassay...

Anne Nguyen
Neuronal and glial cells changes in a transgenic mouse model of retinal neovascularisation

Andrew Crowe
ABCB1 (P-glycoprotein) reduces bacterial attachment to human gastrointestinal LS174T cells

Hamed Shahnam
Investigating the underlying pathophysiology of selective NSAID hypersensitivity and diagnostic...

Matthew Howard
Designing a simple, cost effective and robust assay for measuring CYP2C19 genetic polymorphisms in the...

CP07 Pharmacy Practice: Pulmonary

Sinthia Bosnic-Anticevich
Comparing three different forms of education on health professional inhaler technique and maintenance...

Lynn Cheong
Social network analysis in asthma care: The impact of patients' health connections on interprofessional...

Ming Ley Kong
The information needs of asthma patients and their internet use

Lucille Norton
A review of the management of childhood asthma in Tasmania

Parisa Aslani
Nebulised medicine adherence and factors that affect adherence in patients with cystic fibrosis

Angelina Lim
Asthma during pregnancy: The experiences, concerns and views of pregnant asthmatic women

CP08 Pharmacy Practice: International Perspective

Tuan Nguyen
Why are medicine prices in Vietnam high?

Hanni Puspitasari
A simulated patient study to explore Indonesian pharmacy staff's response to a symptom-based OTC request...

Ho Yan Hidy Chan
Pharmaceutical access in Australia, Hong Kong, Thailand, Vietnam, Singapore and Malaysia

Isaac Joshua
Appropriateness of prescribing in selected locations in Papua New Guinea

Souhiela Fakih
Comparing women pharmacy consumers' experiences with weight loss treatment in Victoria and...

Gereltuya Dorj
Assessment of prescribing practices for community-acquired pneumonia (CAP) in Mongolia

12:30pm

LUNCH

Lunch

Location: City East Plaza

1:00pm

1:30pm

LOCATION LEGEND H2-02 | P5-14 | P5-15 | P5-33 | P5-34 | PM-06 | Brookman Hall

TUESDAY 13 December 2011

1:30pm

SYMPOSIUM 03: New Pharmacist Roles

Roles and Responsibilities of Pharmacist Practitioners in Australia's Reformed Health System

Chris Freeman
Vivienne Mak
Luke Grzeskowiak

Quality Use of Medicines and Pharmacy Research Centre

SYMPOSIUM 04: Nanoparticle Delivery Systems

Toxicological Issues with Nanoparticulate Systems

Rod Minchin
Michael Roberts
Brian Priestly

2:00pm

2:30pm

3:00pm

LUNCH

Afternoon Tea & Poster Presentations (Even Numbered Presentations)

3:30pm

4:00pm

PLENARY: Steve Wesselingh

Steve Wesselingh

Are Academic Health Centres the Key to Linking Science and Practice?

4:30pm

5:00pm

7:00pm

DINNER

APSA Conference Dinner

Location: National Wine Centre of Australia

11:00pm

LOCATION LEGEND H2-02 | P5-14 | P5-15 | P5-33 | P5-34 | PM-06 | Brookman Hall

WEDNESDAY 14 December 2011

8:30am

REGISTRATION

Registration

Location: Foyer, Hetzel Building

9:00am

SYMPOSIUM 05: Medicines' Safety & Effectiveness

Assessing Medicines Safety and Effectiveness: Beyond Randomised Controlled Trials

Sallie-Anne Pearson

Emily Banks

Nicole Pratt

9:30am

SYMPOSIUM 06: Pharmacometrics

Pharmacometrics

David Foster

Richard Upton

Carl Kirkpatrick

University of South Australia | Australian Centre for Pharmacometrics

10:00am

10:30am

MORNING TEA

Morning Tea

Location: City East Plaza

11:00am

CP09 Pharmaceutical Science: Drug Disposition

Cher-Rin Chong
Determinants of perhexiline uptake into the human myocardium

Nathania Leong
The effect of intravenous SBE_7-β-CD on the pharmacokinetics of a series of adamantane-containing compounds

11:30am

Peng Li
Inhibition of sinusoidal membrane Na^+/K^+ ATPase digoxin binding by quinidine is the main determinant of...

Haniza Hassan
Impaired hepatic drug elimination by silica nanoparticles

12:00pm

Sifei Han
Lipophilic prodrugs to target delivery of immunomodulators to lymphocytes in the lymphatic system

Joseph Nicolazzo
Impact of Alzheimer's disease on the blood-brain barrier transport of therapeutic agents

CP10 Pharmacy Education

Gabrielle Cooper
Beyond the dispensary: Innovations in the provision of placements within a pharmacy course that provide...

Pascale Dettwiller
Developing interprofessional teaching and learning: Three universities experience of a remote health day

Maree-Ann Jensen
From the COSE to the OSCE at Auckland School of Pharmacy: Performance based assessment development in the...

Helender Singh
Dose calculations in a virtual world: A pilot evaluation of UQ's compounding dispensary in "Pharmatopia"

Peter Gee
Enhancing placement training: To evaluate the introduction and acceptability of an e-portfolio...

Stacey Gough
NAPSA Indigenous Health Position Statement

CP11 Pharmacy Practice: Drugs in the Elderly

Jenni Ilomäki
Heavy drinking predicts subsequent sedative or anxiolytic medication use in aging men: A longitudinal study

Danijela Gnjidic
High risk prescribing and incidence of frailty among community-dwelling older adults

Imaina Widagdo
Characteristics and criteria of the frail elderly: A review of frailty measures

Jodie Hillen
Fishing in a sea of indicators: Challenges with evaluating QUM in Australian RAC

Sukhpreet Kaur
Evaluation of medication related problems in medication reviews: A comparative perspective?

Julia Gilmartin
A review of dose administration aids: Improving medicine management

CP12 Pharmacy Practice: Practice Roles

Safeera Hussainy
Piloting the role of a pharmacist in a community palliative care multidisciplinary team

Edwin Tan
Is there a role for pharmacists in general practice?

Sara McMillan
Nurse practitioners in community pharmacies: Now a reality, so what do they do?

Amy Tan
An exploratory study of medication supply and management in a rural community in Queensland

Louise Deeks
Do pharmacy staff want to offer chlamydia screening?

Greg Kyle
Can international experience make pharmacist prescribing work in Australia?

12:30pm

LUNCH

Lunch

Location: City East Plaza

1:00pm

1:30pm

LOCATION LEGEND: H2-02 | P5-14 | P5-15 | P5-33 | P5-34 | PM-06 | Brookman Hall

WEDNESDAY 14 December 2011

1:30pm

APSA MEDAL: Ross McKinnon

Ross McKinnon

Integrate or Perish: A Perspective on the Future of Pharmaceutical Research in Australia

2:00pm

2:30pm

CLOSE

Awards & Close

3:00pm

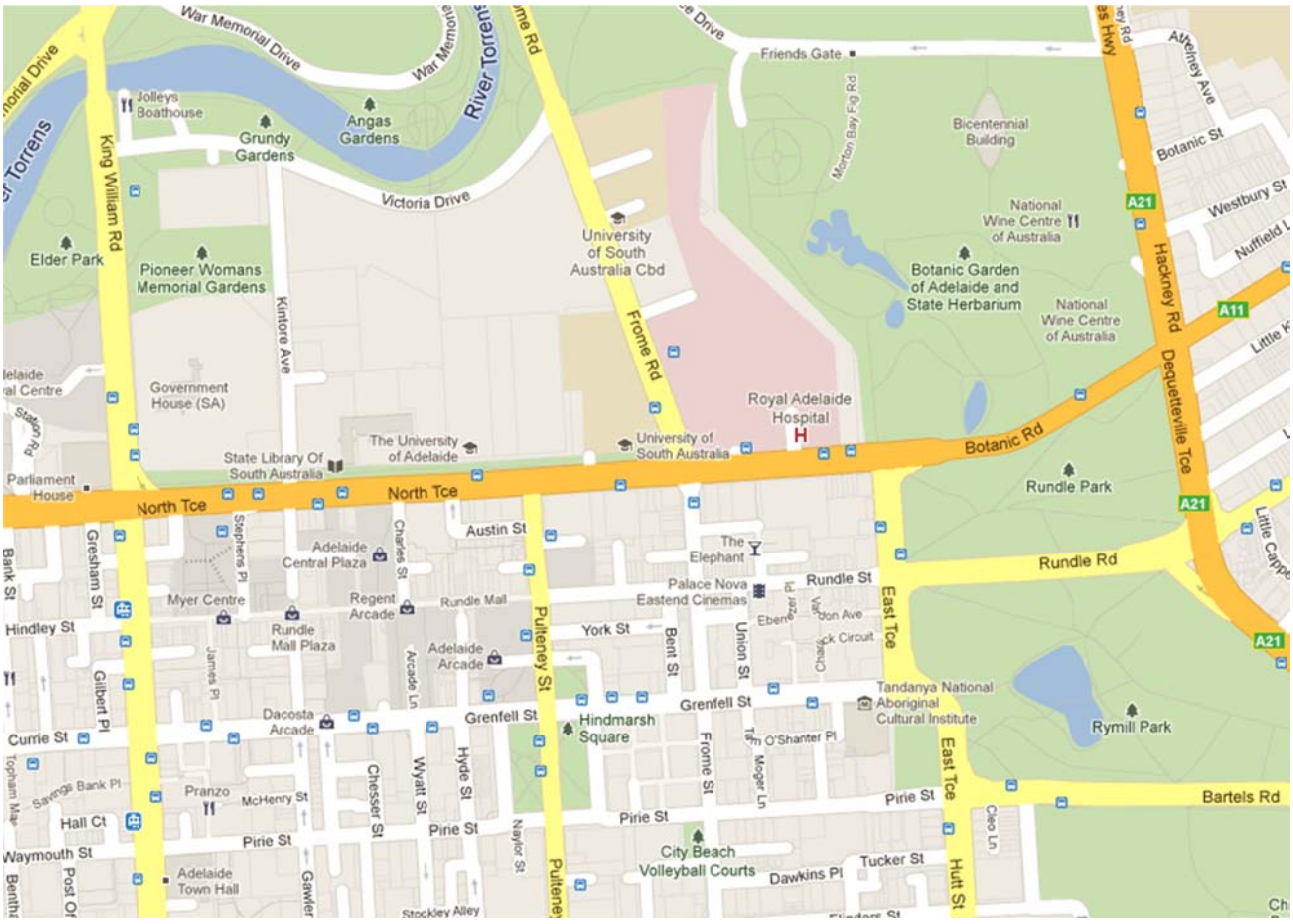
LOCATION LEGEND H2-02 P5-14 P5-15 P5-33 P5-34 PM-06 Brookman Hall

Destination

Adelaide is the capital and most populous city of the Australian state of South Australia, and is the fifth-largest city in Australia with a population of more than 1.1 million. It is a coastal city, situated on the Adelaide Plains, north of the Fleurieu Peninsula between the Gulf of St Vincent and the low-lying Mount Lofty Ranges. The most common day trips from Adelaide are to the Barossa Valley or McLaren Vale for wine-tasting, to Kangaroo Island or Cleland Wildlife Park for nature experiences or a visit to the seaside at either Glenelg or Victor Harbor.

Adelaide is a multi-cultural metropolis, nestled between the sea and the hills. Settled in 1836 and boasting a Mediterranean climate, Adelaide has developed to encompass the vigour and excitement of a modern city, while retaining the charm and tranquillity of the past. The world's best food and wine complement the natural environment in Australia's most convenient city

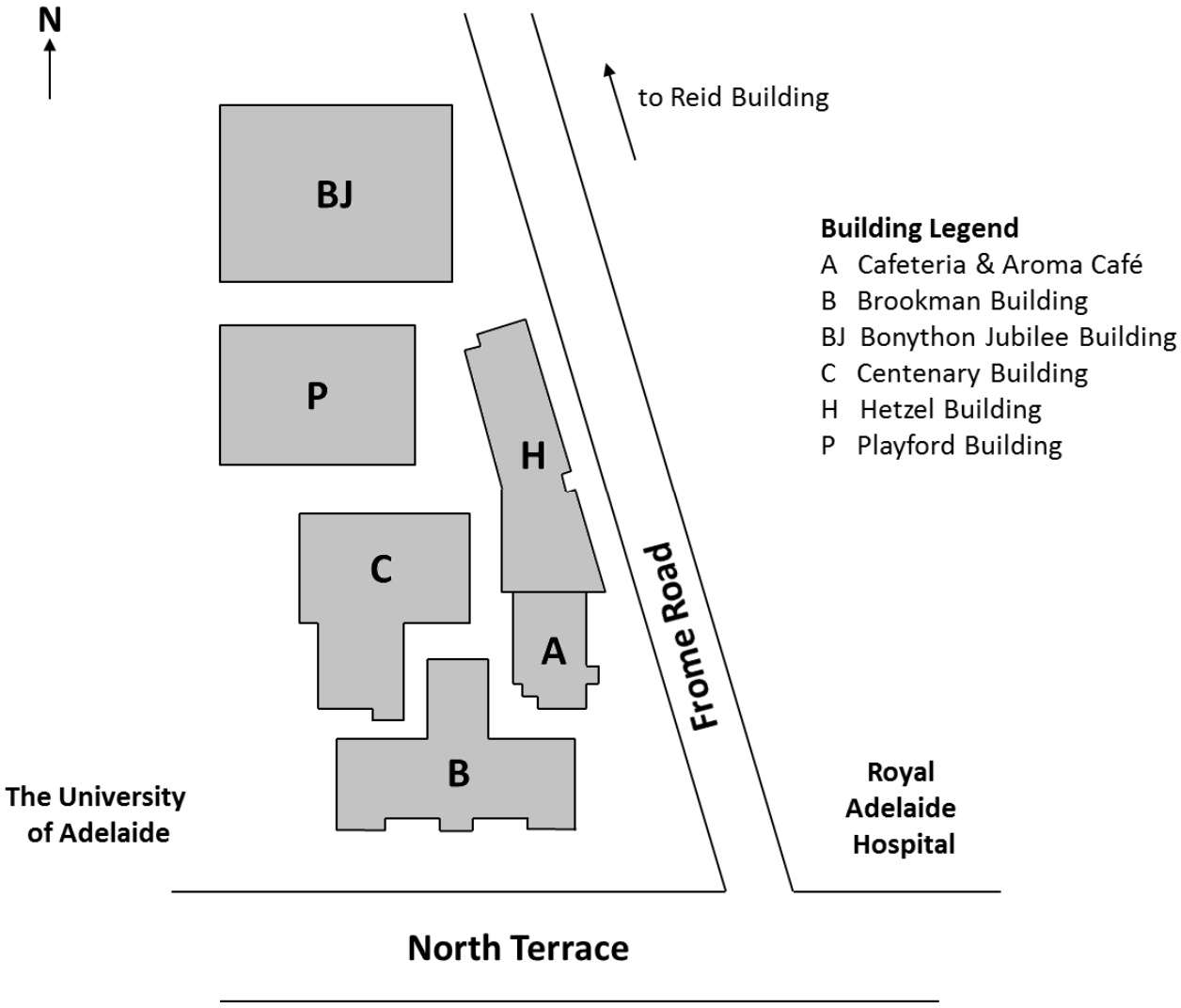
North Terrace is Adelaide's cultural boulevard and is exactly 1 mile (1.6 km) long, featuring the State Art Gallery, Museum of South Australia and the Adelaide Botanic Gardens. One street over is the Rundle Mall shopping precinct, while just east of Rundle Mall is Rundle Street with numerous cafés and restaurants.



Venue

The City East Campus of the University of South Australia is located on the corner of North Terrace and Frome Road, in the busiest part of central Adelaide.

City East has the State's only programs in physiotherapy, podiatry, pharmacy, medical radiation, occupational therapy and human movement. It is also home to medical science programs including laboratory medicine, pharmaceutical science and nutrition and food sciences. Research expertise includes pharmaceutical science at the world class Sansom Institute for Health Research situated on campus.

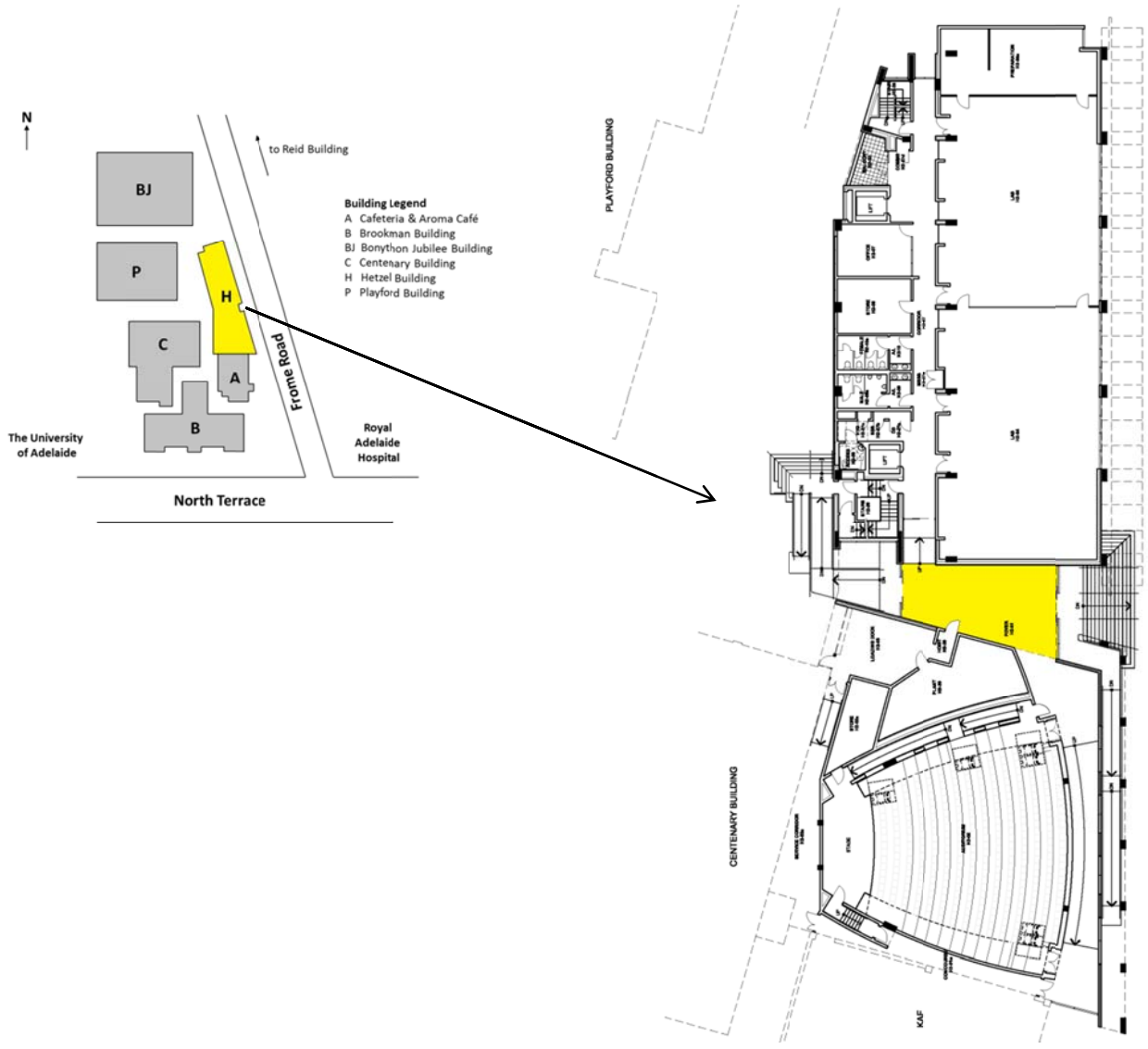


Conference Registration

All delegates must register to attend the conference. The registrtaion desk will be located in the foyer of the Hetzel Building (Level 2), accessible via the Frome Road entrance.

The registration and information desk will be open during the following hours:
Sunday 11 December 2011, 3:00pm – 7:00pm
Monday 12 December 2011, 8:30am – 5:30pm
Tuesday 13 December 2011, 8:30am – 5:00pm
Wednesday 14 December 2011, 8:30am – 3:00pm

Any enquires in relation to the conference may be directed to the Conference Secretariat who will be in attendance at the registration desk for the duration of the conference. Any urgent enquires can be addresed by calling Shanna (0437 377 107) or Kate (0402 946 322) directly. Enquires relating to accommodation should be directed to the relevant hotel.

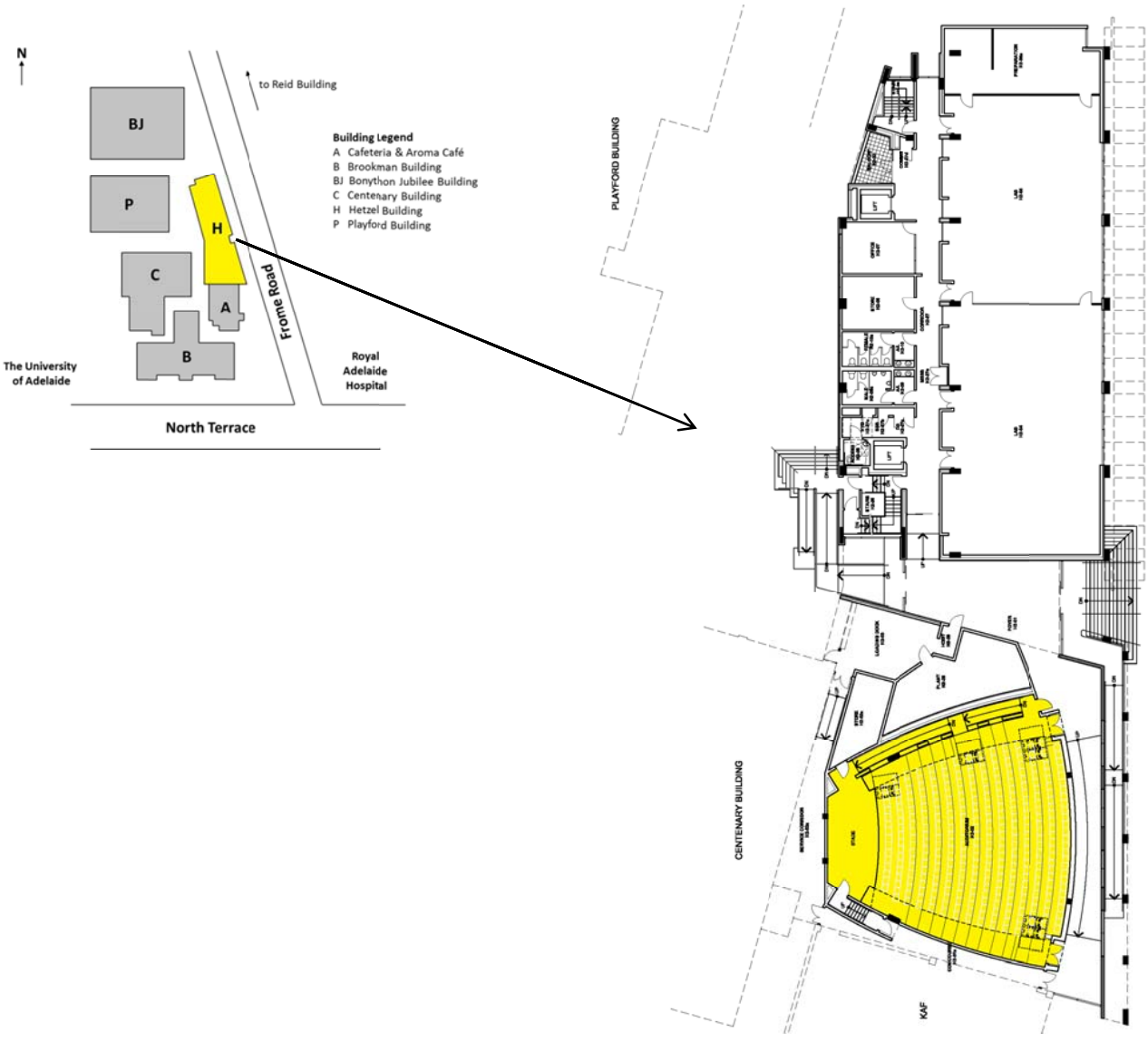


Plenary Sessions

The conference plenary sessions will be presented in the Basil Hetzel Lecture Theatre (H2-02) located on Level 2 of the Hetzel Building.

Plenary presenters are requested to email final versions of their PowerPoint presentations to the APSA email address (info@apsa-online.org) prior to conference commencement for uploading; alternatively, presentations may be uploaded or updated with the assistance of the administrative staff in the School of Pharmacy & Medical Sciences office located on Level 4 of the Playford Building between 8:30am – 5:00pm on Monday, Tuesday or Wednesday.

Plenary presenters will be provided with a laser pointer and lapel microphone for use during their session. Presenters are asked to report to the lecture theatre at least 10 minutes prior to the commencement of their session. A University of South Australia representative will be in attendance for IT support during the session.

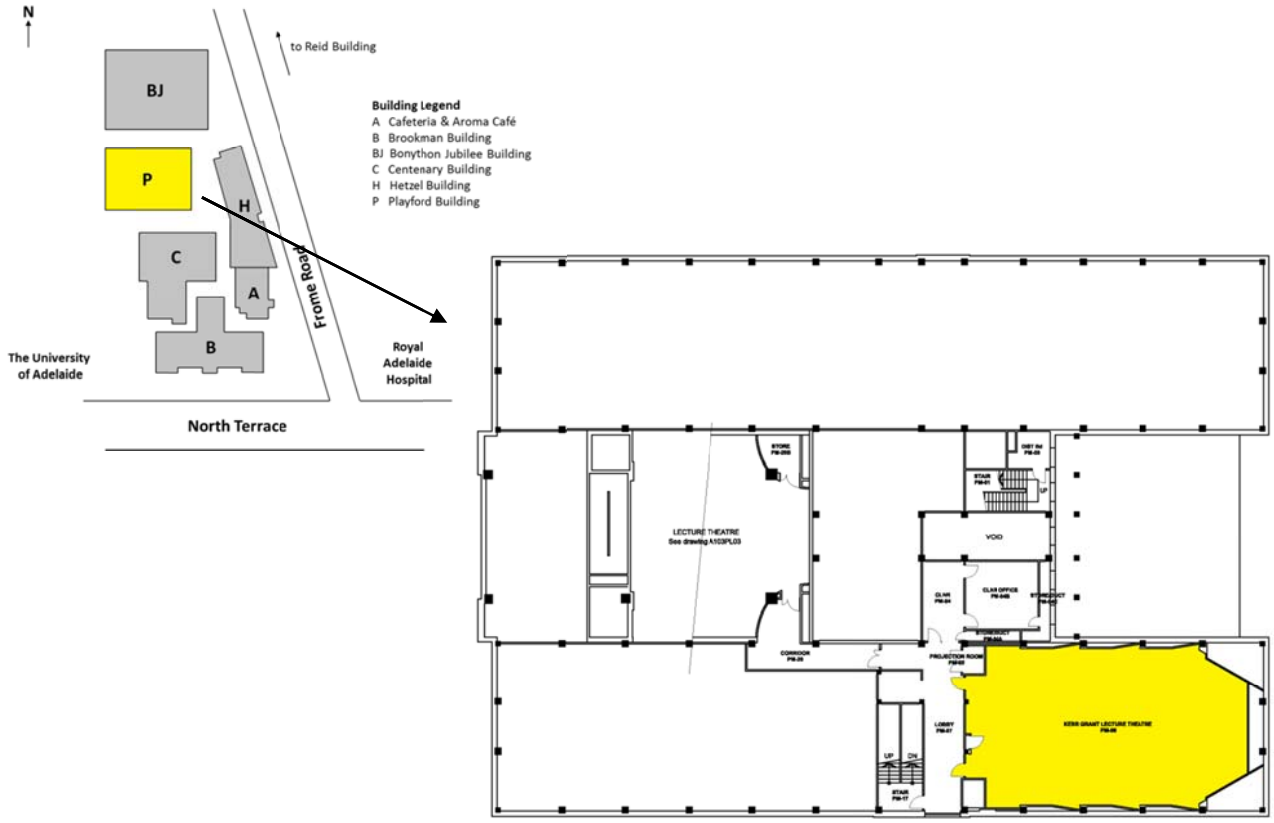


Symposium Sessions

The concurrent symposium sessions will be presented in either the Basil Hetzel Lecture Theatre (H2-02) located on Level 2 of the Hetzel Building or the Kerr Grant Lecture Theatre (PM-06) located on the Mezzanine Level of the Playford Building. The entrance to the Kerr Grant Lecture Theatre is situated between Level 2 and Level 3, accessible via the southern stairwell in the Playford Building.

Symposium presenters are requested to email final versions of their PowerPoint presentations to the APSA email address (info@apsa-online.org) prior to conference commencement for uploading; alternatively, presentations may be uploaded or updated with the assistance of the administrative staff in the School of Pharmacy & Medical Sciences office located on Level 4 of the Playford Building between 8:30am – 5:00pm on Monday, Tuesday or Wednesday.

Symposium presenters will be provided with a laser pointer and lapel microphone for use during their session. Presenters are asked to report to their relevant presentation room at least 10 minutes prior to the commencement of their session. A University of South Australia representative will be in attendance for IT support during the session.

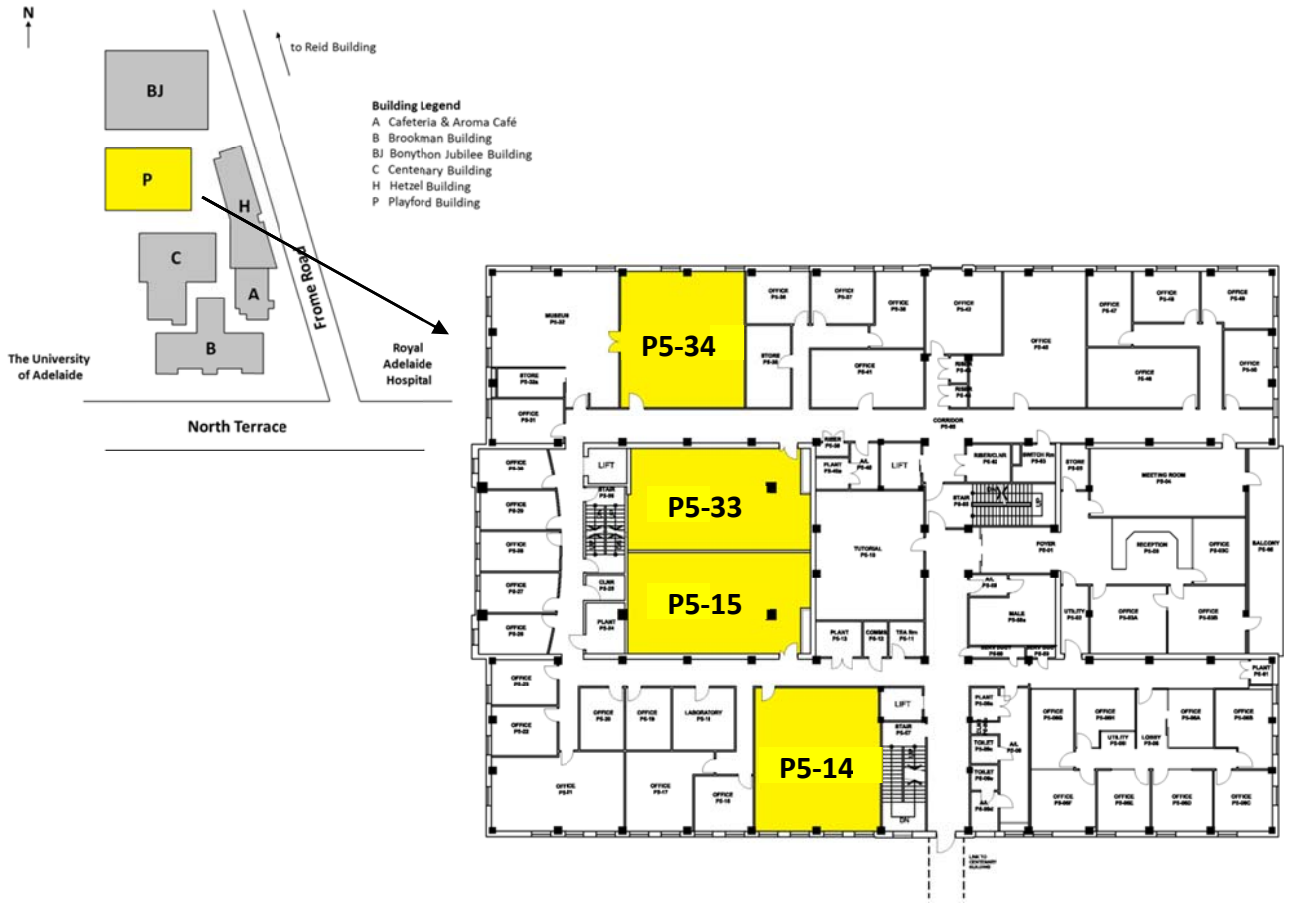


Contributed Paper Sessions

The contributed paper sessions will be presented in rooms P5-14, P5-15, P5-33 and P5-34 located on Level 5 of the Playford Building.

Contributed papers presenters must email final versions of their PowerPoint presentations to the APSA email address (info@apsa-online.org) prior to conference commencement for uploading; minor amendments to presentations may be made with the assistance of the administrative staff in the School of Pharmacy & Medical Sciences office located on Level 4 of the Playford Building between 8:30am – 5:00pm on Monday, Tuesday or Wednesday.

Presenters are asked to report to their relevant presentation room at least 10 minutes prior to the commencement of their session. A University of South Australia representative will be in attendance for IT support during the session.

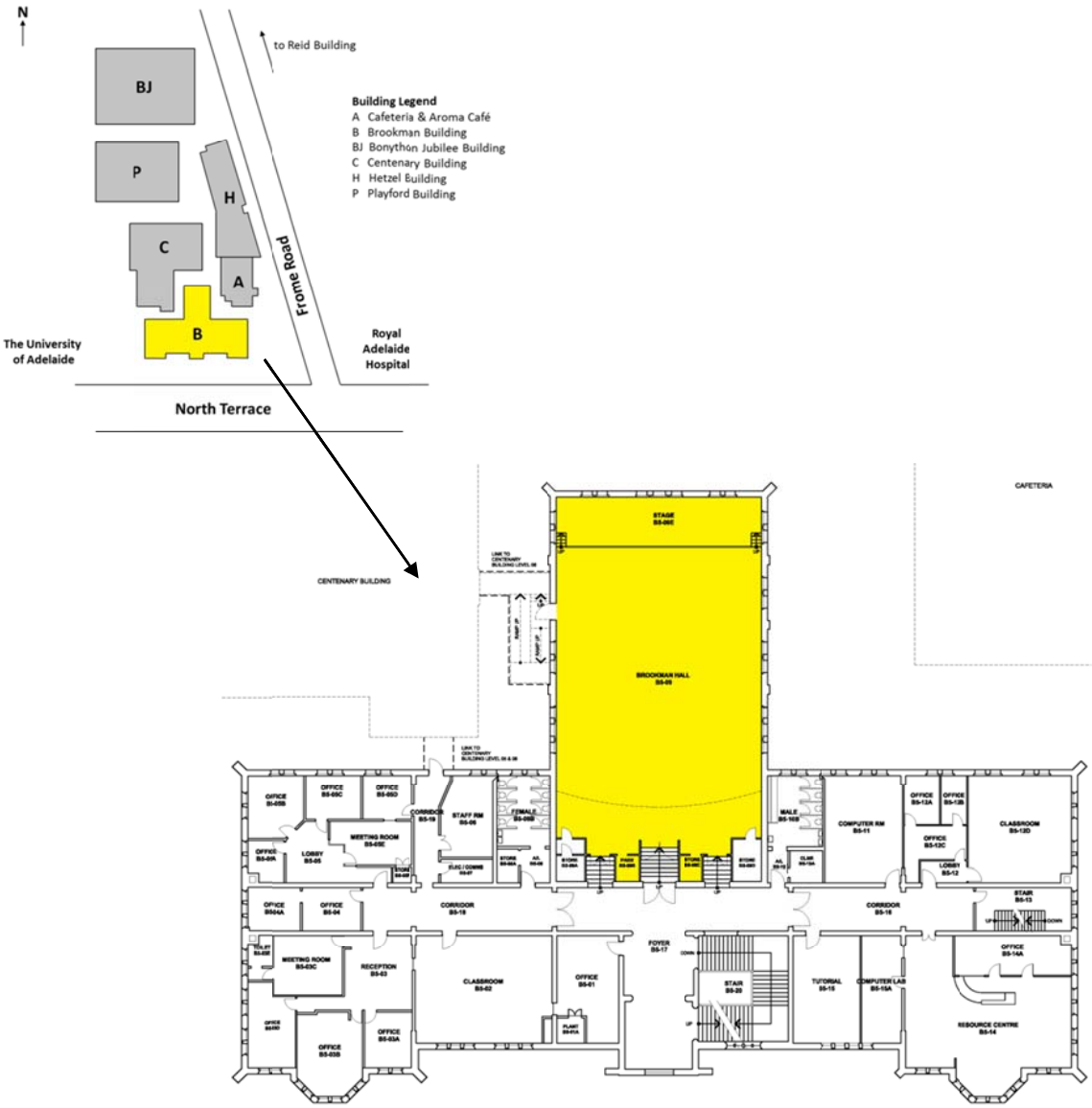


Poster Presentations

The poster exhibition will be held in Brookman Hall, located on Level 5 of the Brookman Building. Brookman Hall is most easily accessed via the North Terrace entrance and up one level via the main staircase.

Posters should be displayed prior to 10:00am on Monday 12 December and should remain until at least 4:00pm on Tuesday 13 December. Posters are to be prepared with dimensions not exceeding 0.8 m wide x 1.0 m high (portrait orientation). Presenters will be required to supply their own pins and/or velcro for affixing their poster to the fabric-covered poster display boards.

Posters will be attended during the afternoon tea breaks on Monday (odd numbered presentations) and Tuesday (even numbered presentations). In addition, students shortlisted for an APSA poster presentation prize will present a 1-minute synopsis of their work as part of the "Poster Presentation Teaser" session on Monday 10:00am – 10:30am in the Basil Hetzel Lecture Theatre (H2-02).



Catering

Morning tea and lunch will be served in the Cafeteria and Plaza area located on Level 3 of the Hetzel Building. Afternoon tea will be served in Brookman Hall as part of the poster presentation sessions. Coffee and tea will be available throughout the conference from 8:30am – 2:00pm in the Cafeteria and from 3:00pm – 4:00pm in Brookman Hall. Special meal requests have been catered for; for assistance please ask the UniSA representative in attendance.

Social Program

Welcome Reception

Renew old acquaintances and meet new contacts at the official Welcome Reception immediately following the opening keynote presentation by Professor Ian Olver. Enjoy a relaxed evening of fine South Australian wine, a gourmet BBQ and excellent company.

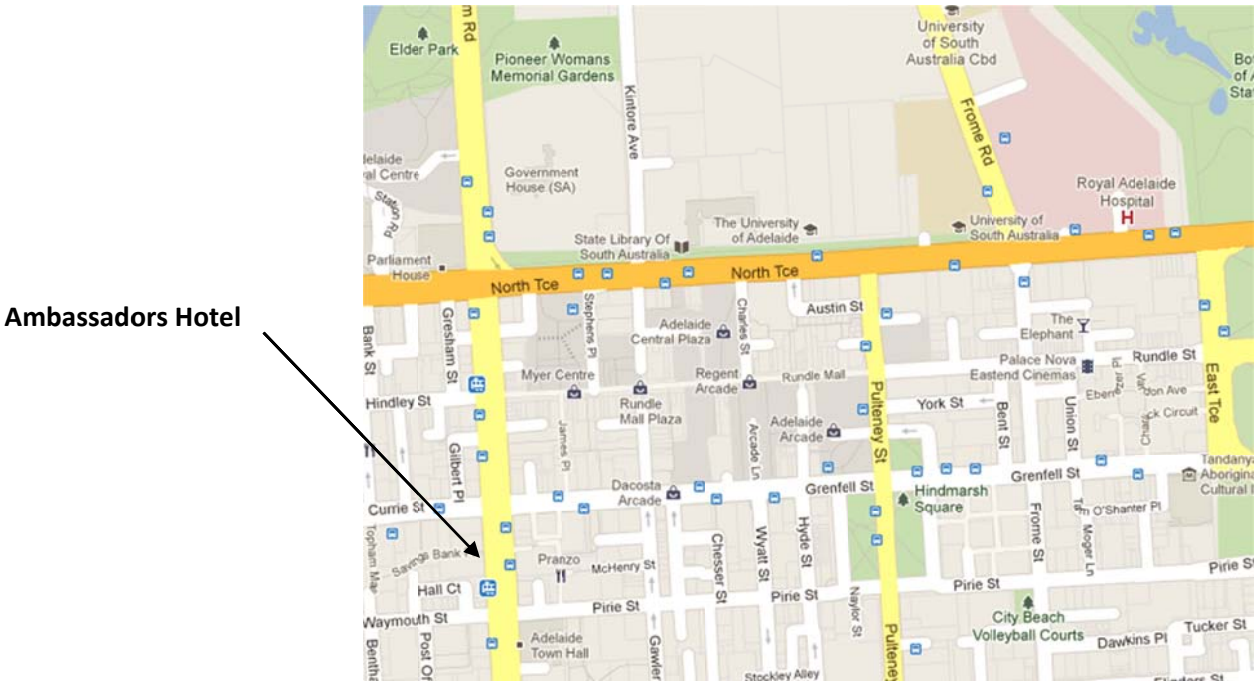
Date: Sunday 11 December 2011
Time: 6:00pm – 8:00pm
Venue: City East Plaza (Level 3, Hetzel Building)
Dress: Smart Casual
Cost: Inclusive for full registrants; additional tickets available for $60.00 per person

Student Dinner

Hosted by the Monash University Student Chapter of the American Association of Pharmaceutical Scientists (AAPS), students, recent graduates, early career professionals and young members new to APSA are all encouraged to attend this event to share experiences and build contacts.

Date: Monday 12 December 2011
Time: 7:00pm – 11:00pm
Venue: Balcony Dining Room, Ambassadors Hotel
Dress: Smart Casual
Cost: $20.00 per person

The Ambassadors Hotel is located at 107 King William Street, Adelaide, approximately 1.3 km from the City East Campus, University of South Australia.



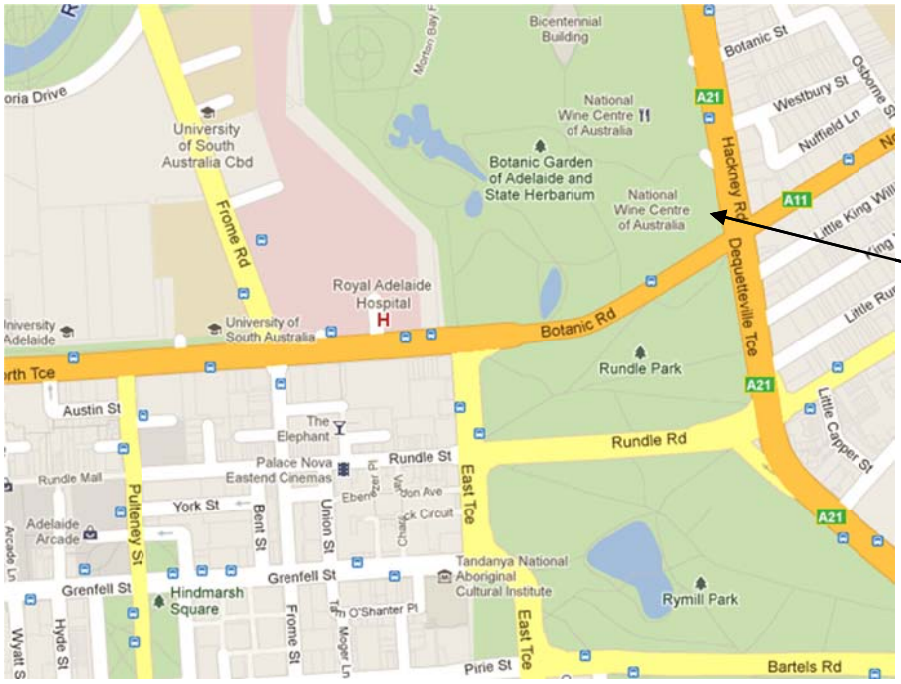
Social Program

Conference Dinner

The National Wine Centre of Australia is a great place to dine. Enjoy a relaxing night showcasing fabulous South Australian food and wine with good company and great entertainement provided by The Germein Sisters.

Date: Tuesday 13 December 2011
Time: 7:00pm – 11:00pm
Venue: National Wine Centre of Australia
Dress: Business/Cocktail (Tie Optional)
Cost: $120.00 per person

The National Wine Centre of Australia is located on the corner of Botanic Road (the continuation of North Terrace) and Hackney Road, Adelaide, approximately 500m from the City East Campus, University of South Australia.



National Wine Centre of Australia

Travel

To/From the Airport

Adelaide Airport is located approximately 6 km west of the city centre. A number of transport modes are available for travel to and from the airport including taxis, shuttle buses and public transport.

Taxi: A taxi rank is located directly outside the terminal on the ground level. Concierges provide a safe environment and allocate taxis to passengers. Taxis cost approximately $15.00 for travel between the airport and the city centre; there is a $2.00 levy for taxis leaving the airport.

Shuttle Bus: The SkyLink Airport Shuttle provides a regular scheduled bus service between Adelaide Airport and the Adelaide CBD, with pick-up and set-down from most major city hotels.

Public Transport: Public transport buses – known as the JetBus (J1 and J2) service – provide travel to and from the city as well as Glenelg and the north-eastern suburbs. Pick-up and drop-off is from the bus stop located at the south-west end of the upper level of the terminal (left as you exit the terminal). All JetBuses are Metroticket services; single trip and daytrip tickets can be purchased from bus drivers. Additional details can be found on the Adelaide Metro website: http://www.adelaidemetro.com.au/routes/jetbus

Within Adelaide

Taxi: The main taxi companies operating in the Adelaide metropolitan area are:
Adelaide Independent Taxi Service (13 22 11)
Suburban Taxi (13 10 08)
Yellow Can Co. (13 22 27)

The most convenient taxi ranks to the University of South Australia, City East Campus are located on the corner of North Terrace and Frome Road (in front of the Royal Adelaide Hospital) and on Pulteney Street at the end of Rundle Mall.

Public Tranport: Adelaide is serviced by bus, train and tram services operated by Adelaide Metro (www.adelaidemetro.com.au); single trip and daytrip tickets can be purchased on board.

The free City Loop (99C service) operates a loop around the city centre, including sites such as the South Australian Museum, The State Library of South Australia, the Art Gallery of South Australia, the Royal Adelaide Hospital, the Adelaide Botanic Gardens, Rundle Street (East End), Tandanya National Aboriginal Cultural Institute, Adelaide Central Market, Hindley Street precinct, The University of South Australia and The University of Adelaide.

The Adelaide Metro tram runs between Moseley Square, Glenelg and the Adelaide Entertainment Centre, Port Road via King William Street, Adelaide. Travel aboard the tram is free within the Adelaide city centre (South Terrace to/from Adelaide Entertainment Centre).

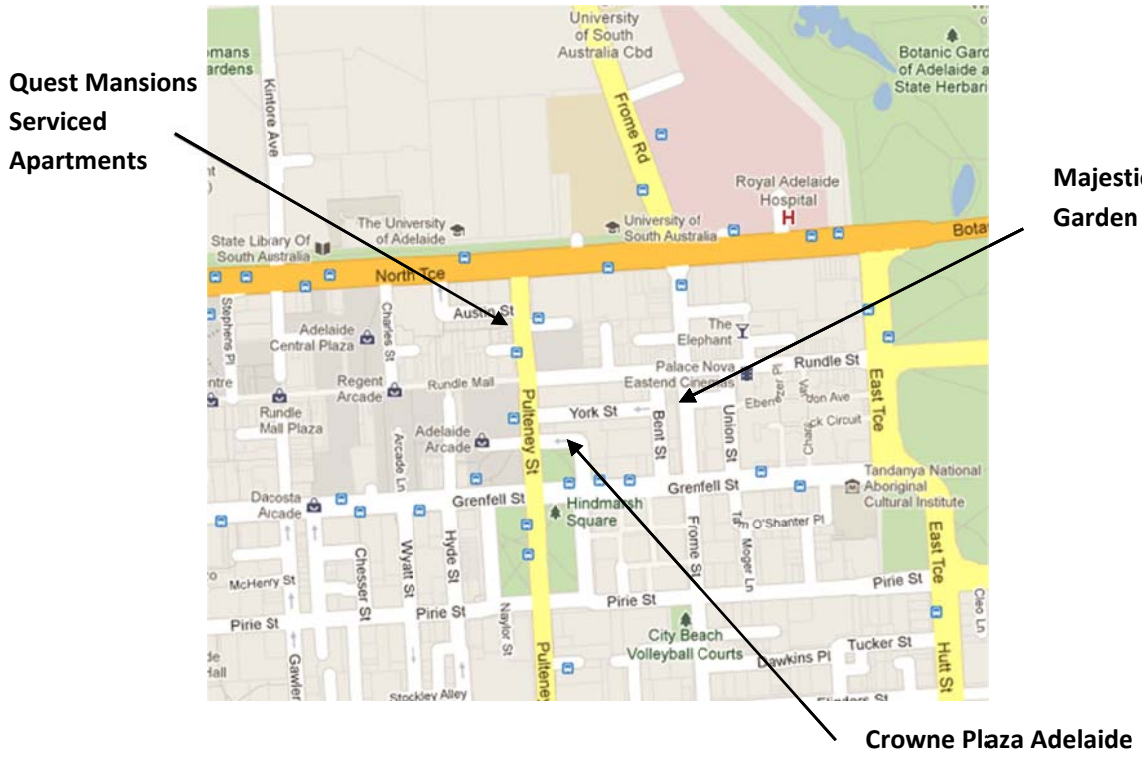
Accommodation

Crowne Plaza Adelaide
16 Hindmarsh Square
Adelaide SA 5000
p: +61 8 8206 8888
w: www.crowneplaza.com/cpadelaide

Majestic Roof Garden Hotel
55 Frome Street
Adelaide SA 5000
p: +61 8 8100 4400
w: www.majestichotels.com.au

Quest Mansions Serviced Apartments
21 Pulteney Street
Adelaide SA 5000
p: +61 8 8232 0033
w: www.questmansions.com.au

Accommodation booked via the Conference Secretariat has been secured using the credit card details supplied; this card will not be charged for your accommodation, you will need to arrange payment directly with your hotel during your stay.



General Information

Shopping/Eating Out

The University of South Australia, City East Campus is within easy walking distance to Adelaide's major shopping and dining precincts. Rundle Street is the home to the popular East End district, including Adelaide's best known cafés, restaurants and wine bars as well as fashion, homewares, jewellery and accessories stores. Rundle Mall offers the largest selection of shopping facilites in Adelaide, including department stores, arcades and centres and over 700 retail stores. A small supermarket (IGA) is located on North Terrace, opposite the Royal Adelaide Hospital, or alternateively a large Woolworths supermarket is located in the centre of Rundle Mall.

Name Badges

All delegates will be provided with a name badge upon registration. Name badges must be worn at all times as this is provides entry to all sessions, lunches/breaks and social funtions; note that social function attendance is signified by coloured dots.

Dress Code

The suggested dress code for all conference sessions, the Welcome Reception and the AAPS Student Dinner is smart casual. Business/cocktail dress is recommended for the APSA Conference Dinner.

Internet Access

Internet access is available for delegates via the dedicated computers located in the Cafeteria area for accessing email. Please ask a University of South Australia representative in attendance for assistance.

Mobile Phones

In consideration of the presenters, please ensure that your phone is switched to silent during all sessions.

Restrooms

Male and female restrooms are located throughout the City East Campus. The most convenient facilities for delegates are located on Level 2 of the Hetzel Building, Levels 3 and 5 of the Playford Building and Level 5 of the Brookman Building.

Smoking

The University of South Australia is a non-smoking environment and therefore smoking in all indoor and outdoor areas is not permitted; a designated smoking area is located on the western side of the Brookman Building (between the University of South Australia and The University of Adelaide).

General Information

Privacy Policy

The All Occasions Group (encompassing All Occasions Management and Travelscene at All Occasions) complies with all legislation which is designed to protect the rights of the individual to privacy of their information, including the Privacy Act 1988 (Cth). Information collected with respect to your registration for participation in this conference will only be used for the purposes of planning, conduct of the event or communication regarding future events. These details may be made available to parties directly related to the conference including but not limited to the All Occasions Group, venues, accommodation and travel providers (for the purposes of room/travel bookings and conference options), key sponsors (subject to strict conditions) and other related parties as deemed necessary. It is also usual practice to produce a 'Delegate List' of attendees at the conference and to include the individual's details in such a list. By completing the registration form, you acknowledge that the details supplied by you may be used for the above purposes. It is your responsibility to ensure that all information provided to the All Occasions Group is accurate and kept up to date. To access or update your information, please email or fax the All Occasions Group on conference@aomevents.com or +61 8 8125 2200.

Liability / Insurance

In the event of industrial disruptions or natural disasters, Australasian Pharmaceutical Science Association, the Organising Committee, and All Occasions Group (encompassing All Occasions Management and Travelscene at All Occasions) cannot accept responsibility for any financial or other losses incurred by the delegates. The Australasian Pharmaceutical Science Association, the Organising Committee and the All Occasions Group take no responsibility for injury or damage to persons or property occurring during the conference. All insurance, including medical cover, or expenses incurred in the event of the cancellation of the conference is the individual delegate's responsibility. Delegates are encouraged to choose a travel insurance policy that includes loss of fees/deposits through cancellation of your participation in the conference, or through the cancellation of the conference itself, loss of airfares for any reason, medical expenses, loss or damage to personal property, additional expenses and repatriation should travel arrangements have to be altered. Australasian Pharmaceutical Science Association, the Organising Committee, and All Occasions Group will take no responsibility for any participant failing to insure.

Pre-Conference Workshops

Moving Forward with Pharmacy Competencies and Quality Experiential Learning Activities

Time: Sunday 11 December 2011, 12:30pm – 4:30pm
Venue: P3-18, Playford Building

This half-day workshop focuses on preparatory programs and collaborative sharing of implementation strategies regarding the updated competencies and quality curriculum learning activities.

Learning Objectives/Outcomes: A greater range of strategies for implementation of updated competencies within preparatory programs are available following collaborative sharing and workshop activities; increased familiarity and use of online website learning materials through collaborative sharing of implementation approaches.

Activities: Website familiarisation; collegial discussion and sharing; skill building.

Cloves, Kerosene and Capsicum: The Chemistry of Wine Aroma

Time: Sunday 11 December 2011, 1:30pm – 4:30pm
Venue: Australian Wine Research Institute

While there can be a degree of scepticism about the subjective nature of wine evaluation, in this fascinating session held at the Australian Wine Research Institute, you will learn how sensory descriptions of wines relate to naturally occurring volatile compounds also found in fruits, vegetables, spices and even rubber and cat urine.

Flavour compounds with a positive influence on wine quality are mainly derived from the grape berry and from the action of yeast on grape components, but the influence of oak, malolactic fermentation and post-bottling storage can also be extremely important. The multitude of aroma compounds present in a finished wine will interact strongly to mask or change the perceived sensory properties, making the ability to predict wine flavour from chemical measurement difficult. The origin of these compounds will be discussed, as well as results of recent research efforts to understand influences of microbiology, winemaking and viticulture on modifying levels of these compounds.

This workshop will give an overview of the main aroma and flavour compounds known to be important to wine, and will have a strong practical element. The chemical components that contribute to particular wine aromas will be introduced, and aroma compounds will be presented for smelling during the talk. Distinctive wines will also be tasted. Transport to and from the Australian Wine Research Institute is included.

This workshop will be run by Dr Leigh Francis, manager of the sensory science and aroma chemistry research teams at the Australian Wine Research Institute. He has more than 20 years' experience in wine flavour chemistry and sensory evaluation research. He has worked on numerous aspects of wine flavour, including flavour precursors, Brettanomyces off-flavour, closure-related flavour changes during storage, tannins, microbiological influences, consumer sensory preferences, and compounds important to fruit flavour in both white and red wines. He is a co-author of more than 60 scientific papers.

University of South Australia

Sansom Institute for Health Research

From identifying better medicines for angina and infection, to developing safer treatment for psoriasis and skin cancer, the Therapeutics and Pharmaceutical Science research group, within the Sansom Institute, is involved in a wide range of projects aimed at treating disease and optimising health.

Led by Professor Michael Roberts and Associate Professor Robert Milne, the concentration brings together more than 30 pharmaceutical and medical scientists investigating a diverse range of health-related issues.

Research strengths are numerous and include synthetic and natural products, drug delivery, pharmacokinetics and computer modelling of drug disposition, fundamental surface science in biochemical processes, pharmacogenetics, pharmacogenomics and ethnopharmacology.

For more information about the Sansom Institute for Health Research and the Therapeutics and Pharmaceutical Science research group, visit www.unisa.edu.au/sansominstitute

NAPE

National Alliance for Pharmacy Education

The National Alliance for Pharmacy Education is a partnership between four leading universities. NAPE leads the development of a common vision for the future of postgraduate pharmacy education in Australia. It assists pharmacy professionals to develop the knowledge and skills required for professional excellence and career advancement.

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To find out more, visit www.nape.edu.au

NAPE

The University Of Queensland AUSTRALIA

The University of Sydney

University of South Australia

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PDL MEMBER BENEFITS

PDL arranges Professional Indemnity cover for registered pharmacists and Provisional Registrants (Interns) in whatever area they practice. This individual cover is for 24/7 at a very low cost.

Other member benefits are:

- **The Australian Journal of Pharmacy (AJP)** free in Australia.
- **Loans and leases to pharmacists**
- **Car service, buying a new vehicle**
- **One-off free legal advice**
- **Discount on selected publications purchased from APPco (ie Pharmpress Books)**
- **Discounts on selected products from the PDL Member Benefits online store**
- **New member benefit: PDL is pleased to introduce you to OnePath (formerly ING) Life's ProSecure Income Replacement Plan** which may help ensure you have a regular monthly income if you are unable to work due to injury or illness
- **New member benefit: PDL is pleased to announce a new member benefit now available to PDL members.** Members can receive new life insurance benefits of up to $1.5m.

Plenary Sessions

Plenary 01

Professor Ian Olver, Cancer Council Australia

Cancer in Australia Over the Next Decade

Plenary 02

Professor Edzard Ernst, Peninsula Medical School

Complementary and Alternative Medicines: Is Evidence Informing Practice or Practice Informing Evidence?

Plenary 03

Professor Chris Porter, Monash University

APSA LECTURE – Endogenous Transport Pathways as a Blueprint for Drug Delivery: Lessons Learnt from Lipid Absorption

Plenary 04

Dr Jill Maxwell (OAM), National e-Health Transition Authority

The promise of e-health, and what barriers are there to realising its full potential?

Plenary 05

Professor Bill Runciman, Australian Patient Safety Foundation

Systems to Improve Medication Safety: Can We Do Better?

Plenary 06

Professor Steve Wesselingh, South Australian Health and Medical Research Institute

Are Academic Health Centres the Key to Linking Science and Practice?

Plenary 07

Professor Ross McKinnon, Flinders University

APSA MEDAL – Integrate or Perish: A Perspective on the Future of Pharmaceutical Research in Australia

Cancer in Australia Over the Next Decade

Chair: Bernie Hughes, University of South Australia

Sunday 11 December 2011, 5:00pm – 6:00pm

Room H2-02, Hetzel Building

Professor Ian Olver, Cancer Council Australia

Professor Ian Olver is currently Chief Executive Officer of Cancer Council Australia, Clinical Professor in the Department of Medicine at the University of Sydney and is an Honorary Associate, Department of Medical Oncology, Royal Prince Alfred Hospital. He has published over 190 articles in journals, 19 book chapters has written two books and edited three others.

In his role as Chief Executive Officer of Cancer Council Australia, he will be able to provide a broad overview of cancer in Australia during his keynote presentation. He will cover issues such as the growing role of community pharmacists in cancer prevention and screening, the benefits and issues arising from the paradigm shift in the treatment of cancer to targeted therapies, and insights into the likely future advances and opportunities for research.

Summary

The next decade will see significant changes both in the diagnosis and treatment of cancer and in prevention and screening. The era of targeted personalised medicine is dawning. In Australia, cancer is the leading cause of disease burden (19%) followed be cardiovascular disease, and this will continue unless prevention and early detection improves. Lifestyle changes alone could account for a 33% reduction in the mortality from cancer. Tobacco control is still the mainstay of prevention and price control is the major influence although plain packaging will reduce the uptake by young people. It is a realistic hope that we can achieve less that 10% of adults smoking in the next decade from the current 15.1%. More problematic will be the need to control obesity and the harmful use of alcohol both of which are risk factors for cancer. Screening and early detection of cancers will improve. Currently the only population screening which exists is for breast cancer, cervical cancer and bowel cancer although that has only been introduced in a rudimentary way in Australia. Screening tests for other tumours are needed. Also screening for genetic risk will become more important as preventive strategies such as aspirin in high risk bowel cancer are developed. Studies of the human genome and the patterns of genetic mutations within tumours will hold the key to diagnosis, prognosis and provided targets for new cancer treatments in future. Targeted therapies such as imatinib in gastrointestinal stromal tumours and trastuzumab in breast cancer have already shown the proof of principle of this approach, which has the advantage of being less toxic and more efficient, in that only cancers expressing the target are treated. Other modalities of anticancer treatment are also increasingly targeted as exemplified by conformal radiotherapy and reduced surgery using sentinel node biopsies. Technological advances will see cancer moving into the digital age with electronic medical records and efficient linkage of registry and clinical data. The mediawiki guidelines project at Cancer Council Australia will improve the currency and reach of treatment guidelines. All of this is underpinned by research investment but we need to continue to fund cancer research and develop priority areas where the research spend will deliver the greatest benefit.

Complementary and Alternative Medicines: Is Evidence Informing Practice or Practice Informing Evidence?

Chair: Allan Evans, University of South Australia

Monday 12 December 2011, 9:00am – 10:00am

Room H2-02, Hetzel Building

University of South Australia | Sansom Institute for Health Research

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Professor Edzard Ernst, Peninsula Medical School

Professor Edzard Ernst received his medical training in Munich, and moved to the University of Exeter (UK) Postgraduate Medical School in October 1993, establishing the first Chair in Complementary Medicine. In 1996 he founded the Department of Complementary Medicine at this University's Postgraduate Medical School and in 2002 his unit became part of the new Peninsula Medical School, Universities of Exeter and Plymouth. He has published over 1000 peer reviewed papers, primarily in the area of efficacy, safety and costs of complementary and alternative medicines. He states that one of his professional aims is 'to be neither promotional nor derogatory, but to struggle for objectivity'.

Summary

Complementary and alternative medicine (CAM) is relevant not least because many consumers use it. In Australia, like in most other countries, pharmacies typically offer a range of CAM-products for sale. This lecture will critically review the evidence for or against aromatherapy, Bach Flower Remedies, static magnets, herbal medicines and homeopathic remedies - all products typically available through pharmacies. In particular, Professor Ernst will evaluate the efficacy and the safety of these treatments. The conclusion is that, in CAM, practice is rarely based on good evidence, and that evidence is often not informed by practice.

APSA LECTURE – Endogenous Transport Pathways as a Blueprint for Drug Delivery: Lessons Learnt from Lipid Absorption

Chair: Roger Nation, Monash University

Monday 12 December 2011, 4:00pm – 5:00pm

Room H2-02, Hetzel Building

Professor Chris Porter, Monash University

Professor Chris Porter is Professor of Pharmaceutics at the Monash Institute of Pharmaceutical Sciences and Associate Dean (Research) of the Faculty of Pharmacy and Pharmaceutical Sciences at Monash University, Melbourne. Chris' research program has focused on understanding and quantifying drug absorption, distribution and elimination profiles and on developing the models and techniques to probe these interactions. A major interest has been the issues and problems surrounding the absorption of poorly water soluble, highly lipophilic drugs and in particular the use of lipid based delivery systems and microemulsions to enhance oral bioavailability and stimulate lymphatic transport. More recently, his interests have expanded into the mechanisms of cellular transport of lipophilic drugs and the potential utility of dendrimers as drug delivery systems. Chris has published more than 120 peer reviewed papers in these areas. He is a current member of the Editorial Boards of Pharmaceutical Research, the Journal of Pharmaceutical Sciences and the Journal of Pharmacy and Pharmacology, a member of the Board of Scientific Advisors of CRS and a fellow of the Royal Australian Chemical Institute.

Summary

Effective drug delivery remains a challenge in many areas of Pharmaceutical Sciences, none more so than in the delivery of drugs where low aqueous solubility limits oral bioavailability. Recent analyses suggests that up to 70% of drug discovery candidates may be classified as 'poorly water soluble' and therefore carry the risk of poor and variable absorption after oral delivery. In contrast the absorption of similarly poorly water soluble dietary fat is astonishingly efficient and somewhat ironically many companies are as committed to reducing lipid absorption as they are to increasing drug absorption. The efficiency of lipid absorption lies in the evolution of a series of interconnected lipid transport pathways. These provide a continuum of lipophilic microenvironments that acts as a transport conduit for dietary lipids across the largely hydrophilic (aqueous) environments of the gastrointestinal tract, the cellular cytosol and the blood. The focus of our laboratories over the last several years has been in better understanding the potential role of these lipid transport pathways in drug absorption and disposition, and in harnessing the power of these highly evolved transport systems to enhance drug exposure. This presentation will explore the interface between lipid and drug absorption and provide a series of examples where 'hijacking' endogenous transport pathways has a beneficial effect on drug delivery.

The promise of e-health, and what barriers are there to realising its full potential?

Chair: Timothy Chen, The University of Sydney

Tuesday 13 December 2011, 9:00am – 9:45am

Room H2-02, Hetzel Building

Dr Jill Maxwell (OAM), National e-Health Transition Authority

A full time GP and practice owner in Adelaide, Jill has also been active in the medico-political and medico-legal area for almost twenty years. She has been a state President of the AMA, the Chair of a number of national medical committees and for ten years was the Chair of Medical Indemnity Insurance Australia (MIGA). Jill is one of the Clinical Leads with NeHTA.

Summary

Not available.

Systems to Improve Medication Safety: Can We Do Better?

Chair: Timothy Chen, The University of Sydney

Tuesday 13 December 2011, 9:45am – 10:30am

Room H2-02, Hetzel Building

Professor Bill Runciman, Australian Patient Safety Foundation

Professor Bill Runciman is President of the Australian Patient Safety Foundation. He played a pivotal role in the conceptualisation and implementation of the Advanced Incident Management System (AIMS) - a system for collection, classification, analysis and management of incidents in health care. Professor Runciman is a member of the International Patient Safety Classification Group and is co-chair of the Research Methods and Measures Group of the World Alliance for Patient Safety, within the World Health Organization. Formerly an Intensive Care consultant for over 30 years, he has published over 220 scientific papers/chapters. In 2008 he was awarded the Sidney Sax Medal of the Australian Healthcare and Hospitals Association for outstanding contribution in the field of health services policy, organisation, delivery and research.

Summary

Over eight years ago, we published a review which showed that 2 – 4% of all hospital admissions in Australia (up to 30% for patients over 75 years of age) were medication related, and that half of these were potentially preventable. Routine discharge coding has indicated that medication adverse events contributed in 27% of deaths, made up 20% of adverse events identified at discharge and 43% of those in general practice. Furthermore, between one third and a half of all incidents reported involve medications directly or indirectly. Besides actual harm, evidence continues to emerge that baseline values for appropriate care are poor (being provided about half the time), and that intensive interventions often result in modest, poorly sustained improvements. As examples, recent work has shown that less than 30% of eligible patients receive appropriate care for high blood lipids or cholesterol, and less than 20% for community acquired pneumonia. It has been clear for some time that conventional interventions ("more of the same") generally result in more of the same. Exhortations to improve "culture" – like exhortations to teenagers to drive carefully – usually produce no measurable changes. "Forcing functions" are needed – preferably subtle ones which make it easier to do the right thing and harder to do the wrong thing – and we now have some evidence that these, when embedded in electronic record and management systems, may produce substantial improvements in contexts in which conventional interventions can be shown to be of no avail. The next frontier is at the interface between practitioners embedded in their work practices and prejudices, and the huge potential power of information technology. The challenge will be to make progress in a healthcare system seemingly bound by homeostatic mechanisms which maintain the status quo; some approaches will be outlined.

Are Academic Health Centres the Key to Linking Science and Practice?

Chair: Ross McKinnon, Flinders University

Tuesday 13 December 2011, 4:00pm – 5:00pm

Room H2-02, Hetzel Building

University of South Australia | School of Pharmacy and Medical Sciences

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Professor Steve Wesselingh, South Australian Health and Medical Research Institute

Professor Steve Wesselingh is currently the Executive Director of the South Australian Health and Medical Research Institute. Previously he was the Dean of the Faculty of Medicine, Nursing and Health Sciences, Monash University, and prior to that was the Director of the Burnet Institute which specialises in infectious diseases, immunology and public health. Professor Wesselingh is an Infectious Diseases Physician with research interests in Neurovirology, HIV and vaccine development. He is internationally recognised as an expert in viruses that affect the human brain, and has held major research grants from the Australian National Health and Medical Research Council (NHMRC) and from the National Institutes of Health in the United States. Professor Wesselingh will speak about the international growth of academic health care centres – close partnerships between a tertiary health care provider and a university with a focus on excellence in research, clinical services and education. Furthermore, he will discuss the challenges and opportunities that surround the use of such a model in Australia with respect to providing opportunities for research and improved health care.

Summary

Medical researchers consistently make global headlines. Yet research strengths do not necessarily connect with the delivery of innovative and high quality health care. The reasons behind this disjunction are complex, including the separate funding models for health, research and higher education, cultural differences and significant gaps in workforce development. However, unless we overcome these issues and develop new structures to forge stronger links between healthcare facilities, universities and medical research institutes, we are going to fall short on our potential to deliver outstanding medical care and the rapid movement of innovation into healthcare delivery.

APSA MEDAL – Integrate or Perish: A Perspective on the Future of Pharmaceutical Research in Australia

Chair: Andrew McLachlan, The University of Sydney

Wednesday 14 December 2011, 1:30pm – 2:30pm

Room H2-02, Hetzel Building

Professor Ross McKinnon, Flinders University

An academic pharmacist, Professor Ross McKinnon joined Flinders University as the Research Director of the Flinders Centre for Innovation in Cancer in 2011 after 16 years with the University of South Australia. At UniSA, Ross was the inaugural Director of the Sansom Institute (2005 – 2009) and was also Associate Head of the School of Pharmacy and Medical Sciences. In 2010, Ross was appointed National Facilitator for the Translating Health Discovery into Clinical Applications Super Science Project. He has broad research interests in the Pharmacology/ Toxicology, Pharmaceutical Biotechnology and Molecular Oncology areas with a particular interest in the influence of genetic background on individual response to drugs, diet and environmental contaminants. Ross is a co-inventor of patents relating to cancer chemoprevention (PharmaQest) and the discovery of novel anti-inflammatory compounds. He is a past-President of APSA, member of the Federation of International Pharmacists Council and Education Steering Committee and also a NHMRC Academy member. Collectively, Ross has been a Chief Investigator on grants attracting over $13.5 million. His outputs include over 100 invited lectures, symposia talks and seminars at national and international level, along with 330 published outputs including over 100 original research manuscripts. He has supervised more than 60 PhD and Honours students.

Summary

Over the last decade, research strategies across many disciplines that are relevant to pharmacy and pharmaceutical science have increasingly focused on a need for integration and aggregation. Through such strategies, many researchers have been successful in gaining access to major infrastructure and resources that are increasingly necessary to secure competitive research funding. Particularly notable over recent years has been an increasing focus in many countries on the development of research policy and infrastructure to heighten translational efficiency of research involving therapeutic innovations such as drugs, companion diagnostics, devices and cell based therapies. In Australia, a series of government infrastructure initiatives including the Department of Innovation, Industry and Research's 'Strategic Roadmap for Australian Research Infrastructure' and the National Collaborative Research Infrastructure Scheme (NCRIS) relate directly to this agenda. In addition, the Clinical Trials Action Group (CTAG), a joint committee of the Parliamentary Secretaries for Health and Innovation was specifically tasked to assess issues related to clinical trial activity in Australia. As a result of this focus, most Australian states are in the midst of major building programs to accommodate translational research. This presentation will critically assess the implications of these various initiatives for pharmacy and highlight the critical need for pharmaceutical researchers to engage in networking strategies both nationally and internationally to remain competitive and secure adequate funding.

Symposium Sessions

Symposium 01

Integrating Complementary and Alternative Medicines into Mainstream Medicine

Professor Edzard Ernst, Professor Michael James & Associate Professor Lisa Nissen

Symposium 02

Trends in Pharmaceutical Formulation: From Bench to the Clinic

Professor Vânia Rodrigues Leite e Silva, Associate Professor Sanjay Garg, Dr Hugo Albrecht & Dr Graham Aldous

Symposium 03

Roles and Responsibilities of Pharmacist Practitioners in Australia's Reformed Health System

Chris Freeman, Vivienne Mak & Luke Grzeskowiak

Symposium 04

Toxicological Issues with Nanoparticulate Systems

Professor Rod Minchin, Professor Michael Roberts & Professor Brian Priestly

Symposium 05

Assessing Medicines Safety and Effectiveness: Beyond Randomised Controlled Trials

Professor Emily Banks, Sallie-Anne Pearson & Dr Nicole Pratt

Symposium 06

Pharmacokinetics

Dr David Foster, Professor Richard Upton & Professor Carl Kirkpatrick

Integrating Complementary and Alternative Medicines into Mainstream Medicine

Chair: Andrew McLachlan, The University of Sydney

Monday 12 December 2011, 1:30pm – 3:00pm

Room H2-02, Hetzel Building

There are a growing number complementary and alternative medicines that have a strong evidence base for their safety and efficacy. The symposium will specifically highlight the opportunities and challenges in integrating these complementary and alternative medicines into mainstream practice. In addition to Professor Ernst, the symposium will feature a number of prominent figures such as Professor Michael James (Rheumatology Department, Royal Adelaide Hospital), who has made significant contributions to the evidence base surrounding the use omega-3 fatty acids in cardiovascular and rheumatological diseases.

Edzard Ernst, Peninsula Medical School

Professor Edzard Ernst received his medical training in Munich, and moved to the University of Exeter (UK) Postgraduate Medical School in October 1993, establishing the first Chair in Complementary Medicine. In 1996 he founded the Department of Complementary Medicine at this University's Postgraduate Medical School and in 2002 his unit became part of the new Peninsula Medical School, Universities of Exeter and Plymouth. He has published over 1000 peer reviewed papers, primarily in the area of efficacy, safety and costs of complementary and alternative medicines. He states that one of his professional aims is 'to be neither promotional nor derogatory, but to struggle for objectivity'.

Michael James, Royal Adelaide Hospital

Professor Michael James is Chief Medical Scientist in the Rheumatology Unit, Royal Adelaide Hospital, and a Professor in the Department of Medicine, University of Adelaide. He is a long-standing researcher on omega-3 fats and has conducted studies on omega-3 fats in cardiac patients, rheumatoid arthritis patients, and in healthy volunteers. He has more than 130 publications in peer reviewed journals and is a member of the board of Directors of ISSFAL, the premier international society for the study of lipids.

Lisa Nissen, The University of Queensland

Dr Lisa Nissen is an Associate Professor of Quality Use of Medicines (QUM) in the University of Queensland, School of Pharmacy and Deputy-Director of the School's Centre for Safe and Effective Prescribing. Lisa has over 18 years experience, having worked in hospital and community pharmacy in both rural and metropolitan areas. Her clinical research focuses on the QUM in the wider community and the expansion of roles for pharmacists, including cognitive services such as chlamydia screening, sleep management, chronic pain management and pharmacist prescribing. Lisa's specific clinical interest is in the management of chronic pain. Lisa was the 2002 Pharmaceutical Society of Australia's (PSA) Young Pharmacist of the Year, and the 2008 PSA Pharmacist of the Year. In 2008 she received an Australian Learning and Teaching Council National University Teaching Excellence Award. Lisa is a past chairman of Society of Hospital Pharmacists of Australia (QLD) Branch, a Fellow of the Society of Hospital Pharmacists, an Honorary Fellow of the Hong Kong Association of Pharmacists, a Fellow of the PSA and the current PSA (QLD) Branch President.

Trends in Pharmaceutical Formulation: From Bench to the Clinic

Chairs: Sanjay Garg, The University of Auckland and Robert Milne, University of South Australia

Monday 12 December 2011, 1:30pm – 3:00pm

Room PM-06, Playford Building

The art and science of pharmaceutical formulation is rapidly evolving due to advances in technology and changing regulatory, marketing, and intellectual property frameworks. The symposium will address formulation development issues at various stages, i.e. drug discovery, preclinical, clinical, and market. Professor Vânia Leite e Silva will discuss formulating topical medications for systemic effects; Associate Professor Garg will compare formulation development for reaserch, clinical trials and the market; Dr Albrecht will speak on the formulation of protein drugs and opportunities for contract research; and finally Dr Aldous will discuss formulating for the market and what is needed to get and keep it there. Share your experiences and thoughts with experts from industry and academia.

Vânia Rodrigues Leite e Silva, Universidade Federal de São Paulo

Professor Vânia Leite e Silva currently acts as a Professor of Cosmetology, Federal University of São Paulo (UNIFESP- Universidade de São Paulo), Brazil. Vania has 22 years' experience in industry, with emphasis on research and development of cosmetics; in particular the research, development and validation of new methodologies and technologies for evaluation of cosmetic performance.

Sanjay Garg, The Unviersity of Auckland

Associate Professor Sanjay Garg is currently active as Deputy Head and Associate Professor, School of Pharmacy, University of Auckland, New Zealand. He acts as Chief Scientific Officer of AnQual GLP analytical laboratory. Sanjay leads a research team focusing on conventional and novel drug delivery systems (human and veterinary products for oral, buccal, topical, vaginal and parenteral routes), regulatory affairs and management. A number of formulations from his laboratory have reached clinical stages and market. Sanjay has interest in regulatory affairs and acts as a consultant to pharmaceutical companies in several countries. He will be joining as Professor in Pharmaceutical Sciences within the School of Pharmacy and Medical Sciences at the University of South Australia from January 2012.

Hugo Albrecht, University of South Australia

Dr Hugo Albrecht has considerable experience gained in both commercial and academic settings in Europe and the US, particularly within the fields of drug discovery, immunology, and neuroscience. Having directed a large number of projects within preclinical drug discovery in his position as Head of R&D for the contract research organisation Discovery Partners International in Basel, he has firsthand knowledge of the pharmaceutical drug discovery process. Hugo was also a member of the Swiss Biotech Network committee founded to encourage collaborations between industry and university research groups in Switzerland, and has an extensive commercial and academic network within Europe. Prior to joining the University of South Australia as a Senior Lecturer in 2011, Hugo was employed as Professor of Bioanalytics at the University of Applied Sciences North-Western Switzerland in Basel, where he played a major role in the establishment of a new undergraduate and master course in drug discovery and bioanalytics.

Graham Aldous, University of South Australia

Dr Graham Aldous has over 30 years experience in the Pharmaceutical Industry, having joined an Australian owned pharmaceutical company, Hamilton Pharmaceutical Pty Ltd as Research Manager, after attaining his PhD in physical organic chemistry at the Flinders University of South Australia. His work at Hamilton included the supervision of all internal product formulation and of research and external collaborative research conducted by the company. In 2000 Graham was invited to join the Board of Hamilton as Director of Scientific Affairs, with Quality Assurance and Research reporting directly to him. In 2011, Graham joined the University of South Australia as a Senior Lecturer. Graham has been a member of the Royal Australian Society of Chemistry for over three decades and is a member and past President of the Australian Society of Cosmetic Chemists.

Roles and Responsibilities of Pharmacist Practitioners in Australia's Reformed Health System

Chair: Andrew Gilbert, University of South Australia

Tuesday 13 December 2011, 1:30pm – 3:00pm

Room H2-02, Hetzel Building

Quality Use of Medicines and Pharmacy Research Centre

Structural changes such as Medicare Locals and GP Super Clinics are already in place. One key objective for government is to better support primary health care professions, including pharmacists, in delivering effective and efficient services through innovative and flexible service delivery models. Three young pharmacists, as part of their PhD research, will discuss their contribution to the evidence base in this area of health care reforms. Chris Freeman will talk on his experiences as a pharmacist working in a General Medical Practitioners surgery; Vivienne Mak will discuss the preparedness of pharmacists to work in innovative and flexible service delivery models and Luke Grzeskowiak will discuss pharmacists' roles in developing the evidence base for safe and effective use of medicines in pregnancy.

Chris Freeman, The University of Queensland

Chris obtained his Bachelor of Pharmacy from James Cook University in 2003. Since then, Chris has had experience in many sectors of pharmacy including hospital, community, and academia. In 2006, Chris gained accreditation to conduct medication reviews and in 2008 completed a Graduate Diploma in Clinical Pharmacy at the University of Queensland. In 2009, Chris commenced practice as a Consultant Pharmacist within the Camp Hill Healthcare medical centre located in Brisbane. In same year, Chris commenced his PhD in which he is investigating the integration of pharmacists into the General Practice environment. Chris is also involved in a large primary care research project describing how multidisciplinary care planning works in practice.

Vivienne Mak, University of South Australia

Vivienne Mak is a community pharmacist and is currently undertaking a PhD focusing on pharmacy practice. Her research focuses on the future of pharmacy in particular the preparedness of pharmacists to contribute to achieving the objectives of Australia's health care reform agenda. Along with her current role as the National Representative of the PSA South Australian Early Career Pharmacists Working Group, Vivienne currently also actively contributes to the profession as a PSA SA/NT Councillor since 2009. She was also recently awarded PSA Australian Young Pharmacist of the Year in 2010.

Luke Grzeskowiak, University of South Australia

Luke is a pharmacist, graduating from the University of South Australia in 2006. During and following his intern year he worked at the Women's and Children's Hospital in Adelaide, where he developed a strong interest in the area of medication safety in pregnancy and evidence-based medicine. He is currently in the final year of his PhD studies which are focused on examining the potential for using linked health data to investigate the potential long-term effects of medication use during pregnancy on infant health and development.

Toxicological Issues with Nanoparticulate Systems

Chair: Robert Milne, University of South Australia

Tuesday 13 December 2011, 1:30pm – 3:00pm

Room PM-06, Playford Building

Nanoparticulate delivery systems may allow important advances in the bioavailability and targeting of pharmaceuticals. While there is much information on the risks associated with environmental exposure to particles in the nano-size range, there is very little related to their therapeutic use. Professor Rod Minchin will speak on the mechanisms of the interactions between therapeutic nanoparticles and cells/tissues; Professor Michael Roberts will speak on the pharmacokinetics of these particles and Professor Brian Priestly will speak on current and possible future regulatory issues that are specific to therapeutic nanoparticles.

Rod Minchin, The University of Queensland

Professor Rod Minchin was appointed to a Chair of Molecular Pharmacology in the School of Biomedical Sciences at the University of Queensland in 2003. He graduated Ph.D. from the Department of Pharmacology, The University of Western Australia, followed by postdoctoral study at the National Cancer Institute in Washington DC. He moved to the University of New South Wales as a Queen Elizabeth II Fellow before returning to Western Australia to take up a teaching and research position. His research career has focussed on toxicology and cancer, and the role of drug metabolizing enzymes such as N-acetyltransferase. His work has been supported extensively by grants from the NHMRC and ARC and other government-funded organizations, and from this has published more than 130 original research articles. While maintaining his interest in the role of N-acetyltransferase, more recently he has turned his attention to the interactions between nanoparticles and biological molecules; hence the request for him to offer insights into his recent work at this symposium.

Michael Roberts, University of South Australia

Professor Michael Roberts graduated in pharmacy from the former SA Institute of Technology and, after a brief encounter with hospital pharmacy plus part-time research, embarked on a Ph.D. in the School of Pharmacy at The University of Sydney; he graduated in 1976. He accepted an academic position at the University of Tasmania before taking up an appointment as Professor at the University of Otago, New Zealand in the mid-1980s and then at The University of Queensland in the late 1980s. Currently, he is an NHMRC Senior Principal Research Fellow and has a shared professorial appointment between Queensland and the University of South Australia. Michael's research seeks to gain a better understanding the spatial disposition of drugs and nanoparticles in the liver, and improve delivery and permeation of substances across the skin. In later years, he has been investigating non-invasive methods for tracking substances in these regions of the body. So that he is fully occupied, he also seeks to improve outcomes in critical care and community care by ensuring that medicines are prescribed and used appropriately. He has enjoyed long-standing support from grants awarded by the NHMRC and ARC, plus numerous other organizations. His work over almost forty years has produced 6 books and over 400 publications, many of them emanating from his collaborations with a host of international researchers.

Brian Priestly, Monash University

Professor Brian Priestly graduated with a Bachelor of Pharmacy from the University of Sydney and then completed a Ph.D. at the same institution in 1968. After a period of postdoctoral research on mechanisms of hepatotoxicity at L'Universite de Montreal, he held Lecturer/Senior Lecturer positions in pharmacology at The University of Adelaide. He moved to Canberra in 1992 to lead the chemicals toxicology programs in the Commonwealth Health portfolio, and in 2001 – 2003, he served as Director of the Laboratories Branch of the Australian Therapeutic Goods Administration. He has chaired the NHMRC Advisory Committee on Health and Nanotechnology and is a member of the Nanotechnology Advisory Group of the National Industry Chemicals Notification and Assessment. He has served on numerous other national and international committees and working parties advising on the risks and adverse effects of chemical used by humans. In 2003 he was appointed as a Professorial Fellow in the Department of Epidemiology and Preventive Medicine at Monash University where he holds the title (part-time since his retirement in 2009) as Director of the Australian Centre for Human Health Risk Assessment.

Assessing Medicines Safety and Effectiveness: Beyond Randomised Controlled Trials

Chair: Libby Roughead, University of South Australia

Wednesday 14 December 2011, 9:00am – 10:30am

Room H2-02, Hetzel Building

A clear understanding of the safety and effectiveness of medicines is critical for informed medical and public decision making. Although randomised controlled trials are an important source of information on medicine safety and effectiveness, they have many important limitations that have been well recognised for a number of years. This symposium will demonstrate, through presentations and panel discussion, the opportunity to utilise pharmacoepidemiology to inform important knowledge gaps for medicines safety and effectiveness. In addition, the observational data sources available in Australia for such research will be reviewed, as will the pros and cons of the available methodologies.

Emily Banks, Australian National University

Professor Emily Banks is a medically trained epidemiologist with interest and expertise in large scale cohort studies, pharmacoepidemiology, women's health, and healthy ageing. She has worked extensively on the health effects of hormone replacement therapy. Professor Banks is currently the Scientific Director of the NSW 45 and Up Study and an NHMRC Senior Research Fellow at the National Centre for Epidemiology and Population Health, at the Australian National University. She was based in the UK from 1995-2003, where she was Deputy Director of the Cancer Research UK Epidemiology Unit at the University of Oxford and joint Principal Investigator of the Million Women Study. In 2000 she was awarded the UK National Woman of Achievement in Science and Technology. She has served as an advisor to the World Health Organization, International Agency for Research on Cancer and the UK National Health Service Breast Screening Programme. She is also a member of the Collaborative Group on Hormonal Factors in Breast Cancer and the Research Advisory Committee to the National Breast Cancer Foundation. Professor Banks is currently head of Chronic Disease Epidemiology at the National Centre for Epidemiology and Population Health and Chair of the Advisory Committee on the Safety of Medicines.

Sallie-Anne Pearson, University of New South Wales

Sallie is a health service researcher specialising in clinician behaviour change, pharmacoepidemiology and pharmaceutical policy evaluation. She has conducted this research in Australia, the United States and the developing world. Sallie completed her doctoral training in 1998 at the University of Newcastle, Australia and was the inaugural Postdoctoral Fellow in Pharmaceutical Policy at Harvard Medical School from 2000 – 2001. She returned to Australia in 2002 where she worked as a consultant to the WHO Collaborating Centre in Pharmaceutical Policy Boston and Medicare Australia for two years. She returned to academia in 2004 and in March 2006 joined the Adult Cancer Program to head the Pharmacoepidemiology and Pharmaceutical Policy Research Group. She currently holds a Cancer Institute NSW Career Development Fellowship (2010 – 2012). Sallie's current research interests focus on three core areas: (i) using secondary data sources to investigate the use and impact of medicines in real world clinical practice, (ii) clinician behaviour change, specifically the use and uptake of electronic decision support to guide prescribing practice (iii) investigating the direct and indirect costs of cancer care from the perspective of health care payers and patients.

Nicole Pratt, University of South Australia

Dr Nicole Pratt is a Senior Research Fellow at the Quality Use of Medicines and Pharmacy Research Centre, University of South Australia. She has a particular interest in new statistical methodologies to study the effectiveness and safety of medicine use and in the development of tools for post-marketing surveillance of medicines. Nicole leads the evaluation of the Veterans' Medicines Advice and Therapeutics Education Service (Veterans' MATES) program which uses administrative claims data to develop and evaluate interventions to improve use of medicines in the veteran population in Australia. She is a founding member of Medicines Utilisation Research Australia (MURA), co-coordinator of the Asian Pharmacoepidemiology Network (AsPEN) initiative and a member of the Therapeutic Goods Administration Advisory Committee on the Safety of Medicines (ACSOM).

Pharmacometrics

Chair: David Foster, University of South Australia

Wednesday 14 December 2011, 9:00am – 10:30am

Room PM-06, Playford Building

University of South Australia | Australian Centre for Pharmacometrics

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Pharmacometrics is the science which deals with the quantitative description of disease, drug effects and variability, often referred to as “modelling and simulation”. This field quantifies drug, disease and trial information to aid efficient drug use, development, and regulatory decisions. The strength of such analyses is the ability to integrate knowledge from prior understanding, related compounds and biology, together with the inclusion of both richly sampled data and more limited/incomplete data typically unusable in traditional statistical approaches. This area has often been poorly understood by mainstream biomedical researchers in the past. However, researchers, regulatory authorities and funding bodies are increasingly recognizing the power and utility of pharmacometric analyses. Dr David Foster will give a broad overview of pharmacometrics, while Professor Richard Upton will provide an example of model development, and Professor Carl Kirkpatrick will present a more clinically orientated perspective. The symposium will finish with a panel discussion.

David Foster, University of South Australia

After completing his PhD in pharmacology, Dr David Foster continued his research at the Drug Metabolism and Pharmacokinetics laboratory of the Discipline of Clinical & Experimental Pharmacology at The University of Adelaide. In 2006 he took up the position of lecturer at the University of South Australia in the School of Pharmacy and Medical Sciences. David’s exposure to the pharmacy profession and drug regulation, combined with his biomedical science training, has focussed his research on identifying the pharmacokinetic and pharmacodynamic factors which govern variability in drug response. This work aims to employ pharmacometric analysis as a tool to translate basic and clinical research into improved pharmacotherapeutic use.

Richard Upton, University of South Australia

Professor Richard Upton splits his time between a chair in Pharmacometrics at the University of South Australia and working as a pharmacometric consultant to industry. He trained in biological science, and completed his PhD in the Department of Anaesthesia and Intensive Care at Flinders University. His research interests include the physiological determinants of the actions of anaesthetics and analgesics. He has used pharmacokinetic-pharmacodynamic modelling extensively to infer the behaviour of physiological and pharmacological systems. Richard has benefited from being a successful basic researcher, from seeing the needs of industry and from close collaboration with clinicians. This wide perspective has led him to the conviction that modelling and simulation provides innovative ways of translating knowledge into strategies for optimising the management of disease.

Carl Kirkpatrick, Monash Univeristy

Professor Carl Kirkpatrick obtained his undergraduate pharmacy qualifications and PhD from the University of Otago, New Zealand. Since graduating he has worked in all aspects of community and hospital pharmacy. Carl's research interests include: population pharmacokinetic and pharmacodynamic modelling, dosing monitoring and Bayesian optimisation (antimicrobials, chemotherapeutic agents and anticoagulants), optimisation of dosing in renal dysfunction, pharmacokinetics and dosing in obesity, drugs in breast milk, and the quality use of medicines. The goal of Carl's research is to optimise pharmacotherapy which should lead to improved patient outcomes.

Pharmaceutical Science: Analytical Techniques

Session Chair: Hywel Williams, Monash University

Monday 12 December 2011, 11:00am – 12:30pm

Room P5-14, Playford Building

CP01-1

Timothy Barnes, University of South Australia

Biophysical characterisation informing the development of protein delivery systems

CP01-2

Clare Strachan, University of Otago

Rapid detection of adulterated herbal products using vibrational spectroscopy

CP01-3

Qiang Huang, The University of Sydney

Development of a simple TLC method for the determination of aristolochic acids

CP01-4

Petra Priemel, University of Otago

Correlating recrystallisation with dissolution behaviour

CP01-5

Atul Awasthi, The University of Auckland

Separation and identification of degradation products in eprinomectin formulation using LC, FT-MS, H/D exchange and NMR studies

CP01-6

Madhur Shastri, University of Tasmania

Development of an effective ion chromatography technique for the separation of intact low-molecular-weight heparin

Biophysical characterisation informing the development of protein delivery systems

Timothy J Barnes [1] Ivan M Kempson [2, 3] Clive A Prestidge [2]

[1] School of Pharmacy and Medical Sciences, University of South Australia, Adelaide, SA

[2] Ian Wark Research Institute, University of South Australia, Adelaide, SA

[3] Institute of Physics, Academia Sinica, Taipei, TAIWAN

Objective

With the prevalence of peptide and protein based therapeutics, as well as the numerous disease states attributed to protein stability, there is a need for advanced methods to characterise protein adsorption. Here, we investigate the role of protein structure, and in particular the influence of subtle changes (e.g. due to denaturation) on the protein adsorption behaviour.

Methods

Using advanced methodologies including Atomic Force Microscopy (AFM), Time-of-Flight Secondary Ion Mass Spectroscopy (ToF-SIMS) and the Quartz Crystal Microbalance (QCM) we characterise protein adsorption on silicon substrates.

Results

The influence of both surface chemistry and protein dimensions on loading into a porous silicon matrix was explored. The importance of optimising surface chemistry to ensure the loaded protein (papain) retained its bioactivity was demonstrated. Using ToF-SIMS and QCM, we demonstrate that it is possible to discriminate between the presence of native and partially denatured human serum albumin (HSA) adsorbed on a solid substrate. With the exceptional surface sensitivity of ToF-SIMS, and the use of Principle Component Analysis to interrogate the complex amino acid fragmentation pattern, it was possible to elucidate changes in HSA adsorbed conformation which occurred as a result of subtle changes in protein tertiary structure. Finally, we could distinguish between the presence of native and denatured HSA from a complex protein (from human serum) mixture from their adsorption behaviour.

Conclusions

Here, we highlight a novel use of advanced biophysical characterisation tools (AFM, ToF-SIMS, QCM) to characterise protein adsorption, and demonstrate their significant potential, particularly in detecting changes in protein structure/conformation.

Rapid detection of adulterated herbal products using vibrational spectroscopy

Friederike Folttmann [1] Sara Fraser [2] James Oughton [3] Keith Gordon [2] Clare Strachan [1]

[1] School of Pharmacy, University of Otago, Dunedin, NEW ZEALAND

[2] Department of Chemistry, University of Otago, Dunedin, NEW ZEALAND

[3] Medsafe, Ministry of Health, Auckland, NEW ZEALAND

Objective

The aim of this study was compare the potential of different vibrational spectroscopy techniques, namely mid-infrared and Raman spectroscopy, for the rapid detection of adulterated herbal products.

Methods

Thirty one herbal medicines intercepted at the New Zealand border and claiming to relieve symptoms of erectile dysfunction or increase libido were selected. LC-MS was used to qualitatively and quantitatively determine the presence of any phosphodiesterase type V inhibitors in the herbal products. Infrared and Raman spectroscopy of the samples were also taken and the resulting spectra analysed using principal component analysis (PCA) and the classification method soft independent modelling of class analogy (SIMCA). The results from the chemometric analysis were compared to the type and quantity of adulterated drug found in the samples based on LC-MS analysis.

Results

Of the 31 samples, 26 were found to be adulterated with sildenafil (n = 17), sildanfil analogues (n = 6), vardenafil (n = 1) and/or tadalafil (n = 5), with 16 adulterated at therapeutic or overdose levels. For both infrared and Raman spectroscopy, samples with a high concentration of sildenafil or containing a similar analogue clustered in a similar region in PC space, and those contaminated with tadalafil clustered in a separate region. The SIMCA analysis was largely successful in identifying herbal products that were adulterated with therapeutic or toxic levels of the drugs, with Raman spectroscopy performing slightly better than infrared spectroscopy, but detection of trace levels was more challenging.

Discussion

Both mid-infrared and Raman spectroscopy combined with PCA and SIMCA analysis show potential for the rapid detection of adulterated herbal products.

Development of a simple TLC method for the determination of aristolochic acids

Qiang Huang [1] Yuling Chen [1] Kong M Li [2] Valentina Razmovski-Naumovski [3] Kelvin Chan [1, 3] Basil Roufogalis [1] Andrew McLachlan [1] George Q Li [1]

[1] Faculty of Pharmacy, The University of Sydney, Sydney, NSW

[2] Bosch Institute, The University of Sydney, Sydney, NSW

[3] Centre for Complementary Medicine Research, University of Western Sydney, Sydney, NSW

Objective

Aristolochic acids (AAs) is a collective name for compounds with a nitrophenanthrene carboxylic acid structure that can be found in the Aristolochiaceae plant family, primarily in the genera Aristolochia and Asarum. AAs are recognised for their nephrotoxic and carcinogenic effects in humans. In Australia, herbs and products for medicinal use suspected to contain AAs are forbidden to be sold, supplied and used. This study aims to develop a simple thin-layer chromatography (TLC) method to identify and screen AAs in highly suspicious raw herbs and products.

Methods

Ultra-sonication was implemented in the extraction of samples. Different common extracting solvents and homogenous solvent mixtures as mobile phase systems were examined. Aristolochic Acid I was used as a reference compound. A silica gel F254 TLC plate was employed as stationary phase. 10% H_2SO_4 was applied as the derivatising agent.

Results

1) Ultra-sonication is an effective and efficient tool in the extraction of AAs. 2) A new mobile phase system consisting of toluene, acetone and formic acid was developed. 3) The TLC fingerprints of a number of herbs in Aristolochiaceae were generated and incorporated in the 'Toxic Chinese Herbal Medicines Database'.

Conclusions

TLC can provide a cost effective and rapid screening method for the detection of AAs in Chinese herbal medicine. It needs to be supported by HPLC for quantitative analysis and LC-MS for structure confirmation. This authentication for the database will provide a platform for the regulation of toxic and scheduled herbs in Australia.

Correlating recrystallisation with dissolution behaviour

Petra Priemel [1] Holger Grohganz [2] Keith Gordon [3] Thomas Rades [1] Clare Strachan [1]

[1] School of Pharmacy, University of Otago, Dunedin, NEW ZEALAND

[2] Faculty of Pharmaceutical Sciences, University of Copenhagen, Copenhagen, DENMARK

[3] Department of Chemistry, University of Otago, Dunedin, NEW ZEALAND

Objective

The aims of this study were: (a) to analyse the stability of quench cooled indomethacin with different analytical techniques, and (b) correlate the quantitative results with the dissolution behaviour of stored samples.

Methods

Quench cooled indomethacin (150 - 250 µm) was stored at 30°C and 23% RH. Samples were analysed with attenuated total reflectance infrared spectroscopy (ATR-IR), differential scanning calorimetry (DSC), X-ray powder diffraction (XRPD) and the amorphous content was quantified. Scanning electron microscopy (SEM) was additionally used to visualise samples. Intrinsic dissolution testing at pH 6.8 was performed with crystalline indomethacin, freshly prepared and stored amorphous samples.

Results

SEM analysis revealed surface crystallisation of amorphous indomethacin. Quantification with different analytical techniques resulted in large differences in re-crystallisation endpoints and kinetics. Analysis with ATR-IR showed the fastest re-crystallisation and XRPD the slowest. This could be explained by the properties of the analytical techniques such as different sampling depths (ATR-IR, XRPD) or sensitivity to extent of long range order. Stored samples with a crystalline shell but an amorphous core showed the same dissolution behaviour as the crystalline form showing that ATR-IR spectroscopy was a suitable analytical technique to predict the dissolution behaviour.

Conclusions

Different analytical techniques resulted in different observed re-crystallisation behaviour. Correlating the quantitative results of the analytical techniques to the dissolution behaviour of stored samples revealed that ATR-IR spectroscopy predicted the dissolution behaviour best. The results emphasise the importance of understanding analytical technique limitations when investigating solid state behaviour and associated critical quality attributes, such as dissolution.

Separation and identification of degradation products in eprinomectin formulation using LC, FT-MS, H/D exchange and NMR studies

Atul Awasthi [1] Majid Razzak [2] Raida Al-Kassas [1] Joanne Harvey [3] David Greenwood [4] Sanjay Garg [1]

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[3] School of Chemical and Physical Sciences, Victoria University of Wellington, Wellington, NEW ZEALAND

[4] School of Biological Sciences, The University of Auckland, Auckland, NEW ZEALAND

Objective

The aim of present study was to develop and validate a new HPLC method for the analysis of eprinomectin (EPM) in pharmaceutical preparations and to identify/characterize its degradation products using current analytical protocols.

Methods

An HPLC method was developed and validated according to international guidelines. Two major degradation products shown in stress study samples were isolated using semi preparative flash chromatography and identified/characterized using LC-PDA, high resolution FT-ICR MS, H/D exchange, and NMR i.e. ^{1}H, ^{13}C, and ^{2}D experiments (COSY, NOESY) studies. MS^{n} studies were applied to establish the degradation pathways. In addition, stereo and structural isomers were distinguished and findings were compared with *in silico* analysis using HiChem MassFrontier 5.1.

Results

The new HPLC method was found selective, precise and stability indicating. FT-MS analysis presented molecular ion peaks for EPM and degradation products at m/z 914.52505 Da, with almost identical fragmentation patterns of accurate masses (mass error <1 ppm). MS^{n} studies helped to establish the origin of fragments, degradation pathways, and distinguished structural isomers. The presence of functions groups with labile hydrogen was confirmed by exchanging hydrogen with deuterium using external experiment. ^{1}H, ^{13}C, and ^{2}D NMR experiments confirm the structure of parent compound and degradation products. The interpretation of experimental data positively identified Unknown 1 as the stereoisomer *2-epimer* and Unknown 2 as the structural isomer Δ-2,3 isomer of EPM.

Conclusions

The alternative HPLC method and identification exercise will contribute towards a better understanding of EPM and degradation chemistry, and establish a platform to facilitate the MS analysis of EPM in biological, environmental, and pharmaceutical samples. The study reveals that pharmaceutical methods have their limitations for the analysis of medicinal products and more importantly HPLC, as well as conventional MS analysis, lacks the ability to distinguish structural and stereoisomers.

Development of an effective ion chromatography technique for the separation of intact low-molecular-weight heparin

Cameron Johns [1] Joseph Hutchinson [1] Madhur Shastri [2] Rahul Patel [2] Amanda Stocks [2]

[1] Australian Centre for Research on Seperation Science, University of Tasmania, Hobart, TAS

[2] School of Pharmacy, University of Tasmania, Hobart, TAS

Objective

It has been long-known that enoxaparin, a widely used anti-coagulant, possesses anti-inflammatory activity. While enoxaparin has shown promising results in the management of asthma, some fractions of enoxaparin have anti-inflammatory properties and other fractions possess the risk of bleeding. The aim of the study was to develop an effective ion-chromatography (IC) technique which allows the isolation and hence identification of enoxaparin fractions with negligible anti-coagulant activity.

Methods

The developed IC method uses a semi-preparative CarboPac PA 100 (9 x 250 mm) ion-exchange column with UV detection at 230 nm, flow rate at 2.0 mL/minute, and a mobile phase gradient of 32-74% NaCl, at pH 6.0. Desalting of the isolated fractions was investigated using HILIC cartridges, a molecular-weight-cut-off (1000 Da) filter or methanol precipitation. This anti-coagulant activity of each IC-derived fraction was determined using anti-factor Xa assay.

Results

The newly developed IC method partially resolved the enoxaparin into more than 30 different peaks without prior depolymerisation. Compared to other desalting methods, the methanol precipitation successfully removed NaCl from the IC-collected fractions and also the recovery of desalted fractions was more than 95%. Various fractions of enoxaparin with high, moderate or negligible anti-coagulant activities were identified.

Conclusions

The developed IC method is relatively quick and provides superior resolution to previously reported methods. It can be useful for the chemical characterisation and stability determination of enoxaparin. This assay can provide a platform to identify the fractions of enoxaparin having high anti-inflammatory properties but devoid of significant anti-coagulant activity.

Pharmaceutical Science: Oncology

Session Chair: Mary Bebawy, University of Technology Sydney

Monday 12 December 2011, 11:00am – 12:30pm

Room P5-15, Playford Building

CP02-1

Vaughan Connell, Curtin University

Durability of low dose cisplatin-induced cell cycle arrest

CP02-2

Ashleigh De Marie, Curtin University

Cytotoxicity and chemo-sensitisation in malignant mesothelioma cells by small molecule Bcl-2 protein inhibitors

CP02-3

Ritu Jaiswal, The University of Sydney

Microparticle-associated nucleic acids mediate trait dominance in cancer

CP02-4

Victoria McLeod, Monash University

Comparison of the pharmacokinetics and anti-tumour efficacy of a PEGylated doxorubicin-conjugated polylysine dendrimer with PEGylated liposomal doxorubicin and a simple doxorubicin solution

CP02-5

Joyce Gong, The University of Sydney

Microparticle-mediated resistance and vesicular drug sequestration in breast cancer

CP02-6

Lisa Kaminskas, Monash University

Targeting methotrexate-conjugated dendrimers to the lymphatics enhances efficacy in a syngeneic rat model of lymph-metastatic cancer

Durability of low dose cisplatin-induced cell cycle arrest

Vaughan Connell [1, 2] Brett Dix [1, 2]

[1] School of Pharmacy, Curtin University, Perth, WA

[2] Curtin Health Innovation Research Institute, Curtin University, Perth, WA

Objective

The generally accepted approach to chemotherapy is to induce apoptosis in cancer cells through the use of high dose treatment. However, research in our laboratory has indicated that comparatively low doses of cisplatin, while failing to induce apoptosis, are able to induce a cell cycle arrest. In this study we sought to investigate how clinically applicable these recent findings may be, by examining the durability of the induced arrest and the effects of prolonged exposure to cisplatin.

Methods

The human lung cancer A549 cell line was used. Cisplatin 1mg/mL (Hospira, Australia Pty Ltd.) was applied in each experiment at 1.25 µg/mL (4.31 µM). Cell cycle arrest was analysed via cell counts and flow cytometry with propidium iodide staining.

Results

A549 lung carcinoma cells exposed to low dose cisplatin enter cell cycle arrest 21 - 24 hours after the commencement of treatment. Durability of cell cycle arrest is directly related to exposure time to drug with 12 hours of exposure necessary to induce an arrest that lasts for 24 hours or longer. Single dose of cisplatin appeared to lose its effectiveness within 24 hours, however reapplication of the drug at 12 hourly intervals resulted in a sustained cell cycle arrest.

Conclusions

These findings suggest that low dose cisplatin could potentially be used in patients where the goal of therapy is no longer curative but rather palliative in nature and where the adverse events associated with high dose cisplatin treatment may not be tolerated.

Cytotoxicity and chemo-sensitisation in malignant mesothelioma cells by small molecule Bcl-2 protein inhibitors

Ashleigh De Marie [1] Simon A Fox [1, 2]

[1] School of Pharmacy, Curtin University, Perth, WA

[2] Curtin Health Innovation Research Institute, Curtin University, Perth, WA

Objective

Anti-apoptotic Bcl-2 proteins are frequently over-expressed in cancers resulting in resistance to apoptosis induced by cytotoxic chemotherapy. Malignant mesothelioma (MM) is a cancer with poor prognosis, highly resistant to chemotherapy and displaying upregulation of anti-apoptotic Bcl-xL and Mcl-1. In this study we explored mechanisms which may underlie its chemo-resistance by examining the effect of small molecule inhibitors of these proteins upon drug induced cell death in mesothelioma cells.

Methods

The human MM cell lines JU77 and ONE58 were used. Bcl-2 inhibitors were ABT-263 (Selleck Chemicals, USA) and HA14-1 (Sigma-Aldrich, Aust.). Cell viability was assayed by MTT assay and apoptotic cell membrane changes were measured by flow cytometry with annexin V/ propidium iodiode staining. Active caspase-3 was measured by alpha-LISA (Perkin-Elmer, Aust.).

Results

ONE58 cells were more resistant to both cisplatin and gemcitabine and did not show caspase-3 activation and membrane phosphatidylserine (PS) as seen in JU77 cells. We found that both ABT-263 and HA14-1 were cytotoxic as single-agents against MM cells. However, the mechanism of this effect varied between the cell lines with differential effects upon caspase activation and membrane PS exposure. In combination experiments pretreatment of MM cells with either inhibitor in combination with drug was more effective than drug treatment alone.

Conclusions

These results provide further insight into apoptotic mechanisms in MM cells following treatment with chemotherapeutics. Furthermore, using the Bcl-2 inhibitors HA14-1 or ABT-263 we were able to induce cell death and modify the sensitivity of both MM cell lines to cisplatin and gemcitabine.

Microparticle-associated nucleic acids mediate trait dominance in cancer

Ritu Jaiswal [1, 2] Joyce Gong [1, 2] Georges E Grau [1] Mary Bebawy [2]

[1] Bosch Institute, The University of Sydney, Sydney, NSW

[2] School of Pharmacy, University of Technology Sydney, Sydney, NSW

Objective

Multidrug resistance (MDR) is a serious cause of anticancer treatment failure whereby cancer cells display cross-resistance to structurally and functionally unrelated drugs. MDR is caused by overexpression of the efflux transporters P-glycoprotein (P-gp) and Multidrug Resistance-Associated Protein 1 (MRP1). These transporters act to maintain sublethal intracellular drug concentrations within cancer cells, making the population treatment unresponsive. Recently, we discovered a novel non-genetic basis to MDR whereby microparticles (MPs) transfer P-gp intercellularly from MDR donor cells to drug-sensitive recipient cells.

Methods

MPs isolated from MDR leukemia and breast cancer cells were co-cultured with their drug-sensitive counterparts. The MP - cell interaction was visualised by scanning electron microscopy. P-gp transfer was assessed by FACS analysis following direct immunolabeling and q RT-PCR. miRNA profiles of MPs, MP cocultured with recipient cells and cells alone were profiled using the affymetrix miRNA microarray platform.

Results

We show that MDR MPs incorporate nucleic acids including transcripts encoding the mediators of miRNA biogenesis. We also show that MPs change the recipient cells' transcriptional environment to reflect donor MDR phenotype with distinct pathways present among cancers of different origin.

Conclusions

We demonstrate that intercellular transfer of MDR exists for both hematological and non-hematological malignancies. By conferring MDR and "re-templating" the transcriptional landscape of recipient cells, MPs provide a novel pathway having implications in the dissemination and acquisition of deleterious traits in clinical oncology.

This work was supported by the NSW Cancer Council and National Health and Medical Research Council (NHMRC).

Comparison of the pharmacokinetics and anti-tumour efficacy of a PEGylated doxorubicin-conjugated polylysine dendrimer with PEGylated liposomal doxorubicin and a simple doxorubicin solution

Victoria McLeod [1] Lisa Kaminskas [1] Brian Kelly [2] David Owen [2] Christopher Porter [1]

[1] Monash Institute of Pharmaceutical Sciences, Monash University, Melbourne, VIC

[2] Starpharma Pty Ltd, Melbourne, VIC

Objective

Liposomal formulations of doxorubicin display improved tumour targeting and reduced cardiotoxicity, but are associated with side effects relating to accumulation in the skin and non-specific drug release in plasma. Here we compare the pharmacokinetics, anti-tumour efficacy and systemic toxicity of PEGylated liposomal doxorubicin (L-DOX) and a simple solution formulation of doxorubicin (DOX) with a novel, biodegradable, doxorubicin-conjugated dendrimer (D-DOX).

Methods

A generation 5 PEGylated polylysine dendrimer was synthesised with doxorubicin conjugated to the surface via an acid labile hydrazone linker to epsilon-amino groups and PEG1100 to alpha-amino groups. The pharmacokinetics, anti-tumour efficacy and systemic toxicity of the three doxorubicin formulations were subsequently compared in a doxorubicin-sensitive rat carcinoma model.

Results

D-DOX and L-DOX significantly increased plasma exposure of total doxorubicin and increased uptake of doxorubicin into solid tumours when compared to DOX. However, D-DOX showed significantly lower uptake into the spleen when compared to DOX and L-DOX. Anti-tumour efficacy studies in rats (bearing Walker 256 carcinomas) and mice (bearing MDA-MB231 carcinomas) revealed similar inhibition of tumour growth after administration of doxorubicin equivalent doses of D-DOX, DOX and L-DOX. However, at higher doses of doxorubicin (4 - 8 mg/kg), D-DOX increased rat survival time when compared to DOX and L-DOX by reducing systemic toxicity.

Conclusions

The data suggest that dendrimers bearing doxorubicin via acid labile covalent linkages have potential as doxorubicin-based nanomedicines with equivalent chemotherapeutic efficacy but significantly reduced side effects when compared to current clinical formulations of doxorubicin.

Microparticle-mediated resistance and vesicular drug sequestration in breast cancer

Joyce Gong [1, 2] Ritu Jaiswal [1, 2] Georges Grau [1] Mary Bebawy [2]

[1] Sydney Medical School, The University of Sydney, Sydney, NSW

[2] School of Pharmacy, University of Technology Sydney, Sydney, NSW

Objective

Multidrug resistance (MDR) occurs when a tumour cell becomes resistant to many cytotoxic drugs following exposure to a single agent, resulting in a tumour cell that no longer responds to therapy. One mechanism contributing to MDR is the over-expression of P-glycoprotein (P-gp), an efflux transporter, which maintains a sublethal intracellular drug concentration, rendering tumour cells treatment unresponsive. Microparticles (MPs) are plasma membrane-derived vesicles 0.1 - 1 µm in diameter that are released by blebbing from various cell types. MPs consist of fragments of the parent cell's plasma membrane, cell surface proteins and cytoplasmic material. We have shown in human acute lymphoblastic leukaemia cells that drug-resistant cells shed MPs that can transfer functional P-gp to drug-sensitive cells, rendering them MDR. We now demonstrate the expanding role of MPs in drug sequestration.

Methods

Flow cytometry confirmed the presence of functional P-gp from MPs released from human MCF-7/Dx breast cancer cells. Transferred P-gp was confirmed functional using the daunorubicin dye exclusion assay. Quantitative real time PCR was used to determine expression levels of transcripts and microRNAs. Drug sequestration profiles were determined by exposing MPs to known concentrations of drugs, subsequently removing MPs and determining remaining drug concentrations by fluorimeter.

Results

We show that MPs shed from MCF-7/Dx cells transfer functional P-gp to recipient cells, resulting in MDR. Furthermore, MPs incorporate and transfer transporter transcripts and microRNAs, resulting in a ‘re-templating’ of recipient cells to reflect the donor cell phenotype. Additionally, MPs effectively sequester some chemotherapeutics resulting in a reduction of the free drug concentration available at the target site.

Conclusions

This study reveals novel parallel pathways by which MPs contribute to MDR in cancer. These findings have significant implications in the rational design of alternative treatment strategies for the prevention and circumvention of drug resistance clinically.

This work was supported by research grants from the NSW Cancer Council and National Health and Medical Research Council.

Targeting methotrexate-conjugated dendrimers to the lymphatics enhances efficacy in a syngeneic rat model of lymph-metastatic cancer

Lisa Kaminskas [1] Victoria McLeod [1] Brian Kelly [2] David Owen [2] Christopher Porter [1]

[1] Monash Institute of Pharmaceutical Sciences, Monash University, Melbourne, VIC

[2] Starpharma Pty Ltd, Melbourne, VIC

Objective

Conjugation of methotrexate (MTX) to the surface of PEGylated polylysine dendrimers (D-MTX) results in rapid uptake into reticuloendothelial macrophages and poor tumour targeting after IV administration. In contrast, tert-butyl capping of the MTX free carboxylate group (D-MTX-CAP) results in reduced macrophage uptake and enhanced activity in SC injected Walker rat tumours. Here we sought to utilise the macrophage targeting properties of D-MTX to promote uptake into lymph nodes after SC administration and to improve chemotherapy against lymph-resident metastases.

Methods

The pharmacokinetics, biodistribution, lymphatic uptake and anti-cancer efficacy of free MTX, D-MTX, D-MTX-CAP and a non-methotrexylated control dendrimer (D) were compared after SC administration in rats.

Results

D and D-MTX-CAP were absorbed primarily via the lymph (~20 - 25% of the injected dose), whereas free methotrexate was largely excluded from the lymph. In spite of good access to the lymph fluid, lymph node retention of D or D-MTX-CAP was poor (<2%/g). In contrast, D-MTX was less well absorbed, but lymph node retention was high (~35%/g). SC administration of D-MTX in rats containing popliteal metastases subsequently resulted in improved chemotherapy when compared to administration of equimolar quantities of D-MTX-CAP or MTX alone.

Conclusions

MTX-conjugated polylysine dendrimers are avidly taken up into lymph nodes draining SC injection sites. Improved targeting to lymph nodes also enhances tumour growth suppression when compared to free MTX or D-MTX-CAP. The data suggest that dendrimers with high affinity for lymph node resident macrophages may provide advantage in selective targeting of sentinel lymph nodes in cancer chemotherapy.

Pharmacy Practice: Cardiovascular

Session Chair: Beata Bajorek, University of Technology Sydney

Monday 12 December 2011, 11:00am – 12:30pm

Room P5-33, Playford Building

CP03-1

Gina Gujral, The University of Queensland

Pharmacists reinforcing patients' beliefs about medications to improve adherence post myocardial infarction

CP03-2

Greg Kyle, University of Canberra

Landmark studies impact on Australian antihypertensive usage trends from 1992 to 2010

CP03-3

Ashraf Eissa, The University of Sydney

Utilisation of thrombolysis in acute ischaemic stroke: A clinical audit

CP03-4

Janet Sluggett, University of South Australia

Patterns of hospital separations after a transient ischaemic attack or ischaemic stroke

CP03-5

Alexandra Madden, University of Tasmania

International normalised ratio control in southern Tasmania

CP03-6

John Shaw, The University of Auckland

Anticoagulation management by New Zealand community pharmacists

Pharmacists reinforcing patients' beliefs about medications to improve adherence post myocardial infarction

Gina Gujral [1] Karl Winckel [1, 2] Paul Garrahy [3] Lisa Nissen [1] Neil Cottrell [1]

[1] School of Pharmacy, The University of Queensland, Brisbane, QLD

[2] Department of Pharmacy, Princess Alexandra Hospital, Brisbane, QLD

[3] Department of Cardiology, Princess Alexandra Hospital, Brisbane, QLD

Objective

To improve medication adherence by reinforcing patients' beliefs about medicines for secondary prevention of myocardial infarction (MI) elicited using the repertory grid technique.

Methods

Two hundred patients discharged from hospital following a MI were randomised into intervention (n = 100) and control groups (n = 100). All patients were interviewed at 5 to 6 weeks, 6 and 12 months post discharge to elicit their beliefs about medicines for MI using the repertory grid technique. In the intervention group, patient's beliefs about their medicines were communicated by the researcher to their community pharmacist, who used this information to reinforce the patient's beliefs about their medicines at designated interviews (3, 6 and 12 months). The control group was provided with usual care. Medication adherence was measured using a medication possession ratio of their lipid lowering agent; less than 80% was categorised as non-adherent.

Results

There were 137 patients (intervention group n = 72, control group n = 65) remaining in the study at 12 months. In the intervention group, 29% (n = 20) of patients were non-adherent compared to 25% (n = 16) in control group, although it was not statistically significant; p = 0.697. Statements used to elicit beliefs about medicines from the repertory grid technique were themed, however there were no significant differences in themes between the intervention and control groups.

Conclusions

Reinforcing patients' beliefs about their MI medicines did not improve medication adherence however, this may reflect the small sample size and research into more regular follow up with a larger sample size is required.

Landmark studies impact on Australian antihypertensive usage trends from 1992 to 2010

Natalie Pastro [1] Greg Kyle [1]

[1] Discipline of Pharmacy, University of Canberra, Canberra, ACT

Objective

To evaluate usage patterns and identify any temporal associations between antihypertensive usage trends in Australia between 1992 and 2010 and landmark hypertension trials published during the same time period.

Methods

Annual dispensing data for all antihypertensives on the Pharmaceutical Benefits Scheme (PBS) were obtained for concessional and Veterans beneficiaries between 1992 and 2010. These data were converted to defined daily doses, and plotted against time to identify usage trends. Landmark studies were overlaid by year of publication to identify temporal associations at the drug class and individual drug level.

Results

Australian trends of growth and decline for antihypertensive medications were identified. Changes in usage trends coincided with the publication of the ALLHAT, ANBP2, EUROPA, TROPHY, PROGRESS, STOP-2 and ASCOT-BPLA trials. The effect of these trials appeared to have an influence only on the subject drug(s) rather than a class effect. Any class effect seen was due to a change in usage of the specific drug(s) in included in the trial. This was particularly seen with EUROPA and perindopril and ASCOT with perindiopril and amlodipine.

Conclusions

Relationships between usage trends and trial results appear to exist for approximately half of the trials studied. Factors other than trial evidence, such as marketing and drug availability may also influence usage trends.

Utilisation of thrombolysis in acute ischaemic stroke: A clinical audit

Ashraf Eissa [1] Ines Krass [1] Beata Bajorek [2, 3]

[1] Faculty of Pharmacy, The University of Sydney, Sydney, NSW

[2] School of Pharmacy, University of Technology Sydney, Sydney, NSW

[3] Department of Pharmacy, Royal North Shore Hospital, Sydney, NSW

Objective

Thrombolysis (tissue plasminogen activator) is the only evidence based pharmacological treatment for acute ischaemic stroke (AIS), however, its utilisation is reportedly extremely low. We aimed to determine the rates of utilisation of thrombolysis in a range of Australian hospitals and to identify the barriers to the use of this treatment.

Methods

A retrospective cross-sectional-study was conducted in five metropolitan hospitals in NSW, comprising two tertiary referral centres (TRC) and three district hospitals (DH). Patients discharged with a principal admission diagnosis of AIS during a 12 month time period (July 2009 - July 2010) were identified and the medical records of a systematically chosen sample reviewed.

Results

A total of 521 records (48.8% females; mean age 74.4 ± 14 years; range 22 - 102 years) of the 1261 patients with AIS, were reviewed; 133 from a 740-bed-TRC, 117 from a 650-bed-TRC, 94 from a 200-bed-DH, 85 from a 400-bed-DH and 92 from a 485-bed-DH. The rates of thrombolysis utilisation were 2.3%, 9.4%, 0%, 1.2% and 9.8%, respectively, with an overall rate of 4.6%. The most common reasons for not considering patients for thrombolysis were late presentation beyond the therapeutic time window (68.7%), minor or rapidly improving symptoms (26.9%), the patient receiving an anticoagulant with an International normalized ratio >1.7 at presentation (5.6%) and severe stroke (2.1%).

Conclusions

Rates of thrombolysis utilisation vary greatly between different hospitals with late patient presentation consistently being the most significant barrier to the utilisation of thrombolysis in stroke. Future efforts should focus on overcoming this barrier and standardising stroke care across Australia.

Patterns of hospital separations after a transient ischaemic attack or ischaemic stroke

Janet Sluggett [1] Gillian Caughey [1] Michael Ward [1] Andrew Gilbert [1]

[1] Sansom Institute for Health Research, University of South Australia, Adelaide, SA

Objective

To investigate the reasons for hospital separations occurring after a transient ischaemic attack (TIA) or ischaemic stroke (IS).

Methods

A retrospective observational study was conducted using claims data from the Department of Veterans' Affairs health administrative database. Data was extracted for subjects with a hospital separation for a TIA or IS in 2008 - 2009. The index separation was defined as the first separation extracted. Reasons for hospital separations in the following two months were determined. A clinical panel assessed the relationship between the reasons for subsequent separations and the index separation, ranking them as probable, possible or unlikely to be related. Disagreement was resolved by discussion.

Results

4882 subjects (2443 TIA, 2439 IS) met the inclusion criteria. Of these, 4520 subjects (2425 TIA, 2095 IS) survived the index separation. 782 TIA (32%) and 1323 IS (63%) subjects had a subsequent hospital separation during the two month follow-up. The number of subsequent separations ranged from 0 to 27. There was moderate agreement amongst panel members when assessing the relationship between index and subsequent separations (Kendall's coefficient of concordance 0.49, $p < 0.0001$). After the final panel ratings were applied to the dataset, 55% and 85% of the subsequent separations were determined to be probably or possibly related to the index TIA and IS separations, respectively.

Conclusions

Individuals hospitalised for a TIA or IS can have multiple hospital separations relating to the same event. These separations will need to be considered when using administrative data to investigate medicine use after a TIA or IS.

International normalised ratio control in southern Tasmania

Alexandra Madden [1] Gregory Peterson [1] Luke Bereznicki [1]

[1] School of Pharmacy, University of Tasmania, Hobart, TAS

Objective

To determine the current level of International Normalised Ratio (INR) control in southern Tasmania, and investigate the influence of testing frequency and patient characteristics on INR control.

Methods

An observational cohort study was conducted to examine INR results of southern Tasmanians taking warfarin from 2003 - 2010 obtained from a major private pathology provider.

Results

A total of 2,477 patients with 149,237 INR results were included. The mean time spent in therapeutic INR range (TTR) ± SD was 67.1 ± 22.4%. There were 1,137 patients with uninterrupted data from 2007 - 2010; this group had a mean TTR of 69.2 ± 21.2%, and 22.3% had a mean TTR of <60%. Patients ≥80 years old spent more time with a sub-therapeutic INR than younger patients (21.2% ± 20.8% in the ≥80 age group vs. 13.9 ± 8.1% in the 60 - 69 age group, $p < 0.01$). Patients who were monitored at a mean interval of 28 days or more had superior INR control compared to those monitored at an interval of less than 14 days (71.1 ± 12.9% vs. 63.3 ± 12% respectively, $p < 0.01$). Patients ≥80 years were monitored more frequently than younger patients, females more frequently than males and patients from lower socioeconomic index (SEI) areas more frequently than those from higher SEI areas.

Conclusions

The INR control in southern Tasmanians was superior to INR control demonstrated in recent international studies comparing warfarin to newer antithrombotics. However, there is room for improvement of INR control in southern Tasmania in certain groups.

Anticoagulation management by New Zealand community pharmacists

John Shaw [1] Jeff Harrison [1] Jenny Harrison [1]

[1] School of Pharmacy, The University of Auckland, Auckland, NEW ZEALAND

Objective

The proportion of time in the therapeutic range (%TTR) is a widely used measure of the quality of anticoagulation control. International guidelines recommend maintaining a %TTR of 60% or above in order to maximise benefits of warfarin and limit adverse events. Standard care by general practice and laboratory testing typically results in %TTRs less than 60%. This study set out to determine if accredited pharmacists using point-of-care (PoC) INR testing and decision-support software could provide safe, effective and cost-effective anticoagulation management that is acceptable to patients and other healthcare providers. Cost-effectiveness and acceptability are not reported here.

Methods

After ethics approval, 15 New Zealand community pharmacies recruited up to 50 patients each in consultation with local general practices and provided anticoagulation management during the period December 2010 to August 2011. PoC INR testing was provided using a capillary blood sample using CoaguCheck XS Plus (Roche) linked to a decision-support system (INR Online). Pharmacists recommended the continuation doses of warfain and timing of the next INR test. All results were communicated to the patient's general practice.

Results

A total of 693 patients was enrolled over the 15 sites. The mean %TTR across all sites was 78.6% (range 71.4 - 84.1%); rising to 80.2% for patients with 26 weeks or more of tests. The mean interval between tests was 14.4 days, rising to 16.7 days in months four to six. In terms of compliance with appointments, 83.1% were on or before the due date, and only 6.5% were more than three days overdue. For 154 patients, the prior six months INR data was obtained; for this cohort the %TTR for "standard care" was 60.4%, whereas it was 77.5% in the study. Adverse events and hospitalisations were no greater than reported events associated with standard care; although the small sample size limits firm conclusions.

Conclusions

The most notable result in terms of safety and effectiveness was the mean %TTR achieved in this study; this was consistent across all sites. It is much higher than reported values for "standard care" and for pre-study values for some of the patients in the study. Although it was not possible to definitely conclude that adverse events were decreased; using %TTR as a marker of anticoagulation control it is reasonable to postulate a reduction. Our conclusion is that accredited community pharmacists can provide safe and effective anticoagulation management services.

The study was funded by Health Workforce New Zealand and administered by the Pharmaceutical Society of New Zealand.

Pharmacy Practice: Counselling

Session Chair: Sara McMillan, Griffith University

Monday 12 December 2011, 11:00am – 12:30pm

Room P5-34, Playford Building

CP04-1

Shirin Hui Tan, The University of Queensland

Optimising pharmacists' counselling for patients with chronic pain

CP04-2

Krishneeta Kashyap, The University of Queensland

Assessment and counselling provided with over-the-counter sleep requests: A secret shopper study

CP04-3

Luma Alkhatib, Curtin University

An evaluation of the impact of down-scheduled ophthalmic chloramphenicol on the management of acute bacterial conjunctivitis in community pharmacies in Western Australia

CP04-4

Lillian Huang, The University of Queensland

Commercial influences on community pharmacist recommendations of S2/S3 medicines

CP04-5

Parisa Aslani, The University of Sydney

The provision of an adherence support service by community pharmacists

CP04-6

Kylie Williams, Unviersity of Technology Sydney

Internet and community pharmacy provision of a children's cough and cold medicine

Optimising pharmacists' counselling for patients with chronic pain

Shirin Tan [1] Christy Noble [1] Lisa Nissen [1]

[1] School of Pharmacy, The University of Queensland, Brisbane, QLD

Objective

To investigate the perceptions of both pharmacists and chronic pain patients of counselling for chronic pain.

Methods

Focus group sessions or semi-structured interviews were conducted with pharmacists and chronic pain patients. Themes generated from the interviews were used to develop survey questions which were then sent to a larger population of pharmacists and chronic pain patients. The results were triangulated to determine the degree of correlation between the groups.

Results

Pharmacists tend to focus on providing information on medications while chronic pain patients would like broader information, including information on other treatment modalities and general lifestyle advice. Chronic pain patients reported shorter interactions with pharmacists than that reported by pharmacists. Both pharmacists and patients identified that a lack of sufficient knowledge of chronic pain by pharmacists' leads to a lack of confidence and understanding (empathy) when counselling chronic pain patients. Pharmacists and patients both identified time and lack of private counselling areas as some barriers to pharmacist counselling.

Conclusions

There are discrepancies between chronic pain patients' expectations and pharmacists' focus when counselling. Pharmacists' have shown a lack of empathy and confidence when working with chronic pain patients, which can be improved with further education and training. The current community pharmacy model needs to reviewed to provide a more patient-centred approach, including sufficient staffing to allow pharmacists to spend more quality time with chronic pain patients in a private counselling area.

Assessment and counselling provided with over-the-counter sleep requests: A secret shopper study

Krishneeta Kashyap [1] Lisa Nissen [1] Simon Smith [2] Greg Kyle [3]

[1] School of Pharmacy, The University of Queensland, Brisbane, QLD

[2] School of Psychology, Queensland University of Technology, Brisbane, QLD

[3] Discipline of Pharmacy, University of Canberra, Canberra, ACT

Objective

To evaluate the current management of over the counter (OTC) sleep requests in Australian community pharmacies using secret shopper methodology.

Methods

Trained secret shoppers visited a sample of 100 randomly selected South East Queensland community pharmacies in June 2011. The secret shoppers enacted two OTC sleep scenarios: a direct product request (n = 50) and a symptom based request (n = 50). Results of the interactions were documented immediately after each visit and evaluated using the Pharmaceutical Society of Australia WHAT STOP GO protocol as a standard comparison.

Results

Of all direct product requests, 30% were handled entirely by the pharmacist, 70% of staff enquired about specific symptoms and 28% investigated the cause of insomnia. No staff investigated the frequency of product use. The direct product request scenario resulted in 92% supply of the requested doxylamine product (Restavit). In the symptom based scenario, 18% of requests were handled entirely by the pharmacist, 58% of staff enquired about specific symptoms and 44% investigated the cause of insomnia. Staff recommended medicated products (38%), herbal (78%) and non-drug techniques (18%). Investigation into smoking and alcohol intake was not undertaken in product or symptom based interactions, while questioning on caffeine intake was undertaken in 2% and 14% of cases respectively.

Conclusions

The secret shopper methodology was a successful way to assess the counselling provided in community pharmacies showing suboptimal staff responses when compared with recommended practice standards. Development of a targeted education program for both pharmacists and assistants may be useful in order to enhance current practice.

An evaluation of the impact of down-scheduled ophthalmic chloramphenicol on the management of acute bacterial conjunctivitis in community pharmacies in Western Australia

Luma Alkhatib [1] Petra Czarniak [1] Richard Parsons [2] Bruce Sunderland [1]

[1] School of Pharmacy, Curtin University, Perth, WA

[2] School of Occupational Therapy and Social Work, Curtin University, Perth, WA

Objective

To evaluate factors influencing pharmacists' management of eye infections following the down-scheduling of ophthalmic chloramphenicol to pharmacist supply.

Methods

Data were collected using a self administered questionnaire posted to a random sample of community pharmacies in Western Australia. Data were analysed using SPSS v17. Descriptive statistics summarised the responses and demographics of respondents. Regression analysis was used to identify relationships between variables. Factor Analysis was conducted to pool variables and the derived factors were subjected to regression analysis.

Results

Of the 240 community pharmacies surveyed, 119 (49.5%) responded (79% urban and 21% rural pharmacies). On average urban and rural pharmacies provided ophthalmic chloramphenicol 3.6 and 2.9 times weekly respectively, with some pharmacies providing 12 or more per week. Over 82% of respondents claimed that sales of other OTC products used for acute bacterial conjunctivitis had "decreased/decreased markedly". A majority of respondents (59%) stated that no change occurred in the number of prescriptions received for ophthalmic chloramphenicol. Most respondents (76.4%) "agreed/strongly agreed" that pharmacist's current level of training was adequate to provide ophthalmic chloramphenicol. However some (21.8%) responded that pharmacists required additional training.

Conclusions

Down scheduling of ophthalmic chloramphenicol has improved pharmacists' capability to treat acute bacterial conjunctivitis, largely as a replacement for products previously available over the counter, rather than less GP consultations. The community may be unaware that pharmacists have access to ophthalmic chloramphenicol. Pharmacists showed overall support for the down-scheduling as it enabled better use of professional skills and increased patient access to treatment.

Commercial influences on community pharmacist recommendations of S2/S3 medicines

Lillian Huang [1] Greg Kyle [1, 2] Taso Raptis [1] Ewa Stoklosa [3] Andrea Mattiazzi [1] Lisa Nissen [1]

[1] School of Pharmacy, The University of Queensland, Brisbane, QLD

[2] Discipline of Pharmacy, University of Canberra, Canberra, ACT

[3] Department of Pharmacy, King's College London, London, UNITED KINGDOM

Objective

Community pharmacy faces an inherent conflict between fulfilling professional responsibilities, including ensuring safe and appropriate use of medicines by consumers, and maintaining a profitable business. Evidence is available showing that prescribing habits of medical practitioners may be influenced by commercial factors. However, similar literature for pharmacists is sparse. This study aims to add to this small body of evidence.

Methods

Twelve community pharmacies around Brisbane were recruited to provide a variety of business types (e.g. banner group and independent) and demographic settings. Observational studies were carried out and up to 150 transactions of Pharmacy Medicines (S2) and Pharmacist Only Medicines (S3) were recorded per pharmacy per visit.

Results

The most commonly requested S2/S3 medicines were analgesics, cold and flu preparations and antihistamines. Approximately 20% of the observed transactions were substituted for a less expensive or "pharmacy-preferred" brand and >70% of consumers reported a positive perception of generic medicines. Banner group loyalties appeared to influence the choice of generic brand. However, some S2/S3 transactions did not appear to be handled to professional standards as insufficient clinical information was gathered by pharmacy staff to determine the safety and appropriateness to supply the requested/recommended product.

Conclusions

Substitution may be necessary to sustain and maximise profitability, however, pharmacy staff must fulfil professional duties. More training may be needed to facilitate quality use of medicines whilst remaining attentive to consumer requests.

The provision of an adherence support service by community pharmacists

Parisa Aslani [1] Sarab Mansoor [1] Ines Krass [1]

[1] Faculty of Pharmacy, The University of Sydney, Sydney, NSW

Objective

Adherence to therapy is important for achieving good clinical outcomes. Improving adherence requires a range of strategies that primarily focus on fostering behavioural change. Community pharmacists are well placed to deliver adherence support services to patients. However the extent to which Australian community pharmacists engage in medication adherence support is unknown.This study aimed to investigate the extent to which community pharmacists are providing adherence support services to patients.

Methods

A random sample of 500 pharmacies, selected from a Pharmacy Board of NSW list of community pharmacies were mailed a questionnaire designed to measure pharmacists' knowledge, attitudes and behaviours in providing adherence services. Two follow-up reminders were sent to non-respondents after 2 and 6 weeks.

Results

A 27.6% (n = 126) response rate was achieved. Approximately 38% of respondents reported providing adherence support services to their patients: dose administration aids was the most common method used (n = 120). According to respondents (78%) the main cause of non-adherence among their patients was having to take a large number of medications. Most (98.4%) agreed that it was their role to promote patients' adherence to therapy. However 63.5% and 52.3% reported that patients' time pressures and poor health literacy, respectively, were the main barriers preventing them from providing an adherence support.

Conclusions

The rate of provision of adherence support services by the participating community pharmacists was low. It is important for pharmacists to more proactively embrace the responsibility of providing medication adherence support and use a wider range of strategies to promote medication adherence among their patients.

Internet and community pharmacy provision of a children's cough and cold medicine

Kylie Williams [1] Yang Xu [2]

[1] School of Pharmacy, University of Technology Sydney, Sydney, NSW

[2] Faculty of Pharmacy, The University of Sydney, Sydney, NSW

Objective

To compare the service provided by Australian Internet and community pharmacies for a children's non-prescription medicine request.

Methods

The simulated patient method was used to evaluate the provision of Demazin® cold relief syrup in 46 community pharmacies (CPs) and 23 Internet pharmacies (IPs). Two scenarios were investigated: one for an 18-month-old child and one for a 5-year-old child. Pharmacies were scored on information gathering and delivery. Scores were analysed using the non-parametric Mann-Whitney U test.

Results

Both CPs and IPs scored poorly, and there was no significant difference between their total scores ($p = 0.771$). CPs and IPs performed similarly for information gathering, however, IPs scored significantly better than CPs for information delivery ($p = 0.029$). Nineteen CPs and 5 IPs did not interact with the patient at all, and scored zero. Pharmacies overall scored better in the 18-month-old scenario compared to the 5-year-old scenario ($p = 0.003$), however 9 CPs and 22 IPs inappropriately supplied Demazin® to the 18-month-old. Demazin® was significantly more expensive to purchase from IPs than CPs due to delivery charges ($p = 0.000$).

Conclusions

This study suggests that pharmacy provision of a children's OTC cough and cold product is poor, regardless of pharmacy type. Pharmacies are not adequately obtaining patient information and making thorough risk-benefit assessments, and are not consistently providing sufficient advice and counselling. These processes need to be improved in order to ensure the safe and appropriate use of cough and cold products in children.

Pharmaceutical Science: Formulation

Session Chair: Clare Strachan, University of Otago

Tuesday 13 December 2011, 11:00am – 12:30pm

Room P5-14, Playford Building

CP05-1

Tri-Hung Nguyen, Monash University

Nanostructured reverse hexagonal liquid crystals sustain plasma concentrations for a poorly water soluble drug after oral administration

CP05-2

Sarah Hook, University of Otago

Thermoresponsive gels as sustained release vaccine delivery systems

CP05-3

Nhung Dang, The University of Queensland

Polycaprolactone matrices for vaginal delivery of microbicides

CP05-4

Darren Svirskis, The University of Auckland

A drug delivery system based on intrinsically conducting polymers

CP05-5

Hywel Williams, Monash University

Solidification of lipid-based formulations via adsorption onto an inorganic high surface-area carrier: Effects on *in vitro* and *in vivo* performance

CP05-6

Angel Tan, University of South Australia

Hybrid nanomaterials that mimic the food effect to enhance and control oral drug absorption

Nanostructured reverse hexagonal liquid crystals sustain plasma concentrations for a poorly water soluble drug after oral administration

Tri-Hung Nguyen [1] Tracey Hanley [2] Christopher JH Porter [1] Ben J Boyd [1]

[1] Monash Institute of Pharmaceutical Sciences, Monash University, Melbourne, VIC

[2] Bragg Institute, Australian Nuclear Science and Technology Organisation, Sydney, NSW

Objective

Non-digestible lipid-based liquid crystals have been proposed as sustained oral drug delivery systems. In this study, selachyl alcohol (SA), which forms stable reverse-hexagonal (H_2) liquid crystals in excess water, was assessed for its ability to sustain the release of cinnarizine (CZ) *in vivo*.

Methods

Selachyl alcohol comprising 7 mg/g CZ was administered orally either as a bolus lipid solution or as dispersed nanoparticles (hexosomes) to rats, with drug plasma concentrations measured via HPLC. The stability of the H_2 nanostructure, in the presence of CZ, was assessed under simulated gastrointestinal conditions using an *in vitro* digestion model and small angle x-ray scattering (SAXS).

Results

Administration of the lipid solution resulted in sustained drug absorption (T_{max}, 23.5 ± 5.9 hr) when compared to a control CZ suspension (1 hr). For SA hexosomes, drug plasma concentrations were maintained from 20 - 40 ng/mL within the first 24 hr, with sustained absorption of CZ leading to a significant enhancement ($p < 0.05$) in oral bioavailability (F = 17%) versus 9% for the control suspension. Analysis of SA hexosomes using SAXS indicated that neither the presence of CZ (7 mg/g) nor simulated intestinal fluid altered the H_2 nanostructure, with SA determined to be non-digested when exposed to a simulated digestion environment.

Conclusions

Prolonged drug absorption from SA H_2 systems was attributed to the non-digestible nature of the lipid, incorporation of SA in solubilising mixed micelles and gastric retention of the formulation resulting in the formation of a non-sink drug reservoir. The results highlight the potential for SA to be used as sustained oral drug delivery systems.

Thermoresponsive gels as sustained release vaccine delivery systems

Thunjiradasiree Kojarunchitt [1] Stefania Baldursdottir [2] Ben Boyd [3] Thomas Rades [1] Sarah Hook [1]

[1] School of Pharmacy, University of Otago, Dunedin, NEW ZEALAND

[2] Faculty of Pharmaceutical Sciences, University of Copenhagen, Copenhagen, DENMARK

[3] Monash Institute of Pharmaceutical Sciences, Monash University, Melbourne, VIC

Objective

Vaccines, as well as containing the correct mix of antigens and adjuvants, must be formulated in such a way as to promote optimal activation of the immune system. The aim of this work is to develop safe, simple and effective formulations that mimic the process occurring in a natural infection, so as to induce both cellular and humoral immunity. One class of formulations showing great promise for vaccine delivery are the thermoresponsive hydrogels. These are liquids at room temperature but gel upon injection, creating a biodegradable depot of vaccine that then releases either soluble antigen and adjuvant or particulate antigen and adjuvant (to mimic release of a pathogen) over a sustained period of time.

Methods

Modified poloxamer 407 (P407) and chitosan thermogels containing soluble antigen and adjuvant or antigen or adjuvant loaded cubosomes were developed and characterized (viscosity, gelling behaviour and stability). Immune responses stimulated by gels containing ovalbumin, the TLR-4 ligand monophosphoryl lipid A and the TLR independent adjuvant Quil A were investigated *in vivo*.

Results

Modified chitosan gels were more stable than the P407 formulations and delivered antigen over a prolonged period of time.

Conclusions

Loading antigen and adjuvant into nanoparticles before inclusion in the gel does not appear to be necessary however functional studies must now be carried out to fully characterise the immune responses generated by these formulations.

Polycaprolactone matrices for vaginal delivery of microbicides

Nhung Dang [1] Allan Coombes [1]

[1] Pharmacy Australia Centre of Excellence, The University of Queensland, Brisbane, QLD

Objective

To evaluate the release behaviour of non-specific (Dextran sulphate (DS)) or specific antiviral microbicides (Tenofovir (TEN)) from polycaprolactone (PCL) intravaginal matrices for prevention of HIV transmission.

Methods

TEN or DS were incorporated in PCL matrices at varying loading doses by rapidly cooling suspensions of the microbicide in acetone solutions of PCL. Daily and cumulative release amounts of TEN were determined in 10 mL simulated vaginal fluid (SVF) by UV assay at 260 nm. Concentrations of DS in SVF were determined by forming a complex with 1,9-dimethyl methylene blue and measuring the absorbance at 537 nm. Release properties were characterized using the zero order, Higuchi and Korsmeyer-Peppas models. Scanning electron microscopy (SEM) was used for analysing matrix morphology.

Results

Dried PCL matrices containing the microbicides present a soft texture and highly flexible character. High incorporation efficiency was gained with both microbicides (80% for TEN and 72% for DS). SEM examination revealed the irregular, porous morphology formed by the PCL lamellar structure. Both microbicides were released in high amounts after the first 2 days. TEN showed zero order kinetics whereas DS displayed anomalous release properties. Microbicide release was maintained for not less than 15 and 32 days from DS and TEN-loaded matrices, respectively, resulting in sustained concentrations in SVF higher than the minimum effective dose for HIV inhibition (143 ng/L for TEN and 5 mg/L for DS).

Conclusions

PCL matrices are able to incorporate small molecule and macromolecular microbicides and exhibit sustained release behaviour, thereby demonstrating their potential as intravaginal inserts.

A drug delivery system based on intrinsically conducting polymers

Darren Svirskis [1] Yang Yu [1] Manisha Sharma [1] Sanjay Garg [1]

[1] School of Pharmacy, The University of Auckland, Auckland, NEW ZEALAND

Objective

Intrinsically conducting polymers (ICP), such as polypyrrole, are organic materials that have electrical, magnetic and optical properties usually associated with metals, whilst retaining the advantageous mechanical properties and ease of processing usually associated with polymers. Due to the inherent properties of ICPs, electrical stimulation can be used to alter the redox state of polypyrrole, which in turn can modify the release rate of drug. This study aimed to develop drug delivery systems based on intrinsically conducting polymers.

Methods

Polypyrrole was prepared following the oxidative polymerisation of monomer units. Risperidone was used as a model drug and was incorporated into polypyrrole. Drug release was tested with no electrical stimulation and on application of +0.6 V or -0.6 V.

Results

Polypyrrole films were prepared containing 8.2% w/w risperidone. After 40 minutes without electrical stimulation 37.3% of drug was released, a similar level of drug was released (37.2%) on application of +0.6 V, while 93.8% of drug that was released on application of -0.6 V. Electrical stimulus altered the out-of-plane volume as determined by atomic force microscopy. Through this mechanism drug release from polypyrrole can be controlled.

Conclusions

The described technology could be utilised for implantable drug delivery devices, where the dose could be adjusted by external signalling, optimising patient benefit to side effect ratios while simultaneously ensuring compliance.

CP05-5

Solidification of lipid-based formulations via adsorption onto an inorganic high surface-area carrier: Effects on *in vitro* and *in vivo* performance

Michiel Van Speybroeck [1] Hywel Williams [2] Tri-Hung Nguyen [2] Christopher Porter [2] Patrick Augustijns [1]

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[2] Monash Institute of Pharmaceutical Sciences, Monash University, Melbourne, VIC

Objective

To assess how the adsorption of lipid-based formulations (LBFs) onto a high surface-area material (Neusilin®US2) affects their performance during *in vitro* dispersion/digestion and *in vivo* bioavailability testing.

Methods

Self-emulsifying LBFs containing medium-chain (Captex-355:Capmul-MCM) or long-chain lipids (Soybean oil:Maisine™ 35-1), 30 - 36% Cremophor-EL, 10% ethanol and danazol (12.5 mg/g) were solidified by adsorption on Neusilin®US2 (Fuji Chemicals, Japan) at a 2:1 liquid:adsorbent ratio. Liquid and solidified-LBFs were assessed for performance during *in vitro* dispersion and digestion in simulated intestinal medium (pH 6.5, 3 mM sodium taurodeoxycholate, 0.75 mM phospholipid). *In vivo* bioavailability of danazol (dosed at 10 mg/kg) administered in solidified LBFs was assessed in fasted rats, with equivalent liquid LBFs used as a control.

Results

Adsorption of long-chain and medium-chain LBFs onto Neusilin®US2 led to a decrease in solubilised danazol concentrations during *in vitro* dispersion and digestion compared with equivalent liquid LBFs. The rank order in formulation performance *in vivo* was highly consistent with *in vitro* performance. Liquid LBFs outperformed equivalent adsorbed formulations with calculated $AUC_{[0\text{-}4h]}$ values following the rank order: long-chain liquid (165.3 ± 69.5 ng/mL) > medium-chain liquid (117.1 ± 12.8 ng/mL) > long-chain adsorbed (59.0 ± 28.4 ng/mL) > medium-chain adsorbed (41.7 ± 16.9 ng/mL). The poorer performance of LBFs following solidification was attributed to a decrease in free drug available for absorption since some adsorbed liquid formulation (and therefore drug) was retained on the solid carrier during dispersion/digestion. The poorer performance of medium-chain liquid LBFs compared with equivalent long-chain liquid LBFs was attributed to greater drug precipitation on digestion.

Conclusions

Solidification of LBFs onto high surface-area materials may lead to decreased performance *in vivo* due to incomplete desorption of formulation components from the carrier.

Hybrid nanomaterials that mimic the food effect to enhance and control oral drug absorption

Angel Tan [1] Ben Boyd [2] Clive Prestidge [1]

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[2] Monash Institute of Pharmaceutical Sciences, Monash University, Melbourne, VIC

Objective

This research focuses on the biopharmaceutical investigation of solid-state hybrid microparticles, composed of lipid colloids and silica nanoparticles, which mimic the food effect to enhance/control the oral absorption of water-insoluble drugs.

Methods

Silica-lipid hybrid (SLH) microparticles have been engineered from precursor Pickering emulsions based on nanoparticle and lipid colloid self-assembly; controlled spray-drying effectively transformed the emulsions into a dry silica-lipid hybrid network composed of internal nanoporous matrices (pore sizes 50 - 200 nm) which stabilizes the model drugs (celecoxib, indomethacin, ibuprofen) in a molecular state. The SLH microparticles were investigated for their *in vitro* solubilisation properties under: (i) non-digesting conditions using the USP Apparatus II and (ii) digesting conditions using the pH-stat titration model. *In vivo* bioavailability studies were undertaken in fasted rats, dogs and humans.

Results

The nanostructured microparticles have been shown to facilitate: (i) more predictable and enhanced lipid digestibility for the SLH formulations (i.e. ~100% lipolysis with up to 20-fold higher digestion rate constants) in comparison with conventional oil solution and emulsions; (ii) enhanced drug solubilisation (i.e. 2- to 7-fold higher) under both digesting and non-digesting conditions; and (iii) significantly improved fasted-state bioavailability and other pharmacokinetic properties of the model drugs, i.e. SLH microparticles > conventional lipid solution and emulsions > pure drug ($p>0.05$).

Conclusions

The nanostructured hybrid microparticles have emerged as an effective approach to enhance the oral absorption of water-insoluble drugs via a smart interplay between the lipid-nanoparticle interaction and the action of lipid-digesting enzymes, which controls drug release, intraluminal solubilisation and absorption.

Pharmaceutical Science: Molecular Biology

Session Chair: Andrew Crowe, Curtin University

Tuesday 13 December 2011, 11:00am – 12:30pm

Room P5-15, Playford Building

CP06-1

Wei Chean Lee, Curtin University

The induction of P-glycoprotein and breast cancer resistance protein by xenobiotics in human carcinoma cell lines

CP06-2

George Li, The University of Sydney

Anti-inflammatory action of propolis extract: Inhibition of endothelial adhesion molecules and bioassay-guided fractionation study of active component

CP06-3

Anne Nguyen, Curtin University

Neuronal and glial cells changes in a transgenic mouse model of retinal neovascularisation

CP06-4

Andrew Crowe, Curtin University

ABCB1 (P-glycoprotein) reduces bacterial attachment to human gastrointestinal LS174T cells

CP06-5

Hamed Shahnam, University of South Australia

Investigating the underlying pathophysiology of selective nonsteroidal antiinflammatory drug hypersensitivity and diagnostic approaches

CP06-6

Matthew Howard, La Trobe University

Designing a simple, cost effective and robust assay for measuring CYP2C19 genetic polymorphisms in the Indonesian Makassar ethnic population

The induction of P-glycoprotein and breast cancer resistance protein by xenobiotics in human carcinoma cell lines

Wei Chean Lee [1] Andrew Crowe [1]

[1] School of Pharmacy, Curtin University, Perth, WA

Objective

To compare the effectiveness of known active efflux protein inducers: rifampicin (PXR agonist), phenobarbital (CAR agonist), 1α,25-dihydroxyvitamin D3 (1,25-VD3) (VDR agonist) and digoxin on the expression of MDR1 P-glycoprotein (P-gp or ABCB1) and breast cancer resistance protein (BCRP or ABCG2).

Methods

The cell lines examined were the highly P-gp expressing Caco-2 sub-clone (CLEFF9), the BCRP expressing breast cancer cells (MCF7), and the lung (A549) and gastrointestinal (RKO) cancer cell line. RT-PCR was performed to determine the presence of ABCB1, ABCG2, PXR and CAR mRNAs. Induction of ABCB1 and ABCG2 protein expression was measured by Western blotting. The changes in expression of ABCB1 mRNA were confirmed by real time RT-PCR.

Results

ABCG2, PXR and CAR mRNA were expressed in all of the selected cell lines whereas ABCB1 mRNA was only detected in CLEFF9 cells. The selected inducers failed to up-regulate ABCB1 expression in MCF7, RKO and A549 cells. Induction capability of phenobarbital was markedly greater than rifampicin in CLEFF9 cells, however required at least a 1 mM concentration to do so. ABCG2 protein expression was induced by phenobarbital but not rifampicin in MCF7 cells. ABCB1 protein and mRNA expression in CLEFF9 cells were significantly induced by digoxin and 1,25-VD3.

Conclusions

Phenobarbital induces ABCB1 and ABCG2 expression to a greater extent than rifampicin, suggesting a central role of CAR in the regulation of efflux proteins. Digoxin and 1,25-VD3 have also been found to be potent inducers of ABCB1.

Anti-inflammatory action of propolis extract: Inhibition of endothelial adhesion molecules and bioassay-guided fractionation study of active component

Eshaifol Omar [1] Benjamin Kimble [1] Georges Grau [2] George Li [1]

[1] Faculty of Pharmacy, The University of Sydney, Sydney, NSW

[2] Sydney Medical School, The University of Sydney, Sydney, NSW

Objective

Intracellular (ICAM-1) and vascular (VCAM-1) adhesion molecules have been shown to play an important role in initiation of inflammation. Propolis has been used since ancient time for the treatment of various illnesses, including as a potent anti-inflammatory agent. The current work aim to determine the effects of propolis and the active compound on the production of adhesion molecules.

Methods

Fractionation of the crude propolis extract by column chromatography fractionation method resulted in six different fractions which were subjected to thin layer chromatography (TLC) and high pressure liquid chromatography (HPLC) to identify the composition of each fraction. Human umbilical endothelial cells (Eahy926) were cultured to confluence and treated with extracts before subjected to 10 ng/mL of tumour necrosis factor (TNF) stimulation. The production of adhesion molecules were measured by mean of flow cytometry.

Results

We demonstrated that propolis crude extract inhibited the production of ICAM-1 and VCAM-1 in the Eahy926 cell lines. Fraction 3 (F3) was found to be the most potent out of the 6 fractions, to inhibit the production of ICAM-1 and VCAM-1. In addition F3 inhibited the adhesion of THP-1 cells on the surface of Eahy926 in a dose-dependent manner.

Conclusions

Further fractionation and thus isolation of active compound(s) of F3 would be a useful future direction of our study. This may provide us with a better understanding of the potential active compound of propolis and its molecular mechanism of anti-inflammatory action.

Neuronal and glial cells changes in a transgenic mouse model of retinal neovascularisation

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[1] School of Pharmacy, Curtin University, Perth, WA

[2] Centre for Ophthalmology and Visual Science, The University of Western Australia, Perth, WA

[3] Department of Molecular Ophthalmology, Lions Eye Institute, Perth, WA

Objective

Retinal neovascularisation is a major clinical complication of diabetic retinopathy. However, the exact mechanism for the progression of retinal neovascularisation and the role of inflammation in retinal neovascularisation remains to be established. This study aimed to investigate the neuronal and glial cell changes in the retina in a transgenic mouse model of retinal neovascularisation and to assess the relationship between the vascular abnormalities with the corresponding changes in the neurons and glial cells.

Methods

The transgenic mouse model, Kimba [1], was used to examine the neuronal and glial cell changes in retinal neovascularisation. Retinal sections of Kimba and wild type (WT) mice were analysed for vascular neuronal and glial cells changes using immunocytochemistry. Mice aged 2, 8, and 20 weeks were used to look at neuronal and glial changes associated with the progressive stages of neovascularisation.

Results

There was an overall decrease in retinal thickness for Kimba mice at all stages with varying patterns of changing thickness in the outer nuclear layer (ONL) and inner nuclear layer (INL) of the retina. Compared to WT, the retinal blood vessels in Kimba mice transgressed into the outer layers of the retina including the ONL which caused disruption to the normally organised retinal layers. There was a significant ($p < 0.001$) decrease in ganglion cell count in Kimba at all age points. Whilst there was no change in the morphology of astrocytes and Müller cells, there was a significant ($p < 0.05$) decrease in Müller cell count in 8 and 20 weeks Kimba.

Conclusions

The study shows changes in both neuronal and glial cells in the retina associated with the different stages of retinal neovascularisation. This study further supports the role of inflammation in the progression of retinal neovascularisation.

[1] Lai C-M, Dunlop SA, May LA, Gorbatov M, Brankov M, Shen W-Y, Binz N, Lai YKY, Graham CE, Barry CJ, Constable IJ, Beazley LD, Rakoczy EP. Generation of Transgenic mice with mild and severe retinal neovascularisation. Br J Ophthalmol (2005); 89(7): 911-916.

ABCB1 (P-glycoprotein) reduces bacterial attachment to human gastrointestinal LS174T cells

Andrew Crowe [1, 2] Cynthia Whitchurch [3] Mary Bebawy [4]

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[3] i3 institute, University of Technology Sydney, Sydney, NSW

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Objective

The aim of this project was to show elevated P-glycoprotein (P-gp) expression being able to decrease bacterial association with LS174T human gastrointestinal cells, and that this effect could be reversed upon blocking functional P-gp efflux.

Methods

Staphylococcus aureus, Klebsiella pneumoniae, Pseudomonas aeruginosa, Lactobacilli spp, and numerous strains of Escherichia coli , from commensal to Enteropathogenic (EPEC) and Enterohaemorrhagic strains (O157:H7) were fluorescently labelled and incubated on confluent LS174T cultures either with or without P-gp amplification using rifampicin. PSC-833 was used as a potent functional blocking agent of P-gp. Green fluorescent protein (GFP)-EPEC E.coli were used as a control to validate the Baclight green dye method for all other bacteria.

Results

Staphylococcus and Pseudomonas displayed the greatest association with these LS174T cells. Surprisingly, Lactobacilli retained more fluorescence than EPEC-E.coli in this system. However, irrespective of attachment differences between the bacterial species, the increase in P-gp protein expression decreased bacterial fluorescence by 25 to 30%. This included the GFP-labelled E.coli, and food poisoning E.coli (O157:H7). Blocking P-gp function resulted in the attachment returning to normal levels. Only Klebsiella did not show a decrease in attachment. In all cases, the coadministration of PSC833 increased the amount of bacteria associated with LS174T cells back to control levels.

Conclusions

P-gp appears to be a significant player in the defence against bacteria. As most bacteria were affected to the same degree, irrespective of pathogenicity, we believe this shows that P-gp is likely to be secreting an endogenous antibacterial peptide into the local environment, and that P-gp may be an integral part of the innate immune system.

Investigating the underlying pathophysiology of selective nonsteroidal antiinflammatory drug hypersensitivity and diagnostic approaches

Hamed Shahnam [1] Michael Wiese [1]

[1] School of Pharmacy and Medical Sciences, University of South Australia, Adelaide, SA

Objective

Nonsteroidal antiinflammatory drug (NSAID) hypersensitivity reactions can be immune and non-immune mediated (anaphylactoid). Patients suffering from immune-mediated reactions demonstrate selective reactions to an NSAID in contrast to the anaphylactoid mechanism. The pathophysiology of selective hypersensitivity is unclear, but hepatic metabolism may play a role. The aim of the study was to explore the concept of selective NSAID hypersensitivity and demonstrate specific immunoglobulin (Ig)E towards haptenated proteins of human liver microsome (HLM) or parent NSAID and/or metabolites.

Methods

Sera from 22 participants with a history of immediate NSAID hypersensitivity were obtained from the Royal Adelaide Hospital Immunology Department. Circulating IgE in pooled sera towards diclofenac/naproxen, as well as metabolites conjugated to human serum albumin and polylysine were investigated via enzyme-linked immunosorbent assay (ELISA) and dot blots. The role of hepatic metabolism was explored via western blotting using HLM incubated with diclofenac/naproxen and co-factors instigating key metabolic pathways in the presence of pooled participant sera.

Results

Clinical data was obtained and 7 participants were classified as selective-reactors, 8 were cross-reactors and 7 were NSAID tolerant. No specific IgE towards parent diclofenac/naproxen and metabolite conjugates were detected, although the carrier polylysine caused non-specific IgE binding. Circulating IgE towards haptenated HLM proteins also appeared to be absent.

Conclusions

The lack of specific IgE towards NSAID/metabolite is incongruence with previously published literature. However, circulating antibodies targeting haptenated hepatic proteins have been detected in particular for diclofenac, contrary to the study findings. Thus, more research is required to explore the pathophysiology of selective NSAID hypersensitivity.

Designing a simple, cost effective and robust assay for measuring CYP2C19 genetic polymorphisms in the Indonesian Makassar ethnic population

Matthew Howard [1] Joseph Tucci [1]

[1] School of Pharmacy and Applied Science, La Trobe University, Bendigo, VIC

Objective

The enzyme CYP2C19 displays inter-individual variation in drug metabolism between ethnic populations. These genetic predispositions contribute to treatment failure with drugs such as clopidogrel, increased adverse effects with diazepam, sertraline, voriconazole and variable success of H.pylori therapy with proton pump inhibitors. The objective was to design a novel, specific and cost effective CYP2C19 assay for the clinically significant CYP2C19 alleles. This assay was applied to DNA samples collected from the Makassar Indonesian ethnic population in partnership with the Faculty of Medicine & Health, University of Gadjah Mada, Yogyakarta, Indonesia.

Methods

Twenty DNA samples were amplified by PCR. The CYP2C19*2, CYP2C19*3 and CYP2C19*17 alleles were selected due to their clinical relevance. The RFLP analysis was performed using novel primers and the restriction enzymes SmaI, BamHI and Hsp9211 for each allele respectively. Wild type and variant alleles were detected following electrophoresis on 3% agarose gel.

Results

For the null CYP2C19*2 allele two homozygotes and fourteen heterozygotes were detected corresponding to a 45% allele frequency. The null CYP2C19*3 allele was less common with two heterozygotes identified amounting to a 5% allele frequency. The increased activity CYP2C19*17 allele was present in two heterozygotes and one homozygote with a 10% allele frequency. These results will contribute to a larger genotyping study on this population.

Conclusions

This Indonesian population displays similar frequencies of null alleles to other Asian ethnicities but a higher incidence of CYP2C19*17. This is the first pharmacogenetic study on the Makassar population and indicates potential differences in the capacity of this population to metabolise certain drugs.

Pharmacy Practice: Pulmonary

Session Chair: Sinthia Bosnic-Anticevich, The University of Sydney

Tuesday 13 December 2011, 11:00am – 12:30pm

Room P5-33, Playford Building

CP07-1

Sinthia Bosnic-Anticevich, The University of Sydney

Comparing three different forms of education on health professional inhaler technique and maintenance of correct technique

CP07-2

Lynn Cheong, The University of Sydney

Social network analysis in asthma care: The impact of patients' health connections on interprofessional collaboration

CP07-3

Ming Ley Kong, The University of Sydney

The information needs of asthma patients and their internet use

CP07-4

Lucille Norton, University of Tasmania

A review of the management of childhood asthma in Tasmania

CP07-5

Parisa Aslani, The University of Sydney

Nebulised medicine adherence and factors that affect adherence in patients with cystic fibrosis

CP07-6

Angelina Lim, Monash University

Asthma during pregnancy: The experiences, concerns and views of pregnant asthmatic women

Comparing three different forms of education on health professional inhaler technique and maintenance of correct technique

Sinthia Bosnic-Anticevich [1] Margaret Williamson [2] Biljana Cvetkovski [1] Sofia Mavritsakis [1] Pippa Travers-Mason [2] Gosia Mendrela [2] Erica Sainsbury [1] Meg Stuart [3] Judith Macksonformerly [2] Carol Armour [4, 5]

[1] Faculty of Pharmacy, The University of Sydney, Sydney, NSW

[2] National Prescribing Service, Sydney, NSW

[3] Faculty of Health Sciences, Australian Catholic University, Sydney, NSW

[4] Sydney Medical School, The University of Sydney, Sydney, NSW

[5] Woolcock Institute, The University of Sydney, Sydney, NSW

Objective

To compare the effect of three education interventions, on the ability of health professionals (HPs) to achieve and maintain correct inhaler technique (IT).

Methods

A parallel group, three arm, repeated measure design was used to implement and evaluate three educational interventions: traditional face-to-face workshop (Model 1), online learning module (Model 2) and a collaborative face-to-face workshop (Model 3). HPs' IT was assessed within a fortnight of competing the modules. If HP IT was not correct, the assessor would provide immediate personal training and assessment until correct IT was achieved. HPs then delivered the Collaborations in Asthma Management in the Community (CAMCOM) protocol, involving optimisation of patient's IT over 6 months. HPs IT was then re-assessed.

Results

A total of 81 HP (27 GPs, 11 practice nurses and 43 pharmacists) participated in the study (28, 17 and 36 HPs in Models 1, 2, and 3 respectively). There was a statistically significant difference in the mean proportion of HPs with correct technique between Modules 1, 2, and 3 initially (72%, 27.4% and 47.8% respectively, Pearson's chi-squared, $n = 81$, $p < 0.05$) and at the 6 month follow-up (57.8%, 44.4% and 25.3% respectively, Pearson's chi-squared, $n = 41$, $p < 0.05$).

Conclusions

Different forms of HP education have had differing effects on inhaler technique of participating HPs. After 6 months this technique had generally deteriorated which has implications for what patients might receive in practice. Reasons for non-maintenance of HP IT need to be further explored.

Social network analysis in asthma care: The impact of patients' health connections on interprofessional collaboration

Lynn H M Cheong [1] Carol Armour [2, 3] Sinthia Bosnic-Anticevich [1]

[1] Faculty of Pharmacy, The University of Sydney, Sydney, NSW

[2] Sydney Medical School, The University of Sydney, Sydney, NSW

[3] Woolcock Institute, The University of Sydney, Sydney, NSW

Objective

While Australia's government has called for collaborative team-based care in chronic disease management, there is a paucity of research on the role of patients in interprofessional care. This project aims to explore the health networks of people with asthma by identifying the individuals involved in each patient's asthma care, to gain an understanding on the foundations of network developments and the impact of patients' health perceptions on network choices.

Methods

Mixed-method approaches to social network analysis were employed. Participants were recruited through advertisements in various settings, including community pharmacies, The University of Sydney campus and the Australian Asthma Foundation. Data were collected at two points over a one month period through semi-structured interviews and surveys (asthma control, perceived control, self-management). The network software, Netdraw, was used to generate visual representations of patients' health networks, while qualitative analysis of data assisted in the interpretation of network structures, providing an insider's view.

Results

A total of 26 asthma patients were recruited. Patients' asthma networks included general practitioners, asthma specialists, pharmacists, family/friends, internet, asthma foundation and alternative care sources. Participants indicated that the most influential health connection in their asthma management was patient's spouse (52%). Participants' choices of individuals were driven by their asthma needs, personal experiences with health professionals, perceived asthma severity, perceived ability to self-manage, and encouragement from family.

Conclusions

The patterns of connections suggested that participants have open asthma networks, lacking interprofessional collaboration whereby patients are placed in a position of power and freedom to achieve optimal asthma control independently.

The information needs of asthma patients and their internet use

Ming Ley Kong [1] Carol Armour [2] Kate LeMay [2] Lorraine Smith [1]

[1] Faculty of Pharmacy, The University of Sydney, Sydney, NSW

[2] Woolcock Institute, The University of Sydney, Sydney, NSW

Objective

The objectives of this study were to investigate the information needs of a sample of people with asthma, the degree to which these needs are being met, and their use of the internet for information about asthma.

Methods

A cross sectional survey was conducted among asthma patients who presented at community pharmacies in metropolitan Sydney. Pharmacists were purposively sampled and invited to assist in participant recruitment. The data were collected between August and October 2011.

Results

Seven pharmacies participated in the study. Fifty completed surveys were collected. Twenty eight respondents (56%) were female. The median patient age group was 36 - 45 years. The majority reported having asthma for more than 10 years. All of the respondents used at least one medication. Eight key information needs were identified: medications; management of asthma; asthma triggers; cure; research; nature or characteristics of asthma; alternative therapies; and government benefits. Forty-six percent of respondents stated "a lot" of their information needs were met and only 8% claimed "all" met. Whilst only 30% of respondents included the internet as a source of information about asthma, 86% agreed that they would access a website recommended by their healthcare providers.

Conclusions

Patients with asthma were able to identify their needs in terms of information and only a small proportion was using the internet as a source of information. Given that a website recommended by a healthcare provider was perceived as an acceptable source for further information we recommend that pharmacists become involved in this process in a structured way.

A review of the management of childhood asthma in Tasmania

Lucy Norton [1] Bonnie Bereznicki [1] Luke Bereznicki [1] Sean Beggs [2]

[1] School of Pharmacy, University of Tasmania, Hobart, TAS

[2] Department of Paediatrics, Royal Hobart Hospital, Hobart, TAS

Objective

To review the current management of childhood asthma in Tasmania and highlight evidence-practice gaps for future interventions.

Methods

A software application (MedeMine) that extracts data from the Fred Dispense pharmacy dispensing software system was modified to identify children with asthma. Participating community pharmacies ran the software application. Caregivers of identified children were mailed a survey to evaluate components of asthma management. Dispensing and survey data were analysed.

Results

Twenty-three community pharmacies were recruited. A total of 948 children were identified by the software and deemed eligible for inclusion. Surveys were received from 362 (38.2%) caregivers. In the past year, short-acting beta-2 agonists were used by 56.1% of the cohort, preventers by 76.5% (inhaled corticosteroids 52.3%; leukotriene receptor antagonists 31.3%; inhaled cromones 0.6%), long-acting beta-2 agonists (LABAs) by 25.7% and oral corticosteroids by 21.5%. Approximately half of the children using inhaled corticosteroids were concurrently using a LABA. Survey data indicated 52.7% had an Asthma Action Plan (AAP), and 49.6% used a spacer regularly. Among children with potential indicators of inadequately controlled asthma (emergency department visits, over-use of reliever medication and oral corticosteroid use), up to 25% were not using a preventer and up to 75% of their parents reported that their asthma was adequately controlled.

Conclusions

These results indicate gaps in childhood asthma management, in particular, underutilisation of preventers in high-risk patient groups, high utilisation of LABAs, insufficient spacer and AAP usage and overestimation of asthma control. These areas could be targeted in future interventions to improve childhood asthma management.

Nebulised medicine adherence and factors that affect adherence in patients with cystic fibrosis

Parisa Aslani [1] Alice Hogan [1] Jo-Anne Brien [1, 2] Mary-Anne Bonney [3] Rita Karamy [3]

[1] Faculty of Pharmacy, The University of Sydney, Sydney, NSW

[2] Therapeutics Centre, St Vincent's Hospital, Sydney, NSW

[3] Novartis Pharmaceuticals Australia, Sydney, NSW

Objective

To explore experiences of patients with cystic fibrosis (CF) when taking nebulised medicines, identify factors that impact adherence and strategies used by patients to adhere to therapy.

Methods

Ten participants with CF were recruited through CF NSW by advertising using electronic methods and a mail-out. In-depth semi-structured face-to-face interviews were conducted with adult patients. After five interviews no new themes emerged and five further interviews were conducted to ensure saturation in themes. The interview protocol covered factors impacting adherence/non-adherence, experiences with nebulised medicines and strategies to help adherence. Interviews were audio-recorded, transcribed verbatim and content analysed for anticipated and emergent themes.

Results

Half of participants were male; age ranging from 22 to 45 yrs. Five broad themes (with more specific sub-themes) were identified: feelings about taking nebulised medicines (necessary/ important, dislike, part of life); experiences with taking nebulised medicines (cleaning, time of use, flexibility, balance in routine); factors leading to non-adherence (time consuming therapy, side effects/effects of medicine, work/social demands, lack of perceived importance); factors facilitating adherence (perceived medicine importance, habit/routine, support, health benefits); strategies for adherence (technology/medicine dose form, timetabling).

Conclusions

Nebulised therapy takes up a substantial amount of time however patients are able to balance and alter their routine to fit nebulising into their daily lives. Several factors impacting adherence and strategies used to enhance adherence were cited. These factors should be examined more closely to assist in the development of future educational tools for adult patients with CF to improve nebulised delivery and adherence to nebulised medicines.

Asthma during pregnancy: The experiences, concerns and views of pregnant asthmatic women

Angelina Lim [1] Johnson George [1] Kay Stewart [1] Michael Abramson [1] Kath Ryan [2]

[1] Faculty of Pharmacy and Pharmaceutical Sciences, Monash University, Melbourne, VIC

[2] Department of Nursing, La Trobe University, Melbourne, VIC

Objective

Poor asthma management during pregnancy is detrimental for both the mother and unborn child. Upon realising they are pregnant, women have been shown to decrease or discontinue their asthma medications, unaware of the potential risks of uncontrolled asthma. Understanding the experiences of asthmatic pregnant women would inform the development of strategies to provide more support and awareness about this topic for these women. This study was conducted to investigate how pregnant women manage their asthma during pregnancy and the factors associated with their behaviour.

Methods

In-depth interviews (phone or face-to-face) with a purposive sample of 23 women at various stages of pregnancy and with varying severity of asthma.

Results

Intentional nonadherence to asthma medicines during pregnancy was described. Participants were found to decrease or discontinue their asthma medications, without consulting their doctors. Reasons behind their decisions included lack of support and information, concerns about safety of medications, past experiences and a desire for an all natural pregnancy. Communication between pregnant women and health professionals regarding asthma management was poor. Asthma monitoring during pregnancy was seen as a low priority for many pregnant women and their doctors.

Conclusions

Pregnant women have not been well supported in regards to how to manage their asthma during pregnancy, causing them concern. Education and more support is warranted and wanted by these women to increase their confidence in managing their asthma. Interventions targeting pregnant women, with a focus on the risks versus benefits of taking asthma medication during pregnancy and the potential harm of uncontrolled asthma, should be developed and evaluated.

Pharmacy Practice: International Perspective

Session Chair: Jasmina Fejzic, Griffith University

Tuesday 13 December 2011, 11:00am – 12:30pm

Room P5-34, Playford Building

CP08-1

Tuan Nguyen, University of South Australia

Why are medicine prices in Vietnam high?

CP08-2

Hanni Puspitasari, The University of Sydney

A simulated patient study to explore Indonesian pharmacy staff's response to a symptom-based OTC request: A dyspepsia case

CP08-3

Ho Yan Hidy Chan, The University of Queensland

Pharmaceutical access in Australia, Hong Kong, Thailand, Vietnam, Singapore and Malaysia

CP08-4

Isaac Joshua, Curtin University

Appropriateness of prescribing in selected locations in Papua New Guinea

CP08-5

Souhiela Fakih, Monash University

Comparing women pharmacy consumers' experiences with weight loss treatment in Victoria and Nottingham: A cross-sectional study

CP08-6

Gereltuya Dorj, Curtin University

Assessment of prescribing practices for community-acquired pneumonia (CAP) in Mongolia

Why are medicine prices in Vietnam high?

Tuan Anh Nguyen [1] Rosemary Knight [2] Andrea Mant [2] Minh Quang Cao [3] Husna Razee [2]

[1] Quality Use of Medicines and Pharmacy Research Centre, University of South Australia, Adelaide, SA

[2] School of Public Health and Community Medicine, The University of New South Wales, Sydney, NSW

[3] Ministry of Health, Hanoi, VIETNAM

Objective

To identify the main reasons for high medicine prices in Vietnam.

Methods

Semi-structured questionnaires were used to conduct 43 interviews with different stakeholders including pharmaceutical companies' representatives, Ministry of Health officials, and prescribers in Vietnam from April 2008 to December 2009. The interviews were all recorded, transcribed, and coded using NVivo8 software. Ethics approval was obtained from the University of New South Wales.

Results

According to participants' responses, originator medicines in Vietnam were too expensive due to a supplier monopoly. Prices of generic medicines were set at around 80%, sometime even higher than those of corresponding originator medicines due to informal payment to authorities, commissions for prescribers, and kickback to hospital pharmaceutical departments. Pressures for survival arising from an imperfectly competitive pharmaceutical market, among other reasons, were believed to force pharmaceutical companies to be inextricably linked to prescribers. Salary pressures and the perpetual corruption in the absence of penalties in Vietnam were given as the main motives for prescribers to collude with the pharmaceutical industry. The magnitude of reported corruption varied across geographic regions, sectors, and prescriber's specialties.

Conclusions

Corruption was reported as a main driver for high medicine prices in Vietnam. Although individual factors such as professional ethics and personal value influenced physician behaviours and their response to corruption, entrenched or intractable systemic issues including lack of transparency and accountability and poor legislation enforcement emerged as important factors perpetuating corruption. Addressing the widespread issue of corruption, both individual and systemic factors, is necessary in developing sound medicine pricing policies in Vietnam.

A simulated patient study to explore Indonesian pharmacy staff's response to a symptom-based OTC request: A dyspepsia case

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[1] Faculty of Pharmacy, Airlangga University, Surabaya, INDONESIA

[2] Faculty of Pharmacy, The University of Sydney, Sydney, NSW

Objective

This study explored provision of patient assessment, types of medicines recommended and medicine information provided by community pharmacy staff to patients with dyspepsia.

Methods

A simulated patient presented a symptom-based request for treatment of dyspepsia to 90 randomly selected community pharmacies in Surabaya. The "patient" was instructed to provide relevant information based on the scenario if the pharmacy staff asked using open-ended questions. Otherwise, she was only allowed to answer "yes" or "no". When no medicine information was given, she was instructed to ask in a standardised manner about "how to take" and "when to take" the medicines. Data about patient assessment, the types of medicines recommended and the content of information given were recorded on data sheets after purchasing the medicine and leaving the pharmacy.

Results

Twelve (13%) pharmacies assessed the patient before giving recommendation. Seventy-five (83%) pharmacies recommended antacids, seven (8%) a combination of H2 blockers and antacids, five (6%) proton pump inhibitors, and three (3%) H2 blockers. Medicine information on "how to take", dosing, and "when to take" was given by 87 (97%), 30 (33%) and 90 (100%) pharmacy staff, respectively. Of all pharmacy staff who provided information on "how to take" and "when to take", 80 (92%) and 58 (64%), respectively, gave the information only when requested.

Conclusions

The findings demonstrate that the response of Surabaya pharmacy staff to the presentation of a self-medication request is suboptimal. This highlights an urgent need for training for pharmacy staff in Surabaya.

Pharmaceutical access in Australia, Hong Kong, Thailand, Vietnam, Singapore and Malaysia

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[1] School of Pharmacy, The University of Queensland, Brisbane, QLD

[2] School of Population Health, The University of Queensland, Brisbane, QLD

Objective

To examine the issues regarding communal pharmaceutical access in developed (Australia, Hong Kong and Singapore) and developing countries (Thailand, Vietnam and Malaysia).

Methods

This study used qualitative methods to conduct interviews with government officials, pharmacy owners, pharmacists and academics to gain an in-depth, local insight into overall communal pharmaceutical access in each country. Topics regarding barriers to access, access differences between certain drugs and ways to improve access were discussed. All interviews were analysed by Leximancer to generate concept maps to identify themes and relationship from the interviews. These were compared within and between the countries.

Results

All countries have a different system for communal pharmaceutical access. Despite this, all interviewees claimed pharmaceutical access to be "good/excellent" in their own countries. Equity in accessing pharmaceuticals was not deemed a problem in Australia, yet delayed access to certain medications can occur due to the geographical vastness of the country. Due to their country's social structure, Thai and Vietnamese interviewees reported inequitable access to pharmaceuticals dependent on social status and health insurance entitlement. Illegal sale of prescription medications (e.g. without a prescription) was common in Hong Kong and Malaysia, raising concern regarding the quality use of medications. There was higher use of traditional medicines in the Asian countries compared to Australia.

Conclusions

This study gave an insight into peoples' opinions on pharmaceutical access in developed and developing countries. Countries were diverse in their socioeconomic status, pharmaceutical systems operations and structure; however, all shared similar access views, concerns and ideas for improvement.

Appropriateness of prescribing in selected locations in Papua New Guinea

Isaac Joshua [1] Phillip Passmore [1] Richard Parsons [1] Bruce Sunderland [1]

[1] School of Pharmacy, Curtin University, Perth, WA

Objective

To assess the level of appropriateness of prescribing to outpatients in selected locations in Papua New Guinea (PNG).

Methods

A prospective study was carried out at Losuia Health Centre (LHC), Alotau Provincial Hospital (APH), and Port Moresby General Hospital (PMGH) in PNG. Each study collected >300 consecutive prescriptions from each location in 2010. Diagnosis and prescribing data were collected from prescriptions and patient interview. Prescribing was assessed with respect to the relevant PNG guidelines. Differences in the elements of the study were evaluated using chi-squared tests as appropriate. Ethical approval was obtained.

Results

There were 1090 patients (765 adults; 325 children) enrolled in the study with 356 at LHC, 318 at APH and 416 at PMGH. A total of 2495 medicines were prescribed. The most common were amoxicillin (n = 351), paracetamol (n = 349), artemether/artesunate (n = 186) and sulphadoxine with pyrimethamine (n = 126). The average number of drugs prescribed per patient was 2.3. Inappropriate prescribing was 34.8% in adults and 46.5% in children mainly arising from drug selection ($p < 0.0001$). There was a statistically significant difference observed on the level of inappropriate prescribing by prescriber category on drug selection ($p < 0.0001$), dosage ($p < 0.0001$), and duration ($p < 0.0001$). The most common diseases treated were malaria (23.2%), acute soft tissue injuries (10.4%), anaemia (8.9%), respiratory problems (8.7%), and cough (5.9%).

Conclusions

The results indicate that the level of inappropriate prescribing in the selected locations in PNG is of great concern. Procedures need to be introduced to address the underlying causes.

Comparing women pharmacy consumers' experiences with weight loss treatment in Victoria and Nottingham: A cross-sectional study

Souhiela Fakih [1] Safeera Hussainy [1] Jennifer Marriott [1] Helen Boardman [2] Claire Andersron [2] Lisa Demos [3] John McNeill [3] Anna Peeters [3]

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[2] School of Pharmacy, The University of Nottingham, Nottingham, UNITED KINGDOM

[3] Department of Epidemiology and Preventative Medicine, Monash University, Melbourne, VIC

Objective

To determine the differences and similarities between Australian and English women pharmacy consumers' attitudes and experiences with weight management approaches.

Methods

Women pharmacy consumers in Victoria, Australia and Nottingham, UK were approached by a researcher and asked to complete a questionnaire regarding their own weight management experiences. The questionnaire was completed by the participant alone or with assistance from the researcher.

Results

The response rates were high: 86% (n = 395/460) in Victoria and 98% (n = 215/220) in Nottingham .Overall the women in Victoria and Nottingham were similar with comparable demographics. Approximately 50% (n = 250/508) of women were in the overweight or obese BMI category, with over 70% (n = 436/610) of women having attempted to lose weight in the past; the majority having tried multiple weight loss methods. Of these women, approximately 30% (n = 128/436) had received advice from their healthcare professional (HCP), with more women in Victoria having received advice. Women who had received HCP advice were significantly less likely to regain the weight they had lost, with over 80% stating the advice received was helpful. The majority of women (n = 334/436) felt comfortable receiving advice from pharmacists with 40% (n = 171/436) wanting a pharmacist in their ideal weight management program and 36% (n = 157/436) wanting their program to be delivered in a pharmacy.

Conclusions

Results from this project have provided information on possible ideal pharmacy weight management services in both Victoria and Nottingham, which will specifically target the needs of women pharmacy consumers.

Assessment of prescribing practices for community-acquired pneumonia (CAP) in Mongolia

Gereltuya Dorj [1] Delia Hendrie [2] Richard Parsons [2] Bruce Sunderland [1]

[1] School of Pharmacy, Curtin University, Perth, WA

[2] School of Public Health, Curtin University, Perth, WA

Objective

To evaluate drug therapy prescribed to patients diagnosed with community-acquired pneumonia (CAP) in Mongolia with respect to national guidelines.

Methods

Prescriptions were collected in sequence prospectively for ten weeks from a representative sample of community pharmacies in rural and urban areas of Mongolia. The data included the diagnosis, patient's age, and gender and medication details including drug name, frequency and number of doses prescribed. Evaluation was with respect to the Mongolian Standard Treatment Guidelines (2008, 2010). Chi-squared and Fisher's exact test were used to evaluate differences.

Results

The study examined 393 (192 adults and 201 children) patients with a diagnosis of mild/moderate CAP. The prescriptions were collected from 22 community pharmacies and the prescribing practice of 118 doctors was assessed. The most commonly prescribed drugs were aminopenicillins, vitamins, and mucolytics. A chi-square analysis showed a statistical difference between inappropriate drug selection ($p = 0.022$) for children and adults with inappropriate drug selection being was greater for children (59.4%) than for adults (52.2%). It was the major reason for inappropriate prescribing for adults (86.7%) and for children (99.4%) ($p < 0.0001$). The proportion of prescribed injections was 28% for adults and 9% for children. This is non-compliant with the prescribing standard for outpatients in Mongolia.

Conclusions

The development of comprehensive and reliable control procedures nationwide to improve prescribing practice is of high importance in Mongolia.

Pharmaceutical Science: Drug Disposition

Session Chair: Michelle McIntosh, Monash University

Wednesday 14 December 2011, 11:00am – 12:30pm

Room P5-14, Playford Building

CP09-1

Cher-Rin Chong, University of South Australia

Determinants of perhexiline uptake into the human myocardium

CP09-2

Nathania Leong, Monash University

The effect of intravenous SBE_7-β-CD on the pharmacokinetics of a series of adamantane-containing compounds

CP09-3

Peng Li, University of South Australia

Inhibition of sinusoidal membrane Na^+/K^+ ATPase digoxin binding by quinidine is the main determinant of digoxin-quinidine drug interactions at therapeutic concentrations

CP09-4

Haniza Hassan, University of South Australia

Impaired hepatic drug elimination by silica nanoparticles

CP09-5

Sifei Han, Monash University

Lipophilic prodrugs to target delivery of immunomodulators to lymphocytes in the lymphatic system

CP09-6

Joseph Nicolazzo, Monash University

Impact of Alzheimer's disease on the blood-brain barrier transport of therapeutic agents

Determinants of perhexiline uptake into the human myocardium

Cher-Rin Chong [1, 2] John Licari [2, 3] Nigel E Drury [2, 3, 4] Wai Ping A Chan [2, 3] Michael Frenneaux [5] John Horowitz [2, 3] Domenico Pangano [4] Benedetta C Sallusito [2, 3]

[1] School of Pharmacy and Medical Sciences, University of South Australia, Adelaide, SA

[2] Department of Cardiology, The Queen Elizabeth Hospital, Adelaide, SA

[3] Department of Clinical Pharmacology, The Queen Elizabeth Hospital, Adelaide, SA

[4] Department of Cardiothoracic Surgery, Queen Elizabeth Hospital Birmingham, Birmingham, UNITED KINGDOM

[5] School of Medicine and Dentistry, The University of Aberdeen, Aberdeen, UNITED KINGDOM

Objective

In theory, the process of drug uptake into the myocardium is the primary determinant of effect and/or toxicity, and is directly correlated with steady-state plasma drug concentrations. However, human data on myocardial drug uptake are currently limited, and predominantly obtained during acute (non steady-state) administration, using indirect mass balance principles. Utilising data from the active treatment arm of the CASPER trial, we evaluated perioperative perhexiline therapy in patients undergoing non-emergent coronary bypass grafting, to identify determinants of steady-state perhexiline uptake into the myocardium and its relationship with plasma perhexiline concentration (PPC).

Methods

PPC and atrial perhexiline concentration (APC) were determined by high performance liquid chromatography for 79 patients who had received total cumulative dose of perhexiline maleate between 1800 - 5600 mg over 8 ± 3 (SD) days. CYP2D6 poor metabolisers were excluded and determinants of PPC and APC were sought utilizing backward stepwise multiple linear regression.

Results

PPC and APC were at steady-state as there was no significant interaction with cumulative dose. PPC was inversely correlated with weight ($p < 0.01$). APC varied (independently) directly with age and inversely with weight (both $p < 0.05$). When PPC was included in the multivariate analysis model, correlates of APC were PPC ($\beta = 0.898$, $p < 0.0001$) and age ($\beta = 0.133$, $p < 0.01$).

Conclusions

This study establishes that both weight and age impact on perhexiline accumulation in human atrium. The inverse relationship between weight and APC is mediated via decreased PPC. However, the direct relationship with age is independent of PPC and reflects a differential effect on the plasma: myocardium partition process.

The effect of intravenous SBE_7-β-CD on the pharmacokinetics of a series of adamantane-containing compounds

Nathania Leong [1] Richard Prankerd [1] David Shackleford [2] Michelle McIntosh [1]

[1] Monash Institute of Pharmaceutical Sciences, Monash University, Melbourne, VIC

[2] Centre for Drug Candidate Optimisation, Monash University, Melbourne, VIC

Objective

Intravenously delivered SBE_7-β-CD has been reported to alter the pharmacokinetics of a novel ozonide antimalarial. It was hypothesised that the adamantane moiety of the drug was contributing to a high binding constant (2.3×10^6 M^{-1}) with SBE_7-β-CD resulting in incomplete complex dissociation *in vivo*. As an extension, the relationship between binding affinity and impact on intravenous pharmacokinetics has been studied using three adamantane-containing compounds, amantadine, memantine and rimantadine.

Methods

Binding constants with SBE_7-β-CD were determined using isothermal titration microcalorimetry. *In vivo* studies to define plasma and urinary pharmacokinetics were conducted in rats using a crossover design; each compound was administered intravenously in either a 0.1 M SBE_7-β-CD or a 0.9% saline formulation. The alternative formulation was administered the following day.

Results

The binding constants for memantine, amantadine and rimantadine were determined to be 0.5×10^4, 1.2×10^4 and 2.2×10^4 M^{-1} respectively. No alteration was observed in either the plasma or urinary pharmacokinetic profiles of amantadine and memantine in the presence of SBE_7-β-CD compared to saline. In contrast, the plasma pharmacokinetics of rimantadine was perturbed and a significant increase in urinary excretion of the drug was observed in the SBE_7-β-CD formulation.

Conclusions

The binding contants of the three compounds with SBE_7-β-CD were within the typical range of drug-like molecules (10^2 - 10^4 M^{-1}). SBE_7-β-CD demonstrated significant impact on plasma pharmacokinetics and urinary excretion profiles of the analogue with the highest binding constant.

Inhibition of sinusoidal membrane Na^+/K^+ ATPase digoxin binding by quinidine is the main determinant of digoxin-quinidine drug interactions at therapeutic concentrations

Peng Li [1] Michael Weiss [2] Michael Roberts [1]

[1] School of Pharmacy and Medical Sciences, University of South Australia, Adelaide, SA

[2] Department of Pharmacology, Martin Luther University Halle-Wittenberg, Halle, GERMANY

Objective

The mechanism by which quinidine affects digoxin pharmacokinetics remains controversial. In this work, we try to explore the displacement of digoxin from hepatic sinusoidal binding sites by quinidine as an important determinant of the digoxin - quinidine drug interaction at the quinidine and digoxin concentrations seen in patients.

Methods

We used the impulse-response technique in the single-pass perfused rat liver and literature data to describe the digoxin hepatic disposition by a physiologically-based pharmacokinetic liver model with and without quinidine. This study involved analysis of outflow curves following two consecutive doses of digoxin (42 and 125 µg) without and with quinidine in perfusate. The effect of quinidine on digoxin binding in liver subcellular fractions was quantified.

Results

Quinidine affected the outflow concentration for digoxin at the low digoxin dose but not at the high dose. At the lower digoxin dose, administration of quinidine was associated with an increase in the outflow concentration of digoxin, a decrease in biliary clearance of digoxin and an increase in the sinusoidal efflux of digoxin's primary metabolite, digoxigenin bisdigitoxoside (Dg2). These changes were only adequately described by a classical physiological based pharmacokinetic model with variable digoxin and quinidine concentrations when digoxin displacement from sinusoidal and intrahepatic binding sites was included.

Conclusions

At therapeutic concentrations for both digoxin and quinidine, the main mechanism by which quinidine affects digoxin outflow concentrations from the liver is not by uptake or efflux transporter inhibition of digoxin by quinidine but by quinidine inhibiting the binding of digoxin to hepatic sinusoidal membrane Na^+/K^+ ATPase.

Impaired hepatic drug elimination by silica nanoparticles

Haniza Hassan [1] Jiping Wang [1, 2] Tom Robertson [1, 2] Michael Roberts [1, 2] Allan Evans [1]

[1] School of Pharmacy and Medical Sciences, University of South Australia, Adelaide, SA

[2] Basil Hetzel Institute, The Queen Elizabeth Hospital, Adelaide, SA

Objective

Previous studies have shown that silica nanoparticles may be trapped in the hepatic sinusoid after entering the Space of Disse. This sinusoidal trapping could potentially reduce the uptake of drugs from blood into hepatocytes by compromising their permeation through the Space of Disse. We hypothesized that nanoparticles may impair the hepatic elimination of drugs, which may compromise their use as drug carriers.

Methods

Livers were perfused with Kreb-Hensenleit buffer containing 4-methylumbelliferone (4MU, 100 µM). Silica nanoparticles were injected into the portal vein of the isolated perfused rat liver. Outflow perfusate and bile was collected and analyzed by HPLC. Livers were also examined histologically. Pharmacokinetics of 4MU and its metabolites, 4-methylumbelliferyl glucuronide (4MUG) and 4-methylumbelliferyl sulfate (4MUS) were determined.

Results

Hepatic clearance of 4MU decreased from 22.64 ± 1.80 to 17.30 ± 4.39 mL/min ($p < 0.05$) after injecting a 5 mg dose of nanoparticles. A greater effect was seen for a 50 mg dose (from 23.32 ± 1.87 to 7.89 ± 1.58 mL/min, $p < 0.01$). Formation and biliary clearance of 4MUG, and bile flow rate decreased significantly in the 50 mg nanoparticles group compared to the control ($p < 0.001$), while no significant difference was observed between the other groups. Cell swelling and protein-like substance accumulation was observed in the livers exposed to the nanoparticles.

Conclusions

Silica nanoparticles reduced the hepatic clearance of 4MU. Structural changes induced by silica nanoparticles may be due to their accumulation in the Space of Disse thereby preventing transfer of drug molecules from hepatic sinusoids into hepatocytes. Further work is needed to determine the full impact of nanoparticles on hepatic drug elimination.

Lipophilic prodrugs to target delivery of immunomodulators to lymphocytes in the lymphatic system

Sifei Han [1] Anisa Wahab [1] Natalie Trevaskis [1] Jamie Simpson [1] Christopher Porter [1]

[1] Monash Institute of Pharmaceutical Sciences, Monash University, Melbourne, VIC

Objective

Enhancing drug transport via the intestinal lymphatic system facilitates targeted delivery to lymphocytes and may thus provide opportunities to enhance the activity of immunomodulators in the treatment of immune diseases. The current study aimed to target the delivery of an immunomodulator, mycophenolic acid (MPA), to the intestinal lymphatics via oral administration of two lipophilic prodrugs: octadecyl-mycophenolate (OM) and 1,3-dipalmitoylglycerol mycophenolate (DPGM). OM and DPGM were expected to access the lymph via different mechanisms.

Methods

Lymphatic drug transport was examined in mesenteric lymph-cannulated rats following intraduodenal infusion of lipid formulations containing oleic acid. Biotransformation of the prodrugs was also assessed via incubation with rat digestive fluid and by examination of the prodrug derivatives in mesenteric lymph by HPLC-MS.

Results

OM (16-fold) and DPGM (52-fold) markedly increased lymphatic drug transport when compared to MPA. The hydrolysis of OM in digestive fluid was relatively slow (half-life 70 min), whereas the lipolysis of DPGM was rapid, instantaneously releasing glycerol-mycophenolate. OM was transported via mesenteric lymph in its original form, whilst DPGM was re-esterified with oleic acid, most likely originating from the co-administered formulation.

Conclusions

The prodrugs successfully improved lymphatic transport of MPA via distinct pathways: OM appeared to passively partition into intestinal lymph lipoproteins, whereas DPGM was hydrolysed and subsequently re-esterified prior to incorporation into endogenous lipoprotein assembly pathways. The data suggest that lipophilic prodrugs may be used to promote lymphatic drug transport and exemplify the potential use of drug delivery principles to guide medicinal chemistry strategies for lymphocyte-related therapeutic indications.

Impact of Alzheimer's disease on the blood-brain barrier transport of therapeutic agents

Dharmini Mehta [1] Jennifer Short [1] Joseph Nicolazzo [1]

[1] Monash Institute of Pharmaceutical Sciences, Monash University, Melbourne, VIC

Objective

Despite reports of blood-brain barrier (BBB) dysfunction in Alzheimer's disease (AD) including altered expression of tight junction proteins, P-glycoprotein (P-gp) and basement membrane proteins, the impact of these alterations on the brain access of drugs remains unknown. The aim of this project was to determine whether brain uptake of drugs with different BBB transport mechanisms is affected in AD.

Methods

Radiolabelled marker compounds were transcardially perfused (0.5 µCi/mL at 2 mL/min for 4 min) to 18 month male wild-type (WT) and 3xTg AD mice. The marker compounds were ^{14}C-sucrose (paracellular marker), ^{3}H-diazepam and ^{3}H-propranolol (passive transcellular markers) and ^{3}H-digoxin, ^{3}H-loperamide and ^{3}H-verapamil (P-gp substrates). Following perfusion, the cortex and hippocampus were dissected, analysed for radioactivity and cortex-to-perfusate (C:P) and hippocampus-to-perfusate (H:P) ratios determined.

Results

The C:P ratio of ^{14}C-sucrose was 0.021 ± 0.003 (mean ± SD) in WT mice and 0.026 ± 0.005 in 3xTg mice, and similarly, the H:P ratios of ^{14}C-sucrose were 0.019 ± 0.004 and 0.023 ± 0.004 in WT and 3xTg mice, respectively. The BBB transport of P-gp substrates was not significantly affected in AD mice, whereas the BBB transport of passive transcellular markers was significantly ($p < 0.05$) reduced (C:P and H:P ratios in 3xTg AD mice being 2.2 - 2.3 fold lower for ^{3}H-diazepam and 1.9 - 2.7 fold lower for ^{3}H-propranolol).

Conclusions

Passive BBB diffusion of drugs appears to be decreased in 3xTg mice, likely due to cerebrovascular membrane thickening. This reduction in transport appears to be counteracted for P-gp substrates, possibly due to the reduced BBB expression of P-gp in AD.

Pharmacy Education

Session Chair: Libby Hotham, University of South Australia

Wednesday 14 December 2011, 11:00am – 12:30pm

Room P5-15, Playford Building

CP10-1

Gabrielle Cooper, University of Canberra

Beyond the dispensary: Innovations in the provision of placements within a pharmacy course that provide learning experinces that broaden graduates understanding of the pharmacists potential scope of practice

CP10-2

Pascale Dettwiller, Charles Darwin University

Developing interprofessional teaching and learning: Three universities experience of a remote health day

CP10-3

Maree-Ann Jensen, The University of Auckland

From the COSE to the OSCE at Auckland School of Pharmacy: Performance based assessment development in the first ten years at the Auckland School of Pharmacy, the journey continues

CP10-4

Helender Singh, The University of Queensland

Dose calculations in a virtual world: A pilot evaluation of The University of Queensland's compounding dispensary in "Pharmatopia"

CP10-5

Peter Gee, University of Tasmania

Enhancing placement training: To evaluate the introduction and acceptability of an e-portfolio in an undergraduate pharmacy course

CP10-6

Stacey Gough, Curtin University

NAPSA Indigenous Health Position Statement

Beyond the dispensary: Innovations in the provision of placements within a pharmacy course that provide learning experinces that broaden graduates understanding of the pharmacists potential scope of practice

Gabrielle Cooper [1] Greg Kyle [1] Ben Gilbert [1] Louise Deeks [1] Mark Naunton [1]

[1] Discipline of Pharmacy, University of Canberra, Canberra, ACT

Objective

To present innovations employed within a pharmacy course that provide practice based learning in novel and relevant environments that will broaden students understanding of possible career opportunities.

Methods

Descriptive and 360 degree feedback from sites, clinical preceptors, students (current and graduated), employers and the Faculty of Health Placement Office was collated and analyses to identify and quantify the impact of innovative placement experiences on future employment and scope of practice in the profession of pharmacy.

Results

Students and graduates from the program identified that a broader experience in the health sector during their course has influenced their professional progression away from a purely "community pharmacy" focus that they has on joining the course. Graduates currently are employed in sectors such as public health, health administration (state and federal), rural practice and therapeutics evaluation.

Conclusions

Pharmacy courses have the obligation to identify to student's career paths that will broaden their scope of practice and provide employability. Courses that engage closely with other health professionals and industries who require graduates with pathophysiology, clinical, pharmacological, analytical, interpersonal and communication skills will position pharmacy graduates well for future success.

Developing interprofessional teaching and learning: Three universities experience of a remote health day

Pascale Dettwiller [1] Tim Earnshaw [2] Teresa Raines [3]

[1] Discipline of Pharmacy, Charles Darwin University, Darwin, NT

[2] NT Medical Program, Flinders University, Darwin, NT

[3] Batchelor Institute of Indigenous Tertiary Education, Batchelor, NT

Objective

Remote health day objectives were to: (a) emphasize health in Aboriginal communities, (b) introduce students to the NT remote health system, (c) discuss the stresses in working in a remote setting and discuss strategies for developing a rewarding career-path in remote health.

Methods

The remote health day was held at BIITE, a remote area 1.5 hrs drive south from Darwin, and was attended by 64 students, comprising: 22 medical (post grad yr1), 30 pharmacy (under-grad yr 3 elective) and 12 aboriginal health workers (dip yr 2 trainees). The day consisted of a traditional welcome to country, presentations by experienced practitioners in the field, and a closing panel in the morning. Eight skill stations were set-up for the afternoon and the multi-disciplinary student groups circulated through the 8 stations. As the day was primarily concerned with outlining health practitioner skills and issues, plus showcasing the experiences and opportunities in remote health work and placements, the evaluation used self-administered questionnaire pre and post activities.

Results

65% of the participants submitted their 2 course and session evaluation forms; 65% submitted a survey form. "Did the course meets it's objectives?" (Likert scales): 100% of the participants stated that all the sessions met their objectives. "Did the course change the participant's list of remote health issues?": 47% of the participants reported changing their issues list. "Would participants do student placement, or work, in a remote community?": 71% of the participants reported willing to work in a remote community after this activity.

Conclusions

The participant students stated their improved awareness of the issues and context of remote health and the benefit from the interdisciplinary learning program.

From the COSE to the OSCE at Auckland School of Pharmacy: Performance based assessment development in the first ten years at the Auckland School of Pharmacy, the journey continues

Maree Jensen [1] Janie Sheridan [1] John Shaw [1]

[1] School of Pharmacy, The University of Auckland, Auckland, NEW ZEALAND

Summary

Structured clinical examinations (OSCEs) are one popular method used to determine both the skills and application of knowledge of health professionals and use performance to demonstrate these abilities to a pre-determined level. They have been used in medical programmes world-wide since the 1970's, and are increasingly used by other health professionals to determine ability to practice in their chosen health care domain. OSCE processes at the School of Pharmacy in Auckland have travelled some distance since the School was first opened in 2000. The first Part 3 students experienced a clinical examination, that was conducted orally as well as in a structured manner (thus the COSE) by travelling out to Middlemore Hospital, some 17 kilometers away from the Medical and Health Faculty, where they participated in a number of "stations" where they were asked about particular conditions which had been studied in that paper that year. On reflection this examination was not as educationally sound as it could be, and over subsequent years the oral examination has undergone several changes of clothing to become more tailored and well groomed, matching learning objectives to assessment. Whilst the OSCE does not map to all course content, and thus requires additional forms of assessment for these, its strength is in its ability to determine evidence of deeper learning, as applied to care planning, and the skills, knowledge and attitudes to provide a better patient journey. This presentation will provide a travelogue of the OSCE journey over the last 10 years, and will allow us to share our insights and learning.

Dose calculations in a virtual world: A pilot evaluation of The University of Queensland's compounding dispensary in "Pharmatopia"

Helender Singh [1] Sally Firth [1] Jacqueline Bond [1]

[1] Pharmacy Australia Centre of Excellence, The University of Queensland, Brisbane, QLD

Objective

To evaluate "Pharmatopia's" virtual compounding dispensary as a resource to improve dosage calculations skills in pharmacy students.

Methods

Phase I: Ten first-year UQ pharmacy students were recruited by email to a 1-day workshop. Students underwent testing for baseline dose calculation proficiency, received a tutorial regarding the virtual dispensary and were given 1.5 h for self-directed learning. Students were re-tested for calculations proficiency and overall feedback was elicited through a focus group. Phase II targeted the entire cohort (n = 249) of commencing 2011 UQ BPharm students. Students were encouraged to engage with the new resource and were surveyed regarding its usefulness.

Results

Phase I: Nine students attended the workshop. The average pre-Pharmatopia score was 5.8/10 and the average post-Pharmatopia score was 7.7/10, yielding an average performance increase of 18.9% ($p < 0.0061$). Common themes noted during the focus group included that the virtual dispensary was a helpful, enjoyable resource with potential for use in both collaborative and individual settings. All students would recommend Pharmatopia to a peer. Phase II: The survey was completed by 76.7% of students. Fifty-four students reported use, comprised of 3 heavy, 15 moderate and 36 once-off users. Feedback from users was predominantly positive; however there was no significant difference between the academic performance of those using the virtual dispensary and those who did not use the resource. Eighty-four percent of students who used the resource would recommend Pharmatopia's virtual dispensary to a peer.

Conclusions

Pharmatopia shows promise as an immersive, pedagogical tool to improve confidence and academic performance of students.

Enhancing placement training: To evaluate the introduction and acceptability of an e-portfolio in an undergraduate pharmacy course

Juanita Westbury [1] Peter Gee [1]

[1] School of Pharmacy, University of Tasmania, Hobart, TAS

Objective

Students in their fourth year attend a three week placement in a community pharmacy at various Australian locations. During their placement they complete a daily log and also reflect on three "clinical encounters" in depth. In previous years students used a paper-based system, submitting this for assessment. The benefits of an electronic portfolio are that it can be read by assessors whilst students are away on placement, thus enabling student support and feedback. This study was conducted to subjectively evaluate an e-portfolio tool to help facilitate interaction between final-year pharmacy students and their preceptor whilst on placement in community pharmacy settings.

Methods

Two evaluation on-line questionnaires were given to fourth year pharmacy students before and after exposure to the e-portfolio tool.

Results

All 52 final-year students completed the pre-evaluation questionnaire. When asked about their understanding of an e-portfolio, 64% of the students thought they might be useful for storing information; however, a lower proportion (40%) thought it would be useful as a reflective tool. As the majority of students had used a social networking site (92%) they were generally positive about using the e-portfolio (74%). Fewer students responded to the post-evaluation questionnaire (n = 24, 46%). Although the majority liked to receive feedback regularly (65%), when student responses were compared before and after using the e-portfolio tool, students were significantly less positive after using the e-portfolio (χ^2, p = 0.004, df = 1). Many students (57%) reported that they found the interface of the tool to be cumbersome and difficult to use and some students felt that increased training on using the e-portfolio was required (27%).

Conclusions

Many pharmacy students were less positive about using an e-portfolio after trialling it on placement. This was probably impacted by difficulties encountered with the tool itself and the necessity for increased training.

NAPSA Indigenous Health Position Statement

Ellen Pedler [1] Briohny Gillespe [2] Stacey Gough [3]

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Summary

The National Australian Pharmacy Student's Association (NAPSA) is the representative body for over 3500 pharmacy students across Australia. NAPSA's Rural and Indigenous Affairs (R&I) Committee recognise the need for Indigenous health education as an area for concern for our members, and in May 2011, conducted a survey to investigate members' views on rural placements and Indigenous health education. 83% of the 414 respondents felt it is important to be taught about Aboriginal and Torres Strait Islander health issues, but only 60% have access to such education and furthermore, only half of those respondents felt they are taught enough about this topic. It is the belief of the NAPSA R&I Committee that Australia's future pharmacists should be committed to closing the gap, and be competent and confident in all aspects of Aboriginal and Torres Strait Islander health. As a result, the NAPSA R&I committee has developed a Position Statement, which proposes all pharmacy schools across Australia incorporate the following into their core curriculum, and strive to set and meet national standards for these competencies: (i) awareness of the social, environmental and historical influences on current Aboriginal and Torres Strait Islander health outcomes, (ii) appreciation of the diversity of Aboriginal and Torres Strait Islander peoples throughout Australia, (iii) the principles behind cultural awareness, competency and culturally safe practice in regard to Aboriginal and Torres Strait Islander health, (iv) encouragement and support of student placements that enable greater learning opportunities in Aboriginal and Torres Strait Islander settings, where possible, with Aboriginal Community Controlled Health Service (ACCHO) or Aboriginal Medical Services (AMS).

Pharmacy Practice: Drugs in the Elderly

Session Chair: Simon Bell, University of South Australia

Wednesday 14 December 2011, 11:00am – 12:30pm

Room P5-33, Playford Building

CP11-1

Jenni Ilomäki, University of South Australia

Heavy drinking predicts subsequent sedative or anxiolytic medication use in aging men: A longitudinal study

CP11-2

Danijela Gnjidic, The University of Sydney

High risk prescribing and incidence of frailty among community-dwelling older adults

CP11-3

Imaina Widagdo, University of South Australia

Characteristics and criteria of the frail elderly: A review of frailty measures

CP11-4

Jodie Hillen, University of South Australia

Fishing in a sea of indicators: Challenges with evaluating QUM in Australian RAC

CP11-5

Sukhpreet Kaur, University of South Australia

Evaluation of medication related problems in medication reviews: A comparative perspective?

CP11-6

Julia Gilmartin, Monash University

A review of dose administration aids: Improving medicine management

Heavy drinking predicts subsequent sedative or anxiolytic medication use in aging men: A longitudinal study

Jenni Ilomäki [1] J Simon Bell [1] Jussi Kauhanen [2] Hannes Enlund [3]

[1] School of Pharmacy and Medical Sciences, University of South Australia, Adelaide, SA

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[3] Finnish Medicines Agency, Helsinki, FINLAND

Objective

Cross-sectional studies have found an association between alcohol consumption and psychotropic medication use. However, evidence for a possible temporal association is lacking. The objective of this study was to prospectively investigate whether heavy drinking predicts initiation or continuation of sedative/anxiolytic medication at four and 11 years and, conversely, whether sedative/anxiolytic medication use predicts heavy drinking.

Methods

This longitudinal population-based study was conducted in Kuopio, Finland. A random sample of 1516 men aged 42, 48, 54, and 60 years received a structured clinical examination at baseline (1986 - 1989). Follow-up examinations were conducted at four (n = 1038) and 11 years (n = 854). Multinomial logistic regression was used to compute odds ratios (ORs) and 95% confidence intervals (CIs) for the association between sedative/anxiolytic medication use and initiation and continuation of heavy drinking (4 drinks/week) adjusted for age, working status, smoking and depressive symptoms. The reverse associations were also investigated.

Results

At baseline 12.9% (n = 134) of participants were heavy drinkers and 4.0% (n = 41) used sedative/anxiolytic medicines. In multivariate analyses, baseline heavy drinking predicted initiation of sedative/anxiolytic medication at four years (OR = 2.96; 95% CI: 1.23 - 7.15). Furthermore, baseline sedative/anxiolytic medication use predicted continuation of heavy drinking for 11 years in unadjusted (OR = 3.30; 95% CI: 1.19 - 8.44) but not in adjusted analyses (OR = 2.69; 95% CI: 0.86 - 8.44).

Conclusions

Baseline heavy drinking predicted subsequent initiation of sedative/anxiolytic medicines that was not fully explained by depressive symptoms. This finding may inform strategies to optimise the use of sedative/anxiolytic medicines, and assist in the early identification of patients at risk of heavy drinking.

High risk prescribing and incidence of frailty among community-dwelling older adults

Danijela Gnjidic [1, 2, 3, 4] Sarah Hilmer [1, 2, 4] David Le Couteur [3, 4] Andrew McLachlan [3, 5]

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[2] Department of Aged Care, Royal North Shore Hospital, Sydney, NSW

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[5] Faculty of Pharmacy, The University of Sydney, Sydney, NSW

Objective

Evidence on the association between treatment with high risk medicines and frailty in older adults is limited. The aim of this study was to investigate the relationship between high risk prescribing and frailty at baseline, and 2-year incident frailty in older adults.

Methods

A total of 1662 community-dwelling males, aged ≥70 years enrolled in the Concord Health and Ageing in Men Project were studied. Measurements were obtained at baseline (2005 - 2007) and 2-year follow-up (2007 - 2009). High risk prescribing was defined as polypharmacy (use of ≥5 medicines), hyperpolypharmacy (use of ≥10 medicines) and by the Drug Burden Index (DBI), a dose-normalised measure of anticholinergic and sedative medicines. Frailty was defined according to validated criteria. Odds ratios (OR) of frailty were modelled using logistic regression, and adjusted for sociodemographics and comorbidities.

Results

There were 9.4% participants who were identified as frail at baseline. At baseline, frail participants had adjusted ORs of 2.55 (95% confidence interval, CI: 1.69 - 3.84) for polypharmacy, 5.80 (95% CI: 2.90 - 11.61) for hyperpolypharmacy and 2.33 (95% CI: 1.58 - 3.45) for DBI exposure, compared with non-frail. Among the 1242 men who were non-frail at baseline, 6.2% developed frailty over two years. Adjusted ORs of incident frailty were 2.45 (95% CI: 1.42 - 4.23) for polypharmacy, 2.50 (95% CI: 0.76 - 8.26) for hyperpolypharmacy, and 2.14 (95% CI: 1.25 - 3.64) for DBI.

Conclusions

Older frail men were significantly more likely to be exposed to high risk prescribing than non-frail at baseline, and exposure to high risk medicines was significantly related to the development of frailty over two years.

Characteristics and criteria of the frail elderly: A review of frailty measures

Imaina Widagdo [1] Libby Roughead [1] Nicole Pratt [1]

[1] Quality Use of Medicines and Pharmacy Research Centre, University of South Australia, Adelaide, SA

Objective

To identify the common criteria used in measures of the frail elderly.

Methods

A comprehensive literature review on the frailty measures published in the peer reviewed literature.

Results

21 frailty measure studies were reviewed. Six dimensions of frailty were identified including: age, physical, psychological, social, environmental and medical dimensions. Frailty was generally characterised by the presence of problems in one or more assessed dimensions. One measure also considered assets as a characteristic that may offset frailty. The majority of frailty measures were multi-dimensional but the measures varied according to the number of dimensions they considered. All frailty measures included a physical dimension. Psychological and medical dimensions were considered in 12 and 10 measures respectively. Only one measure considered the environmental dimension. No uniform assessment criteria were observed across the frailty measures. For example, the physical dimension factors were assessed either by self-report or direct examinations of nutrition, muscle strength, energy levels, sensory ability, physical activity, mobility or disability. Only three of the 12 measures that assessed the psychological dimension used standardised measures, which were the mini-mental state examination (MMSE), the geriatric depression scale (GDS) or the centre for epidemiological study depression scale (CES-D). Assessment of the medical dimension was made according to the presence of diseases; number of medications or, laboratory markers.

Conclusions

Frailty was commonly characterised by the presence of deficits in the physical dimension. There was a variety of assessment criteria used among different frailty measures.

Fishing in a sea of indicators: Challenges with evaluating QUM in Australian RAC

Jodie Hillen [1] Agnes Vitry [1] Gillian Caughey [1]

[1] Quality Use of Medicines and Pharmacy Research Centre, University of South Australia, Adelaide, SA

Objective

To identify suitable medication-related quality of care (QOC) indicators for evaluating the quality use of medicines (QUM) in Australian residential aged care (RAC).

Methods

A systematic review of the scientific and grey literature using the PRISMA guidelines was conducted. Medline, Embase, CINAHL, Psychinfo, Google and relevant websites were searched for articles discussing the development, application or validation of medication-related QOC indicators relevant to aged care. Articles meeting the inclusion criteria were further assesssed for quality using the critical appraisal skills program (CASP). Key indicator qualities were extracted and synthesised using content analysis.

Results

127 of 1960 articles were deemed relevant and subsequently reviewed. Fifty articles met the inclusion and quality criteria, which identified 27 unique indicator sets. Twenty-six percent of the sets were developed for the Australian health care system, 52% addressed prescribing practices soley, 30% were developed specifically for aged care, 44% contained explicit indicators exclusively and 26% are currently operational (none in Australia). Whilst the majority of indicator sets have been developed through expert consensus techniques, few have been validated beyond this.

Conclusions

Whilst many potential indicators were identified, few have been specifically developed and validated for the evaluation of QUM in Australian RAC. The challenge is to select those indicators which best address the medication-related needs of Australian aged care residents and then to determine the suitability and feasibility of identified indicators for evaluating QUM in Australian RAC.

Evaluation of medication related problems in medication reviews: A comparative perspective?

Sukhpreet Kaur [1] Jason Roberts [1, 2, 3] Michael Roberts [1, 2, 4]

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[2] Quality Medication Care Pty Ltd, Brisbane, QLD

[3] Burns Trauma and Critical Care Research Centre, The University of Queensland, Brisbane, QLD

[4] Therapeutics Research Centre, Princess Alexandra Hospital, Brisbane, QLD

Objective

To evaluate medication related problems in residential facilities routinely reviewed by pharmacists.

Methods

This study included de-identified resident's health and medication data from six aged care facilities with regular medication reviews over 20 years was collected for 296 residential aged care residents by 3 accredited clinical pharmacists over a two year period. This data was then used as a baseline in analysing other published data for residential aged care facilities and for patients at home.

Results

A total of 802 (range 0 - 12) medication related problems were identified in patients prescribed 2 to 29 medicines, with a mean of 2.7 medicine related issues per review (95% confidence interval 2.43 - 2.98). An analysis of the literature showed that the length of service, inclusion criteria used and the definition of medicine related problems has great impact on the results obtained. However, application of the same criteria to the present data resulted in similar findings as the published Australian average for residents of aged care facilities and patients living independently at home (3.9 and 4.8 medicine related issues per patient respectively).

Conclusions

Medicine related issues identified during a pharmacist review varies widely between studies but can normalised by inclusion criteria, length of service and the nature of the identified issue. It is recommended that a benchmark for best practice be an average of <3 medication issues for patients receiving at least yearly reviews , with at least half actioned by medical practitioners.

A review of dose administration aids: Improving medicine management

Julia Gilmartin [1] Safeera Hussainy [1] Jennifer Marriott [1]

[1] Centre for Medicine Use and Safety, Monash University, Melbourne, VIC

Objective

To determine the accuracy and appropriateness of packing of pharmacy supplied dose administration aids (DAAs - blister packs and sachets) used in Victorian residential aged care facilities (RACFs) for medicine administration. To identify perceptions of DAA accuracy, contributing factors to inaccuracies and suggestions for improvement, from RACF and pharmacy staff.

Methods

Newly supplied DAAs at 49 Victorian RACFs were compared with RACF resident medicine records. Incidents identified included: discrepancies between DAAs and medicine records; medicines that shouldn't be packed according to pharmaceutical guidelines; and damaged or inappropriately altered/divided medicines. Participating RACFs and pharmacies completed a questionnaire to identify their perceptions of the problem.

Results

Victoria's overall incident rate was 17.3% (total incidents/total DAAs audited) affecting 11.6% of DAAs (total DAAs affected/total DAAs audited). Sachets had a higher incident rate (24.1% and 14.5%) compared to blister packs (14.9% and 10.5%). Top five incident types were: shouldn't be packed; addition; incorrect quantity; omission and damage. Rates of particular incident types varied between the two forms of DAA. Incident rates according to region (total incidents/total DAAs audited for that region) included: regional (28.4%), inner metropolitan (18.0%), outer metropolitan (15.6%) and rural (15.4%). Questionnaire results showed that RACF and pharmacy staff perceptions of DAA accuracy underestimated observed incident rates and factors that contribute to incidents included: technical issues, staff, communication and pharmacy DAA checking. Communication was a common suggestion to improve DAA accuracy.

Conclusions

Incident rates were higher than for previous studies and quality improvement activities are needed to improve pharmacy-supplied DAAs for RACFs.

The authors would like to acknowledge Denise van den Bosch and Clare Walsh for their contribution.

Pharmacy Practice: Practice Roles

Session Chair: Lynne Emmerton, Curtin University

Wednesday 14 December 2011, 11:00am – 12:30pm

Room P5-34, Playford Building

CP12-1

Safeera Hussainy, Monash University

Piloting the role of a pharmacist in a community palliative care multidisciplinary team

CP12-2

Edwin Tan, Monash University

Is there a role for pharmacists in general practice?

CP12-3

Sara McMillan, Griffith University

Nurse practitioners in community pharmacies: Now a reality, so what do they do?

CP12-4

Amy Tan, The University of Queensland

An exploratory study of medication supply and management in a rural community in Queensland

CP12-5

Louise Deeks, University of Canberra

Do pharmacy staff want to offer chlamydia screening?

CP12-6

Greg Kyle, University of Canberra

Can international experience make pharmacist prescribing work in Australia?

Piloting the role of a pharmacist in a community palliative care multidisciplinary team

Safeera Hussainy [1] Margaret Box [2] Sandy Scholes [1, 2]

[1] Centre for Medicine Use and Safety, Monash University, Melbourne, VIC

[2] Calvary Health Care Bethlehem, Melbourne, VIC

Objective

The resolution of drug related problems (DRPs) by a pharmacist in the community palliative care setting can potentially reduce medication misadventure and patient hospitalisation. The study objective was to pilot a model of care that supports the pharmacist's role in a community palliative care team.

Methods

Phase 1 (Development) involved undertaking a literature review; scoping the pharmacist's role; and creating tools for recording DRPs and interventions, a care pathway and evidence based patient information. These were implemented in Phase 2. Evaluation (Phase 3) of the impact of the pharmacist's role from the perspectives of the team members was undertaken using an online survey and focus group. Impact on clinical outcomes was determined by the number of patients screened to assess their risk of medication misadventure, and the number of medication reviews and interventions performed to resolve DRPs.

Results

The pharmacist screened 88.4% (n = 373/422) of patients referred to the palliative care service and undertook 52 home visits. Medication reviews were commonly conducted at the majority of home visits (88%, n = 46/52), and 113 DRPs were detected at this point. The pharmacist made 120 recommendations in relation to her interventions. All 20 of the survey respondents felt that the pharmacist helped improve their knowledge of palliative care medications. Similar findings were reported by the six focus group participants.

Conclusions

The inclusion of a pharmacist in a community palliative care team led to an increase in the medication-related knowledge and skills of its members, improved patients' medication management, and minimised related errors.

Is there a role for pharmacists in general practice?

Edwin Tan [1] Kay Stewart [1] Rohan Elliott [1] Johnson George [1]

[1] Centre for Medicine Use and Safety, Monash University, Melbourne, VIC

Objective

Studies from other countries have shown that pharmacists working collaboratively with other primary healthcare professionals can optimise patient outcomes. Our aim was to explore stakeholder views on the integration of pharmacists into Australian general practices.

Methods

Qualitative interviews with a sample of Australian general practitioners, other practice staff and pharmacists were undertaken. Interviews (n = 30) were transcribed verbatim, managed using Nvivo 9 and analysed for emerging themes using the framework approach. Interviews were continued until data saturation was reached.

Results

Five major themes emerged: the current GP-pharmacist relationship; the general practice pharmacist and models of collaboration; the pros and cons of integration; the barriers and facilitators of integration; and the viability and sustainability of the role. Various roles were identified for pharmacists in general practice including medication reviews, drug education and advice, drug use evaluation, new prescriber mentoring, case conferencing, adverse drug event monitoring and others. Pharmacist participants perceived integration as an opportunity for role expansion. Participants agreed that the practice pharmacist needed certain attributes including excellent clinical knowledge, competence, tact and communication skills. There were different views on the level of training and experience required by a pharmacist in this position. The practicalities, logistics and viability of pharmacist integration were also explored.

Conclusions

Our findings could guide the development of collaborative models of care involving pharmacists and other health professionals in general practice. The feasibility and effectiveness of such collaborations should be evaluated in prospective studies.

Nurse practitioners in community pharmacies: Now a reality, so what do they do?

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[1] School of Pharmacy, Curtin University, Perth, WA

[2] School of Pharmacy, Griffith University, Gold Coast, QLD

[3] Revive Clinic, Perth, WA

Objective

Nurse practitioners (NPs) can legally prescribe a range of medicines and perform clinical services. Some community pharmacies have purchased a Revive Clinic franchise to offer NP services to meet client demand for such services. The Revive Clinic is the dominant model in Australia and has been operating since 2008. This study explored the integration of Revive Clinic NPs in community pharmacies, to inform collaborative patient care.

Methods

Interviews and observational data collection were undertaken in August - September 2011 with five Revive Clinic NPs, 10 pharmacists, 12 pharmacy staff and 17 clients of the clinics, in five metropolitan and four regional sites in Western Australia. Telephone interviews were conducted with key staff of three of the regional sites. Questions explored the operation of the clinic, workflow arrangements and procedures in the pharmacy.

Results

As independent practitioners, the NPs perform patient management services within their self-declared scope of practice. Pharmacists' roles, including provision of Pharmacist Only Medicines, clinical monitoring services, advice and consumer medicines information, were not impacted by the NP. NPs complement these roles by providing more intensive and physical diagnostic services (e.g. ordering pathology) and prescribing via clinical guidelines. Clients were not pressured to have their NP-issued prescriptions or non-prescription product recommendations filled at that pharmacy.

Conclusions

Given the complementary nature of the NPs' and pharmacists' roles, further developments might focus on the ideal balance between independence of both practitioners and integration of the NP into the pharmacy team. The model suggests a strong future for collaborative patient care.

An exploratory study of medication supply and management in a rural community in Queensland

Amy Tan [1] Lynne Emmerton [1, 2] Laetitia Hattingh [3] Victoria Jarvis [1]

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[2] School of Pharmacy, Curtin University, Perth, WA

[3] School of Pharmacy, Griffith University, Gold Coast, QLD

Objective

This research explored issues with medication supply and management in a rural Queensland community, specifically: (1) the roles of rural healthcare providers in the medication pathway, (2) challenges facing these providers in provision of medication services, and (3) the community's medication-related needs.

Methods

A geographical mapping exercise enabled identification of a rural study community in Queensland, Australia. Interviews with 12 stakeholders external to this community informed the research topics based on the above objectives. These topics were then explored in interviews with 49 healthcare providers within the study community. Perspectives of local consumers (n = 69) were also sought regarding access to medication services.

Results

Thematically analysed interview data revealed general support for extended prescribing and medication supply/administration roles to improve access to medications. Healthcare providers and consumers reported difficulties in continuing medication therapy and reliance on hospital services for medical care and medication supply when primary care services were unavailable. Challenges impacting optimal medication management include ineffective medication information transfer between health service providers and inadequate medication support systems. Further exploration revealed potential models for rural pharmacists' increased involvement in the medication cycle, which is currently restricted by workforce capacity, prioritisation of dispensing tasks, and lack of remuneration pathway to support extended medication roles.

Conclusions

There is potential for pharmacists to better support the medication cycle and enhance medication management in rural areas. Models worthy of further exploration, to address the shortcomings, include tele-pharmacy, outreach services, sessional employment, and role extension for pharmacy support staff in rural areas.

Do pharmacy staff want to offer chlamydia screening?

Louise Deeks [1, 2] Gabrielle Cooper [1] Ben Gilbert [1] Marian Currie [2] Rhian Parker [3] Sarah Martin [2, 4] Rendry Del Rosario [4] Jane Hocking [5] Frank Bowden [2, 4]

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[3] Australian Primary Health Care Research Institute, The Australian National University, Canberra, ACT

[4] Canberra Sexual Health Centre, Canberra Hospital, Canberra, ACT

[5] Melbourne School of Population Health, The University of Melbourne, Melbourne, VIC

Objective

To determine the acceptability of a pharmacy staff training package and pharmacy-based chlamydia screening when participating young people and the pharmacy are remunerated.

Methods

Training comprised two manuals (chlamydia knowledge, study processes), practical sessions and assessment. Acceptability was determined by: number of staff completing training; total number of samples collected; anonymous questionnaire and focus group responses.

Results

Of 54 staff from 6 pharmacies, 25 completed all training, 35 completed the questionnaire and 15 attended focus groups. Over 29 days, 671/979 urine samples from unique individuals were returned. Pharmacy assistants recruited the majority of participants. The training was ranked as effective (mean visual analogue scale score >8.5). Before the study 31 (91%) respondents never/only sometimes discussed STIs with consumers but during the study 28 (90%) of these recruited participants. Reported barriers to screening were perceived consumer embarrassment, privacy concerns and increased workload. In respect to continuing the program, 14 staff (41%) wanted to continue, 14 (41%) were unsure (citing repeat testers and the financial reward given to participants as reasons) and 4 (12%) did not want to continue.

Conclusions

Pharmacy staff were satisfied with their training and rapidly recruited a large number of people. Recruitment by pharmacy assistants demonstrates the significant role para-professionals can play in public health. Although pharmacy staff had privacy concerns, the speed of recruitment suggests lack of privacy was not an issue for young people. Implementation of strategies to minimise repeat testers, promote training and manage the pharmacy workload would make this model more acceptable to pharmacy staff.

Can international experience make pharmacist prescribing work in Australia?

Greg Kyle [1] Lisa Nissen [1]

[1] Discipline of Pharmacy, University of Canberra, Canberra, ACT

[2] School of Pharmacy, The University of Queensland, Brisbane, QLD

Objective

To utilize international experience to determine the evidence base for a pharmacist prescribing model in Australia. The aim was to determine the evidence density across practice settings and within a health evaluation framework to improve patient access to prescribing services and continue the progressive reform commenced in October 2010 when nurse practitioner and midwife access to PBS and MBS items was introduced.

Methods

Major medical databases were searched for literature regarding pharmacist prescribing. Each reference was assessed across 6 domains: Type; Country; Practice setting; Prescribing model; Research subject; and the Australian Institute of Health and Welfare (AIHW) National Health System Performance Framework evaluation criteria: Accessible; Appropriate; Capable; Continuous; Effective; Efficient; Responsive; Safe; Sustainable.

Results

From 51,417 articles identified, 74 were relevant to the study aim. Prescribing by pharmacists in the UK was most widely reported (31 articles) utilizing independent, supplementary, protocol and repeat prescribing. Australia contributed 26 studies with protocol, formulary and referral methodologies. The top five AIHW criteria indicated pharmacist prescribing were "Capable", "Appropriate", "Effective", "Safe" and "Efficient". Hospital and GP/community practice settings provided the bulk of the evidence in support of pharmacist prescribing.

Conclusions

Pharmacist prescribing has an evidence base across the spectrum of prescribing models and AIHW evaluation criteria. Australian pharmacist prescribing should commence in collaboration with GP and hospital practice to further drive health reform, extend scope of practice and improve patient access to prescribing services.

Poster Presentations

Do pharmacy students value the National Prescribing Curriculum as a learning resource?

Juanita Westbury [1] Santosh Khanal [2] Greg Peterson [1] Michelle Koo [2] Yeqin Zuo [2] Anna Ryan [3] Chris Harnden [4] Justin Tse [5] Tom Buckley [6]

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[2] NPS: Better Choices, Better Health, Sydney, NSW

[3] Austin Health, The University of Melbourne, Melbourne, VIC

[4] Rural Health Academic Centre, The University of Melbourne, Melbourne, VIC

[5] Clinical School - St Vincent's Hospital, The University of Melbourne, Melbourne, VIC

[6] Sydney Nursing School, The University of Sydney, Sydney, NSW

Objective

The National Prescribing Curriculum (NPC), freely available to Australian pharmacy, medical and nurse practitioner schools, is a series of 27 online clinical case-based modules on quality use of medicines and good prescribing. The School of Pharmacy, University of Tasmania (UTAS) has used the NPC in 4th year of its undergraduate course since 2009.

Methods

In 2010, 27 UTAS students (64% of Year 4) completed an NPC evaluation survey. In 2011, another cohort of 40 students participated in a multidisciplinary quality assessment study in which students' perception of the usefulness of answering multiple choice questions (MCQs) before and after completing the modules was evaluated.

Results

From the 2010 survey, 81.5% and 96.0% of students found the modules and the expert clinical feedback useful, 74.0% believed their knowledge was extended, and 92.3% said they would attempt further modules. In the 2011 study, 40.0% of pharmacy students found the MCQs at pre-module stage easy compared to 12.4% of medical students ($n = 14/113$; $p < 0.001$). However, more pharmacy students (80%) found the pre-module MCQs a useful learning tool than medical students (73.1%; not statistically significant, $p = 0.18$). Almost all students found the post-module MCQs (pharmacy 100%, medical 97.8%; $p = 0.87$) and feedback (pharmacy 97.5%, medical 95.5%; $p = 0.51$) useful, and said that completing NPC modules helped them answer the MCQs (pharmacy 95.0%, medical 94.0%; $p = 0.29$).

Conclusions

Pharmacy students consider the NPC to be a valuable learning resource. Further analysis of the quality assessment study will determine whether the perception of easiness by pharmacy students corroborates with their knowledge.

Influence of professional experience placements on selection of internship site

Kay Stewart [1] Anne Leversha [1, 2]

[1] Centre for Medicine Use and Safety, Monash University, Melbourne, VIC

[2] Latrobe Regional Hospital, Traralgon, VIC

Objective

To identify the impact of professional experience placements on selection of internship site.

Methods

Monash University pharmacy students participate in four three-week practical experience placements (PEPs) during their third and fourth undergraduate years; two PEPs are conducted at metropolitan hospitals, one in metropolitan community pharmacies, and another in rural sites. Fourth year students were surveyed in April after completing 2 - 3 and again in October after completing all placements.

Results

Of the 180 students enrolled, 100 (56%) responded to the April survey and 60 (33.3%) to the October round, only 9 of whom had not previously responded. Total responses: n = 109 (61%). Of the April respondents, all had completed at least one hospital PEP; 23 two hospital PEPs; 22 both metropolitan community and rural; 32 metro only and 41 rural only. Most of the 89 students intending to undertake an internship in Australia rated the influence of the PEPs on their choice of intern placement site as "major" (n = 38; 43%) or "moderate" (n = 39; 44%). Of these, the metropolitan hospital site was identified as being most influential by 61 (69%); 11 (10%) said metro community and 5 (5%) said rural community pharmacy. Students who indicated that they gained information from their PEPs that was useful in their choice of site "clinical experience", "pharmacy team perspectives" and the site's "intern training program" as contributing to their decisions.

Conclusions

The PEPs have a strong influence on students' intern site preference.

Using iFeedback increases measures of pharmacy student satisfaction

Simon Young [1] Katherine Baverstock [1]

[1] Discipline of Pharmacy, RMIT University, Melbourne, VIC

Summary

Considerable emphasis is placed upon such survey results as measures of student satisfaction, engagement and their perception of the quality of the course and teaching staff; both within institutions and as a comparative measure. However, a perennial difficulty exists in the expectation of students (and consequently institutions) to furnish high-quality and detailed feedback on assessed works with the time constraints required for the provision of such feedback. This is particularly acute where the student cohort is large or where the cohort is especially discerning; these are challenging to pharmacy. Moreover, the drive to collect flattering survey data leads to a pressure towards grade inflation, to which junior staff members are evidenced to be susceptible. Unlike most other offerings in the market, iFeedback runs as a stand-alone application on the assessor's computer; removing the limitations of web-based interfaces. Using a simple grading workflow based upon a marking rubric, the net result is a considerable improvement in the efficiency and reliability of the assessment process. In development, consistent anecdotal evidence supporting a substantially reduced assessor workload together with the rapid delivery of results and feedback to students has resulted. Moreover, a limited trial of iFeedback in semester 1, 2011 lead to an improvement of 33% on the University-wide satisfaction in the provision of feedback.

Evaluation of a novel IT teaching tool in pharmacy practice

Peter Gee [1] Angus Thompson [1] Luke Bereznicki [1]

[1] School of Pharmacy, University of Tasmania, Hobart, TAS

Objective

Third and fourth year students in the pharmacy practice stream at the Tasmanian School of Pharmacy are taught aspects of pharmacy practice using a simulated learning environment. This poster describes the development and evaluation of an information technology innovation designed to better approximate community pharmacy practice in this setting.

Methods

Previously, students were given a written case history along with a list of the hypothetical patient's medications, and asked to dispense a mock prescription using the FRED dispensing software. During 2010 a software program was developed and trialled that created tailored medication histories for each student, so a student could see a list of their patient's medications in the FRED dispensing software instead of a written drug list. Extra additional information such as allergies and patient's notes were also included. Third year students were surveyed at the end of Semester Two to evaluate this initiative and its effect on their learning experience.

Results

Feedback was received from 41 students. Respondents were very supportive of the system, 93% of respondents agreed that it added real-world relevance to the practical classes. Crucially, 78% of respondents indicated they would like to see the initiative continued into the future.

Conclusions

The customised software written to create detailed dispensing histories for students in our pharmacy practice classes provided a useful addition to the simulated learning environment.

Employers' and supervisors' opinions of La Trobe pharmacy graduates

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Objective

The faculty responsible for the Bachelor of pharmacy course at La Trobe University, Bendigo campus undertakes self-evaluation processes to maintain and enhance teaching methods and curriculum. This aims to ensure the quality of graduates. This study was conducted to validate a survey tool to assess employers' and supervisors' opinions of La Trobe pharmacy graduates and to use the data obtained to explore these opinions.

Methods

Cross-sectional survey of practicing Victorian pharmacists with experience supervising and/or employing graduates from La Trobe University's, Bendigo campus.

Results

Validation of the survey tool was demonstrated through high Cronbach α coefficients, demonstrating internal consistency, and Spearman rank order correlations. Most of the competency standards and domains were perceived by employers and supervisors to be met at a high standard. Generally scores for interns were lower than for graduate pharmacists.

Conclusions

La Trobe University's Bachelor of Pharmacy course was perceived to adequately prepare graduates for their role as a pharmacist.

Transformation of health professional roles in an interprofessional learning workshop

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Objective

To investigate the impact of a sociocultural interprofessional learning (IPL) intervention on health professional (HP) development and team dynamics.

Methods

Four pharmacists and 3 GPs participated in an interactive problem-based IPL workshop. Participants were required to jointly reflect on a clinical scenario and identify issues, goals and strategies for optimising patient management. Audio and video recordings were transcribed, and individual HP behaviours and group interactions analysed for evidence of transformations. Behaviour change was observed within the context of three domains: participant engagement within the group, body language and discourse.

Results

Individual HPs differed on entry in topic interest, confidence, professional concerns, experiences and perspectives. By the end most showed evidence of role transformation to a level of common understanding, displaying trust, respect, and interprofessional collaboration. Some participants evolved into team members while others evolved into team leaders. One did not participate as either leader or member.

Conclusions

Previous research has involved bringing together HPs and using interactive educational methods to facilitate interprofessional engagement, understanding and knowledge outcomes. This innovative study used sociocultural theory as a framework for investigating role transformations during the IPL process. Three distinct roles evolved: team leader, team member and outsider, with the team leader emerging as most critical in shaping team dynamics through engaging, facilitating, overcoming barriers and achieving team goals. The extent and rate of individual transformation was influenced by personality, gender, past experiences, professional socialisation and stereotypes. Future work should explore the sustainability and impact of "transformation" on long-term collaborative behaviours in practice.

Factors predicting GP - pharmacist interprofessional collaboration: A structural equation modelling approach

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Objective

To investigate factors predicting GP - pharmacist interprofessional collaboration.

Methods

Self-administered questionnaires were administered to 586 pharmacists in eight divisions of general practice in New South Wales, Australia. The questionnaires measured frequency of collaborative behaviours as well as practitioner attitudes on a five-point scale. The questionnaire was developed after a literature review and qualitative interviews with GPs and pharmacist and is based on environmental, practitioner and interactional factors believed to influence interprofessional collaboration. Structural equation modelling was used to determine the factors that predict GP - pharmacist collaboration.

Results

Two hundred and twenty-four pharmacist surveys (38%) were completed and returned. The "pharmacist's relationship with the GP" was found to be the strongest predictor of collaboration and this factor was in turn influenced by the "pharmacist's perception of the GP". Other factors found to predict collaboration included the pharmacist's age, the proximity of the pharmacy from the GP's surgery, the pharmacist's participation in interprofessional continuing education events and whether the pharmacy was Quality Care Pharmacy Program (QCPP) accredited. The final model had reasonable fit indices (χ^2 ratio = 1.54, RMSEA = 0.052, CFI = 0.945).

Conclusions

An understanding of the factors which predict GP - pharmacist collaboration may serve to inform the development of strategies to increase and improve future collaboration in the interest of better quality use of medicines and health outcomes.

This research is funded by the Australian Government Department of Health and Ageing under a postgraduate research scholarship forming part of the Fourth Community Pharmacy Agreement Research and Development program.

Could community pharmacies help to meet the unmet health needs of New Zealand's Youth?

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Objective

Although young people are generally considered to be fit and healthy, many have unmet health issues. Community pharmacies are developing services in areas relevant to youth health and are readily accessible to young people. Despite this potential, there have been few studies in this area. This research aims to provide evidence of the potential for community pharmacy to help meet unmet youth health needs in New Zealand (NZ). The objectives of the study were: to quantify the proportion of NZ secondary school students experiencing healthcare access barriers that would not be a problem if they were accessing healthcare through pharmacies; to characterise and quantify the unmet health needs of young people in NZ secondary schools which are relevant to community pharmacy service provision.

Methods

Descriptive secondary analysis of the Youth '07 health and wellbeing survey data.

Results

Seventeen percent of all students had been unable to access care when needed in the last 12 months. Of these students, 86.0% cited barriers to accessing healthcare that would not be considered as barriers to accessing healthcare from a community pharmacy (e.g. couldn't get an appointment). Thirty percent of students had difficulty accessing healthcare in the past 12 months for certain health issues. Just over half of these students cited a health issue for which community pharmacies provide services (e.g. minor health issues; smoking cessation).

Conclusions

This research indicates that there is potential for community pharmacies to improve healthcare access for young people in NZ, and the role of pharmacy in youth health should be explored further.

An evaluation of community pharmacists' responses to ethically challenging requests for emergency contraception

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Objective

The aim of this study was to assess the management of ethical dilemmas involving over-the-counter requests for emergency contraception in community pharmacies.

Methods

Mystery patient visitations were presented to 23 consenting community pharmacies in the Gold Coast region during December 2010. Trained actors attended participating pharmacies as mystery patients, and presented one of two ethically challenging scenarios involving a request for emergency contraception. Semi-covert data was collected throughout the mystery patient visits, utilising qualitative methods of observation, and open questioning. Immediately following each pharmacy interaction, the mystery patient relayed a verbal transcript to the research officer, to eliminate bias and premature analysis.

Results

The data suggests that there are identifiable learning and training gaps amongst pharmacists and pharmacy staff with respect to professional and ethical obligations associated with complicated Schedule 3 (Pharmacist Only) medicines requests. Deficits were particularly noted in history taking, clinical assessment, comprehensive counselling, utilisation of professional resources and ethical reasoning skills.

Conclusions

Targeted training is required across community pharmacy staff to enhance patient confidence in community pharmacy and its' provision of advanced services. However, the impact of time pressures and financial burdens on the quality of pharmaceutical services need to be acknowledged. Further studies could enable development of training tools to address practice shortcomings that were identified through this pilot research.

Development of a behavioural assessment scale for the Australian pharmacy context

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Objective

The practice of pharmacy requires a unique set of professional behaviours, which require development over time. The Australian pharmacy profession lacks a standardized method to ascertain pharmacists' mastery levels of these specific behaviours. The aim of the study is to develop a behavioural professionalism assessment scale for the Australian pharmacy context.

Methods

We conducted a literature review of existing pharmacy professionalism assessment tools. The review included peer reviewed English language articles only with no limit on date of publication. We identified the Behavioural Professionalism Assessment (BPA) scale developed and validated in United States for preceptors to assess pharmacy students. An academic team from The University of Western Australia (UWA) adapted it for the Australian context (with permission).

Results

We identified seven international articles. Three of them used a professionalism tool specific to pharmacy. No Australian research was identified. Two of these three articles assessed professional attitudes and one BPA assessed professional behaviours. We adapted the BPA to the Australian context for readability and terminology, as well as modified it from a preceptor assessment questionnaire of student behaviours (5 point rating scale) to a student or practicing pharmacist self-administrated questionnaire (5 point Likert frequency scale).

Conclusions

We identified the BPA - a professionalism preceptor assessment questionnaire - and adapted it to a self assessment questionnaire to suit the Australian pharmacy context. The self assessment questionnaire will be piloted at The University of Western Australia. We will perform exploratory factor analysis and will derive reliability and validity coefficients.

Population-based studies highlighting the prevalence of sleep-related disorders in adults with respect to ethnicity

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Objective

To eliminate disparities in health outcomes due to sleep disorders there is a need to not only focus on social and environmental factors, but also possible biological or genetic differences. This paper highlights studies investigating ethnic prevalence of certain sleep-related disorders in different populations.

Methods

Recent studies focusing on ethnic differences in sleep-related disorders representing three different regions were selected.

Results

A total of eight papers were reviewed; New Zealand (n = 3), USA (n = 3) and Singapore (n = 2). Studies showed that there were significant differences between ethnic populations in certain sleep-related disorders. In New Zealand, studies showed Maori and Pacific Islanders have higher prevalence and were at higher risk for sleep-related disorders compared to Caucasians and Asians. In the USA, African-Americans showed higher prevalence for sleep-related disorders compared to Caucasians and Hispanics. As for Singapore, the studies compared three major ethnicities in South East Asia: Chinese, Indians and Malays. Studies showed that Chinese have the lowest prevalence and the lowest risk for sleep-related disorder compared to Indians and Malays.

Conclusions

Differences in prevalence of sleep-related disorders with respect to ethnicity have implications in the development of treatment and services. There is a need for more consistent and reliable ethnic data for sleep-related disorders to enable the development and implementation of effective prevention, intervention and treatment.

Changes in medication beliefs over time in adherent and non-adherent patients post myocardial infarction

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Objective

To determine if medication beliefs changed over time in adherent and non-adherent patients post myocardial infarction (MI).

Methods

Patients discharged from hospital after experiencing a MI were followed over one year. Patients were interviewed at 6 and 12 months post discharge utilising the Beliefs about Medicines Questionnaire (BMQ) Specific. Medication adherence was measured using a medication possession ratio of their lipid lowering agent; <80% was categorised as non-adherent. The median BMQ differential was compared within four patient groups; adherent at 6 and 12 months; non-adherent at 6 and 12 months; adherent at 6 months and non-adherent at 12 months and; non-adherent at 6 months and adherent at 12 months. An increase in the BMQ differential indicated higher necessity beliefs.

Results

At 6 months there were 139 patients prescribed a lipid lowering agent of whom 118 (84.9%) were adherent compared to 97 (73.5%) of 132 patients prescribed this at 12 months, p = 0.02. Patients adherent throughout had a significant increase in their necessity beliefs (p = 0.02; small effect size [r = -0.25]), whilst those non-adherent throughout had a non-significant decrease in their necessity beliefs. There was no change to beliefs for patients adherent at 6 months and non-adherent at 12 months. Patients non-adherent at 6 months and adherent at 12 months had a non-significant increase in their necessity beliefs (p = 0.06; large effect size [r = -0.57]).

Conclusions

Beliefs changed between 6 and 12 months. Adherent patients at 12 months had a higher belief in the necessity of their medication than at 6 months.

Characteristics of hyperkalaemia cases amongst hospital inpatients: Aetiology, management and response to treatment

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Objective

This research explored underlying causes of hyperkalaemia amongst hospital inpatients, analysing associations with specific medications and other risk factors, and evaluating clinical management and response to treatment.

Methods

This prospective cohort study analysed incident cases of hyperkalaemia observed over three months. Cases were identified using an automated notification system and subsequently analysed to assess possible relationships with various risk factors. The study also evaluated clinical management and response to interventions.

Results

50 cases were analysed; 35 male (70%) and with a mean age of 78.5 years. Common diagnoses included diabetes mellitus (40%) and ischaemic heart disease (34%). 22 subjects (44%) had a documented diagnosis of renal failure. Hyperkalaemia was thought to be attributable to drug treatment in 41 subjects, including angiotensin converting enzyme inhibitors (n = 11), angiotensin receptor blockers (n = 5) non-steroidal anti-inflammatory drugs (n = 3), and spironolactone (n = 8). In many cases, several drugs were thought to contribute concurrently. The mean length of stay was 14.8 days and four subjects died, but no deaths were attributed to hyperkalaemia. 56% of cases were managed with cation exchange resin, 12% received combined insulin/glucose and 8% were treated with calcium gluconate. All but one case hyperkalaemia were correctable.

Conclusions

Drugs contributed to the majority of hyperkalaemia cases here. Polypharmacy, advanced age, and multiple medical comorbidities are known risk factors for adverse outcomes from hospitalisation. Caution is required when treatment involves medications associated with hyperkalaemia, but conventional approaches to management were effective in the management of majority of cases in this study.

Knowledge and behaviours of osteoporosis prevention in suburban community in Khon Kaen Province, Thailand

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Objective

To explore the knowledge of communities in Thailand regarding osteoporosis prevention, and identify demographic predictors of preventive behaviours.

Methods

A structured interview was used to measure participant's knowledge of calcium and osteoporosis and behaviours promoting bone health including milk consumption, calcium intake, exposure to sunlight and weight bearing movement. People ≥ 50 years of age in each house in a suburban community were asked to participate in the survey. Frequency distributions were generated for knowledge, preventive health behaviours and demographics. Association between demographic-factors and preventive behaviours were assessed by Chi-squared test.

Results

A total of 150 people were interviewed. In response to the 13 five-choice knowledge questions, only 4% (n = 6/150) of respondents answered >7 questions correctly with a mean knowledge score of 4.7 (SD = 1.78). With regard to behaviours promoting bone health, on average respondents consumed milk 3 days/week (SD = 2), whilst taking calcium 1.4 days/week (SD = 1.9). A median of exposure to sunlight 20 minutes/day (IQR: 10, 60) in 5.6 days/week (SD = 1.9) and weight bearing movement 20 minutes/day (IQR: 10, 40) in 5.7 days/week (SD = 1.7). Factors statistically significantly associated with milk consuming, calcium intake, and exposure to sunlight, were occupation and having heard about calcium. None of studied demographic factor statistically significantly associated with undertaking weight bearing movement.

Conclusions

There is a need to design interventions to promote osteoporosis prevention and calcium consumption from various sources. Thai communities had insufficient knowledge of calcium and osteoporosis. Having heard about calcium showed to determine preventive behaviours.

Women's perception of alendronate and bone health

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Objective

Alendronate belongs to the bisphosphonate drug class, which exhibits effects on bone. Since late 1996, alendronate has been indicated in Australia as a first line agent in the prevention and treatment of osteoporosis, a condition with greater prevalence amongst women than men. Consequently, this qualitative research project aims to gain a greater insight into women's perception of alendronate and the bones, via the reporting of personal views and experiences.

Methods

A descriptive, qualitative study design was adopted for this research project whereby data were collected through semi-structured interviewing. Women who were either current users, or previous users, of alendronate were invited to participate through 7 participating community pharmacies. An initial question guide was formulated and adapted according to any emergent themes throughout the data collection period. Subsequent verbatim transcriptions and thematic data coding followed.

Results

Nine women were interviewed. Ten primary themes were extracted from the data, with some overlap between thematic categories. These themes included: perceived reason for use, information sources and influencing factors, patient knowledge, adherence, formulation of a routine, benefits of alendronate use, perceived disadvantages and fears, use of additional supplementation and exercise-related therapies, lifestyle changes and the pharmacist's involvement. Collectively, these themes gave a wide overview of the perceptions of women in this context.

Conclusions

The findings of this study provide additional insight into womens' perceived reasons for alendronate use. Notable gaps in knowledge and specific lifestyle-related changes have been identified, indicative of the importance of empowering women by providing this information.

"Knowing how" is not enough: An empirical and theory based investigation of why people with asthma do not maintain correct inhaler technique over time

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Objective

The aim of this study was to determine the patient-, education- and device-related factors that predict inhaler technique maintenance.

Methods

Thirty one community pharmacists were trained to deliver inhaler technique education to people with asthma. Pharmacists evaluated (based on published checklists), and where appropriate, delivered inhaler technique education to patients (participants) in the community pharmacy at baseline (Visit 1) and one month later (Visit 2). Data were collected on participant demographics, asthma history, current asthma control, history of inhaler technique education and a range of psychosocial aspects of disease management. Stepwise backwards logistic regression was used to identify the predictors of inhaler technique maintenance at one month.

Results

One hundred and forty five and 127 participants completed Visits 1 and 2 respectively. At baseline, 17% of patients (n = 24) demonstrated correct technique (score 11/11) which increased to 100% (n = 139) after remedial education by pharmacists. At follow up 61% (n = 77) of patients maintained correct technique. The predictors of inhaler technique maintenance were: use of a Dry Powder Inhaler (DPI) over a pressurised Metered Dose Inhaler (pMDI) (OR 2.6), having better asthma control at baseline (OR 2.3) and being more motivated to practice correct inhaler technique (OR 1.2) (χ^2 (n = 125,3) = 16.22, p = 0.001).

Conclusions

Contrary to what is typically recommended in previous research, correct inhaler technique maintenance may involve more than repetition of instructions. This study found that past technique education factors had no bearing on technique maintenance, whereas patient psychosocial factors (motivation) did.

Asthma management by patients purchasing salbutamol over the counter from community pharmacy

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Objective

Due to the easy availability of reliever medications (such as salbutamol) available over the counter (OTC) from pharmacies in Australia, there is a concern that asthmatic patients will not be managed effectively according to the current guidelines. The aim of this study was to determine whether patients who purchase the reliever salbutamol as an OTC product from pharmacies are managing their condition adequately according to accepted clinical guidelines.

Methods

A structured questionnaire, administered to patients presenting to a community pharmacy requesting the reliever salbutamol as an over the counter sale was undertaken to investigate the patient's level of asthma control as well as their use of preventer medications, frequency of doctor visits and ownership of an Asthma Management Plan (AMP).

Results

18 patients participated in the study. Of those 35% did not use preventer medications even when indicated. Only 50% reported regular visits to their doctor and only 22% were in possession of a written AMP.

Conclusions

This study concluded that patients who purchase salbutamol OTC were not managing their asthma according to the guidelines that are currently in place, with a substantial proportion of patients unlikely to use inhaled corticosteroids even if indicated or prescribed. These patients also visit doctors less often and are less likely to possess an asthma management plan, resulting in poor health outcomes for these patients.

Implementation strategies used to disseminate information about new asthma management tools in Western Australia

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Objective

Two asthma management tools (Short Acting Beta Agonist (SABA) guidelines for pharmacists and the Asthma Action Plan card) were developed to facilitate best practice in asthma care. The objective of the implementation project was to publicise and implement the use of the tools into practice. It was envisaged that successful implementation would require a widespread, collaborative and long-term approach.

Methods

A key stakeholder group was convened to collaborate on the project, which included representatives from The University of Western Australia, the Health Department of Western Australia, the Asthma Foundation of Western Australia and the Pharmaceutical Society of Western Australia. Target groups included all health professionals involved in asthma management and consumers. The strategy was to provide information to target groups multiple times, in a variety of ways, to reinforce the message. Dissemination methods included; direct detailing, lectures, workshops, web-based information, emails and printed resources.

Results

In the four month implementation period >45,000 Asthma Action Plan cards were distributed throughout Western Australia. Direct detailing was carried out in >400 community pharmacies. Lectures and workshops reached (n ~ 1800) health professionals and consumers. Emails, e-newsletters and e-news publications were sent to members by professional organizations (n = 13) or media outlets. Printed media included newspaper articles (n = 5) and journal articles (n = 2).

Conclusions

Stakeholder collaboration provided access to a variety of resources that achieved the widespread dissemination of information.

P-021

Evaluation of the Community Pharmacy "ABC" pilot quit smoking service on smoking cessation outcomes and the provision of smoking cessation pharmacotherapy

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Objective

To determine the effectiveness of the Community Pharmacy "ABC" (CPABC), a quit smoking pilot on smoking cessation outcomes and the access to smoking cessation pharmacotherapy.

Methods

A descriptive study involving quantitative and qualitative data of the CPABC quit smoking pilot was undertaken. 282 patient service documents were available for analysis (n = 282). A retrospective analysis of smoking cessation pharmacotherapies and quit card data from participating pharmacies (n = 20) was undertaken. Data were entered and analysed using IBM SPSS Statistics and thematic analysis was undertaken for the qualitative data.

Results

Self-reported quit rates at four weeks, eight weeks and six months were 53%, 44% and 38% respectively. Quit rates were greater in non-highly dependent smokers when compared to highly-dependent smokers. Quit rates were greater for NZ European and European compared to other ethnicities. Five main themes identified that may have influenced quit rates were; motivation, support, correct and appropriate use, side effects and alternatives to nicotine replacement therapy (NRT). There was an increase in the provision of subsided NRT after the commencement of the pilot with a general increase in both the quantity and number of prescription items dispensed. The provision of over-the-counter (OTC) NRT remained consistent prior to and during the pilot with no overall change in the volume of OTC NRT sales.

Conclusions

Outcomes from this study are encouraging. Community pharmacy is well positioned to deliver smoking cessation services and has the skills and capacity to be a recognised provider of smoking cessation service.

The feasibility of implementing the Ministry of Health's "ABC" smoking cessation in New Zealand community pharmacy

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Objective

The aim of this study was to determine the barriers and facilitators that need to be considered for the successful implementation of a quit smoking service in a community pharmacy setting in NZ.

Methods

Cross sectional study design involving self-completion postal questionnaires was undertaken. Participants were pharmacy staff members aged 18 years or over, who participated in the Community Pharmacy "ABC", a quit smoking pilot in West Auckland and Canterbury. A mixed format questionnaire, containing qualitative and quantitative sections, was posted to 124 pharmacy staff in West Auckland, and 225 pharmacy staff in Canterbury, NZ. Quantitative data was entered and analysed using IBM SPSS Statistics version 19 and thematic analysis was used to evaluate qualitative data.

Results

Overall response rate was 17%. West Auckland's response rate was 40%, and Canterbury 5%. Barriers identified were; lack of time, financial reimbursement, and documentation. Facilitators of the service were; "Quit Card" provision, staff smoking cessation training, tailored resources and access to community pharmacy. Most staff held positive attitudes towards smoking cessation services, and would continue to provide the service in the future. A possible association between the number of prescription items dispensed daily by a pharmacy with difficulty in asking patient' smoking status was identified.

Conclusions

The "ABC" model of smoking cessation support can be successfully implemented in community pharmacies in NZ. Key barriers and facilitators identified such as refined service documentation using electronic systems, appropriate financial reimbursement and an approved provision "Quit Card" system will need to be considered.

Exposure to tobacco smoke in pregnancy: A survey of out-patients

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Objective

To gather information about pregnant women's smoking patterns, attitudes towards smoking cessation and treatment/support preferences.

Methods

Pregnant women attending the out-patient pregnancy clinics of The Royal Women's Hospital and The Mercy Hospital for Women were asked to complete a questionnaire regarding their socio-demographics, smoking habits and attitudes towards quitting. Data are currently being entered into an SPSS database (Version 16.0).

Results

Of the 553 pregnant women who completed the questionnaire 38 (7%) were smokers; 29 (5%) were daily smokers, 9 (2%) were occasional smokers and 168 (31%) were ex-smokers. The median (interquartile range) for motivation and confidence to quit were 7 (5 - 10) and 4 (3 - 8), respectively, on a scale of 1 to 10 (very low - very high). The main treatment/support preferences reported by smokers were patch (n = 9, 36%), Quitline (n = 4, 16%), tablet (n = 3, 12%) and counselling (n = 2, 8%). Two in five pregnant women who smoked reported that their health professionals did not discourage them from smoking during pregnancy. The study is in progress.

Conclusions

The prevalence of smoking found in this study is lower than previous studies, which could be attributed to the self-reporting method used. Health professionals should be more proactive in offering appropriate smoking cessation support to pregnant women. Our findings could inform the development of an out-patient smoking cessation program for pregnant women.

Medicine use and safety whilst breastfeeding: Investigating the perspectives of community pharmacists in Australia

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Objective

To investigate Australian community pharmacists' decision-making around medication use and safety in breastfeeding.

Methods

An anonymous postal survey was sent (October 17th, 2011) to a national random sample of 1200 community pharmacies.

Results

As of October 26th, 85 pharmacists have responded (54% female). 55% had children and 70% had breastfeeding experiences for more than 27 weeks. Respondents were generally supportive of breastfeeding, agreeing with supportive statements: "Breastfeeding is more convenient than formula feeding", and disagreeing with unsupportive statements: "In most cases, a breastfeeding mother must temporarily stop breastfeeding her baby while she is taking prescription medications". 88% had, on average, at least one conversation per week about medicine use in breastfeeding and 94% were confident about supplying or counselling on medication during breastfeeding. The most commonly used resources were drug company information, the Australian Medicines Handbook, and dedicated books like the Royal Women's Pregnancy and Breastfeeding Medicines Guide. 80% believed the available information about medicines and breastfeeding to be adequate and 85.9 % thought it is readily accessible. Over one-third of pharmacists were unaware that ibuprofen and metronidazole are considered compatible with breastfeeding. 82% were able to name at least one medicine that may decrease breast milk supply; pseudo-ephedrine was most commonly named.

Conclusions

Preliminary results indicate that community pharmacists are supportive of breastfeeding, regularly discuss medicine use in breastfeeding and are confident of their ability to do so; however, their knowledge may be variable.

Did landmark studies on the effects of menopausal hormone therapy influence usage patterns in Australia?

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Objective

To evaluate usage patterns and determine any effect of landmark studies published between 1992 and 2010 on the usage of menopausal hormone therapy in Australia over the same time period.

Methods

Annual dispensing data were obtained for concessional and Veterans beneficiaries for each menopausal hormone therapy available on the Pharmaceutical Benefits Scheme (PBS) between January 1992 and December 2010. The dispensing data were converted to defined daily dose (DDD)/year and accumulated into; oestrogen only, progestogen only, combination oestrogen and progestogen HRT categories and total hormone therapy usage. These categories were plotted against year to analyse usage trends over time. The Pearson's correlation coefficient (K) was calculated to assess correlations between usage trends for each hormone therapy group.

Results

During the study period, total Australian menopausal hormone therapy usage experienced growth and decline. Market growth was evident from 1992 until 2001, where usage peaked and then substantially decreased from 2002. Menopausal hormone therapy usage reached its lowest point in 2010. Total hormone usage was highly correlated with oestrogen use (K = 1.00) and well correlated with progestogen usage (K = 0.84). Oestrogen and progestagen usage were also well correlated (K = 0.83). The only studies which appeared to have any impact on Australian hormone usage were HERS II and WHI.

Conclusions

Australian menopausal hormone therapy usage was not altered by the publication of many landmark studies. The WHI trial produced the most substantial effect on menopausal hormone usage patterns.

The impact of cholestatic hepatitis on antibiotic usage in Australia 1992-2010

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Objective

To determine whether ADRAC warnings regarding cholestatic hepatitis as an adverse effect of flucloxacillin and amoxycillin-clavulanic acid had any impact on their use between 1992 and 2010 and to investigate whether cephalexin and macrolides (recommended alternative therapy), respectively filled any gap caused by reduced usage.

Methods

Annual dispensing data for all oral forms of flucloxacillin, amoxycillin-clavulanic acid, cephalexin and each macrolide were obtained between 1992 and 2010 for concessional and Veterans beneficiaries. These data were converted to the number of defined daily doses (DDD) and plotted against time. The usage trend of each medicine was compared to determine any temporal associations in changing usage patterns.

Results

A dramatic decrease of flucloxacillin use occurred between 1993 and 2002, after flucloxacillin induced cholestatic hepatitis featured prominently in ADRAC bulletins and warnings were issued in 1994. Cephalexin usage increased markedly, but to a greater extent during the same period. The use of amoxycillin-clavulanic acid declined between 1995 and 1997 after it was associated with hepatitis in a 1996 ADRAC bulletin. However, the amoxycillin-clavulanic acid usage increased again in 1998 and continued to do so throughout the study period. Total macrolide usage also increased during this time, but the usage trend was not changed.

Conclusions

Cholestatic hepatitis appeared to impact flucloxacillin usage in Australia, and the data suggests cephalexin was the alternative that filled the gap. The use of amoxycillin-clavulanic acid was only transiently affected between 1995 and 1997 and it is not clear if macrolides filled this gap.

P-027

Assessment of upper gastrointestinal management and referral rates with the supply of nonprescription pantoprazole: A simulated patient study

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Objective

To assess upper gastrointestinal management and investigate referral rates in Australian community pharmacies.

Methods

Researchers posing as simulated patients visited Perth metropolitan pharmacies in March and April 2011. Using two standardised scenarios, the simulated patient presented as someone with upper gastrointestinal symptoms requesting the purchase of the proton pump inhibitor pantoprazole. In scenario one the simulated patient has used the product before, in scenario two the product has not been used before. In both scenarios the appropriate outcome was immediate medical referral. Results of the encounter were recorded immediately after the visit. Descriptive statistics were used to report demographic, assessment, counselling and referral data.

Results

One hundred and forty one community pharmacies were visited (71 were given scenario one and 70 were given scenario two). Appropriate medical referral for both scenarios was achieved in 7% (n = 10) of the pharmacies visited. The number of assessment questions asked, counsellor's position and consultation time were key predictors for appropriate referral. There was no significant difference in referral rates between pharmacy type or scenario.

Conclusions

Inadequate patient assessment translated to inadequate medical referrals. This research indicates the need for substantial pharmacy practice improvements in line with Australian pharmacy professional organisation guidelines in order to create consistent professional advice across the industry.

Audit of antiplatelet drug use for high cardiovascular risk patients at Repatriation General Hospital, Daw Park, South Australia

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Objective

To audit the prescription of antiplatelet drugs in hospital inpatients assessed at high cardiovascular risk by the Australian absolute cardiovascular risk calculator.

Methods

This was a cross-sectional retrospective study that recorded antiplatelet drug use for all medical inpatients on a specified audit day. Non-medical unit patients were excluded. Cardiovascular risk was assessed by using the Australian absolute cardiovascular risk calculator. Data regarding antiplatelet drug use and cardiovascular risk was obtained from case note review and computer pathology results.

Results

94 cases (42 males, 52 females) with a mean age of 80.2 years (SD ± 1.29) were reviewed. 80 subjects (85%) were categorized as at high cardiovascular risk based (>15%). Of the 80 patients assessed as being at high cardiovascular risk, 43 (54%) were prescribed antiplatelet agents (aspirin n = 29, clopidogrel n = 14) and 16 subjects (20%) were prescribed anticoagulant drugs. 21 (26%) of high risk patients were not prescribed an antiplatelet agent or other anticoagulant. Of these 21 subjects, only 8 subjects had a clearly documented reason (bleeding disorder, previous haemorrhagic complication, or drug contraindication).

Conclusions

A significant proportion of medical inpatients 21 subjects (26%) assessed as at high cardiovascular risk were not prescribed an antiplatelet drug or anticoagulant. Although there are potentially many reasons why patients cannot, or will not take prescribed antiplatelet agents, pharmacists should become proactive and raise the issue of prescription of antiplatelet agents for high cardiovascular risk patients with prescribers.

Educating patients about warfarin using Information Technology (IT): A survey on healthcare professionals' perspectives

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Objective

To explore healthcare professionals' views about the benefits and challenges of using IT resources for educating patients about their warfarin therapy.

Methods

A cross-sectional survey of both community and hospital-based healthcare professionals (e.g., doctors, pharmacists and nurses) was conducted during May - August 2011 using a purpose-designed questionnaire.

Results

107 healthcare participants responded to the 300 questionnaires distributed (34.4% response rate). Over half (53.3%) of them were aged between 40 - 59 years, and 59.5% were female. Fifty nine (55.1%) of the 107 participants, reported having had no access to warfarin-specific IT-based patient education resources. Further 37.5% of the participants, who had IT-access, reported that they had never used such resources. The main challenges of patients' warfarin education as reported by the participants included: patient-related factors, such as older age, language barriers and/or cognitive impairments, as well as their own time constraints. Computers and interactive touch screen kiosks were the most preferred tools to the participants to help deliver warfarin education in different practice settings. The participants also identified some benefits (e.g., reinforcement of warfarin education, offering reliable and easily understood information), and barriers (e.g., time and costs of using IT resources, difficulty in operating the resources) of using warfarin-specific IT resources.

Conclusions

This study suggests that many healthcare professionals do not use or access IT-based warfarin education resources for their patients. Perhaps, by addressing the concerns raised by the participants regarding the implementation of warfarin-specific IT resources, they could be used more effectively when educating patients about their warfarin therapy.

Provision of warfarin education to hospital in-patients: A clinical audit

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Objective

To review the provision of education to hospital in-patients who were prescribed warfarin therapy during their admissions.

Methods

A prospective study was undertaken in two large metropolitan Australian hospitals. The provision of warfarin education was identified by auditing the medication charts and clinical notes of hospitalised older patients (≥65 years), as well as by interviewing patients about their recall of having received any warfarin education.

Results

Data was collected from a total of 96 in-patients with a mean age of 74.4 (± 12.7) years. The majority (78%) of these in-patients were admitted to medical wards, were taking warfarin for atrial fibrillation (56%), and had commenced warfarin prior to admission (54%). In regard to warfarin education, 36% of all in-patients had the provision of their education documented in medication charts and notes, and in the majority (69%) of cases the education was provided by a pharmacist. Among the 68 in-patients able to be interviewed, only 47% recalled having received any warfarin education; in the majority (69%) of cases they cited pharmacists as having provided the education.

Conclusions

The study findings highlight the need for improvements in both documentation and provision of warfarin education to all relevant hospital in-patients.

A retrospective study on statin use in children and adolescents

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Objective

To (a) profile children with lipid disorders; (b) investigate initial intervention, treatment and doses; (c) explore the effectiveness of statins compared to dietary interventions.

Methods

A computerised search of The Children's Hospital's (Westmead) database was conducted to produce a list of out-patient children (n = 64) treated at the Lipid Clinic and in-patients (n = 25) who were prescribed statins (January 2000 - July 2011). Children were profiled and their plasma lipid levels recorded. Total cholesterol (TC) and low density lipoprotein (LDL) levels were grouped based on 6-monthly intervals from baseline to 2 years starting from either a diet or statin intervention.

Results

Only 25 out-patients and all in-patients had a record of statin use, with average age of statin commencement as 10.6 years (range: 2 - 17). The most commonly used statin was atorvastatin (n = 23). Thirty-six of the out-patients had a dietary intervention with 15 eventually requiring a statin. There was no apparent trend in the choice of starting statin or dose, or any evidence of weight-dependent dosing. There was a drop of 1.3 mmol/L in TC levels between initial and 12 months post-statin treatment ($p < 0.05$) and 1.4 mmol/L LDL levels of initial and 18 months post-statin ($p < 0.05$). There were no statistically significant drops in plasma lipid levels in any other time points or for diet intervention.

Conclusions

Statins have been shown to be beneficial in children with cholesterol disorders when dietary interventions have failed. Despite their accepted use in this population, there appears to be no consensus in the choice of statin type or dose.

Antipsychotic utilisation among individuals receiving compulsory treatment for mental illness in the community

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Objective

Community treatment orders (CTOs) are legal orders which require individuals with mental illness to accept treatment in the community. Studies have determined that long-acting injectable antipsychotic (LAI) use is associated with CTOs however little is known about the specific drug regimens prescribed in CTOs. The objective of this study was to evaluate the use of antipsychotic drugs among CTO recipients.

Methods

This was a descriptive study of individuals issued a CTO by the New South Wales Mental Health Review Tribunal in 2009 (n = 2856). A random sample of case notes and treatment plans were retrospectively reviewed using tribunal records (n = 378). Following the initial development and piloting of a standardised pro-forma, de-identified information relating to individuals' treatment management plans as well as demographic, clinical, and psychosocial details were systematically recorded.

Results

In total, 378 cases were reviewed. More than 75% of individuals had a diagnosis of psychosis and 377 were prescribed an antipsychotic. 307 (81.2%) were receiving a LAI, either alone or in combination with, an oral antipsychotic. Risperidone was the most commonly used antipsychotic, evident in 164 (43.4%) individuals. Most antipsychotics were prescribed at doses higher than the World Health Organization's Defined Daily Doses (DDDs) however were within international consensus guideline recommendations. 148 (31.5%) individuals were receiving at least 2 antipsychotics concurrently.

Conclusions

This study confirms the association between LAIs and CTOs and provides an insight into antipsychotic use in a challenging population averse to treatment.

Exploring the relationship between mental health stigma, knowledge and provision of pharmacy services for consumers with schizophrenia

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Objective

To explore the relationship between pharmacists' level of mental health stigma, their beliefs about the helpfulness of interventions in schizophrenia and their self-reported behaviour in relation to providing pharmacy services for consumers with schizophrenia.

Methods

A survey instrument, containing a measure of mental health literacy, the 7-item social distance scale and 16 items relating to the provision of pharmacy services for consumers with schizophrenia compared to cardiovascular disease, was mailed to a random sample of 1000 pharmacists registered with the Pharmacy Board of New South Wales in November 2009. Multiple linear regression models were fitted to assess the relationship between stigma, knowledge and behaviour.

Results

Responses were received from 188 pharmacists. Pharmacists were significantly more confident and comfortable to provide services to consumers with a cardiovascular illness than a mental illness. Social distance, $\beta = 0.11$ (0.01, 0.22), and schizophrenia knowledge scores, $\beta = -1.02$, (-1.50, -0.54), were strongly associated with medication counselling. While schizophrenia literacy was also a strong predictor of identifying drug related problems, $\beta = -1.09$ (-1.79, -0.39).

Conclusions

Low levels of mental health stigma and high levels of schizophrenia literacy were associated with pharmacists being more willing to provide medication counselling and identify drug related problems for consumers with schizophrenia. This demonstrates the importance of improving knowledge and stigma surrounding schizophrenia to improve service delivery for consumers taking medicines for schizophrenia.

Effectiveness of interventions to improve antidepressant medication adherence: A systematic review

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Objective

Non-adherence to antidepressant medications is a significant barrier to the successful treatment of depression in clinical practice. This review aims to systematically assess the effectiveness of interventions for improving antidepressant medication adherence among patients with unipolar depression, and to evaluate the effect of these interventions on depression clinical outcomes.

Methods

Medline, PsycInfo and Embase databases were searched for English-language randomised controlled trials published between January 1990 and December 2010 on interventions to improve antidepressant adherence. The impact of interventions on antidepressant medication adherence and depression clinical outcomes was evaluated.

Results

Twenty-six studies met the inclusion criteria. Interventions were classified as educational, behavioural and multifaceted interventions. A total of 28 interventions were reviewed, as 2 studies investigated 2 interventions each. Sixteen (57%) of the 28 interventions showed significant effects on antidepressant adherence outcomes, whereas 12 (43%) interventions demonstrated significant effects on both antidepressant adherence and depression outcomes. The interventions which showed significant improvement in outcomes were primarily multifaceted and complex, with proactive care management and involvement of mental health specialists. Overall, educational interventions alone were ineffective in improving antidepressant medication adherence.

Conclusions

Improving adherence to antidepressants requires a complex behavioural change and there is some evidence to support behavioural and multifaceted interventions as the most effective in improving antidepressant medication adherence and depression outcomes. More carefully designed and well-conducted studies are needed to clarify the effect of interventions in different patient populations and treatment settings.

Health care providers' perspectives of medication adherence in the treatment of depression: A qualitative study

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Objective

Non-adherence to antidepressant medications has been associated with adverse outcomes such as relapse and recurrence. The objective of this study was to explore the views and perspectives of health care providers on antidepressant medication non-adherence in clinical practice settings.

Methods

Individual semi-structured interviews were conducted with a purposive sample of 31 health care providers from a range of disciplines and settings. Interviews focused on medication adherence issues in depression and providers' strategies in dealing with them. Interviews were audio-recorded, transcribed verbatim and thematically content analyzed using a constant comparison approach.

Results

Four broad themes were identified from the interview transcripts: scope of antidepressant non-adherence problems, issues of antidepressant non-adherence, approaches to managing antidepressant non-adherence and challenges in implementing approaches. Health care providers generally acknowledged medication non-adherence to be an important problem in depression. They attributed this problem to patient, medication and environmental-specific issues. Five approaches in addressing non-adherence were reported: patient education, building partnerships with patients, pharmacological management, developing behavioural skills and building supportive networks. Challenges perceived to be complicating the management of antidepressant non-adherence were lack of time and skills, assessment of medication adherence, transition period immediately post-discharge and conflicts in views between health care providers.

Conclusions

The study has highlighted the complexity of antidepressant medication adherence problem from the perspective of health care providers. Future research should take into account health care providers' perspectives when developing multidisciplinary interventions to improve antidepressant medication adherence.

Sedative load and physical function in community-dwelling people aged 75 years and older in Finland: A population-based study

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Objective

Sedative load refers to the cumulative effect of taking multiple medications with sedative properties. The objective of this study was to investigate the association between sedative load and balance, mobility and muscle strength in community dwelling older people in Finland.

Methods

Cross-sectional analyses were conducted for 700 community-dwelling people aged ≥75 years (mean age 81.3 years, 69% women) who participated in the Geriatric Multidisciplinary Strategy for the Good Care of the Elderly (GeMS) study in Kuopio, Finland. Demographic, diagnostic and medication use data were collected during structured clinical examinations in 2004. Balance, mobility and muscle strength were assessed by trained physiotherapists using validated and objective measures. Sedative load was computed using a previously published model. ANCOVA and logistic regression were utilised to assess the cross-sectional association between sedative load and balance, mobility and muscle strength.

Results

Twenty-nine percent of participants (n = 205) used one or more medications with sedative properties on a regular or when-required basis. After adjusting for confounders, exposure to higher sedative load ranges was associated with slower walking speed (p = 0.0003), longer time to perform the Timed Up and Go test (p = 0.005), and lower scores on Berg Balance Scale (p = 0.005), but not with self-reported ability to walk 400 metres. Use of medications with sedative properties was associated with poorer performance in grip strength (p = 0.009), knee extension strength (p = 0.02) and completion of five chair stands (p = 0.003).

Conclusions

Use of medications with sedative properties was associated with impaired balance, mobility and muscle strength in community-dwelling older persons in Finland.

Sedative load and functional outcomes in older Australian men: The Concord Health and Ageing in Men project

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Objective

The objective of this cross-sectional study was to investigate the association between sedative load and functional outcomes in a random population-based sample of community-dwelling older Australian men.

Methods

A total of 1696 males aged ≥70 years underwent structured clinical assessments from 2005 - 2007. Sedative load was computed using a previously published model. Logistic regression models were used to compute unadjusted and adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for the association between sedative load and functional outcomes. Analysis of covariance (ANCOVA) was used to investigate mean differences in physical performance.

Results

Of the participants, 15.3% took medications with sedative properties. After adjusting for age, education, depressive symptoms and comorbidities, participants who took one medication with sedation as a prominent side-effect (sedative load = 1) had an OR of 2.15 (95% CI: 1.20 - 3.85) for Activities of Daily Living (ADL) disability, compared to participants with sedative load = 0. Participants who took at least one primary sedative or two medications with sedation as a prominent side-effect (sedative load ≥2) had an OR of 1.55 (95% CI: 1.02 - 2.35) for Instrumental Activities of Daily Living (IADL) disability, compared with participants with sedative load = 0. Mean 6 m walking speed ($p = 0.001$) and grip strength ($p = 0.003$) were significantly different between sedative load groups in unadjusted models only. No association between sedative load and cognitive impairment or performance in balance and chair stands tests was observed.

Conclusions

Higher sedative load is associated with ADL and IADL disability, but not with poorer physical performance or cognitive impairment in older Australian men.

Adverse drug reactions prevalence and risk factors in elderly hospitalized patients: A review

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Objective

To review the prevalence of adverse drug reactions (ADRs) in elderly hospital patients and to identify potential risk factors associated with ADRs in the elderly.

Methods

A search of Medline, Embase, and International Pharmaceutical Abstracts was conducted using the terms "adverse drug reaction", "hospital" and "elderly". Literature searches were limited to English language and no time limitation or exclusion criteria were used. All titles and abstracts of identified studies were examined for potential relevance. The reference lists of relevant studies were also reviewed to identify other relevant articles.

Results

Twenty-one studies included a measure of ADRs prevalence. The reported prevalences varied widely, from 10.6% to 64.8% .ADRs were recorded as the reason for hospitalisation in between 5.8% and 45% of admissions in the elderly. A number of potential ADRs risk factors were identified. These mainly included age, gender, polypharmacy, renal impairment, length of stay and medication type. The main medication classes implicated were neurological, psychotropic, NSAIDs, antibiotics and cardiovascular agents. There was marked heterogeneity in the study methodologies and ADR definitions used. Eight studies used the WHO definition while rest used study specific definitions. Eighteen studies were conducted prospectively and three studies were retrospective studies with a variety of methodologies.

Conclusions

Despite the lack of consistency in the published literature regarding the prevalence of ADRs in elderly hospital patients, ADRs remain a significant clinical issue in this population. A number of potential risk factors were identified however little is known about the clinical outcomes or clinical relevance associated with each factor.

Sensitivity of sequence symmetry analysis in detecting adverse drug reactions (ADRs) from an administrative database

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Objective

To determine the sensitivity of sequence symmetry analysis to detect known adverse drug reactions (ADRs) identified in randomized controlled trials (RCTs).

Methods

Published RCTs of five medicines; risperidone, sertraline, donepezil, strontium ranelate and tramadol extended release were identified through search databases, product information or the United States Food and Drug Administration website. Adverse events were independently extracted from the RCTs by two clinical researchers. Adverse events that were adequately powered in the clinical trials (≥80%) were tested with symmetry analysis using administrative claims data from the Department of Veteran's Affairs. The symmetry analysis examines asymmetry in the distribution ratio of an incident event (either prescription of another medicine or hospitalisation) before and after the initiation of the five tested medicines. Crude and adjusted sequence ratios with 95% confidence interval were calculated.

Results

A total of 16 adverse events were identified with sufficient power in RCTs. Of these, 12 were detected by symmetry analysis. These included nausea induced by all tested medicines, diarrhoea induced by donepezil and sertraline, and peripheral oedema induced by risperidone. The sensitivity of symmetry analysis was 75%.

Conclusions

The sequence symmetry technique was found to have high sensitivity for detecting known adverse events. The technique could be an additional pharmacosurveillance tool for detecting ADRs from administrative databases. More work is required to determine whether the sensitivity of PSSA is affected by the background prevalence of the ADR in the population.

Determining the prevalence and reasons for medication swallowing difficulties in the general population

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Objective

Difficulties with swallowing solid dosage forms is a common problem among patients who are classified as dysphagic. These patients or their carers modify their medications by crushing tablets and opening capsules, and mixing the powder with various food-based items. Dosage form modification similar to this also occurs amongst people who can swallow food but who find it difficult to swallow whole tablets and capsules. This project investigates the issues around medication swallowing in non-dysphagic people.

Methods

Healthy volunteers completed a survey that included food-related questions around food textures, memory of choking incidents, and willingness to try new foods, and medication-related questions around regularity of medication use and memory of choking or swallowing problems. The person's gag reflex, taste receptor density and chewing efficiency were then assessed. Finally, the person was observed while swallowing a capsule.

Results

Difficulties swallowing whole tablets and capsules was associated with their size, shape and coating, and strong memories of previous choking incidents. A variety of manoeuvres were used to help swallow the whole capsule such as adding to a mouthful of pre-chewed food and tipping the head back. Placing the capsule far back in the mouth was used successfully by those with a weak or absent gag reflex.

Conclusions

This pilot study has determined that many otherwise healthy people find whole tablets and capsules difficult to swallow. Tilting the head back while swallowing was worryingly a common approach to swallowing medications, as this preferentially opens the airway and could result in medication entering the lungs.

Design and evaluation of written medicine information for Riamet® users

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Objective

Written medicine information is poorly valued by patients, with length, presentation and readability considered to be key factors in their opinions. This notion is more significant in low-health literate population groups. This study aimed to re-design a Consumer Medicine Information (CMI) leaflet to improve its comprehension by patients with low health literacy.

Methods

The CMI leaflet for Riamet Dispersible® was re-designed based on key guidelines for medicine information writing. Pictograms were also included to enhance readability and comprehension of dosage instructions. The two modified CMI leaflets were user tested [1] with 31 people, who were asked to find information and explain answers to 12 questions about the medicine found in the CMI.

Results

The implementation of key design principles, re-formatting and re-wording the content improved readability, comprehension, presentation and the CMI length in both modified CMIs. Consumers generally required less time and had less difficulty in finding and answering a question about the CMI content, compared to the original CMI. Thus both modified CMIs were considered to be more superior to the currently available CMI. User testing was a useful tool in identifying aspects in the CMI leaflets that needed improvement to enhance comprehensibility. These included the dosage table which required re-formatting, re-wording of some headings and dosage instructions.

Conclusions

This research suggests that modifying currently available CMI based on key design principles and writing guidelines, and user testing with consumers, resulted in improved CMI. Consumers were better able to find and understand the information in the modified CMI.

[1] Jay E, Aslani P, Raynor DK. User testing of Consumer Medicine Information in Australia. *Health Education Journal* (2010); DOI: 10.1177/0017896910376131

DIY OTC: Reclassification of a medicine without a manufacturer's application

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Objective

Reclassification of medicines is generally driven by pharmaceutical manufacturers. However, multiple barriers exist for sponsors to reclassify. In 2010, the world's first reclassification of topical calcipotriol for psoriasis was uniquely driven by a pharmacy retail group in New Zealand (NZ). This study was conducted to describe a case of reclassification by a pharmacy retail group without manufacturer support.

Methods

This case study is nested within a larger project using interviews, document analysis and a heuristic qualitative approach. The lead author initiated this reclassification application on behalf of Pharmacybrands Limited. Information sources included interviews, the reclassification submission, and the Medicines Classification Committee meeting minutes.

Results

Reclassification of topical calcipotriol in NZ was relatively straightforward, despite lack of manufacturer support, use for a chronic condition, and no international experience of non-prescription calcipotriol. Difficulties encountered included an inability to change packaging, a requirement for blood tests, no funding for pharmacist training and no consumer leaflet. Unusually, rather than being designated as Pharmacist-Only medicine, topical calcipotriol became exempt from prescription "...when sold in a pack of not more than 30 grams or 30 millilitres by a pharmacist to an adult with mild to moderate psoriasis previously diagnosed by a doctor". The collaborative care model included the pharmacist or consumer informing the doctor of calcipotriol usage.

Conclusions

This practical example shows lack of manufacturer support is not an insurmountable barrier to reclassification of medicines. An exemption to prescription status may be workable in other countries. Pharmacy and other organisations could be proactive to improve access to medicines.

Behind the times in the antipodes? Barriers and enablers to medicine reclassification in Australasia

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Objective

Australia and New Zealand (NZ) have participated in the worldwide trend for prescription to non-prescription reclassification. However, medicines such as simvastatin, oral contraceptives, mebeverine, and domperidone have reclassified elsewhere, but remain prescription-only here. With pressure on the medical workforce, taxpayer-funded health, and an international trend to self-management, a review of the environment for reclassification in Australasia is warranted. The objective of this study was to elucidate barriers and enablers for rescheduling of medicines in Australia and NZ.

Methods

Using a qualitative, heuristic approach, in-depth interviews were conducted face-to-face or by telephone with 23 purposively selected key informants from Australia and NZ between November 2009 and September 2011. Analysis of minutes and other documents provided supplemental information and triangulation.

Results

These medicines remain prescription-only in Australasia primarily because reclassification applications have not been forthcoming. Numerous barriers to sponsor interest in reclassification emerged including advertising restrictions and a conservative committee in Australia, the negative pharmaceutical environment and low prescription cost in NZ, and lack of market exclusivity post-rescheduling in both countries. Enablers include Pharmacist-Only and Pharmacy-Only schedules in both countries, and a pragmatic approach in NZ. Factors may act as both barriers and enablers, such as small population, subsidised healthcare, and transparency of process. Certain barriers have limited scope for change. Modification of others may allow greater consumer access to medicines which may reduce the health spend and improve doctor availability for appointments.

Conclusions

Barriers to rescheduling in both countries inhibit consumer access to some medicines. Modification of barriers whilst capitalising on enablers may increase reclassification.

Why "half" a tablet is the wrong medicine in Australia

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Summary

The practice of patients or carers splitting tablets into two or more pieces is largely caused by economic gain caused by a "flat" pricing policy. In most cases, the cost of medicines can be halved. In addition to those tablets that are generally considered unsuitable for splitting (because of coating, lack of score or modified release nature) there is the concern that doses may vary as a result of unequal division of tablets or unanticipated loss of material in the splitting process. However, unlike the European Union, New Zealand and (most recently) the USA, Australia sets no limits for such divided dose variability and is silent on the matter. The disturbing findings resulting from of a group of young adults splitting (scored) dispersible aspirin 300 mg tablets labelled to allow such a division are reported. In twenty samples, all samples of whole tablets passed the BP Uniformity of Mass Test, whereas all samples of half tablets failed. Assuming uniformity of drug distribution throughout tablets, the considerable (33%) variation in mass of half tablets observed leads to a tenfold increase in dose variability. Whilst not of therapeutic concern in this case, a similar result for a drug of more narrow therapeutic index could lead to therapeutic failure or toxicity. This study emphasises the importance of the pharmacist in considering the suitability of the formulation, drug and patient if "half" tablet doses are to be administered; and highlights the need to review the current Standard for Tablets and Capsules (TGO 78).

Disposal practices for unused medications in New Zealand community pharmacies

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Objective

One of the recommended methods for households to dispose of unused medications in many countries is to return them to community pharmacies. However, such a practice will only reduce the environmental levels of pharmaceuticals if the medications are also disposed and destroyed properly by the pharmacies. This study reports the results of a questionnaire sent to New Zealand community pharmacists regarding disposal practices for unused or expired medications in their workplaces.

Methods

A pre-tested, self-administered questionnaire was sent to 500 randomly selected community pharmacies from all areas of New Zealand. The participants were asked how they disposed of a variety of medications. In addition, participants were also asked about whether they knew how unused medications were destroyed if their pharmacy used a third party contractor or distributor to dispose of them.

Results

Of the 265 respondents, 80.4% and 61.1% respectively reported that solid and semi-solid medications were removed by contractors. However liquid (44.7%) and Class B controlled drugs (58.5%) were predominantly disposed of down the pharmacy sink. Over 60% of the participating pharmacists indicated that they believed the contractors incinerated the collected pharmaceutical waste, and over 90% of the participating pharmacists indicated their wish for a state-run disposal and destruction system.

Conclusions

Liquid medications and Class B controlled drugs, which were commonly reported to be rinsed down the sewage system, may increase the potential for environmental pollution by pharmaceuticals in New Zealand. There is a need for increased environmental awareness amongst community pharmacists in New Zealand.

Investigating unused medications

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Objective

The objective of this study was to identify unused medications within household in New Zealand. Specifically the proportion of households, the reasons for unused medications, the storage locations and how the participants intended to dispose of these medications.

Methods

An online survey was placed on the New Zealand National Poison Centre website for a three month period. This consisted of a series of questions with predefined answer sets and asked about collection of medication, unused medications, storage of medications and disposal of medications.

Results

This survey was completed by 452 individuals. Irrespective of whether they "felt" they needed them or not, 56% of respondents collected all items prescribed. 62% of respondents currently had unwanted medications in their house. The most common reason for people to have left over medication was "condition improve or resolved" (n=307). Most respondents kept unwanted medications "in case they needed them later" (n=222) and almost a quarter kept unwanted medications because they did not know how to dispose of them. Depending on formulation type only between 13 - 24% of unused medications were returned to pharmacies for disposal.

Conclusions

A significant amount of medication is collected from pharmacies and subsequently unused. Reducing excess medications and subsequent wastage may reduce stockpiles of unused medications that may be implicated in accidental ingestions and will reduce the financial and environmental burden of the disposal of these medications.

Development of a toxic Chinese herbal medicines database in Australia

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Objective

In Australia, commercial herbal products are regulated by the Therapeutic Goods Administration (TGA) and toxic herbal medicines are regulated by The Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP). The implementation of SUSMP is controversial to Chinese medicine professionals as it differs from the toxic schedule in China and the Victoria Chinese Medicine Registration Board has requested revision of the scheduling. This study aims to review the current literatures on scheduled and toxic Chinese herbs in Australia and build a database.

Methods

Systematic searches on toxic Chinese herbs were conducted to collect basic information and toxicity of the herbs. Class system was applied for the toxicity ranking of the herbs. Filemaker Pro software was used to develop an online database of these herbs.

Results

Prototypes of the online database and a mobile phone version of the website were developed. Recommendations on 73 species of the scheduled and toxic Chinese herbs, including Aristolochia, Aconite, Asarum, Ephedra and Farfara, were made by ranking them according to their toxicity evidence.

Conclusions

This study has provided the foundation for the further studies on the safety, the regulation and the authentication of the scheduled and toxic Chinese herbs in Australia. Guidance for the health care professionals and the public has been established and may provide suggestions for the revision of current toxic herbs in SUSMP.

Enhancing quality use of medication self-reported questionnaire (EQUIM-SRQ) among mental health consumers: A pilot study

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Objective

To assess the uptake, return and completion rates of an adverse event screening questionnaire (the Enhancing Quality Use of Medication Self-Reported Questionnaire (EQUIM-SRQ)) in an Australian mental health outpatient population.

Methods

Questionnaires were distributed amongst two Australian adult mental health clinics for completion either at the clinic (onsite), or externally (postal option), from March - May 2011. Assistance was offered to participants completing the questionnaire onsite. Clients who were visited in their homes by clinic staff were invited to participate as external participants.

Results

Of 160 questionnaires distributed, 29 (18%) were completed. Of those, 22 (76%) were completed onsite, and seven (24%) were completed externally. Of the questionnaires completed onsite, 11 (50%) were fully completed, with 4 participants requiring assistance. A further 11 (50%) questionnaires were partially completed, with 2 participants requiring assistance. Of the questionnaires completed externally, 5 (71%) were fully completed.

Conclusions

This pilot study demonstrated the use of the EQUIM-SRQ in research. Further development and validation of the EQUIM-SRQ is required. This will include identifying optimal delivery methods of the tool as well as consumer and expert feedback via focus groups to evaluate perceptions of the tool.

Development and validation of a questionnaire to investigate pain management of community-dwelling chronic pain sufferers'

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Objective

Assessing the quality and adequacy of pain management is complex. There is currently no validated tool that assesses such areas in community-dwelling chronic pain sufferers. Consequently, the development and validation of a tool was desired.

Methods

The newly developed tool was a modified form of the American Pain Society's Patient Outcome Questionnaire (APS-POQ-R). It was tested in the Australian state of Victorian where participants were recruited when they had an oral or transdermal analgesic preparation dispensed by a participating pharmacy. The data was analysed to psychometrically evaluate the questionnaire and investigate the ability of the Pain Management Index (PMI) and pain severity scores to differentiate between adequately and inadequately managed chronic pain.

Results

The tool has good validity and reliability. Four subscales; emotions and activities out of bed, side effects, sleep and activities in bed and perception of management represent the quality of pain management. Pain management adequacy was assessed using PMI or pain severity scores. The PMI proved unhelpful, pain severity score is a better determinant of pain management adequacy.

Conclusions

The questionnaire displayed the potential for use by health professionals to understand the adequacy and quality of their patients' chronic pain management.

Evaluation of the Anaphylaxis Training Pharmacist Assessment Tool (AT-PAsT): A pilot study

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Objective

Pharmacists play an important role in managing patients at risk of anaphylaxis. The Anaphylaxis Training Pharmacist Assessment Tool (AT-PAsT) was developed to measure the effectiveness of anaphylaxis training programs delivered to pharmacists by the Australasian Society of Clinical Immunology and Allergy (ASCIA). The pilot study evaluates AT-PAsT prior to use in a larger study.

Methods

AT-PAsT is a twelve-question knowledge assessment tool developed by ASCIA in collaboration with The University of Western Australia. Pharmacists and pharmacy interns attending anaphylaxis training presented jointly by ASCIA and the Pharmaceutical Society of Australia in Adelaide, South Australia, were eligible to participate. AT-PAsT was administered to all participants before and after training. Mean scores before and after training were compared to determine knowledge change. The number of correct answers for each question before and after training was compared to measure each question's ability to measure knowledge change.

Results

Sixty-four people participated (54 pharmacists and 10 intern pharmacists) with 57 (89%) fully completing AT-PAsT. The mean knowledge score before training was 8.2 points (95% CI: 7.76 - 8.66), and after training was 11.2 points (95% CI: 10.95 - 11.5) Participants' knowledge significantly increased after training ($p < 0.001$). Participants' knowledge significantly increased after training ($p < 0.001$). There was no significant change in individual question response before and after training, for four of the twelve AT-PAsT questions ($p \geq 0.5$).

Conclusions

The AT-PAsT demonstrated a significant improvement in knowledge scores after ASCIA anaphylaxis training. The four questions that did not show response change have been replaced in the AT-PAsT for use in future research.

Sugar and spice: The clinical effectiveness of cinnamon for diabetes mellitus

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Objective

Diabetes mellitus is a chronic metabolic disorder, which is associated with an increased risk of cardiovascular disease, eye disease, nephropathy, neuropathy, and sexual dysfunction. Improvements in glycaemic control may help to reduce the risk of these complications. One intervention that has been shown in a number of animal studies to improve glycaemic control is cinnamon bark. This study aimed to evaluate the safety and efficacy of cinnamon in patients with diabetes mellitus via a Cochrane systematic review and meta-analysis.

Methods

Fourteen electronic databases were searched for randomised controlled trials investigating the effects of orally administered mono-preparations of cinnamon (Cinnamomum spp.) in adults with type 1 or type 2 diabetes mellitus. Data were extracted using standard templates, and risk of bias assessed using Cochrane risk of bias criteria.

Results

Eight randomised controlled trials, involving a total of 523 participants with type 1 and type 2 diabetes mellitus, were identified. Risk of bias of these trials was generally high. Cinnamon was shown to be effective in reducing fasting blood glucose level when compared to controls; however, substantial heterogeneity was present. No statistically significant difference in glycosylated haemoglobin (HbA1c) or serum insulin was found between cinnamon and control groups. Adverse reactions to oral cinnamon were infrequent and generally mild in nature.

Conclusions

There is insufficient evidence to support the use of cinnamon for type 1 or type 2 diabetes mellitus.

The effect of gastric acid suppression with pantoprazole on the efficacy of calcium carbonate as a phosphate binder in haemodialysis patients

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Objective

Metallic phosphate binders require an acidic environment to dissociate to the free metallic ion and bind gastrointestinal phosphate. Changes in gastric acidity with acid suppressants may therefore alter the efficacy of phosphate binders. Given the high consumption of acid suppressants there is potential for a common significant drug interaction to occur. We evaluated the *in vivo* effect of gastric acid suppression on the efficacy of calcium carbonate as a phosphate binder.

Methods

We conducted a two period, interventional, crossover, double blind, randomised, placebo controlled trial in 26 haemodialysis patients randomly assigned to pantoprazole 40 mg daily or placebo for two consecutive six week periods.

Results

Serum phosphate was significantly higher during pantoprazole treatment compared to placebo (1.59 ± 0.3 vs. 1.42 ± 0.3 mmol/L, p = 0.0051). Serum calcium (2.37 ± 0.2 vs. 2.46 ± 0.2 mmol/L, p = 0.012) and ionised calcium (1.17 ± 0.1 vs. 1.22 ± 0.1 mmol/L, p = 0.013) were lower during pantoprazole. Ca x PO_4 (3.76 ± 0.7 $mmol^2/L^2$ vs. 3.48 ± 0.7 $mmol^2/L^2$, p = 0.032) and iPTH (31.9 ± 21.4 vs. 23.6 ± 17.7 pmol/L, p = 0.004) were higher on pantoprazole. There were no differences in URR, Kt/V or dietary phosphate intake. Most patients did not show objective evidence for the need of gastric acid suppressants.

Conclusions

Our data suggested that calcium carbonate efficacy as a phosphate binder is negatively affected by the co-administration of pantoprazole. This may be the reason why hyperphosphataemia is not properly controlled in some haemodialysis patients.

Pharmacogenomics of leflunomide in the treatment of rheumatoid arthritis

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Objective

Aggressive treatment in rheumatoid arthritis (RA) is warranted due to early irreversible joint damage that causes significant morbidity. At the Royal Adelaide Hospital (RAH) treatment of early RA is with triple DMARD therapy and if this is ineffective, leflunomide is added. Approximately two-thirds of patients will not respond to leflunomide therapy and a large number will suffer significant toxicities like diarrhoea, nausea and leukopenia. Leflunomide is converted to its active metabolite teriflunomide via CYP2C19 and CYP1A2 and teriflunomide is a substrate for ABCG2, which may be responsible for significant enterohepatic recycling, explaining teriflunomides long half life. The primary site of action of teriflunomide is the mitochondrial enzyme dihydro-orotate dehydrogenase (DHODH). This study aimed to investigate the associations of SNP's in enzymes inherent to the pharmacology of leflunomide on response and toxicity, with the premise to improve leflunomide therapy by pinpointing robust predictors.

Methods

80 RA patients treated with leflunomide at the RAH were genotyped by TaqMan assays and assessed for response and toxicity. At 6 months post leflunomide commencement 72 and 53 patients were analysed for toxicity and response respectively to identify potential associations.

Results

Patients carrying the A allele of CYP2C19 rs4244285, which is associated with lower enzyme activity, were more likely to suffer toxicity (OR = 4.40, p = 0.05), and patients carrying the A allele of ABCG2 rs2231142, associated with lower ABCG2 activity, appeared more likely to suffer side effects to leflunomide (OR = 3.94, p = 0.12).

Conclusions

Carriage of the A allele in both CYP2C19 rs4244285 and ABCG2 rs2231142 may predict toxicity to leflunomide.

Vitamin D levels do not appear to be a predictor of statin-induced myopathy

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Objective

To determine the relationship between incidence of statin-induced myopathy and patients' vitamin D levels at time of statin initiation.

Methods

A prospective, observational design was adopted. Eligible patients were commencing a statin for the first time and were ezetemibe, fibrate and vitamin D supplement naive. Patients were recruited from four wards of SCGH. Patients giving informed consent were administered a standardised questionnaire regarding muscle symptoms prior to admission and at follow-up 4 to 8 weeks later. Information regarding patients' medical conditions, statin use, other medications and muscle symptoms were recorded. Blood for a vitamin D level was taken before the patient was discharged. Samples were stored at PathWest laboratory situated at SCGH and analysed after administering the second questionnaire.

Results

Seventy-one patients were enrolled (mean age 60.2 ± 13.2 years; 74.6% males). The mean vitamin D level was 69.7 ± 23.8 nmol/L, with 47.9% of participants having vitamin D levels <70 nmmol/L and 4.2% <25 nmol/L. Over 90% of patients were initiated on 40mg or 80 mg of atorvastatin daily. Incidence of statin-induced myopathy was 12.8%. Univariate analysis failed to show an association between myopathy and vitamin D levels at statin initiation ($p = 0.16$). Multivariate analysis was not undertaken due to the small cohort size.

Conclusions

Considering the data available, a relationship between vitamin D levels at the commencement of statin treatment and subsequent development of muscle symptoms is not apparent. Since evidence exists that vitamin D may alleviate statin-induce symptoms, a larger study is required to verify this finding.

Unlocking mechanisms implicated in drug-induced bizarre idiosyncratic behaviours: Learning from people, molecules and possible targets

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Objective

Zolpidem, an imidazopyridine hypnotic, which acts on GABA-A receptors has been associated with the development of a number of disturbing adverse drug reactions (ADRs) including amnesia, hallucinations and parasomnias. Other medications are also implicated in the induction of such adverse events; however, the mechanism behind these ADRs remains elusive. Retrospective disproportionality analysis of pharmacovigilance data investigated these ADRs and revealed drug-event associations (DEAs) for a number of compounds. DEA signals were coupled with ligand-based pharmacophore analyses to gain insights into the mechanisms underlying the induction of these ADRs.

Methods

Data from 208 drugs from various classes in the Australian Adverse Drug Reaction Systems (ADRS) database was analysed using case/non-case methods. Multivariate logistic regression was used to determine adjusted reporting odds ratios (RORs) for drugs associated with the following ADRs; amnesia, hallucination, parasomnia, movement-related parasomnia and non-movement related parasomnia. The RORs subsequently served as an indicator for activity in the Quantitative Structure Activity Relationship (QSAR) analysis in Schrodinger's PHASE program.

Results

6 drugs (zolpidem, zopiclone, nitrazepam and three β-adrenergic antagonists) were identified to possess significant associations with movement-related parasomnias. A 3-point pharmacophore hypothesis was generated that matched each of the 6 active drugs. Similarly, other pharmacophores were shared among large proportions of drugs that possess signals for activity for other classes of adverse event studied.

Conclusions

Specific motifs were shared among many of the investigated active drug structures associated with amnesia, hallucinations or parasomnias. These may represent pharmacophores that interact with unidentified off-target receptors to induce these events.

QSAR: An *in silico* approach for predicting pesticide toxicity to the nursing infant

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Objective

Most research on environmental pollutants is concentrated on highly lipophilic chemicals such as pesticides that accumulate in the environment and can be detected in contaminated water, air and soil. Human exposure to environmental pollutants is known to be responsible for a range of diseases such as cancer, birth defects, and learning disabilities. There is also increasing concern regarding the presence of drugs and pesticides in breast milk, leading to potentially harmful effects to the nursing infant. The aim of this study was to develop an *in silico* QSAR model capable of predicting partitioning of pesticides into breast milk.

Methods

A large data set of 190 diverse compounds, including drugs and pesticides with experimentally derived M/P values taken from the literature, were used to train, test and validate a predictive model. Each compound was then encoded with 70 calculated molecular structure descriptors and used as the inputs. The averaged literature M/P values were used as the ANN's output. Sensitivity analysis was used to select descriptors that best described the transfer of pesticides into breast milk and an artificial neural network (ANN) was used to develop a QSAR.

Results

This study developed an ANN QSAR model that is able to predict the partitioning of unseen pesticides into breast milk, from 26 molecular descriptors deemed important in milk plasma partitioning. The model's average correlation for training, testing and validation was 0.77.

Conclusions

The QSAR model can be used as a suitable tool for screening a wide range of compounds without the need for actual compound synthesis and subsequently prioritizing potentially toxic compounds for further testing.

Prediction of taxane clearance from *in vitro* metabolism data

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Objective

Docetaxel and paclitaxel are cytotoxic drugs that are extensively metabolised by CYP enzymes. Simcyp® is a population-based ADME simulator that predicts the pharmacokinetics of drugs from *in vitro* data. This study aimed to predict the clearances of docetaxel and paclitaxel using Simcyp®.

Methods

In vitro kinetic constants (Km and Vmax) for the pathways of taxane metabolism were retrieved from the literature and entered into Simcyp® (V9.0) along with relevant physicochemical and pharmacokinetic parameters. Using the "PK Profiles" mode, 10 virtual trials comprising 10 subjects each were run for single infusions of docetaxel or paclitaxel, with population demographics matched to the participants in published clinical studies.

Results

The simulated clearance of docetaxel via tert-butylhydroxylation was consistent with estimates from clinical studies (simulated = 27.4 L/hr [5.89 - 63.2 L/hr] vs. clinical = 25.1 L/hr [2.88 - 65.5 L/hr]). Likewise, paclitaxel 6α-hydroxylation clearance and paclitaxel 3'-phenyl-hydroxylation clearance were predicted accurately (simulated 6α-hydroxylation clearance = 8.46 L/hr [1.41 - 30.0 L/hr] vs. clinical 9.79 L/hr [2.54 - 21.1 L/hr], and simulated 3'-phenyl-hydroxylation clearance = 3.19 L/hr [0.36 - 15.0 L/hr] vs. clinical 1.65 L/hr [0.429 - 3.58 L/hr]). For both taxanes, the simulated clearance via CYP pathways was approximately half the total drug clearance reported in clinical studies.

Conclusions

The clearance of taxanes via CYP pathways was accurately predicted using Simcyp®. However, these pathways account for only half total drug clearance. Collectively, undefined elimination pathways, possibly mediated by transporters, may contribute significantly to taxane clearance.

Clinical utility of posaconazole therapeutic drug monitoring

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Objective

Posaconazole has an important role in the prophylaxis and salvage treatment of invasive fungal infections (IFI), although its limited absorption remains an important clinical concern. Few studies have examined the utility of monitoring posaconazole plasma concentrations. This study aimed to investigate the factors affecting posaconazole pharmacokinetics, and evaluate the clinical utility of therapeutic drug monitoring (TDM) for posaconazole.

Methods

Patient medical records from 6 Australian hospitals (Dec 2008 - Dec 2010) were reviewed to collect information on dosing and clinical outcome for all patients who had ≥1 plasma concentrations measured. Ethics approval was received.

Results

85 patients received posaconazole during the study period, with 538 plasma concentrations available. Posaconazole concentrations were frequently low in most patients (median 467 ng/mL). Among 72 patients taking posaconazole for prophylaxis against IFI, 12 patients developed fungal infection (17%); posaconazole concentrations were significantly reduced in these patients compared to those who did not develop fungal infection (median 289 ng/mL vs. 485 ng/mL respectively, $p < 0.05$). Multivariate analysis of posaconazole concentrations identified a number of significant factors associated with reduced posaconazole exposure, including co-administration with proton pump inhibitors, metoclopramide, phenytoin or rifampicin, the presence of mucositis or diarrhoea, as well as a novel finding of significantly reduced posaconazole exposure in the early post-transplant period in haematopoietic stem cell transplant recipients.

Conclusions

This study is the largest investigation of posaconazole TDM to date. Low posaconazole concentrations are common and are associated with a poor clinical outcome, supporting the utility of monitoring posaconazole concentrations to ensure optimal systemic exposure.

Voriconazole pharmacokinetics and therapeutic drug monitoring: A multi-centre analysis

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Objective

Voriconazole is widely used in the treatment of invasive fungal infections (IFI). Studies of therapeutic drug monitoring (TDM) for voriconazole have typically used a limited sample size at a single institution. This study aimed to investigate the role of TDM for voriconazole, examining relationships between voriconazole concentration and clinical outcome and adverse events as well as the factors affecting voriconazole pharmacokinetics.

Methods

In this multi-centre study across 7 Australian hospitals (Dec 2008 - May 2010), patient medical records were reviewed to collect information on clinical outcome and adverse events for patients who had ≥1 plasma concentrations measured. Ethics approval was received.

Results

202 patients received voriconazole during the study period, with 760 trough concentrations measured. Among patients administered voriconazole for the treatment of proven/probable IFI, treatment failure was more common in patients with voriconazole concentrations <1.7 mg/L ($p < 0.05$). Twenty-two patients (10.9%) experienced hallucinations while taking voriconazole; concentrations were measured during this event in 12 patients and were significantly higher (median 6.5 mg/L (range 2.9 - 10.9 mg/L), $p < 0.05$). Multivariate analysis of voriconazole concentrations identified a number of significant factors; most notably co-administration of prednisone, dexamethasone or methylprednisolone was associated with significantly reduced voriconazole concentrations ($p < 0.01$), implying a novel potential drug interaction between glucocorticoids and voriconazole.

Conclusions

Investigation of voriconazole TDM identified a greater incidence of treatment failure among patients with low voriconazole exposure, with high concentrations associated with an increased risk of hallucinations. A previously unreported potential drug interaction between glucocorticoids and voriconazole resulting in reduced voriconazole concentrations was identified.

Population pharmacokinetics of melfoquine in healthy adults and patients with uncomplicated *Plasmodium falciparum* malaria

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Objective

The determination of dosing regimens for the treatment of malaria is largely empirical and thus a better understanding of the pharmacokinetic and pharmacodynamic properties of anti-malarial agents such as mefloquine is required to ensure rational use and optimal dosing regimens. Research has suggested that patients with *Plasmodium falciparum* malaria exhibit altered mefloquine pharmacokinetics compared to healthy volunteers; it is not known whether these differences are due to the presence of malaria infection or if they could be accounted for by differences in other factors such as body weight, gender, etc. A population pharmacokinetic approach was used to provide estimates of mefloquine pharmacokinetic parameters and an assessment of the sources of variance in these parameters in patients and healthy volunteers.

Methods

The pharmacokinetics of mefloquine were assessed in 24 healthy adult male and non-pregnant female volunteers and 43 male and non-pregnant female patients with slide-proved *Plasmodium falciparum* malaria. Population pharmacokinetic modelling was conducted using NONMEM VI.

Results

A two-compartmental model with a single transit compartment and first-order elimination from the central compartment was found to most adequately describe mefloquine concentration-time data. Introduction of covariates into the structural model identified a significant effect of weight on CL/F, and weight and the presence of malaria on V_C/F. The population parameters estimates were CL/F = 1.22 L/hr; V_C/F = 677 L; Q/F = 1.34 L/hr; V_P/F = 186 L; K_A = 0.985 hr^{-1}, with the presence of malaria infection associated with a 40% reduction in V_C/F.

Conclusions

Alterations in apparent volume of distribution, and hence elimination half-life, are thought to be due to changes in α_1-acid glycoprotein levels. Further modelling of mefloquine pharmacokinetics with respect to plasma α_1-acid glycoprotein levels is needed in order to clearly establish this relationship and to ascertain the most appropriate dosing regimens, in particular in vulnerable patient populations.

Pharmacokinetics of gentamicin: The impact of frailty and implications for dosing

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Objective

Frailty is a biological syndrome characterized by a decrease in physiological reserve. The aim of this study was to characterize the pharmacokinetics of gentamicin in hospitalized older people and determine the impact of frailty on gentamicin clearance (CL).

Methods

Data was available on 38 patients from two studies on first dose gentamicin in older people (30 prophylaxis; 8 treatment) with median (range) age 80 (65 - 96) years, 26% female and 50% frail, as measured by the Reported Edmonton Frailty Scale. Simulations were performed at 3, 4, 5, 6, 7, 9 and 11 mg/kg to determine the percentage of patients reaching a target AUC between 70 - 100 mg/mL*min. Pharmacokinetic parameters were estimated and simulations were conducted in NONMEM.

Results

A one-compartment linear model with between subject variability (BSV) on CL and volume (V) best described the data. The addition of creatinine clearance calculated using Cockcroft-Gault with Lean Body Weight to the covariate model reduced the random component of BSV from 32 to 23%, with a further reduction to 20% with the addition of frailty. The final estimates for a non-frail patient were 6.1 L/hr and 14.6 L, for CL and V respectively. Frail patients showed a ~15% decrease in gentamicin CL. Simulations showed that dosing based on weight, renal function and frailty at 7 mg/kg gave the highest percentage (>81%) of patients achieving target AUC, with <3% of patients reaching toxic levels. Without the adjustment for frailty, 6% of patients fell into the toxic-range.

Conclusions

In an older hospital population, variability in gentamicin CL can be partly explained by frailty, even after adjusting for renal function.

Oral bioavailability and lymphatic transport of a highly lipophilic drug differs across pre-clinical species

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Objective

The current study aimed to (i) establish a method to examine intestinal lymphatic drug transport in mice, (ii) compare oral bioavailability and lymphatic transport of a model lipophilic drug (halofantrine) in different pre-clinical species (mice, rats and dogs), (iii) examine the impact of lipid dose and sex on lymphatic lipid and drug transport in different species.

Methods

Animals were administered 1.6 mg/kg halofantrine in a low (18.1 mg/kg) or high doses (100 - 1000 mg/kg) of ^{14}C long-chain lipid orally or intraduodenally. For calculation of bioavailability, separate animals were administered 0.3 - 1.6 mg/kg halofantrine in intralipid via IV infusion. Lymph or blood samples were taken and halofantrine (HPLC), triglyceride and phospholipid (colorimetric assay) and/or ^{14}C exogenous lipid (scintillation counting) concentrations measured.

Results

The oral bioavailability and lymphatic transport of halofantrine was in the order: dogs > rats > mice. For example, 28%, 7% and 2% of the dose were transported in lymph after administration with 18.1 mg/kg lipid. Lymphatic drug transport was markedly different across species despite similar lymph lipid transport and plateaued when lipid transport was >250 mg/kg over 8 h. Lymphatic lipid and drug transport was lower in female animals after administration of low lipid doses.

Conclusions

Highly lipophilic drug candidates are a frequent outcome of modern drug discovery programs. The current data suggests, at least for halofantrine, that the extent of absorption and lymphatic transport may be reduced in smaller pre-clinical animals. Care should therefore be taken when extrapolating data from small animals to larger animals or humans for compounds of this type.

P-067

Impact of lymphatic transport on systemic clearance and organ deposition patterns of highly lipophilic compounds

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Objective

This study aimed to investigate the influence of drug transport to the systemic circulation via the intestinal lymphatic system, rather than the intestinal blood supply, on clearance and organ deposition patterns using a lipophilic model compound (DDT).

Methods

Two parallel groups of rats were intravenously dosed with 1mL lymph or plasma containing 0.15 mg and 0.5 µCi ^{14}C-DDT. Lymph containing DDT was collected from donor rats after intra-duodenal infusion of ^{14}C-DDT in a lipid-based emulsion. Plasma containing ^{14}C-DDT was obtained by incubating plasma with ^{14}C-DDT. Recipient rats were either sacrificed 4 h post-dosing and organs/tissues removed to determine ^{14}C-DDT deposition or blood samples were taken over 30 h to examine ^{14}C-DDT systemic clearance. ^{14}C-DDT in dosing formulations, plasma and organs/tissues were determined by scintillation counting.

Results

Systemic clearance of DDT was >2-fold greater when delivered in lymph. DDT deposition into adipose tissue, heart, pancreas, brain, testes and lymphoid organs was significantly greater when delivered in lymph, whereas deposition in the GIT was significantly lower. No difference in DDT deposition was seen in the liver (highest recovery of any organ, ~15%), kidneys or lungs (1 - 2%).

Conclusions

The clearance and patterns of systemic distribution of DDT were markedly different when delivered into the circulation in lymph as opposed to plasma. This suggests that like DDT, the clearance, organ accumulation and therefore activity and toxicity profiles of highly lipophilic compounds may be altered as a result of changes to the extent of lymphatic transport (e.g. with formulation changes or in the fed vs. fasted state).

The impact of bovine serum albumin, oleic acid and linoleic acid on the metabolism of antipyrine in liver microsomes and isolated perfused liver

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Objective

This study investigated the impact of albumin on antipyrine metabolism and the interplay between fatty acids (FAs), albumin and antipyrine metabolism. Antipyrine does not bind strongly to albumin and a previous study had shown albumin to stimulate the metabolism of antipyrine in the perfused rat liver, via an unknown mechanism.

Methods

In vitro microsomal studies and *ex vivo* isolated perfused rat liver (IPL) were performed. Microsomal studies were conducted for the control, oleic acid (OA, 1 mM), linoleic acid (LA, 1 mM), bovine serum albumin (BSA, 15 g/L) and BSA + LA groups. Antipyrine concentration in the microsomal incubation and IPL samples was determined by HPLC. Pharmacokinetic parameters of antipyrine in the IPL were determined.

Results

In rat liver microsomal incubations, the presence of BSA facilitated antipyrine metabolism, LA inhibited antipyrine metabolism whereas OA had no effect. BSA counteracted the impact of LA on the metabolism of antipyrine catalysed by microsomal CYPs. The addition of BSA, OA or LA into the IPL perfusate had no impact on the hepatic clearance of antipyrine.

Conclusions

In the microsomal system, the effect of albumin was consistent with its sequestration of inhibitory FAs that are released from microsomal membranes during incubation. The lack of effect of albumin in the IPL was contrary to previous findings but in keeping with a lack of impact on antipyrine uptake or intracellular metabolism. The effect of FAs and albumin on drug metabolism is primarily dependent on the experimental system used (*in vitro* vs. *ex vivo*).

Effect of garlic, ginkgo and St. John's wort on the expression of rat intestinal P-glycoprotein and organic anion transporting polypeptide

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Objective

Previous perfused liver studies suggested that garlic and ginkgo induced the activity of hepatic Oatp, whereas SJW induced both P-gp and Oatp. *In vivo*, garlic increased the oral absorption of fexofenadine, possibly via induction of intestinal Oatp, whereas SJW and ginkgo did not affect absorption; however, a dual effect on opposing transport by Oatp and P-gp could not be excluded. This study examined the effects of garlic, ginkgo and SJW on the expression of intestinal P-gp and Oatp in the rat.

Methods

Male rats were dosed orally with garlic (120 mg/kg), ginkgo (17 mg/kg), SJW (1000 mg/kg) or water (control) for 14 days. On day 15, rats were anesthetized and the small intestine removed and divided into four equal segments, with segment I being the most proximal. Crude membrane fractions were prepared from the mucosa and analysed for P-gp and Oatp expression by Western blotting.

Results

Oatp content in segment I was increased significantly ($p < 0.05$) from control by treatment with garlic (88%) and SJW (63%). P-gp in segment II was increased significantly by SJW (43%).

Conclusions

Induction of intestinal Oatp by garlic may explain the increased absorption of fexofenadine. Lack of effect from SJW *in vivo* might arise from the combined impact of induced P-gp and Oatp in liver and of P-gp in intestine facilitating removal from plasma but compensated for by increased intestinal absorption via induced Oatp. The lack of effect from ginkgo on intestinal expression of both may explain its lack of effect on absorption.

Absorption of zinc related to nano- and micro-particles of ZnO by everted intestinal sac of rat

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Objective

This study aimed to compare the intestinal absorption of zinc (Zn) related to ZnO nanoparticles (nZnO) and micro-particles (μZnO) and to determine the absorption rate of Zn at different segments of small intestine.

Methods

The rat everted intestinal sac was incubated with Medium 199 (saturated with 95% O_2 and 5% CO_2, pH 7.4) containing nZnO or μZnO (20 μg/mL) for 1 h. The free Zn ions and ZnO particles were separated by ultracentrifugation. Zn in the mucosal and serosal medium and tissue was quantified by atom absorption spectrometer.

Results

Zinc in the forms of dissociated zinc ions and ZnO particles was absorbed, with Zn^{2+} being more extensively absorbed (ca. 80%). Higher intestinal absorption of Zn^{2+} and ZnO particles was observed for nZnO as compared to μZnO ($p < 0.05$). The absorption varied between different segments of small intestine, with the jejunum having the highest permeability. Retention of Zn in the intestine tissue was observed, with higher retention observed for nZnO as compared to μZnO. There was no difference in the amount of Zn retained in the intestine tissue between different segments.

Conclusions

Zinc can be readily absorbed through all segments of the small intestine in the forms of zinc ions and ZnO particles, with jejunum being the most permeable section. Higher intestinal absorption of zinc can be achieved when exposed to nZnO as compared to μZnO, suggesting potential higher toxicity of nZnO than bulk ZnO particles after oral exposure.

P-071

Oral bioavailability of a poorly soluble CETP inhibitor is enhanced by dosing in lipidic formulations, but is insensitive to formulation change

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Objective

To assess the use of an *in vitro* lipid digestion model to predict the *in vivo* exposure of a poorly water soluble CETP inhibitor (CETPi) after oral administration of a series of lipid based formulations (LBF).

Methods

Solubilised drug concentrations in the aqueous phase (AP) after *in vitro* digestion were assessed for a range of LBFs and compared to *in vivo* drug exposure after oral administration of the same lipid formulations and a suspension formulation to beagle dogs.

Results

Drug solubilisation after *in vitro* digestion of LBFs varied significantly (~14 fold) from 0.03 to 0.42 mg/mL. In contrast, administration of the LBFs to beagle dogs resulted in much lower (~2 fold) differences *in vivo* exposure, and oral bioavailability (BA) was surprisingly high (49 - 97%). Drug BA from the suspension formulation was low (4%). Initial drug solubility in biorelevant media alone was also quite high (0.18 mg/mL), but declined rapidly after 30 min.

Conclusions

Formulation as a LBF overcomes the dissolution limitations associated with the CETPi suspension formulation. However LBFs that resulted in significant drug precipitation after *in vitro* digestion remained capable of significant increases in BA *in vivo*. The high *in vivo* exposure after administration of all the LBFs may reflect the intrinsic initial solubility of the CETPi in intestinal fluids (regardless of formulation composition), high intestinal permeability (and therefore lowered solubilisation requirements) or precipitation of drug in a readily re-solubilised amorphous form.

Methimazole: Preparation, stability and *in vitro* penetration for transdermal delivery in cats

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Objective

This study was conducted to evaluate the stability and *in vitro* bioavailability of a methimazole dosage form for transdermal delivery in the management of feline hyperthyroidism.

Methods

The preparation of methimazole in a Lipoderm® base was optimised, the stability of the formulation was determined, and *in vitro* tests were designed to measure the absorption of methimazole across a membrane, using Franz cells.

Results

The study findings indicated that uniform distribution of methimazole throughout the Lipoderm® base was optimised using the tile method, with a mean percentage yield of 99.17 ± 0.60%. Formulated in the Lipoderm® base, methimazole was found to be stable over a 3 month period when protected from light and stored at 30°C, with a mean percentage of 99.9 ± 1.8%. However, storage under accelerated conditions (40°C/75% RH) with light exposure, resulted in significant degradation of methimazole, which occurred over a 28 day period, with a mean percentage of only 84.9 ± 4.4% A non-polar photodegradant formed during this process was detected using a validated high performance liquid chromatography (HPLC) method. Methimazole is freely released from the Lipoderm® base, with between 70 and 100% of the total methimazole dose present in the receptor fluid after 30 minutes. The Franz cell study using the calf skin showed that almost 90% of the total methimazole dose is able to penetrate a full thickness skin barrier after only 3 hours.

Conclusions

Methimazole which was uniformly distributed throughout the Lipoderm® base, was stable for 3 months when stored protected from light and is capable of diffusing through full thickness skin.

Flow rate modulated drug release kinetics from nanoporous implant studied by *in situ* monitoring using microfluidic reflectometric interference Fourier transform spectroscopy (RIFTS)

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Objective

Porous materials based on porous silica, alumina and nanotubular titania have been demonstrated as excellent candidates for the design of therapeutic implants, not only because porous structures support tissue integration, but also because pores act as remarkable reservoirs for slow drug elution over extended time periods, from several days to several weeks. *In vitro* drug release studies from these implants are commonly performed by batch methods and periodic spectrophotometric determination of amount of released drug into buffer solution. However, there are considerable disadvantages of this approach because human body is a highly dynamic system and kinetics of drug release is highly influenced by flow rate of body fluids at the porous interface of the implant. The aim of this work is to develop a new microfluidic optical method able to directly monitor drug release from the porous layer of implants with specific focus to study influence of flow rate on drug release kinetics.

Methods

Nanoporous anodic aluminium oxide (AAO) prepared by electrochemical anodization regarding its tuneable pore geometries, high surface area, biocompatibility, unique optical properties and proved drug delivery application is used as the model substrate and poorly soluble drug indomethacin loaded into AAO is used as a model for this study. To mimic the effect of the blood flow rate on drug release kinetics from the porous implant, we developed a special a microfluidic system, capable of integrating of drug loaded AAO nanoporous platform and reflectometric interference Fourier transform spectroscopy (RIFTS) with ability to continuously monitor the changes optical properties (effective refractive index) as result of drug release from AAO pores.

Results

Developed RIFTS device is a compact and highly sensitive to any changes in the refractive index and thickness of the porous film (recorded as changes in effective optical thickness, EOT) which was used for precise determination of drug release kinetic from the pore structures influenced by many parameters including: flow rate of buffer, pore dimensions and their surface chemistry, temperature and chemical properties of drug molecules. The changes in EOT as result of drug release from pores were continuously monitored for approximately 2 hours to capture kinetics of burst release. Comparative spectrophotometric measurements of released drugs in buffers were also performed, which align completely with the RIFTS measurements (at 30 µl/min).

Conclusions

Our initial results are promising toward development of simple microfluidic system to perform dynamic drug release characterisation of implantable drug delivery systems.

Kafirin microparticles for targeted drug delivery

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Objective

Sorghum is a major grain crop grown in Queensland. It is known to be incredibly indigestible. This characteristic is thought to be due to kafirin, a storage protein found in the seeds of the sorghum grain. The aim was to formulate and analyse kafirin microparticles loaded with prednisolone, and evaluate their potential as a targeted release oral delivery device.

Methods

Kafirin microparticles loaded with prednisolone were formulated using a phase separation method. The microparticles were freeze-dried, then analysed to quantify the amount of prednisolone loaded. Prednisolone release from microparticles was measured over a total of 7 h in conditions simulating the stomach followed by the small intestine. Drug release was also measured in the simulated conditions with enzymes – pepsin in the gastric environment and pancreatin in the conditions mimicking the small intestine.

Results

Based on the combination of kafirin and prednisolone that resulted in the highest drug loading, approximately 30 mg of microparticles contained 5 mg of prednisolone. From these microparticles, approximately 20% of the prednisolone was released over the 7 h period – with the extent and rate of release being comparable irrespective of whether any enzymes were present in the media.

Conclusions

The small amount of prednisolone released in the simulated conditions of the stomach and small intestine over the 7 h suggests that kafirin microparticles may have potential as an oral drug delivery device targeting the large intestine.

P-075

Investigating the role of drug properties on formation and loading capacity of zein microparticles

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Objective

Zein, a storage protein found in maize has been investigated for its use in drug delivery. Following previous work in which zein microparticles were successfully loaded with hydrocortisone, current work has investigated the loading of mesalazine into zein.

Methods

Zein was loaded with mesalazine using a previously optimised coacervation method for formulating zein-hydrocortisone microparticles. The starting quantities of zein and mesalazine were varied, and their effects on drug loading were analysed. Modifications to the method were investigated to optimise mesalazine loading into the microparticles.

Results

Loading of mesalazine into zein microparticles were compared with that of hydrocortisone. The chemical nature of mesalazine makes it difficult to load into zein microparticles using this coacervation process.

Conclusions

Difference in drug loading may be explained by the different chemical properties of the drugs. Investigating the microparticle formulation process for mesalazine loading will help to further the understanding of zein as a suitable drug delivery device in targeted release.

Development of a novel cell-based system for screening epigenetic drugs: Application for development of liposomal-based delivery of decitabine

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Objective

Our research focuses on: (i) development of a novel bioassay system for rapid screening of epigenetic drugs and (ii) improvement of the delivery and potency of decitabine by liposomal formulation.

Methods

(i) A cell-based assay system was designed based on a triple-mutated bacterial nitroreductase gene, TMnfsB, that encodes an oxygene insensitive flavin mononucleotide-dependent enzyme, which has no phenotypic consequences when expressed in the non-malignant human cell line, MCF10A. TMnfsB and the Red Fluorescent Protein (RFP) coding sequences were fused and expressed as a RFP-TMnfsB fusion protein under the control of a exogenous promoter, CMV. These cells containing expression of the RFP-TMnfsB gene are rapidly killed by CB1954 (5-(azaridin-1-yl)-2,4-dinitro-benzamide). Following treatment of MCF10A- RFP-TMnfsB with CB1954, surviving colonies where identified where the TMnfsB gene was epigenetically silenced. In these isolates, the TMnfsB gene can be reactivated after treatment with epigenetic drugs such as 5-aza-2'-deoxycytidine (decitabine) and suberoylanilide hydroxamic acid (SAHA) and assayed using flow cytometry since reactivation of the RFP-TMnfsB gene is associated with increased red fluorescent. This provides a rapid system to assay the activity of epigenetic drugs. (ii) Formulation of hydrophilic decitabine with liposome protects the drug from degradation. The size and zeta potential of liposomal decitabine were investigated. The potency of liposomal decitabine will be assayed using the developed bioassay system.

Results

The RFP expression of the derivative MCF10A cells was shown to significantly increase after treatment with epigenetic drug such as 1 µM of decitabine. The combination of both SAHA and decitabine showed an additive effect on gene reactivation. The liposome formulation of decitabine has achieved a particle size of ~150 nm and zeta potential of -55 mV. Controlled release from liposomal decitabine and enhanced potency are anticipated.

Conclusions

The developed bioassay system provides a novel and rapid system to compare the efficiencies of epigenetic drugs.

Optimization of a 5-fluorouracil loaded sterically stabilized liposomal formulation

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Objective

Liposomes are recognized as effective carriers for anticancer drugs as they can prolong the plasma retention and increase tumour distribution of encapsulated drugs. This study aimed to prepare 5-fluorouracil (5-FU) loaded sterically stabilized liposomes and to optimize the formulations by using lipids with different phase transition temperature (Tm) and varying ratios of cholesterol and PEG-lipids, thus increasing their loading capacity and prolonging their release.

Methods

Small uni-lamellar liposomes were prepared by thin film hydration and membrane extrusion. Different ratios and types of lipids (HSPC, DSPE, PEG2000-DSPE, PEG2000-DMPE and cholesterol) were used. The release kinetics of 5-FU from loaded liposomes was measured through a dialysis-bag by HPLC.

Results

Increasing the molar ratio of cholesterol (30% to 40%) reduced the loading capacity. Application of lipids with higher phase Tm (e.g. DSPC and PEG2000-DSPE) resulted in more prolonged release: <80% within 110 min, compared with 60 min when prepared with HSPC and PEG2000-DMPE. The release behaviour was fitted to the Weibull equation. Liposomes prepared with 5% PEG-lipids showed more sustained release compared with higher molar ratios of PEG-lipids (8% and 10%). This confirms the complex role of PEG in liposomal formulation. A preliminary microdialysis study showed a greater tendency for distribution of 5-FU into tumour tissue relative to s.c. tissue of rats after being encapsulated into the PEGylated liposomes.

Conclusions

Liposomes prepared with DSPC: Cholesterol: PEG2000-DSPE (65:30:5, molar ratio) demonstrated a high loading capacity and the most prolonged release profile. An optimized liposome formulation was identified for further pharmacokinetic studies.

Lyophilisation for the production of silica-lipid hybrid (SLH) drug delivery systems

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Objective

Lyophilisation has been investigated as an alternative to spray drying for the production of silica-lipid hybrid (SLH) microcapsules as a controlled drug delivery system for poorly water soluble drugs. The NSAID celecoxib (CEL) was employed as a model drug.

Methods

The SLH microcapsule system was produced by freeze drying of silica-stabilized submicron emulsions in the presence and absence of maltodextrin (acting as a cryoprotectant). Negatively charged lecithin was used as the emulsifier. CEL was dissolved in the lipid oil phase before emulsification. HPLC was used for determination of CEL loading levels and release kinetics. The freeze-dried SLH microcapsules were investigated for their physicochemical and biopharmaceutical properties: lipid carrier digestion and drug dissolution properties.

Results

The use of maltodextrin as a low as 2% was effective in preserving the structure of silica- stabilized emulsions after lyophilisation and produced well encapsulated, spherical SLH microcapsules (1% CEL loaded) of 2 - 5 µm in diameter. *In vitro* dissolution study performed under simulated sink conditions (pH 7.2) revealed that micro-encapsulation of CEL in the SLH matrix improved the dissolution kinetics of CEL. *In vitro* lipase mediated digestion studies performed under simulated fasting intestinal conditions showed lipolysis kinetics can be controlled by varying the silica and maltodextrin content in the microcapsules. Both silica and maltodextrin were shown to exert synergistic inhibitory effect on the digestion of SLH microcapsules.

Conclusions

Maltodextrin containing SLH microcapsules produced by lyophilisation are promising as an oral delivery system for poorly soluble drugs. Their mechanism for action includes increasing drug release kinetics and controlling carrier digestion.

Liposomal micellar hybrid (LMH) carriers for enhanced loading and delivery of poorly soluble drugs

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Objective

We report on the fabrication of a novel multi-component hybrid drug delivery system for hydrophobic therapeutics: liposomal micellar hybrid (LMH) carriers consist of drug loaded micelles encapsulated into liposomes. The LMH carrier is engineered to facilitate: (a) higher drug loading level, (b) protection of micelles from dissociation and (c) controlled drug release.

Methods

LMH are prepared in a two-step process, initially hydrophobic drugs (Coumarin 102 and Itraconazole) are loaded into micelles, and then these drug loaded micelles are used to rehydrate a lipid film and form liposomes by membrane extrusion. The drug content was quantified by using fluorescence spectroscopy and reverse phase HPLC. *In vitro* dissolution tests were carried out in sink conditions using either a USP 23 type II apparatus or a dialysis bag method.

Results

The average size of LMH carriers was 167.7 nm, PDI was 0.55 and zeta potential was found to be -70.6 mV. In comparison the average size, PDI, and zeta potential of liposomes was 150.1 nm, 0.38 and -29.7 mV. LMH was shown to enhance the overall drug loading of poorly soluble drugs, i.e. ~3 fold increase compared to conventional liposomes. *In vitro* dissolution studies indicated a slow (sustained) rate of drug release from LMH in comparison with the conventional liposomes.

Conclusions

LMH carriers are being developed to increase drug loading and modify drug release profile. Our hypothesis is that liposomes can act as molecular fences for the drug loaded micellar structures and isolate them from the biological environment. Successful development of LMH carriers would open new avenues for liposomal controlled drug delivery of hydrophobic agents.

Novel liquid crystalline lipid dispersions stabilized by silica nanoparticles for the delivery of poorly soluble drugs

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Objective

Liquid crystalline lipids are promising drug delivery systems for poorly soluble drugs because of their high internal surface area, biodegradability and bioadhesiveness. The major limitation of these systems is their susceptibility to digestion by gastric enzymes. The main objective of this project was to formulate glyceryl monooleate (GMO) liquid crystalline dispersions stabilised using silica nanoparticles. The influence of silica nanoparticles on lipid digestion rate and model drug (Coumarin 102) release was explored, as well as their freeze-thaw stability.

Methods

GMO (cubic) liquid crystal dispersions were prepared by high-speed homogenisation using either aerosil A380 or ludox silica nanoparticles as stabilisers. GMO dispersions were characterized in terms of particle size and zeta potential, lipid digestion and *in vitro* release, as well as their behaviour following redispersion after freeze-drying.

Results

The GMO disperse phases were ~160 nm in diameter, while the zeta potential decreased (to ~-30 mV) with increasing silica nanoparticle concentration. GMO dispersions stabilised by silica particles exhibited a reduced digestion rate as well as sustained Coumarin 102 release, compared to the control (copolymer stabilised) dispersions. Freeze-dried nanoparticle stabilised GMO dispersions showed further reduction in the digestion rate compared to the wet dispersion, with no effect observed for the control.

Conclusions

Silica nanoparticles stabilised cubic GMO dispersions were successfully prepared, providing enhanced protection against enzymatic digestion and controlled drug release, compared to copolymer stabilised systems.

Formulation, characterisation and *in vitro* haemolytic evaluation of cryptolepine-loaded gelatine nanoparticles

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Objective

Cryptolepine hydrochloride-loaded gelatine nanoparticles were developed and characterised as a means of exploring formulation techniques to improve the pharmaceutic profile of the compound.

Methods

Cryptolepine hydrochloride-loaded gelatine type(A) nanoparticles were developed based on the double desolvation approach, using glutaraldehyde as the cross linker. After optimisation of formulation parameters, the rest of the study was conducted at two different formulation pH (2.5 and 11.0) and by two different approaches to drug loading. Formulations were characterised by size, zeta potential, polydispersity index, morphology, *in vitro* haemolytic activity and stability. Release characteristics were investigated by the beaker method and by dialysis. Three cryoprotectants were investigated for preparation of freeze-dried samples.

Results

Nanoparticles of size mostly less than 350 nm and zeta potential above ±20 mV were obtained when formulation pH was between 2.5 and 5 and above 9. Entrapment efficiency was higher at pH 11.0 than pH 2.5 and for products formulated when drug was loaded during second desolvation. Further investigation of pH effect showed a new isoelectric point of 6.23 - 6.27 at which zeta potential of nanoparticles was zero. Sucrose and glucose were effective in low concentrations as cryoprotectants. The best formulation produced an EC_{50} of 227.4 µM compared to 51.61 µM by the free compound, indicating reduction in haemolytic effect. Drug release from formulation 2.5 ds prepared at pH 2.5 with drug loading carried out during second desolvation stage was the most gradual. Formulations were stable at 4°C over 52 weeks, but less so at room temperature.

Conclusions

Cryptolepine-loaded gelatine nanoparticles exhibited reduced haemolytic effect compared to the pure compound.

Titania nanotubes for drug delivery into trabecular bone: *Ex vivo* study using bovine bone model

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Objective

The purpose of this study is to investigate the application of titania nanotube arrays (TNT) on Ti wires as an implantable device for predictable drug delivery into bovine trabecular bone cores.

Methods

Titania nanotube arrays were fabricated 360° around titanium (Ti) wires of 0.75 mm width, which were then embedded in bovine trabecular bone cores *ex vivo*. The loading characteristics of Rhodamine B into the TNT and its flux, concentration and rate of diffusion into the bone were measured at different time intervals (1 h, 4 h, 5 h, 12 h, 24 h and 5 days). To maintain viability of the bone cores, they were perfused with cell culture media at 7 mL/h.

Results

Fully loaded TNTs contain a drug flux of 0.30 ± 0.04 mg/cm².s. Perfusion media flow plays a part in influencing the release pattern, as the drug flux with perfusion was significantly greater, i.e. an order of magnitude higher (10.73 ± 0.60 mg/cm².s) than the flux of drug release without perfusion flow. Nevertheless, a consistent, gradual release of Rhodamine B was observed, with the model drug spreading radially into the surrounding bone core over a period of 1 week.

Conclusions

This novel system presents a promising strategy for TNT synthesized on titanium wires, as a drug eluting device to encapsulate desired drugs and provide controlled release into bones, for targeting orthopaedic conditions such as treating bacterial infections, wound inflammation in bones, the improvement of osteoblast functions during tissue regeneration or bone healing.

Electrochemically-engineered nanotubular titania with biopolymer thin film deposition as implantable device for prolonged delivery of drugs and drug carriers

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Objective

In this work, we present an improved strategy for local drug administration using nanotubular titania (TNT) arrays prepared by simple electrochemical anodisation. Biopolymer surface coatings were applied, in an effort to address the limitations of systemic therapy, low efficacy of poorly soluble drugs, and therefore to extend the delivery of these drugs in a localized, implantable drug delivery system.

Methods

Indomethacin, an anti-inflammatory drug, was used as an example of a poorly soluble drug. Polymeric micelle, D-α-tocopheryl polyethylene glycol 1000 succinate (TPGS) was used as the model for drug nano-carrier. Upon drug loading in TPGS, TNT was coated with thin films of polymers prepared by two techniques: plasma polymerisation (poly-allylamine) and dip-coating (chitosan and poly (lactic-co-glycolic) acid, PLGA). TNT implants before and after drug loading and polymer deposition were characterised by scanning electron microscopy (SEM), thermogravimetric analysis (TGA) and time-of-flight secondary ion mass spectrometry (ToF-SIMS). The release of drug and micelle (drug nano-carrier) was monitored using UV-Vis spectroscopy over 3 - 4 weeks.

Results

Drug-loaded micelles were encapsulated inside the nanotubes and a high drug loading (>15 wt%) was achieved. Biopolymer deposition on TNT was confirmed and initial burst release was significantly reduced. An extended elution of drugs and drug-loaded micelles with minor burst release over a period of more than 4 weeks was obtained.

Conclusions

The design of TNT therapeutic implants, integrating micelles as drug nanocarriers and biopolymer film deposition to suppress burst release, was successfully demonstrated to extend the drug delivery of poorly soluble therapeutics to more than 30 days.

Surface modification of diatomite silica microcapsules for improved drug delivery applications

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Objective

The aim of this work is to address conventional drug delivery problems, namely, poor drug bioavailability, low biodistribution and undesirable pharmacokinetics. We are developing a new approach using natural silica microcapsules as drug carriers for poorly water soluble drugs. Considering their outstanding properties, i.e. excellent biocompatibility, high porosity and surface area, non-toxicity, low cost and abundance in nature, we propose in this study that there is much underlying potential to replace their synthetic counterparts (MCM-41, SBA-15).

Methods

Raw diatomaceous earth (DE) material was purified and classified to obtain diatom silica microcapsules as drug microcarriers. Various hydrophilic and hydrophobic silanes (3-aminopropyltrimethoxysilane, 3-glycidyloxypropyl trimethoxysilane, mPEG-Silane and 7-octenyltrichlorosilane) and phosphonic acids (2-carboxyethyl-phosphonic acid and 16-phosphono-hexadecanoic acid) were used to achieve surface modification of diatom microcapsules via standard silanisation and phosphonation techniques. Indomethacin was selected as the model hydrophobic drug. Thermogravimetric analysis (TGA) and UV-Vis spectrophotometer were used to characterise the drug loading and *in vitro* release studies respectively.

Results

Release studies showed two phase drug release which includes: an initial burst release for 6 hrs, followed by zero-order sustained drug release kinetics for up to 26 days . Variations in drug release profiles and loading capacity of 6 - 20% for DE was observed, which was attributed to the various active functional groups that render its surface hydrophilic or hydrophobic for drug deposition, thus offering flexibility in adjusting dosage and time for the delivery of therapeutics.

Conclusions

This study demonstrates the potential of natural DE material as an effective drug carrier for poorly water-soluble drugs, which can be tailored via proposed versatile surface functionalisations to achieve controlled drug release and hence, sustained therapeutic effects.

Propranolol hydrochloride-loaded alginate gel microspheres produced by a novel impinging aerosols method for oral delivery

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Objective

To encapsulate propranolol hydrochloride in alginate gel microspheres to improve protection of therapeutic drug in the gastric environment and investigate their potential as controlled release oral formulations.

Methods

Propranolol hydrochloride was directly encapsulated in alginate gel microspheres (40 - 50 µm in diameter) using a novel method involving impinging aerosols of $CaCl_2$ cross-linking solution and sodium alginate solution containing dissolved drug. Microspheres were characterized in terms of size, morphology, drug loading and drug release behaviour.

Results

Microspheres formulated using the lowest $CaCl_2$ crosslinking concentration (0.1 M) exhibited the highest drug loading (14%, w/w of dry microspheres) and highest encapsulation efficiency (66.5%). Less than 4% propranolol release occurred from hydrated alginate gel microspheres and 35% from dried microspheres in 2 h in simulated gastric fluid (SGF). The majority of the drug load (90%) was released in 5 and 7 h from hydrated and dried microspheres respectively in simulated intestinal fluid (SIF).

Conclusions

Incubation of hydrated microspheres (crosslinked using 0.5 M $CaCl_2$) in SGF prior to SIF prolonged the time of release in SIF to 10 h which has implications for the design of test protocols and their correlation with *in vivo* release behaviour. Restricted propranolol release in SGF and complete extraction in SIF demonstrates the potential of alginate gel microspheres, produced using the impinging aerosols technique, for oral delivery of pharmaceuticals.

The potential for controlled delivery of antivirals to the female genital tract using microporous polymer matrices

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Objective

Acyclovir (ACV) is a synthetic nucleoside analogue with activity against herpes simplex virus 2 (HSV-2). The virus causes genital ulcers and is known to increase the risk of HIV transmission in persons infected with HSV-2. Since mucous membrane of the vagina provides a suitable site for local delivery of antiviral agent, vaginal ring has been designed to prevent sexual transmitted disease.

Methods

ACV was incorporated in controlled-release polycaprolactone (PCL) matrices designed for application as intravaginal ring inserts (IVRs) to treat HSV infection and to provide a barrier against HIV transmission. The release behaviour of drug from matrices during 30 days and antiviral activity of released medium were studied.

Results

Around 55% of the ACV content was gradually released from matrices containing a theoretical 10% drug loading over 30 days in simulated vaginal fluid (SVF) at 37°C. No significant differences were detected in the morphology of drug-free matrices or ACV-loaded matrices before and after release testing. Plaque reduction and tissue culture infectious dose (TCID50) assays confirmed the antiviral activity of released ACV against HSV-2 replication in primate cells (Vero).

Conclusions

The release kinetics could be described effectively by the Higuchi model, suggesting that Fickian diffusion of ACV is occurring; although the Korsmeyer-Peppas model indicated the involvement of multiple release phenomena. Sustained release of active ACV demonstrates that PCL matrices offer possibilities for vaginal delivery of antiviral agents in the treatment and prevention of sexually transmitted infections.

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Controlled ocular drug delivery using polycaprolactone (PCL) inserts

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Objective

Polymeric matrices of polycaprolactone (PCL), a biodegradable polymer, were employed to encapsulate a small molecule active (dexamethasone (Dex)). Ocular inserts containing Dex were developed for treating anterior inflammatory diseases, such as iritis and iridocyclitis, and posterior inflammatory diseases, such as retinitis and choroiditis.

Methods

Different PCL matrix formulations with varying amounts of Dex (10%, 15% and 20%) were produced and characterised via *in vitro* testing and texture analysis.

Results

In vitro drug release studies showed the release rate of Dex from PCL matrices over 24 hours was gradual and complete and could be described by the anomalous, non-Fickian, model. The compression resistance of Dex-loaded PCL matrices decreased with increasing Dex content and following drug release.

Conclusions

The ability of PCL matrices to control the release of small molecule illustrates promise for fabricating controlled-release PCL inserts for future ophthalmic applications.

Improved dissolution of poorly water-soluble drug dapivirine by solid dispersion technique

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Objective

Dapivirine is an antiretroviral drug used to prevent the replication of human immunodeficiency virus (HIV) in host cells via inhibition of the enzyme reverse transcriptase. Dapivirine is of great clinical value as it acts synergistically with most of the other antiretroviral drugs. However, its use is limited by its poor solubility and dissolution rate which results in poor bioavailability. One way to improve the dissolution rate of dapivirine and thereby the bioavailability is by adopting solid dispersion technique. This study aimed to improve the dissolution of dapivirine by solid dispersion technique.

Methods

Solid dispersion of dapivirine were prepared by solvent and fusion method using 1:1, 1:4 and 1:6 ratios of drug and polymers (PEG 8000 and PVPk30). Fourier transform infrared (FTIR) spectroscopy, powder X-ray diffraction (XRD), thermal analysis (DSC) and *in vitro* dissolution studies were studied to characterize the prepared solid dispersion. The physical appearance of solid dispersions was also investigated by scanning electron microscopy (SEM).

Results

The results indicated that *in vitro* dissolution rate of dapivirine was improved in the solid dispersion of the drug compared with physical mixture and drug alone. The drug release was 65% from solid dispersion; 19% from physical mixure and 18% from drug alone after 60 mins. The results obtained from FTIR and XRD showed good evidence of drug-carrier interaction.

Conclusions

In conclusion solid dispersions of dapivirine in water-soluble carriers proved to be an effective means of increasing the dissolution rate which in turn enhances bioavailability of the drug.

Evaluation of HPTLC for the quantification of phenylpropanoids in commercial echinacea products using video densitometry

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Objective

There is currently large chemical variability between *Echinacea* products available for both research and consumption. This variability impacts both the quality and efficacy of these products. High performance thin-layer chromatography (HPTLC) provides several advantages for quality control in terms of its simplicity, cost-effectiveness and efficiency. This is particularly when coupled with video densitometry, a rapid method of detection which allows for high sample throughput. This paper aimed to validate a method for the quantification of commercial *Echinacea* products using HPTLC and video densitometry. The method was developed in the hope that it may provide a foundation for a future method used in quality control settings.

Methods

Products were analysed based on the presence of markers commonly found in echinacea. Three phenylpropanoids were quantified as markers: chlorogenic acid, cichoric acid and echinacoside. Levels of these standards present in the products were quantified based on calibration curves constructed. The developed method was validated according to current International Conference on Harmonisation (ICH) guidelines in terms of accuracy, precision, linearity, specificity, limits of quantification and detection. Sample application and development were performed manually and derivatisation was not used.

Results

The method was able to successfully quantify these markers in three commercial *Echinacea* formulations. It was found that the method achieved better limits of detection than previous assays, despite exhibiting lower repeatability particularly when quantifying cichoric acid.

Conclusions

It is speculated that with automation and derivatisation the method may demonstrate further improvements with respect to validation parameters. This work has established a basis for the incorporation of HPTLC coupled with video densitometry for the quantitative analysis of commercial *Echinacea* products and other herbal formulations.

UPLC-MS analysis of cotinine and 3'-hydroxycotinine in urine

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Objective

To develop a simple and robust UPLC-MS method for the detection and measurement of nicotine metabolites from urine. There is increasing evidence that genetic differences in nicotine metabolism are important determinants of smoking cessation.

Methods

Free and total (post enzymatic hydrolysis) levels of urinary nicotine metabolites were analysed after 25x dilution and addition of deuterated internal standard. Diluted samples were injected directly into the UPLC-MS onto a BEH C18 column (2.1 x 100 mm x 1.7-micon particles) with tandem mass spectrometric identification and quantification using positive ion electrospray ionization with multiple reaction monitoring on a quadrupole ion trap mass analyzer. Chromatography utilised water and acetonitrile at a flow rate of 0.3 mL/min. A linear eluent gradient was employed; initial eluent 100% water for 3 minutes then to 18% acetonitrile over 6 minutes.

Results

The LOD and LLOQ for *trans*-3'-hydroxycotinine were 0.03 and 0.1 ng/mL respectively and for cotinine, were 0.2 and 0.6 ng/mL respectively. Precision: RSD ranged from 0.5% to 1.2% for 770 ng/mL cotinine; RSD ranged from 2.0% to 3.4% for 1300 ng/mL trans-3'-hydroxycotinine. In smokers (1 - 45 cigarettes/day), the total urinary cotinine ranged from 490 to 10600 ng/mg creatinine and total 3'-hydroxycotinine ranged from 17 to 15400 ng/mg creatinine. The ratio of 3'-hydroxycotinine to cotinine ranged from 0 to 3.66.

Conclusions

A highly sensitive, specific and rapid UPLC-MS assay was developed for detection and quantification of two major nicotine metabolites in urine from smokers. This assay is suitable for genetic studies involving metabolism of nicotine, smoking prevalence and cessation.

Investigating the potential of a new pre-processing method for analysing Raman spectra containing fluorescence

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Objective

To investigate the potential of a new spectral pre-processing method for analysing Raman spectra containing fluorescence.

Methods

Different indomethacin-polyvinylpyrrolidone solid dispersions were prepared and Raman spectra of the samples were recorded. The spectra exhibited auto-fluorescence. Two pre-processing approaches were used on the spectra, and their effect on the spectra of the different solid dispersions was compared using principal component analysis (PCA). Firstly, the traditional pre-processing method of standard normal variate (SNV) transformation, which can mitigate but does not separate the fluorescence signal, was applied. In the new pre-processing method, a polynomial baseline correction that separates the fluorescence signal from the Raman signal, and retains the fluorescence signal in a separate data set was used.

Results

Both processing methods resulted in a similar ability to resolve the different solid dispersions in this study. The potential advantage of the second approach is that more information is retained, and PCA can be performed on the Raman or fluorescence signal alone or on both the Raman and fluorescence signals. Since more information was retained with the new approach, improved understanding of the Raman and the fluorescence signals was obtained.

Conclusions

Fluorescence and Raman signals were separated using the new pre-processing approach. While the new approach did not increase the ability to resolve different solid dispersion samples in this study, it may be valuable in the analysis of other fluorescing samples since more information is retained.

Application of HPLC-QTOF-MS/MS to assess the chemical diversity of the marine actinobacterial genus *Salinispora*

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Objective

The genus *Salinispora*, like many actinobacteria, produces a host of secondary metabolites with many pharmaceutical applications, including the antibiotic rifamycin, and the anticancer compounds salinosporamide A and staurosporine. It has been determined that *Salinispora* produces secondary metabolite profiles that are species-specific. This feature of *Salinispora* is unique amongst actinobacteria and could provide a useful basis for identifying strains with unique secondary metabolite profiles. This project is a preliminary examination of the application of HPLC-QTOF-MS/MS to determine the chemical diversity of genus *Salinispora* at the species and intra-species levels.

Methods

Bacterial extracts were prepared by solvent extraction (ethyl acetate) of bacterial cell mass of *Salinispora*, followed by evaporation and reconstitution. An HPLC-QTOF-MS/MS metabolic fingerprinting approach was developed and applied to two species, *S. arenicola* (n = 6) and *S. pacifica* (n = 6). Principal component analysis (PCA) was used to identify the chemical variation among the metabolite profiles.

Results

It was found that the analysis of HPLC-QTOF-MS/MS data with PCA could identify both species and intra-species diversity in the strains tested.

Conclusions

Analysis of metabolic fingerprinting derived from HPLC-QTOF-MS/MS using PCA was applied to assess the secondary metabolite diversity of marine actinobacterial genus *Salinispora*. Our preliminary results demonstrate that this technique can identify strains of *Salinispora* with variations in their secondary metabolite profiles and is therefore suitable for application to a larger sample set.

Identification of antimicrobial compounds in the crude extracts of the Australian macrofungi, *Hohenbuehelia* sp. and *Ramaria* sp., through bioassay-guided fractionation

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Objective

Crude water and ethanol extracts of *Hohenbuehelia* sp. and *Ramaria* sp. collected in Queensland exhibited promising antimicrobial activity previously prompting identification of component(s) responsible for this activity via bioassay-guided fractionation.

Methods

Extracts were fractionated using preparative HPLC. Based on previous bioactivity, fractions from *Hohenbuehelia* water extract (HWE) were tested against Gram +ve (*Listeria monocytogenes*) and Gram -ve (*Pseudomonas aeruginosa*) bacteria, and two fungi (*Geotricum candidum* and *Saccharomyces cerevisiae*), whereas *Ramaria* ethanol extract (REE) fractions were tested against another Gram +ve (*Bacillus cereus*) and Gram -ve bacteria (*Acinetobacter baumannii*) and the same fungi. The fractions from *Hohenbuehelia* ethanol extract (HEE) and *Ramaria* water extract (RWE) were tested against the fungi only. Minimum inhibitory concentrations (MIC) were calculated for the active fractions.

Results

Water extracts of both fungi showed little activity, except for one HWE fraction which inhibited growth of *S. cerevisiae* (MIC 125 µg/mL) that was associated with phenylalanine and/or dipeptides. Three fractions from HEE had MICs of 16 - 250 µg/mL against *S. cerevisiae* and 125 - 250 µg/mL against *G. candidum*. Four REE fractions had MICs of 125 - 1000 µg/mL against *B. cereus*, 31.2 - 250 µg/mL against *S. cerevisiae* and 62.5 - 250 µg/mL against *G. candidum*. Analytical techniques revealed the presence of a mixture of saturated and unsaturated fatty acids as the active components in the ethanol extracts from both macrofungi.

Conclusions

Unfortunately, no potential antimicrobial lead compounds were discovered in this study. Fatty acids and phenylalanine and/or dipeptides were apparently responsible for bioactivity.

Development and characterization of topical formulation products of the Northern Kaanju traditional medicinal plant, *Dodonaea polyandra*

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Objective

To develop and characterize topical use formulations containing active extracts from *Dodonara polyandra*, which could be used to treat acute inflammatory skin disorders.

Methods

Topical formulations includingtwo oil-in-water (O/W) creams, two hydrogels and one self-emulsion were designed and optimised. *In vitro* permeation tests with human skin epidermis mountedon Franz diffusion cells was used to characterize formulations containing active extract. The permeated amount was quantified by high performance liquid chromatography (HPLC) over several time points.The anti-inflammatory activity of these formulations was assessed in a TPA-induced mouse ear oedema model of acute inflammation. Histological analysis was subsequently conducted on mouse ear tissue using haematoxylin and eosin (H & E) staining. Neutrophil infiltration was quantified as a measure of anti-inflammatory effect.

Results

Permeability and efficacy of active compounds from five different formulations were evaluated respectively. The highest permeability was achieved by self-emulsion containing 1% active extract. The corresponding permeated amount for two active components at 8 hours was 7.53 and 55.11 µg per cm^2. All formulations displayed anti-inflammatory effects *in vivo* ranging from 62.3 - 95.7% inhibition of oedema at 8 hours. A positive correlation existed between *in vitro* permeation and *in vivo* activity. Histological examination further supported the *in vivo* results in terms of decreasing neutrophil infiltration into the inflamed tissue.

Conclusions

Active extracts from *Dodonara polyandra* were successfully incorporated into a number of topical vehicles with each displaying anti-inflammatory activity. Histological examination further supported the ability of these formulations to reduce inflammation.

Ranunculin, the antibacterial constituent in *Clematis aristata*, and its mode of action

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Objective

Leaf of some *Clematis* spp. has been used in traditional Chinese medicine for the treatment of infection. The aim of this study was to determine the antibacterial activity and mechanism of action of ranunculin, which was isolated from *Clematis aristata*.

Methods

Minimum inhibition concentrations (MICs) of ranunculin against some Gram-positive and Gram-negative bacteria were determined by resazurin-indicated broth dilution in 96-well microplates. Scanning electron microscopy, antibiotic interaction with gentamicin by a chequerboard technique, deoxycholate-inducated lysis, induction of antibiotic resistance and headspace-GC/MS-SPME were employed to study the antibacterial mechanism of ranunculin against *Pseudomonas aeruginosa*.

Results

Ranunculin was selective active against Gram-negative bacteria. The MIC of ranunculin against clinically-isolated multi-drug resistant *P. aeruginosa* strains (PA124 and PAu19b) was the same as that against a sensitive *P. aeruginosa* strain (PAO1). It was found that ranunculin is a pro-toxin of protoanemonin. The antibacterial mechanism of ranunculin (protoanemonin) against sensitive and multi-drug resistant *P. aeruginosa* strains appeared to be different. The MexXY multidrug efflux system was detected in PA124 and PAu19b, but this system did not confer resistance to ranunculin (protoanemonin).

Conclusions

Ranunculin is selective for Gram-negative bacteria. It is equally effective against antibiotic-sensitive and -resistant *P. aeruginosa* but appears to have different mechanisms of action in the different strains. Its mode of delivery and hydrolysis *in situ* may represent a useful model of antibiotic action.

The effects of saliva on the chemistry and biological activity of *Dodonaea viscosa* extracts

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Objective

To investigate the traditional use of chewed *Dodoneae viscosa* leaf as a poultice for wounds by determination of the effect of saliva treatment of on the antibacterial activity, cytotoxicity and chemistry of leaf extracts.

Methods

Foliage was obtained from four plants at different locations. The leaves were macerated, incubated with or without saliva for 24 hours, extracted, fractionated and tested for activity against *S.aureus*, *S. pyogenes*, *B. cereus* and *E. coli* using a disk diffusion assay, and for cytotoxicity against murine P388 cells. Chemical analysis by HPLC was performed.

Results

Saliva treatment increased activity against *S. aureus* and *S. pyogenes* in the methanol and petroleum ether fractions compared with untreated extracts. There was no change in activity against *B. cereus*. All extracts failed to inhibit the growth of *E. coli*. Cytotoxic activity of *D. viscosa* extracts was unchanged by saliva pretreatment. Formation of new compounds in the least and most polar fractions, and corresponding decreases in some compounds in the intermediate polarity fractions, was observed by HPLC after saliva treatment.

Conclusions

Saliva treatment of *Dodonaea viscosa* increased the antimicrobial activity of some extracts against *Streptococcus* spp., but not cytotoxic activity. Associated chemical differences were also observed. Evidence supports the traditional use of chewed *D. viscosa* leaf. Enzymatic pretreatment of plant tissues may be a useful step prior to screening plant extracts for biological activities of potential pharmaceutical significance.

The effect of isosteviol on hyperglycemia and hyperlipidemia in rats fed with high-fat emulsion

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Objective

The study aimed to investigate the effect of isosteviol on hyperglycemia and hyperlipidemia in rats fed with high-fat emulsion (HFE).

Methods

Hyperglycemia and hyperlipidemia rat model was established by daily ingestion of HFE for 14 days. The rats were then given isosteviol (0.2, 1.0, or 5.0 mg/kg/day) or rosiglitazone maleate (5.0 mg/kg/day, as the positive control) orally for 7 days. The levels of fasting serum glucose (FSG), fasting serum insulin (FSI), total cholesterol (TC), triglyceride (TG), high density lipoprotein (HDL), and low density lipoprotein (LDL) were measured. Intravenous glucose tolerance test (IVGTT) was performed with serum glucose and insulin levels monitored. The effect of the supplement with palmitate in HFE on the activity of isosteviol was investigated. Ultrastructural changes in islet β-cells and PPARα mRNA expression profile were determined.

Results

The administration of isosteviol led to decrease in FSG, FSI, TC and LDL levels and insulin resistance index (IRI) and increase in HDL level. During IVGTT, serum glucose levels were decreased by isosteviol and no significant differences were observed in insulin release between isosteviol-treated and control groups. The effects of isosteviol were attenuated by palmitate. In isosteviol-treated groups, damage to pancreatic islet cells was partially attenuated, and enhanced expression profile of hepatic PPARα mRNA was observed.

Conclusions

Antihyperglycemic effects of isosteviol may enhance utilization of glucose in the periphery and reduce β-cell damage induced by dyslipidemia. Lipid-modulating effects of isosteviol may be related to the potential enhancement of liver PPARα mRNA expression.

Mad Maggots: Forensic investigations of a psychotropic drug using a rat brain model

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Objective

To develop an analytical method suitable for the detection of methylphenidate from maggots (*Lucilia sericata*). To investigate the role of maggots as an alternative toxicological specimen using an *in vivo* rat brain model.

Methods

Maggots (*Lucilia sericata*) were reared for five days on methylphenidate spiked foodstuff (2 mg/g) and stored at -80°C until analysis. Following a liquid-liquid extraction of methylphenidate from the maggots, the drug was detecting using LC-MSMS. The pilot study consisted of six male Sprague-Dawley rats (380 ± 45 g). Rats were dosed with methylphenidate at 100 mg/kg PO (n = 3) or 20 mg/kg IV (n = 3). Rats were sacrificed by guillotine and brain tissue was dissected. Maggots were reared on one hemisphere of the rat brain. Methylphenidate was extracted from maggots and brain (positive control) and analysed by LC-MSMS.

Results

Maggots show a high tolerance for methylphenidate and can grow on foodstuff spiked with methylphenidate corresponding to LD_{50} in rats. The maggots were not affected by drug-induced toxicity during the *in vivo* study. Methylphenidate partitioned rapidly into the rat brain with T_{max} at 2 minutes (IV) and 10 minutes (PO). Maggots completely ingested the rat brain (0.99 ± 0.20 g) within five days. Methylphenidate could be detected both from maggots reared on spiked foodstuff and from the rat brains using LC-MSMS.

Conclusions

Methylphenidate from maggots can be detected using LC-MSMS. The rat brain model provides a realistic forensic model for future forensic investigations. Maggots are suitable as an alternative toxicological specimen when traditional specimen such as tissue or blood are not available for analysis.

Picropodophyllin: An inhibitor of mesothelioma cell growth and inducer of apoptosis

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Objective

Malignant mesothelioma (MM) is a fatal rare tumour that responds poorly to currently available therapeutic treatment. Studies have suggested that the insulin-like growth factor 1 receptor (IGF-1R) is a critical pathway in MM cell growth and survival. We investigated the potential for targeting this pathway in MM cells using the cyclolignan picropodophyllin (PPP) an IGF-1R inhibitor.

Methods

The human MM cell lines JU77 and ONE58 were used. PPP was obtained from Sigma-Aldrich. Cell viability was assayed by MTT assay. Active caspase-3 was measured by alpha-LISA (Perkin-Elmer, Aust.). Phosphorylation of IGF-1R, Akt and GSK3β were assayed by AlphaScreen Sure-Fire kits (TGR BioSciences, SA, Aust.).

Results

PPP as a single agent showed dose dependent cytotoxicity in both cell lines killing up to 50% of cells at 0.5 µM and above. This was associated with caspase-3 activation in ONE58 but not in JU77. In combination with either cisplatin or gemcitabine, pretreatment with PPP showed additive effects upon cell viability. Both cell lines expressed IGF-1R by RT-PCR but receptor phosphorylation was not detected following treatment with either recombinant IGF-1 or insulin. In contrast the downstream Akt and GSK3β pathways were constitutively activated in JU77 cells but not ONE58.

Conclusions

The results of this study suggest that PPP has cytotoxic potential in mesothelioma and may have some benefits in combination with other chemotherapeutics. Our data is consistent with PPP exerting its effects through pathways other than IGF-1R inhibition and suggest further investigation is needed into the mechanism of action of this molecule.

In vitro method for propagation of varicella zoster virus (VZV)

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Objective

Following chicken pox infection in childhood, the varicella zoster virus (VZV) remains in the dorsal root ganglia thereafter. When immunity is lowered, VZV may re-activate to cause shingles. Pain that persists for greater than 3 months after the shingles rash has healed is known as postherpetic neuralgia (PHN). PHN is difficult to relieve with existing analgesic agents. Hence, there is a large unmet medical need for new treatments to alleviate PHN. This study aimed to compare the *in vitro* infectivity of several strains of VZV in cultured MRC-5 cells and subsequent selection of VZV strain(s) for establishment of a rat model of PHN.

Methods

The VZV strains compared were Schenke, Ellen and AV-92. Briefly, MRC-5 cells (ATCC, CCL-171; 2 x 10^5 cells/mL) were seeded into 96 well plates and grown at 37°C in 5% CO_2 for 24 - 48 hours to achieve 80% confluence. MRC-5 cells were infected by co-culturing with 10-fold serial dilutions of VZV-infected MRC-5 cells for 7 days. VZV infectivity was assessed qualitatively using crystal violet staining with 10 fold serial dilution of 100 µl aliquots of 80% confluent infected cells. Immunohistochemistry was used to identify the VZV IE-62 protein.

Results

The Schenke and Ellen strains of VZV had similar infectivity in cultured MRC-5 cells. VZV infection of cultured MRC-5 cells was confirmed by IE-62 immunohistochemistry.

Conclusions

The method for propagation of VZV in MRC-5 cells has been optimized and two strains have been selected for progression to establishment of a rat model of PHN. Work is ongoing to optimize this model.

Advanced degradation of trimethoprim by UV/H_2O_2 and photoFenton processes

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Objective

The discharge of antibacterial agents into the environment are a major concern as resistant microbes may develop from chronic exposure to such agents. It is thus of benefit to investigate alternative strategies for the removal of these compounds from sewage treatment facilities, in order to minimize their discharge into the environment from improper medication disposal down the sink or toilet. In this study, the UV-induced degradation kinetics of trimethoprim in water when irradiated with H_2O_2 and the photoFenton process ($FeSO_4.7H_2O$ and H_2O_2) are reported.

Methods

Aqueous trimethoprim (90 mg/L) was irradiated with UV-C (254 nm, 2 x 10^{16} photons/s) alone or in combination with H_2O_2 (3 g/L) or H_2O_2/iron (II) sulfate (1 g/L) (photoFenton process). Two mL samples were collected at various time points during the irradiation process and 1 mL of bromothymol blue (0.62 g/L) was mixed with the collected sample. The yellow trimethoprim-bromothymol blue complex produced was extracted into 3 mL of dichloromethane and the concentration of trimethoprim remaining was determined by spectrophotometry at 420 nm.

Results

Trimethoprim photodegradation with the photoFenton process was more efficient than the UV/H_2O_2 system when pH = 3 (0.38 ± 0.03 min^{-1} vs 0.24 ± 0.03 min^{-1} respectively) however the efficiency of the photoFenton system decreased with increasing pH.

Conclusions

While trimethoprim degrades with the UV/H_2O_2 and the photoFenton systems applied in this study, further work is necessary to determine whether trimethoprim is completely mineralized to inorganic compounds by these advanced degradation processes.

Effect of pH and temperature on the physical stability of amorphous indomethacin in aqueous suspensions

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Objective

To study the crystallisation behaviour of amorphous indomethacin in aqueous suspensions at different pH and temperature.

Methods

The crystallisation behaviour in amorphous suspension was studied by adding amorphous solid (20 mg/mL) to buffered aqueous media of different pHs (2.0, 4.5, and 6.8) at 5 and 25°C. Both the solid and solution were analysed at different time points up to 24 h. FTIR-spectroscopy (with principal component analysis) was used to study phase-transformation in the solid. Solution concentration-time profile was assessed by UV-spectroscopy. Crystal forms observed were also examined by DSC, SEM and XRPD.

Results

At 25°C, onset of crystallisation for all the samples was observed at 5 min. The fastest rate was observed at pH 6.8 where complete recrystallisation to α-form occurred within 1 - 2 h, while complete recrystallisation took 5 - 6 h at pH 4.5 and 24 h at pH 2.0. At 5°C, onset of crystallisation was increased to 1 h for all pHs. At this temperature three additional polymorphic forms were observed. After 1h, a ε-form reported only once, started appearing at all pHs. Subsequently, this form converted to the α-form at pH 6.8, but to the unreported ζ-form at pH 4.5 and pH 2.0. At pH 2.0, the ζ-form then converted to another unreported η-form after 8 h. Crystallisation was associated with a drop in dissolved drug concentration. The drug concentrations depended on pH and resulting polymorphic form.

Conclusions

The pH and temperature of the suspensions affected not only the crystallisation rate, but also the resulting polymorphic forms. New forms were identified.

The physical stability of amorphous indomethacin aqueous suspension: Effect of polymers

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Objective

To investigate the effect of type of polymer and addition method on crystallisation behaviour and solution concentration-time profile of amorphous indomethacin.

Methods

Pure amorphous indomethacin (IND) and solid dispersions (SD) of IND with polymers (PVP, HPMC and Soluplus®) at a 1:1 drug to polymer ratio (w/w) were prepared by quench cooling. Suspensions were prepared by either (i) adding the SDs into water (20 mg/mL), or (ii) adding pure amorphous IND into aqueous media containing predissolved polymer (PVP, HPMC and Soluplus®), with the total drug and polymer concentration equivalent to the SD formulations. Crystallisation and concentration of dissolved IND were studied. FTIR spectroscopy (with principal component analysis) was used to determine the onset of crystallisation. Concentration of dissolved drug over the time was assessed by UV-spectroscopy.

Results

Solid dispersions were better at inhibiting the crystallisation of excess amorphous solid than when the polymer was added into solution. Of the three solid dispersions, Soluplus® inhibited crystallisation the longest (>30 days), followed by PVP (12 h) and HPMC (7 h). Interestingly, polymer solutions generated higher IND concentrations than SDs, despite a faster onset of crystallisation. The use of Soluplus® led to more than 20-fold higher IND concentration in solution than when the corresponding Soluplus® SD was used. Other polymer solutions maintained 2 - 10-fold higher drug concentrations at 24 h in comparison to their corresponding SDs.

Conclusions

The ability of polymers to inhibit crystallisation of amorphous IND depends on the type of polymer used, and on the method used to add the polymer (SD or polymer in solution).

Effects of filtration on the presence of particulate and oxycodone content of injections prepared from crushed OxyContin tablets

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Objective

It is common for injecting drug users (IDU) to prepare injections by crushing tablets which are not designed for parental administration. The injection of insoluble tablet excipients can lead to serious local and systemic medical complications. The aim of the study was to investigate the effectiveness of various types of filters in removing harmful insoluble particles from the injections prepared using crushed oxycodone tablets.

Methods

Injections were prepared from a sustained-release oxycodone tablet formulation. The filtration of tablet extracts was carried out following procedures used by IDU using makeshift filter and commercially available filters. Particulate contamination and oxycodone content were analysed using light microscopy and spectrophotometer.

Results

Unfiltered extracts contained hundreds of thousands of particles of sufficient size to cause harms. Cigarette filters removed large particles but failed to remove small particles. The combination of cigarette filter and syringe filter (0.45 µm or 0.22 µm) reduced the particle count by 90 - 95%. A double membrane syringe filter (0.8/0.2 µm) removed more than 99% of the particles. Recovery of oxycodone was more than 95% with the tested syringe filters.

Conclusions

Particulate contamination in injections prepared from crushed tablets can be effectively removed using a combination process of cigarette filter and syringe filters, or a 0.8/0.2 µm syringe filter. Compared to other filters, the 0.8/0.2 µm syringe filter did not block, the filtration was quick and easy to perform, and did not retain oxycodone. The use of a 0.8/0.2 µm syringe filter can provide an important harm reduction measure for IDU.

Thermodynamic study of the solubility of ibuprofen in cosolvent mixtures

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Objective

Ibuprofen is widely used in oral or topical formulations. Liquid formulations are available in Australia but they are prepared as suspensions and relatively expensive. Liquid formulations are not available in Colombia, where this research was conducted. Solubility was studied in some pharmaceutical cosolvents formed by ethanol, propylene glycol and water to evaluate the effect of their composition and the temperature-solubility dependence for thermodynamic data based on van't Hoff methods.

Methods

Solubility was determined by preparing mixtures of EtOH-H_2O, EtOH-PG, PG-H_2O by changing their relative composition in steps of 10%. An excess of ibuprofen was added and the isothermal equilibrium at each temperature (20, 25, 30, 35 and 40°C) was reached. Samples were collected and concentration of dissolved ibuprofen was determined by measuring absorbance.

Results

Experimental solubility of ibuprofen reached a maximum as temperature, EtOH and PG proportion in mixtures increased; Enthalpy values and free energy of solution were also positive in all systems studied. Nevertheless, at the majority of compositions, the entropy showed positive values while for some aqueous mixtures, where composition involved 10% PG or 20% EtOH, entropy was negative.

Conclusions

Enthalpy of solution is endothermic, while the entropy indicates that it leads the solution process for mixtures and where negative values were found, ibuprofen and cosolvent are likely to be separated, whereas free energy showed that ibuprofen tends to be in its original physical state. Additionally, thermodynamics of solution, solvation and mix were energetically favourable due to the enthalpy contribution, bonding formation and specific solute-solvent interactions between ibuprofen and the mixtures.

Recrystallization of amorphous nifedipine induced by milling

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Objective

To investigate the effect of ball milling on the physical stability of amorphous nifedipine.

Methods

Amorphous nifedipine (prepared by quench cooling) was milled in an oscillatory ball mill at three different frequencies, 5 Hz, 15 Hz and 30 Hz for up to 30 min. Samples milled at 15 Hz for different times were subjected to stability testing. Analysis was conducted using Raman spectroscopy with multivariate data analysis and X-ray powder diffraction (XRPD).

Results

Amorphous nifedipine recrystallized into two different polymorphic forms, the metastable β-form and the stable α-form during milling. XRPD showed that recrystallization to the β-form began after 18 min of milling at 5 Hz. At the end of milling process, an amorphous halo remained. At 30 Hz, small crystalline peaks could be observed after 4 min milling. Further milling led to an increase in crystallinity and the disappearance of the amorphous halo. Both amorphous nifedipine and samples milled for 4 min at 15 Hz recrystallized only to the β-form after two day's storage. After one week's storage, conversion to the α-form was observed, and the samples were mainly a mixture of α- and β-form. When amorphous nifedpine was milled for a longer time, although only the β-form was detected initially, a conversion to the α-form was apparent after two day's storage.

Conclusions

The solid-state composition of nifedipine during ball milling was influenced by two milling parameters, time and frequency. The physical stability of amorphous nifedipine can be strongly affected by ball milling.

Evaluation of vitamin D medicines and dietary supplements and the physicochemical analysis of selected formulations

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Objective

The objective of this study was to identify vitamin D formulations from the global market, procure selected formulations from the New Zealand market and to analyse these products using a validated HPLC method.

Methods

The first component of the study consisted of a market search of vitamin D formulations available around the world, including New Zealand, Australia, USA, Japan, and India. The second component of the study involved analysing selected vitamin D formulations available in New Zealand. Vitamin D was extracted from capsule, tablet and emulsion formulations and quantified using high performance liquid chromatography (HPLC). The data obtained was compared with the labelled vitamin D content of the product.

Results

Formulations containing vitamin D from eight countries were identified, variations were found between countries in terms of content and dosage forms. 14 formulations were selected from the New Zealand market; these were either registered medicines or dietary supplements. 60% of the formulations were within 100 ± 10% of the label claim. Three of the dietary supplements had levels well under the label claim of vitamin D3, with one containing 8 ± 2%. Three dietary supplements contained significantly higher levels than their label claim; including a formulation containing 201 ± 29% of vitamin D3. In contrast, registered formulations displayed values within the acceptable range.

Conclusions

A large range of vitamin D products exist in the global market which related to a growing interest in the therapeutic effects of vitamin D. Due to the inaccuracy of label claims of some dietary supplements containing vitamin D in New Zealand there is a need for tighter regulation of these products.

Implications on stability of repackaging drugs into Dose Administration Aids

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Objective

This study was conducted to present evidence of the stability of drugs commonly repackaged into Dose Administration Aids (DAAs), as although increasing use of these aids is resulting in improved clinical outcomes for patients, there is limited availability of relevant stability data.

Methods

Tablets (clozapine, paracetamol, frusemide, sodium valproate and prochlorperazine) were repackaged into DAAs, exposured to different light, temperature and relative humidity (RH) storage conditions (40 °C/75% RH; 25 °C; 2 - 8 °C) for periods of up to 56 days, and evaluated for their chemical, physical and photo-stability.

Results

The findings indicated the chemical content, determined by validated high-performance liquid chromatography (HPLC) methods to be within British Pharmacopoeial (BP) limits for clozapine, paracetamol, frusemide, sodium valproate and prochlorperazine, confirming their chemical stability. Physical stability, relating to hardness, thickness, friability, disintegration, and dissolution was also confirmed for all tablets except sodium valproate, where the weight gain due to its hygroscopicity was about 12%, under accelerated conditions. For the photostability studies, a noticeable difference in colour was observed between the exposed and unexposed frusemide and prochlorperazine tablets, while for clozapine the orange colouration, attributed to photo-oxidation was found to be due to removal of these tablets from the DAA by the patient.

Conclusions

Although the quality of three medications commonly repackaged into DAAs has been compromised, it is recommended that in the case of the light-sensitive drugs patients are counseled on their appropriate storage. This highlights an important role for the pharmacist in the delivery of safe, effective and quality drug products.

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