

Sixty-fourth Annual Conference

Of

Association of Faculties of
Pharmacy of Canada

"International Symposium on Pharmacy &
Pharmaceutical Sciences:
From bench to market"

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Welcome from Dr. Daniel Thirion AFPC Co-Chair



Dear AFPC Members, Conference Delegates and Visitors:

Welcome to the 64th Annual General Meeting and Conference of AFPC! The University of Montreal is pleased to have the honour of hosting this year's lively downtown Montreal event. We join the Canadian Society for Pharmaceutical Sciences (CSPS) and the Pharmaceutical and Biomedical Analysis (PBA) to offer an international research and academic programme dedicated to excellence. This is reflected in the event where you have the great opportunity to choose from three synchronized tracks to tailor your learning experience. AFPC has carefully selected speakers and topics to provide a vision of clinical practice and pharmacy programmes in this time of recent legislative reform. As pioneers in this changing environment, come challenge your mentoring and leadership skills that serve to shape practice and research! Also, explore the interesting cross-curricular competency evaluation now being integrated into health education.

I hope you will enjoy this experience and take advantage of what the AFPC 2007 conference has to offer: opening reception and award dinner, posters, exhibits, the annual general meeting, evening activities, and closing banquet in the exciting downtown Montreal!

J'aimerais remercier profondément mes collègues du comité organisateur pour leur dévouement sans relâche et le souci d'un travail de qualité ainsi que les généreux commanditaires sans qui cette conférence ne pourrait être le succès que vous connaissez aujourd'hui.

Yours sincerely,

Daniel J.G. Thirion, B.Pharm., M.Sc., Pharm.D., BCPS
Co-Chair
Councillor, Faculté de pharmacie, Université de Montréal



Welcome from Anne Marie Whelan
AFPC PRESIDENT



Dear AFPC Members, Conference Delegates and Visitors:

Welcome to the 64th Annual General Meetings and Conference of AFPC! I would also like to welcome the delegates from the concurrent 10th Canadian Society for Pharmaceutics Sciences (CSPS) Annual Meeting and the 18th Pharmaceutical and Biomedical Analysis (PBA) Annual Meeting. It is exciting to be meeting with these organizations as it is obvious from the program that we share many of the same interests! I 'm sure you will enjoy the speakers, posters and discussions highlighting new drugs, impacts of legislative changes, mentoring, and cross curricular competencies. Please join us for the Opening and Award Dinners, where we will have the opportunity to acknowledge the award winners from our Faculties across Canada.

On behalf of the executive and council of AFPC, I would like to gratefully thank the Montreal Organizing Committee co-chaired by Daniel Thiron from the University of Montreal and Fakhreddin Jamali from the University of Alberta. Under their leadership the committee has worked endlessly to put together a joint program and social activities that are of interest to all three organizations. I would also like to extend our gratitude to all of our sponsors who make these meetings possible.

Please enjoy the meeting and your visit to beautiful Montreal!

A handwritten signature in blue ink that reads "A Whelan". The signature is fluid and cursive.

Anne Marie Whelan, BSc (Pharm), PharmD
President, AFPC (2006-2007)



Welcome from Dr Pierre Moreau Dean of the Faculty of Pharmacy



Dear colleagues and friends,

As the new dean of the Faculty of Pharmacy of Université de Montréal, it is a real pleasure for me to welcome you to Montréal for this year's edition of the AFPC meeting.

As some of you may well know, we will offer a Pharm D program starting this September and the timing for the meeting is simply excellent. Indeed, the program centers around legislation modifications that impact on the practice and training of pharmacy. Our new program was developed to account for these changes in order to provide all the skills necessary to tackle the new challenges. Other provinces are also experiencing similar changes and their reaction will surely provide valuable information for those who will face similar challenges in the future.

Among necessary skills, general competencies are increasingly recognized as a major contributor to the overall quality of health care professionals. These skills were incorporated into our curriculum and the meeting program also includes topics related to this issue and more precisely on how to properly evaluate them. As the role of the pharmacist is expanding, its ability to communicate, manage, stay scientifically informed, collaborate and be critical will also prove to be tremendously valuable in order for the transition to be successful. Collective reflections on these topics is indeed timely.

Montreal is a dynamic city, but pales in comparison to the organizing committee who has put tremendous time and energy to offer you this meeting. I sincerely hope that you will enjoy your stay with us for yet another successful AFPC meeting.

Bienvenue,

A handwritten signature in black ink, appearing to read 'Pierre Moreau', followed by a long, sweeping horizontal line.

Pierre Moreau, Ph.D.
Professeur et Doyen



AFPC Conference Planning Committee

Chair

Daniel Thirion

Registration / Logistics

Sylvie Marleau / Daniel Thirion / Sophie Brisebois / Lyne Levesque / Leila Andraos

Conference Budget

Pierre Moreau / Frank Abbott / Daniel Thirion / Michelle Savoie

AFPC Pharmacy Practice Research Session

Chair: Pierre Moreau

Faculty: Daniel Thirion / Frank Abbott

AFPC/CSPS/PBA Joint Opening Session

Mo Jamali / Daniel Thirion / Frank Abbott

AFPC Teacher's Conference I and II

Daniel Thirion / Nancy Winslade

Conference Program

Sylvie Marleau / Daniel Thirion / Line Labbé / Frank Abbott / Lyne Levesque / Gisèle Gagné

Banquets / Receptions (Opening Dinner, Awards Dinner)

Sylvie Marleau / Sophie Brisebois

GRUM/AFPC Poster Session and Exhibits

Chair : Line Labbé / Sylvie Marleau

Faculty : Daniel Thirion / Frank Abbott / Lyne Levesque

Looking Ahead to the AFPC Conference 2008

The upcoming 2008 AFPC annual meeting will be held with the AACP at the Sheraton Chicago Hotel & Towers Chicago Illinois.

Joint American Association of Colleges of Pharmacy/Association of Faculties of Pharmacy of Canada Meeting

July 19–23 2008

AACP Teachers Seminar, Leadership Seminar and AACP Annual Meeting
Sheraton Chicago Hotel & Towers, Chicago, Illinois

Education Advancing Practice

For only the second time, pharmacy educators in Canada and the United States will hold a joint annual meeting in July 2008 in Chicago Illinois. The opportunity to learn from colleagues from across North America and around the world, and the ability to showcase our own innovations in pharmacy education in Canada will make this conference a premier continuing professional development event for pharmacy educators - book your calendars now to make sure you don't miss this important event! On behalf of AFPC, the Universities of Toronto and Waterloo will be organizing this meeting - we look forward to welcoming you to Chicago in 2008!

Conference Theme:

Pharmacy education and practice have always had a synergistic relationship. Practitioners have been intimately involved in education, either as lecturers, teaching assistants, lab demonstrators or experiential preceptors and co-ordinators. Similarly, educators have made a significant contribution to practice, through development of advanced practice models and roles, providing continuing education, and through mentorship of others. Collaboration across the continuum of practice and education has created an excellent platform for many research endeavors. The relationship between education and practice requires nurturing, yet the advantages for the profession are many.

Objectives:

- a) To describe and showcase practice-academia innovations in Canada
- b) To discuss barriers and facilitators to practice-academia innovations
- c) To identify emerging practices related to practice-academic innovations

Structure:

Three, 3-hour sessions will be planned focused on the following areas:

- 1) Structured Practical Experience
- 2) Performance Based Teaching, Learning and Assessment
- 3) Integrating practice in large-group teaching

For each session, 2-3 innovations will be showcased and discussed. Emphasis will be placed on innovations for which evidence exists regarding the benefit of the practice-academia relationship. These innovations will be utilized as case studies to allow participants to examine promising practices and lessons learned regarding these innovations. Our goal is to showcase at least one innovation from each of the 10 pharmacy schools in Canada.

Calls for papers, posters, and presentations will be published in late fall 2007. Plan now to attend this important meeting, and share your experience with pharmacy educators from across North America!

AFPC Council and Executive

AFPC Executive

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EXHIBITS



Information companies offering specialized publications and software for physicians, nurses, students and specialized clinicians. Our educational division, which is represented at this conference, provides information, materials and support to faculty who are considering adopting our textbooks in their courses. For more information, please visit our exhibit, or have a look at our website www.lww.com, or contact Carol.McGimpsey@wolterskluwer.com.



La librairie de l'Université de Montréal est heureuse de contribuer à la conférence AFPC/CSPS.

The bookstore of the Université de Montréal is happy to be part of the AFPC/CSPS conference in Montreal.

Sciences sociales

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**ASSOCIATION OF FACULTIES OF PHARMACY OF CANADA
64TH ANNUAL MEETINGS AND CONFERENCE**

**May 30 – June 2, 2007
The Queen Elizabeth Hotel
Montréal, Québec**

The 2007 AFPC conference is being held in conjunction with the 10th Canadian Society for Pharmaceutical Sciences (CSPS) Annual Meeting and the 18th Pharmaceutical and Biomedical Analysis (PBA) Annual Meeting.

**International Symposium on Pharmacy & Pharmaceutical Sciences:
From bench to market**

AFPC Program

WEDNESDAY, MAY 30

4:00 – 6:00 pm	Registration	Alcôve
5:30 pm	Opening reception CSPS / PBA / AFPC	Duluth - Mackenzie
7:00 pm	Dinner and Presentations by Award Winners	Hochelaga 4

THURSDAY, MAY 31

8:00am – 3:00 pm	Registration	Alcôve
8:00am – 3:00 pm	Poster viewing and Exhibits	Hochelaga 1 - 3
9:00 – 10:00am	Joint Session with CPS and PBA Drugs on the Horizon Julie Ducharme, Director, Department of Drug Metabolism and Pharmacokinetics (DMPK), AstraZeneca R&D Montreal and Global Discipline Leader, Discovery DMPK, AstraZeneca	Duluth - Mackenzie
10:00am	Break	

Program



10:20 – 11:20am	Joint session with CSPS and PBA Today's Challenges in Pharmacotherapy Patrick DuSouich, Professor of Pharmacology, Faculty of Medicine, University of Montreal, Montreal, Canada	Duluth - Mackenzie
11:20am	Poster Viewing and Exhibits	Hochelaga 1 - 3
11:30am – 1:00pm	AFPC Annual General Meeting Lunch served for members	Montréalais 2
1:00–4:30pm	Pharmacy Practice Research Session: Impact of recent legislation on pharmacy practice, curriculum changes and pharmacy practice research. Moderator: Pierre Moreau, University of Montreal, Qc., Canada	Mackenzie
1:00pm	Legislative Changes in Quebec: Impact on Patient Care Jean-François Bussi�res, University of Montreal, QC, Canada	Mackenzie
1:45pm	Legislative Changes: Impact on Pharmacy Programs in Ontario A: Nancy Waite, University of Waterloo, Waterloo, ON B: Lalitha Raman-Wilms, University of Toronto Bill C102	Mackenzie
2:30pm	Break, Poster Viewing and Exhibits	Hochelaga 1 - 3
3:00pm	Legislative Changes and changes in Pharmacy Programs in Alberta Greg Eberhart, Registrar, Alberta College of Pharmacists	Mackenzie
3:45pm	Expected competencies of graduate and undergraduate students in preparation for the biopharmaceutical industry. Lyne Fortin Vice President Sales & Marketing, Business Unit #3 Merck Frosst Canada Ltd.	Mackenzie
5:00pm	GRUM Poster viewing	Hochelaga 1 - 3
6:45pm	Evening activities – Amphibus Tour	Alc�ve

FRIDAY, JUNE 1

8:00 – 10:30am	Registration	Alcôve
8:00am – 5:00pm	Poster Presentations	Hochelaga 1 - 3
8:30am - 12:00pm	Teachers Conference I: Mentoring	Mackenzie
8:30am	Mentoring and Leadership Workshop Laurel Taylor, Hema Patel, and Saleem Razack, McGill University, Montreal, QC, Canada	
10:00am	Break, Poster Viewing and Exhibits	Hochelaga 1 - 3
10:30am	Mentoring and Leadership Workshop Laurel Taylor, Hema Patel, and Saleem Razack, McGill University, Montreal, QC, Canada	Mackenzie
12:00pm	Lunch Break, Poster Viewing and Exhibits	Hochelaga 1 - 3
1:00-5:00pm	Teacher's Conference II: Cross Curricular Competencies	Mackenzie
1:00pm	Fundamentals of Evaluating Cross Curricular Competencies Nancy Winslade, McGill University, Montreal, QC, Canada	Mackenzie
1:45pm	Tools for Assessing Cross Curricular Competencies Gilles Leclerc, University of Montreal	Mackenzie
2:30pm	Break, Poster Viewing and Exhibits	Hochelaga 1 - 3
3:00pm	Tools for Assessing Cross Curricular Competencies Continued	Mackenzie
3:45pm	PEP Canada: Supporting Pharmacists to be Effective Practice Based Teachers: Developing a National Pharmacy Preceptor Development Strategy Annie Lee, University of Toronto, Toronto ON and Cheryl Cox, University of Alberta, Edmonton, AB	Mackenzie
6:00pm	AFPC Awards Banquet (Departure 5:00pm)	Hélène de Champlain Île Ste-Hélène

SATURDAY, JUNE 2

8:30am –12:00pm	AFPC registrants will be free to attend CSPA/PBA sessions To see program go to: http://www.cspscanada.org/symposium2007/programme.html CPHA Centennial Conference begins in Ottawa.
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ORAL PRESENTATIONS

AWARD WINNERS

AND

SPEAKERS

AFPC/GLAXOSMITHKLINE GRADUATE STUDENT RESEARCH AWARD

Patrick Ronaldson, PhD Candidate, Leslie Dan Faculty of Pharmacy, University of Toronto.



Patrick Ronaldson is a Ph.D. candidate at the Leslie Dan Faculty of Pharmacy, University of Toronto under the supervision of Dr. Reina Bendayan. Patrick's doctoral research has focused on characterizing the localization, expression, and activity of drug efflux transporters in glial cells and understanding their relationship to the treatment of brain HIV-1 infection. He has currently published seven papers in peer-reviewed journals as well as a book chapter describing mechanisms of drug transport in the brain. He has also been invited to present his work at several national and international conferences and has received various awards in recognition of his research accomplishments. Patrick was elected by his peers to the post of President of the Pharmaceutical Sciences Graduate Students' Association (2003-2006) at the Leslie Dan Faculty of Pharmacy. He recently received a Gordon Cressy Student Leadership Award (2007), which is awarded by the University of Toronto Alumni Association and the Division of University Advancement for his contributions to the University of Toronto community. After completion of his Ph.D. degree in June 2007, Patrick intends to do a postdoctoral fellowship in the field of drug transport.

Abstract: HIV-1 Viral Envelope Glycoprotein Gp120 Triggers an Inflammatory Response in Cultured Rat Astrocytes and Regulates the Functional Expression of P-glycoprotein.

In the present work, we have examined i) the ability of gp120, an HIV-1 viral envelope glycoprotein, to trigger the innate immune response in astrocytes, an HIV-1 brain cellular target and ii) investigated the functional expression of the ABC membrane transporter P-glycoprotein (P-gp), in primary cultures of rat astrocytes treated with gp120 or cytokines (TNF- α , IL-1 β , IL-6). Standard MTT and D-mannitol uptake assays confirmed that HIV-1_{96ZM651} gp120 treatment did not alter cell viability or membrane permeability. Semiquantitative RT-PCR analysis and ELISA demonstrated increased TNF- α , IL-1 β and IL-6 mRNA and protein expression in cultures treated with HIV-1_{96ZM651} gp120, suggesting *in vitro* activation of immune responses. Cytokine secretion was detected when CXCR4, but not CCR5, was inhibited with a specific antibody, implying cytokine secretion is primarily mediated via CCR5 in astrocytes triggered with HIV-1_{96ZM651} gp120. P-gp protein expression was increased in astrocyte cultures exposed to TNF- α (2.9-fold) or IL-1 β (1.6-fold) but profoundly decreased in the presence of IL-6 (8.9-fold), suggesting IL-6 is primarily involved in modulating P-gp expression. In parallel, following HIV-1_{96ZM651} gp120 treatment, immunoblotting analysis showed a significant decrease in P-gp expression (4.7-fold). Furthermore, the accumulation of two P-gp substrates, digoxin and saquinavir (an HIV-1 protease inhibitor) was enhanced (1.5-1.8-fold) in HIV-1_{96ZM651} gp120 treated astrocyte monolayers but not altered by P-gp inhibitors (i.e., PSC833, GF120918) suggesting a loss of transport activity. Taken together, these data imply that HIV-1_{96ZM651} gp120 or cytokine treatment modulate P-gp functional expression in astrocytes which may lead to complex drug-transporter interactions during HIV-1 encephalitis-associated immune responses.



AFPC-BRISTOL-MYERS SQUIBB NATIONAL AWARD FOR EXCELLENCE IN EDUCATION
PRIX NATIONAL AFPC-BRISTOL-MYERS SQUIBB POUR EXCELLENCE EN
ENSEIGNEMENT

Louise Mallet, BSc. Pharm., Pharm. D.

Professeure titulaire de clinique, Faculté de pharmacie, Université de Montréal.



Louise Mallet, a reçu son Baccalauréat en pharmacie à l'Université Dalhousie à Halifax. Par la suite elle a effectué une résidence en pharmacie d'hôpital à « University of Alberta Hospital » à Edmonton en Alberta. Elle obtient un Pharm.D. de Massachusetts College of Pharmacy à Boston puis effectue 2 années de fellowship en gériatrie à l'Université de la Georgie à Athens.

Mme Mallet est présentement professeure titulaire de clinique à la Faculté de Pharmacie de l'Université de Montréal et également pharmacienne en gériatrie au Centre universitaire de santé McGill. Elle est l'auteur de nombreuses publications et co-auteur du livre en gériatrie- Manuel des soins pharmaceutiques en gériatrie.

Abstract: La gériatrie: Application et implication en enseignement

La conférence portera sur mon implication au niveau de l'enseignement en gériatrie, de l'enseignement en interdisciplinarité et à la participation à l'application des soins pharmaceutiques à la Faculté de pharmacie de l'Université de Montréal. Les différentes méthodes pédagogiques utilisées seront présentées pour illustrer l'interaction entre les étudiants et le professeur ou conférenciers dans le cours de Pharmacothérapie gériatrique. Ces méthodes pédagogiques sont: les principes gériatriques, la rencontre avec l'expert- la question préalable, la solution collective de problèmes et l'approche interdisciplinaire. La résidence spécialisée en pratique gériatrique représente une autre initiative d'une formation spécialisée permettant de dispenser des soins pharmaceutiques. La « Journée de consultation avec les personnes âgées » mise en place dans le but de favoriser le développement du professionnalisme chez l'étudiant permettra d'illustrer une autre implication gériatrique. L'enseignement en interdisciplinarité en collaboration avec les Facultés de physiothérapie et d'ergothérapie permet aux étudiants de mieux comprendre le rôle de chacun des intervenants dans une équipe de soins. Enfin, une rencontre avec les membres de l'équipe interdisciplinaire permet de découvrir le rôle de chacun. Les outils développés pour favoriser la continuité des soins ainsi que mon implication au niveau de l'équipe de soins de gériatrie au Centre universitaire de santé McGill seront aussi présentés.

AFPC/ASTRAZENECA NEW INVESTIGATOR RESEARCH AWARD

Zubin Austin, BScPhm, MBA, MISC, PhD

OCP Professor in Pharmacy, Leslie Dan Faculty of Pharmacy, University of Toronto



Zubin Austin completed his pharmacy degree at the University of Toronto in 1988. Upon graduation, he began working as a clinical pharmacist at Mount Sinai Hospital, with a specialty in psychiatry. He completed graduate degrees in business administration and information science and began working as a lecturer at the Faculty of Pharmacy in 1994, where he coordinated senior level pharmacy practice lectures and labs. In 2002, after completion of a PhD in cognitive science, he was appointed Assistant Professor. In 2003, he was appointed the inaugural holder of the Ontario College of Pharmacists' Professorship in Pharmacy. His research interests include bridging education for internationally educated health care professionals and interprofessional education and practice. He has published over 45 peer reviewed manuscripts, and has received over \$4 million in external competitive funding as principal investigator. In 2006, he was awarded the American Association of Colleges of Pharmacy Lyman Award for outstanding article published in the American Journal of Pharmaceutical Education. He is a past recipient of the AFPC/Bristol Myers Squibb Award of Excellence in Pharmacy Education, and has been named "Professor of the Year" at the Faculty of Pharmacy on five separate occasions.

Abstract: Social values research in pharmacy education

Social values researchers examine attitudes towards secular and religious authority, social status, the role of the sexes, and well as orientations towards personal autonomy, informality and immediate gratification. Social values have been studied and described in the general population, and in university-aged students, but there has been little published on the attitudes, values, and beliefs of pharmacy students. The measurement and understanding of social values within a group was described by Rokeach, de Vulpian, and others, and includes a systematic linking of behavioural and attitudinal questions. Since 1997, a longitudinal study of 4th year pharmacy students has been undertaken at the University of Toronto. Through this survey, and using "motivational cognition" methods described by Adams, a model of pharmacy students' social values is emerging. This presentation will outline key findings regarding a model for understanding the evolution of social values of pharmacy students and will discuss implications for pharmacy education, professional practice, and interprofessional collaboration.



AFPC-PFIZER RESEARCH CAREER AWARD

Thomas R. Einarson Associate Professor, Ph.D. (Arizona), Leslie Dan Faculty of Pharmacy, University of Toronto



Tom Einarson received his bachelor of science in pharmacy degree from the University of Manitoba in 1968. Thereafter, he worked in various community pharmacies in Ontario and in community hospitals (mostly small community hospitals) until 1982. Tom then traveled to Tucson to obtain his Master of Science degree with a major in Pharmacy from the College of Pharmacy, University of Arizona. He completed this degree in 1984. Continuing on in Arizona, Tom completed his Master of Education degree in 1986 with a major in Educational Psychology. In 1987, Tom obtained his PhD degree with a major in Pharmacy and a minor in Educational Psychology. He then proceeded to join the Faculty of Pharmacy at the University of Toronto. Tom's current research is aimed at the development and application of quantitative methods for the evaluation of drug use. This includes the fields of pharmacoepidemiology, pharmacoeconomics, meta-analysis, and statistical methodology. As well, evaluation of methods in the literature is a focus. He has consulted extensively with government (PMPRB, CCOHTA, CADTH, Ontario MoH, Cancer care Ontario) and with both the brand name and generic pharmaceutical industry.

ABSTRACT: Development and Application of Quantitative Methods to Drugs and Drug Services.

Today's healthcare system is facing cost constraints while at the same time increasing consumer demand and increased number of new drug entities entering the market. A need exists for methods to evaluate these new drugs and their place in the system from a variety of viewpoints. Pharmacy administration addresses these and other issues with respect to drugs, drug use, and pharmacy services.

Current research is aimed at the development and application of quantitative methods for the evaluation of drug use. That includes the fields of pharmacoepidemiology, pharmacoeconomics, meta-analysis, and statistical methodology. As well, evaluation of methods in the literature is a focus.



Award Winners

PHARMACY PRACTICE RESEARCH SESSION

Nancy Waite, Pharm D, FCCP, Associate Director, Practice-Based Education, School of Pharmacy, University of Waterloo, Waterloo



Nancy Waite Pharm D, FCCP is Associate Director of Practice-Based Education at the new School of Pharmacy, University of Waterloo where she oversees experiential programming, practice-based courses/labs, residencies/fellowships and continuing professional development. In her previous position at the Leslie Dan Faculty of Pharmacy she was responsible for the development of a plan for implementation of an Entry-level Pharm D program. Through various academic and clinical positions in Canada and the United States, she has experience providing clinical pharmacy services in ambulatory care practice settings, teaching professional and student audiences, pharmacy practice research and academic managerial responsibilities. Participating and leading curricular reform to meet changing health care needs and advancing pharmacy practice through innovative programs have been two of her key responsibilities over the last 10 years.

Abstract: University of Waterloo School of Pharmacy: Impact of Legislative Changes

The School of Pharmacy at the University of Waterloo (UW) has the rare opportunity to create a wholly new pharmacy program, graduating professionals who embrace both the current and future roles of pharmacists. Recent legislative initiatives are shaping and informing these roles. UW has modified almost every element of a traditional pharmacy curriculum. Our admissions process, through the use of student profiles and personal interviews, is identifying students who are motivated, courageous and innovative. We are committed to identifying and supporting students with interests in a range of professional career paths. Interprofessional team skills will be developed through joint learning opportunities with medicine, optometry, pharmacy technicians and Family Health Teams. Introducing a co-operative model of education has allowed us to increase the amount of experiential learning, early and throughout the curriculum, and provide it in a variety of practice settings. This unique real-world exposure provides students with practical skill sets, on-the-job problem-solving abilities, and allows early and frequent application of classroom learning in an applied context. In turn, the students' employment experiences will continually inform the curriculum. All students will be encouraged to engage with their community through service learning. To facilitate these changes, we have increased the number of pre-requisites and introduced integrated courses. Further details of our new curricular delivery models will be presented.

Speakers



PHARMACY PRACTICE RESEARCH SESSION

Lalitha Raman-Wilms, BSc(Phm), PharmD, FCSHP, Associate Professor, Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto.



Lalitha Raman-Wilms is an Associate Professor and Director of the Division of Pharmacy Practice at the Leslie Dan Faculty of Pharmacy. She has experience teaching in both the undergraduate and the Doctor of Pharmacy programs. She is also the faculty advisor for the University of Toronto's International Health Program. Her interests include interprofessional teaching and practice, problem-based learning, pharmaceutical care, and geriatric pharmacotherapy. Lalitha also has many years of hospital and community pharmacy experience, and currently provides pharmaceutical care at a community health centre. Presently, Lalitha has been seconded as Project Leader, Curricular Renewal, as the Faculty is in the process of renewing its curriculum. Lalitha has received several teaching awards

and recently, as a member of the Interprofessional Pain Curriculum Committee, was awarded the University's Northrop-Frye award, recognizing distinguished achievements in linking teaching and research.

Abstract: Curricular Renewal: Preparing Graduates to meet the Evolving Pharmacy-related needs of Canadians

Across Canada, university pharmacy curricula prepare students effectively to provide direct patient care. However, with changes both in health service delivery and the needs of Canadians, the role of the pharmacist will continue to evolve and expand. In Ontario, there is a strong move towards a team-based approach to care, along with a renewed focus on primary care, as seen by the development of Family Health Teams and Community Health Centres. New legislation related to pharmacists' services are also reflective of the change in the expectation of the pharmacist's role. Pharmacy curricula need to be abreast of these changes in order to ensure that graduates continue to meet the pharmacy-related health care needs of Canadians. This discussion will address the pharmacy curriculum renewal development process and the proposed educational changes at the University of Toronto. The proposed educational changes are based on extensive stakeholder feedback, and reflect the need to enhance education in areas such as personalized therapeutics, pharmacy informatics and patient safety initiatives. In addition, skills and competency in collaborative, interprofessional team-building, retrieval and effective use of health information, knowledge translation at the patient and health care provider levels will enable graduates to develop strong clinical skills, preparing them to be competent and confident in meeting their patient's drug-related needs.



Speakers

PHARMACY PRACTICE RESEARCH SESSION

Greg Eberhart, Registrar Alberta College of Pharmacists, Edmonton, Alberta



Greg Eberhart graduated from the Faculty of Pharmacy and Pharmaceutical Sciences at the University of Alberta in 1979. He practiced in both independent and corporately owned community pharmacies for over 10 years. During this period he had opportunity to provide services to a rural hospital and auxiliary care centre, and a federal penal institute.

In 1984 Greg was elected to the council of Alberta Pharmaceutical Association, serving as president in 1989. During his tenure he chaired the Association's Pharmacy Technician Advisory Committee, and was a member of the Professional Affairs and Drug Caution Code committees. He represented Alberta on the Council of Delegates to the Canadian Pharmaceutical Association from 1986-1989, serving on the association's Audit Review Committee, which he chaired during the 1988/89

term.

Since January 1990 Greg has been Registrar of the Alberta Pharmaceutical Association and its successor, the Alberta College of Pharmacists. Highlights of his career include the inception of NAPRA, the development of Alberta's Pharmacy Information Network and Electronic Health Record, and achieving an expanded scope of practice for pharmacists that formally recognizes the full spectrum of pharmacists' knowledge and skills, positioning Alberta pharmacists as care providers – not simply dispensers of medications.

Abstract: "Legislative Changes and Changes in Pharmacy Programs in Alberta"

Effective April 1, 2007 pharmacists in Alberta are practicing under a new regulatory and practice framework that recognizes their knowledge and skills as prescribers.

The Health Professions Act (1999) accommodates overlapping scopes of practice amongst 30 regulated health professions. Activities such as dispensing, compounding, selling schedule 1 and schedule 2 drugs, prescribing and administering drugs by injection are restricted to health professionals regulated by a college that has demonstrated that its members have the competencies to safely and effectively perform these activities. These are all roles that Alberta pharmacists have been authorized to perform.

The Alberta College of Pharmacists (ACP) developed a unique model to define pharmacist prescribing as a foundation to extensive consultation and negotiation required to bring the legislation to fruition. Most prescribing will be conducted in a collaborative environment; however, the regulations recognize that some patients will benefit from the ability of pharmacists to prescribe when they are the "initial point of contact" with the health system.

The privilege to prescribe is a new tool that will be used by some pharmacists, in some situations, to resolve drug related problems. Basic privileges have been provided to all pharmacists on ACP's clinical (practicing register). Additional privileges will be granted to pharmacists who successfully complete an evaluation process being administered by ACP.

Tools have been developed to support pharmacists identify their learning needs and to support professional development. New standards have been developed for the practice of pharmacists and for the operation of pharmacies. The college's Code of Ethics is scheduled to be reviewed later this fall.

Greg Eberhart, Registrar of the Alberta College of Pharmacists, will introduce the prescribing model, critical success factors important to achieving this legislated authority, ACP's implementation strategy, and discuss experiences to date since implementation.



PHARMACY PRACTICE RESEARCH SESSION

Lyne Fortin, Vice President, Sales and Marketing, Merck Frosst Canada Limited.



Lyne Fortin is currently Vice-President, Sales & Marketing responsible for the Specialty and Hospital Business Unit at Merck Frosst Canada, Ltd.

Ms. Fortin graduated in 1982 from l'Université de Montréal with a Bachelor of Pharmacy including a Minor in chemistry. She subsequently obtained a Master of Business Administration from Concordia University. At Merck Frosst since 1985, she held various positions in Market Research, Product Management, Marketing Planning, Sales Management as well as Public Affairs. Ms. Fortin also had international experience when appointed in 1994 as Senior Business Director for the Los Angeles region with Merck & Co. prior to being promoted in November 1998 to Executive Director, Sales & Marketing in Canada. In April 2005, she became Vice-President for one the company's Business Unit and more recently was appointed Member of the Board of Directors for Merck Frosst Canada Ltd. Ms. Fortin is also a member of l'Ordre des pharmaciens du Québec.

Abstract: What Industry Expects From Pharmacy Graduates: A Biopharmaceutical Perspective

Over the past few decades, the Canadian health care sector has experienced constant growth. In its most recent projections, the Canadian Institute for Health Information (CIHI) reports that Canadians invested over \$148 billion in health care in 2006, representing more than 10% of Canada's GDP. This investment trend is expected to continue as the Canadian population ages. In 1981, Canadians over 65 years of age represented 10% of the population. In 2016, less than a decade from now, this number is expected to reach 16% or almost 6 million people.

Within health care spending, health care technology, and drugs in particular, are often seen as cost drivers. However, they can and should be looked at as a way of optimizing the health status of Canadians and as a tremendous opportunity for economic development. The Canadian government, along with some provincial governments, has repeatedly suggested that the future of Canada's economy lies in the knowledge industry. The biopharmaceutical sector, comprised of a wide range of pharmaceutical and biotech companies, is one of the key sectors of the knowledge economy where Canada can develop a competitive advantage. To build that competitive edge, highly-skilled human resources are a must. In this presentation, we will explore how the field of pharmacy can contribute to build that competitive edge by developing the talent required for a striving biopharmaceutical sector in Canada.



Speakers

TEACHERS CONFERENCE I

Saleem Razack, Associate Professor Pediatrics, McGill University Montreal.



Saleem Razack is a pediatric intensivist and Associate Professor of Pediatrics at McGill University. He completed his medical school training at the University of Toronto and his residency and fellowship training at McGill University. His academic interests lie within the field of medical education and he is currently the director of the pediatric residency program at McGill University and a member of the Centre for Medical Education at McGill University. He is involved primarily in scholarly projects concerning core competencies training such as leadership skills, communication skills, and training in social accountability. He is the recipient of a 2007 Canadian Association for Medical Education certificate of merit.

Hema Patel, Associate Professor, Pediatrics, McGill University Health Centre, Montreal



Hema Patel is an Associate Professor in Pediatrics with the McGill University Health Centre, working at the Montreal Children's Hospital (MCH) since 1997. She undertook her medical school training at the University of Western Ontario, followed by pediatric residency training at Dalhousie University in Halifax, Nova Scotia. Next, she completed a fellowship in Academic General Pediatrics at The Hospital for Sick Children in Toronto. Concurrently with her fellowship, she completed her Masters in Clinical Epidemiology at the University of Toronto. Currently, her clinical activities are centred in the Intensive Ambulatory Care Service at MCH, where she is interim Program Head. She is also the Academic General Pediatrics Fellowship supervisor at MCH. She is active in research and teaching and has been a Chercheur-Boursier Clinicien with the FRSQ since 2000. Her research now focuses on the theme of Education

in Medical Leadership.

Speakers



TEACHERS CONFERENCE I

Laurel Taylor, Assistant Professor, Departments of Medicine and Neurology, McGill University, Montreal.



Laurel Taylor has a background in business administration (MBA University of Alberta) and organizational analysis (PhD University of Alberta). She is an Assistant Professor in the Departments of Medicine and Neurology, at McGill University. She is currently on the use of pharmacy and e-health technologies and the impact of information technology on the provision of health care. Dr. Taylor is a member of the Medical Office of the Twenty-first Century (MOXXI) project team. In this innovative health research team, she has project management and liaison functions, while pursuing a stream of research concerning the integration of technology to provide improved quality and safety of health care to Canadians. Dr. Taylor's current research interests include: understanding predictors for adoption and utilization of technology in primary care; assessing the prevalence of electronic drug alerts in primary care settings with an integrated drug management system; analyzing the predictors of physician response to drug alerts; and identifying facilitators and barriers to the integration of decision support tools for the treatment of asthma into community care practices. Before relocating to Quebec, she was part of a team that introduced the principles of total quality management to the administrative and clinical functions of the University of Alberta hospitals. She has been a leading instructor in McGill University's annual Health Challenge: Integrating Management and Medicine workshop for graduating MD-MBA students. She is also active in promoting management education for physicians and is currently a co-investigator for a unique and important clinical trial providing leadership and management education to residents.

Abstract: Teaching Cross Curricular Competencies: A Focus on Teamwork

The current focus on utilizing multidisciplinary teams for the provision of health care requires an additional skill set for providers, one that is not commonly offered as part of the training for providers. This workshop will provide an interactive overview of the concepts of teamwork and multidisciplinary practice, including the potential advantages and disadvantages. An additional requirement for effective teamwork is the ability to manage conflict and understand negotiation tactics. The session will introduce this concept and provide attendees with some tools to understand their own, and other, conflict management styles and review the central concepts for successful negotiation. The goal of the workshop is to introduce a framework for optimal team interactions and conflict management.

TEACHERS CONFERENCE II

Nancy Winslade, B.Sc.Pharm., Pharm.D., M.H.P.E., Medical Office of the 21st Century Project (MOXXI), Faculties of Medicine, and Epidemiology & Biostatistics, McGill University, Montreal.



Nancy Winslade obtained her Bachelors of Science in Pharmacy from the University of Toronto in Canada and her Doctor of Pharmacy from SUNYAB in United States. During her early career she practiced at Sunnybrook Health Sciences Centre and was an Associate Professor at the Faculty of Pharmacy in Toronto. At the University she developed and administered the Pharm.D. program that focused on teaching pharmacists to provide direct patient care. Nancy changed to a consulting role upon her relocation to Europe in 1994. Since receiving her Masters in Health Professions Education from the University of Maastricht in the Netherlands, she has worked mainly in the area of assessment of students and practicing health care professionals. Based on this expertise, she was invited by the American Association of Colleges of Pharmacy to prepare their position paper on systems for assessing achievement of pharmacy students. Upon her return to Canada in 2004, she joined the Medical Office of the 21st Century project at the Departments of Medicine and Epidemiology & Biostatistics at McGill University. The MOXXI project investigates the use of e-based technologies to improve physician prescribing. Her research expands this focus to include the community pharmacist's role in optimizing patient's use of medications. She continues her consulting in assessment of competence of health professionals, primarily with the Canadian Examiners of Optometry, the Physicians Assistants of the Canadian Forces and the University of Montreal, Faculty of Pharmacy. Her project with the latter includes assistance with the design of a student assessment program for the proposed entry-level doctor of pharmacy program.

Abstract: Fundamentals of Evaluating Cross Curricular Competencies.

Many health professions have focused on the importance of practitioners' skills related to, for example, professionalism, communication and ethics. Various terms have been used for these skills including cross-curricular competencies, professionalism and general attributes. In pharmacy, both the National Association of Pharmacy Regulatory Authorities' competency-based standards of practice and the Association of Faculty of Pharmacy's educational outcomes for Bachelor of Science in Pharmacy programs emphasize that such general attributes are critical to competent performance as a pharmacist. Similar to other professions, initial approaches to assessment of these attributes conceptualized them as separate from other areas of core professional competence such as provision of pharmaceutical care or management of medication distribution. However, the separation of these attributes from core professional competencies created difficulties since these skills are needed to competently perform the core competencies. Alternative assessment methods evaluate performance of these general attributes within the context of performance of professional competencies. Several models for assessing these attributes will be discussed, with focus on the integrated models proposed by the Competence Committee of the Canadian Examiner's of Optometry and by the University of Montreal, Faculty of Pharmacy.



TEACHERS CONFERENCE II

Monsieur Gilles Leclerc. B.Pharm., Faculté de pharmacie, Université de Montréal, Montreal.



Gilles Leclerc is a former member of the AFPC experiential task force and is presently acting as clerkship coordinator at the Faculté de pharmacie, Université de Montréal. Monsieur Leclerc was involved substantially in the Pharm.D. clerkship program design and has shown specific interest in practice oriented assessment of professional and cross-curricular competencies.

Furthermore, he was asked to join the Pharm.D. Steering committee. He has planned and developed UGO, an Academic program management system, winning an honourable mention at the IMS Global Learning Impact Award 2007 conference. He shows a growing interest in Instructional Engineering in Networked Environment focusing on reusability of learning resources,

interoperability of learning systems and adaptive testing. Lately he became a member of the CREPUQ IT task force.

Abstract: ***Tools for Assessing Cross-Curricular Competencies: listening to students and preceptors workshop.***

While developing its Pharm.D. curriculum, the University of Montreal explored new ways to assess student's competencies. This has led to the design of the ECO Model. The challenge was to develop standard direct observation tools that could be used for assessment during practice labs, integration activities and clerkships. A pilot project has allowed students and preceptors to apply the ECO Model during clerkship and to comment on this new approach. Based on the preliminary results of this experience, this workshop will focus on challenges raised by students and preceptors on competency assessment and make participants exchange their own views and experiences.

PEP CANADA

Annie Lee, BScPhm, MSc(T), Lecturer, Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto



Annie Lee received her B.Sc.Pharm from the University of Toronto and a Master of Science in Teaching degree from McMaster University. She completed a hospital residency at St. Joseph's hospital, Hamilton, followed by clinical, research and management positions at various hospitals. Annie is a coordinator for the Structured Practical Experience Program and the coordinator of the third year professional practice lab course at the University of Toronto. She is actively involved with the delivery and development of preceptor training programs for new and returning pharmacist preceptors. Annie is currently co-chair of the PEP Canada committee that consists of experiential program coordinators from across Canada.

Cheryl Cox, BSP, MBA - Director of Clinical Placements, Faculty of Pharmacy & Pharmaceutical Sciences University of Alberta, Edmonton



Cheryl completed a Bachelor of Science in Pharmacy at the University of Saskatchewan and a hospital residency at the Royal University Hospital in Saskatoon. Cheryl's research interests are within the field of curriculum studies with a focus on the transition of students from the classroom to the practice setting. This is the focus of her interdisciplinary Ph. D program in Clinical Education in the Faculty of Education. Currently she coordinates three experiential education courses within the pharmacy program at the University of Alberta.

Abstract: “Supporting Pharmacists to be Effective Practice Based Teachers – Developing a National Pharmacy Preceptor Development Strategy”, Annie Lee, University of Toronto and Cheryl Cox, University of Alberta

A component of experiential programs across Canada is providing support to preceptors to be effective practice based teachers. This presentation by members of PEP Canada will highlight initiatives taken by the committee as part of the strategic plan to develop a National strategy for preceptor development. PEP Canada is a national committee of experiential program coordinators from each of the Faculties of Pharmacy in Canada. The proposed strategy will explore issues such as the desired qualities of a preceptor, key components of an introductory preceptor workshop, the selection of preceptors, topics for advanced preceptor workshops, implementation issues for preceptor development including mandatory participation and quality assurance. This presentation will focus on two components of this strategy. The survey results from the Canadian program coordinators will be presented that highlight the desired qualities of a preceptor and the key components for a preceptor workshop for advanced experiential rotations.



Sixty-fourth Annual Conference

Of

Association of Faculties of
Pharmacy of Canada

"International Symposium on Pharmacy &
Pharmaceutical Sciences:
From bench to market"

POSTERS

Abstract Compendium

**“International Symposium on Pharmacy
& Pharmaceutical Sciences:
From bench to market”**



64th AFPC Annual Conference

May 30 – 31, June 1, 2007

**Hôtel Reine Élisabeth
Montréal, Québec**



Posters - Thursday May 31, 2007

CATEGORY	TITLE	AUTHORS
PHARMACY PRACTICE RESEARCH		
PPR47-AFPC	Nouvelle méthode de revue d'utilisation des médicaments : exemple pratique du pantoprazole intraveineux en réanimation pédiatrique	Jean-François Bussi�res, Denis Lebel, Catherine Litalien, Sonia Prot-Labarthe, V�ronique Bouche, Bao Nguyen
PPR48-AFPC	Int�gration de la pharmacovigilance � la pratique clinique	<i>Jean-Fran�ois Bussi�res</i> , Mariane Blond, Denis Lebel, Brigitte Martin, Pierre Barret, Karine Touzin
PPR49-AFPC	Perspective qu�b�coise et canadienne de la pratique pharmaceutique en �tablissement – 2005-2006	<i>Jean-Fran�ois Bussi�res</i> , Patricia Lefebvre
PPR50-AFPC	Metoclopramide and diphenhydramine in the treatment of hyperemesis gravidarum	<i>An�is Lacasse</i> , BSc, Amandine Lagoutte, Ema Ferreira, PharmD and Anick B�rard, PhD
PPR51-AFPC	�valuation de la conformit� des pratiques en h�mato-oncologie au CHU Sainte-Justine	<i>Jean-Fran�ois Delisle</i> , Jean-Fran�ois Bussi�res
PPR52-AFPC	Risk evaluation of <i>Clostridium difficile</i> -associated diarrhea following antimicrobial prophylaxis in patients undergoing cardiac, vascular or thoracic surgery in a tertiary care trauma center	<i>Daniel. J. G. Thirion</i> , D. Banon, C. Ferland, A. Thibodeau, K. Wilhelmy, L. Blais, A. Fillion, T. Bigras, G. Pichette, P. Laflamme
PPR53-AFPC	Prevalences and trends in medication use during pregnancy and lactation	<i>Marie-Pierre Gendron</i> , BSc, Brigitte Martin, BPharm MSc, Driss Oraichi, PhD and Anick Berard, PhD
BASIC RESEARCH		
BR54-AFPC	Involvement of elastases in elastocalcinosis	<i>C�line Bouvet</i> , Simon Moreau & Pierre Moreau
BR55-AFPC	Chemical and enzymatic synthesis of sugar nucleotides for glycosylation engineering of natural products	<i>Shannon C. Timmons</i> , Roy H. Mosher, Sheryl A. Knowles, and David L. Jakeman
BR56-AFPC	Gender-related differences in potassium channel block; Modulatory role of verapamil	<i>Raymond Hreiche</i> , Pierre Morissette, Hubert Zakrzewski-Jakubiak and Jacques Turgeon
BR57-AFPC	Polyion complex micelles of carboxymethyldextran-block-poly(ethylene glycol) and diminazene diaceturate: preparation and physicochemical characterization	<i>Ghareb M. Soliman</i> and Fran�oise M. Winnik
BR58-AFPC	Cholesterol efflux mediated by ABC transporters is upregulated with EP 80317, a growth hormone releasing peptide in a PPAR�-dependent manner	<i>Kim Bujold</i> , Sylvie Marleau and Huy Ong
BR59-AFPC	Ser/Thr cluster I and II located in C-terminal end of IRF3 are both important for its optimal transactivation ability and are involved in different aspects of IRF3 life cycle	<i>Jean-Fran�ois Clement</i> , Annie Bibeau-Poirier, Simon-Pierre Gravel, Nathalie Grandvaux, Sylvain Meloche and Marc J Servant
BR60-AFPC	The transcription factors Nur77 and retinoid X receptors participate in amphetamine-induced locomotor affects	<i>Emmanuelle Bourhis</i> , J�r�me Maheux ¹ , Claude Rouillard ² and Daniel Levesque

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BR61-AFPC	A physiologically based pharmacokinetic model to assess the role of ABC transporters in drug distribution	<i>Frédérique Fenneteau</i> , Jun Li, Lucie Couture, Jacques Turgeon, Fahima Nekka
BR62-AFPC	Induction of the transcription factor <i>Nur77</i> by antipsychotic drugs is dependant upon metabotropic glutamate subtype 5 and adenosine A _{2A} receptors	<i>Jérôme Maheux</i> , Michel St-Hilaire, Emmanuelle Bourhis, Claude Rouillard, Daniel Levesque
BR63-AFPC	Rôle du monoxyde d'azote dans la rigidité artérielle et l'élastocalcinose	<i>Liz-Ann Gilbert</i> , Richard Larivière et Pierre Moreau
BR64-AFPC	Rôle du TGF-B1 dans l'élastocalcinose	<i>Simon Moreau</i> , Céline Bouvet, Pierre Moreau
BR65-AFPC	Novel CD36 ligands with hypocholesterolemic and anti-atherosclerotic properties	<i>Valérie L. Bessi</i> , Kim Bujold, Sylvie Marleau and Huy Ong
BR66-AFPC	Implication of the renin-angiotensin-aldosterone pathway-related polymorphisms to heart failure predisposition	Marcin Zakrzewski-Jakubiak M.Sc., 1Simon de Denus M.Sc., 2Marie-Pierre Dubé Ph.D, 1François Bélanger M.Sc., 2Michel White MD, 1Jacques Turgeon Ph.D
EDUCATION AND TEACHING		
ET67-AFPC	Évaluation de la qualité des résumés publiés dans le Pharmactuel de 1993 à 2006	<i>Bénédicte Coureau</i> , Jean-François Bussièrès, Sonia Prot-Labarthe, Denis Lebel
ET68-AFPC	Development and preliminary evaluation of a training workshop for pharmacists assessing students in an OSCE setting	<i>Debra M. Moy</i> B.Sc. Pharm, Anthony Marini PhD, Greg Morris, B.A
ET69-AFPC	Evaluation of a complementary pharmacy day within an interprofessional pain curriculum	<i>Debra M. Moy</i> , B. Sc. Pharm., Lalitha Raman-Wilms, Pharm D
ET70-AFPC	The ability of interprofessional and uniprofessional student teams to assess the quality of a patient care plan as compared to an experienced evaluator	<i>Roy Dobson</i> , Jane Cassidy, Peggy Proctor, Doreen Walker
ET71-AFPC	Self-directed learning at the University of Manitoba: implementation of a new elective program at the Faculty of Pharmacy	<i>Silvia Alessi-Severini</i> , Colleen Metge, Rehana Durocher, Tamara Buchel and Brent Kvern
ET72-AFPC	ECO project: A new competency assessment model for clerkships	<i>Gilles Leclerc</i> , Ema Feirreira, Guylaine Bertrand, Johanne Collin, Marie Dubois, Tania Choquette
ET73-AFPC	Educational resources management model: From cross-curricular to trans-curricular	<i>Gilles Leclerc</i> , Michel Leblanc, Guylaine Bertrand
ET153 - AFPC	Transforming healthcare through collaboration "in-BC"	<i>Rosemin Kassam</i> ¹ , Lesley Bainbridge ² , Grant Charles ³ , Kathy Copeman-Stewart ⁴ Grace Mickelson ⁵ , Provincial Project Leaders

Posters - Friday June 1, 2007

CATEGORY	TITLE	AUTHORS
PHARMACY PRACTICE RESEARCH		
PPR118-AFPC	Feasibility of conducting a pragmatic cluster cohort study using administrative databases to evaluate the effectiveness of an osteoporosis workshop	<i>Marie-Claude Laliberté</i> , Sylvie Perreault, Alice Dragomir, Johanne Goudreau, Isabel Rodrigues, Lucie Blais, Nicole Damestoy, Diane Corbeil, Lyne Lalonde
PPR119-AFPC	Évaluation de la conformité de la chaîne thermique en établissement de santé	<i>Jessica McMahon</i> , Jean-François Bussi�res
PPR120-AFPC	Plasma concentrations of Bupivacaine and Ropivacaine in combined femoral-sciatic block	<i>Mohamad-Samer Mouksassi</i> , Pierre Beaulieu, France Varin and Line Labb�
PPR121-AFPC	Population Pharmacokinetics of Intravenous Pantoprazole in Pediatric Intensive Care Patients	<i>Mohamad-Samer Mouksassi</i> , <i>G�raldine Pettersen*</i> , Yves. Th�or�t, Line Labb�, Christophe Faure, Bao Nguyen and Catherine Litalien
PPR122-AFPC	Population pharmacokinetic of intravenous busulfan in children	<i>Nastya Kassir</i> , Yves Th�or�t, Martin A. Champagne, Michel Duval, Diane Larocque, Line Labb�
PPR123-AFPC	Physician readiness to collaborate with community pharmacists on drug therapy management	<i>Nedzad Pojskic</i> , Linda MacKeigan, Heather Boon, Curtis Breslin and Philip Ellison
PPR124-AFPC	Facteurs influen�ant la prestation des soins pharmaceutiques visant la ma�trise de l'asthme par le pharmacien communautaire : �tude PRO-RESPIR	<i>Nola Ren�-Henri</i> , <i>B.Pharm</i> , Natalie Nadaira B.Pharm, Yvonne Khamla B.Pharm, Catherine Ouellet B.Pharm, Lyne Lalonde, Marie-France Beauchesne, Johanne Collin, Lucie Blais
BR134-AFPC	Early systemic exposure to inhaled milrinone in cardiac patients	<i>Anne QN Nguyen BSc</i> , Dr. Andr� Denault MD, Dr. Yves Th�or�t BPharm PhD, Dr France Varin BPharm PhD
BASIC RESEARCH		
BR125-AFPC	Design, synthesis, and biological evaluation of thieno[2,3- <i>b</i>]quinolones as topoisomerase II inhibitors with potential antineoplastic activity	<i>Ranjith Garlapati</i> and Mohsen Daneshtalab
BR126-AFPC	EP80317, a ligand of CD36 receptor, protects against remote lung injury after hindlimb ischemia/reperfusion	<i>Diala Harb</i> , Leila Hamdan, Caroline B�langer, Val�rie L.Bessi, Marie-Christine Koutsing Tine, Huy Ong, Sylvie Marleau
BR127-AFPC	Induction and inhibition of cytochrome P450 and phase II enzymes by the flaxseed plant lignans secoisolariciresinol and secoisolariciresinol diglucoside	<i>Erin Boyd</i> , Ed S. Krol and Jane Alcorn
BR128-AFPC	P-glycoprotein and HERG closely interact in cardiac ventricular myocytes	<i>Hakima Yahi-Kerbane</i> , Raymond Hreiche, Fran�ois B�langer and Jacques Turgeon
BR129-AFPC	The QFRP peptides modulate adipogenic genes in differentiated 3T3-L1 cells	<i>Mukandila Mulumba</i> , Sylvie Marleau, Huy Ong
BR130-AFPC	Synthesis of 2-deoxy-2-fluorosugars for use as glycosyltransferase enzyme probes	<i>Stephanie S. Lucas</i> , Shannon C. Timmons and David L. Jakeman

Posters – Friday June 1, 2007

BR131-AFPC	Effect of polyethylene oxide (PEO) content and drug solubility on polymer swelling and drug dissolution	<i>Robert Hardy</i> , Hongtao Li, Xiaochen Gu
BR132-AFPC	Electrical remodeling in a transgenic mouse model of cardiac-specific overexpression of type 1 angiotensin II receptor	<i>Katy Rivard</i> , Pierre Paradis, Mona Nemer and Céline Fiset
BR133-AFPC	The effect of metoprolol on energy metabolism in the diabetic heart	<i>Pavan Dhillon</i> , Vijay Sharma, Michael Allard and John H. McNeill
BR135-AFPC	Design, synthesis, biological evaluation and determination of the mechanism of action of new anticancer agents: the arylchloroethylurea-combretastatin hybrids	<i>Sébastien Fortin</i> , Emmanuel Moreau, Jean-Claude Teulade, René C.-Gaudreault
BR136-AFPC	Outward K ⁺ current is decreased in ventricular myocytes isolated from adult mice with elevated levels of serum TNF α	<i>Scott A. Grandy</i> , Marie-Andrée Lupien and Céline Fiset
BR137-AFPC	Influence of short and long-term exposure to tamoxifen on cardiac repolarization in mice	<i>Gracia El Gebeily</i> and Céline Fiset
BR138-AFPC	Dendritic Cell Targeted Nanovaccine Formulations	<i>Welson Wen-Shang Wang</i> , Dipankar Das and Mavanur R. Suresh
SOCIAL AND ADMINISTRATIVE RESEARCH		
SAR139-AFPC	Évaluation de la conformité à la politique de double-vérification dans un centre hospitalier mère-enfant	<i>Jean-François Bussièrès</i> , Karine Touzin, Bénédicte Coureau, Sylvie Legault, Ginette Quesnel
SAR140-AFPC	Antihypertensive agents' adherence level and primary prevention of non fatal strokes	<i>Fatima-Zohra Kettani</i> , Pharm., Alice Dragomir, MSc, Robert Côté, MD, FRCPC, Louise Roy, MD, Pierre Moreau, PhD, Sylvie Perreault, PhD
SAR141-AFPC	Association between antidepressant use during pregnancy and infants born small for gestational age	<i>Ramos Elodie</i> , Driss Oraichi, Anick Bérard
SAR142-AFPC	Are controlled asthmatic pregnant women more at risk of prenatal outcomes than non-asthmatic women?	<i>Faranak Firoozi</i> , Francine M Ducharme, Catherine Lemièrre, Marie-France Beauchesne, Anick Bérard, Amélie Forget, Lucie Blais
SAR143-AFPC	Impact of non-adherence to bisphosphonates on the incidence of osteoporotic fractures : a nested case-control study	<i>Julie Blouin</i> , Alice Dragomir, Yola Moride, Louis-Georges Ste-Marie, Julio C Fernandes, Sylvie Perreault
SAR144-AFPC	Population-based study: statin adherence on non fatal stroke among patients for primary prevention	<i>Laura Ellia</i> , Alice Dragomir, MSc, Lucie Blais, PhD, Robert Côté, MD, FRCPC, Sylvie Perreault, PhD
SAR145-AFPC	Two-stage nested case-control study of the control and severity of maternal asthma during pregnancy and the incidence of asthma in the offspring	<i>Marie-Josée Martel</i> , Evelyne Rey, Marie-France Beauchesne, Jean-Luc Malo, Sylvie Perreault, Amélie Forget, Lucie Blais

Posters - Thursday May 31, 2007

Please note that numbering corresponds to the placement of the AFPC abstract in the joint listing of poster abstracts by CSPA, PBA and AFPC

PHARMACY PRACTICE RESEARCH

47. Nouvelle méthode de revue d'utilisation des médicaments : exemple pratique du pantoprazole intraveineux en réanimation pédiatrique

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Objectif : L'objectif de cette étude est de présenter la première RUM rapide au sein de notre établissement. Elle concerne le pantoprazole intraveineux administré en réanimation pédiatrique. Le pantoprazole est le seul inhibiteur de la pompe à proton (IPP) disponible pour administration intraveineuse au Canada. **Méthodologie :** La méthode de RUM rapide est une démarche qui permet une évaluation structurée dans un temps limité. Elle comporte 15 étapes (Tableau 2) qui doivent être réalisées en 30 jours sur un maximum de 30 patients incluent consécutivement à rebours à partir d'une date donnée sur une période ne dépassant pas 12 mois. La méthode détaillée et les résultats de la RUM rapide portant sur le pantoprazole par voie injectable sont présentés. **Résultats :** L'étude a été réalisée au CHU Sainte-Justine, Montréal, Québec, Canada. Il s'agit d'un centre hospitalier universitaire mère-enfant québécois de 400 lits de pédiatrie dont 24 lits de réanimation pédiatrique. La RUM rapide s'est réalisée sur une période de 40 jours au lieu des 30 jours prévus. Un total de 30 patients (14M; 16F) consécutifs ont été inclus du 1^{er} février 2004 au 30 septembre 2005, ce qui représente une période d'étude de 21 mois. En prophylaxie de l'ulcère de stress, l'utilisation du pantoprazole était conforme aux critères de prescription dans 17 % des cas. La non-conformité s'explique principalement par la non-conformité au critère 2 (i.e. utilisation en première intention de ranitidine à raison de 6 mg/kg/jour). Pour le traitement d'un saignement digestif haut actif, la conformité était de 100 %. Une endoscopie a été réalisée dans 28% des cas avant l'instauration du pantoprazole. **Conclusion :** Cette étude illustre une première démarche de revue d'utilisation de médicaments rapide en établissement de santé. L'utilisation du pantoprazole est peu conforme en prophylaxie de l'ulcère de stress mais conforme en traitement de saignement digestif haut actif.

48. Intégration de la pharmacovigilance à la pratique clinique

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Objectif: Comparer les systèmes et les formulaires de déclarations utilisés dans 5 pays différents à partir d'une revue de la documentation afin d'en évaluer l'efficacité et présenter une démarche active permettant l'intégration de la pharmacovigilance à la pratique clinique dans un centre hospitalier universitaire.

Méthodologie: À partir d'une revue de la documentation, on a comparé les systèmes et les formulaires de déclarations utilisés dans 5 pays différents. On a revu les méthodes de codification des dossiers patients et l'identification des effets indésirables aux médicaments (EIM) pour en déterminer l'efficacité. À partir de l'intranet pharmacie, on a élaboré et développé un concept d'intégration de la pharmacovigilance dans notre établissement de santé. **Résultats:** Les systèmes de déclaration diffèrent entre les cinq pays étudiés alors que les formulaires de déclaration contiennent les mêmes renseignements. Les données de la documentation suggèrent qu'un nombre important d'EIM n'est pas codifié, déclaré et documenté au dossier du patient et que l'intégration de la pharmacovigilance doit être améliorée en établissement de santé afin d'en augmenter l'efficacité. Le concept développé est composé de trois volets soit la détection, la documentation et le retour d'informations. Le modèle proposé relance les activités d'un sous-comité de pharmacovigilance avec une représentation adéquate des cliniciens et permet l'intégration du dossier pharmacologique, du dossier des examens biologiques et des rapports d'EIM colligés via intranet. **Conclusion:** Les effets indésirables des médicaments doivent être documentés pour assurer leur utilisation optimale. La sous-déclaration des EIM est fréquente dans de nombreux pays. Cet article présente une démarche permettant l'intégration de la pharmacovigilance à la pratique clinique dans un centre hospitalier universitaire, en profitant de la présence des pharmaciens dans les équipes cliniques.

49. Perspective québécoise et canadienne de la pratique pharmaceutique en établissement – 2005-2006*Jean-François Bussières¹, Patricia Lefebvre.*¹ Unité de recherche en pratique pharmaceutique, Département de pharmacie, CHU Sainte Justine, Montréal, Québec, Canada / Faculté de pharmacie, Université de Montréal

Objectif: Présenter les faits saillants de la 16^{ème} édition du rapport 2005-06 et les différences observées en ce qui a trait à la pratique québécoise par rapport à l'ensemble de la pratique canadienne. **Méthode:** Il s'agit d'une enquête canadienne réalisée aux deux ans auprès des chefs de département de pharmacie des établissements de santé de plus de 100 lits dont au moins 50 lits courte durée. Les différences observées sont interprétées en tenant compte du nombre absolu de répondants à chaque question. **Résultats:** Les données québécoises 2005-06 (n = 42 répondants) et 2003-04 (n = 48 répondants) sont mises en perspectives données canadiennes en ce qui concerne les indicateurs de structure, les indicateurs de tâches reliées à la pratique pharmaceutique, les indicateurs de ressources humaines, les indicateurs de dépenses en médicaments, le profil des programmes de soins et la présence de pharmaciens, les indicateurs de services cliniques et académiques, les indicateurs de prestation sécuritaire. **Conclusion:** Cette perspective québécoise 2005-06 de la pratique pharmaceutique est publiée dans le cadre d'un supplément du Pharmactuel en ligne au printemps 2007. Cette enquête est réalisée grâce à la contribution financière sans restriction de Eli Lilly Canada.

50. Metoclopramide and diphenhydramine in the treatment of hyperemesis gravidarum*Anaïs Lacasse, BSc¹, Amandine Lagoutte², Ema Ferreira, PharmD¹ and Anick Bérard, PhD¹.*¹Faculty of Pharmacy, University of Montreal, Montreal, Quebec, Canada; ²Faculty of Pharmacy, Université de Bourgogne, Dijon, France.

Introduction: Hyperemesis gravidarum (HG) is the second most common reason for hospitalisation during pregnancy. Since 2002, a new HG treatment protocol consisting of metoclopramide plus diphenhydramine was put in place at CHU Sainte-Justine, Quebec. **Objectives:** We compared the effectiveness and the safety of this new HG protocol with what has been used previously (droperidol plus diphenhydramine) by comparing length of hospitalisation for HG, rate of rehospitalisations, evolution of nausea and vomiting symptoms, pregnancy outcomes, and rate of adverse events between the two groups. Predictors of rehospitalisation for HG in women treated with the new HG protocol were also identified. **Methods:** A retrospective cohort study was conducted from 2002 to 2006 on the population of pregnant women diagnosed with HG, and treated at CHU Sainte-Justine with the new protocol consisting of intravenous metoclopramide 1.2-1.8 mg/h plus diphenhydramine 50mg every 6h. These women were compared to a historical control group consisting of women diagnosed with HG, and treated in the same institution with intravenous droperidol 0.5-1mg/h plus diphenhydramine 25-50mg every 6h between 1998-2001. **Results:** During the study period, 30 pregnant women were exposed to the new HG protocol versus 99 that were exposed to the droperidol and diphenhydramine combination between 1998-2001. Our study showed that the new HG protocol was associated with a greater improvement of vomiting symptoms (36% vs. 21%;p=0.0397), and with less adverse events. The new HG protocol was not better than the droperidol and diphenhydramine combination to reduce nausea symptoms, length of hospitalisation (3.7 vs. 3.1 days; p=0.0096), and rehospitalisations for HG (19.23% vs. 24.44%;p=0.3536); the new protocol did not increase rate of major malformations. In women treated with the new protocol, adjusted analysis revealed that race was the only predictor of rehospitalisation for HG (Black vs. Caucasian;OR: 8.52; 95% CI 1.15-63.34). **Conclusion:** The combination of metoclopramide and diphenhydramine appears to be a good option in the management of HG.

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51. Évaluation de la conformité des pratiques en hématologie-oncologie au CHU Sainte-JustineJean-François Delisle¹, Jean-François Bussières¹,¹Unité de recherche en pratique pharmaceutique (URPP), Département de pharmacie, CHU Sainte Justine, Montréal, Québec, Canada / Faculté de Pharmacie, Université de Montréal

Objectif : Évaluer la conformité des pratiques en hématologie-oncologie au CHU Sainte-Justine à partir d'une version préliminaire du Guide sur les médicaments dangereux de l'Association pour la santé et la sécurité au travail – secteur des affaires sociales. **Méthode :** À partir d'un comité pharmacie soins-infirmiers avec la participation active d'un pharmacien résident, complétion d'une grille d'auto-évaluation comportant 189 critères de conformité pour 11 domaines. À partir des éléments non conforme, rédaction d'un plan d'action incluant un échéancier en tenant compte d'un nouvel aménagement physique à partir de juin 2007. On a tenu 4 réunions de travail afin de compléter l'outil et de valider les informations recueillies. **Résultats :** Au terme de l'exercice, on obtient le profil de conformité suivant : 30 % des critères sont conformes, 37 % sont partiellement conformes, 30 % sont non conformes et 3 % ne sont pas applicables. Les principaux secteurs de non conformité sont liés aux domaines suivants en ordre décroissant: déballage et entreposage (52 %), aménagement de la pharmacie d'oncologie (42 %), administration des médicaments (21 %). Un plan d'action par domaine a été déterminé incluant un échéancier. **Conclusion :** Une auto-évaluation de la conformité aux pratiques en hématologie-oncologie à partir du guide de l'ASSTSAS est une démarche pratique et applicable qui peut mener à un plan d'action concret.

52. Risk evaluation of *Clostridium difficile*-associated diarrhea following antimicrobial prophylaxis in patients undergoing cardiac, vascular or thoracic surgery in a tertiary care trauma centerDaniel J. G. Thirion^{1,2}, D. Banon^{1,2}, C. Ferland^{1,2}, A. Thibodeau^{1,2}, K. Wilhelmy^{1,2}, L. Blais^{1,2}, A. Fillion², T. Bigras², G. Pichette², P. Laflamme²¹Université de Montréal, Montréal, ²Hôpital du Sacré-Coeur de Montréal, Montréal, Canada.

Background: Since 2002, a *C. difficile* associated diarrhea (CDAD) outbreak has been affecting institutions in the Canadian province of Quebec. CDAD has since become the most common nosocomial infection diagnosed. The purpose of this study is to evaluate the risk of CDAD and its complications following antimicrobial prophylaxis (AP) in patients undergoing cardiac, vascular or thoracic surgery at a university affiliated tertiary care trauma center. **Methods:** We reviewed the charts of patients aged 18 years or older and who received an AP for surgery between January 1st 2002 and December 31st 2004. The primary outcomes were the occurrence of CDAD and its complications and the occurrence of surgical site infections (SSI). Rates were estimated with their 95% confidence intervals (CI). AP conformity was also documented. **Results:** Overall, 1524 charts were reviewed. In total, 837 cardiac, 335 thoracic, and 352 vascular surgeries were evaluated. CDAD and SSI rates are presented in the following table. Rate of complications associated with CDAD was 20.8 % (95% CI 12.7-28.9 %).

Rates of CDAD and SSI in cardiac, thoracic and vascular surgery patients

Outcome	Cardiac n = 837	Thoracic n = 335	Vascular n = 352	Total n = 1524
CDAD (%) (95%CI)	4.3 (2.9-5.7)	10.2 (6.9-13.4)	7.1 (4.4-9.8)	6.3 (5.1-7.5)
SSI (%) (95%CI)	4.1 (2.7-5.4)	0.9 (-0.1-1.9)	5.1 (2.8-7.4)	3.7 (2.7-4.6)

Conclusions: AP exposes patients to an increased risk of CDAD. This risk may outweigh its benefit, especially in thoracic surgery. AP needs to be re-evaluated in the context of CDAD outbreaks, and more specifically in surgeries at low risk of SSI. Improving surgical methods is required to alleviate the necessity of AP in specific situations. Previously presented at ICAAC 2006, and CSHP 2007.

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53. Prevalences and trends in medication use during pregnancy and lactation.

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Background: Although women are having children at an increasingly older age, and thus can be exposed to medications during gestation, little is known about the prevalences and trends of medication exposures during pregnancy and lactation. **Objectives:** Identify the major classes of medications used during pregnancy and lactation, estimate the prevalence of medication use, and determine the overall and yearly trends in medication exposures during pregnancy and lactation for 2003-2007. **Methods:** A cross-sectional study was conducted on the population of women calling IMAGE, a teratology information service based at CHU Ste-Justine in Montreal, Canada, for questions regarding risks/benefits of medication use during pregnancy or lactation. To be eligible in this study, women had to call IMAGE between 12/01/2003 and 01/31/2007, and be pregnant or nursing while using medications at the time of call. Data collected included socio-demographic data, lifestyle variables such as smoking status, alcohol and illicit drug use, pregnancy and lactation history, current pregnancy or lactation data such as gestational age or time since birth, co-morbidities, and complete current medication utilization. Medication data were coded using Health Canada medication library, and disease status using the MedDRA coding system. Time-series modelling was used for the trend analyses. **Results:** A total of 10,506 pregnant women, and 12,982 lactating women were included for analyses. The most frequently used medications during pregnancy were: antidepressants (16.8%), benzodiazepines (5.1%), antipsychotic agents (4.2%), gastro-intestinal agents (4.2%), sympathomimetics (3.9%), NSAIDs (3.6%), and antiemetics (3.1%). The most frequently used medications during lactation were: antidepressants (10.6%), gastro-intestinal agents (6.0%), NSAIDs (5.9%), oral contraceptives (4.5%), antihistaminics (4.0%), opiate agonists (3.3%) and benzodiazepines (3.2%). Significant increases in the number of calls to IMAGE were observed after the paroxetine warnings (Oct.05), and the signal on the possible teratogenic effect of NSAIDs (Aug.06). **Conclusions:** Our findings show that there is increasing use of, and awareness to medications during pregnancy and lactation.

BASIC RESEARCH**54. Involvement of elastases in elastocalcinosis.**

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Introduction: Elastocalcinosis is a form of vascular calcification associated with aging and localized on the elastic lamellae. It is associated with a reduction of collagen/elastin ratio and a fragmentation of elastin. **Purpose:** Determine if elastases are important in the development of elastocalcinosis. **Methods:** Male Wistar rats were treated with warfarin (20 mg/kg/d) and vitamin K (15 mg/kg/d) (WVK) during 1, 2, 3 and 4 weeks. Untreated rats were used as control (Ctrl). Pulse wave velocity (PWV, an index of vascular stiffness) was evaluated. In the aorta, calcium content and elastin fragmentation were measured. Gelatinase activity was evaluated by zymography. To determine the involvement of different families of elastases, ex vivo experiments of calcification were performed with aprotinin, E-64, 1,10-phenanthroline (1,10-phen) and doxycycline (Doxy). Finally, additional rats received Doxy in association with the WVK treatment during 4 weeks. **Results:** WVK treatment induced a progressive accumulation of calcium and fragmentation of elastin in the aortic wall, associated with a gradual increase of PWV. Gelatinase activity, especially MMP-9 activity, was enhanced after 1 week of WVK treatment (WVK1: 217±52 vs Ctrl: 100, P<0.05). The activity returned to baseline at 4 weeks of treatment. Ex vivo experiments demonstrated that only metalloproteinases inhibitors (1,10-phen or doxy) prevented the calcification. Doxy also prevented calcification (Doxy: 0.78±0.18 vs WVK4: 2.27±0.36 µg/mg of tissue, P<0.05) and elastin fragmentation in rats. Moreover, it reduced vascular stiffness. **Conclusion:** WVK treatment induced a progressive calcification and elastin fragmentation associated with arterial stiffening. It was associated with a transient activation of MMP-9. Considering that metalloproteinases inhibitors were able to prevent calcification ex vivo and in vivo, our results suggest that MMPs are key players in the process of elastocalcinosis.

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55. Chemical and enzymatic synthesis of sugar nucleotides for glycosylation engineering of natural productsShannon C. Timmons¹, Roy H. Mosher^{2,3}, Sheryl A. Knowles³, and David L. Jakeman^{*1,3}¹Department of Chemistry, Dalhousie University, Halifax, NS, ²Department of Biological Sciences, Wagner College, Staten Island, NY, ³College of Pharmacy, Dalhousie University, Halifax, NS

Introduction and objectives: Despite advances in modern drug discovery, a significant number of pharmaceuticals continue to be derived from natural products, many of which contain one or more carbohydrate functionalities. Sugar appendages are often important in conferring bioactivity, although their precise function remains unclear in many cases. To further understand the medicinal role of carbohydrates attached to natural products, access to a variety of differentially glycosylated compounds is required. As the chemical synthesis of these derivatives is often challenging, glycosyltransferase enzymes are increasingly being used to generate libraries of structurally related glycosylated natural products. These enzymes utilize sugar nucleotides as substrates to transfer carbohydrates to natural products. A major limitation of this approach is poor access to sugar nucleotide substrates. Thus, the development of efficient synthetic and enzymatic methodologies to prepare sugar nucleotides is of particular importance for advancing natural product glycosylation studies (Figure 1).

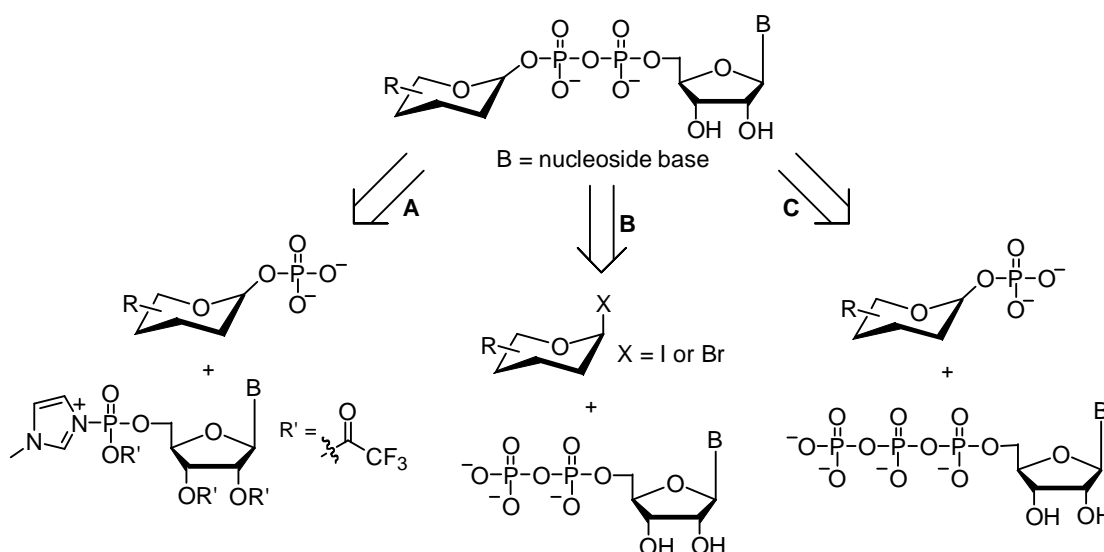


Figure 1. Retrosynthetic strategies for preparing sugar nucleotides

Methods: Sugar nucleotides were prepared using chemical and enzymatic approaches. Compounds were purified using reversed-phase chromatography and characterized via NMR spectroscopy and mass spectrometry. **Results:** Eight sugar nucleotides were chemically synthesized by coupling various sugar-1-phosphates with activated nucleoside 5'-monophosphates (**A**) while five sugar nucleotides were chemically synthesized by coupling electrophilic carbohydrates with nucleoside 5'-diphosphates (**B**). Fifteen sugar nucleotides were also prepared by exploiting the substrate flexibility of three bacterial thymidyltransferases (**C**). **Conclusions:** Chemical synthesis represents a robust and versatile method of preparing structurally diverse sugar nucleotides, although the enzymatic synthesis of sugar nucleotides using nucleotidyltransferases is a more convenient and higher yielding method of preparing these substrates when enzymes are substrate flexible. Sugar nucleotides prepared via both chemical and enzymatic methods will be used to probe the substrate specificity of the JadS glycosyltransferase enzyme, which transfers a carbohydrate appendage to the angucycline antibiotic aglycon of jadomycin B.

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56. Gender-related differences in potassium channel block; Modulatory role of verapamil.*Raymond Hreiche, Pierre Morissette, Hubert Zakrzewski-Jakubiak and Jacques Turgeon.*

Faculté de Pharmacie, Université de Montréal.

Background: Gender-related differences observed in drug-induced Long QT syndrome (LQTS) are well established, while their mechanisms remain largely undefined. Our laboratory previously reported that a treatment with verapamil, a well-known membrane transporters modulator, can potentiate the electrophysiological effects of an I_{Kr} blocker, cisapride. Therefore, the objective of the present study was to evaluate, with or without verapamil treatment, gender-related differences during block of I_{Kr} , I_{Ks} , and $I_{Kr}+I_{Ks}$.

Method: Hearts ($n=120$) from Hartley male and female guinea pigs were isolated and buffer-perfused in the Langendorff mode. After a 10min perfusion with Krebs-buffer containing no drug, hearts were perfused for 10min with buffer containing [20nM dofetilide], [100nM domperidone], [66 μ M indapamide], [20nM dofetilide + 66 μ M indapamide] or [100nM domperidone + 66 μ M indapamide].

Results: In non-treated guinea pigs, indapamide 66 μ M used as a selective I_{Ks} blocker caused a more pronounced prolongation of MAPD₉₀ in female (17.0 ± 5.7 msec) compared to male (11.8 ± 3.5 msec) ($p<0.05$). In opposite, the MAPD₉₀ prolongation induced by I_{Kr} blockers (domperidone and dofetilide) alone or associated with indapamide was not significantly different in male versus female. Independently from the gender effect, we demonstrated that the treatment with verapamil induced a higher MAPD₉₀ prolongation when hearts were perfused with dofetilide or domperidone ($p<0.01$). Independently from the verapamil treatment, our results showed that the gender parameter exhibits a significant effect ($p=0.091$) with a significant superior MAPD₉₀ prolongation observed in females. Yet, verapamil treatment does not seem to show a significant difference when I_{Kr} or I_{Ks} blockers are perfused.

Conclusion: Gender-related differences were observed in MAPD₉₀ of hearts exposed to I_{Ks} blockers but not with I_{Kr} blockers. In addition, we confirmed the modulatory effect of verapamil on the prolongation of cardiac repolarization with I_{Kr} blockers. Finally, we lacked to demonstrate an implication of verapamil treatment - via a potential modulatory role of membrane transporters - in the gender-related differences in drug-induced LQTS.

57. Polyion complex micelles of carboxymethyl dextran-block-poly(ethylene glycol) and diminazene diaceturate: preparation and physicochemical characterization.*Ghareb M. Soliman and Françoise M. Winnik,*

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Purpose: The purpose of this study is to prepare and characterize the polyion complex micelles (PIC) of novel carboxymethyl dextran-block-poly(ethylene glycol) (CMD-PEG) and diminazene diaceturate, a model water soluble cationic drug. The effect of PEG chain length and dextran degree of carboxymethylation on micelle formation and stability was studied.

Methods: CMD-PEG block copolymers with different PEG chain lengths and different degrees of dextran carboxymethylation were synthesized by coupling of PEG-NH₂ and dextran-lactone followed by carboxymethylation of dextran. ¹H NMR was used to determine the drug: carboxylate molar ratio corresponding to micellization. The micellar properties, such as their hydrodynamic radius (R_H) and polydispersity index (PI), were determined for solutions of various salt concentrations and over a wide pH range, using dynamic (DLS) and static (SLS) light scattering. The micelle morphology was examined by environmental scanning electron microscopy (ESEM). In-vitro drug release from the micelles was measured using the dialysis bag method.

Results: Four CMD-PEG block copolymers were synthesized, two have different PEG chain length and two have different dextran degrees of carboxymethylation. DLS studies showed that CMD-PEG formed PIC micelles upon the interaction with diminazene diaceturate with $R_H \sim 40$ -60 nm and low PI, depending on the type of CMD-PEG block copolymer. The micelle R_H and PI were constant over the 4 to 11 pH range. The micelles were able to withstand salt concentrations up to 400 mM. Diminazene loading ranged from 40-60 % w/w, depending on the dextran degree of carboxymethylation. ESEM showed that the micelles have spherical shape and uniform size. No aggregation was detectable. The micelles were able to sustain the drug release for 8 h under physiological pH and salt conditions.

Conclusion: Electrostatic interactions between CMD-PEG and diminazene trigger the formation of small, monodispersed and stable micelles. These nanoparticles are expected to find applications in oral drug delivery systems for charged hydrophilic molecules such as peptide drugs.

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58. Cholesterol efflux mediated by ABC transporters is upregulated with EP 80317, a growth hormone releasing peptide in a PPAR γ -dependent manner.

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Cholesterol homeostasis within macrophages relies in part on efficient efflux pathways supplying cholesterol for its reverse transport to the liver. We have recently shown that CD36 ligands such as EP 80317 exerted striking hypocholesterolemic and anti-atherosclerotic effects in apoE-deficient mice fed a high fat high cholesterol diet. These effects were associated with an increased expression of ATP-binding cassette (ABC) transporters and an increased efflux of cholesterol from peritoneal macrophages. The present study aims to assess the role of nuclear receptors and of the different ABC transporters in EP 80317-mediated cholesterol efflux in macrophages. **Methods:** J774 cells were loaded with [3 H]-cholesterol (1 μ Ci/ml) and incubated \pm EP 80317 (10^{-7} M). Cholesterol efflux from J774 cells was determined following a 4 and 16 hours incubation with HDL (50 μ g/ml) or apoA-I (20 μ g/ml) as cholesterol acceptors. The expression of proteins involved in reverse cholesterol transport was determined by western blot. **Results:** With apoA-I as the cholesterol acceptor, EP 80317 induced a significant increase of cholesterol efflux by 163% and 95% ($p < 0.001$) after 4 and 16 hours, respectively. In contrast, EP 80317-mediated efflux to HDL increased by only 32-26% ($p < 0.001$), under the same conditions. The significant increase of EP 80317-mediated cholesterol efflux was completely inhibited with DIDS, an ABC transporter inhibitor, with either acceptor. In contrast, no change in EP 80317-elicited cholesterol efflux was found following the incubation of J774 cells with BLT-1, a SR-B1 inhibitor. To assess the effect of EP 80317 on PPAR γ in the regulation of cholesterol efflux, J774 cells were incubated with GW 9662, a PPAR γ inhibitor. A complete inhibition of EP 80317-mediated efflux was found. The expression of proteins involved in cholesterol efflux, as assessed by Western blot, was increased by 2.5-, 2.2- and 7.3-fold for LXRA, ABCG1 and ABCA1, respectively, without significant change in the PPAR γ protein levels. **Conclusions:** EP 80317 induces a significant increase in cholesterol efflux from murine macrophages. EP 80317-mediated efflux is mainly mediated through ABC transporters in a PPAR γ -dependent manner.

59. Ser/Thr cluster I and II located in C-terminal end of IRF3 are both important for its optimal transactivation ability and are involved in different aspects of IRF3 life cycle.

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Introduction: The IKK related kinases, IKKi and TBK1, were recently shown to be responsible for the C-terminal phosphorylation of IRF3. However, different conclusions were raised about the phosphoacceptor site(s) targeted by these two kinases. **Purpose:** In order to evaluate with accuracy the physiological relevance of the different Ser/Thr clusters, we chose to study the effect of alanine mutations on anti-viral cytokines productions. **Methods:** For this purpose, we took advantage of a biological assay where supernatants of HeLa cells overexpressing the different C-terminal IRF3 mutants were collected and used to pretreat Vero cells before further challenge with VSV. The effects were evaluated through VSV-induced cell lysis using a standard plaque assay procedure. **Results:** Our data revealed that both Ser/Thr clusters are required for optimal transactivation capacity of IRF3, but that the S385 and S386 are the first one targeted by TBK1/IKKi. *In vitro* kinase assay using full length IRF3 harboring C-terminal mutations as substrates also demonstrate that clusters I and II are both targeted by the kinases as opposed to published results using a GST-IRF3 as substrate. Analysis of Ser/Thr to Ala mutants also reveals that S396A, located in cluster II, abolished IRF3 homodimerization, CBP association and nuclear accumulation. However, the production of anti-viral cytokines is still present in IRF3 S396A expressing cells. Moreover, the phosphomimetic mutant S396D is constitutively active and homodimerize. These data reveal an intriguing role of S396 that lead us to reconsider the current model of IRF3 activation. **Conclusion:** We propose that some read out of IRF3 activation needs to be reconsidered for a better understanding of its regulation. Our data also reconcile published data by showing that both clusters are essential for IRF3 activity. However, our study clearly demonstrates that the different sites are involved in different steps of IRF3 life cycle. CIHR (MOP-53282), CIHR/RxD and FRSQ

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60. The transcription factors Nur77 and retinoid X receptors participate in amphetamine-induced locomotor affectsEmmanuelle Bourhis¹, Jérôme Maheux¹, Claude Rouillard² and Daniel Levesque¹¹ Faculty of Pharmacy, University of Montreal, Montreal, Qc, Canada, ² Neuroscience unit, Laval University Research Center, Quebec city, Qc, Canada

Introduction: In the brain, dopaminergic systems integrate and respond to stimuli coming from internal and external environment. Psychostimulants such as amphetamine (AMPH) represent some external stimuli that alter dopamine neurotransmission. However, the molecular and cellular mechanisms underlying psychostimulant responses are still incompletely understood. In recent years, evidences emerged that certain transcription factors of the nuclear receptor family, specifically Nur77 and retinoid X receptors (RXR), play an important role in adaptation and homeostatic regulation of dopaminergic systems. **Objective:** In this study, we investigate the role of these transcription factors in the locomotor response induced by AMPH. **Methods:** We used a combination of genetic (Nur77) and pharmacological (retinoid drugs) approaches to evaluate the role of these factors. We compared locomotor responses induced by repeated AMPH administration between wild type and Nur77 knockout mice in the presence or not of various synthetic retinoid drugs (RXR and retinoic acid receptor (RAR) agonists and antagonists). We measured 3 components of locomotor activity: horizontal locomotion, vertical locomotion or rearings and stereotyped behaviors. **Results:** The results show that HX531, a synthetic RXR antagonist, reduces AMPH-induced horizontal locomotor activity, while RAR drugs remain inactive. Rearing and stereotyped behaviours are not altered by the Nur77 gene deletion or by retinoid drugs. Interestingly, the effect of the RXR antagonist on horizontal locomotor activity induced by AMPH is abolished in Nur77 deficient mice, suggesting that this orphan nuclear receptor partner is essential for the effect of this RXR drug. **Conclusion:** This study indicates that RXR and Nur77 represent neuronal substrates for AMPH effects. It suggests an involvement of RXR in interaction with the orphan nuclear receptor Nur77 rather than a classic RAR-RXR-mediated retinoid signaling activity. Thus, these transcription factors might play a role in long-term neuroadaptation related to drug-taking and selective RXR antagonists might represent interesting pharmacological tools to reduce motor activation induced by drugs of abuse.

61. A physiologically based pharmacokinetic model to assess the role of ABC transporters in drug distribution.Frédérique Fenneteau¹, Jun Li^{1,3}, Lucie Couture^{1,2}, Jacques Turgeon¹, Fahima Nekka^{1,3}¹ Faculté de Pharmacie, Université de Montréal, Montréal, Québec, Canada, ² Charles River Laboratories Preclinical Services Montréal Inc., Montréal, Québec, Canada, ³ Centre de Recherche Mathématiques, Université de Montréal, Québec, Canada.

Background: Drug interactions affecting the expression and/or activity of ATP-Binding Cassette (ABC) transporters may have a significant impact on drug disposition, drug effectiveness or drug toxicity. The main objective of our study was to develop an innovative model that takes into account the involvement of ABC transporter activities in different tissues, in order to improve prediction of drug distribution in the various conditions surrounding ABC transporter activities. **Method:** A PBPK model was developed in order to consider various conditions of P-gp transporters activities in mouse brain, liver, kidney and heart tissues. Drug distribution was represented either by variants of well-stirred model or permeability rate limited model. Input parameters related to the activity of P-gp in these tissues were mainly extrapolated from in vitro data. A global sensitivity analysis (SA) was also performed from 500 multivariate log-normal Monte-Carlo simulations to account for the variability of input parameters and their influence on the following model outputs obtained on each tissue: C_{max}, C_{last} and AUC_{0-tlast}. The measure of input-output sensitivity was performed using the partial rank correlation coefficient (PRCC) concept which has been designed for correlated inputs. **Results:** Our model was successfully validated from experimental data collected on wild type and mdr1a/1b(-/-) mice which were intravenously administered 5mg/kg of 3H-domperidone. PBPK model simulations in brain and heart tissues confirmed and quantified a significant involvement of additional efflux transporters at the blood-brain barrier as well as of cardiac influx transporters in domperidone distribution. Further investigations are required to determine the exact nature of additional transporters involved in domperidone distribution at the blood-brain barrier. **Conclusion:** This PBPK model is novel and unique while defined in general terms that can be applied to other drugs and transporters.

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62. Induction of the transcription factor *Nur77* by antipsychotic drugs is dependant upon metabotropic glutamate subtype 5 and adenosine A_{2A} receptors.

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Introduction: Recent observations have shown that transcription factor of the *Nurs* family, mainly *Nur77*, could play a major role in the generation of extrapyramidal effects induced by first generation antipsychotic drugs. Indeed, *Nur77* is strongly induced in motor area of the striatum following administration of a typical neuroleptic. Although antipsychotic actions are generally associated with interaction with dopamine D₂ receptor subtypes, the contribution of metabotropic glutamate and adenosine receptors have been demonstrated. To better understand the role of these neurotransmitters in antipsychotic drugs action, we investigated the role of mGluR5 and A_{2A} receptors in antipsychotic-induced *Nur77* mRNA levels in the mouse brain. **Methods:** Groups of mice received acute injections of vehicle, MPEP (specific mGluR5 antagonist), SCH58261 (specific A_{2A} antagonist), eticlopride (D₂ antagonist), a combination of eticlopride and MPEP or SCH58261 and finally a combination of the eticlopride, MPEP and SCH58261. *Nur77* mRNA levels were detected by in situ hybridization with a specific radiolabeled ribonucleic probe. **Results:** Both MPEP and SCH58261 have no effect on *Nur77* mRNA levels when administered alone. While SCH58261 has no effect on eticlopride-induced *Nur77* mRNA levels, MPEP administration partially prevents this up-regulation. Interestingly, administration of both antagonists abolishes eticlopride-induced *Nur77* mRNA levels in the striatum and nucleus accumbens suggesting a synergistic effect of these two receptors in the up-regulation of *Nur77* mRNA level after eticlopride administration. **Conclusion:** This study indicates that up-regulation of *Nur77* mRNA levels induced by antipsychotic drugs is dependant upon mGluR5 and A_{2A} receptors and might not implicate direct blockade of D₂ receptors in the striatum. These results indicate that the mechanism of action of antipsychotic drugs is not as straightforward as previously proposed and needs to be reconsidered.

63. Role du monoxyde d'azote dans la rigidité artérielle et l'élastocalcinoïse

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Introduction : L'hypertension systolique isolée (HSI) est associée à une calcification physiologique de l'aorte contribuant à l'augmentation de la rigidité artérielle mesurée par la vitesse de l'onde de pouls (PWV). Objectifs: Déterminer l'implication du NO dans la modulation de la rigidité artérielle et l'élastocalcinoïse. **Méthodes:** Des rats ont reçu une injection s.c de vitamine K 3 fois par semaine pendant 4 semaines, ainsi que de la warfarine administrée dans l'eau de boisson (WVK). Pendant les 4 semaines suivantes, le traitement WVK a été poursuivi en ajoutant du L-NAME (20mg/kg/jour) dans la nourriture. Les traitements ont été arrêtés 24 heures avant la mesure des paramètres hémodynamiques (pression pulsée et PWV). Les concentrations de calcium aortique ont été mesurées par une méthode spectrophotométrique et sa localisation sur coupe d'aorte a été faite par coloration Von Kossa. L'endothéline (ET) tissulaire a été mesurée par essai radioimmunologique. **Résultats:** Le L-NAME a fait varier de manière significative la déposition de calcium au niveau de l'aorte comparativement aux rats WVK, et conséquemment les rats ayant reçu du L-NAME ont un PWV significativement augmenté. Le traitement WVK augmente significativement la production d'ET dans l'aorte, mais l'administration de L-NAME n'augmente pas davantage sa concentration tissulaire. Sur des coupes transversales d'aorte, chez des rats WVK, il est possible d'observer une distribution du calcium sur les lamelles élastiques les plus près de l'adventice. Chez des rats L-NAME, en plus de la déposition de calcium sur les lamelles près de l'adventice, il y a également accumulation de calcium sur les lamelles près de l'endothélium. **Conclusion:** Le NO endogène limite le développement de l'élastocalcinoïse et l'augmentation de la rigidité artérielle, en agissant principalement sur la partie interne de la tunique médiane.

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64. Rôle du TGF-B1 dans l'élastocalcinose

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Introduction: Le vieillissement est associé à la calcification élastocalcinose et la dégradation progressives des lamelles élastiques de la média, menant à l'augmentation de la rigidité artérielle et au développement de l'hypertension systolique isolée (HSI). Sachant que la dégradation de l'élastine libère certains produits, dont le TGF-B1, nous avons voulu déterminer leur implication dans l'élastocalcinose. **Méthodes:** L'élastocalcinose a été induite chez le rat par le traitement warfarine (20mg/kg/j)-vitamine K(15mg/kg/j) (WVK). Les paramètres hémodynamiques et la rigidité artérielle (vitesse de l'onde de pouls) ont été mesurés, de même que le calcium (colorimétrie). La fragmentation de l'élastine a été évaluée avec la coloration de Weigert. L'activité de TGF-B1 a été évaluée par co-immunoprécipitation de smad 2/3 – smad 4. Le SB-431542 a été utilisé ex-vivo pour bloquer les effets de TGF-B1 et le lactose pour bloquer les récepteurs des peptides d'élastine de façon à évaluer leur rôle dans la calcification vasculaire. Le Cbfa-1 a été mesuré par western blot comme indice de changement phénotypique des cellules musculaires lisses vasculaires. **Résultats:** La calcification était augmentée significativement après 3 semaines de traitement WVK pour atteindre un maximum à 4 semaines. La fragmentation de l'élastine et l'augmentation de l'expression de Cbfa-1 ont suivi la même progression. SB-431542 a prévenu la calcification de façon significative, alors que le lactose n'a pas eu d'effet. In vivo, la liaison de Smad 2/3 à Smad 4 était augmentée à une semaine de traitement WVK, pour ensuite revenir à des valeurs témoin. **Discussion:** TGF-B1 semble être impliqué dans la calcification vasculaire, tant dans le modèle in vivo qu'ex vivo. Puisqu'il est également connu que TGF-B1 est impliqué dans la fibrose, peut-être est-il le lien entre la calcification et la fibrose, qui mènent au développement de la rigidité artérielle.

65. Novel CD36 ligands with hypocholesterolemic and anti-atherosclerotic properties

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Introduction. Atherosclerosis develops as a consequence of oxidized low density lipoprotein accumulation and their uptake through the scavenger receptor CD36 into intimal macrophages which develop into foam cells. We have previously reported that EP 80317, a selective CD36 ligand, and to a lesser extent hexarelin, a growth hormone-releasing peptide (GHRP) that also binds CD36, exert significant CD36-dependent anti-atherosclerotic effect in mice. Whether this anti-atherosclerotic effect is shared by other analogs is not known. A new analog EP 80318 (Atab-D-MeTrp-D-Lys-Trp-D-Phe-Lys-NH₂) with specific binding affinity towards CD36 at 2.5 µM was used to document anti-atherosclerotic properties in apolipoprotein E (apoE)-null mice. **Methods.** ApoE-deficient mice fed a high fat high cholesterol diet from 4 weeks old were administered a daily s.c. dose of either one of two selective CD36 ligands, EP 80317, EP 80318, 300 µg/kg or 0.9% NaCl from 6 to 18 weeks of age (n = 6-9 per group). Blood was withdrawn from the subclavian vein and aortas were isolated from the aortic arch to the iliac bifurcation and cut longitudinally under stereomicroscope. Neutral lipids were colored by Oil Red O staining and the percentage of atherosclerotic lesions was determined by morphometric analysis. **Results.** A chronic treatment with EP 80318 or EP 80317 reduced the percentage of total aortic lesions by 30% (p < 0.01) and 41% (p < 0.01), compared to 0.9% NaCl, respectively. This effect was associated with a hypocholesterolemia, as shown by a reduction of 31% (p < 0.05) of total plasma cholesterol in mice treated with EP 80318 and of 26 % (p < 0.05) for mice treated with EP 80317 (22.6 ± 2.2 mmol/L in controls, 15.5 ± 1.3 mmol/L and 16.8 ± 2.1 mmol/L in mice treated with EP 80318 and EP 80317, respectively). In contrast, neither triglycerides, nor HDL cholesterol plasma concentrations were modulated by either one of the treatments. **Conclusion.** Our results support the potential application of GHRP derivatives, targeting CD36 for the prevention of atherosclerotic lesions development.

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66. Implication of the renin-angiotensin-aldosterone pathway-related polymorphisms to heart failure predisposition.

1Marcin Zakrzewski-Jakubiak M.Sc., 1Simon de Denus M.Sc., 2Marie-Pierre Dubé Ph.D., 1François Bélanger M.Sc.,
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Aims: Racial differences in survival outcomes point toward a genetic role in the pathophysiology of heart failure. Furthermore, contemporary evidence links genetics to heart failure predisposition. We tested for a difference in prevalence of 10 RAAS-related gene polymorphisms between a homogenous population of maximally treated heart failure patients and healthy controls. **Methods:** 111 healthy volunteers and 58 heart failure patients were included in this study. The healthy control group consisted of males aged between 18 and 35 years old. The heart failure group consisted of patients that were at least 18 years old, were in NYHA class II-III and had a documented LVEF of at most 40% within the previous 6 months. Despite being maximally treated for their condition with ACE inhibitors and beta-blockers, they continued to be symptomatic and, as such, compose a highly specialized and homogeneous patient population. Both groups were composed of Canadian Caucasians. The analysed polymorphisms were: ACE (I/D), AGTR1 (A1166C), AGT (M235T & T174M), eNOS (T-786C & Glu298Asp), ADRB2 (Gln27Glu), BDKRB2 (+9/-9), CYP11B2 (T-344C) and ADD1 (Gly460Trp). **Results:** The AGT T235 allele ($p<0.0025$) and the AGT M174 allele ($p<0.05$) were found to be more prevalent in our heart failure group. The AGT(174M)-AGT(235T) haplotype was also associated with the heart failure phenotype ($p=0.0069$). Exploratory evaluation of gene-gene combinations revealed an indicative association of the AGT(235T)-ACE(D) combined polymorphisms in the heart failure population ($p<0.02$). **Conclusion:** This study demonstrates that the SNPs of AGT may be associated with heart failure in our population and that the AGT/ACE gene combination may play an important role in disease predisposition.

EDUCATION AND TEACHING**67. Évaluation de la qualité des résumés publiés dans le Pharmactuel de 1993 à 2006**

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Objectif : R  aliser une   valuation de la qualit   des r  sum  s publi  s dans le Pharmactuel. L'objectif secondaire est de d  crire les r  sum  s publi  s. **M  thodologie :** Il s'agit d'une   tude descriptive et r  trospective des r  sum  s publi  s dans le Pharmactuel du 1er janvier 1993 au 31 d  cembre 2006. Un r  sum   sur deux a   t   s  lectionn   de fa  on al  atoire parmi ceux recens  s durant cette p  riode de publication du Pharmactuel. Le r  sum   a   t     valu   selon une   chelle de cotation publi  e dans la documentation et compos  e de 33 crit  res de qualit   regroup  s en 8 sections. Deux scores de qualit   ont   t   calcul  s: conformit   globale et conformit   si crit  re applicable. **R  sultats :** Des 416 r  sum  s publi  s dans le Pharmactuel de 1993    2006, 209 ont   t   inclus. Une proportion significativement plus   lev  e de r  sum  s proviennent des centres hospitaliers affili  s    l'Universit   Laval (i.e. 66%) que de l'Universit   de Montr  al (34%). Plus de 90% des r  sum  s sont issus de projets de ma  trise en pharmacie. Pour l'ensemble des r  sum  s   valu  s, le score moyen de conformit   est de 67,9% en prenant les crit  res applicables    chaque r  sum   et de 53,4% en prenant l'ensemble des crit  res (n=33). **Conclusion :** Il s'agit de la premi  re   tude   valuant la qualit   des r  sum  s publi  s dans le Pharmactuel. Pour l'ensemble des r  sum  s   valu  s, on observe un bon score moyen de conformit  . L'activit   de publication par les pharmaciens en poste doit   tre mieux encourag  e, ainsi que la finalisation des projets pr  sent  s par les r  sidents (pourcentage de r  sum  s ayant men      une publication faible : 6,7%).

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68. Development and preliminary evaluation of a training workshop for pharmacists assessing students in an OSCE setting.*Debra M. Moy* B.Sc. Pharm¹, Anthony Marini PhD², Greg Morris, B.A.¹¹University of Toronto, ²University of Calgary

Introduction: As the number of assessors has increased in an Objective Structured Clinical Evaluation (OSCE)-based 4th year undergraduate pharmacy course, to accommodate increased student enrolment, a lack of consistency and reliability in assessment between assessors for the same student performance has been observed by the course instructor and reported by students. **Objective:** To create a workshop for assessors to develop the skills needed to effectively assess OSCE-based student performance with the same reliability. **Methods:** Six steps followed in this developmental study. First an OVID search of the medical literature was undertaken looking for articles on how to improve assessor verbal/cognitive assessment in an OSCE-based teaching environment. Second, key concepts and strategies were identified to create a framework for the workshop. Third, a three-hour workshop was designed. Fourth, evaluation criteria were established and a questionnaire was developed to evaluate assessors' perceptions of the effectiveness of the workshop. Fifth the workshop was delivered to 32 assessors. In the final step a post workshop evaluation was conducted. **Results:** The literature review produced 4 key articles with the work by Brukner being most relevant. An expert facilitator, familiar with pharmacy practice outcomes, was hired. The workshop design included four components; didactic teaching, small and large group discussion, and a DVD, was used depicting simulated students role-playing different student performances. Thirty-one assessors attended the workshop and 29 completed the questionnaire. All respondents indicated the workshop will help them be more consistent when assessing students. Ninety-three percent (93%) of respondents indicated they have both a better understanding of bias/diversity issues that influence their own assessment decisions and how their peers are assessing the same student performance. **Conclusions:** The response by participants to the workshop was overwhelmingly positive. It was suggested that this workshop be offered annually. Anecdotally the number of student complaints related to assessor inconsistency declined dramatically.

69. Evaluation of a complementary pharmacy day within an interprofessional pain curriculum*Debra M. Moy*, B. Sc. Pharm., Lalitha Raman-Wilms, Pharm D.

Leslie Dan Faculty of Pharmacy, University of Toronto.

In the first year of an interprofessional pain curriculum pharmacy student feedback indicated they were not prepared with the knowledge and skills required to engage effectively in interprofessional discussions. To augment student's ability to contribute to interprofessional discussions we strategically designed a half-day program for our students. **Objective:** To evaluate, from the student's perspective, their experience in the half-day program and their perception of its impact on subsequent interprofessional discussions. **Methods:** Four content components were determined and included. 1. The management of constipation in chronic narcotic use, 2. Methadone in managing pain, 3. Dose conversions, and 4. Chronic pain in the elderly. The teaching design criteria were then established and included. (1) relevant, immediately transferable competency that can be applied the following day, (2) applicable to hospital and community practice and (3) patient-case based. A questionnaire was then developed. It was administered at the end of each half-day pharmacy program between 2004 and 2005. **Results:** For each content area the questionnaire asked if it increased the student's knowledge on how to manage pain-related issues, as well as if it stimulated student's thinking in this area. In addition questions about specific speakers were asked. Students were asked to rate the program overall. In 2004, 90% of students who participated in the half-day program completed the survey and in 2005, 92% of students completed the survey. In both years, 75% of respondents agreed, or agreed strongly that the topics increased their knowledge on managing pain related issues. In both years, more than 87% of respondents rated the day as useful and complementary to the pain curriculum. **Conclusions:** Development of a complementary pharmacy day within an interprofessional pain curriculum, with strategic teaching design criteria, resulted in increased student knowledge on this topic and allowed them to be more active participants in interprofessional discussions.

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70. The ability of interprofessional and uniprofessional student teams to assess the quality of a patient care plan as compared to an experienced evaluator.

Roy Dobson¹, Jane Cassidy¹, Peggy Proctor², Doreen Walker¹

¹. College of Pharmacy and Nutrition and ². School of Physical Therapy, University of Saskatchewan

Purpose: To give students working in interprofessional and uniprofessional teams the opportunity to assess a simulated hospitalized patient, develop a comprehensive patient care plan, and assess the quality of that plan. **Methods:** Pharmacy, nutrition and physical therapy students were assigned to work in small interprofessional or uniprofessional (pharmacy only) teams of 2-3 students. Together, each team interviewed a patient-actor role-playing a hospitalized postmenopausal woman with a newly diagnosed vertebral compression fracture, and together developed a comprehensive care plan. At a follow-up tutorial, the teams self-assessed the quality of their care plans using an evaluation tool based on published clinical practice guidelines for the management of osteoporosis, and input from dietitians, pharmacists and physical therapists. The care plans were also assessed by an experienced external evaluator using the same tool. Students were also asked to complete a questionnaire about their experiences with intra-peer assessment of the patient care plan. **Results:** Overall, student groups tended to score their care plans higher than the experienced evaluator (34.8 vs 30.5; $p < 0.001$). Individual portions of the plans scored higher by the student teams included calcium supplement (4.6 vs 3.7; $p < 0.001$), pain management (4.1 vs 3.7; $p < 0.05$), exercise (4.4 vs 4.2; $p < 0.05$), education (3.5 vs 2.5; $p < 0.001$), patient follow-up (3.7 vs 3.3; $p < 0.05$), and global assessment (5.7 vs 4.3; $p < 0.001$). No differences in scoring were seen for recommendations regarding Vitamin D or choice of pharmacologic agent. Students indicated value in assessing their own plans, confidence in their ability to carry out the task, working together was helpful in assessing the plan, and the evaluation tool was helpful. **Implications:** Self-assessment of the quality of their patient care plan provides students with an opportunity to enhance their understanding of the comprehensive management of osteoporosis and to practice self-evaluation skills as an important professional competency.

71. Self-directed learning at the University of Manitoba: implementation of a new elective program at the Faculty of Pharmacy

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Background: The Electives Program (PHRM 4800), offered for the first time in 2007R at the Faculty of Pharmacy (University of Manitoba), was developed to provide senior pharmacy students with opportunities for self-directed learning in areas of basic and clinical research, professional practice, and education that are beyond the boundaries of the required undergraduate curriculum. **Methods:** Students can choose to conduct projects at sites pre-approved by the Faculty or to propose alternative avenues. Under the guidance of a preceptor, students increase their depth of knowledge in the areas of interest and enhance their skills in reflection-in-practice. Students are required to produce a written report of their experience to complete the evaluation provided by their preceptor. **Results:** In addition to the Faculty of Pharmacy, pre-approved sites included the National Microbiology Laboratory, the Wellness Institute, the Addiction Foundation of Manitoba and the RCMP Toxicology Laboratories. The Department of Family Medicine provided a unique opportunity for interdisciplinary education where pharmacy students interacted with medical residents and various health professionals with the purpose of gaining insights into and improving patients' primary care. Students also pursued sites abroad which included the University of Bonn, the University of Queensland and the International Pharmaceutical Federation. **Conclusion:** A research project aimed at evaluating the entire elective program is on going. Results of this study will contribute to our understanding of how well this new course in pharmacy helps students reach the educational outcome of being able to self-assess their learning needs and develop and implement strategies to promote lifelong learning and continuing professional competences. Upon analysis of the reflective outcomes, recommendations will be made to improve the quality of this educational experience.

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72. ECO project: A new competency assessment model for clerkships

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Purpose: To compare students and preceptors perception between the actual assessment model and a new cross-curricular assessment model (ECO Model). To measure the validity, reliability and convenience of appraisal forms (AF). **Methods:** All active students and preceptors during 4th year clerkship were asked to join in. Participants had to assist to a training session, use ECO Model tools (Direct observation booklet (DOB) and Competency Global Assessment Form (CGAF)), complete an AF, and participate in a focus group. **Results:** Preliminary analysis suggest that the training sessions and informative material were well received by both students and preceptors; that the ECO Model offers an easy process and proposes practice oriented outcomes, enables frequent feedback and allows clear professionalism assessment. On the other hand, preceptors and students have reported resistance to change, an unclear 3-level assessment scale and a too crowded and literal tool display affecting usability. DOB was used 2,2 times/week/preceptor. Preceptors would have appreciated using the ECO Model from the beginning of the clerkship. Online availability of the ECO Model was also requested. **Conclusion:** Relevant modifications will be made to the DOB, CGAF and AF prior to implementation. Preceptors will be trained for accurate use of the ECO Model. Phase 2 of the study will focus on measuring validity, reliability and convenience at a larger scale by using the revised AF.

73. Educational resources management model: From cross-curricular to trans-curricular

Gilles Leclerc, Michel Leblanc, Guylaine Bertrand
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Purpose: Design an online system that supports a collaborative management approach and enables Cross-Curricular and Trans-Curricular reusability of numerical educational resources in order to meet the educational outcomes of pharmacy undergraduate, graduate and professional development programs. **Methods:** A sequential process of preliminary needs analysis, case utilization review, conceptual analysis, international standards review and model design has lead to an iterative development of an online system. **Results:** The model refers to three levels of educational resources management: learning objects (LO), learning units (LU) and course information systems/websites (CIW). The development of these educational resources was driven by a collaborative and multidisciplinary approach. Learning Objects are defined as any digital resource designed to support learning. The model focuses on reusability of LO in various learning context and for diverse education levels. Furthermore, the Learning Units gathers selected LO with formative assessments and external links to service a desired learning domain. Finally the CIW combines and contextualized LUs according to user's educational level. The LU and CIW are designed to support future development toward adaptive learning/ testing and SCORM interoperability. In order to favor usability, a web template was designed for all the courses with common basic features. **Conclusion:** The model will be implemented and tested during the following academic year (2007-2008) in the Pharm.D. first year courses and specific professional development courses.

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153. Transforming healthcare through collaboration "in-BC"

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Introduction. It is becoming increasingly evident that processes by which health professionals are educated and supported will be integral to health human resource planning in Canada. Amongst the many strategies currently being examined, interprofessional education and collaboration is one practice that is thought to be key in maintaining a workforce for a sustainable and quality health care system. **Methods and Goals:** Funded by Health Canada and the BC Ministry of Health, the Interprofessional Network of BC (*In-BC*) is a collaborative initiative amongst the College of Health Disciplines at the University of British Columbia and the six health authorities and post-secondary education institutions across British Columbia. Through this partnership, *In-BC* has brought together health and education stakeholders to share resources and expertise to achieve four overarching goals: 1. Promote and demonstrate benefits of interprofessional education and collaborative patient-centred practice, 2. Foster system change in health and education, 3. Promote knowledge translation/exchange, and 4. Increase capacity to teach and learn from an interprofessional perspective. **Results:** The *In-BC* outcomes include: (i) Implementation of five provincial projects; (ii) Development of a multiple level evaluation framework; (iii) Development of an interprofessional curriculum framework; and (iii) Implementation of infrastructure to support knowledge translation initiatives. **Conclusion:** The *In-BC* initiative has been integral in transforming health and education systems in British Columbia.

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Posters – Friday June 1, 2007

PHARMACY PRACTICE RESEARCH

118. Feasibility of conducting a pragmatic cluster cohort study using administrative databases to evaluate the effectiveness of an osteoporosis workshop

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Background: A one-hour osteoporosis workshop offered to family physicians may influence their prescribing practices. **Objectives:** To evaluate the feasibility of using the RAMQ administrative databases to build a cohort of elderly patients candidate for an osteoporosis screening and followed-up by exposed and unexposed physicians to the workshop. **Methods:** Each exposed physician was matched to 10 unexposed physicians from the RAMQ database based on gender and year of graduation. Patients' eligibility criteria were: be alive and 70 years or older at the index date (date of the workshop), have at least one medical visit with a participating physician during the year preceding and following the index date, no bone mineral density testing, no osteoporosis treatment, and not be institutionalized 5 years prior to the index date. The number (proportion) of non-eligible patients is computed after applying each eligibility criteria. **Results:** 26 (76%) out of 34 exposed physicians agreed to participate and were matched with 260 unexposed physicians. A total of 55445 elderly patients alive at the index date were followed-up by these physicians. Among those, 35339 (64%) had no medical visit with the same physician during the year following the index date, 13555 (24%) had bone mineral density testing, 14494 (26%) had an osteoporosis treatment, and 4,696 (9%) were institutionalized 5 years prior to the index date. Overall, 11472 patients fulfilled the eligibility criteria. **Conclusions:** Using the RAMQ databases, with 26 exposed physicians, it is feasible to constitute a sufficiency large cohort to detect, with a power of 80%, a difference of 7% in the proportion of patients having a bone mineral density testing in the exposed and unexposed groups.

119. Évaluation de la conformité de la chaîne thermique en établissement de santé

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Objectif : Cet article vise   pr senter une  valuation de la conformit  de la gestion des r frig rateurs dans un centre hospitalier qu b cois ainsi qu'un plan d'action. **M thode :** Sant  Canada a publi  des lignes directrices sur le contr le de la temp rature des m dicaments pendant leur entreposage et leur transport,   l'intention des fabricants, des distributeurs et des pharmaciens.   partir de cette politique en vigueur, nous avons  tabli douze crit res de conformit . On a proc d    une  valuation de la pratique par le biais d'une tourn e de tous les r frig rateurs de l' tablissement pouvant contenir des m dicaments en appliquant les crit res de conformit . **R sultats :** La conformit  des r frig rateurs utilis s dans notre  tablissement de sant  varie de 21%   96 % et 7 des douze crit res sont  gaux ou inf rieurs   50 % de conformit . Le degr  de propret  est jug  acceptable pour presque la majorit  des r frig rateurs  valu s. **Conclusion :** Cette  valuation nous permet de constater que le niveau de conformit  des r frig rateurs pr sent dans notre  tablissement de sant  doit  tre am lior . Elle nous am ne   mettre en place une d marche pratique de mise   jour en ce qui concerne la conservation des m dicaments. Cette  tude d montre la n cessit  de diffuser l'information et de former davantage le personnel clinique et celui des unit s de soins sur tout ce qui concerne la conservation des m dicaments au r frig rateur dans un centre hospitalier qu b cois afin d'en assurer la conformit . La possibilit  de recourir   de nouvelles technologies (traceurs) pour  valuer ponctuellement d'autres aspects du circuit du m dicament fait aussi partie int grante de notre plan d'action visant l'am lioration de la conformit  de la cha ne thermique.

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120. Plasma concentrations of Bupivacaine and Ropivacaine in combined femoral-sciatic blockMohamad-Samer Mouksassi¹, Pierre Beaulieu², France Varin¹, and Line Labbé¹,¹Faculty of Pharmacy, University of Montreal, Montreal, Canada, ²Faculty of Medicine, Pharmacology department, University of Montréal, Montreal, Canada

Purpose: The objective of our analysis is to describe the population pharmacokinetic (PK) of bupivacaine (BUP) and ropivacaine (ROP) in combined femoral-sciatic nerve block (CFSB) and to identify factors explaining the interindividual variability (IIV). **Methods:** A randomized double blind study comparing ROP (n=8) and BUP (n=8) in CFSB for knee arthroplasty was conducted. Sciatic nerve block was performed first by injecting 15 ml of a 0.5% solution of either anesthetic using the Labatt approach; femoral nerve block was then performed with 25 ml using a classical anterior approach. Plasma samples were drawn up to 32 h after the first block. Data analysis was performed with NONMEM. The covariates studied were: age, sex (ROP group only), height, weight, and drugs affecting CYP1A2 or CYP3A4. **Results:** For BUP no covariate relationships were discovered and apparent clearance (CL/F) was 14.5 L/h with an IIV of 164%. The apparent central volume of distribution (Vd/F) of BUP was 371 L with an IIV of 99 %. For ROP CL/F was 7.7 L/h with an IIV of 23%. The Vd/F of ROP in men was 1.76 greater than in women (366 vs. 208 L; p=0.028). **Conclusions:** No covariate effects were detected for BUP but there were no men in this group. For ROP, sex differences in Vd/F that are not fully explained by weight differences, were observed. Studies with larger number of subjects are needed to fully characterize the PK of both drugs and to detect significant covariate relationships if any.

This abstract was presented at the ASCPT meeting 2006

Mouksassi MS, Varin F, Beaulieu P and Labbé L. Population Pharmacokinetics of Bupivacaine and Ropivacaine in Combined Femoral-Sciatic Nerve Bloc. : PIII-65. Clinical Pharmacology & Therapeutics. 79(2):P76, February 2006.

121. Population Pharmacokinetics of Intravenous Pantoprazole in Pediatric Intensive Care PatientsMohamad-Samer Mouksassi¹, Géraldine Pettersen^{2*}, Yves. Théorêt³, Line Labbé¹, Christophe Faure⁴, Bao Nguyen⁵ and Catherine Litalien⁶

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Introduction: Intravenous (IV) pantoprazole, the only proton pump inhibitor (PPI) with IV formulation in Canada, is an attractive drug for critically ill children who require gastric acid suppression. To date, there is very scarce data regarding the pharmacokinetics of pantoprazole in children, with essentially no data in infants less than 2 years. **Purpose:** To determine the pharmacokinetics of intravenous pantoprazole in critically ill children and to identify factors responsible for interindividual variability. **Methods:** Pantoprazole was administered to twenty patients at risk for or with upper gastrointestinal bleeding in whom intensive blood sampling was performed. A population analysis was conducted via a two-compartment pharmacokinetic model using NONMEM. **Results:** The total interindividual variability for clearance in the base model was estimated to be 132 %. Weight, systemic inflammatory response syndrome (SIRS), age, hepatic dysfunction, and presence of a CYP2C19 inhibitor were the significant covariates, accounting for 77 % of the observed variability. For a typical five year old child weighing 20 kg, the clearance and central volume of distribution were 5.5 L/hr and 2.22 L, respectively. Pantoprazole clearance was decreased by 68 % in the presence of SIRS (p < 0.001), by 57 % in the presence of hepatic dysfunction (p < 0.001) and 60 % in the presence of a CYP2C19 inhibitor (p < 0.001). **Conclusions:** The pharmacokinetics of IV pantoprazole in critically ill children is extremely variable and affected by inflammation. Our results emphasize the importance of dosing individualization in pediatric intensive care patients.

*The first two authors equally contributed to this research

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122. Population pharmacokinetic of intravenous busulfan in childrenNastya Kassir¹, Yves Théorêt², Martin A. Champagne², Michel Duval², Diane Larocque², Line Labbé¹¹Faculty of Pharmacy, University of Montreal, Montreal, Canada, ²Service d'hématologie-oncologie, Département de pharmacie, Centre Hospitalier Universitaire Sainte-Justine Montréal, Canada, H3T 1C5

Purpose: Busulfan is an alkylating agent used, in combination with cyclophosphamide +/- other drugs, as a radiomimetic in a variety of preparative regimens for hematopoietic stem cell transplantation (HSCT). Intravenous preparation provides better predictable pharmacokinetic than oral formulation, although wide inter and intra-individual variability may subsist. The objective of our study is to describe the population pharmacokinetic of intravenous busulfan and to identify the covariates that allow a better dosing and a lesser variability. **Methods:** A retrospective population pharmacokinetic analysis was performed on 41 consecutive children (0.21 – 20 years old) receiving intravenous busulfan. Initial dose of intravenous busulfan was 0.8 mg/kg for 33 patients and 1mg/kg for 8 patients, in a 2 hour infusion, and then every 6 hours, for a total of 16 doses. Pharmacokinetic parameters were determined on the first dose, and subsequent doses were adjusted, if needed, to achieve an area under the curve of 900-1500 µMol*min. Data analysis was carried out by a population approach using NONMEM. The influence of the covariates age, sex, actual body weight and body surface area (BSA) was studied. **Results:** Clearance (CL) and volume of distribution (VD) of busulfan were found functions of BSA and BSA + sex, respectively. The clearance was 3.24 ml/min/kg and the volume of distribution was 0.68 L/kg. Busulfan VD was significantly reduced in girls (-12%). Patient BSA was associated with an increase of busulfan CL and VD (9.9% and 10.7% per 0.1 m², respectively; p<0.05). The inter-patient variability was decreased from 77.52% to 18.49% in CL and from 76.35% to 7.94% in VD. Inter-occasion variability was 13.34% in CL and 9.41% in VD. **Conclusion:** Different dose regimens were tested, the dosing based on BSA was found to be more appropriate in children than the dosing per kg. Due to the existing variability, an association with therapeutic drug monitoring is considered more efficient.

123. Physician readiness to collaborate with community pharmacists on drug therapy management.Nedžad Pojskic¹, Linda MacKeigan¹, Heather Boon¹, Curtis Breslin², and Philip Ellison³¹Department of Pharmaceutical Sciences, Leslie Dan Faculty of Pharmacy, University of Toronto, ²Institute for Work and Health and Department of Public Health Sciences, University of Toronto, ³University Health Network and Faculty of Medicine, University of Toronto, Toronto, ON, Canada

Introduction: With the increasing importance of drugs in patients' therapy and their rising costs, health policy makers are focusing attention on strategies to enhance the safety and effectiveness of drug prescribing and use. Close pharmacist-physician collaboration has been shown to increase the safety and cost-effectiveness of drug therapy, however, it occurs relatively infrequently in the community setting, with respect to drug therapy management. The main **goals** of this study were to assess Ontario family physicians' readiness to collaborate with community pharmacists on drug therapy management, as well as to identify predictors of physicians' readiness to collaborate. **Methods:** A 22-item survey instrument was developed based on information from two qualitative studies conducted in Ontario and the Transtheoretical Model of Behaviour Change. The questionnaire enquired about 3 types of physician-pharmacist interactions on a collaborative continuum. The survey was distributed to a stratified random sample of 842 family physicians across Ontario, with physicians stratified based on urban or rural practice location. **Results:** The survey response rate was 36.8%. Most respondents were male (65.5%), practiced in urban locations (83.2%) and non-interdisciplinary settings (75.5%), and had no academic affiliation (70.9%). Preliminary results indicated that 84.2% of respondents regularly take community pharmacists' phone calls, pertaining to drug therapy management, while 77.8% sometimes seek pharmacists' recommendations regarding their patients' drug therapy. Only 28.8% of physicians, however, refer their patients to community pharmacists for medication reviews, with 45.4% unaware such a service exists. Respondents perceived more accurate medication lists as the primary advantage of collaborating with pharmacists, and pharmacists' lack of patient information as the primary disadvantage. **Conclusion:** Overall, Ontario physicians were more engaged in lower level collaborative behaviours, than higher level collaborative behaviours, regarding drug therapy management.

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124. Facteurs influençant la prestation des soins pharmaceutiques visant la maîtrise de l'asthme par le pharmacien communautaire : Étude PRO-RESPIR.

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pharmaceutique AstraZeneca en santé respiratoire, Montréal, Québec.

Objectifs : Identifier les facteurs organisationnels, professionnels et relationnels influençant la prestation de soins pharmaceutiques (SP) par le pharmacien communautaire afin d'optimiser la maîtrise de l'asthme et décrire les interventions habituellement prodiguées aux patients asthmatiques. **Méthodologie :** En novembre 2006, un questionnaire pré-testé et un rappel ont été envoyés par la poste aux 4587 pharmaciens communautaires du Québec inscrits sur le tableau de l'Ordre des Pharmaciens du Québec avant le 1er janvier 2006 et travaillant au moins 15 heures/semaine. Le questionnaire comprenait 35 questions ouvertes et fermées (échelle de Likert 1 à 4) portant sur les interventions (21), sur les facteurs organisationnels, professionnels et relationnels (14) et sur les caractéristiques socio-démographiques (17). Pour les questions fermées, la proportion (intervalle de confiance à 95% ou IC95%) des réponses rapportées a été calculée. **Résultats :** Parmi les 917 questionnaires retournés (taux de réponse de 20.1%), 877 répondaient aux critères d'admissibilité. 33.9%;IC95%:30.8% à 37.1% des pharmaciens rapportent que le manque de temps restreint leur prestation des SP, alors que près de 20%;IC95%:17.4% à 23.6% des pharmaciens disent que le support des autres pharmaciens et l'intérêt des patients vis-à-vis leur condition médicale les incitent à prodiguer plus de soins. Les 3 interventions les plus souvent prodiguées consistent à donner de l'information verbale sur la nouvelle médication (97.7%;IC95%:96.6% à 98.6%), à enseigner la technique d'inhalation (96.6%;IC95%:95.2% à 97.7%) et à vérifier la sur-utilisation des bronchodilatateurs à courte durée d'action (91%;IC95%:89.0% à 92.8%) tandis que le suivi du journal de bord est la moins fréquente (0.6%;IC95%:0.07% à 1.1%). **Conclusion :** Bien que la majorité des pharmaciens communautaires interviennent principalement au moment d'une nouvelle ordonnance dans le but d'optimiser la maîtrise de l'asthme, il semble que l'organisation du travail restreint la prestation de SP.

134. Early systemic exposure to inhaled milrinone in cardiac patients.

Anne QN Nguyen BSc¹, Dr. André Denault MD², Dr. Yves Théorêt BPharm PhD³,

Dr France Varin BPharm PhD.¹,

¹Faculté de pharmacie de l'UdeM, ²Département d'anesthésiologie de l'ICM, ³Département de pharmacologie de l'UdeM et Département de biochimie du CHU Ste-Justine.

Background: Milrinone is a vasoactive drug administered intravenously or through inhalation to patients undergoing cardiac surgery under cardiopulmonary bypass (CPB) for the treatment and prevention of pulmonary hypertension (PHT) associated with difficult separation from bypass (DSB)(1,2). Targeted steady-state concentrations during intravenous administration are considered to be 100-300 ng/ml. However, when given intravenously milrinone is associated with a high occurrence of systemic hypotension while this is not the case after inhalation. The blood concentrations of milrinone administered through inhalation have never been measured but the absence of hypotension could be secondary to lower systemic concentrations. Our **objective** was to confirm that the safer profile of inhaled milrinone could be secondary to lower systemic exposure. **Method:** A pilot observational study was carried out in patients scheduled for elective cardiac surgery requiring CPB and admitted at the Montreal Heart Institute. Patients with preoperative PHT and for whom administration of inhaled milrinone was indicated were enrolled. Milrinone (5 mg) was administered before CPB (Pre-CPB) by nebulization (conventional or ultrasonic) over 15 min. Arterial blood samples were obtained before starting inhalation (time zero), at 20, 25, 30 min thereafter, and immediately after CPB (Post-CPB). Milrinone concentrations were determined by HPLC with UV detection with a lower limit of quantification of 2.5 ng/ml. **Results:** In 2 out of 5 patients dosed so far, peak systemic levels of milrinone were 50 and 90 ng/ml. Arterial levels were undetectable in the other patients. **Discussion:** Because the first sample was drawn 5 min after stopping inhalation, peak concentrations could have been underestimated. However, these concentrations remain significantly below those measured after intravenous administration of milrinone. **Conclusion:** Our pilot study suggests that a negligible systemic availability may explain the higher therapeutic index of inhaled milrinone.

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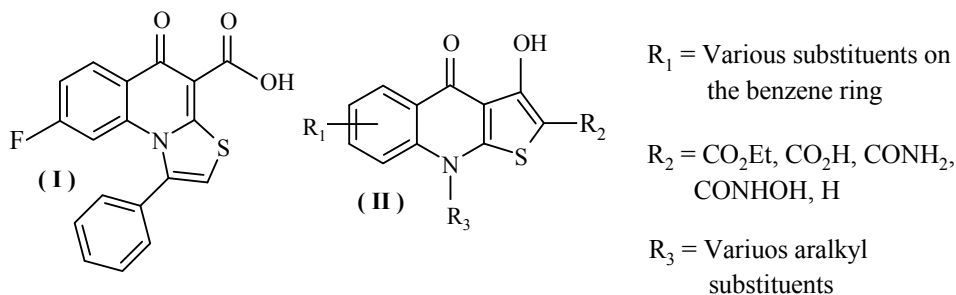
BASIC RESEARCH

125. Design, synthesis, and biological evaluation of thieno[2,3-*b*]quinolones as topoisomerase II inhibitors with potential antineoplastic activity

Ranjith Garlapati and Mohsen Daneshtalab

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Study Objectives: Based on the previously reported topo-II inhibitory and anticancer activity of 5-fluoro-3-phenyl-8-oxo-3a,8-dihydro-thiazolo[3,2-*a*]quinoline-9-carboxylic acid (**I**)¹ and application of structure-based molecular modeling approach, we designed and synthesized novel 2-substituted-3-hydroxy-9-aralkyls substituted-4,9-dihydrothieno[2,3-*b*]quinoline-4-one derivatives (**II**) in order to investigate the potential of these molecules as selective inhibitors of topoisomerase-II and antitumor agents.



Methods: Using Hyperchem-3TM program, the optimum geometry of **I** was determined through molecular mechanic optimization. Based on the above data, the linear analogue **II** ($R_1 = 7\text{-F}$; $R_2 = \text{H}$, and $R_3 = \text{CH}_2\text{Ph}$) was designed, which was perfectly overlapping with the optimized geometry of compound **I**. Based on this information, different derivatives of compound **II** were synthesized using appropriate synthetic approaches. **Results:** Preparation of compound **II** was achieved by either conventional synthesis of the relevant 2-mercaptoquinolone carboxylic acid followed by N-alkylation and cyclization, or through convergent synthesis starting with appropriate benzoylacetoacetate intermediate and further cyclization. During this process we were able to improve the synthetic feasibility of the final products via regioselective alkylation of quinolones using a modified Mitsunobu reaction. This process would help in further structural modifications using parallel syntheses approach with an appropriately substituted N_1 -aralkyl (or alkyl)-2-mercapto-1,4-dihydroquinolin-4-one-3-carboxylate as the building block. The synthesized compounds were preliminary evaluated for their toxicity against brine shrimps. Further biological evaluation of the synthesized compounds against KB and L-1210 cell lines, as well as topo-II inhibitory activity, is in progress to identify the compound with optimized activity profile (lead compound). **Conclusions:** Through this study, we were able to introduce novel synthetic methodologies for the preparation of linear thieno-quinolone derivatives with potential topo-II inhibitory and cytotoxic activities.

¹ Hosomi J, Asahina Y, Suzue S (1989). WO8912055. published, Dec 14, 1989

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126. EP80317, a ligand of CD36 receptor, protects against remote lung injury after hindlimb ischemia/reperfusion
Diala Harb¹, Leila Hamdan¹, Caroline Bélanger¹, Valérie L.Bessi¹, Marie-Christine Koutsing Tine¹, Huy Ong¹, Sylvie Marleau¹

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Introduction: Increased numbers/trafficking of primed/activated circulating leukocytes to remote organs is a cause of tissue injury associated with the reperfusion of ischemic limbs. The **aim** was to assess whether EP80317, a ligand of the CD36 scavenger receptor present on endothelial cells and circulating monocytes, may alter the course of the inflammatory response. **Methods:** ApoE^{-/-} mice or apoE apoE^{-/-}/CD36^{-/-} mice were treated daily with a s.c. injection of EP80317 or saline for 14 days. Hindlimb ischemia was induced for 30 minutes followed by 180 minutes reperfusion. Lung samples were collected for measurement of leukocyte accumulation (myeloperoxidase assay). Blood samples were harvested to assess luminol-induced blood chemiluminescence (opsonized zymosan-elicited generation of reactive oxygen species). **Results:** As compared to mice on normal diet (ND), mice fed a high fat diet (HFHCD) showed a significant increase of 177% of leukocyte accumulation into lungs (1.3 ± 0.3 to $3.6 \pm 0.7 \times 10^7$ leukocytes/g lung). In mice fed ND, EP80317 did not modulate leukocyte trafficking to the lungs (1.3 ± 0.3 in control mice and $1.3 \pm 0.2 \times 10^7$ leukocytes/g lung in EP80317-treated mice). In contrast, in mice fed a HFHCD, a condition further promoting increased circulating numbers of primed/activated leukocytes, EP80317 significantly reduced leukocyte accumulation by 56% in the lungs (3.6 ± 0.7 in control mice to $1.6 \pm 0.6 \times 10^7$ leukocytes/g lung in EP80317-treated mice). This was associated with 56% reduction of ROS release in whole blood. Neither blood chemiluminescence nor leukocyte accumulation in the lungs was significantly modulated in apoE^{-/-}/CD36^{-/-} mice (1.9 ± 0.5 in control mice to $1.9 \pm 0.8 \times 10^7$ leukocytes/g lung in EP80317-treated mice). **Conclusion:** EP80317 protects from ischemia/reperfusion-elicited remote lung injury in hypercholesterolemic mice. This effect appears to be mediated through a CD36 pathway. These results suggest a potentially beneficial role for selective CD36 ligands in hindlimb ischemia-reperfusion injury associated with other cardiovascular risk factors such as hypercholesterolemia.

127. Induction and inhibition of cytochrome P450 and phase II enzymes by the flaxseed plant lignans secoisolariciresinol and secoisolariciresinol diglucoside

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Flaxseed contains the highest levels of the plant lignan Secoisolariciresinol Diglucoside (SDG) a precursor of Secoisolariciresinol (SECO). Flaxseed and the plant lignans have beneficial effects on cardiovascular disease, cancer and diabetes. Induction and inhibition of metabolic enzyme activity must be investigated to determine the safety of lignan use. **Purpose:** To assess the induction and inhibition of phase I and phase II enzymes by SECO and SDG. **Methods:** **Induction Studies:** Male Sprague-Dawley primary rat hepatocytes, purchased from Cellz Direct (pooled n=2) or isolated with a modified two-step collagenase procedure, were incubated with 0, 1, 10 or 100 μ M SECO for 24 hours. Cells were harvested and RNA isolated and purified with QIAGEN RNeasy Mini kits. Induction of CYP2C11, 2B1, 1A1, 1A2, 3A1 and 3A2, GSTA2 and A5 and UGT2B1 was assessed with real time RT-PCR. **Methods:** **Inhibition Studies:** Male, Sprague-Dawley, 12 week, rat liver microsomes were prepared and pooled (n=4). The inhibition of CYP3A, 2B and 2C11 was measured by testosterone metabolism to 6 β -, 16 α - and 2 α -OH testosterone with a gradient HPLC system (UV detection at 240nm). For irreversible inhibition, hepatic microsomes were pre-incubated with various concentrations (0-2000 μ M) SECO or SDG for 0, 5, 10 or 20 minutes prior to the addition of testosterone (250 μ M). For reversible inhibition, hepatic microsomes were incubated with SECO and SDG (0-2000 μ M) concurrently with testosterone (25-250 μ M). **Results:** Rat primary hepatocytes have been successfully isolated and cultured. Primers for all gene targets have been optimized for real-time RT-PCR. Inhibition was not observed with SDG at any concentration. For SECO, a concentration dependent decrease in 6 β -OH testosterone formation indicated inhibition of CYP3A with an approximate IC₅₀ of 300 μ M. A concentration dependent increase in 16 α -OH testosterone without an effect on 2 α -OH testosterone formation indicated an increase in CYP2B activity. Secoisolariciresinol alters CYP enzyme activity *in vitro*.

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128. P-glycoprotein and HERG closely interact in cardiac ventricular myocytes.

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Faculty of Pharmacy, Université de Montréal

Aims: The drug transporters present in cardiac tissues are key determinants of drug concentrations in the heart and therefore, of cardiac drug action. The rapid component of the delayed rectifier cardiac potassium current (I_{Kr} ; HERG) represents a major target for drugs associated with drug-induced Long QT syndrome (LQTS). Binding to HERG is intracellular and several drugs associated with HERG block have also shown affinity for the ATP-binding cassette efflux membrane transporter P-glycoprotein (P-gp). **Methods:** Extraction of membranes protein, co-immunoprecipitation, immunohistochemistry study. The presence of P-gp and HERG was demonstrated in membrane protein extracts from human hearts; Protein extracts were then exposed to non-selective IgG antibodies and to anti-P-gp antibodies where P-gp could be detected after 24 and 4 hours of exposure. Membrane protein extracts from human and guinea pigs hearts were separated by 8% SDS-PAGE and then transferred to nitrocellulose filters (Amersham-Biosciences). Western blotting then separated co-immunoprecipitated proteins. The localization of HERG and P-Gp was revealed by immunochemistry and confocal microscopy following appropriate treatment of a slice of human cardiac ventricular tissue. The co-localization of the two proteins was revealed by simultaneous exposure to wavelengths for both P-gp and HERG antibodies. **Results:** We demonstrated the presence of HERG and P-gp in human heart. In addition, using co-immunoprecipitation procedures, we demonstrated a close relationship between HERG and P-gp. Using immunohistochemistry procedure, we demonstrated the colocalisation of these two proteins. **Conclusion:** We demonstrated in our study, for the first time a tight physical interaction between a cardiac potassium channel protein (HERG) and a membrane drug efflux transporter (P-gp) in human and guinea pig cardiac ventricular myocytes. The close relationship between these two proteins provides new information for our better understanding of mechanisms underlying the drug-induced Long QT syndrome (LQTS). This syndrome has been associated with major cardiac side effects in patients including deaths and has forced removal from the market of otherwise very efficacious drugs.

°This work was supported by Genome Quebec – Genome Canada

129. The QRFP peptides modulate adipogenic genes in differentiated 3T3-L1 cells.

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A novel neuropeptide of 43 aa belonging to the QRFP (RF amide peptide) family, and its constitutive part, QRFP-26, have been recently identified as endogenous ligands of the orphan G-coupled receptor GPR103. Two receptor subtypes 103A and B were identified, and were found to be mainly expressed in the hypothalamus regions involved in the regulation of appetite. Chronic intracerebroventricular injections of these peptides in mice were shown to induce hyperphagia and to increase body weight and fat mass. However, whether the adipogenic effect of QRFP results from a direct effect on peripheral adipose tissue or occurs secondary to alteration of vagal activity has yet to be determined. **Objectives:** 1) To document the effect of QRFP on the expression of genes involved in the differentiation of 3T3-L1 cells towards an adipocyte phenotype 2). To characterize the receptor mediating the adipogenic effect of QRFP in differentiated 3T3-L1 adipocytes. **Methods:** The effect of QRFP-43 and -26 on 3T3-L1 cell differentiation was quantified by measuring the optical density (510 nm) following QRFP-elicited oil red O (ORO) uptake by 3T3-L1 cells. Lipolysis was assessed by quantifying glycerol in the medium after 90 minutes of treatment on 3T3-L1 differentiated cells. **Results:** Four-day treatment with QRFP-43 and -26 increased ORO uptake by 50% and 42%, ($p < 0.001$) respectively compared to control (10% FBS). In parallel, both peptides inhibited isoproterenol-induced lipolysis in a dose-dependent manner in differentiated adipocytes with IC50s of 2.2 and 1.1 nM, respectively. GPR103B mRNA was found to be specifically expressed in 3T3-L1-differentiated adipocytes, and its expression was upregulated during differentiation together with that of adipocyte differentiation markers including PPAR- γ 2 and perilipin. **Conclusion:** These results suggest that QRFP peptides induce adipogenesis through the activation of GPR103B and may play a key role in energy homeostasis by a direct action on adipose tissue.

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130. Synthesis of 2-deoxy-2-fluorosugars for use as glycosyltransferase enzyme probesStephanie S. Lucas¹, Shannon C. Timmons², and David L. Jakeman^{*1,2}¹College of Pharmacy, ²Department of Chemistry, Dalhousie University, Halifax, NS

Introduction and Objectives: Recent research has shown that the carbohydrate units attached to many natural products are essential for bioactivity. The natural product of interest in our laboratory is jadomycin B, an angucycline antibiotic produced by *Streptomyces venezuelae* ISP 5230 in response to environmental stress. In one of the final steps of the biosynthesis of jadomycin B the antibiotic is glycosylated by the JadS glycosyltransferase enzyme, which accepts β -L-digitoxose deoxythymidine diphosphate and the jadomycin B aglycone as its natural substrates (Figure 1). Synthesizing fluorosugar analogues and converting these derivatives into sugar nucleoside diphosphates will provide novel compounds that will be used to probe the substrate flexibility of the enzyme and potentially produce novel compounds for biological testing.

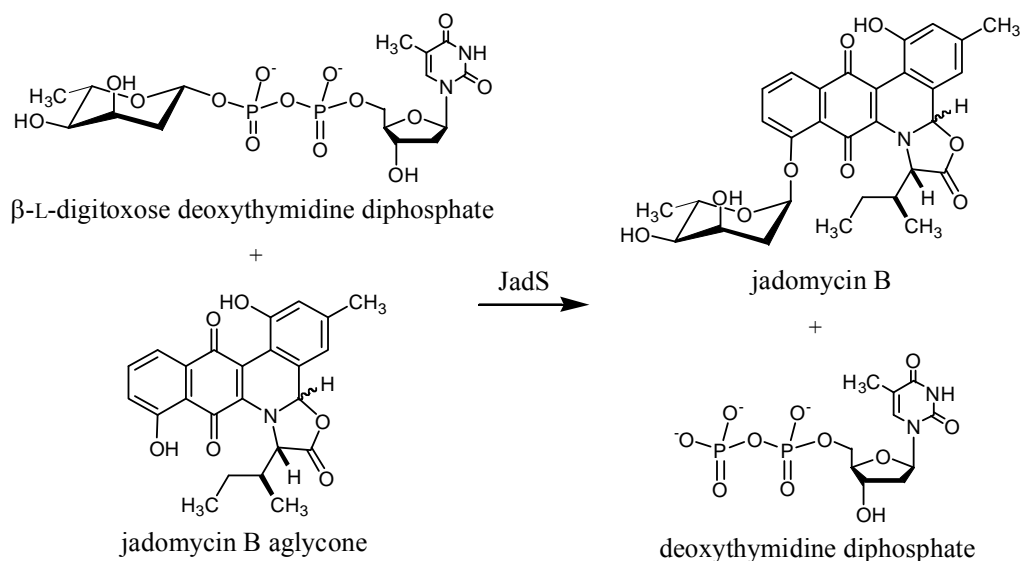


Figure 1: The enzymatic biosynthesis of jadomycin B

Methods: Fluorosugar analogues were synthesized by various multi-step routes in good yield. Compounds isolated in each synthetic step were purified by extraction and/or column chromatography. Purified compounds were characterized using nuclear magnetic resonance (NMR) spectroscopy. **Results:** Four fluorosugar analogues were prepared using novel synthetic routes: 1,3,4-tri-O-acetyl-2-deoxy-2-fluoro-L-fucose, 1,3,4-tri-O-acetyl-2-deoxy-2-fluoro-L-arabinose, 1,3,4-tri-O-acetyl-2-deoxy-2-epifluoro-L-rhamnose and 1,3,4-tri-O-acetyl-2-deoxy-2-fluoro-L-rhamnose. The two fluorosugar analogues derived from L-rhamnose were used to synthesize sugar-1-phosphates, which will be coupled with activated nucleoside monophosphates to prepare sugar nucleotides. All compounds were characterized using NMR spectroscopy, which confirmed the structure and purity of the isolated products. **Conclusions:** Four 2-deoxy-2-fluorosugars were efficiently prepared *via* multi-step synthetic pathways. These sugars will be converted to sugar nucleoside diphosphates and used to probe the substrate specificity of the JadS glycosyltransferase enzyme and potentially produce novel compounds for biological testing. **Acknowledgements:** Funding was provided by the Dalhousie Pharmacy Endowment Fund.

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131. Effect of polyethylene oxide (PEO) content and drug solubility on polymer swelling and drug dissolution*Robert Hardy, Hongtao Li, Xiaochen Gu*Faculty of Pharmacy, University of Manitoba, Winnipeg, Manitoba R3T 2N2

Purpose: To investigate the effect of PEO content and drug solubility on polymer swelling and drug dissolution from a series of modified release matrix tablets. **Methods:** Nine different formulations of modified release PEO matrix tablets were prepared by direct tableting compression. Acetaminophen (AMP), ibuprofen (IBU) and pseudoephedrine (PSE) were used as model compounds in the preparations for their varying aqueous solubility. Thickness of hydrogel layer formed by PEO during dissolution was measured using a texture analyzer. Tablet dissolution was carried out using a USP II Apparatus. Relationships among hydrogel thickness, PEO ratio, drug solubility and dissolution were correlated and interpreted. **Results:** Hydrogel formation and drug dissolution were directly influenced by drug solubility and PEO content in the formulations. Lower drug solubility resulted in smaller polymer hydration due to slower water penetration; higher PEO content allowed for greater hydrogel formation. Thickness of PEO hydrogel at 30 and 360 minutes ranged 1.82-2.01/6.34-6.76 mm for PSE, 1.67-1.78/5.73-6.25 mm for IBU and 1.23-1.44/3.61-4.63 mm for AMP, respectively. The time required for 50% of drug release ($DT_{50\%}$) from the tablets were 83-92 minutes for PSE, 323-354 minutes for IBU and >6 hours for AMP, respectively. The diffusional release exponents were 0.492-0.498 for PSE, 0.674-0.698 for IBU and 0.746-0.802 for AMP, respectively, indicating a diffusion-controlled release mechanism for both PSE and IBU tablets but an erosion-controlled release mechanism for AMP tablets. **Conclusion:** Drug solubility and PEO content in the modified release matrix tablets directly influenced the hydration of PEO polymer and diffusion and dissolution of drug from the preparations. The study also demonstrated the applicability of a texture analyzer in designing tablet formulation and characterizing drug dissolution.

132. Electrical remodeling in a transgenic mouse model of cardiac-specific overexpression of type 1 angiotensin II receptor*Katy Rivard, Pierre Paradis, Mona Nemer and Céline Fiset*University of Montreal.

Background Cardiac-specific overexpression of the human type 1 angiotensin II receptor (AT1R) in mice leads to ventricular hypertrophy and heart failure. Moreover, AT1R mice die prematurely of sudden cardiac death suggesting that in pathological condition angiotensin II could be responsible of severe arrhythmias leading to sudden death. Accordingly, the objective of this study was to characterize cardiac repolarization in AT1R mice to establish whether there is a relationship between angiotensin II, delayed repolarization and cardiac arrhythmias. **Methods and Results** To achieve this objective we combined electrophysiology and molecular biology techniques. We first observed that compared to aged-matched littermate controls (CTL), 6-8 month old AT1R male mice present spontaneous ventricular arrhythmias, longer QTc interval (CTL: 53.6 ± 1.5 ms, AT1R: 64.2 ± 1.4 ms, $p = 0.0005$) and prolonged action potential duration (at 90% repolarization, CTL: 19.0 ± 1.8 ms; AT1R: 39.1 ± 4.7 ms, $p = 0.0001$). We then studied the K^+ currents in ventricular myocytes and their underlying K^+ channels. These currents (channels) include (1) the Ca^{2+} -independent transient outward, I_{to} (Kv4.2/Kv4.3), (2) the ultrarapid delayed rectifier, I_{Kur} (Kv1.5), (3) the steady-state outward, I_{ss} (Kv2.1) and (4) the inward rectifier, I_{K1} (Kir2.1). Our results revealed a significant reduction of I_{to} , I_{Kur} and I_{K1} in cardiac myocytes isolated from AT1R mice and Western Blot analysis showed a corresponding reduction of protein expression for Kv4.2, Kv1.5 and Kir2.1. To ascertain that the repolarization defects seen in AT1R were not secondary to cardiac hypertrophy and failure, we characterized ventricular repolarization in younger (50 days) AT1R mice confirming that the delayed repolarization seen in AT1R mice did not occur as a consequence of cardiac remodeling. **Conclusion** Altogether, these results indicate that chronic stimulation of type 1 angiotensin II receptor is responsible for the delayed ventricular repolarization phenotype observed in AT1R mice and for the increase incidence of cardiac arrhythmias and sudden death observed in AT1R mice.

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133. The effect of metoprolol on energy metabolism in the diabetic heart.*Pavan Dhillon¹, Vijay Sharma¹, Michael Allard², and John H. McNeill¹.*¹ Faculty of Pharmaceutical Sciences, University of British Columbia. ² James Hogg iCapture Center, St. Paul's Hospital, Vancouver, Canada.

Background: Diabetic myocytes are unable to use glucose as an energy source forcing them to rely on free fatty acids (FFA). This shift in substrate utilization has been associated with lipotoxic oxidative stress, which may lead to cardiomyopathy. We have previously shown that the β -blocker metoprolol inhibits carnitine palmitoyltransferase 1 (CPT-1), a major control step of fatty acid oxidation. Furthermore, it also decreases the sensitivity of CPT-1 to its major inhibitor, malonyl CoA (MCoA). The heart expresses two CPT-1 isoforms, CPT-1Muscle (CPT-1M) and CPT-1Liver (CPT-1L); CPT-1L is less sensitive to MCoA inhibition than CPT-1M. We therefore hypothesized that metoprolol decreases the expression of CPT-1 and induces an isoform shift from CPT-1M to CPT-1 L. **Objective:** To determine whether chronic metoprolol treatment decreases the expression of CPT-1 and induces an isoform shift from CPT-1M to CPT-1L. **Methods:** Male Wistar rats were randomly assigned to one of four groups: control, control treated, diabetic and diabetic treated. Diabetes was induced by injection of 60 mg/kg streptozotocin into the tail vein. Treated groups received 75 mg/ kg/ day metoprolol by intraperitoneal injection. Six weeks after the induction of diabetes, the rats were euthanized and the hearts excised, flash frozen in liquid nitrogen and stored at -70°C until the day of assay. On the day of assay, the heart tissue was homogenized and subjected to SDS-PAGE and Western Blotting to probe for CPT-1 total expression, CPT-1M and CPT-1L. **Results:** The total expression of CPT-1 was decreased by metoprolol. The expression of CPT-1M was decreased by metoprolol, but CPT-1L was detected only at low levels and its expression was not altered by metoprolol. **Conclusions:** The decrease in CPT-1 activity produced by metoprolol may be partially explained by a decrease in CPT-1M expression. However, the decrease in the sensitivity in CPT-1 to malonyl CoA cannot be explained on the basis of an isoform shift.

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135. Design, synthesis, biological evaluation and determination of the mechanism of action of new anticancer agents: the arylchloroethylurea-combretastatin hybridsSébastien Fortin^{1,2}, Emmanuel Moreau³, Jean-Claude Teulade³, René C.-Gaudreault²¹Faculté de pharmacie, Université Laval, Québec, ²Centre de recherche, CHUQ, Hôpital Saint-François d'Assise, Québec,³Université Clermont1, laboratoire de Chimie Organique, Clermont-Ferrand, France

Introduction: Arylchloroethylureas (CEU) are a new class of soft alkylating agents that inhibit cell division through their irreversible binding to the colchicine-binding site on tubulin. Recently, combretastatin-A4 (CA-4), a newer and simpler antitubulin molecule was found to bind also to the colchicine-binding site. In the course of our research program, we have evaluated the chemical interactions occurring between CEU and CA-4, and the colchicine-binding site using molecular modeling tools. Our studies revealed important structural similarities between CEU, CA-4 and other antimitotic agents.

Objectives and methods: In the aim to increase the inhibition activity and the selectivity of our CEU for the colchicine-binding site we have used those structural similarities to design and prepare a new series of CEU that are "hybrids" of the molecular structures of CEU and CA-4. Conventional organic reactions such as Wittig addition, hydrogenation and reduction were used to synthesize the new derivatives and bioisosteres. Cytotoxicity was evaluated on four tumor cell lines. Effect of the drugs was assessed using flow cytometry experiments. The specificity and the irreversible binding of the drugs toward the colchicine-binding site were evaluated by SDS-PAGE and western analysis. **Results:** CEU-CA-4 hybrids showed that they inhibit tumor cell proliferation at the micro molar level on the four tumor cell lines tested. Flow cytometry experiments evidenced the arrest of the cell division in the G₂/M phase. In addition, competition essays confirmed that the new compounds are still irreversibly binding to the colchicine-binding site. **Conclusion:** The new pharmacophoric moiety of CEU-CA-4 hybrids might be an alternative of the trimethoxyl group present in all the typical colchicine-binding site inhibitors. The antineoplastic activity and the biopharmaceutical properties of these new CEU will soon be evaluated on animal models and compared with the CA-4.

136. Outward K⁺ current is decreased in ventricular myocytes isolated from adult mice with elevated levels of serum TNF α

Scott A. Grandy, Marie-Andrée Lupien and Céline Fiset

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Background: Previous studies have shown repolarizing currents are altered in isolated cardiomyocytes treated with tumor necrosis factor alpha (TNF α). Repolarization also is altered in cardiac tissue that overexpresses TNF α . However, the effect(s) of serum TNF α on the K⁺ currents that underlie cardiac repolarization are not clear. **Objective:** The purpose of this study was to determine the effects of elevated levels of serum TNF α on cardiac repolarization. **Methods and Results:** C3H mice were treated with TNF α (200 ng) biweekly for 6 weeks. Serum TNF α levels were 27.4 \pm 6.5 pg/ml in TNF α treated mice compared to 9.0 \pm 5.6 pg/ml in control mice. Mice were then sacrificed and ventricular myocytes were isolated for voltage-clamp experiments. Patch-clamp techniques were used to investigate K⁺ currents. The results showed that total K⁺ current (I_{peak}) was significantly reduced in myocytes isolated from the hearts of TNF α treated mice compared to myocytes from control (CTL) mice (at +40 mV: CTL 101.1 \pm 5.6 pA/pF; TNF 78.3 \pm 5.0 pA/pF). Examination of the underlying components of outward K⁺ current revealed that the Ca²⁺-independent (I_{to}) and the ultrarapid delayed rectifier (I_{Kur}) K⁺ currents were significantly reduced in ventricular myocytes from TNF α treated animals (I_{to} at +40 mV: CTL 56.0 \pm 4.3 pA/pF; TNF 39.9 \pm 3.9 pA/pF; I_{Kur} at +40: CTL 36.3 \pm 4.2; TNF 22.9 \pm 3.9). In contrast, the steady-state K⁺ current (I_{ss}) and the inward K⁺ current (I_{K1}) were comparable in both groups. To determine if TNF α had a direct effect on outward K⁺ current, myocytes isolated from control animals were superfused with TNF α (100 ng) for 10 minutes. The results showed that acute exposure to TNF α had no effect on outward K⁺ current. **Conclusion:** This study shows that elevated levels of serum TNF α can alter ionic currents, but that TNF α does not directly modulate K⁺ currents in mouse ventricular myocytes.

The data in this abstract was previously presented at the 51st annual meeting of the Biophysical Society (presentation date: March 6, 2007).

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137. Influence of short and long-term exposure to tamoxifen on cardiac repolarization in mice.

Gracia El Gebeily and Céline Fiset

Faculté de pharmacie, Université de Montréal.

Tamoxifen (Tam) is a selective estrogen receptor modulator that has both agonist and antagonist activities depending on the molecular profile of its target. Tam is the most widely used in the treatment and prevention of breast cancer from more than 20 years. Experimental studies have reported that acute exposure to Tam or to its active metabolite the 4-hydroxytamoxifen (4 OH-Tam) could reduce cardiac ionic currents. However, despite widespread clinical use, TAM is not associated with a prolongation of the QT interval and a development of ventricular arrhythmias. In order to verify if the treatment duration of Tam could explain these contradictory results, the **objective** of this study was to compare the acute and chronic effects of 4 OH-Tam on K^+ currents in mouse female ventricular myocytes. These currents include the transient outward (I_{to}), the ultrarapid delayed rectifier (I_{Kur}), the steady state (I_{ss}) and the inwardly rectifying (I_{K1}) K^+ currents. **Methods:** First assessed was the acute exposure to 4 OH-Tam on these currents. Using whole-cell voltage-clamp technique, K^+ currents were recorded before and after perfusion of the cells with 4 OH-Tam applied at different therapeutic concentrations. Results indicated that 4 OH-Tam significantly decreased the density of I_{to} , I_{Kur} , I_{K1} whereas I_{ss} was unaffected. Then, it was determined whether a long term exposure to Tam also affected the density of these K^+ currents. To reproduce similar hormonal environment as the one observed in postmenopausal women receiving Tam, ovariectomized (OVX) mice were used. These animals were treated with placebo or Tam pellets. **Results:** The density of I_{to} , I_{Kur} , I_{K1} and I_{ss} were significantly increased in the ventricular myocytes of the Tam treated OVX mice compared to the OVX mice. **Conclusion:** These results suggest that while blocking the estrogen receptors, TAM would remove the inhibitory effect of estrogen on K^+ currents. This would explain the increase of K^+ currents observed in this study as well as the absence of harmful effect of TAM on QT interval and cardiac rhythm defects with chronic Tam treatment.

138. Dendritic Cell Targeted Nanovaccine Formulations

Welson Wen-Shang Wang, Dipankar Das and Mavanur R. Suresh.

Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta, Edmonton, AB

Purpose: Our lab has designed a dendritic cells (DC) targeting vector for delivering low dose vaccines. The *in vivo* study of targeting antigens to DC stems from our hypothesis that efficient targeting of the antigen to the desired cell population enhances the immune response. A universal DC targeting vehicle such as the bifunctional fusion protein (bfFp) that can bind to a mixture of biotinylated antigens may be useful to induce polyvalent immune responses. **Methods:** scFv in V_L - V_H orientation that recognizes the DEC-205 receptor of DC was fused to core-streptavidin and expressed in *E.coli* using T7 expression system. ELISA and Western blot were performed using different secondary reagents to demonstrate the bifunctional activity employing DC to show the anti-DEC-205 activity and biotinylated OVA or biotinylated BSA to confirm anti-biotin activity. *In vivo* immune response studies in mice with biotinylated OVA, Ebola virus GP1, SARS Spike RBD, MUC-1 cancer peptide, Anthrax RBD, GM3, GM2, and WEE structural DNA were performed. **Results:** Construction, cloning, expression and purification of the bfFp in *E.coli* using T7 expression system was successful. In step purification using IMAC, we were able to obtain pure monomeric fusion protein. Both ELISA and Western blot results have shown the bifunctional activity of the fusion protein. *In vivo* studies in mice with biotinylated OVA has shown that in the presence of bfFp and anti-CD40 mAb, both humoral and cell-mediated responses can be augmented. In this targeting formulation, low concentration of antigen (200 ng) in saline is adequate to achieve a strong immune response in mice. In the multiple antigens targeting strategy, we also achieved humoral and cell-mediated responses for SARS Spike RBD, MUC-1, Anthrax RBD, GM3, GM2 and WEE E1, E2. **Conclusions:** In the absence of traditional adjuvants and *ex vivo* stimulation of DC, bfFp targeting of biotinylated antigens to DC could be a convenient method to deliver multiple antigens to DC. Such nanovaccine formulations can induce immune responses towards peptide, protein, glycoprotein, hapten and DNA encoding structural protein (DNA vaccine).

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Introduction: Although it has been clearly proven that controlled blood pressure decreases cardiovascular morbidity and mortality, a high proportion of hypertensive patients do not have adequate blood pressure control. This may result from poor adherence to therapy. The consequences of non-adherence on the real-life efficacy of drugs need more studies. **Objective:** To evaluate the impact of antihypertensive agents' adherence level on the rate of non fatal strokes. **Methods:** A cohort of 31,905 patients was reconstructed using the RAMQ databases. All patients aged from 45 to 75 years old who were newly treated with antihypertensive agents between 1999 and 2000 were eligible. A nested case-control design was conducted. Every case of non fatal stroke was matched for age and period with 15 controls. Adherence level was reported as the percentage of the prescribed doses of antihypertensive agents used during follow-up period, and was classified as $\geq 80\%$ or $< 80\%$. Conditional logistic regression models were used to estimate the rate ratio (RR) of non-fatal strokes adjusting for several covariables. **Results:** The overall rate of non-fatal strokes was at 3.8%. Among patients followed for more than one year, those with adherence level of $\geq 80\%$ had less non-fatal stroke (RR: 0.84; 0.71-0.98). The fact of being male (RR: 1.41; 1.22-1.64), welfare recipients (RR: 1.44; 1.11-1.88) or having higher chronic disease score (RR: 2.39; 2.02-2.82) increased significantly the risk of non-fatal stroke. **Conclusion:** Our analysis shows that adherence to therapy of $\geq 80\%$ for more than one year is essential to reduce non-fatal strokes among patients in primary prevention. These results confirm the importance of a long term therapy with antihypertensive agents.

141. Association between antidepressant use during pregnancy and infants born small for gestational age.*Ramos Elodie*^{1,2}, *Driss Oraichi*², *Anick Bérard*^{1,2}¹Faculty of Pharmacy, University of Montreal, Montreal, Quebec, Canada; ²Research Centre, CHU Sainte-Justine, Montreal, Quebec, Canada

Background: Studies have suggested a possible association between antidepressant use during pregnancy, low birth weight, and prematurity. Outcome measures combining birth weight and age e.g. 'Small for Gestational Age' (SGA) have rarely been investigated. **Objective:** To determine the association between class of antidepressant and the risk of infants being born SGA, according to trimester of exposure. **Methods:** A 'Medication and Pregnancy' registry, built by linking three databases (RAMQ, Med-Écho, ISQ) and data from a questionnaire was used. Eligible women had 1) to be 15-45 years of age at the beginning of pregnancy, 2) be insured by the RAMQ drug plan for ≥ 12 months prior to the first gestational day and during pregnancy, 3) have ≥ 1 diagnosis of psychiatric disorder before pregnancy, 4) have used antidepressants for ≥ 30 days in the year prior to pregnancy, and 5) have a pregnancy ending with a live singleton birth. Cases were defined as newborns with birth weight $\leq 10^{\text{th}}$ percentile for that gestational age. Relative risks were estimated using modified Poisson regression. **Results:** Among the 3061 pregnancies meeting inclusion criteria, 419 (13.7%) infants were born SGA. New antidepressants used during the second trimester such as SNRIs were associated with SGA at birth (new antidepressants vs. none: aRR 1.88, 95% CI 1.05, 3.34). However, SSRIs and tricyclics were not associated with an increased risk of infants being born SGA. **Conclusion:** These data suggest that the use of new antidepressants during the second trimester of pregnancy is associated with an increased risk of infants being born SGA.

142. Are controlled asthmatic pregnant women more at risk of prenatal outcomes than non-asthmatic women?*Faranak Firoozi*¹, *Francine M Ducharme*², *Catherine Lemi re*³, *Marie-France Beauchesne*^{1, 3}, *Anick B rard*¹, *Am lie Forget*³, *Lucie Blais*^{1,3}¹UdeM, Qc, ²Children hospital, Qc, ³Sacr -C ur hospital, Qc

Background: It is reported that the risk of adverse infant outcomes, such as preterm birth, low birth weight and small for gestational age (SGA) does not seem to differ significantly between optimally treated asthmatic women and women without asthma. However, the scientific evidence related to this topic is scarce. **Methods:** A large population-based cohort of pregnant asthmatic and non asthmatic women was reconstructed by linking three administrative databases of the Canadian province of Quebec, between 1990 and 2002. Asthma during pregnancy was considered controlled if a woman did not have any short-course of oral corticosteroids, hospitalisation or ED visit for asthma, and had low dose of inhaled short-acting beta₂-agonists (SABA). Outcomes under study were SGA defined as a birth weight below the 10th percentile for gestational age, using new Canadian standards, preterm birth (< 37 weeks of gestation) and low birth weight (LBW: < 2500 g). Logistic regression models were used to obtain odds ratios adjusted for several potential confounders related to asthma, pregnancy and maternal chronic diseases. **Results:** The cohort included 40893 pregnancies from asthmatic and non-asthmatic women. 13040 pregnancies were from asthmatic women and 35.9% of them had uncontrolled asthma. The risk of adverse infant outcomes was found to be significantly higher in controlled asthmatic women than in non-asthmatic women: SGA (adjusted odds ratio (aOR) = 1.29; 95% CI: 1.21-1.38), preterm birth (aOR = 1.56; 95% CI: 1.45-1.69), and LBW (aOR=1.59; 95% CI: 1.47-1.73). Moreover, women with uncontrolled asthma were found to be more likely to have a SGA baby than women with controlled asthma (aOR=1.17; 95% CI: 1.07-1.27). **Conclusions:** Women with controlled asthma may have minimal symptoms but still are potentially more at risk to deliver SGA, premature or low birth weight babies. Asthma in itself appears to be risky for the fetus, but asthma control should be attained since uncontrolled asthma can even further increase the risk.

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143. Impact of non-adherence to bisphosphonates on the incidence of osteoporotic fractures : a nested case-control studyJulie Blouin¹, Alice Dragomir¹, Yola Moride¹, Louis-Georges Ste-Marie², Julio C Fernandes³, Sylvie Perreault¹¹Faculty of Pharmacy, University of Montreal; ²Centre de Recherche du CHUM, Montreal; ³Orthopaedic Research Laboratory, Sacre-Coeur Hospital, Montreal

Background: Suboptimal adherence to bisphosphonates (alendronate and risedronate) has been reported in many observational studies. We aimed to evaluate the association between non-adherence to bisphosphonates and the risk of osteoporotic fracture among postmenopausal women. **Methods:** We conducted a nested case-control study using the RAMQ databases. The cohort consisted of 49 755 women ≥ 68 yr old who started alendronate or risedronate between January 1998 and June 2005. Cases included all women with an incident osteoporotic fracture (defined by ICD-9 or medical procedure code) after ≥ 6 months of therapy. Each case was matched with up to 10 controls using incidence density sampling, according to age and duration of follow-up. The index date was defined as the date of fracture for cases and the date of selection for controls. Adherence was calculated using medication possession ratio. A woman was non-adherent if she was exposed to therapy $< 80\%$ of time. Rate ratios (RR) for fractures were estimated through conditional logistic regression analysis, adjusting for potential confounders: prior osteoporotic fracture, diagnosis of osteoporosis, socioeconomic status, co-medications (glucocorticoids, anticonvulsants, narcotics, etc), and co-morbidities (rheumatoid arthritis, risk of fall, etc). **Results:** There were 3340 fracture cases, corresponding to an incidence rate of 3 fractures/100 person-years. Mean age was 78 yr. Median duration of follow-up was 1.5 yr. Among women followed ≤ 1 yr, compared to adherent, non-adherent women did not show a higher risk of fracture. For women followed > 1 year, the risk of total, nonvertebral (including hip) and hip fracture was statistically significantly increased in non-adherent women: RR 1.18 (95% confidence interval (CI), 1.08-1.29), RR 1.21 (95% CI, 1.10-1.32), and RR 1.28 (95% CI, 1.09-1.49), respectively. **Conclusion:** For a duration of therapy > 1 yr, postmenopausal women exposed to alendronate or risedronate $< 80\%$ of time have a higher risk of all types of osteoporotic fractures compared to those exposed $\geq 80\%$ of time.

144. Population-based study: statin adherence on non fatal stroke among patients for primary prevention.Laura Ellia¹, Alice Dragomir¹, MSc, Lucie Blais¹, PhD, Robert Côté², MD, FRCPC, Sylvie Perreault¹, PhD.¹Faculty of Pharmacy, Université de Montréal and ²Faculty of Medicine, McGill University, Montréal, Québec

Aim: Clinical trials have demonstrated that statins can reduce cerebrovascular disease among patients having hyperlipidemia. Observational studies reported that more than 50% of patients stop their therapy after 2 years, but no study has evaluated the impact of statin adherence on stroke for primary prevention. **Objective:** To evaluate the impact of statin adherence on the rate of stroke. **Methods:** A cohort of 29,926 patients was reconstructed using the RAMQ databases. All patients aged from 45 to 75 years old who were newly treated with statins between 1999 and 2000 were eligible. A nested case-control design was used to study non fatal stroke. Every case was matched for age and follow-up period with 15 controls. Adherence level was reported as the percentage of the prescribed doses of statin used during follow-up period, and was classified as $\geq 80\%$ or $< 80\%$. Conditional logistic regression models were used to estimate the rate ratio (RR) of non fatal stroke adjusting for covariables. **Results:** The rate of stroke was at 3.4%. Among patients followed up for more than one year, those with adherence of $\geq 80\%$ had less stroke (RR=0.74, 0.62-0.88). Risk factors such as male (RR=1.27, 1.07-1.52), diabetes (RR=1.23, 1.02-1.48), hypertension (RR=1.35, 1.12-1.63) and higher CDS score (RR=1.82, 1.50-2.20) had a significantly higher risk of non fatal stroke. **Conclusion:** This analysis indicated that adherence of $\geq 80\%$ and for more than 1 year is essential to reduce non fatal stroke. Our results confirm the importance of a long term adherence with statins.

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145. Two-stage nested case-control study of the control and severity of maternal asthma during pregnancy and the incidence of asthma in the offspring.

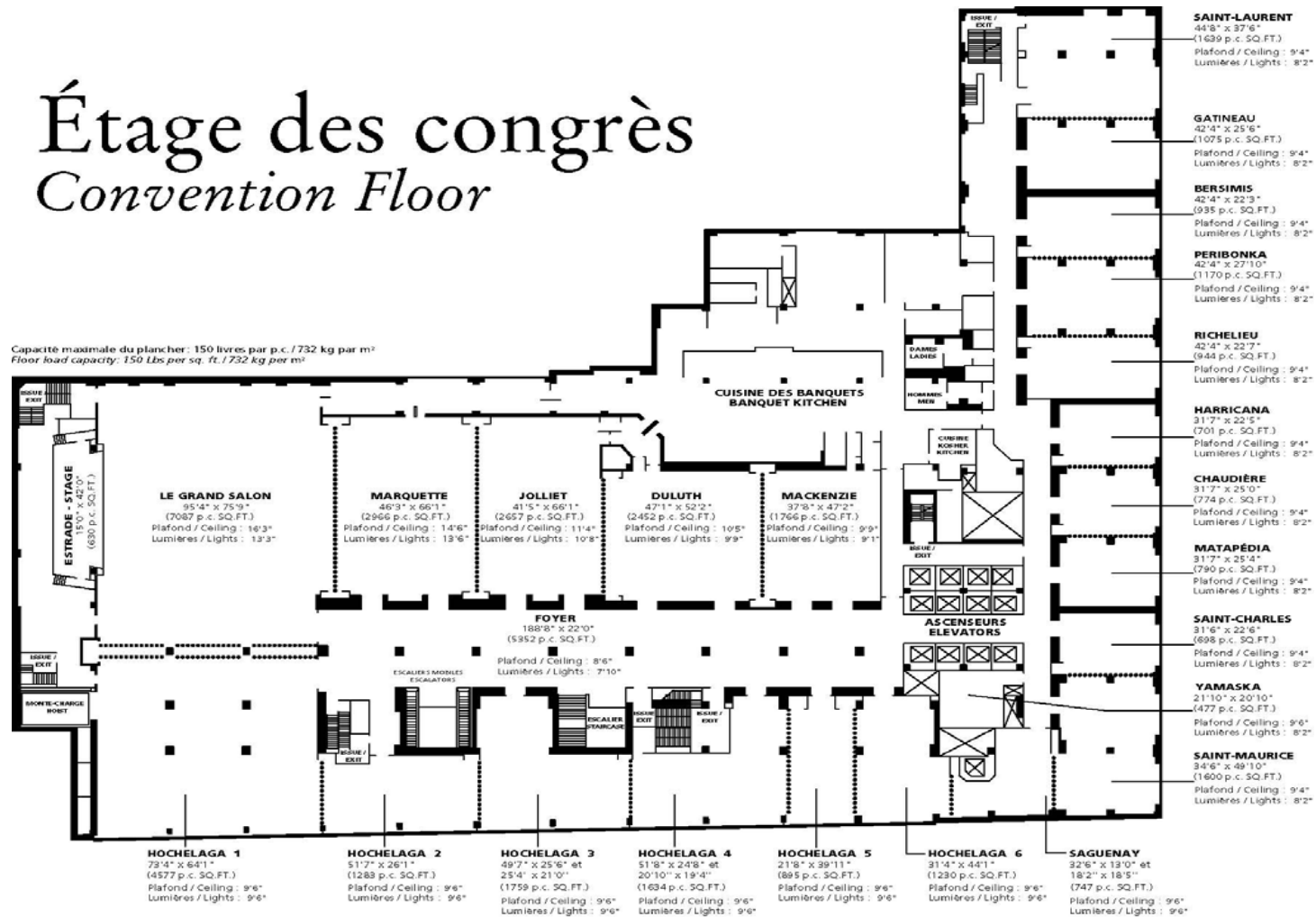
Marie-Josée Martel, Evelyne Rey, Marie-France Beauchesne, Jean-Luc Malo, Sylvie Perreault, Amelie Forget, Lucie Blais.

Universite de Montreal, Faculty of Pharmacy and affiliated hospitals, Montreal, Quebec, Canada

Background: Children of asthmatic mothers tend to have a higher risk of asthma than those of non-asthmatic mothers, but the extent to which the incidence of asthma in children is influenced by maternal asthma control and severity in pregnancy is unknown. **Objectives:** To evaluate the association between maternal asthma control and severity during pregnancy and the incidence of asthma in the offspring in the first 10 years of life. **Methods:** A two-stage case-control study, nested in a cohort of 8 226 children born to asthmatic mothers between 1990 and 2002, was conducted using 3 interlinked administrative health databases from Quebec and a mailed questionnaire. A child was considered as a case if it had received at least one diagnosis and a prescription for asthma within a 2-year period. Up to 20 controls/case were selected and matched for age at case occurrence. Maternal asthma control and severity were measured with validated indexes. Using a balanced two-stage sampling strategy, 3 254 randomly selected mothers were mailed questionnaires to obtain information on additional confounders. The final estimates, adjusted odds ratios, were obtained using logistic regression and were corrected with corresponding sampling fractions. **Results:** From the cohort, 2 681 asthma cases and 30 381 controls were identified. The questionnaire response rate was 44% (671 cases, 758 controls). Among children of asthmatic mothers, the increased risk of asthma in the offspring seen in the adjusted first-stage analysis (adjusted rate ratio:1.24 95%CI:1.11-1.38, comparing children of mothers with moderate-to-severe uncontrolled asthma during pregnancy vs those of mothers with mild controlled asthma), did not remain statistically significant in the final model (adjusted odds ratio:1.15 95%CI:0.95-1.40) combining first- and second-stage variables. **Conclusions:** This study showed no statistically significant increases in the risk of asthma among children whose mothers had a poorer control and increased severity of asthma during pregnancy.

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