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CONFERENCE 2004 POSTER SESSION

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BASIC RESEARCH

**BasicRes No. 1**: ABC transporters as a key determinant of sex-related differences in drug-induced Long QT syndrome, Pierre Morissette, Jacques Turgeon, Faculte de pharmacie, Universite de Montreal

**BasicRes No. 2**: The effect of modulating glucuronidation on VPA-associated 8-isoprostaglandin F2α levels in rats, Vincent Tong, Xiaowei Teng, Thomas K.H. Chang and Frank S. Abbott, Faculty of Pharmaceutical Sciences, University of British Columbia

**BasicRes No. 3**: Postnatal maturation of cytochrome P450 2E1 and glutathione-S-transferases, pharmacokinetic model validation, Fawzy A. Elbarbry, Jane Alcorn, College of Pharmacy and Nutrition, University of Saskatchewan

**BasicRes No. 4**: Heat treated fungizone® (HFZ) maintains amphotericin B's (AmB) antifungal activity while decreasing its renal cytotoxicity: role of fungal phospholipases, Erin Chew, Stephen D. Lee, Nancy S. Chung and Kishor M. Wasan, Faculty of Pharmaceutical Sciences, University of British Columbia

**BasicRes No. 5**: Changes in gene expression of natriuretic peptides and myosin heavy chain isoforms in cardiomypathic hamsters after treatment with growth hormone, Mukandila Mulumba, Huy Ong and Sylvie Marleau, Faculty of Pharmacy, Université de Montréal

**BasicRes No. 6**: Mechanisms involved in the modulation of aryl hydrocarbon receptor-regulated genes by tumor necrosis factor-α and lipopolysaccharide, Negar Gharavi and Ayman O.S. El-Kadi, Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta

**BasicRes No. 7**: Cytokine-mediated regulation of the rat mdr1b promoter in Huh7 hepatoma cells, Emmanuel Ho and Micheline Piquette-Miller, Department of Pharmaceutical Sciences, University of Toronto

**BasicRes No. 8**: Effect of warfarin on haloperidol lipoprotein and protein association within normolipidemic and hyperlipidemic human plasma, Tiffany Ho, Ric M. Procyshyn and Kishor M. Wasan, Faculty of Pharmaceutical Sciences, The University of British Columbia

**BasicRes No. 9**: Electrophysiological characterization of mutations found in the gene Kv1.5 in patients with different forms of atrial fibrillation, Isabelle Plante, Dominique Fournier, Chantal Guillemette, Gilles O'Hara, Jean Champagne, Patrick Mathieu, Richard Baillot, Pascal Daleau. 1 Quebec Heart Institute, Laval Hospital, 2 Faculty of Pharmacy, Laval University

**BasicRes No. 10**: Study on the correlation of drug dissolution and polymer swelling from a matrix tablet using texture analyzer, Hongtao Li, Xiao Chen, Faculty of Pharmacy, University of Manitoba

**BasicRes No. 11**: Pharmacokinetic study of methotrexate loaded poly(L-lactic acid) microspheres following intra-articular injection in rabbits, Linda Liang, Wesley Wong, and Helen Burt, Faculty of Pharmaceutical Sciences, University of British Columbia

**BasicRes No. 12**: In vitro and in vivo percutaneous permeation of insect repellent N, N-Diethyl-m-toluamide (DEET) and sunscreen oxybenzone, Sreeneeranj Kasichayanula, Xiao Chen, Faculty of Pharmacy, University of Manitoba

**BasicRes No. 13**: 3-Hydroxy-4,9-dihydroisothiazolo[5,4-b]quinoline-4-ones as topo-II inhibitors with antitumor activity, Zohreh Amoozgar and Mohsen Daneshzalab, School of Pharmacy, Memorial University of Newfoundland

CLINICAL RESEARCH

**ClinRes No. 1**: Optimizing care of diabetes patients with ischemic heart disease at Burnaby Hospital, Wendy A. Leong, Lorna S. Leckie, Marshall Dahl, Burnaby Hospital; University of British Columbia

**ClinRes No. 2**: Validation of logistic regression models for the development of thrombocytopenia in critical care patients, Arun K. Verma; Marc Levine, Stephen J. Shalansky, John J. Spinelli and Peter M. Dodek. Faculty of Pharmaceutical
Sciences, University of British Columbia; ²Children’s & Women’s Health Centre of B.C.; ³Pharmacy Department, St. Paul’s Hospital; ⁴B.C. Cancer Agency; ⁵Critical Care Medicine, St. Paul’s Hospital and the University of British Columbia

ClinRes No. 3: Phenotypic strategies, a better approach for individualized warfarin therapy

Veronique Michaud, Denis Brouillette, Denis Roy, Lucie Verret, Nicolas Noel, Isabelle Taillon, Gilles O’Hara, Denis Gossard, Monique Champagne, Marie-Claude Vanier, Jacques Turgeon. Faculté de pharmacie, Université de Montréal, Institut de cardiologie de Montréal, Institut de cardiologie de Québec, Hôpital Haut-Richelieu, Hôpital Maisonneuve-Rosemont, Xanthus Life Sciences

ClinRes No. 4: Evaluation of mitoxantrone in secondary progressive multiple sclerosis (SPMS),

M. Namaka, M. Melanson, J. Major, MNL. Klassen, S. Slobodian, D Ruhlen. Faculty of Pharmacy, University of Manitoba

ClinRes No. 5: A novel genotyping algorithm for the CYP2D6*10 allele in Asians using real-time rapid-cycle PCR and multiplex PCR, Evan H. Kwong¹, Marc Levine¹, Carolyne J. Montgomery², and Thomas K.H. Chang¹, ¹Faculty of Pharmaceutical Sciences, University of British Columbia, ²Department of Anesthesiology, Children’s and Women’s Health Centre of British Columbia

EDUCATIONAL AND TEACHING RESEARCH

Edu/Teach No. 1: Anticoagulation training and certification in Canada. Wendy A. Leong and The Anticoagulation Resource Team, Burnaby Research & University of British Columbia

Edu/Teach No. 2: Self-care Curriculum Revitalized: The Experience Within University of Toronto’s International Pharmacy Graduate Program. Janet Sio, Diem Cong & Karen Elaine Edge. International Pharmacy Graduate Program, Faculty of Pharmacy, University of Toronto

Edu/Teach No. 3: Electronic portfolios: a novel approach for assessing learning outcomes. Ingrid V. Price, Jennifer A. Shabbits, Marion L. Pearson, Lynda M. Eccott. Faculty of Pharmaceutical Sciences, University of British Columbia

Edu/Teach No. 4: Investigating the ‘Future’ of Pharmacy: the professional maturation and training of nascent pharmacists at one Canadian faculty of pharmacy. Jennifer D. Beales and Zubin Austin, Leslie Dan Faculty of Pharmacy

Edu/Teach No. 5: Investigating socio-cultural awareness in pharmacy curricula: The role of case examples. Jennifer D. Beales, Leslie Dan Faculty of Pharmacy, University of Toronto

Edu/Teach No. 6: Evaluating First Year CAPS-I – Cases in Pharmaceutical Sciences: Educational successes and challenges. Ingrid Price. Faculty of Pharmaceutical Sciences, University of British Columbia

Edu/Teach No. 7: Characterization and analysis of direct observation forms completed by preceptors during final year pharmacy experiential rotations. Andrea J. Cameron, Lesley A. Lavack. Leslie Dan Faculty of Pharmacy, University of Toronto

Edu/Teach No. 8: Experiences with collaborative practice among pharmacy and nutrition students assessing a standardized patient. Roy Dobson; Jeff Taylor; Jane Cassidy; Doreen Walker. College of Pharmacy and Nutrition, University of Saskatchewan

Edu/Teach No. 9: Feasibility of a web-based therapeutics course – a pilot evaluation. Heather R Kertland,¹² Natalie R Kennie,¹² Lori A May,¹ Thomas ER Brown ¹,³. Leslie Dan Faculty of Pharmacy, University of Toronto,¹ St Michael’s Hospital², Sunnybrook and Women’s College Health Science Centre³

Edu/Teach No. 10: Pilot trial of online training of evidence-based practice within the pharmacy curriculum at the Université de Montréal. Geneviève Gauthier,¹ Daniel J. G. Thirion,² Marie-France Beauchesne,² Lucie Blais,² and Claudine Laurier,² ¹. Department of Educational Psychology, McGill University. ². Faculté de pharmacie, Université de Montréal

Edu/Teach No. 11: Re-structuring of pathophysiology and therapeutics in the Doctor of Pharmacy program. Thomas ER Brown¹,
Clarence Chant2, Artemis Diamantorous1, Linda D Dresser2, Heather R Kertland2, Debora W Kwan7

Leslie Dan Faculty of Pharmacy University of
Toronto, Sunnybrook and Women’s College Health
Science Centre1, St Michael’s Hospital2, Mount Sinai
Hospital3, University Health Network4

Edu/Teach No. 12: Development of a first year
community practice experiential program. Debra
M. Moy, Michael R. Heffer. Leslie Dan Faculty of
Pharmacy, University of Toronto

Edu/Teach No. 13: An objective competency
level-based method to assess student performance
in experiential training. Christopher J. Turner,
Ralph Altiere, Larry Clark, Carrie Maffeo and Connie
Valdez. University of Colorado Health Sciences
Center School of Pharmacy

Edu/Teach No. 14: The integrated laboratory
network pilot project: a virtual approach to
teaching pharmaceutical analysis. Simon P.
Albon1, Devon A. Cancilla2, 1Faculty of
Pharmaceutical Sciences, University of British
Columbia, 2Scientific Technical Services, Western
Washington University.

Edu/Teach No. 15: An interfaculty pain
curriculum for health professional students: an
evaluation. Lalitha Raman-Wilms1, Judith
Hunter2, Judy Watt-Watson3, Leila Lax3, Glenn
Regehr3, Larry Librach3, Peter Pennefather1. 1.
Leslie Dan Faculty of Pharmacy, 2Department of
Physical Therapy, 3Faculty of Medicine, 4Faculty of
Nursing, University of Toronto

PHARMACY PRACTICE RESEARCH

PPR No. 1: Evaluation of pharmacist practice in
an interdisciplinary primary care team-based
setting: Implications for pharmacy education. Jana M. Bajcar1,2, Natalie Kennie1,2, Tom
Einarson1. 1. Leslie Dan Faculty of Pharmacy,
University of Toronto and 2. Department of Family
and Community Medicine, St. Michael’s Hospital

PPR No. 2: Involvement of a community
pharmacist research network in evaluating
outcomes of bisphosphonate therapy. Judith A.
Soon, Mary H.H. Ensom, D.W. Fielding, Marc
Levine, James P. McCormack, Selena M. Santi.
Collaboration for Outcomes Research and
Evaluation (COR, E), Faculty of Pharmaceutical
Sciences, University of British Columbia

PPR No. 3: Drug utilization review (DUR) for the
treatment of asthma. Joëlle Mimeault, Diane
Blais. Conseil du médicament, Direction du suivi
et de l’utilisation optimale

PPR No. 4: The provision and reimbursement of
home care services by community pharmacists in
Canada. Jennifer Alissa Lawrence 1 and A.
Kirsten Woodend2. 1University of Saskatchewan,
2Director, Research, CPhA

PPR No. 5: Pictographic instructions for
medications: Do other cultures interpret them
accurately? Zahra Sadikali1, LCol Régis
Vaillancourt2, John B. Collins3, Rosemin Kassam1. 1.
Faculty of Pharmaceutical Sciences, University of
British Columbia; 2Directorate of Medical Policy,
Pharmacy Policy and Standards, The Canadian
Forces; 3Department of Education Studies,
University of British Columbia

PPR No. 6: Community-based warfarin co-
prescribing and point of care INR testing. Wendy
A. Leong,* and London Drugs Anticoagulation
Team; Jenny Chiang, Daniel Choi, Nelson Costa,
Sanja Ivankovic, Allen Jang, Cecilia Lee, Winnie
Lee, Joyce Tan, Robert Tong, John Tse, Annie
Wang, Grace Yeung, }.,# Burnaby Research* &
University of British Columbia*

SOCIAL AND ADMINISTRATIVE
RESEARCH

Soc Admin No. 1: Hot on the Net: pharmaceutical policy/PDAs, Timothy Rees and
Elizabeth Foy, College of Pharmacy, Dalhousie
University
BASIC RESEARCH

BasicRes No. 1: ABC transporters as a key determinant of sex-related differences in drug-induced Long QT syndrome

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Sex-related differences in drug-induced Long QT syndrome are well recognized. Recently, our laboratory has demonstrated that ATP binding cassette (ABC) membrane transporters play a key role in the regulation of intracellular drug accumulation and cardiac toxicity. Purpose: 1) To determine whether an ABC transporter modulator can alter the effects of LQT blockers on cardiac repolarization, and 2) To determine if these effects are modulated by gender. ABC transporter activity was modulated by pre-treating male and female guinea-pigs (n=96) for 5 days with verapamil (1.5 to 15 mg/kg/day), prior to EP studies. Duration of monophasic action potential duration measured at 90% repolarization (MAPD90) was evaluated at baseline and following a 5 minute perfusion period with cisapride (50 nM). Intracellular cisapride concentrations were evaluated in myocytes of pre-treated animals using an HPLC method. At a basic cycle length of 250 msec, MAPD90 was prolonged by cisapride +5 msec in male but 22+6 msec in female hearts from vehicle pre-treated animals. In contrast, a much greater increase in MAPD90 was noticed in hearts isolated from animals pre-treated with verapamil (11.6 mg/kg/day). Indeed, MAPD90 was prolonged 28±9 msec in male but 48±9 msec in female hearts (p<0.05). Additional experiments were conducted to demonstrate an increase in intracellular concentrations of cisapride in pre-treated animals. Cisapride concentrations were 12±4 and 14±3 ng/mg protein in control male and female hearts, respectively. Much higher concentrations of cisapride were observed in hearts from animals pre-treated with verapamil (11.6 mg/kg/day): intracellular concentrations were 22±4 and 30±4 ng/mg protein, respectively (p<0.05). This study demonstrates that ABC membrane transporter activity modulates I\(_\text{K}\) block by non-antiarrhythmic agents such as cisapride. We identify for the first time ABC transporters as a key determinant of mechanisms underlying sex-related differences in drug-induced Long QT syndrome.

BasicRes No. 2: The effect of modulating glucuronidation on VPA-associated 8-iso-prostaglandin \(F_{2\alpha}\) levels in rats.

Vincent Tong, Xiaowei Teng, Thomas K.H. Chang and Frank S. Abbott
Faculty of Pharmaceutical Sciences, University of British Columbia

Increased production of reactive oxygen species (ROS) has been associated with valproic acid (VPA) treatment and studies are ongoing to examine the relationship between VPA biotransformation and oxidative stress.

Objectives. (A) To biosynthesize VPA-1-O-acyl glucuronide (VPA-G) and to develop a quantitative LC/MS assay for VPA-G in rat liver. (B) To investigate the effect of modulating VPA-G formation, the major VPA biotransformation pathway, on ROS production in rats.

Methods. Urethane anesthetized male Sprague Dawley rats were administered intraperitoneally with VPA or \(^{[3]H}\)-VPA. VPA-G and \(^{[2]H}\)-VPA-G were extracted and purified from bile by HPLC. A quantitative LC/MS method was developed and validated for the determination of VPA-G from liver homogenates. To modulate VPA-glucuronidation pathway, rats (n=8/group) were pretreated with [\((1S)-endo\)]-(-)-borneol (1mmol/kg, i.p.) at 0.5 hr prior to VPA treatment (500mg/kg, i.p.). VPA-G levels were determined by LC/MS and oxidative stress was measured by 8-iso-prostaglandin \(F_{2\alpha}\) levels using an EIA method.

Results. The identities of VPA-G and \(^{[2]H}\)-VPA-G were confirmed by NMR and mass spectrometry. The LC/MS method using negative electrospray ionization was linear over the range 0.5-50 \(\mu\)g/mL. Intra- and inter-assay validation results indicated that the accuracy and precision was <15 % bias and 15% C.V. (n=5 days). (-)-Borneol pretreatment reduced the levels of VPA-G by ~90% compared to animals treated with VPA alone. Furthermore, plasma levels of 8-iso-prostaglandin \(F_{2\alpha}\) were found to be reduced from 93±8 pg/mL to 60±4 pg/mL in (-)-Borneol and VPA treated animals compared to VPA treated animals alone.

Conclusion. (-)-Borneol pretreatment significantly inhibited VPA-glucuronidation, and the modulation of this major metabolic pathway was associated with an apparent decrease in levels of 8-iso-prostaglandin \(F_{2\alpha}\). (Supported by CIHR).

BasicRes No. 3: Postnatal maturation of cytochrome P450 2E1 and glutathione-S-transferases, pharmacokinetic model validation

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Maturation of systemic clearance mechanisms during postnatal development produces dramatic and rapid improvements in a neonate’s capacity to eliminate drugs. Our study’s objective was to evaluate underlying assumptions of a pharmacokinetic model that describes hepatic Cytochrome P450 (CYP) enzyme activity ontogenesis and to extend the model to Phase II enzymes. We tested the hypothesis that age-dependent changes in intrinsic clearance are attributed only to changes in \(V_{\text{max}}\). CYP2E1 and GST ontogenesis were determined in male Sprague-Dawley rat (n=4) hepatic microsomes and cytosols at day 20 of gestation and at postnatal ages 1, 3, 5, 7, 10, and 14 days, and 3, 4, 6, 9, 12, and 16 weeks. Body and liver weights, hepatic microsomal and cytosol protein content, and total CYP protein content were measured to calculate age-dependent hepatic scaling factors. CYP2E1 activity ontogenesis was monitored with Chlorozoxazone (CZX) and \(p\)-nitrophenol (PNP) using HPLC analysis. Spectrophotometric analysis of glutathione conjugation of 2, 4- dinitro-1-chlorobenzene was used to monitor general GST enzyme activity ontogenesis. Metabolite
formation velocities were measured at concentrations of 0 to 1000 µM to determine age-dependent $V_{\text{max}}$ and $K_m$ values. The results showed a similar pattern of postnatal increase in CYP2E1 and GST enzyme activity up to 4 weeks of age. Age-dependent changes in $V_{\text{max}}$ with CZX were significantly different ($P<0.05$) between the different age groups and covaried with PNP. $K_m$ values were similar with adult values at all stages of postnatal maturation except in fetal, and 1 and 3 day old livers. Microsomal protein (MP) contents increased with postnatal age with dramatic increase after day 14 of age. Although the data are not totally consistent with the model assumptions and hypothesis, further work is needed to determine whether the model may allow predictions of in vivo hepatic metabolic clearance.

**BasicRes No. 4: Heat treated fungizone® (HFZ) maintains amphotericin B's (AmB) antifungal activity while decreasing its renal cytotoxicity: role of fungal phospholipases**

Erin Chew, Stephen D. Lee, Nancy S. Chung and Kishor M. Wasan

Faculty of Pharmaceutical Sciences, University of British Columbia

**Purpose:** The purpose of this investigation was to determine if the addition of fungal phospholipases to pig kidney cells would restore HFZ's cytotoxicity to those observed when these cells were treated with fungizone® (FZ).

**Methods:** LLC-PK₁ cells, a pig kidney cell line, were grown in T75 flasks and seeded in 96 well plates at a density of 40,000 cells/cm². FZ and HFZ treatment solutions containing a concentration of 10, 20, and 50 g AmB/ml were prepared. HFZ was prepared by heating the drug in a 70°C water bath for 20 minutes. A concentration of 0.43 units/ml of Fungal Phospholipases A₂ was added to all treatment groups and incubated for 1 h at 37°C before the cells were further incubated for an additional 18 h with different concentrations of FZ and/or HFZ. Following this incubation, an MTS assay was performed to determine the mitochondrial respiration as a function of cell proliferation, thereby indicating the viability of cells post treatment.

**Results:** HFZ was significantly less toxic than FZ to renal cells. However, the addition of fungal phospholipases to the cell culture increased HFZ cytotoxicity to the levels seen for FZ. FZ treatment resulted in 80% toxicity in LLC-PK₁ cells versus control whereas HFZ showed a dose-dependent increase in cytotoxicity from 20% to 50% over AmB concentrations from 10µg/ml to 50µg/ml versus control. In the presence of fungal phospholipases, HFZ renal cytotoxicity was similar to FZ renal cytotoxicity.

**Conclusions:** The addition of fungal phospholipases to pig kidney cells restores HFZ cytotoxicity to those observed when these cells were treated with FZ.

**Acknowledgements:** Funding provided with a grant from the Canadian Institutes of Health Research.

**BasicRes No. 5: Changes in gene expression of natriuretic peptides and myosin heavy chain isoforms in cardiomyopathic hamsters after treatment with growth hormone.**

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Idiopathic dilated cardiomyopathy (IDC) is a cardiac disease known to correlate with changes in hypertrophic biomarkers gene expression including natriuretic peptides (NPs) and myosin heavy chain isoforms ($\alpha$ and $\beta$-MHC), for which a switch from $\alpha$ to $\beta$ isoform is associated with a reduced energy spent. The cardiomyopathic hamster (CMH) is a suitable model of the human IDC showing multifocal necrosis, dilatation and severe HF. Clinical observations have shown that the administration of growth hormone (GH) may improve cardiac function in patients with IDC. The aim of the present study is to examine the gene expression of NPs and MHC isoforms by RT-PCR in the left ventricle following GH administration at a daily dose of 1 mg/kg s.c. to female CMH, starting at either 30 days (early phase of the disease) or 200 days old (late phase), until they reach 240 days old. Vehicle-treated CMH show elevated ventricular ANP (3- to 4-fold) and BNP (1.3-fold) mRNA levels compared to controls (Golden Syrian hamsters). Following GH treatment, BNP gene expression is further increased by 2.6- and 3.4-fold versus controls when treated from the early or late phase of the disease, respectively. In contrast, ventricular ANP gene expression is reduced to control levels in the late phase treatment. As expected, $\beta$-MHC expression is increased in vehicle-treated CMH compared to controls (~1.6 fold), and GH administration further increased $\beta$-MHC expression (~2.2 fold versus controls) in the late phase of the disease. We conclude that GH therapy is associated with changes in cardiac hypertrophic biomarkers expression and with an increase in the low ATPase myosin isoform.

**BasicRes No. 6: Mechanisms involved in the modulation of aryl hydrocarbon receptor-regulated genes by tumor necrosis factor-α and lipopolysaccharide**

Negar Gharavi and Ayman O.S. El-Kadi

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Little is known about the mechanisms involved in the modulation of aryl hydrocarbon receptor (AHR)-regulated genes during pathophysiological conditions such as inflammation. In the present study the effect of tumor necrosis factor (TNF) - and lipopolysaccharides (LPS) on the constitutive and inducible expression of the AHR-regulated genes: cytochrome P450 1a1 (cyp1a1), glutathione S-transferase Ya (GST Ya), and NAD(P)H:quinone oxidoreductase (QOR) were determined. Murine hepatoma Hepa 1c1c7 (WT), AHR-deficient (C12) and AHR nuclear translocator protein (ARNT)-deficient (C4) cells were incubated with recombinant murine TNF-α (1-10 ng/ml) or LPS (1-5 g/ml) with or without the AHR ligand, - naphthoflavon (NF, 10 M). We found that TNF-α and LPS strongly repress the constitutive expression and the NF-mediated induction of cyp1a1, cyp1a2, GST Ya and QOR in WT but not in C12 and C4 cells dose-dependently. TNF-α and LPS did not significantly alter the mRNA expression of the stress...
protein, heme oxygenase (HO-1) in WT cells, suggesting that HO-1 is not involved in the modulation of AHR-regulated genes by TNF-α and LPS. In addition, significant increase in reactive oxygen species (ROS) was observed in WT, C12 and C4 cells treated with TNF-α or LPS. The production of ROS was higher in WT cells than in C12 and C4 cells, suggesting the involvement of AHR in the ROS production. In conclusion, the downregulation of AHR-regulated genes by inflammation is dependent on the presence of both heterodimeric transcription factors, AHR and ARNT. Furthermore, ROS may directly or indirectly be involved in the downregulation of AHR-regulated genes.

Acknowledgement, Negar Gharavi is nominated for Canadian Foundation for Pharmacy National Student Research Poster Award.

BasicRes No. 7: Cytokine-mediated regulation of the rat mdr1b promoter in Huh7 hepatoma cells
Emmanuel Ho and Micheline Piquette-Miller
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Background. Decreased efficacy of chemotherapy often occurs due to a mechanism known as multidrug resistance (MDR). Acute inflammation induced by cytokines or lipopolysaccharide (LPS) has been shown to decrease basal expression of the multidrug resistance gene mdr1b as well as suppress its induction in rodents. We hypothesize that binding of negative regulatory transcription factors (NF-IL6 or STAT3) may be involved in the cytokine-mediated down regulation of mdr1b transcription.

Methods. Sprague-Dawley rats were administered 5mg/kg LPS i.p. or saline, livers removed at various times and nuclear proteins isolated. Electrophoretic mobility shift assays (EMSA) were performed with 32P-radiolabelled mdr1b promoter fragments (nt –291 to –278). Influence of cytokines on transcriptional activity was examined in chloramphenicol acetyltransferase (CAT)-promoter construct fragments (wildtype or deletion construct- Del nt –291→–278).

Results. EMSA revealed an increased binding of nuclear fractions with the nt –291→–278 promoter region in LPS-treated rats. Competition and supershift experiments indicated that neither NF-IL6, STAT3 nor NF-κB interacted at this region, suggesting binding of a novel transcription factor. CAT assays detected a dramatic decrease in basal mdr1b transcriptional activity (P<0.005) in deletion constructs. Reporter assays also revealed dose-dependent induction of transcription in both wild type and deletion constructs in cytokine-treated cells. This site appeared to be involved, in part, in LPS and IL-1β mediated induction of transcription.

Conclusions. A novel transcription factor appears to interact at the promoter region nt –291→–278. Reporter assays also reveal that this region is required for basal transcriptional activity of the rat mdr1b and that cytokines may modulate mdr1b transcription through interaction at this region. These studies significantly increase our basic understanding of cytokine-mediated regulation of the MDR genes in malignant hepatocytes.

BasicRes No. 8: Effect of warfarin on haloperidol lipoprotein and protein association within normolipidemic and hyperlipidemic human plasma

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Purpose: The objective of this study was to determine the protein and lipoprotein association of Haloperidol in the presence of different concentrations of warfarin in normolipidemic and hyperlipidemic human plasma.

Methods: Warfarin sodium was pre-incubated in normolipidemic and hyperlipidemic human plasma at different concentrations (1, 5, 10 µg/mL) for 24 hours at 37 C (n=6). Following the pre-incubation with warfarin, [3H]Haloperidol mixed with unlabeled Haloperidol (total concentration = 18 ng/mL) was incubated in this plasma for 1 hour at 37 C. Treated plasma samples were separated into four fractions: triglyceride-rich lipoproteins (TRL), low-density lipoproteins (LDL), high-density lipoproteins (HDL), and lipoprotein-deficient plasma (LPDP) by density gradient ultracentrifugation. Each lipoprotein and lipoprotein-deficient fraction was assayed for [3H]Haloperidol by radioactivity. In addition, 100µL of the LPDP fraction from each treated plasma samples were pipetted into an ultrafiltration column to distinguish free Haloperidol from protein-bound Haloperidol. The filtrate and filter from the devices as well as 100µL of each LPDP sample were assayed for [3H]Haloperidol by radioactivity to determine the amount of free compared to protein-bound Haloperidol.

Results: In normolipidemic plasma, increasing concentrations of warfarin did not significantly alter the lipoprotein distribution of haloperidol. In the presence of warfarin, the percentage of protein-bound Haloperidol increased from 25.5% ± 1.0% (0µg/mL) to 32.2% ± 2.8% (10µg/mL). In hyperlipidemic plasma, increasing concentrations of warfarin correlated with an 11.5% decrease in the amount of haloperidol recovered in the LPDP fraction and a concurrent 4.8% and 5.2% increase in the amount of haloperidol recovered in TRL and LDL fractions, respectively. As warfarin concentration increased, the percentage of protein-bound Haloperidol decreased from 65.8% ± 2.2% (0µg/mL) to 57.0% ± 3.2% (10µg/mL).

Conclusion: In hyperlipidemic plasma, increasing concentrations of warfarin correlated with a significant decrease in amount of haloperidol recovered in the LPDP fraction and concurrent increases in the amount of Haloperidol recovered in the TRL and LDL fractions.

Acknowledgements: Funding for this project was provided by CIHR and Riverview Hospital

BasicRes No. 9: Electrophysiological characterization of mutations found in the gene Kv1.5 in patients with different forms of atrial fibrillation
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Atrial fibrillation (AF) is the most prevalent form of cardiac arrhythmias. Shortening of the atrial effective refractory period is an important factor contributing to AF, involving functional
changes in ion channels. AF could be familial, idiopathic (without identified cause) or consecutive to a cardiac surgery. The gene Kv1.5 encodes an atrial potassium channel. Considering the important role of Kv1.5 in atrial repolarization, we hypothesized that mutations in Kv1.5 are implicated in AF. We searched for the presence of mutations in the gene Kv1.5 of patients with idiopathic (6), familial (10), and post-surgery (26) AF. Healthy patients (20) and others (10) having undergone a coronary artery bypass surgery without developing post-surgery AF were used as controls. Total DNA of patients was extracted from blood. The gene Kv1.5 (promoter and coding region) was amplified using PCR, and sequenced. Three mutations were identified: R87Q (1 patient with post-surgery AF), A251T (1 patient with familial AF, 1 with post-surgery AF and 1 having undergone the surgery without developing AF) and P307S (2 patients with post-surgery AF). These mutations were reproduced by directed mutagenesis and their effects on channel functions were evaluated using the whole-cell patch-clamp technique on transfected CHO cells. The mutations R87Q and P307S accelerate the channel opening and A251T shifts the I-V curve towards more negative voltages compared to the wild type. The effects of these mutations will tend to enhance the Kv1.5 current and could thus be involved in the pathogenicity of AF.

BasicRes No. 10: Study on the correlation of drug dissolution and polymer swelling from a matrix tablet using texture analyzer

Hongtao Li, Xiaochen Gu
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Purpose: To study the relationship between drug dissolution and polymer swelling from a controlled release matrix tablet of pseudoephedrine using texture analyzer.

Methods: A series of controlled release matrix tablets of pseudoephedrine were prepared by direct compression method using identical compression force. Controlled release of pseudoephedrine was achieved by combined use of matrix excipients Compritol® 888 ATO (C) and Polyox® WSR 301 (P). Dissolution profiles of the tablets were evaluated using USP Method II. Thickness of gel formation and area under the curve (AUC, product of the force of the probe sensed and the distance the probe traveled) during drug dissolution were also recorded using a Texture Analyzer. The relationship between drug dissolution and polymer swelling was correlated and interpreted.

Results: Drug dissolution within the first 90 minutes reduced with the increased proportion of C and P in tablet formulation. However, drug dissolution was complete in 6 hours due to the aqueous solubility of pseudoephedrine. Thickness of gel formation as well as the AUC increased linearly with the dissolution time, indicating first-order kinetics of water penetration into the tablet matrix. Linear correlation was also observed between thickness of gel formation and square of drug release percentage. Various dissolution parameters are tabulated.

Conclusion: There was a linear relationship between drug dissolution and polymer swelling of a controlled release matrix tablet of pseudoephedrine. The study demonstrated a unique application of Texture Analyzer in characterization of tablet quality control and drug dissolution.

BasicRes No. 11: Pharmacokinetic study of methotrexate loaded poly(L-lactic acid) microspheres following intra-articular injection in rabbits

Linda Liang, Wesley Wong, and Helen Burt
Faculty of Pharmaceutical Sciences, University of British Columbia

Purpose: The plasma concentrations and tissue distribution of methotrexate (MTX) were investigated following intra-articular injection of either free MTX or controlled release MTX loaded microspheres in healthy rabbit joints.

Methods: MTX loaded poly(L-lactic acid) (2000g/mole) microspheres (30-90µm) were manufactured using the solvent evaporation method. Free MTX or MTX loaded microspheres (10mg MTX) was injected into the right knee joint cavity of rabbits. Blood samples were taken at predetermined times from the jugular vein. Urine samples were also collected over time periods up to 24 hours. The rabbits were sacrificed and the major organs and synovial tissues were removed 6 hours and 24 hours post injection (n=4). MTX concentrations in the plasma and major organs were determined by HPLC.

Results: For rabbits injected with free MTX, the plasma MTX concentration reached a maximum at 15 minutes (Cmax 2.5µg/mL) and declined to undetectable levels 8 hours following the injection. The plasma MTX concentrations of rabbits injected with MTX microspheres peaked at 15 minutes (Cmax 0.5µg/mL) and declined to undetectable levels 4 hours following the injection. Analysis of urine collected showed that 19 times more MTX was excreted in the urine from rabbits injected with free MTX compared to those injected with MTX loaded microspheres in the period of 0 to 3 hours. The concentration of MTX in the synovial fluid 6 hours following intra-articular injection was 10 times higher in the rabbits injected with microspheres than in the rabbits injected with free MTX.

Conclusion: Free MTX was rapidly cleared from the joint cavity while MTX encapsulated microspheres decreased the clearance and retained MTX in the joint cavity.

BasicRes No. 12: In vitro and in vivo percutaneous permeation of insect repellent N, N-Diethyl-m-toluamide (DEET) and sunscreen oxybenzone

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The objective of this study was to investigate concurrent skin absorption of DEET and oxygenzene in vitro and in vivo.

Methods: In vitro diffusion studies were conducted at 45°C, using Franz-style cells with piglet epidermis (300-500μm) as membrane model. DEET and oxygenzene at 5 mg/mL in 50% ethanol (E), polyethylene glycol 400 (PEG-400) and propylene glycol (PG) were used either separately or in combination. Three commercially available repellent and sunscreen products (Coppertone® Sunblock Lotion, OFF!® Repellent Lotion and OFF!® Repellent Lotion with Sunscreen) were applied to the back of 6 piglets. Tape strippings were collected at 2, 12 and 48 hours after the application. Concentrations of DEET and oxygenzene were analyzed using a validated HPLC assay.

Results: Overall in vitro permeation ranged 0.6-18% for DEET and 0.4-20% for oxygenzene respectively. Enhanced permeation across piglet skin was found for both DEET and oxygenzene when the two compounds present concurrently (DEET: 289% in PG, 243% in E and 112% in PEG-400; oxygenzene: 139% in PEG-400, 120% in PG and 112% in E). E and PG significantly increased the permeation of DEET across the membrane. Recovery of DEET and oxygenzene from in vivo tape stripping varied dependent upon sampling time and formulation applied. Overall recovery amounts at 48 hours were 5.3% for DEET and 22.4% for oxygenzene respectively. Combined formulation showed higher recovery of 81.8% for DEET and 135.0% for oxygenzene respectively compared to single-component counterpart.

Conclusions: Permeation of DEET and oxygenzene was synergistically enhanced when they were applied simultaneously. Mechanisms of such absorption synergy as well as approaches to reduce permeation of DEET and oxygenzene need to be systematically identified.

BasicRes No. 13: 3-Hydroxy-4,9-dihydroisothiazolo[5,4-b]quinoline-4-ones as topo-II inhibitors with antitumor activity
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Objectives: Based on the previously reported topo-II inhibitory and anticancer activity of 8-oxo-1,2,4-thiadiazolo[4,5-a]quinoline-9-carboxylic acids (I) and application of structure-based molecular modeling approach, we designed and synthesized novel 3-hydroxy-4,9-dihydroisothiazolo[5,4-b]quinoline-4-one derivatives (II) in order to investigate the potential of these molecules as selective inhibitors of topoisomerase-II and potential antitumors.

Methods: Using Hyperchem program, the optimum geometry of I (R3 = 5-F; R5, Ph) was determined through molecular mechanic optimization. Based on the above data, the linear analogue II (R3 = 7-F; R5, CH2Ph) was designed, which was perfectly overlapping with the optimized geometry of compound I. Compound II was then synthesized through different synthetic approaches.

Results: Preparation of compound II was achieved by either conventional synthesis of the relevant 2-mercaptoquinoline carboxylic acid followed by N-alkylation and cyclization, or through convergent synthesis starting with appropriate benzoylacetocacetate intermediate and further cyclization. The synthesized compounds were evaluated for their topo-II inhibitory and cytotoxic activity. Based on the successful synthesis of parent N9-benzyl analogue, and in order to study the effect of different substituted alkyl, cycloalkyl, aryl, and heteroaryl moieties on the overall Topo-II inhibitory and cytotoxic activities of this class of compounds, several new N9-substituted analogues of structure II were synthesized and evaluated for the targeted activities.

Conclusions: Through this study, we were able to introduce novel synthetic methodologies for the preparation of linear isothiazolo-quinoline derivatives with potential topo-II inhibitory and cytotoxic activities.

CLINICAL RESEARCH

ClinRes No. 1: Optimizing care of diabetes patients with Ischemic heart disease at Burnaby Hospital
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Objectives: Ischemic heart disease (IHD) is the #1 cause of death in diabetes (DM) patients. The study objectives were: (i) to establish patterns of practice; (ii) to identify key problems; and (iii) to improve care of DM-IHD patients at our busy, 515-bed, university-affiliated, primary and secondary care centre (i.e. 60,000 emergency visits per year).

Methods: This retrospective, open evaluation included all Type 2 DM patients admitted with a primary or secondary diagnosis of IHD, from April 1998 to March 1999.

Results: For the 130 study patients included: average (avg.) age of 71 years (yrs); avg. age at DM diagnosis 59 years; 45% female; 22% ethnic; 74% overweight; 75% hyperlipidemia; 78% HT; 63% smokers; 54% family history of IHD; and an avg. of 5 cardiovascular risk factors. DM complications included: 18% eye surgery; 2% limb amputation; 36% coronary angiography; 15% PTCA; and 14% CABG. The most common reasons for admission were: IHD, CHF and AMI. During hospitalization, there was also: (a) more ASA, diuretics, beta-blockers, digoxin, and ACE inhibitors were prescribed compared to medications used prior to admission; (b) hyperglycemia and hypoglycemia in 43% and 36%, respectively; (c) HT in 70% and (d) thrombolysis in 17%. Routine lab monitoring did not include HbA1c, lipids, or microalbuminuria.

Of the 130 study patients, 75% were discharged alive and 8% died. Referrals to our Diabetic Education Centre, and Healthy Heart Program were low (19%, 9%, respectively). Our
recommendations included: (i) more intensive control of blood glucose, IHD, hypertension and diet; and (ii) more DM-IHD patient education and discharge follow-up.

**CONCLUSION:** IHD management in DM patients could be improved by referring more patients to a Diabetic Education Centre and a Healthy Heart (cardiac prevention) Program.

**ClinRes No. 2: Validation of logistic regression models for the development of thrombocytopenia in critical care patients.**

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**Objectives:** Thrombocytopenia is common and clinically relevant in critically ill patients. The objectives of this study were to identify explanatory variables for thrombocytopenia at and after admission, and to evaluate the generalizability of these statistical models by internal and external validation procedures.

**Methods:** Logistic regression was used to identify predictors for thrombocytopenia (< 100 × 10⁹/L) using data from 792 intensive and coronary care unit (ICU/CCU) patients at a community hospital. Admission and post-admission models were developed and validated internally using bootstrap resampling techniques. Subsequently, the admission model was validated externally using data from 572 patients admitted to a tertiary care ICU.

**Results:** Predictors were identified for the admission (admission diagnoses, APACHE II score, age, surgery within 24 hours of admission, and admission platelet count) and post-admission (admission diagnoses, APACHE II score, admission platelet count, fresh frozen plasma transfusion, packed red blood cell transfusion, Swan-Ganz catheters, imipenem, and heparin) models, respectively. The area under the receiver operating characteristic (ROC) curve (95% confidence interval) of the admission and post-admission models were 0.925 (0.897–0.957) and 0.942 (0.920–0.963), respectively. Based on the bootstrap method, the optimism in these estimates was shown to be 0.008 (0.006–0.010) and 0.021 (0.019–0.023), respectively. For the external validation set, the area under the ROC of the admission model was 0.808 (0.757-0.860).

**Conclusions:** Both models demonstrated excellent discriminating ability and low bias. The admission model demonstrated very good predictive performance in the external validation dataset. Clinicians should consider the identified predictors in diagnostic and treatment decisions involving critically ill patients who may be at risk of thrombocytopenia.

**ClinRes No. 3: Phenotypic strategies, a better approach for individualized warfarin therapy**

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CYP2C9 metabolizes drugs such as losartan and (S)-warfarin. CYP2C9 is polymorphic and correlation between warfarin clearance and CYP2C9 genotype had been demonstrated in healthy volunteers but not in patients undergoing treatment with various drugs under usual clinical conditions. The overall objective of our study was to determine, in patients with a multiple drug regimen, correlations between required doses of warfarin and 1) CYP2C9 genotypes, 2) CYP2C9 phenotypes losartan metabolic ratio or S- and R-warfarin ratio. Losartan and its main metabolite EXP 3174 were analysed by HPLC in 6-hour urine samples collected from 77 subjects after a single 12.5 mg oral dose of losartan before initiating warfarin therapy. S- and R-warfarin concentrations were analyzed by HPLC in blood samples collected from 96 subjects at 3, 14 and 24 hours following initiation of warfarin treatment. The three most common CYP2C9 allelic variants were analysed by PCR-RFLP using genomic DNA of 121 patients. Two multiple linear regression analysis models were developed using phenotype, age, weight, gender, amiodarone treatment (only for phenotype based on losartan metabolic ratio) and genotype (only for phenotype using warfarin as probe drug) as cofactors. These models explain 40% of variability in warfarin dose. In contrast, a genotype analysis correlated with phenotype values only in patients carrying two copies of variant alleles. Our results indicate that in more than 90% of patients, a genotypic approach does not predict required doses of warfarin. CYP2C9 phenotype could represent a more favorable strategy to explain intersubject variability in warfarin disposition.

**ClinRes No. 4: Evaluation of mitoxantrone in secondary progressive multiple sclerosis (SPMS)**

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**Purpose:** To evaluate the efficacy and safety of Mitoxantrone (Novantrone) in patients diagnosed with SPMS.

**Methods:** An open-label study was conducted in 42 patients that were diagnosed with SPMS. Eligibility of all screened patients was determined in accordance with previously established criteria. All eligible patients were separated into treatment (n=31) or control groups (n=11) based on their informed decision to receive or not receive mitoxantrone treatment. Both treatment and control groups received baseline assessments that included: urinalysis, serum pregnancy test, blood work, cardiac monitoring (MUGA scans) and expanded disability status scale (EDSS) scoring. All treated patients were scheduled to receive an intravenous infusion of 12 mg/m² of mitoxantrone every 3 months up to a maximum of 10 treatments...
or a cumulative dose of 120 mg/m² over a 27-month period. Urinalysis, serum pregnancy test, blood work, drug related adverse effects (nausea, hair loss) and EDSS scoring were conducted prior to each successive treatment and 10 days post treatment. MUGA scans were scheduled every 6 months up to 8 treatments or 100mg/m² after which were conducted following each successive treatment until study completion. All control patients received standard blood work, urinalysis and EDSS scoring with each regularly scheduled clinic visit.

**Results:** Interim analysis revealed that 17 out of 31 patients (~55%) in the active treatment group had withdrawn from the study after receiving an average of approximately 3 treatments or 36 mg/m². Reasons for premature study termination included: cardiac complications (~47%), patient concerns (~29%), quality of life concerns (~29%), urinary tract complications (~6%) and other (~12%). In addition, patients receiving active treatment did not display a statistical significant improvement in the average EDSS scoring.

**Conclusions:** Preliminary results obtained from the interim analysis suggest insufficient evidence to validate the use of mitoxantrone in the treatment of SPMS. Although target recruitment numbers have been reached, final conclusions will be determined once all remaining participants in the active treatment group complete or withdraw from the study.

**ClinRes No. 5: A novel genotyping algorithm for the CYP2D6*10 allele in Asians using real-time rapid-cycle PCR and multiplex PCR**

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**Objectives:** The CYP2D6*10 allele is common among Asians and associated with decreased metabolism of some CYP2D6 substrates. To study the effect of this allele on drug metabolism, it is necessary to accurately genotype patients for CYP2D6*10 (C188T). Based on reported allele frequencies among Asians, it is necessary to rule out CYP2D6*4 (C188T, G1934A) and CYP2D6*5 (gene deletion) before inferring the presence of CYP2D6*1 or CYP2D6*2 (C188). The project objectives are to devise a genotyping algorithm and to develop and validate genotyping methods for detecting the C188T and G1934A single nucleotide polymorphisms (SNPs) and CYP2D6*5.

**Methods:** Long PCR was used to amplify the CYP2D6 gene. Nested real-time PCR methods to detect the C188T and G1934A SNPs were developed and validated by restriction fragment length polymorphism (RFLP) and sequencing analyses of previously genotyped reference samples (CYP2D6*1/*1, CYP2D6*1/*4, CYP2D6*4/*4). A multiplex PCR method to detect CYP2D6*5 using published primer sequences was developed and validated using reference samples (CYP2D6*1/*1, CYP2D6*1/*5, CYP2D6*5/*5).

**Results:** C188T and G1934A genotyping results using real-time PCR were consistent with RFLP analyses, sequencing analyses, and the genotypes of the reference samples. CYP2D6*5 genotyping results were also in agreement with the genotypes of the reference samples.

**Conclusions:** The combination of real-time PCR to detect the C188T and G1934A SNPs and multiplex PCR to detect CYP2D6*5 provides an efficient approach for CYP2D6 genotyping in Asian patients. These methods can be applied to a novel genotyping algorithm for future clinical trials studying the effect of CYP2D6*10 on drug metabolism in Asians.
Purpose: To redesign and implement a self-care course for the International Pharmacy Graduate (IPG) program, a bridge program for foreign-trained pharmacists housed within the Faculty of Pharmacy at the University of Toronto.

Methods: In 2003, interview and focus group feedback data about IPG student and faculty perceptions of IPG instruction and curriculum was collected. Based on this data and literature detailing adult education methods, the self-care course was revised, employing a triad of pedagogical strategies including: collaborative learning projects, facilitated case study seminars, and role-playing over a 7 week period covering 9 self-care topics. On completion of the course, self-care participants filled out a quantitative survey, gauging perceived improvement within peripheral skills such as research, computer, collaboration, and communication skills. Participants also noted significant challenges with the course including intense workload and challenges in keeping up with the quantity of assignments.

Conclusions: This paper suggests that a three dimensional approach to self-care instruction is the most effective means of information acquisition for adult learners. These findings have implications for undergraduate and bridge program instruction within Pharmacy and other professional adult training programs.


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Background: An electronic portfolio (e-portfolio) is an electronic repository of critical reflections and artifacts (documentation) that allows students to demonstrate evidence of learning and competency in a number of areas.

Objective: To pilot test the use of e-portfolios as a learning and assessment tool for first year Pharmacy students in the new outcomes-based curriculum.

Methods: From the Faculty’s list of ability based outcomes, four general ability outcomes were selected as the focus for the first year. Students were introduced to e-portfolios during orientation week and developed their collection of artifacts over the year. A multi-course, year-end assignment will require students to submit a reflective statement and supporting artifacts to demonstrate their achievement of the selected outcomes. A grading rubric was developed for use by e-portfolio evaluators. A year-end survey will be used to gather information from students and assessors related to aspects such as ease of use of marking rubric and software, technical difficulties, and the perceived value of the e-portfolio for individual learning and skill development.

Results: The project has been implemented in four of the five required first year courses and is currently ongoing. Results of the year-end survey will be available in May 2004.

Conclusions: Results of the survey will be used to inform future use of e-portfolios by Pharmacy students.

Edu/Teach No. 4: Investigating the 'Future' of Pharmacy: the professional maturation and training of nascent pharmacists at one Canadian faculty of pharmacy

Jennifer D. Beales and Zubin Austin

Leslie Dan Faculty of Pharmacy, University of Toronto

To investigate how 4th year pharmacy students understand their professional training, future practice, and the profession, a survey and follow-up group interviews were conducted with a small sample of students (n=82) attending a prominent Canadian university. Students reflect on four years of schooling and data illustrate their perceptions of how they see their professional education and socialization. Findings suggest that there are significant gender and cultural differences among pharmacy students that influence interpretations of their professional training and future career aspirations. Gender is an important social variable that influences why students choose pharmacy and what they seek from the profession. Students’ perceptions of their professional training suggest that they are satisfied that they have acquired the necessary skills to practice pharmacy, yet doubt their competence within a practice setting. Moreover, students question their professional training, as their program emphasizes theoretical over practical courses. Thus, professional education instills competence yet may not adequately prepare students for the working world. Implications of the research are discussed in relation to the graduating students, pharmacy practice and other professions.

Edu/Teach No. 5: Investigating socio-cultural awareness in pharmacy curricula: The role of case examples

Jennifer D. Beales

Leslie Dan Faculty of Pharmacy, University of Toronto

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Edu/Teach No. 6: Evaluating First Year CAPS-I – Cases in Pharmaceutical Sciences: Educational successes and challenges

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In 2003/04, UBC implemented a new outcomes-based curriculum. One of the cornerstones of this curriculum is the four-year Cases in Pharmaceutical Sciences (CAPS) course stream. The goal of CAPS is to support students towards achieving the curriculum outcomes through the use of real-life cases. While CAPS promises the opportunity for rich and experiential learning, it remains an untested approach that warrants evaluation to corroborate its effectiveness in meeting its curriculum goals.

Objectives: 1) To evaluate the initial offering of CAPS-I to determine its success in achieving set objectives; 2) To gain both formative and summative insights into course improvements.

Method: Ongoing narrative evaluations were collecting from students throughout the year. Detailed November mid-term and April year-end evaluations assembled student self-reports on two views of 30 specific objectives: progress already achieved, and skills yet-to-be-acquired. Data were analyzed for both formative and summative course improvements.

Results: Student self-reports showed improvements in all 30 objectives; 20 of the ‘progress already achieved’ improvements were statistically significant (p<.05), as were eight of the ‘skills-yet-to-be-acquired’ objectives. Summed over all objectives, these pre-to-post changes represent a better than one-half sigma improvement ( = .567) for the ‘already achieved’ objectives ( = .93) and a quarter sigma improvement ( = .262) for the ‘yet-to-be-acquired’ skills ( = .95).

Conclusion: Evaluation of this first round of CAPS-I has achieved multiple goals for both student outcomes and course delivery strategies. Selected improvements were implemented into the routine course delivery methods as quickly as they were recognized, others will await integration over the summer by the CAPS-II course design team and in time for the second iteration of CAPS-I. Meanwhile, students report significant progress toward curriculum outcomes.

Edu/Teach No. 7: Characterization and analysis of direct observation forms completed by preceptors during final year experiential rotations

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Objectives: To characterize types and relative frequency of comments and summarize average ratings.

Methods: Using mid rotation (week 4) evaluations from the first rotation of 2003 (January-February), a random sample of 24 evaluation sets was selected: 12 community (C) and 12 institutional (I). OBS forms (10 per set) were analyzed to characterize the type of comments written by preceptors, and relative frequency, using a coding system adapted from Salerno et al in J Gen Intern Med 2003. The types of feedback in the C and I settings were compared, as was the number of feedback phrases written on each OBS. Other data included the overall rating (1 to 7) and correlation with the biweekly pharmaceutical care evaluation.

Results: Most of the 742 phrases were specific (84% in C, and 86% in I) versus (vs) general, and positive (64% in both C and I) vs corrective. Formative feedback related to skills (67% C, 60% I), knowledge (25% C, 30% I), and attitudes (6% C, 10% I). Summative phrases occurred only in 2% of C. The average OBS rating was 5.1 ± 0.5 for C and 5.3 ± 0.4 for I rotations. An average of 10.5 ± 1.1 forms were completed for C and 9.8 ± 1.3 for I rotations. Each form had an average of 3.0 ± 1.2 phrases (C), and 3.1 ± 1.4 (I). Correlation coefficient of OBS with biweekly ratings was 0.60.

Conclusions: The types and frequency of feedback inform and guide development of specific educational interventions for students and preceptors. The data also provide a baseline for further analysis, including comparison to other rotations or final week-8 feedback.

Edu/Teach No. 8: Experiences with collaborative practice among pharmacy and nutrition students assessing a standardized patient

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Study Objective: To determine student perceptions of participating in an interdisciplinary team-based patient assessment lab.

Methods: Participants consisted of 21 third year Nutrition students (100%) and 54 fourth year pharmacy students (73%). Groups consisted primarily of pharmacy-nutrition (PN) or pharmacy-pharmacy pairings (PP). Due to scheduling constraints, there were also two groups of three pharmacy students (PPP). Students completed a questionnaire relating to their experience at the end of the assessment lab. Analysis included frequency and comparative statistics. Comments arising from open-ended questions were collected into themes.

Results: Most students agreed or strongly agreed: the objectives of the lab were clear (74.3%); the lab objectives had been met (79.7%); they were able to obtain a sufficient range of information from the patient (75.7%); their partner’s knowledge and skills increased their ability to gather information (76.4%); it was easy to work together (90.5%); and working together was beneficial (89.2%). No significant differences were seen between PN and PP groups. Themes emerging from written comments included: the quality of the simulated practice setting; the scope of the patient interview; awareness of the role of another health profession; enhanced clinical knowledge; and interdisciplinary teamwork.

Discussion: The assessment lab’s collaborative approach was well received by the students, with most reporting a real benefit from working with another person. Comments indicated enthusiasm for the scenario and the opportunity to work with “real” patients, and a greater awareness of the benefits of working together. Conclusions: Working with another health discipline did not appear to affect the assessment lab experience. However, comments suggest students working with another discipline may gain in their appreciation for the contributions made by another health profession.

Edu/Teach No. 9: Feasibility of a web-based therapeutics course – a pilot evaluation
Edu/Teach No. 10: Pilot trial of online training of evidence-based practice within the pharmacy curriculum at the Université de Montréal

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Introduction: The strategic plan for the Doctor of Pharmacy program included the development of a part-time distance program. This program is intended to have the same academic rigor as the current full-time program. Currently small group tutorials are used to teach therapeutics. A pilot tutorial was developed and delivered using WebCT as the course management software.

Objectives: To evaluate the feasibility of conducting small group tutorials via WebCT. To determine the limitations and benefits of providing tutorials on-line

Methods: A tutorial from the full-time program was selected. Educational materials were developed using WebCT. The online tutorial was designed to mimic a current tutorial. Two groups participated in the pilot. Group 1 consisted of current full-time students. This group would be able to give feedback on how web-based learning compared to face-to-face. Group 2 consisted of graduates of the program. These individuals would comment on the feasibility of completing a tutorial on a part-time basis.

Results: Group 1 adapted well to the new format. Student’s learning was assessed via written assignment, documented comprehension and application of materials. Group 1 had minimal difficulties with WebCT. Group 2 encountered greater difficulties, mainly due to older computers and lack of orientation to WebCT. Group 2 also identified the need to have specific times set aside for coursework.

Conclusions: WebCT is suitable for delivering small group tutorials on-line. However, students of the distance part-time program have to have reasonable expectations of time requirements. It will also be necessary to orient students to the use of course management software and to provide support to address technology problems.

Edu/Teach No. 11: Re-structuring of pathophysiology and therapeutics in the Doctor of Pharmacy program

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Introduction: The two largest courses in the first year of the PharmD program were Pathophysiology and Therapeutics. These courses were coordinated and delivered separately. However the courses were fundamentally interrelated. Lectures from the pathophysiology course were used to provide a knowledge basis for the case-based tutorial sessions in therapeutics.

Objective: To integrate the pathophysiology and therapeutics courses to provide a coordinated approach for the problem-based learning process. To address workload issues in providing 432 hours of educational instruction.

Methods: Faculty met to determine how to integrate the courses. Content was reviewed for each course. Subject matter was clustered into disease-state themes. These themes were used as the basis to create Advanced Pharmacotherapy courses. Workload issues were evaluated.

Results: There were 36 pathophysiology lectures (108 hours) and 36 therapeutic tutorial cases (324 hours). The pathophysiology lectures were matched to each therapeutic case and grouped into the following themes: cardiology, infectious diseases (ID), neurology/psychiatry and general medicine. Each became a new course. Cardiology, ID and neurology/psychiatry each had 7 pathophysiology lectures and 7 corresponding therapeutic cases. General medicine had 15 different subjects; therefore it was divided into General Medicine

Corroboration of content in lectures and cases during classroom time was also included. Five modules were revised by a panel of students and pharmacists and implemented within the 1st and 2nd years of the curriculum. Baseline knowledge on EBP was assessed prior to accessing the content by an online anonymous survey. After completing the survey, students had a sequential access to the different modules and interactive activities. Knowledge and competency performance following completion of modules was evaluated through traditional examination.

Results: From the 340 students having access to the course, ninety percent of them (305/340) accessed the online content. Eighty-five percent of students (228/268) who completed the survey mention having heard of EBP, and believe it is important for their practice. However, only 8% (21/268) mention being at ease to retrieve clinical information on the web.

Conclusion: Several methods are currently used to implement EBP teaching within pharmacy curriculum. A longitudinal implementation of a web-based approach can be used to facilitate learning of EBP.
I (8 lectures and cases) and General Medicine 2 (7 lectures and cases). A clinical faculty member with a specialty practice in the content area coordinated each course, which allowed for a better focus on course content.

**Conclusion:** Combining Pathophysiology and Therapeutics established integration of course content. The courses are now coordinated by 5 faculty members rather than two, therefore, redistributing workload.

**Edu/Teach No. 13: An objective competency level-based method to assess student performance in experiential training.**

*Christopher J. Turner, Ralph Altiere, Larry Clark, Carrie Maffeo and Connie Valdez*

University of Colorado Health Sciences Center School of Pharmacy

**Objective:** To implement a competency-based assessment system in a sequence of three introductory pharmacy practice experience (IPPE) courses in a new entry-level Pharm.D. program.

**Method:** The University of Colorado Health Sciences Center School of Pharmacy implemented a sequence of three 2nd and 3rd year IPPE courses in its new entry-level Pharm.D. program. The primary component of each course is eight community pharmacy visits to conduct “OTC” counseling and health-promotion and disease prevention activities. Students are required to write statements that described their counseling activities, link each statement to an AACP Center for the Advancement of Pharmaceutical Education (CAPE) outcome-competency, and self-assess their level of competency. Each student, for selected CAPE competencies, must reach a pre-set number of competency statements graded as “exceeds” or “meets expectations” by the course directors to pass each course. Students with competency statements graded “below expectations” are asked to revise and re-submit their work or submit replacement statements. The work submitted by students in the first iterations of these courses was used by the course directors to establish required levels of performance for each competency in each course.

**Results:** For each course, multiple examples of competency statements graded “exceeds”, “meets” and “below expectations” were selected by the course directors to create rubrics that define levels of performance for the CAPE competencies. Thinking, Communication, Valuing and Ethical Decision Making, Social Interaction, and Provide Pharmaceutical Care.

**Conclusions:** A competency-based assessment system has been successfully introduced for a series of three IPPE courses in a new entry-level Pharm.D. program.

**Edu/Teach No. 14: The integrated laboratory network pilot project: a virtual approach to teaching pharmaceutical analysis**

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**Background:** The B.Sc.Pharm program at UBC includes a compulsory lecture-laboratory course in pharmaceutical analysis (enrollment: 137). One lecture topic, gas-liquid mass spectrometry (GCMS), has no corresponding laboratory as there is no GCMS instrument available for teaching purposes. Through a collaboration with WWU’s Integrated Laboratory Network (ILN), which connects laboratory, computer and instructional technology (two-way audio and video) through high-speed networks, pharmacy students at UBC used a GCMS instrument at WWU to gather data to solve an in-class case-study.

**Objective:** To pilot test the WWU ILN as a teaching tool in the pharmaceutical analysis course at UBC.

**Methods:** The pilot project took place during the last two lecture-blocks of the term (four hours). A case-study, involving drug profiling of a neurosurgery team, was developed focusing on qualitative and quantitative GCMS analysis. The WWU ILN.
was demonstrated in-class to generate additional data to complement the chromatographic and mass spectral data provided to students along with the case. A survey was used to gather impact data on the activity.

**Results:** The ILN pilot project was successfully completed. While students (response rate 85%) gave the activity an overall rating of “fair”, 70% of students felt it helped their learning about chromatography and mass spectrometry. Students commented that the pilot project helped them to learn general concepts, to integrate and visualize theory and practical applications of GCMS, and provided a good review. Approximately 10-15% of students felt the pilot project was not helpful preferring “hands-on” access to instrumentation to virtual access through the ILN.

**Conclusions:** The WWU ILN was pilot tested in a compulsory pharmaceutical analysis course providing access to scientific instrumentation not available to students at UBC. Impact data suggest that the ILN has the potential to support student learning.

**Edu/Teach No. 15: An interfaculty pain curriculum for health professional students: an evaluation**

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**Background:** Effective pain management requires health professionals to understand pain assessment and management and to have a commitment to work together. No models of an interfaculty pain curriculum for six health professions were found at the undergraduate level.

**Objective:** The University of Toronto Centre for the Study of Pain organized an Interfaculty Pain Curriculum Committee to develop, implement and evaluate an integrated pain curriculum for students from six Faculties. The evolving model has been implemented over two years.

**Methods:** Students from six disciplines participated in an integrated 20-hour pain curriculum in March 2002 (N=540) and 2003 (N=565). Learning occurred through presentations, panel patient, small group work and use of standardized patients or cases. Group work was facilitated by clinicians (N=63 2002, N=78 2003). Students were assessed in a pre- post-test design on knowledge and beliefs about pain and their understanding of interdisciplinary roles. A paired t-test was used to compare pre- & post-test student scores. Daily surveys were also completed.

**Results:** For 2002 and 2003, the change in correct scores from the pretest to the post-test was 17% and 16% respectively. The difference in the mean was 6.5 for 2002 and 6.7 for 2003 (p < 0.05 for both). Most responders (85%-95%) agreed or strongly agreed that the interfaculty pain curriculum was relevant and informative.

**Conclusion:** The interfaculty pain curriculum was effective in increasing students’ knowledge of pain assessment and management and their awareness of related health professional roles in both 2002 and 2003. This program is scheduled to be offered again in March 2004.

**PHARMACY PRACTICE RESEARCH**

**PPR No. 1: Evaluation of pharmacist practice in an interdisciplinary primary care team-based setting: Implications for pharmacy education**

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**Purpose:** To evaluate an innovative, functional prototype of pharmacist best-practice in an interdisciplinary primary care team. The goals were to conduct a process evaluation to characterize activities and functions that were needed to meet the needs of the team and explore processes and structures used by the pharmacist to contribute to collaborative medication management (CMM).

**Methods:** This study used mixed (quantitative and qualitative) methods: (a) a retrospective chart review of 105 patients to study the type of drug-related problems and their relationship to pharmacist’s role and pharmacist-physician collaboration; and (b) a grounded theory method to data collection and analysis of case scenarios of pharmacist’s involvement in patient cases to identify key categories, their properties, and relationships to the pharmacist’s role in CMM.

**Results:** The findings revealed that in addition to the philosophy of pharmaceutical care, there are six more principles that need to guide pharmacist practice in CMM. To contribute to CMM pharmacists will need to become competent to perform multiple functions that form a foundation for a repertoire of core expertise. A key finding was the characterization of a reflective approach that defines the nature of involvement and level of pharmacist responsibility in different patient situations which is an essential reflective competency that will need to be acquired by pharmacists if they are to integrate effectively into primary care teams.

**Conclusions:** There is large variability in the functions and the nature of involvement potentially required of a pharmacist in primary care, thus pharmacy students will need to become highly reflective practitioners competent to perform a wide repertoire of specific expanded patient care functions.

Parts of the results were previously presented: CSHP Professional Practice Conference, January 2004. Also parts of the study have been submitted for presentations as poster or oral presentation at the following conferences but results of the reviews are still pending: Qualitative Health Research Conference, April 2004; CPhA Annual Meeting, May 2004; Canadian College of Clinical Pharmacy Conference, June 2004.

**PPR No. 2: Involvement of a community pharmacist research network in evaluating outcomes of bisphosphonate therapy**
**PPR No. 3: Drug utilization review (DUR) for the treatment of asthma**

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Conseil du médicament, Direction du suivi et de l'utilisation optimale

**Background:** The appropriateness of inhaled β₂ agonists and leukotriene receptor antagonists (LRA) for the treatment of asthma in Québec was assessed and compared with the results of a first DUR. The initial use of a combined product, containing a long acting inhaled β₂ agonist (LA) [salmeterol] and an inhaled corticosteroid (IC) [fluticasone], in treating asthma was also documented.

**Methods:** This retrospective study using provincial database included subjects, aged 5 to 45, enrolled in the public drug insurance plan who received, in 2001, at least one prescription of short acting inhaled β₂ agonists (SA) or LA or LRA. Appropriateness of use was assessed according to criteria developed in consultation with a group of experts and based on the 2001 update of recommendations by the 1999 Canadian Consensus Conference on Asthma.

**Results:** Although there was a significant improvement in the percentages of appropriate frequency of use for SA in 2001 compared to 1997-1998 (41% vs 8%; p<0.01) and in the continued use of corticosteroids with LA (35% vs 15%; p<0.01), SA are still overused and IC are still underused. Use of LA and LRA was not optimal. Furthermore, the combined product was often used improperly: In the subjects who received this product for the first time, 68% had not received an IC and 42% had received neither an IC or SA for a period of at least 7 months prior to the first prescription.

**Conclusion:** Although an improvement was noted in some respects, utilization of main drugs for treating asthma is not optimal. The Conseil du médicament, in collaboration with many healthcare stakeholders, will suggest various strategies to promote better use of asthma therapy.

**PPR No. 4: The provision and reimbursement of home care services by community pharmacists in Canada**

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**Objectives:** A survey was done to determine the proportion of Canadian community pharmacists providing home care services; roles of community pharmacists in home care; types of patients currently reached; and barriers to providing these services.

**Methods:** The survey was mailed to a random sample of 406 Canadian community pharmacists, stratified by province. Follow-up contacts were made at two weeks and one month in order to maximize returns.

**Results:** The response rate was 49%. Most pharmacies (96%) sold one or more home care products (i.e. monitors, aids, parenterals) and 93% of these pharmacies provided patient training for these products. Only one-quarter (23%) of pharmacists were reimbursed for providing training. Most frequent services provided were compliance packaging, medication reviews, and providing therapeutic alternatives. Prevention/monitoring services were offered by three-quarters of pharmacists, with 34% in patients’ homes. Eighteen percent of the pharmacists were reimbursed for providing the above services and most often this was by 3rd party or patient payers. Eighty-one percent of these pharmacists said they spent at least 0.5% of their time each week providing home care.

**Conclusions:** While the majority of Canadian community pharmacists said they provide some sort of home care service, a much smaller proportion made home visits. Barriers to providing home care services included lack of reimbursement, time, lack of specialized training, shortages of pharmacists, legal issues, and paperwork. Ways of reducing these barriers need to be identified and implemented.
PPR No. 5: Pictographic instructions for medications: Do other cultures interpret them accurately?

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Background: Dispensing medication is a major service provided by the Canadian Forces’ humanitarian relief missions around the world, often taking place in developing countries. This study tested a set of sixteen pre-developed pictograms to determine whether they accurately communicated the written directions found on medication labels to ethnic respondents who neither speak nor read English, French or Spanish.

Objective: (1) To determine whether ethnically diverse individuals could understand the pictogram meanings without additional aids such as verbal instructions or explanations, and (2) to identify appropriate modifications to the pictograms to reduce interpretation errors.

Method: Both qualitative and quantitative methods evaluated the pictograms’ interpretability among three ethnic groups, Cantonese, Somali and Punjabi. Standard ANOVAs tested for differences due to ethnicity and other demographics.

Key Findings: Only four of the 16 initial pictograms tested were interpreted correctly by 80% of participants. Relaxing the criterion from 80% to 50% included eight more. Modifications to problem icon elements further improved interpretation accuracy levels by 22% for a ‘best-of-three’ tally of 67.15%. Quantity errors were twice as common as timing, administration route or auxiliary instruction errors.

Conclusions: Participants could identify particular pictographic symbols they found confusing or ambiguous. Basic education and time since immigration predicted interpretation accuracy better than ethnicity or any other demographic characteristic.

PPR No. 6: Community-based warfarin co-prescribing and point of care INR testing

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Background: Traditionally, hospital and community pharmacists have avoided warfarin management. The major problems are lack of warfarin expertise, subtherapeutic dosing, inconsistent lab monitoring, etc. For over 20 years, outpatient anticoagulation services have provided safe, effective care in the USA.

Methods: In November 2001, a community anticoagulation management program was implemented in BC at 2 London Drugs locations (Brentwood & Kerrisdale). The outpatient service was created to assist physicians with warfarin management. The program met the 12 Anticoagulation Forum Consensus Guidelines and the College of Pharmacists of BC’s approval.

Results: The service included training and certification of 10 anticoagulation pharmacist, warfarin co-prescribing, protocols, point-of-care INR testing (POCT), counseling rooms, physician referrals, etc. We created a mobile anticoagulation cart; patient chart (i.e. monitoring forms, warfarin dosing grid, progress notes, etc); a reference binder; cheat sheets; POCT INR log book; patient education materials, etc.

At each brief visit, the patient’s INR and daily warfarin dosage were determined. The finger stick method required only 1 drop of blood with the result ready in 2 minutes. The pharmacist co-prescribed and scheduled the patient’s next INR. Audits for safety and efficacy were completed in May 2002, September 2002 and December 2003. Satisfaction surveys were completed for patients, physicians and pharmacy staff with excellent feedback.

Conclusion: The London Drugs Anticoagulation Service with warfarin co-prescribing and point of care INR testing was safe, reliable, faster and more convenient for physicians and patients.

SOCIAL & ADMINISTRATIVE RESEARCH

Soc Admin No. 1: Hot on the Net: pharmaceutical policy/PDAs

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Purpose: Our goal was to make information on pharmaceutical policy, as well as personal digital assistants (PDAs), more accessible to those who need it. The objectives of this project were to: 1) identify journals and institutions publishing a significant number of articles on pharmaceutical policy as well as relevant websites; 2) identify PDA software websites with programs relevant to pharmacy practice; 3) create two new categories for Drug Information Resources: A Guide for Pharmacists (DIR) and; 4) present a talk to Dalhousie IMPART Drug Use Management and Policy Residents on the topic of pharmaceutical policy on the Internet.

Methods: To identify “hot journals” and “hot institutions”, six pharmaceutical policy areas were chosen and ideal names of pharmaceutical policy departments were devised. PubMed was searched using these names, limiting citations to English-language and those published in the past five years. Both journals and departments having less than 10 occurrences were rejected. Pharmaceutical policy websites were identified using Google® and by scanning relevant print publications. Articles on PDA drug- and pharmacy-related applications were reviewed to identify software programs, commercial and educational mega-websites and useful “how to do it” references.

Results: Thirteen “hot journals” and fourteen “hot institutions” in the area of pharmaceutical policy were identified. The new DIR pharmaceutical policy and PDA categories were uploaded to the Internet in June and September 2003, respectively. The
new DIR pharmaceutical policy category was presented to the IMPART Residents on June 24, 2003.

**Conclusion:** Pharmaceutical policy websites and journals and institutions publishing in this area were identified. PDA websites and useful journal articles relevant to pharmacy practice also were identified. As a result, two new categories were added to DIR.