PROCEEDINGS OF
THE INAUGURAL SYMPOSIUM OF AAPS,
CPU, FUDAN, NJU AND NUS

March 25, 2006 Saturday
Lecture Theatre of Level 2 of Zhi Xing Lou
Nanjing University, China
**Message from the Symposium Committee**

Welcome to the Inaugural Symposium of AAPS, CPU, Fudan, NJU and NUS!

AAPS (the American Association of Pharmaceutical Scientists) is a professional, scientific society of more than 12,000 members employed in academia, industry, government and other research institutes worldwide. The mission of AAPS is to serve the pharmaceutical sciences, promote the economic vitality of the pharmaceutical sciences and scientists, and represent scientific interests within academia, industry, government and other private and public institutions.

NUS (National University of Singapore) is one of the finest universities in the Asia-Pacific region, a comprehensive university offering a broad-based curriculum underscored by multi-disciplinary courses and cross-faculty enrichment. NUS has 13 faculties, with an enrollment of more than 22,000 undergraduate and 8,000 graduate students. NUS enjoys a close teaching-research nexus with 13 national-level, 12 university-level and more than 60 faculty-based research institutes and centers.

Fudan (Fudan University) and NJU (Nanjing University) are the top 10 universities in China. CPU (China Pharmaceutical University) is the leading university in pharmaceutical sciences in China.

The American Association of Pharmaceutical Scientists (AAPS) – National University of Singapore (NUS) Student Chapter is a non-profit student organization. AAPS-NUS Student Chapter aims to facilitate local student participation in the activities of AAPS and increase student awareness of career opportunities and latest advances and discoveries in the pharmaceutical sciences.

AAPS-NUS Student Chapter is the first student chapter in Asia while all the other established chapters are located in Canada, US and Mexico. Starting from 2005, three universities in China are in the progress of application to become official chapters of AAPS. They are AAPS-CPU Student Chapter, AAPS-Fudan Student Chapter and AAPS-NJU Student Chapter. It is important that they receive guidance from AAPS and share their application experiences. This symposium will provide an ideal opportunity to acquire necessary experiences of organizing regional conferences in Asia for AAPS student chapters, since such an event has yet no precedents in the history of AAPS. Furthermore, it will helpful for peers in pharmaceutical sciences to network with one another and to gain access to educational opportunities in various aspects of drug development and latest advances in pharmaceutical sciences.

Welcome, everyone! We hope this meeting is truly a memorable experience to all participants!

Regards,
Lifeng Kang, Chair of AAPS-NUS Student Chapter
On behalf of the Symposium Committee
Feng Zhi (NJU), Jie Feng (CPU), Tian Zhang (CPU) and Yaju Zhou (Fudan)
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0800-0900  Registration

0900-0915  Introduction by Prof Yiqiao Hu, School of Life Science, Nanjing University (NJU)

0915-0945  Skin lipid organization by Prof Joke A Bouwstra, Head of Leiden Amsterdam Center for Drug Research (LACDR), Leiden University

0945-1015  Pharmacy education and research at National University of Singapore, by Associate Prof Sui Yung Chan, Head of Dept of Pharmacy, National University of Singapore (NUS)

1015-1045  The roles of endogenous reactive oxygen species and nitric oxide in triptolide-induced apoptotic cell death in macrophages, by Prof Pingping Shen (NJU)

1045-1100  Rapid liquid chromatography/tandem mass spectrometry method for the determination of apomorphine in canine plasma and its pharmacokinetic studies, by Miss Yang Bei, Fudan University (Fudan)

1100-1115  A novel p-gp inhibitor, by Mr Feng Zhi (NJU)

1115-1130  Closing speech by Mr Lifeng Kang, Chair of AAPS-NUS Student Chapter.

1130-1330  Poster viewing
Podium Presentations
Skin lipid organization

JA Bouwstra, MW de Jager, GS Gooris, M Ponec.

Leiden/Amsterdam Center for Drug Research, Leiden University, The Netherlands

Lipid lamellae present in the outermost layer of the skin, the stratum corneum, form the main barrier for diffusion of molecules through the skin. Due to the exceptional stratum corneum lipid composition, with long chain ceramides, free fatty acids and cholesterol as the main lipid classes, their lipid phase behavior is different from that of other biological membranes. In stratum corneum, crystalline phases are predominantly present, but most probably a subpopulation of lipids also forms a liquid phase. Both the crystalline nature and the presence of a 13 nm lamellar phase are considered to be crucial for the skin barrier function. Recently X-ray diffraction was used to examine the organization in lipid mixtures prepared with synthetic ceramides with uniform chain length. The ceramides varied from each other in the acyl chain length and closely mimic the head group architecture of the ceramides in pig stratum corneum. The results show that mixtures of cholesterol, free fatty acids and synthetic ceramides closely resemble the lamellar and lateral stratum corneum lipid organization, both at room and elevated temperatures. Exclusion of several ceramide classes from the mixture does not affect the lipid organization. However, the head group architecture of acylceramides considerably affects the lipid organization. In conclusion, lipid mixtures prepared with well-defined synthetic ceramides offer an attractive tool to unravel the importance of molecular structure of individual ceramides on the lipid organization.
Pharmacy education and research at National University of Singapore

Sui Yung Chan, Dept of Pharmacy, National University of Singapore

The lecture will cover the history of the university, the pharmacy department, overview of our education philosophy, curriculum, graduate studies and research.
The roles of endogenous reactive oxygen species and nitric oxide in triptolide-induced apoptotic cell death in macrophages

Pingping Shen, School of Life Science, Nanjing University
Rapid liquid chromatography/tandem mass spectrometry method for the determination of apomorphine in canine plasma and its pharmacokinetic studies

Bei Yang, GL Duan

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Objective: Apomorphine is a potent dopamine receptor agonist used in the management of Parkinson’s disease, which requires repeated subcutaneous injection. Due to its low dosage and short duration time, a highly sensitive and rapid analytical technique is indispensable for its clinical and pharmacokinetic studies. In this study, a rapid and sensitive LC/MS/MS method was developed and validated for this purpose.

Method: The analytes were prepared using one-step liquid-liquid extraction and analyzed on a Waters Symmetry C18 column interfaced with triple quadrupole tandem mass spectrometer. A mixture of methanol-0.1% formic acid in water (70: 30, v/v) was employed as the isocratic mobile phase. Positive electrospray ionization was utilized as the ionization source. The analyte and internal standard clenbuterol were both detected by the use of multiple reaction monitoring (MRM) mode.

Results and Discussion: The method was linear in the concentration range of 0.1–100 ng/mL. The limit of detection (LOD) was 30 pg/mL. The intra- and inter-day relative standard deviations (RSDs) across the validation runs over the entire concentration range were less than 8.0%. The accuracy determined at three concentrations (0.1, 10 and 100 ng/mL for apomorphine) was within ±6.0% in terms of relative error. The described method was successfully applied to a pharmacokinetic study after intranasal administration of 0.5 mg apomorphine to 4 healthy beagle dogs.

Conclusions: In this study, for the first time we developed a LC-MS/MS method to determine the concentration of apomorphine in canine plasma. The determination of the sensitivity, precision, accuracy, selectivity, matrix effect, recovery, and stability in plasma samples and solutions demonstrated that the proposed method was successfully validated for routine use.
A novel p-gp inhibitor

Feng Zhi, School of Life Science, Nanjing University
Posters
Structure-based 3D-QSAR studies on thiazoles as 5-HT$_3$ receptor antagonists

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Structure-based 3D-QSAR studies were performed on 20 thiazoles against their binding affinities to 5-HT$_3$ receptor with comparative molecular field analysis (CoMFA) and comparative molecular similarity indices analysis (CoMSIA). The thiazoles were initially docked into the binding pocket of a human 5-HT3A receptor homology model, constructed on the basis of the crystal structure of the snail acetylcholine binding protein (AChBP), using GOLD program. The docked conformations were then extracted and used to build the 3D-QSAR models, with cross-validated $r^2$ cv values 0.785 and 0.744 for CoMFA and CoMSIA respectively. Additional 5 molecules were used to further validate the models, giving satisfactory predictive $r^2$ values of 0.582 and 0.804 for CoMFA and CoMSIA, respectively. The results would be helpful for the discovery of new potent and selective 5-HT3 receptor antagonists.
Simultaneous determination of the contents of three stilbene oligomers in *Caragana sinica* collected in different seasons using an improved HPLC method

N Shu, H Zhou, and CQ Hu
Department of chemistry of Natural Drugs, School of Pharmacy, Fudan University, Shanghai, China

**Objective** To determine simultaneously the contents of two stilbene tetramers, carasinol B (1) and kobophenol A (2), and one stilbene trimer, (+)-á-viniferin (3), in the roots, tubers, and leaves of *Caragana sinica* in various seasons.

**Methods:** Quantitative analyses were performed on an Agilent 1100 series chromatography system (Agilent Tech, Germany) with a photodiode array detector (DAD). An ODS-2 RP-C18 column (150 × 4.6 mm, 5im) (Thermo Electron Corp, UK) was used with column temperature set at 30 Ž. The mobile phase was a mixture of methanol/acetonitrile-buffer (16.2:12.8:71.0) (v/v/v) at a flow rate of 1.0 mL/min. The pH value of the buffer was 4.50. The detection wavelength was set at 284 nm. The injection volume was 20 ìL

**Results:** Using this method, different samples of *Caragana sinica* were evaluated. The results showed that the contents of 1, 2, and 3 in the roots were much higher than those in the tubers, and the contents of stilbene tetramers were maximal in winter while the contents of the stilbene trimer were maximal in summer. Compounds 1, 2, and 3 could not be detected in the flowers of *Caragana sinica* in our detection ranges.
Stability of haloperidol in SMGA gels

T Toh, L Kang and SY Chan
Department of Pharmacy, Faculty of Science, National University of Singapore,

**Objective**: Stability of haloperidol in ISA-based SMGA gel when exposed to stress condition of temperature and light was investigated in this short-term stability study, with the aim and objective to identify the degradation kinetic model; to determine a tentative expiry date and an overview of it photostability profile.

**Method**: Sample of gel used for study consisted of haloperidol, and GP-1 in the concentration of 0.003% w/v and 5 %w/v respectively, dissolved in ISA under heat. For temperature study, triplicates of the samples were stored in temperature 60, 70, 80 and 90 °C (± 2 °C). Content of haloperidol were assayed using HPLC and expressed relative to content of haloperidol in samples stored at 5 °C. The data were then fitted to zero- and first-order degradation kinetic models and the adequacy of the model was evaluated through lack-of-fit test. Determination of tentative expiry period was made through the application of Arrhenius equation. For light study, triplicates of samples with thickness maintained at 25 mm were exposed to white fluorescent light; change in content haloperidol with time was compared with that of samples protected from light.

**Results and discussion**: Degradation of haloperidol in ISA-based gel under effect of temperature followed first-order kinetic reaction and determination of tentative expiry date from data from temperature stress study was not possible due to the inadequacy of the Arrehnius equation in describing the relationship of inverse of temperature and logarithm of degradation rate constant. Photostability study indicated that the translucent appearance of the gel did not confer extra stability to haloperidol against photodegradation.

**Conclusion**: The study can served as prior information for a better study design such that the tentative expiry period of haloperidol can be determined. Furthermore, the thermal stability profile of the drug in such system provides an indication that drug loss might be incurred even during the making of drug-gel preparation; hence a revisit to steps in the making might be essential to find the optimum conditions for the making of the preparation. No extra photostability is conferred to the drug by the gel appearance indicating that protection against light is essential to prevent drug loss through photodegradation.
Announcing the 2nd Joint Symposium

The venue for the 2nd Joint Symposium is expected to be at Fudan in 2007. Please check the AAPS-NUS Student Chapter web pages for updates. http://www.pharmacy.nus.edu.sg/asc
For inquiry, please contact Yaju Zhou (Email: 042103117@fudan.edu.cn School of Pharmacy, Fudan University).