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ANTIFUNGAL, ANTIVIRAL AND ANTIRETROVIRAL

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SESSION CHAIR : **DR. BHASWAT CHAKRABORTY**
Sr. Vice President, R&D, Cadila Pharmaceuticals, India

SESSION CO-CHAIR: DR. JOON MYONG SONG
Associate Professor, College of Pharmacy
Seoul National University, South Korea

SESSION INTRODUCTION

TITLE: THERAPEUTIC DRUG MONITORING OF ANTI-RETROVIRAL DRUGS

DR. BHASWAT CHAKRABORTY, Sr. Vice President, R&D, Cadila Pharmaceuticals, India

TITLE: MATRIX EFFECTS, A MAJOR CONCERN DURING LC-MS/MS BIO-ANALYSIS

DR. CHINMOY GHOSH, Cadila Pharmaceuticals Limited, India

TITLE: ANTIBACTERIAL METALLOPHARMACEUTICALS: INTO THE NANOSCALE REGIME OF SILVER

DR. JOON MYONG SONG, Associate Professor, College of Pharmacy, Seoul National University, South Korea

TITLE: OCULAR PHARMACOKINETICS OF ANTIVIRAL NANOFORMULATIONS BY ULTRA HIGH-PRESSURE LIQUID CHROMATOGRAPHIC METHOD

DR. SOHAIL AKHTER, Department of Pharmaceutics, F/O Pharmacy, Hamdard University, India

COFFEE BREAK & POSTER SESSION

TITLE: NEGLECTED TROPICAL DISEASE MANAGEMENT: PROBLEMS AND PROSPECTS

DR. SUNIT K. SINGH, Laboratory of Neurovirology and Inflammation Biology, Centre for Cellular and Molecular Biology (CCMB), India

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Therapeutic Drug Monitoring of Anti-Retroviral Drugs

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Most current highly active antiretroviral therapy (HAART) regimens for HIV-positive patients contain two nucleoside reverse transcriptase inhibitors (NRTIs) with either a Protease inhibitor (PIs) or a non-nucleoside reverse transcriptase inhibitors (NNRTI). Notwithstanding the regulatory guidelines recommending therapeutic drug monitoring (TDM) for these drugs, therapeutic failure is a very serious concern implying drug induced toxicity and more importantly viral rebound and viral resistance.

Single dose, steady state and dose ranging studies have all more or less demonstrated that there is a positive correlation between plasma concentrations and therapeutic effects of anti-retrovirals (ARVs). However, one of the main challenges still seems to be the target concentrations for these drugs and their relevant inhibitory quotient. In this talk, we are going to examine these issues along with bioanalytical challenges, drug-effect and drug–toxicity relationships and finally drug-drug interactions within different HAART regimes.

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Matrix Effects, a Major Concern During LC-MS/MS Bio-analysis

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In LC-MS/ MS bio-analysis matrix effects influencing the ionization process are a major concern with respect to the quality of the results obtained. Matrix effects and selectivity issues have long been associated with bioanalytical techniques. A number of approaches have been investigated to improve the reproducibility and robustness of LC-MS/ MS methods that are subjected to matrix effect. In general such matrix effects are directly related to an insufficient sample clean-up of the biofluids. Phospholipids are known to cause matrix ionization effects during the analysis of biological samples (i.e. blood, plasma, urine etc.) in LC-MS/ MS. However the high incidence of matrix effects in liquid chromatographic tandem mass spectrometric (LC-MS/ MS) methods help to a greater understanding of the factors which contribute to these effects. There are qualitative and quantitative ways to determine matrix effects. Matrix effect is mainly determined in terms of ion suppression or enhancement. Post column infusion technique is very popular for qualitative analysis of matrix effects. Whereas, for quantitative determination of matrix effects more than one techniques are available, among them determination of matrix factor and calculating the precession and accuracy of quality control samples are widely used. Among many factors, some of the causes of matrix effects are presence of endogenous compounds i.e. different phospholipids, inefficient chromatographic conditions, ionization polarity, ionization source design, ionization technique i.e. ESI/ APCI, presence of exogenous materials, presence of anticoagulants etc plays an important role. So to remove or minimize the matrix effects the above mentioned factors should be optimized.

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Antibacterial Metallopharmaceuticals: Into the Nanoscale Regime of Silver

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Bacterial resistance towards to common antibiotics, results development of antibacterial metallopharmaceuticals (silver nanoparticles) (AgNP). AgNPs of different shapes were synthesized by solution phase routes, and their interactions with *E.coli* were studied. The antibacterial activity of silver compounds loaded on porous host matrices are evaluated under short contact time where in the bacterial load was exposed not directly to the metal-loaded material but to distilled water pretreated with them, was mainly attributed to generation of reactive oxygen species (ROS). In this work we first investigated the shape dependence of the antibacterial activity of silver nanoparticles. We also developed highly antibacterial porous carbon matrices supporting nano-silver by simple and cost effective way. EFTEM micrographs of the bacterial cells showed considerable changes in the cell membranes upon AgNP-treatment.

Truncated triangular silver nanoplates with a {111} lattice plane as the basal plane displayed the strongest biocidal action compared with spherical, rod shaped nanoparticles or with silver ions. Nanocrystalline silver-supported carbon composite was fabricated by directly loading AgNPs into the porous host matrix from a preformed nanosilver hydrosol. The method eliminates the high temperature decomposition step, thereby minimizing the possibilities of formation of larger silver particles. XRD calculation indicated the presence of Ag crystallites in nanometer range; silver nanoparticle hydrosol-treated composite having the finest crystallite size (<14.4 nm). Ag crystals coalesced significantly with increasing temperature resulting in much larger particle size in thermally impregnated silver-carbon composites. The results demonstrate for the first time that silver nanoparticles undergo a shape dependent interaction with bacteria.

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Ocular Pharmacokinetics of Antiviral Nanoformulations by Ultra High-pressure Liquid Chromatographic Method

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The present work describes a rapid and sensitive advance liquid chromatographic technique, *ultra high-pressure liquid chromatography (UHPLC) method* with UV detection to quantify antiviral drug ganciclovir (GCV) in rabbit aqueous humor. After deproteinisation with acetonitrile, gradient separation of GCV was achieved on a Waters Acquity BEH C18 (50 mm x 2.1 mm, 1.7 µm) column at 50°C. The mobile phase consisted of 0.1% trifluoroacetic acid in water (pH 3.5) and acetonitrile (95:5, v/v) at a flow rate of 0.45 mL/min. GCV analysis was performed at a wavelength of 254 nm with total run time of 3 min. Method was found to be selective, linear (r^2 = 0.999), accurate (recovery, 97.0–100.2%) and precise (CV, ≤ 3.1%) in the selected concentration range of 0.1–1.0 µg/mL. Detection and quantitation limit of GCV in aqueous humor were 3.0 and 10.0 ng/mL, respectively. The method was applied to compare aqueous humor levels of GCV after single topical instillation of GCV solution, GCV nanoparticles, GCV nanocomplexes and GCV niosomal dispersions. Topical instillation of GCV-NCs ($AUC_{0\rightarrow t}$, 3440.7±26.2 ng.hr/mL) and GCV-NDs ($AUC_{0\rightarrow t}$, 3380.5±29.3 ng.hr/mL) provided approximately 5 fold increase in the relative ocular bioavailability compared with GCV solution ($AUC_{0\rightarrow t}$, 650.8±14.9 ng.h/mL) and nearly 2.5 fold higher than the GCV-NPs ($AUC_{0\rightarrow t}$, 1350.2±18.5 ng.h/mL). The results indicate that the nanocomplexes and niosomal dispersions increases ocular bioavailability of GCV and prolong its residence time in the eye.

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Neglected Tropical Disease Management: Problems and Prospects

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Neglected tropical diseases represent one of the most serious burdens to public health. Many of these diseases can be treated cost-effectively, but most of them could not attract the attention of policy makers associated with global health policy formulations. The 13 parasitic and bacterial infections known as the neglected tropical diseases include three soil-transmitted helminth infections (ascariasis, hookworm infection, and trichuriasis), lymphatic filariasis, onchocerciasis, dracunculiasis, schistosomiasis, Chagas' disease, human African trypanosomiasis, leishmaniasis, Buruli ulcer, leprosy, and trachoma. An expanded list could include dengue fever, Japanese Encephalitis, Chikungunya, treponematoses, leptospirosis, strongyloidiasis, foodborne trematodiases, neurocysticercosis, and scabies, as well as other tropical infections. Polyparasitism has become very common rather than the exception in many under developed and developing countries. It has been reported that a large number of individuals harbor three or more parasites in remote areas of Sub-Saharan Africa, due to lack of adequate facilities of health and hygiene. Co-infection with malaria and HIV has recently been reported as a source of increased severity of both of these diseases in sub-Saharan Africa. Scientific literature focused on co-infection with diverse combinations of helminths, HIV, malaria, and tuberculosis is growing tremendously. Neglected tropical diseases have been ignored for a long time due to the negligence of health policymakers at national, regional, and global levels. During the past few years, several research and development agencies have shown their interest and started supporting the programs related to control of neglected tropical diseases. There is a need of concerted effort to face the challenges associated with diversity of disease control approaches and health policy structures-both nationally and internationally in controlling neglected tropical diseases.