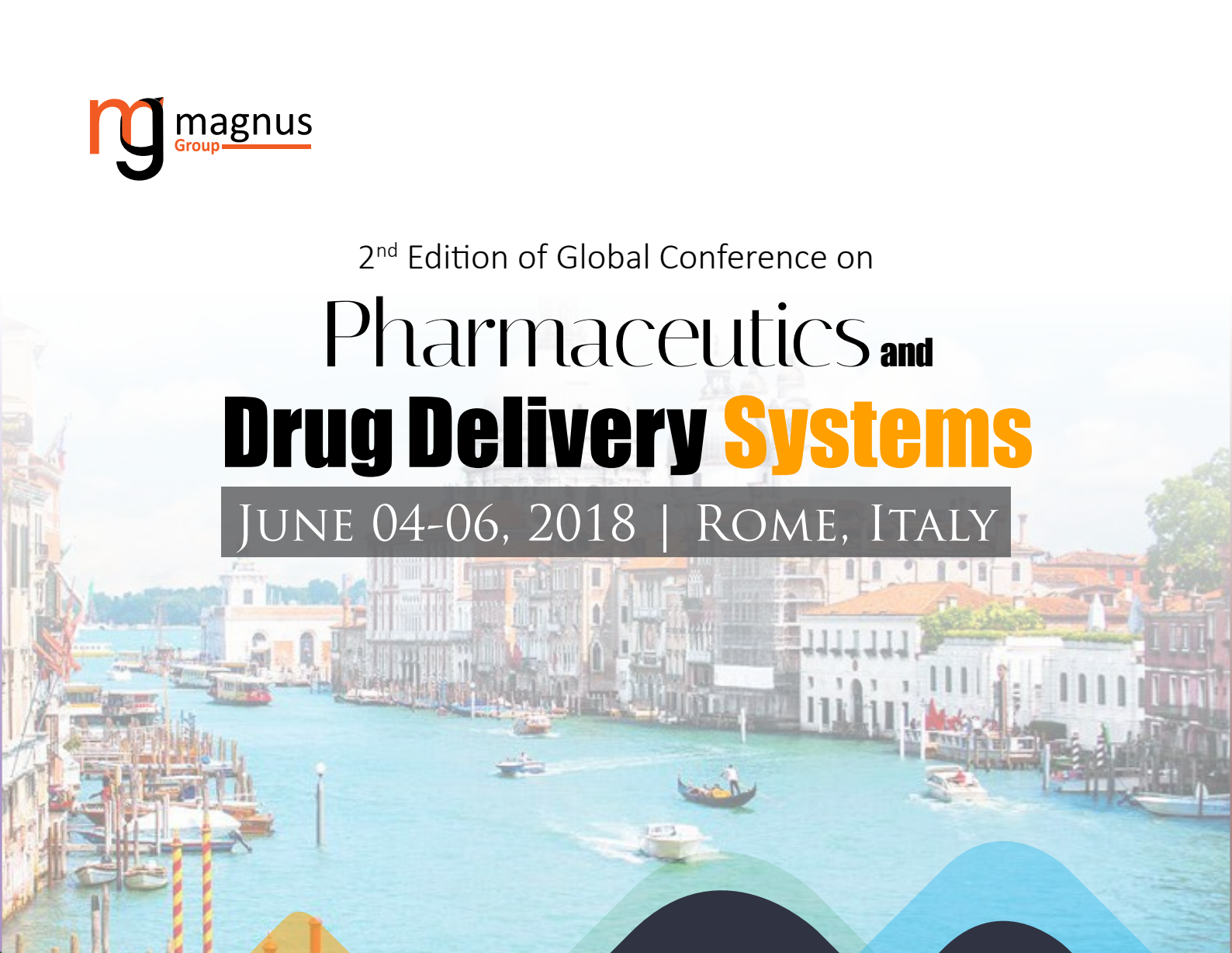
magnus Group

2nd Edition of Global Conference on

Pharmaceutics and Drug Delivery Systems

June 04-06, 2018 | Rome, Italy



PDDS 2018

The multifaceted aspects of drug delivery

VENUE

Holiday Inn Rome Aurelia
Via Aurelia, Km 8.400, 00165
Rome, Italy

https://pharmaceuticsconference.com

Presenters

Ana Carolina Kogawa
Universidade Estadual Paulista – UNESP, Brazil

Ali Dehshahri
Shiraz University of Medical Sciences
Iran

Anayanti Arianto
University of Sumatera Utara
Indonesia

Attila Gacsi
University of Szeged
Hungary

Biana Godin
Houston Methodist Research Institute, USA

Chaodong Wu
Texas A&M University
USA

Csaba Hetenyi
University of Pecs
Hungary

Daniel Zucker
NOF Europe GmbH
Germany

El Hassane Larhrib
University of Huddersfield
UK

Elaine Frances Enright
University College Cork
Ireland

Enise Ece Gurdal
Yeditepe University
Turkey

Esmaiel Jabbari
University of South Carolina
USA

Eugenia V. Gurevich
Vanderbilt University
USA

Faiza Naseer
University of Huddersfield
UK

Georgina Kate Such
University of Melbourne
Australia

Gerald H Tomkin
Beacon Hospital and Trinity College Dublin, Ireland

Gerhard Winter
LMU Munchen
Germany

Gillian Hutcheon
Liverpool John Moores University, UK

Guo-Ping Zhou
Guangxi Academy of Sciences
China

Hadrien Calmet
Barcelona Supercomputing Center (BSC-CNS), Spain

Hakim Bangun
University of Sumatera Utara
Indonesia

Hassan Saeiahan
Iran University of Medical science, Iran

Hemant K. S. Yadav
RAK Medical & Health Science University, UAE

Hyung Jun Ahn
Korea Institute of Sceince and Technology, Republic of Korea

Ilya Yakavets
Universite de Lorraine
France

Irina Ermolina
De Montfort University School of Pharmacy, UK

Jeong Kyu Bang
Korea Basic Science Institute
Republic of Korea

Joanna Jaworska
Polish Academy of Sciences
Poland

Joe E. Springer
University of Kentucky
USA

K.V.R.N.S.Ramesh
RAK Medical & Health Sciences University, UAE

Presenters

PDDS 2018

Katarzyna Jelonek
Polish Academy of Sciences
Poland

Kira Astakhova
Technical University of
Denmark, Denmark

Ivana Hrebickova
Charles University
Czech Republic

Lourdes Amable Vega Rasgado
Escuela Nacional de Ciencias
Biológicas del Instituto
Politecnico Nacional, Mexico

Luis Jesus Villarreal Gomez
Universidad Autónoma de
Baja California, Mexico

Marc Du Jardin
Janssen
Belgium

Marcelle Machluf
Technion – Israel Institute of
Technology, Israel

Marcelo Nacucchio
University of Buenos Aires
Argentina

Mario Jug
University of Zagreb
Croatia

Matej Dobravc Verbic
University Medical Centre
Ljubljana, Slovenia

Maya Bar-Zeev
Technion – Israel Institute of
Technology, Israel

Mehrdad Azarmi Aghajan
Shahid Beheshti University
Iran

Michal Abrahamowicz
McGill University
Canada

Mikhail V. Khvostov
N.N. Vorozhtsov Institute of
Organic Chemistry SB RAS
Russia

Mino R. Caira
University of Cape Town
South Africa

Monika Eniko Balint
University of Pecs
Hungary

Nataliya Storozhylova
University of Santiago de
Compostela, Spain

Natassa Pippa
University of Athens
Greece

Pawel Brzuzan
University of Warmia and
Mazury in Olsztyn, Poland

Prashant G. Upadhaya
Institute of Chemical
Technology, India

Yulia Svenskaya
Saratov State University
Russia

Selene Baschieri
ENEA
Italy

Sergey Bachurin
Russian Academy of Sciences
Russia

Takahisa Yamamoto
National Institute of
Technology, Gifu College, Japan

Tatyana V. Leshina
Voevodsky Institute of Chemichal
Kinetics & Combustion SB RAS
Russia

Tomasz Osmalek
Poznan University of
Medical Sciences (PUMS),
Poland

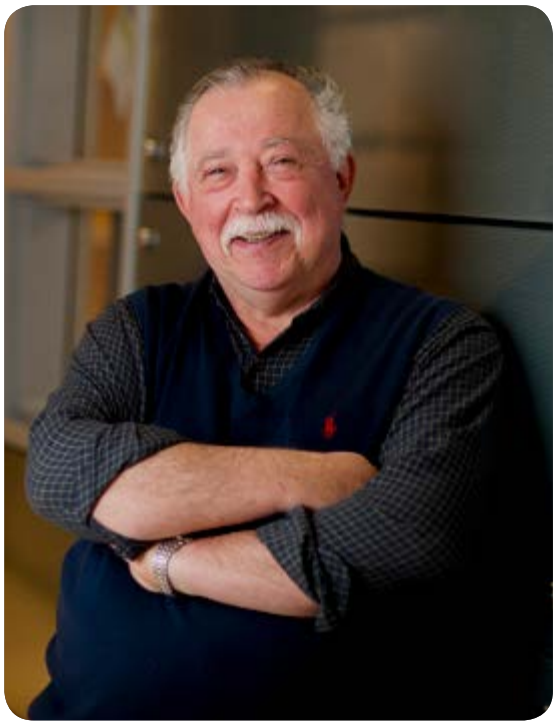
Ursula Thevarajah
University of
Huddersfield, UK

Vandana B. Patravale
Institute of Chemical
Technology
India

Vladimir Muzykantov
University of Pennsylvania
USA

Vladimir P. Torchilin
Northeastern University
USA

Welcome Message



Dear participants of PDDS 2018!

Welcome to Rome, Italy, to participate in 2nd Edition of Global Conference on Pharmaceutics and Drug Delivery Systems 2018!

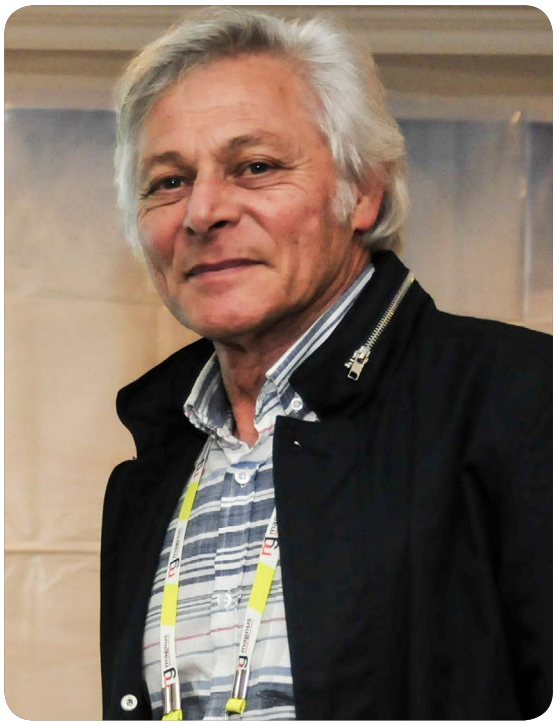
PDDS 2018 should serve as a platform for the interaction between experts in the areas of biotechnology, nanotechnology, nanomedicine, pharmaceutics, and drug delivery around the world and aims in sharing some unique research and translational studies on various advances in the related fields. The conference opens the doors for many researchers, clinicians, and industry representatives working in these exciting areas. It is expected to bring together both reputable scientists in advanced stages of their career and young researches from many related disciplines. The conference expects many new ideas to emerge at the interfaces between disciplines aiming to solve the most important problems relating to the health and wellbeing of the humanity.

The conference will take place in Rome, one of the greatest world cities, an important site for pharmaceutical science and industry and just a great place to visit.

With our warmest regards, the Organizing Committee of the PDDS 2018 wishes you the most productive work and the most pleasant stay in beautiful Rome.

Professor Vladimir P. Torchilin
University Distinguished Professor
Director, Center for Pharmaceutical Biotechnology and Nanomedicine
Northeastern University, USA

Welcome Message



Following the very successful Global Conference on Pharmaceutics and Drug Delivery Systems (PDDS 2017) held in Valencia, Spain last year, the Magnus Group warmly welcomes you to participate at PDDS 2018, the second edition of this event, which will be held in Rome, Italy during 04-06 June 2018.

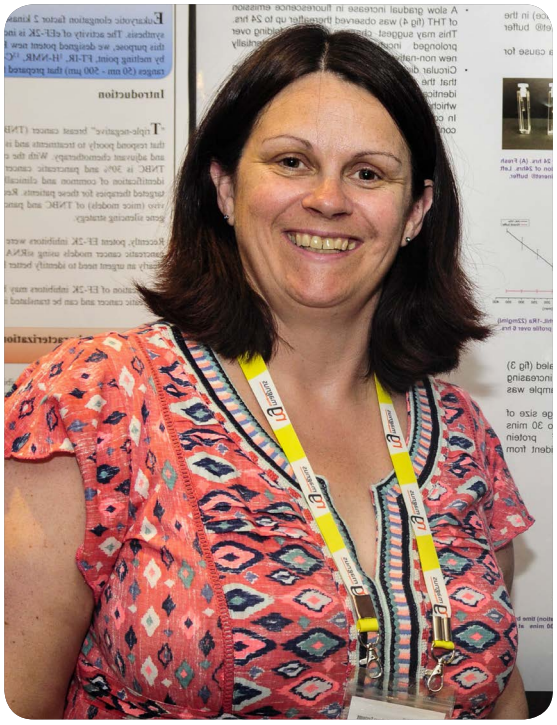
The growing urgency for the development of new medicinal agents and ensuring their efficient delivery continues to be a major concern of worldwide relevance. At this conference, renowned specialists in the fields of Pharmaceutics and Drug Delivery systems will assemble to share their multi-faceted expertise with the audience by presenting accounts of wide-ranging studies that reflect current and possible future strategies for addressing the serious challenges encountered in these disciplines.

This event will provide an excellent opportunity for participants to keep abreast with new developments in the field, engage in discussions of topics of mutual interest and forge new professional relationships and collaborations.

Your attendance at PDDS 2018 should be a rewarding experience and we look forward to welcoming you in Rome!

Professor Mino R Caira
Emeritus Professor
Senior Research Scholar
Department of Chemistry
University of Cape Town, South Africa

Welcome Message



As a member of the scientific committee, I cordially invite you to participate in the '2nd Edition of Global Conference on Pharmaceutics and Drug Delivery Systems' during June 4th – 6th in Rome, Italy.

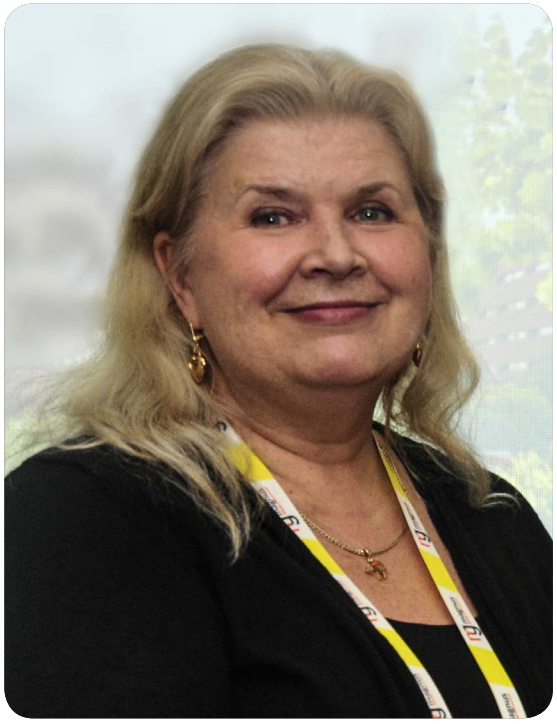
Conference (PDDS 2018) topics include pharmaceutics, drug delivery and development of healthcare products. I will be presenting a keynote lecture on the delivery of peptides to the brain for migraine treatment and chairing sessions on 'Biodrugs, Biomolecules and Therapeutics' and 'Therapeutic drug carrier systems'. This meeting will also provide you a great opportunity to share ideas, knowledge, and network with other scientists from a wide variety of disciplines.

I look forward to seeing you in Rome.

Gillian Hutcheon

Dr. Gillian Hutcheon
Head of Institute of Health Research
Liverpool John Moores University, UK

Welcome Message



On behalf of the Magnus Group and organizing committee, we would like to cordially invite you to participate in the "2nd Edition of the Global Conference on Pharmaceutics and Drug Delivery Systems" (PDDS 2018) taking place Monday June 4 through Wednesday June 6, 2018 at Holiday Rome Aurelia in Rome, Italy.

The PDDS 2018 conference is an opportunity for researchers in academia and industry from around the world to discuss critical issues in the field of pharmaceutics and drug delivery systems. With its strong emphasis on innovative approaches, the conference offers a chance for scientists and physicians working in different areas of drug development to learn of the new ideas that could help them advance their own research. The conference provides just the right setting to establish fruitful collaborations with the colleagues with similar research interests and complementary expertise.

We look forward to seeing you in Rome, Italy!

Eugenia V. Gurevich, Ph.D.
Associate Professor of Pharmacology
Vanderbilt University, USA

keynote speakers

Vladimir P. Torchilin
Northeastern University
USA

Esmaiel Jabbari
University of South Carolina
USA

Vladimir Muzykantov
University of Pennsylvania the
Perelman School of Medicine, USA

Joe E. Springer
University of Kentucky
USA

Eugenia V. Gurevich
Vanderbilt University
USA

Mino R. Caira
University of Cape Town
South Africa

Gillian Hutcheon
Liverpool John Moores
University, UK

El Hassane Larhrib
University of Huddersfield
UK

Michal Abrahamowicz
McGill University
Canada

About MAGNUS GROUP

Magnus Group (MG) is initiated to meet a need and to pursue collective goals of the scientific community specifically focusing in the field of Sciences, Engineering and technology to endorse exchanging of the ideas & knowledge which facilitate the collaboration between the scientists, academicians and researchers of same field or interdisciplinary research. Magnus group is proficient in organizing conferences, meetings, seminars and workshops with the ingenious and peerless speakers throughout the world providing you and your organization with broad range of networking opportunities to globalize your research and create your own identity. Our conference and workshops can be well titled as 'ocean of knowledge' where you can sail your boat and pick the pearls, leading the way for innovative research and strategies empowering the strength by overwhelming the complications associated with in the respective fields.

Participation from 80 different countries and 688 different Universities have contributed to the success of our conferences. Our first International Conference was organized on Oncology and Radiology (ICOR) in Dubai, UAE. Our conferences usually run for 2-3 days completely covering Keynote & Oral sessions along with workshops and poster presentations. Our organization runs promptly with dedicated and proficient employees' managing different conferences throughout the world, without compromising service and quality.

About PDDS 2018

PDDS 2018 will bring together a collection of investigators who are at the forefront of their field and will provide opportunities for junior scientists and graduate students to interactively present their work and exchange ideas with established senior scientists. It is an assemblage of scientists and research professionals in the field of Pharmaceutics and Drug Delivery systems.

PDDS is designed to assist fellow researchers by reviewing current practice and policies while disseminating examples of successful innovation. It is a great platform for top researchers, experts and thinkers in academia, industry, and government from around the world to exchange ideas on number of critical topics in the field.

Our expert honorary speakers will provide you with the most clinically up-to-date relevant information, you'll leave better educated and more invigorated than you thought possible.

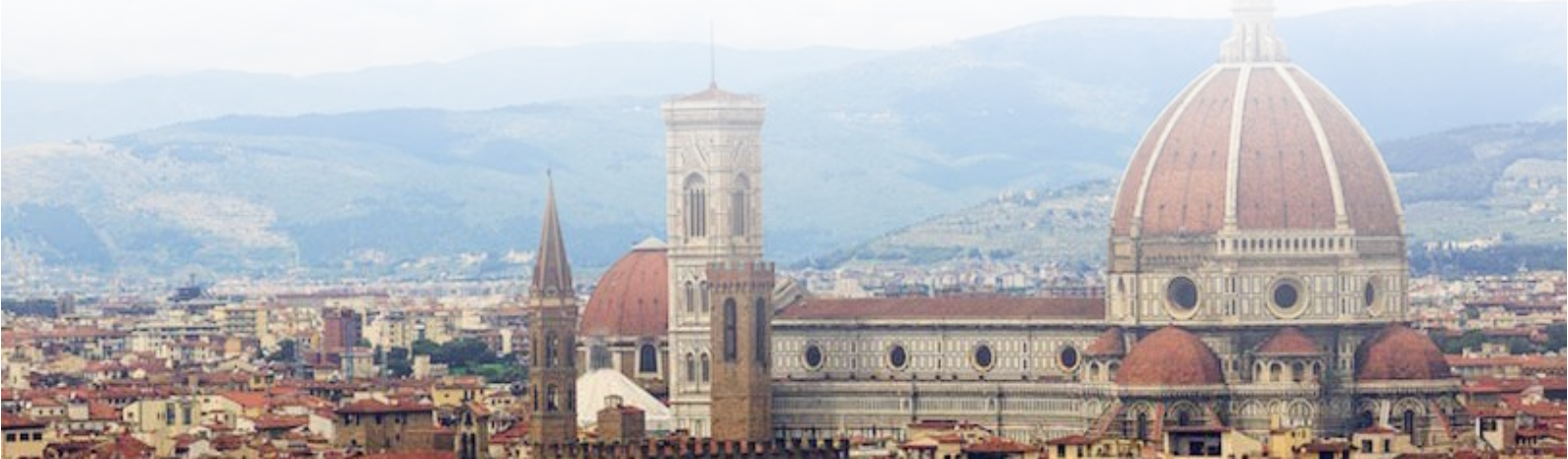


TABLE OF CONTENTS

magnus Group

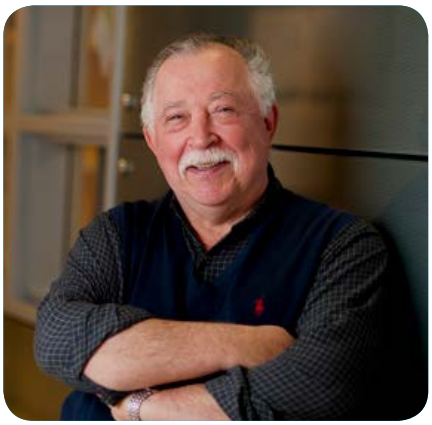
DAY 1

KEYNOTE FORUM

2ND EDITION OF GLOBAL CONFERENCE ON

Pharmaceutics and Drug Delivery Systems

JUNE 04-06, 2018
ROME, ITALY



Biography

Vladimir P. Torchilin, Ph.D., D.Sc. is a University Distinguished Professor of Pharmaceutical Sciences and Director, Center for Pharmaceutical Biotechnology and Nanomedicine, Northeastern University, Boston. His interests include drug delivery and targeting, nanomedicine, multifunctional and stimuli-sensitive pharmaceutical nanocarriers, biomedical polymers, experimental cancer therapy. He has published more than 400 original papers, more than 150 reviews and book chapters, wrote and edited 12 books, and holds more than 40 patents. Google Scholar shows more than 53,000 citations of his papers with H-index of 103. He is Editor-in-Chief of Current Drug Discovery Technologies, Drug Delivery, and OpenNano, Co-Editor of Current Pharmaceutical Biotechnology and on the Editorial Boards of many other journals. He received more than $30 M from the governmental and industrial sources in research funding. He has multiple honors and awards and in 2011, Times Higher Education ranked him number 2 among top world scientists in pharmacology for the period of 2000-2010.

Next generation of drug delivery system: Stimuli-sensitive combination nanopreparations

Vladimir P. Torchilin, Ph.D., DSc

Northeastern University, USA

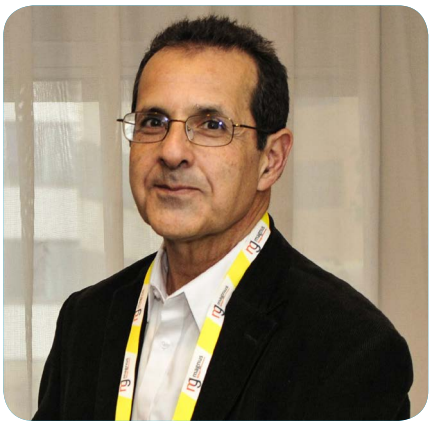
Tumor therapy, especially in the case of multidrug resistant cancers, could be significantly enhanced by using siRNA down-regulating the production of proteins, which are involved in cancer cell resistance, such as Pgp or survivin. Even better response could be achieved is such siRNA could be delivered to tumors together with chemotherapeutic agent. This task is complicated by low stability of siRNA in biological surrounding. Thus, the delivery system should simultaneously protect siRNA from degradation. We have developed several types of lipid-core polymeric micelles based on PEG-phospholipid or PEI-phospholipid conjugates, which are biologically inert, demonstrate prolonged circulation in the blood and can firmly bind non-modified or reversibly-modified siRNA. Additionally, these nanopreparations can be loaded into their lipidic core with poorly water soluble chemotherapeutic agents, such as paclitaxel or camptothecin. In experiments with cancer cell monolayers, cancer cell 3D spheroids, and in animals with implanted tumors, it was shown that such co-loaded preparations can significantly down-regulate target proteins in cancer cells, enhance drug activity, and reverse multidrug resistance.

In order to specifically unload such nanopreparations inside tumors, we made them sensitive to local tumor-specific stimuli, such as lowered pH, hypoxia, or overexpressed certain enzymes, such as matrix metalloproteases. Using pH-, hypoxia-, or MMP2-sensitive bonds between different components of nanopreparations co-loaded with siRNA and drugs, we were able to make the systems specifically delivering biologically active agents in tumors, which resulted in significantly improved therapeutic response.

Audience Take Away:

- Will learn new technologies to prepare effective anticancer nanomedicines
- The talk will provide novel information on solving practical problems in drug delivery in cancer
- The material can be used for educational perposes

CONTENTS



Biography

Esmaiel Jabbari completed his Ph.D. in Chemical Engineering, Purdue University in 1993. He is Tenured Full Professor of Chemical and Biomedical Engineering at the University of South Carolina. Prof. Jabbari's Biomaterials, Tissue Engineering, and Drug Delivery laboratory specializes in creation of 3D tissue models for skeletal tissue engineering and cancer drug delivery. He is the author of >250 research articles. He received Berton Rahn Award from AO Foundation and Stephen Milam Award from Oral & Maxillofacial Surgery Foundation. He was elected to the College of Fellows of AIMBE in 2013. He serves as Academic Editor for PLOS ONE.

Drug screening and targeting against the stem subpopulation of cancer cells

Esmaiel Jabbari, Ph.D.

University of South Carolina, USA

A major contributing factor to mortality in cancer patients is relapse after therapy, and developing resistance. Cancer recurrence and resistance is related to the existence of a very small population of initiating stem cells (CSCs) in the tumor tissue with high expression of ATP-binding cassette (ABC) transporter proteins associated with drug resistance. After therapy, the bulk of tumor shrinks to <1% of its initial volume and the tissue becomes enriched with CSCs that are highly resistant to therapies. Further, as much as 40% of the volume of solid tumors is occupied by tumor-associated macrophages (TAMs), specifically immunosuppressive M2-macrophages, which play a central role in cancer progression. In my presentation, I will present a 3D co-culture system consisting of enriched CSCs and TAMs as a platform for preclinical drug screening and toxicity evaluation against the most aggressive cell colonies in the population of cancer cells. Using this novel 3D drug screening platform, we discovered that TAMs phenotype changes when co-cultured with CSCs and TAMs release factors that promote CSC maintenance. I will also discuss in my presentation the role of nanoparticles in overcoming resistance to drug uptake by cancer stem cells co-cultured with TAMs.

Audience Take Away:

- Cancer stem cells control the phenotype of TAMs
- TAMs contribute to the niche for maintenance of stemness in cancer cells
- TAM-CSC tumor model as a preclinical drug efficacy platform
- Nanoparticles can overcome resistance to drug delivery to cancer stem cells

Biography

Vladimir Muzykantov (MD from First Moscow Medical School, 1980 and Ph.D. in Biochemistry from Russian National Cardiology Research Center, 1985), joined PENN in 1993 and in 2010 became a Professor and Vice-Chair of the Department of Systems Pharmacology and Translational Therapeutics. He established and since 2010 directs the Center for Targeted Therapeutics and Translational Nanomedicine. He published >200 papers and edited a book "Biomedical Aspects of Drug Targeting" (Kluwer, 2003). Honors include Established Investigator (1996) and Bugher Stroke (2000) Awards from the American Heart Association, the Keynote and Chairing forums including Transatlantic Airway Conference on Targeting Molecular Signatures in Lungs (Luzerne, 2009), Gordon Conference on Drug Carriers (2012) and HLBI Division of Lung Diseases Workshop "Precision Therapeutics Delivery for Lung Diseases" (2014), Annual Italian Society of Biochemistry and Molecular Biology Conference (2015). His research focuses on drug delivery by red blood cells and endothelial targeting for treatment inflammation, thrombosis and ischemia.

Targeting nanomedicine to the vascular endothelium

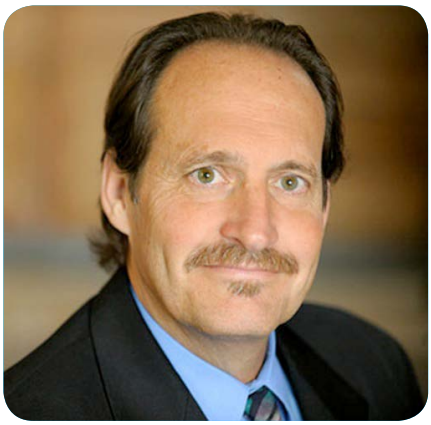
Vladimir Muzykantov, MD/Ph.D.

University of Pennsylvania the Perelman School of Medicine, USA

Endothelial cells lining the vascular lumen represent an important therapeutic target in many dangerous maladies. Some of them have no effective pharmacotherapy, at least in part due to inadequate drug delivery to intended site of action. Coupling drugs and carriers with specific affinity ligands enables targeted endothelial drug delivery in animal studies. Combining *in vivo* and *in vitro* approaches provide the insights into the complex mechanistic aspects of endothelial targeting. Briefly, endothelial drug targeting, uptake, traffic and effects are governed, among other design parameters, by: i) ligand nature, affinity and conjugation; ii) carrier's size, shape and plasticity; iii) supramolecular configuration of assembled targeted carrier (valence, ligand's steric freedom). Biological factors modulating targeting include carrier's interactions with molecules and cells en route, target accessibility, functional consequences of anchoring to specific epitope and its location. Pathological factors alter perfusion, vascular permeability, epitope accessibility and endothelial status and carrier uptake. Permutations of design and biological factors yield complex and somewhat difficult to reduce to practice, yet multifaceted and diversified paradigms for vascular drug delivery and targeting. In animal models of human diseases, endothelial targeting of antioxidant, anti-thrombotic and anti-inflammatory agents provides beneficial effects unrivaled by untargeted counterparts. This approach may provide tangible therapeutic benefits in conditions including acute lung injury, ischemia-reperfusion and sepsis. Current studies aim to define mechanisms and utility of "endothelial nanomedicine".

Audience Take Away:

- They will be able to use this in their research and educational activities in the fields of nanomedicine and drug delivery.
- The ideas and results shown in the presentation will guide their research and educational activities, support their own design of drug delivery systems, help solve practical and translational problems, provide examples and facilitate the interpretation of their own and literature data.



Biography

Joe Springer is a Professor of Neuroscience and Interim Director of the Spinal Cord and Brain Injury Research Center at the University of Kentucky. His lab was one of the first to demonstrate the potential therapeutic potential of riluzole as a treatment for acute spinal cord injury (SCI) and riluzole is now in phase III clinical trials. His lab also was the first to characterize the molecular signaling events linking mitochondria associated caspase-dependent activation and apoptotic oligodendroglia cell death in SCI. Most recently, his lab is collaborating with Dr. Wangxia Wang, who is a recognized expert in miRNA biology to examine the role of mitochondria in regulating the cellular activity of inflammatory miRNA following traumatic brain injury.

Nanoparticle delivery of mitochondria-associated microRNA regulating inflammation in the central nervous system

Joe E. Springer, Ph.D.

University of Kentucky, USA

Traumatic brain injury (TBI) is a leading cause of long-term impairments in higher cognitive function. Ongoing destructive secondary injury events occur minutes to days after the initial insult characterized by a cascade of pervasive biochemical and pathophysiological stressors including mitochondrial dysfunction, free radical-mediated oxidative damage, and inflammation. A rapid and sustained phase of mitochondrial dysfunction after TBI impacts a number of important cellular events. Our recent studies revealed that the levels of several mitochondria-associated miRNAs regulating inflammation (e.g., miR-146a) are altered early on after TBI at times that corresponds to a loss of mitochondrial function. Knowledge of the temporal changes in mitochondria associated miRNA levels after TBI provides an opportunity to target specific miRNA at specific time points. Two validated targets of miR-146a (TRAF6 and IRAK1) are thought to be involved in the differential expression of the M1 pro-inflammatory and M2 anti-inflammatory macrophage/microglia phenotypes. Recently, we employed a peptide-based miRNA nanoparticle delivery approach as a strategy to favor M2 microglia/macrophage expression and promote tissue repair following TBI. Specifically, we found that *in vitro* and *in vivo* nanoparticle delivery of miR-146a mimic reduced expression of TRAF6 and IRAK1, decreased expression of several pro-inflammatory markers (e.g., Marco, IL-6, and Nos2) and increased expression of anti-inflammatory markers (IL-4, Mrc1, and Arg1). The outcomes of our studies suggest a temporally dynamic interaction of miRNAs with mitochondria and point a potential role for mitochondria in directing the cellular function of specific miRNA regulating inflammatory responses in the central nervous system (CNS). Our studies also demonstrate the use of a peptide-based nanoparticle approach to effectively deliver miRNA mimics as a way to target specific miRNA activities following TBI and possibly other CNS-related injury events.

Audience Take Away:

- The audience will gain a better understanding of signaling events regulating inflammatory miRNA expression after traumatic brain injury.
- The ability to manipulate the activity of miRNAs regulating inflammation has therapeutic potential in the treatment of traumatic brain injury.
- Regulation of key mitochondria- associated inflammatory miRNA in response to CNS injury may be tissue and cell specific.
- Our current studies utilize microinjections of miR-146a containing nanoparticles directly into the CNS tissue, which is not clinically optimal. Therefore, identification of delivery strategies that obviate the need for direct injections into the CNS is a high priority.

CONTENTS

Biography

Eugenia V. Gurevich completed her doctorate in neuroscience in Moscow State University. She trained as a postdoctoral fellow with Dr. Jeffrey Joyce at the University of Pennsylvania, Pennsylvania, USA, and then accepted the position as the Brain Bank Director and Staff Scientist at Sun Health Research Institute in Sun City, Arizona, where she conducted research on dopamine receptor functions in Parkinson's disease and schizophrenia with the focus on postmortem studies of the human brain. Since 2003, Dr. Gurevich is a faculty member of the Department of Pharmacology at Vanderbilt University, Tennessee, (Assistant Professor 2003-2009, Associate Professor from 2009), where she conducts research on the regulation of dopaminergic signaling in the normal and diseased brain. She is particularly interested in the functional role of proteins, G protein-coupled receptor kinases (GRKs) and arrestins, controlling desensitization of G protein-coupled receptors n neural pathologies such as Parkinson's disease, L-DOPA-induced dyskinesia, and drug addiction. She is an expert on the use of viral gene transfer technology to induce protein expression or knockdown in the brain of living animals. Dr. Gurevich has pioneered the study of the role of GRKs and arrestins in L-DOPA-induced dyskinesia with the goal of targeting these proteins to control dyskinesia and other L-DOPA-induced motor complications. This work may eventually lead to the development of novel therapies for Parkinson's disease and drug discoveries targeting GRK proteins.

Signaling peptides for brain diseases: Delivery and action

Eugenia V. Gurevich, Ph.D.

Vanderbilt University, USA

Arrestins were discovered as the key proteins responsible for the shutoff of the G protein-dependent signaling by G protein-coupled receptors (GPCRs). Later it was discovered that arrestins regulate multiple signaling pathways, including mitogen activated protein (MAP) kinase pathways, by scaffolding the pathways' components. One of the two ubiquitously expressed arrestin subtypes, arrestin-3, is the only isoform capable of activating the JNK pathway, with the preference for the JNK3 neuro specific isoform. We show that short peptides derived from the JNK3-binding region of arrestin-3 effectively mimic the full-length arrestin-3 protein in the ability to activate the JNK pathway. Further deletion of a few amino acids yields peptides that bind some, but not all kinases in the JNK pathway, thereby recruiting them away from productive arrestin-3-dependent scaffolds and inhibiting JNK3 activation via the dominant-negative mechanism. Therefore, such peptides should act as selective inhibitors of arrestin-3-dependent activation of JNK3. We recently found that arrestin-3-dependent JNK activation is a contributing factor to L-DOPA-induced dyskinesia (LID), a severe side effect of the most commonly used L-DOPA therapy in Parkinson's disease. We show that lentivirus-mediated delivery of peptides activating JNK3 promote LID, whereas inhibitory peptides alleviate it in animal models of LID without interfering with the beneficial effect of L-DOPA. These data suggest that signaling peptides could be used as highly selective therapeutics for brain diseases. Such protein-derived peptides capable of fulfilling select functions of the parent multi-functional protein have a great potential as therapeutic tools, specifically to target protein-protein interactions, which are notoriously hard to modulate with small molecule therapeutics. We will show the data on the effectiveness of inhibitory arrestin-3-derived peptides rendered cell penetrating as anti-LID therapeutics. The issue of the best way of delivering the peptide therapeutics into the brain will be addressed.

Audience Take Away:

- Our experience in using peptides to treat a brain disease would be helpful to other scientists interested in neurodegenerative and other brain disorders;
- The design of the therapeutics targeting protein-protein interactions could also be advanced by our studies. Since most regulatory functions in the cells are performed via protein-protein interactions, this would help to open up a large pool of novel therapeutic targets that would become "druggable".
- Scientists engages in studies of delivery methods will find our experience with testing cell penetrating peptides in cultured cells and living animals informative for their own research.

magnus Group

DAY 1

SPEAKERS

2ND EDITION OF GLOBAL CONFERENCE ON

Pharmaceutics and Drug Delivery Systems

June 04-06, 2018
Rome, Italy

CONTENTS

Understanding the Impact of nanoparticle structure on cellular response

G.K. Such[1]*, N. Kongkatigumjorn[1], A. S. M. Wong[1], E. Czuba[2], A.S.M.Wong[2], M. Chen[2], A. P. R. Johnston[2]
[1]The University of Melbourne, Australia
[2]Monash University, Parkville, Australia

Nanoparticle delivery systems have potential for biomedical applications due to the ability of the nanoparticles to better target diseased cells or tissue, and therefore optimise the therapeutic payload to a treatment site. Self-assembled polymeric carriers have generated particular attention for delivery applications due to their simple and versatile synthesis. However, such carriers are still limited by inefficient delivery to target regions within the cell. Therefore, there is still a need to better understand their cellular response. Recently, our research group developed pH responsive nanoparticles that could be used as a model to investigate targeting, internalisation and the trafficking of the nanoparticles into the cytosol. One of the key bottlenecks of interest in our work is escape of the polymeric carrier from acidic, cellular compartments (lysosomes/endosomes) into the cytosol, referred to as endosomal escape. PH responsive materials have shown potential for endosomal escape but the mechanisms for this response are still unclear. One interesting pH responsive polymer is poly(2-(diethylamino)ethyl methacrylate) (PDEAEMA) as it undergoes a transition from hydrophobic to hydrophilic in a pH range consistent with endosomal compartments.

In this presentation, the synthesis of pH responsive nanoparticles based on (2-(diethylamino)ethyl methacrylate and related monomers will be reported. PDEAEMA particles (pHlexi particles) were assembled using a simple one-pot synthesis approach and demonstrated rapid pH disassembly when the pH was decreased. A library of nanoparticles with different pH of disassembly were synthesised and the effect on hemolysis, internalisation and endosomal escape investigated. Interestingly, high endosomal escape was observed for nanoparticles at the extremes of the pH disassembly range (pH 5 and pH 7.2) with low amounts of escape at intermediate pH. In addition, a fluorescent internalisation probe was used to investigate the internalisation kinetics of these nanoparticles. The relationship of internalisation to association kinetics was found to be highly dependent on cell line. The responsive and modular nature of these materials provides new insights into the design of nanoengineered materials for application in therapeutic delivery.

Audience Take Away:

- Demonstrate the simple and versatile synthesis of pH responsive nanoparticles.
- Show how endosomal escape can be engineered by changing composition of polymer building blocks.
- Demonstrate the use of an internalisation sensor to probe internalisation and internalisation pathways.

This talk provides important insights into how particle engineering can play a significant role in cellular trafficking, factors that should be considered for applications that require delivery of biological therapeutics.

Biography

Georgina Such completed her PhD in 2006 from the University of New South Wales. After her PhD, Dr Such commenced postdoctoral work in the Nanostructured Interfaces and Materials Science (NIMS) group headed by Professor Frank Caruso. Her research in this group focused on making nanoscale polymer carriers for targeted drug delivery. In 2013, she commenced a Future Fellowship in the School of Chemistry, The University of Melbourne, enabling her to start her own research group in the area of stimuli-responsive materials. Dr Such is now a senior lecturer at the University of Melbourne. Dr Such has authored 65 peer-reviewed publications including 3 book chapters. Her work has been recognized with the 2011 L'Oreal Women in Science Fellowship. Her research interests include polymer synthesis, self-assembly and stimuli-responsive materials.

Overcoming the barriers to effective targeted drug delivery through stem cell-derived nano-ghosts

Marcelle Machluf*, Ph.D. and Tomer Bronshtein, Ph.D.
Technion – Israel Institute of Technology, Israel

Targeted drug and gene delivery technologies, mostly for oncological applications, have been extensively investigated for more than three decades. With only seven passively-targeted systems and just two actively-targeted antibody-drug conjugates in oncological use, it seems, however, that the clinical translation of targeted drug delivery technologies suffers from relatively slow progression compared to other advanced cancer therapies. This limited translatability, despite overwhelming preclinical data, was largely attributed to wide variations in the tumor presentation of distinctive targetable characteristics. Such variations, seen both between patients and among the same patients during disease progression, limit the selectivity of targeted delivery technologies while giving rise to off-target effects and restricting their use to small population groups. Overall, these reduce the cost-effectiveness of targeted-delivery technologies and lower their industry appeal. Allogeneic mesenchymal stem cells (MSCs) engineered *ex vivo* to secrete bioactive compounds were suggested as a natural alternative to synthetic delivery systems. This alternative builds on MSCs allogeneic tolerability and their multiple evolutionarily-optimized inflammation-targeting mechanisms, which should allow them to home in on and deliver their payloads to different and evolving cancers. Despite ample advancements, this approach is still limited by MSC susceptibility to host-induced changes, permitting them to exert a short-term effect only and restricting repeated administrations.

In recent years, our lab has been developing a proprietary drug and gene delivery system termed Nano-Ghosts (NGs) that are based on nanometric vesicles manufactured through a scalable process from the cytoplasmic membranes of allogeneic MSCs following the removal of the cells' cytoplasm and organelles. While excluding MSCs' cytoplasmatic machinery, the NGs' retention of MSC membranes equips them with a multitude of surface proteins that are regularly involved in MSC homing and immune evasion. This makes the inanimate NGs less susceptible to host-induced changes and safer than living cells while arming them with a targeting capacity similar to the MSCs. To date, we have demonstrated the NGs' ability to selectively target models for metastatic lung tumors, prostate tumors, and orthotopic pancreas and brain tumors as well as models for neurological and degenerative diseases. NGs were shown to actively traffic across the BBB and infiltrate the bulk of even highly desmoplastic tumors. Inside the tumor niche, the NGs were found to interact with cancer cells and stem cells and endothelial and immune cells, while avoiding such interactions in other parts of the body. Different methods were developed to load the NGs with a variety of bioactive compounds including small molecule drugs, proteins, and nucleic acids, which have dramatically improved the drugs' therapeutic outcomes in all oncological models tested. Safety studies revealed no immunotoxicity or organ toxicity in response to more than ten times the NGs' effective therapeutic dose as well as no primary or secondary immune response. Collectively, our results demonstrate the translational potential of harnessing the homing capabilities of MSC in an imamate NG platform that requires no materials from the patient himself and that can be used as an off-shelf-product delivering diverse payloads for treating a broad range of indications.

Audience Take Away:

- The audience will understand the major limitations to the clinical translation of targeted drug and gene delivery technologies.
- The audience will understand the concept of drug and gene delivery by Nano-Ghosts.
- The audience will understand how Nano-Ghosts can potentially overcome some of the drawbacks of current delivery technologies.
- The audience will be exposed to a unique platform they can use to selectively deliver their own APIs to different pathologies.

Biography

Marcelle Machluf received her PhD in Biotechnology from the Ben-Gurion University, after which she went on to complete a post-doctoral fellowship at the Harvard Medical School. Since joining the Technion in 2001, Marcelle's research focused on the bioengineering of drug and gene delivery systems, and of cell-based and cell-free therapies. Prof. Machluf's papers appeared in leading journals including Nature Biotechnology, Nano Letters, and Blood, and have been cited over 3,200 times. In 2017 she was appointed Head of the Faculty of Biotechnology & Food Engineering. She is also the President of the Israeli chapter of the Controlled Release Society and holds an Adjunct Professor position at the Nanyang Technological University of Singapore.

Chimeric and multicompartment drug delivery systems: Lessons learned and future perspectives

Natassa Pippa, Msc, Ph.D.
University of Athens, Greece

The aim of this investigation is to present the novel progress performed in recent years in the field of design and development of new nanocarriers used in pharmaceutical nanotechnology. Special attention is assigned to chimeric and multicompartment drug delivery systems. Chimeric drug delivery systems are those that consist of different materials i.e. lipids and polymers. Polymer-grafted liposomes and niosomes are presented in this study. The physicochemical characteristics of L-α-phosphatidylcholine, hydrogenated (Soy) (HSPC) and dipalmitoyl phosphatidyl choline (DPPC) liposomes, caused by the incorporation of a poly (oligoethylene glycol acrylate)-b-poly(lauryl acrylate) (POEGA-PLA) block copolymer at different molar ratios (chimeric liposomes) are investigated using Light Scattering and Imaging Techniques. Polymer-grafted liposomes composed of non-ionic surfactants i.e. Tween 80 and Span 80, cholesterol with and without poly(ethylene oxide)-b-poly(ε-caprolactone) (PEO-b-PCL) block copolymer are also studies with different and complementary techniques. These chimeric vesicles (liposomes and niosomes) exhibited stealth properties due to limited interactions between the plasma proteins and nanocarriers' components. The results from the *in vitro* screening in cells showed low toxicity of the majority of the chimeric vesicles. The aforementioned chimeric systems found to be ideal for the loading and controlled release of model drug, especially those with water-insolubility problems.

Additionally, for this purpose, MWCNTs were oxidized via two different oxidation procedures and the oxidized MWCNTs were treated, in order to induce different surface charges onto MWCNTs-based materials. Then, we studied the cooperativity between the functionalized MWCNTs and DPPC and HSPC, by Differential Scanning Calorimetry. Strong interactions between the functionalized MWCNTs and the polar groups of phospholipids were observed in some cases, while in some other cases the nanotubes were oriented parallel to the membrane and located at the center of lipid bilayers. The presence of MWCNTs causes alterations of the size, size distribution and surface charge of the conventional HSPC and DPPC liposomes. The results from *in vitro* screening experiments showed low toxicity of the vast majority of the lipid/MWCNTs nanocarriers, even at high concentrations. The last observation indicates than the prepared systems are suitable and safe vectors for encapsulation of active pharmaceutical ingredients.

Furthermore, multicompartmentalized systems have been developed both for controlled delivery purpose and as models for cell biomimicry. Giant unilamellar polymersomes were prepared using an emulsion- centrifugation process, for which preformed liposomes were encapsulated into giant unilamellar poly-(butadiene)-b-poly(ethylene oxide) (PBut-b-PEO) vesicles (GUVs). Different types of liposomes were prepared using the thin-film hydration method followed by extrusion. Confocal microscopy and specific labeling using dyes was used to access the multicompartmentalized structure and morphology. As a proof of concept, we show an *in vitro* double-triggered release of dyes from the encapsulated liposomes using temperature variations.

Finally, from all the above examples, we can conclude that chimeric and multicompartment drug delivery vesicles are ideal technology platforms due to their biocompatibility and physicochemical properties.

Audience Take Away:

- The design and the development of advanced drug delivery systems composed of different biomaterials
- The advantages of these prepared systems
- The preparation protocol
- Their characteristics (physicochemical, morphological and thermodynamic)
- Their application in Nanomedicine

Biography

Natassa Pippa is post-doctoral researcher in Department of Pharmaceutical Technology, University of Athens. Her research is focused on the design and development of nanoparticles (i.e. liposomes, micelles etc.) as nanopharmaceuticals. She has published more than 60 peer –review papers and 6 chapters in Books. She has been awarded in Congresses for her oral and poster presentations. She also participated in several research programs with pharmaceutical industries in order to develop medicines, cosmetics and food supplements. She was awarded by International Association of Advanced Materials with the prestigious "International Association of Advanced Materials Scientist Medal (IAAM Scientist medal) for the year 2016" due to her contribution in the field of "Advanced Materials Science and Technology" (at European Advanced Materials Congress on 24th August 2016 Stockholm, Sweden).

Delivery of siRNA *in vivo* to the liver using redox sensitive and ionizable lipids

Daniel Zucker[1]*, Ph.D., Kota Tange[2], Yuta Naki[3]
[1]NOF Europe GmbH
[2]NOF Corporation America
[3]NOF Corporation Japan

A lipid nanoparticle (LNP) composed of a series of disulfide bridge cleavable and pH-reponsive lipid-like materials (COATOSOME SS-E-P4C2) was developed as a platform of a gene delivery system. The LNP showed good stability in the serum. The tertiary amine and disulfide bridge of COATOSOME SS-E-P4C2 lead to destabilization of the endosomal membrane and for intracellular collapse. We would like to present our development of a hepatocyte-targeting siRNA carrier by the molecular tuning of the hydrophobic scaffold, and tertiary amine structures. The gene knockdown activity against a hepatocyte-specific marker (factor VII) was improved when a more fat-soluble vitamin (vitamin E) was employed as a hydrophobic scaffold. Moreover, to allow the tertiary amines to accept protons by sensing a slight change in endosomal acidification, its structural flexibility was minimized by fixing it in a piperidine structure, and the distance between the surface of the particle to the ternary amine was increased. As a result, the pKa value was increased to the approximately 6.18 depending on its distance, while the pKa reached plateau when the tertiary amine was linked by an excess number of linear carbon chains. The pH-dependent membrane destabilization activity, as assessed by a hemolysis assay, was increased in parallel with the pKa value. Moreover, the gene knockdown activity was improved in parallel with hemolytic activity. Finally, further optimization of the lipid/siRNA ratio, and the use of chemically (2′-fluoro) modified siRNA synergistically improved the gene knockdown efficacy to an effective dose (ED50) of 0.035 mg/kg. The developed COATOSOME SS-E-P4C2 represents a promising platform for use as a hepatocyte-targeting siRNA carrier.

Audience Take Away:

- How to optimize the chemical environment around amine groups of ionizable lipids in order to transfect nucleic acids into cells
- How to utilize the difference in the redox-potential between the plasma and the cytoplasm for in-vivo delivery of nucleic acids
- How to optimize the stability of lipid nanoparticles with RNA
- Specific targeting of nanoparticles to the liver after intravenous injection
- Optimization of lipid nanoparticles for transfection of nucleic acids
- Methods for in-vitro optimization of ionizable lipids for efficient complexation of nucleic acids and transfection
- Strategies to develop biodegradable lipids with low toxicity

Biography

Daniel Zucker has completed a Ph.D. in the field of drug delivery and biochemistry at the Hebrew University of Jerusalem in Israel. Next, he did a postdoc in the field of liposomal drug delivery at the Technical University of Denmark. Afterwards, he worked as a senior scientist for RNA delivery at BioNTech RNA Pharmaceuticals GmbH in Germany. Currently, he works as business development manager for drug delivery systems at NOF Europe GmbH in Germany. Daniel is the co-author of 7 peer-reviewed research articles, 4 patent applications, and 1 book in the field of drug delivery. Daniel's publications were cited 379 times in Google Scholar.

CONTENTS

Getting health allies from agriculture enemies: Plant viruses as smart nanoparticles for vaccine/drug delivery

Selene Baschieri
Italian National Agency for New Technologies, Energy and Sustainable Economic Development (ENEA), Italy

Plant virus nanoparticles (pVNPs) might represent an ideal delivery tool in terms of biocompatibility and biodegradability. They have evolved to use plants as their reproductive hosts, and to this aim, have developed infection strategies very different from those adopted by their animal counterparts, so that if injected into animals they behave as unreplicative nanobjects. Moreover, they offer a wide range of shape diversity, are easy to be chemically/biologically engineered on both the surface and/or the internal cavity of the capsid, are easy, safe and rapid to be produced at low costs in plants. In this perspective, we are exploring the potential for biomedical applications of two structurally different plant viruses, the filamentous Potato Virus X (PVX) and the icosahedral Tomato Bushy Stunt Virus (TBSV) that we produce inoculating the tobacco-relative Nicotiana benthamiana. In previous studies, we have defined how, by biotechnology interventions, we can produce particles carrying antigens for vaccination purposes, and demonstrated that these particles work excellently in activating different types of immune responses (innate and adaptive, humoral and cell-mediated). Because intrinsic toxicity cannot be taken for granted, we have also verified that PVX and TBSV are neither toxic nor teratogenic. To complete the picture, more recently we observed that, when injected in mice, these structurally robust pVNPs do not induce alterations of tissues architecture, although having different behaviours in terms of persistence in the blood stream and biodistribution, probably as a function of their shape and surface characteristics. Overall, these information sets a solid ground reference for future testing of pVNPs designed to answer to specific health challenges, and there is no reason to suppose these nanoparticles will not progress rapidly contributing to widen the number of devices available to face evolving issues in biomedicine.

Audience Take Away:

- The audience will discover that plant virology is a field of research only apparently very distant to those of pharmacology and drug delivery.
- My presentation by illustrating a new fascinating use of plants in the field of biomedicine will stimulate new multidisciplinary collaborations.

Biography

Selene Baschieri has thirty years of experience in Immunology and Biotechnology research. She is currently involved in developing new strategies for the use of plant systems for the innovation of vaccine formulations (vaccine delivery) and for the development of novel diagnostic/therapeutic technologies.

Main research interests: Vaccine/drug delivery, Molecular farming (production of proteins of biopharmaceutical interest in plants), Plant virology, Expression of recombinant proteins in heterologous hosts.

The influence of gut microbiota-mediated bile acid metabolism on the cellular response to therapeutics at the intestinal barrier

Elaine F. Enright[1,2*], MPharm, , Kalaimathi Govindarajan[2], Ph.D., Rebecca Darrer[2], MSc, John MacSharry[2,3,4], Ph.D., Brendan T. Griffin[2], Ph.D., Susan A. Joyce[2,5], Ph.D., Cormac G.M. Gahan[1,2,3], Ph.D.

[1]School of Pharmacy, [2]APC Microbiome Institute, [3]School of Microbiology, [4]School of Medicine, [5]School of Biochemistry and Cell Biology, University College Cork, Cork, Ireland

Once regarded obscure, the cohabitation of man and microbe has gained increasing recognition as a determinant of the health status of the host. To date, pharmacokinetic research at the host-microbe interface has been primarily directed towards effects on metabolism. Microbial bile acid metabolism, deconjugation and dehydroxylation of the steroidal nucleus by the gut bacteria, may constitute a source of pharmacokinetic variability, and has been shown to impact bile acid solubilization capacity for poorly water-soluble drugs. Previous work within our research group involving germ-free and conventionalized mice (each group possessing distinct bile acid signatures) identified altered transcriptional expression of genes encoding intestinal transporters involved in lipid translocation. The purpose of this work was to investigate if microbial bile acid metabolism could similarly influence intestinal drug transporter expression and thereby drug uptake.

The impact of microbial bile acid metabolism on the transcriptional expression of genes encoding common influx and efflux transporters (including ABCB1, encoding P-glycoprotein) in Caco-2 cells was assessed. The ability of host (conjugated) and microbial (deconjugated/dehydroxylated) bile acids to differentially affect drug uptake and activity was investigated using the P-glycoprotein substrates, cyclosporine A (CsA) and rhodamine 6G (Rho 6G). Cell viability was used as a preliminary marker of altered CsA uptake/activity. Potential mechanisms by which bile acids could affect P-glycoprotein functioning was evaluated using ATPase and bidirectional transport assays.

Unconjugated bile acids significantly augmented CsA toxicity and reduced Rho 6G efflux, compared to tauro-conjugates ($P < 0.05$). These effects could not be explained by changes to ABCB1 mRNA transcripts. Bile acids were determined to inhibit, rather than stimulate, basal P-gp ATPase suggesting a non-competitive interaction with the transporter.

Overall, microbial bile metabolism was demonstrated to affect the uptake and activity of efflux transporter substrates. The physicochemical properties of unconjugated bile acids, including their capacity for passive membrane diffusion, is speculated to underpin their preferential attenuation of P-glycoprotein-mediated efflux.

Learning objectives:

- To differentiate between host- and microbe- derived bile acids and to gain an appreciation of their altered physicochemical properties.
- To identify the key physicochemical descriptors influencing the differential effect of bile acids on the transcriptional expression and functionality of clinically relevant intestinal drug transporter proteins.
- To discuss the potential significance of altered bile acid "signatures" in the context of multidrug resistance and clinical pharmacokinetic variability.

Audience Take Away:

- The aim of the outlined oral presentation is to provide an insight into the possible mechanisms by which the gut microbiota may affect the uptake and efficacy of multidrug resistant transporter substrates. It is envisaged that this topical subject matter will stimulate discussions on the need to consider both the human host and the gut microbiota in individualized dosage regimen design (PharmacoMicrobiomics).

Biography

Elaine Enright is a registered pharmacist, having graduated from University College Cork, Ireland, in 2014 as "Highest Achieving Student" in the BPharm degree. Elaine subsequently obtained a Masters in Pharmacy from the Royal College of Surgeons in Ireland in 2015. During her studies, Elaine gained experience in the pharmaceutical and regulatory sectors at Servier Laboratories Ireland and at the Health Products Regulatory Authority. Elaine is presently pursuing a PhD in Pharmaceutics (year 3), funded by an Irish Research Council Government of Ireland Postgraduate Scholarship. Elaine's PhD research, which is a collaboration between the APC Microbiome Institute and the School of Pharmacy, UCC, is supervised by Dr Cormac Gahan and Dr Susan Joyce. This four year trans-disciplinary work programme seeks to explore the effect of the gut microbiota on altering drug uptake from the gastrointestinal tract and, in particular, the potential clinical implications of this interplay. It is expected that this research will uncover new mechanisms by which the microbiota can influence individual patient responses to medicines.

Cyclodextrin-based photoactive liposomal nanoparticles for tumor targeting

Ilya Yakavets[1,2,3]*, M.Sc.; Vladimir Zorin[3,4] Ph.D.; Henri-Pierre Lassalle Ph.D.[1,2]; Lina Bezdetnaya M.D., Ph.D.[1,2]

[1] CRAN, CNRS UMR 7039, Université de Lorraine, Nancy, France

[2] Institut de Cancérologie de Lorraine, Vandoeuvre-lès-Nancy, France

[3] Belarussian State University, Minsk, Belarus

[4] International Sakharov Environmental Institute, BSU, Minsk, Belarus

Application of meta-tetra(hydroxyphenyl)chorin (mTHPC), one of the most potent photosensitizer (PS), in the photodynamic therapy (PDT) of solid tumors encounters several complications resulting from its insolubility in aqueous medium. It requires low light doses and concentrations to be photoactive (Senge & Brandt, 2011), however mTHPC aggregation results in reduced photodynamic activity, moderate selectivity and skin photosensitivity (Kachatkou et al., 2009). To improve the transport of mTHPC to target tissue and to strengthen its intra-tissue accumulation, several nanoconstructions have been investigated such as liposomes, polymeric nanoparticles, inclusion complexes etc.

In the present study, we suggested the coupling of two independent delivery systems by encapsulating Cyclodextrin/mTHPC inclusion complexes into liposomes to achieve drug-in-cyclodextrin-in-liposome (DCL) nanoparticles. DCL could circumvent the drawbacks of each separate system. Liposomes offer an excellent opportunity to achieve selective drug targeting which is expected to optimize the pharmacokinetic parameters, prevent local irritation, and reduce drug toxicity. In its turn, cyclodextrins (CDs) are cyclic oligosaccharides, which have been utilized as independent carriers for improvement of pharmaceutical properties such as solubility, stability and bioavailability of various drug molecules, including mTHPC (Yankovsky et al., 2016, Yakavets et al., 2017). Therefore, encapsulation of CD-complexed drug into liposomes may increase the drug loading capacity, entrapment efficiency, restrain the dissociation of drug-CD complexes and prolong its systemic circulation. The aim of this study was to evaluate the effect of DCLs on mTHPC behavior at various stages of its distribution in tumor models *in vitro*.

For this purpose, we have prepared DCL with various compositions to optimize DCL structures in terms of mTHPC delivery. We have studied the influence of DCLs on mTHPC accumulation, distribution and photodynamic efficiency in human adenocarcinoma HT29 cellular monolayer and spheroid models. We have demonstrated that mTHPC-DCLs are stable and almost all PS is bound to β-CDs in the inner aqueous liposome core. We studied mTHPC accumulation and localization in both HT29 monolayer and spheroid cells. Cellular uptake and intracellular localization of mTHPC-based DCL was similar to liposomal mTHPC in monolayer cultures. However, in HT29 3D multicellular tumor spheroids the application of DCLs significantly improved PS compared to other formulations resulting in homogeneous distribution of mTHPC across spheroids.

The data obtained confirm the interest of hybrid nanostructures in mTHPC-PDT.

Acknowledgements: This study was supported by Belarussian Republican Foundation for Fundamental Research, the Ministry of Education of the Republic of Belarus and French "Ligue National contre le Cancer". The authors thank biolitec research GmbH (Jena, Germany) for providing mTHPC.

Audience Take Away:

- This presentation establishes the action of cyclodextrins as nanoshuttles for aryl porphyrin molecules used as photosensitizers. This is the new action mechanism of cyclodextrins application in pharmaceutics.
- The combined action of liposomes and cyclodextrins as nanocarriers could provide the new strategy in nanoparticles design.
- Our study offers a smart selection of essential parameters for nanoparticles screening based on several tumor models and analysis techniques

Biography

Ilya Yakavets is a co-directed PhD student in Université de Lorraine (Nancy, France) and in Belarussian State University (Minsk, Belarus). He defended his Master degree in Belarussian State University (Minsk, Belarus) in 2016 in the field of Biophysics.

Presently, his PhD research focuses on the application of hybrid nanosized photosensitizer carriers based on liposomes and cyclodextrins in photodynamic therapy. The current abstract describes PhD study results of development and application of drug-in-cyclodextrin-in-liposome nanoparticles to improved delivery of porphyrin photosensitizer to the tumor targets. The presentation this PhD project at BioSE Doctoral School (Nancy, France) was awarded by the first prize in 2017.

CONTENTS

Arabinogalactan and glycyrrhizic acid as promising agents for oral drug delivery

Mikhail V. Khvostov[1,2*], Ph.D., Tatjana G. Tolstikova[1,2], Prof., Sergey A. Borisov[1], Ph.D., Tatjana S. Frolova, Ph.D.[1,2], Alexander V. Dushkin [3], Prof., Yulija S. Chistyachenko[3], Elizaveta S. Meteleva[3], PhD, Nikolay E. Polyakov [4], Prof.

[1]N.N. Vorozhtsov Institute of Organic Chemistry SB RAS, Russia
[2]Novosibirsk State University, Russia
[3]Institute of Solid State Chemistry and Mechanochemistry SB RAS, Russia
[4]Voevodsky Institute of Chemical Kinetics and Combustion SB RAS, Russia

Oral drug delivery is the most popular route because of the low expenses and long-term compliance. However, this introduction route has several limitations for drug molecules. Some of them are low water solubility and poor bioavailability. To overcome these limitations "host-guest" inclusion complexes of drugs with natural polysaccharide arabinogalactan (AG) and saponin glycyrrhizic acid (GA) can be applied. Arabinogalactan is a polysaccharide found in the wood cell walls of higher plants. Most of the commercially available AG is obtained from woody tissue of larches, in Russia it is Larix sibirica and gmelinii. Its LD_{50} > 5 g/kg and its usage approved by FDA and Russian pharmacopeia. GA is the chief sweet-tasting constituent of Glycyrrhiza glabra. It is used worldwide as a food sweetener and as part of licorice preparations, as a medicinal product.

All studied inclusion complexes were synthesized mechanochemically and characterized by water solubility, electron microscopy, differential scanning calorimetry, X-ray powder diffraction analysis and 1H-nuclear magnetic resonance spectroscopy. For all of them primary pharmacological properties were evaluated in vivo. For the several complexes pharmacokinetic parameters after oral introduction were obtained (Cmax, Tmax, AUC, $T_{1\backslash 2}$, MRT) and Caco-2 permeability experiments were carried out.

We have studied AG and/or GA inclusion complexes with following drugs: NSAIDs aspirin, ibuprofen, naproxen; antihypertensive drug nifedipine; broad-spectrum antihelminthic agents albendazole and praziquantel; cholesterol lowering drugs simvastatin and atorvastatin. In all cases it was found that such complexation results in significant drug's bioavailability enhancement and effective dose reduction.

Thus, inclusion complexes with AG and GA are a simple and effective way to enchase oral bioavailability of different drugs.

Biography

Mikhail V. Khvostov has completed his Ph.D at the age of 26 years from N.N. Vorozhtsov Institute of Organic Chemistry SB RAS. He is a senior researcher in the Laboratory of pharmacological researches of the NIOCH SB RAS. He has published more than 45 papers in reputed journals and is a co-author of 1 monograph and 2 patents.

Polyethylenimine-based nanoparticles decorated with small molecules mimicking RGD peptide for targeted plasmid DNA delivery

Ali Dehshahri[1*], Hossein Sadeghpour[1], Fatemeh Sheikhsaran[2], Narjes Savadi[1], Elaheh Entezar Almahdi[1]

[1] School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

[2]Fatemeh Sheikhsaran, Ph.D., Tehran University of Medical Sciences, Tehran, Iran

Targeted delivery of polymer-based nanoparticles has been considered as an efficient approach to transfer genetic materials into cells. Considering the over expression of integrin $\alpha_V\beta_3$ receptor on tumor cells and the presence of the binding site for tetraiodothyroacetic acid (tetrac) and L-thyroxine on integrin receptor, we hypothesized that the conjugation of these small molecules to polyethylenimine (PEI) at different conjugation degrees might be an effective strategy for pDNA delivery into the cells over-expressing integrins on their surfaces. In order to test the hypothesis, the conjugated PEI/plasmid DNA complexes were prepared and their ability in the delivery of plasmid encoding IL-12 gene was investigated. Moreover, the conjugates were characterized with respect to plasmid DNA condensation ability, particle size and zeta potential as well as cell-induced toxicity, apoptotic effects and plasmid protection against DNase degradation. The results demonstrated that the majority of the conjugated derivatives of PEI were able to condense the plasmid and protect it against enzyme degradation. The results of dynamic light scattering (DLS) and atomic force microscopy (AFM) revealed that the formed nanoparticles were in the size range of 85-200 nm. The highest level of IL-12 gene expression was achieved by terac-conjugated PEIs at where they could increase the level of gene expression up to 4 fold in the cell lines over-expressing integrin $\alpha_V\beta_3$ receptor whereas no increase in the level of IL-12 expression in the cell lines lacking integrin receptors was observed. Also, the results of the competitive inhibition of the receptors demonstrated the specificity of transfection for the cells over expressing $\alpha_V\beta_3$ receptor. On the other hand, tetrac and L-thyroxine conjugation of PEI significantly reduced the polymer-induced apoptotic effects. Also, the results of in vivo imaging of the polyplexes revealed that ^{99m}Tc-labeled PEI/pDNA complexes accumulated in kidney and bladder 4 h post injection. The results obtained in this investigation suggest the potential of tetrac and L-thyroxine as small molecules mimicking the binding properties of integrin binding peptides (e.g., RGD) for targeted gene delivery.

Audience Take Away:

- The audience will learn the importance of small molecules mimicking RGD properties for integrin targeting.
- These small molecules can be conjugated on various delivery systems using simple conjugation strategies and might be used for targeted gene and drug delivery.
- Since there are some limitations for the application of peptide or proteins as targeting ligands, small molecules with targeting properties might be considered as alternative ligands.

Biography

Ali Dehshahri is currently associate professor of pharmaceutical biotechnology at Shiraz University of Medical Science, Iran. He earned his Ph.D. at Mashhad University of Medical Sciences, Iran, in 2009, working with Prof. Mohammad Ramezani. In his thesis, he investigated the role of polymer amine content on its efficiency for gene delivery. As a distinguished Ph.D student, he was awarded a short-term research grant from the Iranian Ministry of Health to pursue his investigation at LMU, Munich, Germany under the supervision of Prof. Ernst Wagner on polymeric nanoparticles for siRNA delivery. In 2014, Dr. Dehshahri accepted an Associate Professor position at Shiraz University of Medical Sciences, where he has been since that time.

magnus Group

DAY 2

KEYNOTE FORUM

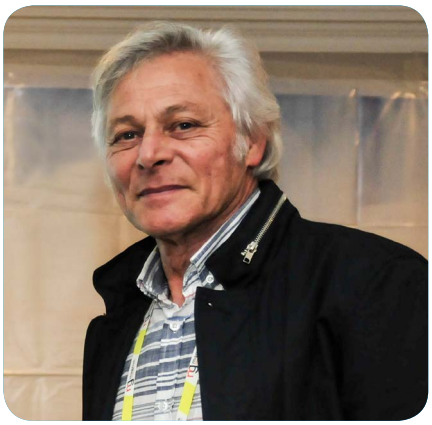
2ND EDITION OF GLOBAL CONFERENCE ON

Pharmaceutics and Drug Delivery Systems

JUNE 04-06, 2018
ROME, ITALY

PDDS 2018

CONTENTS



Biography

Following retirement as Chair of Physical Chemistry at the University of Cape Town (UCT), Professor Mino Caira was appointed as Senior Research Scholar in the same Department in 2015. He has served as Director of the Science Faculty's Centre for Supramolecular Chemistry Research at UCT since 2005, where he supervises the synthesis and physicochemical characterization of multi-component solids containing bioactive molecules (active pharmaceutical ingredients, new drug candidates, bioactive natural products, agrochemicals). He has published over 300 research articles in peer-reviewed journals and several reviews on crystal polymorphism, co-crystallization and cyclodextrin inclusion of drugs.

Physicochemical characterization of co-crystals and cyclodextrin inclusion complexes of bioactive molecules

Mino R. Caira, Ph.D.

University of Cape Town, South Africa

Significant reduction or elimination of unfavourable properties of both well-established drugs and new drug candidates (e.g. poor aqueous solubility, thermal instability, hygroscopicity) can often be achieved via relatively simple strategies such as co-crystallization with partner molecules, namely GRAS (generally recognized as safe) co-former compounds to form co-crystals, and with biodegradable macrocyclic oligosaccharide carriers (cyclodextrins, CDs) to produce CD inclusion complexes. Such products may be binary or higher-order (multi-component) systems and can be regarded as 'supramolecular derivatives' of the bioactive component. By varying the physicochemical properties of the respective partner molecules, the structures and properties of the solid products (co-crystals, CD inclusion complexes) can be tuned, leading to e.g. higher effective melting points for low-melting bioactives and resistance to absorption of water vapour (i.e. reduced hygroscopicity). Furthermore, the solid products are designed to be more soluble in aqueous media than the untreated bioactive molecule and in each case the latter molecule is typically linked to its respective partner (co-former or CD) via combinations of 'soft' interactions (hydrogen bonds, π-π and van der Waals interactions). The reversibility of these linkages ensures that on dissolution of the co-crystal and the CD inclusion complex, they dissociate into their original components, thus liberating the bioactive molecule intact. Significant increase in the solubility of the bioactive molecule (and hence possibly enhanced bioavailability in humans) may result if dissociation of the co-crystal or CD inclusion complex produces high concentrations of the bioactive at sites of absorption. This presentation focuses on the preparation of co-crystals and CD inclusion complexes containing bioactive molecules and their definitive characterization via a variety of techniques (primarily X-ray diffraction, thermo-analytical and spectroscopic methods), as well as assessment of the extent to which supramolecular derivatisation has resulted in property enhancement. Representative bioactive molecules that feature in the presentation fall into several classes, including those with antioxidant, antilipidemic, estrogenic and antimalarial activities.

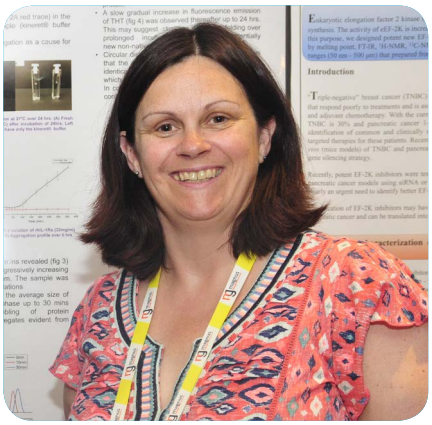
Audience Take Away:

- Awareness of the utility of approaches such as co-crystallization and cyclodextrin inclusion in the treatment of small bioactive molecules (APIs, new drug candidates) to enhance their pharmaceutically relevant properties and performance
- Familiarity with the methodology of solid-state preparation and definitive physicochemical characterization of multi-component systems containing small molecules
- Awareness of potential advantages of implementing such studies on new drug candidates soon after their discovery
- The presentation should facilitate entry into the literature on the topic of multi-component systems containing small drug molecules and their potential advantages for drug delivery. The practical approaches to beneficiation of drugs described in the presentation may be applicable as replacements for more complex and/or expensive strategies currently employed

Peptide Delivery to the brain: A novel treatment for migraine

G.A. Hutcheon, Ph.D.

Liverpool John Moores University, UK



Biography

Gillian Hutcheon graduated from Strathclyde University, Scotland in 1996 with a PhD thesis on Biocatalysts is non-aqueous media. She then undertook postdoctoral research at Queens Medical Centre, Nottingham investigating Protein:Biomaterial interactions. She joined Liverpool John Moores University in 1999 as a lecturer in Organic Chemistry and leads the Formulation and Drug Delivery Research Group. She has evolved her interest in proteins and biomaterials towards drug delivery applications looking at the enzyme catalysed synthesis of novel materials for micro and nanoparticle delivery of small molecule drugs and biomolecules. In 2008 she was conferred as a Reader in Biomaterials and she is currently Head of the LJMU Institute for Health Research.

Migraine is an extremely common, disabling condition which ruins the lives of millions of patients worldwide and is hard to treat effectively. Existing migraine medications are only partially effective, they have unwanted side effects and some patients are resistant to any current treatment.

CGRP is an abundant neuropeptide, consisting of 37 amino acids that plays key roles in cardiovascular homeostasis and nociception and is recognised as an important mediator of neurogenic inflammation and a very likely key contributor to migraine pathology. GPCRs in general have proved to be prime targets for drug discovery, and selective CGRP antagonists with clinical efficacy against migraine have now been produced. Our approach has been to design small 8-10 amino acid peptide antagonists of the CGRP receptor.

Peptides are naturally occurring biologics and, hence, tend to be safer than synthetic drugs and less immunogenic than proteins and antibodies. However, it is challenging to effectively deliver peptides via the oral route due to the harsh stomach environment that results in degradation. By comparison, the nasal route offers several advantages for both local and systemic delivery such as; a large surface area, a thin epithelium, dense vasculature, less enzymatic activity and is non-invasive. For delivery to the brain, the nasal route offers the possibility of adsorption via the nasal mucosa or direct delivery via the olfactory nerve. We have utilized design of experiment to prepare peptide loaded; Poly lactic-co-glycolic acid (PLGA), poly(glycerol adipate-co-ω-pentadecalactone), PGA-co-PDL and various chitosans nanoparticles (NPs). Mucoadhesive microparticles containing either peptide or peptide loaded NPS were prepared by spray drying from chitosans.

The small peptide antagonists that we have developed to date have demonstrated high potency in *in vitro* pharmacological testing and further pre-clinical development is now underway.

Audience Take Away:

During this talk, the following information will be provided:

- An understanding of migraines and current treatment
- An introduction to novel peptides for migraine treatment
- The evaluation of peptide-loaded polymeric nanoparticles
- Spray-drying of mucoadhesive microparticles for nasal delivery
- Evaluation of this delivery system as a novel migraine medicine

magnus Group

DAY 2

SPEAKERS

2ND EDITION OF GLOBAL CONFERENCE ON

Pharmaceutics and Drug Delivery Systems

JUNE 04-06, 2018
ROME, ITALY

Lipid based parenteral depots for biomolecules, an update on recent work

Gerhard Winter*, Ph.D., Michaela Breitsamer, WeiWei Liu, Moritz Vollrath, Ph.D.
LMU München, Germany

A wide range of new data on recent work with solid and semisolid lipid based depot formulations will be presented. As an alternative to PLGA based implants, lipid based rods for long term delivery of protein drugs have been studied in detail. The depot systems consist only of biocompatible glycerides, mainly triglycerides and are biodegraded by lipases over time. The manufacture of such systems is possible with easy to scale up twin screw extrusion technologies. We now can deliver large molecules like e.g. mabs over more than 6 months in a continuous manner. Comprehensive analytical data on the quality of released proteins are presented as well as data on process engineering and stability of the resulting DDS. 4 marketed antibodies were studied in such lipid based depots and, interestingly, showed very different stability profiles. In a second part, our recent work on lecithin based depots for the delivery range of 2-6 weeks is presented. By using s.c. needle free injection such highly viscous systems can be applied very conveniently and allow the most simple formulation and sustained delivery approach for peptides and other biomolecules. Besides the traditional processing by dual asymmetric centrifugation a novel manufacturing process will be introduced. Recently it became clear, that the ultrafine dispersion of the liposome compartments might not be the most relevant parameter to achieve long term retardation with such systems. We have studied this aspect in more detail and can provide insight into the role protein-lipid interaction, vesicle dispersion and other parameters play.

Audience Take Away:

- The audience shall understand the options to design depots for biomolecules with simple lipid systems
- The selection of an appropriate design for a certain purpose (a desired release duration) will be explained
- The chances and limits of lipid based depot systems will be critically discussed, also with a side view on competitive approaches
- Overall the state of the art regarding such depots is laid out

Biography

Gerhard Winter is a pharmacist by training. After his Ph.D. he worked as a R&D manager in the pharmaceutical industry for 12 years. During this time he co-developed marketed formulations for e.g. Neo-Recormon, Retevase, Bonviva. He focused on protein formulation research and lyophilisation, topics he kept for his academic research when he became a professor for Pharmaceutical technology and Biopharmaceutics at the University of Munich (LMU) in 1999. Since then he has published about 50 patent applications, > 160 papers and innumerate abstracts in the field. 60 Ph.D. students have graduated under his supervision. Protein depots are a research topic he has bene working on since more than 20 years.

The effects of drug encapsulation into gellan gum matrix by the example of roxithromycin, naproxen and meloxicam

Tomasz Osmałek[1*], PhD.,Anna Froelich[1], PhD.,Bartłomiej Milanowski[1], PhD.,Mirosław Szybowicz[2], Prof., Marcin Skotnicki[1], PhD.,Barbara Jadach[1], PhD.,Piotr Gadziński[3] MSc.,Katarzyna Ancukiewicz[3], MSc., Marcin Soból[4], PhD.,Urszula Kowalska[4], PhD., Artur Bartkowiak[4], Prof

[1]Poznan University of Medical Sciences (PUMS), Department of Pharmaceutical Technology, Poznań, Poland

[2]Poznan University of Technology, Faculty of Technical Physics, Poznań, Poland

[3]PUMS Pharmaceutical Technology Student Research Group, Department of Pharmaceutical Technology, Poznan University of Medical Sciences, Poznań, Poland

[4]Center of Bioimmobilisation and Innovative Packaging Materials, West Pomeranian University of Technology, Szczecin, Poland

Gellan gum is a linear, anionic biopolymer produced by the bacteria Sphingomonas elodea. Its chain consists of a tetrasaccharide repeating unit of L-rhamnose, D-glucose and D-glucuronate. Due to the unique structure and beneficial properties, gellan is broadly described as a potent multifunctional additive for various pharmaceutical products. There are two main types of gellan gum in use, native (high-acyl, HAG), which contains acyl substituents and deacetylated (low-acyl, LAG). Both are soluble in hot water (>70°C). As a result of temperature decrease, HAG hot solution forms soft and deformable gels, whereas LAG gives hard and brittle ones. The gelation of LAG can be accelerated by the presence of cations. Rapid gelation of LAG solution after instillation to salt solutions is called ionotropic gelation and can be applied in the encapsulation of drugs or other actives. The obtained formulations (beads, capsules, matrices) show the evidence of pH-sensitivity as they are stable in the acidic environment and start to absorb water and degrade during the pH increase. Therefore the matrices based on LAG can be used to shift the drug release to the distal parts of the gastrointestinal tract.

The presented work aimed at the preparation of gellan beads loaded with three different drugs and to evaluate their macroscopic and physicochemical properties, especially regarding pH-dependent behavior. Naproxen, meloxicam and roxithromycin were used as the active compounds. The beads were obtained by ionotropic gelation technique with $CaCl_2$ solution used as a cross-linking medium. Gellan alone or its mixtures with other naturally derived polysaccharides, i.e. carrageenans, guar gum, cellulose sulfate, dextran sulfate, were used for the preparation of the formulations. First, the surface and morphology of the dried beads were analyzed with scanning electron microscopy (SEM). Pure drugs and the beads were also evaluated with Raman spectroscopy and differential scanning calorimetry (DSC) technique. Next, the drug encapsulation efficiency and drug content were determined. The swelling and degradation behavior was evaluated in four simulated gastrointestinal fluids at different pH (1.2; 4.5; 6.8 and 7.4). The last step included *in vitro* drug release studies.

The work was funded by National Science Center (Poland) grant ID 370652, PUMS grants No. 502-14-03314429-09983 and 502-01-033-14-429-03439 and 502-05-03314429-09983.

Audience Take Away:

- The presentation will be the source of information concerning the potential application of low-acyl gellan gum as a pH-sensitive carrier for various drugs in oral delivery.
- The presented material will indicate some important aspects that have to be considered during the design and manufacturing of gellan beads.
- Both the advantages and limitations of ionotropic drug encapsulation will be discussed.

Biography

Tomasz Osmałek is an assistant professor at the Department of Pharmaceutical Technology at Poznan University of Medical Sciences in Poland. His current scientific experiences focus mainly on the technology of semi-solid dosage forms, such as hydrogels or organogels, prepared on both natural or synthetic polymers. The ongoing projects also deal with the application of gellan gum and its mixtures with various natural polysaccharides in the production of hydrophilic matrices as carriers for NSAIDs or other drugs in oral dosage forms with modified release. Earlier studies focused on the application of novel macrocyclic compounds in the photodynamic therapy of localized tumors.

5-Tiered (pre-) formulation approach to support toxicology studies

Marc Du Jardin
Janssen, Belgium

The Beerse developability groups provides physchem and formulation support to both discovery and toxicology teams within Janssen Belgium. In early discovery, it is essential to keep pace with the discovery teams and assure timely delivery of solubility results using Semi High Throughput screens. Besides generating and interpreting data it is essential to align with medicinal chemists and take into account the solid-state optimization of certain lead candidates. Once moving into LO (lead optimization) and LLO (Late Lead Optimization) it is important to support the numerous efficacy and pharmacokinetic studies, taking key deliverables of discovery into account. At this stage, optimization of bioavailability by increasing the absorption potential (if possible), is usually limited to conventional formulation platforms. All knowledge gained during the previous phases, guides the development of formulations used in tolerance studies. Purpose of the non-GLP tolerance studies is to:

1) Determine exposures associated with chemical toxicities in relation to the anticipated clinical efficacious exposures

2) Determine MTD and establish target organs of toxicities

3) Assist in determining dose levels for GLP studies

4) Successful outcome should be a suitable margin between the observed toxicity and the concentration required for efficacy

Formulation and dose should be selected to maximize exposure in toxicity studies, rather than to maximize the dose. Formulation volumes to be administered should be based on anatomical and physiological attributes of the test species and the properties of the formulation. Chemical & physical stability of the formulation are important criteria for suitability for use in toxicity studies and could limit the selection of vehicles available for determining the MFD. To facilitate & support these studies a formulation decision tree of 5 tiers was developed. Conventional aqueous solutions or suspensions are preferred, but when exposures need to be improved exploration of non-conventional systems will be explored.

Audience Take Away:

- How the introduction of a semi-HT Equilibrium screen allowed to assess pH dependent solubility as well as solubility in biorelevant media to support early MAD limitations
- Specific tox findings of certain vehicles will be presented
- Guidelines apply to the assessment and selection of which vehicle(s) can be used for pre-clinical non-GLP and GLP toxicity studies as a function of overall compound developability

Biography

Marc holds a Master's degree in Pharmaceutical sciences from the University of Antwerp. He joined Janssen in 1993, held various positions with increasing responsibility and is now head of the Beerse Preclinical Developability Department. The developability group is responsible for preformulation characterization, form selection and preclinical formulation development.

Porous biodegradable particles for efficient transfollicular drug delivery

Yulia Svenskaya[1]*, Elina Genina[1], Bogdan Parakhonskiy[2], Dmitry Gorin[3], Valery Tuchin[1], Gleb Sukhorukov[4]

[1]Saratov State University, Russia
[2]Ghent University, Belgium
[3]Skolkovo Institute of Science and Technology, Russia
[4]University of London, UK

Porous calcium carbonate submicron particles are proposed as effective carriers for transdermal drug transportation. Administration of bioactive substances via skin appendages arouses a scientific interest regarding to reduced systemic toxicity in terms of targeted delivery. A drug transportation to different regions of the hair follicle holds out the perspective for localized therapy, since they are the sites of interest for regenerative medicine, immunomodulation and aetiology of androgenetic alopecia, acne and other sebaceous gland dysfunctions. In the meantime, a dense capillary network ensures the systemic uptake of transported drug opening up perspectives beyond the scope of dermatology.

The proposing carriers are biodegradable and pH sensitive as they can be decomposed at pH bellow 6.5. Furthermore, the particles have a large surface area and high drug payload ability. The transdermal transportation of such carriers loaded with a fluorescent dye was studied in vivo after their topical application in rats. The optimal protocol for their efficient intrafollicular delivery was elaborated. A deep penetration of the carriers along with plentiful follicle filling was demonstrated using optical coherence tomography and confocal laser scanning microscopy. The process of intrafollicular particle degradation and diffusion of the fluorescent payload was studied in vivo in rats. The total degradation of $CaCO_3$ particles within 12 days was demonstrated together with the storage of the fluorescent dye inside the hair follicles up to 2 weeks. The 3-week investigation of the dye elimination kinetics in urine of experimental animals has proved out these data.

By this means, $CaCO_3$ submicron carriers provide efficient transfollicular delivery of compounds with consequent prolonged degradation-driven in situ release of delivered payload. This effect allows the prolongation of therapeutic intervention for more than 12 days revealing the promising outlook of the proposed system for transdermal drug transportation.

Audience Take Away:

A novel non-invasive protocol for an efficient drug delivery to the deepest regions of hair follicles can be used in scientific and medical practice.

- Practical approaches towards the investigation of skin appendages using such techniques as scanning electron microscopy, optical coherence tomography and confocal laser scanning microscopy, can be applied in future studies.
- Effective biodegradable drug carrier system can be adopted for other administration routes.

Biography

Yulia Svenskaya currently works at Research and Education Institution of Nanostructures and Biosystems at Saratov State University (Saratov, Russia) holding the position of the Senior Research Associate. She leads the project "Mesoporous vaterite submicron particles for transdermal delivery of bioactive molecules" in terms of Presidential funding program for scientific groups under the supervision of young scientists. Yulia received the Ph.D. degree in biophysics in 2013. Her research interests include the synthesis of micro- and submicron carriers for drug delivery, encapsulation of bioactive molecules; targeted delivery of photosensitizers in photodynamic therapy; transdermal delivery of bioactive compounds for photochemotherapy of skin disorders and for antifungal therapy.

Novel RNA-carbohydrate conjugates for modulation of LDLR and cholesterol by transcriptional silencing

Kira Astakhova[2*], Roslyn M Ray[1], Anders Højgaard Hansen[2], Maria Taskova[2], Kevin V Morris[1]
[1]The Center for Gene Therapy, Beckman Research Institute - City of Hope, Duarte CA, USA
[2]Department of Chemistry, Technical University of Denmark, Lyngby, Denmark

The Low Density Lipoprotein receptor (LDLR) is a cell surface expressed protein that binds and internalizes low density lipoprotein (LDL), resulting in cholesterol being made available to the cell. A method to stably over-express LDLR could result in an increased removal of LDL from the blood and subsequent lowering of cholesterol. Previous studies have uncovered an antisense non-coding transcript that overlaps the LDLR promoter, EST BM450697. We investigated the role of this transcript on LDLR gene expression and screened several siRNAs targeted towards either BM450697 or its promoter in Hep 3B and Hep G2 hepatocellular carcinoma cell lines.

Chemically modified RNA have advantages of enzymatic stability, specificity and efficient uptake. In particular, carbohydrate modification such as GalNAC increases the therapeutic activity of RNA. Nevertheless, the synthesis of RNA derivatives remains being a challenge. This is mainly due to chemical instability of RNA and folding into stable 2D structures.

This talk will cover our recent results on the synthesis and tests of chemically modified RNA therapeutics. Our data suggests that small RNAs can functionally activate LDLR expression by the targeted inhibition of the LDLR regulatory lncRNA, BM450697. Notably, these small RNAs are amendable to liver targeted conjugations, such as GalNAC and target the repression of BM450697 in an epigenetic manner, suggesting that long-term activation of LDLR might be feasible by stable silencing of BM450697.

By describing a novel approach to therapeutically actionable RNA molecules, the presentation will provide the audience with new ideas and synthetic methods for developing effective gene therapeutics. The talk will cover both the conceptual novelty of transcriptional gene silencing using synthetic RNA, and practical solutions to preparing and testing this type of therapeutics.

Biography

Kira Astakhova obtained a PhD degree in bioorganic chemistry in 2009. She continued as a postdoc in the group of Prof. Jesper Wengel at the University of Southern Denmark. In 2012 she became an Associate Professor at the University of Southern Denmark. Until 2015, she was also a visiting professor at the University of California Santa Barbara, Department of Chemistry and Biochemistry, and at Stanford University, USA. She is the author of 45 research publications, 5 book chapters and 4 patents. She was awarded with several research prizes and fellowships including Marie Curie Early Stage Research Training Fellowship and Lundbeck Foundation research prize. Her research interests are interdisciplinary, combining organic chemistry, biomedicine, biophysics and nanobioscience.

Myometrium-targeted liposomes for prevention of preterm labor

Biana Godin*, Ph.D., Jerrie Refuerzo, M.D., Francisca Leonard, Ph.D., Monica Longo M.D., Ph.D.
Houston Methodist Research Institute, USA

Preterm labor, leading to preterm birth (birth prior to 37 weeks of pregnancy) is a leading cause of perinatal morbidity and mortality affecting estimated 15 million births worldwide annually. Since the fetus is not yet fully developed before 37 weeks of pregnancy, health problems associated with preterm birth include a variety of acute and chronic health/developmental deficiencies. Among these are acute respiratory, gastrointestinal, immunologic, CNS, hearing and vision issues, as well as cerebral palsy, cognitive, visual, hearing, behavioral, social-emotional, learning, health, and growth problems. Indomethacin (IND) is a tocolytic that prevents uterine contractions and, thus, preterm birth, improving neonatal outcomes. Unfortunately, this efficient tocolytic is limited in its use due to associated cardiac, renal, neurological and other toxicities to the fetus. Fetal exposure to harmful medications is based on the ability of drug molecules to pass transplacentally from mother to fetus, which commonly involves simple passive diffusion. Having a low-molecular weight IND readily crosses the placenta as reflected in complications related to the fetal exposure to the drug. We have designed a liposomal delivery system (LIP) of IND that is targeted to the uterus through oxytocin receptor antagonist (ORA) expressed on the pregnant myometrium, thus increasing the concentration of the agent in the affected organ and minimizing the circulating free drug fraction available for placental passage. LIP-IND-ORA system design, *in vitro* studies in primary human uterine cells, *ex vivo* contractility studies in human myometrium strips and in vivo biodistribution and efficacy studies in pregnant rodents will be discussed.

Audience Take Away:

- The use of nanomedicine in the field of obstetrics is a novel topic.
- We believe that using nanocarriers for preventing the translacental passage of medications can open new avenues for safer therapeutics in the preganancy.
- Additionally, we have used a currently existing medication of targeting our system, which can significantly decrease the path to the regulatory approval. These concepts can also be used in other fields.
- In the presentation I will also briefly discus the pathway we are undertaking for initiating clinical studies with this delivery system.

Biography

Biana Godin earned her Ph.D. in Pharmaceutical Sciences focusing on lipid nanocarriers from the Hebrew University in 2006 and completed her postdoctoral training in the field of Nanomedicine at the University of Texas Health Sciences Center in 2010. In 2010, She joined as a faculty at the Department of Nanomedicine at Houston Methodist Research Institute. She also holds adjunct positions at the University of Houston and University of Texas Health Sciences Center in Houston. Research in Dr. Godin's lab, largely funded by federal and foundation grants, focuses on developing physiologically relevant *in vitro* and *in vivo* disease models and exploiting physical and biological mechanisms to improve currently available therapeutic options in oncology and obstetrics. She has more than 200 scientific publications, received multiple federal and foundation-based grants and participated in multiple national and international grant review panels.

Poly (vinyl pyrrolidone) nanofibers as drug delivery of sildenafil citrate

Luis Jesús Villarreal Gómez[1,2,6*], Erick José Torres Martínez[1,2], José Manuel Cornejo Bravo[1,2], Ricardo Vera Graziano[3], Juvenal Pantoja[4], Aracely Serrano Medina[1,5], Ana Leticia Iglesias[1,6], Graciela Lizeth Pérez González[1,2,6]

[1]Universidad Autónoma de Baja California, Calzada Universidad 14418, Parque Industrial Internacional, Tijuana Baja California C.P. 22390
[2]Facultad de Ciencias Químicas e Ingeniería, Universidad Autónoma de Baja California, Unidad Otay, Tijuana, Baja California, México.
[3]Instituto de Investigaciones en Materiales, Universidad Nacional Autónoma de México, Distrito Federal, México
[4]Hospital General de Tecate, Tecate, Baja California, México.
[5]Facultad de Medicina y Psicología, Universidad Autónoma de Baja California, Unidad Otay, Tijuana, Baja California, México.
[6]Escuela de Ciencias de la Ingeniería y Tecnología, Universidad Autónoma de Baja California, Unidad Valle de las Palmas, Tijuana, Baja California, México.

Pulmonary arterial hypertension (PAH) is one of the main risk factors for cardiovascular, cerebrovascular and heart failure diseases, which are important causes of mortality in Mexico. In just six years, between 2000 and 2006, HBP prevalence increased 19.7% to one in three Mexican adults (31.6%). An increase in substances that close the arteries (vasoconstrictors) such as endothelin or thromboxane and at the same time a decrease in the arteries (vasodilators), such as prostacyclin and nitric oxide, have been shown. The drugs for the treatment of the PAH have a very high cost (depending on the variations in the market), which is a limiting factor in our country. In Mexico, there are only three drugs FDA approved for HAP: Ilioprost (Ventavis®), Bosentan (Tracleer®), Tadalafil (Cialis®) and one available: Sildenafil (Viagra®), which will be studied. Optimizing the absorption and efficacy of the drug sildenafil is the main objective of this research. Therefore, the purpose of this project is to synthesize and characterize electrospun nanofibers containing fast dissolving sildenafil for the treatment of chronic pulmonary hypertension. To accomplish this, sildenafil citrate was loaded onto poly (vinyl pyrrolidone) nanofibers (PVP). These nanofibers were synthesized through the electrospinning technique. The loading of the drug was performed by mixing it into the polymer solutions. The modified PVP nanofibers were then chemically characterized for the analysis of functional groups, as well as the integrity of the chemical composition of the nanofibers and the binding of the nanofibers and the drug, FTIR and UV were performed for the physicochemical characterization. Regarding thermal stability, DSC and TGA were used. For the analysis of the surface of the nanofibers, average fiber diameter and percentage of membrane porosity, SEM studies were used. Finally, nanofibrous degradation studies and drug release studies were performed. The results will serve as a basis for further studies, evaluating biocompatibility in cell cultures and using experimental models to evaluate the effectiveness of the system in small animals, with the aim of making the data useful for transfer to clinical trials.

Audience Take Away:

- We will discuss electrospun nanofibers as a potential strategy of drug delivery of sildenafil in children. This information can be applied to different drug delivering in children, nanofibers allow an easier administration of the drug when the treatment is chronical and acute, and will help to avoid issues about correct dose administration and psychological fears in kids when they must be treated.

Biography

Luis Jesús Villarreal Gómez received the Ph.D. degree in Chemistry Sciences (2013) from the Autonomous University of Baja California (UABC), México. He completed a two years' research stay at the SCRIPPS, University of California, San Diego, USA, from 2007 until 2009, where he worked applying molecular biology and microbiology techniques. He is now a full-time research-professor at the School of Sciences of Engineering and Technology (ECITEC). He is a member of the National Researcher System (SNI-CONACYT) of Mexico. His current research interests include biomaterials, tissue engineering and drug delivery systems. Have published 11 articles, 3 books and 4 chapter books.

The reversal of type 2 diabetes - The role of the bile acids

Gerald H Tomkin
Beacon Hospital, and Trinity College Dublin, Ireland

Type 2 diabetes is a complex disorder. A relative rather than an absolute lack of insulin allows blood sugar to rise above normal even though the patients secret excess insulin. This is termed insulin resistance and is preceded by a hyperinsulinaemia phase where blood sugars still remain normal. The hyperinsulinaemia reflects good islet cell function even if not sufficient to control hyperglycaemia. At this stage in the disease there is an opportunity to reduce insulin resistance and to improve beta cell function and to control/reverse diabetes Bile plays an important regulatory function in carbohydrate and fat metabolism and signals beta cell stimulation and insulin secretion. Abnormalities in bile have been well documented in obesity and type 2 diabetes, and alterations have been shown with weight reduction and following bariatric surgery. Reversal of diabetes has been shown to occur following lifestyle changes and weight reduction and the recent DiRECT study has shown that many obese patients are able to follow a meaningful weight reduction program with 85% of patients who lose more than 15% of body weight being able to reverse their diabetes. Most dietary programs prior to this study, incurred large expenditure but the DiRECT study showed the possibility of general practice being able to deliver a program with little in the way of cost implications. The research showed that about 25% of obese patients with type 2 diabetes were willing and able to complete a years program, with many being successful in reversing their diabetes. Bariatric surgery has a similar impact on diabetes reversal. It is of course more successful in weight reduction in that more patients will lose more than 15% of body weight but at a cost of more complications and a greater financial cost. The role of pharmaceutical agents in preserving beta cell function, improving satiety and diminishing hunger will be discussed.

Audience Take Away:

- The audience will take away an understanding of type 2 diabetes and methods available to treat the condition
- The audience will learn the influence of insulin in carbohydrate, fat and protein metabolism. The importance of bile as a regulator of carbohydrate, fat and protein will be explained and
- The importance of bile in stimulating molecules in the bowel that have an effect on insulin secretion and appetite
- The hypothalamic targets for drug intervention and the role of the stomach and intestine on modulating brain peptides involved in appetite and satiety

Biography

Gerald Tomkin is president of diabetes Ireland and a consultant Endocrinologist/diabetologist in Beacon Consultant Clinic. He has been a vice president of the European Association for the study of Diabetes (EASD) and president of the Association of Physicians of Great Britain and Ireland. His research has focused on cholesterol metabolism in diabetes. He qualified in Trinity College Dublin and spent time training in the UK and USA before coming back to Dublin as a consultant Physician. He has published numerous papers including chapters in some text books and has been invited lecturer in many countries. Outside interests include tennis, golf and gardening.

New potential nanotechnology-based therapy with novel Gal-3 inhibitor for the treatment of rheumatoid arthritis

Nataliya Storozhylova[1,2*] Ph.D., José C. Campo[1], Ph.D., David C. Álvarez[3] Ph.D., Luis Lugo[3] Ph.D., Sandra I. D. Simões[4] Ph.D., Cyrille Grandjean[2] Ph.D., Prof. María J. Alonso[1]

[1]Center for Research in Molecular Medicine and Chronic Diseases (CIMUS), Department of Pharmacology, Pharmacy and Pharmaceutical Technology, University of Santiago de Compostela, Campus Vida, Santiago de Compostela, 15706, Spain
[2]UFIP - UMR CNRS 6286, UFR Sciences and Technology, University of Nantes, Nantes, 44322, France
[3]Department of Applied Physics, Faculty of Science, University of Vigo, Vigo, 36310, Spain
[4]Department of Farmacy, Universidade de Lisboa, Lisboa, 1649-003, Portugal

Intra-articular (IA) administration of drugs is an appealing therapy for the effective treatment of joint diseases; however, challenging due to premature elimination of injected drugs and drug delivery systems (DDSs) from the synovial cavity.

Aiming at increased retention and prolonged drugs release in the joints, a novel DDS composed of an *in situ* hydrogel combined with hyaluronic acid (HA) nanocapsules (NCs) is developed upon this study. NCs, consisting of an olive oil core surrounded by a HA shell, exhibit a particle size of 135 ± 9 nm, a negative surface charge (−31 ± 5 mV) and a capacity to encapsulate model drugs. Subsequently, two injectable *in situ* hydrogel compositions of HA-fibrin and fortified HA-fibrin (with crosslinker factor XIII and α2-antiplasmin) loaded with up to 30% (v/v) of NCs are developed. The morphology and porosity of the hydrogels show a regular structure with a mean pore diameter of 4.88 ± 1.12 μm. They display adjustable gelation time, the moderate initial viscosity that allows good syringeability, while rheological properties of the assembled DDS enable resistance to high deformations, displaying the hydrogel suitable for IA application. In this regard, to validate the new delivery system, dexamethasone is used as a model drug. The non-fortified HA-fibrin hydrogels with 30% NCs show the capacity to control the dexamethasone release in simulated synovial fluid during 72 h. Besides, a novel and potential lead compound for immunotherapeutic anti-rheumatic drug candidate – galectin-3 antagonist – is synthesized, characterized and evaluated in this study. The preliminary *in vivo* results demonstrated remarkable suppression of acute joint inflammation in rats by galectin-3 inhibitor encapsulated within this DDS and administrated IA at microgram scale doses compared to the non-treated control.

Overall, these findings highlight the potential of the DDS with encapsulated synthetic galectin-3 inhibitor as a capable in situ nanotechnology-based platform for rheumatoid arthritis treatment, intended to contribute to efficient joints therapies.

Audience Take Away:

- A new approach in the treatment of non-curable autoimmune diseases such as rheumatoid arthritis is based on the inhibition of a novel immune target galectin-3, a primer trigger of inflammation, by the developed highly specific and selective antagonists of this protein.
- Challenges of IA drug delivery - premature elimination of the DDS from the synovial cavity along with fast synovial fluid (SF) turnover could be overcome by the development of advanced formulations involving a combination of nano-/microcarriers and hydrogels. Such DDSs allow increased retention and prolonged release and improve the efficacy/toxicity balance of the drug.
- Additionally, articular cartilage has a limited ability for self-regeneration and synovial fluid greatly loses its intrinsic functions at pathological joints conditions. Having this in mind, multifunctional drug delivery carriers should contribute to diarthrosis healing. They should not only provide a controlled and prolonged drug release, but also be composed of deformation-resistant materials that may have a prolonged retention in the articulation. Simultaneously, such a nanotechnology-based platform should ideally work as a viscosupplementation agent for improving the knee homeostasis, and as an in situ cell scaffold for cartilage tissue regeneration.
- Sharing the results of my interdisciplinary project will extend the scientific horizons, elucidate the state-of-the-art in the field of joint diseases treatment, contribute to the understanding of the etiology of the rheumatoid arthritis and its treatment, and stimulate new collaborations and new efforts towards the development of the efficient therapies for the treatment of arthropathies.

Biography

Nataliya Storozhylova is finishing her joint-doctoral degree in Nanomedicine and Pharmaceutical innovation in University of Nantes, France and University of Santiago de Compostela, Spain by May 2018. During her interdisciplinary PhD project (2013-2018), she has designed and developed a novel nanotechnology-based therapy for the treatment of rheumatoid arthritis. She is experienced in development, synthesis and screening of anti-inflammatory drugs, an in situ nanotechnology-based drug delivery systems engineering and in vivo evaluation in autoimmune diseases models. She has performed extensive trainings in translational research and bio business (Germany, France) and made an expert-internship in Charité Hospital, Berlin, Germany. Earlier her research was focused on cardiovascular diseases and preparation of lab-on-chip systems for pre-thrombotic conditions diagnostics. In 2011 she has got an annual Mykola Kravets's Award for her scientific and practical contribution to the development of Ukraine.

New aerosol treatment for human nasal cavity through numerical simulation

H. Calmet[1]*, T. Yamamoto[2], B. Eguzkitza[1], O. Lehmkuhl[1], E. Olivares[1], Y. Kobayashi[3], K. Tomoda[3], G. Houzeaux[1], M. Vázquez[1]

[1]Barcelona Supercomputing Center (BSC-CNS), Department of Computer Application in Science and Engineering, Edificio NEXUS I, Gran Capitán 2-4, 08034 Barcelona, Spain

[2]Dept. Mech. Eng., National Institute of Technology, Gifu College, Japan

[3]Dept. Otolaryngology, Head and Neck Surgery, Kansai Medical University, Japan

New treatment in aerosol medicine exhalation through the nose (ETN) is one of promising and comprehensive methods for Eosinophilic Chronic Rhinosinusitis (ECRS) with asthma. The patient inhales aerosol of inhaled corticosteroid (ICS) medicine from mouth using portable inhaler. Then a part of the aerosol still floats and remains in upper airway. When the patient exhales inhaled air through the nose, the aerosol is effectively transported on the walls of meatuses and olfactory clift. This work performed Computational Fluid Dynamics (CFD) and Large eddy simulation (LES) analysis for the transport phenomena of aerosol medicine during exhalation period in order to evaluate the curative effect of ETN numerically. Since the efficacy of ETN strongly depends on expiration condition, this study proposes analysis during exhalation for exercise and quiet breathing states.

Eosinophilic chronic rhinosinusitis (ECRS) is considered a refractory and intractable disease. Patients with ECRS present with asthma, thick mucus production, long-term nasal congestion, loss of sense of smell, and intermittent acute exacerbations secondary to bacterial infections. Despite medical and surgical interventions, there is a high rate of recurrence with significant impairment to quality of life. The recent increasing prevalence of ECRS in east and south Asian countries and the strong tendency of ECRS to reoccur after surgery should be considered. The majority of cases need repeat surgery, and histological examinations of these cases show eosinophilic-dominant inflammation. The degradation and accumulation of eosinophils, release of cytokines, and mucus secretion have important roles in the pathogenesis of ECRS. Almost of all patients with ECRS obtain the efficacy of ETN. On the other hand, there are some patients who could not obtain the efficacy. The detail mechanism of how ETN improves ECRS with asthma is still controversial even though ETN gets a lot of attention as a treatment method for ECRS. In fact, it has been found that the efficacy of ETN strongly depends on expiration condition (expiration velocity, time and pattern) from clinical findings.

In this study we propose to investigate the particle deposition carry on in a real human nasal cavity geometry using a massively parallel simulation software in which both continuum mechanics CFD and Lagrangian particle model are simultaneously solved in a one-way coupling scheme.

Audience Take Away:

- Inform the audience to new treatment to deliver drug into the nasal cavity, more precisely into the sinuses.
- Applications of drug delivery reaching the sinuses are very large and must be interested the scientific community.
- Interact with researchers to share results.

Biography

Hadrien calmet studied Applied Physics of Ocean and Atmosphere and he obtained a Master degree in UTV (University of Toulon Var in France) with 6 months exchange Erasmus in UPC (University polytechnic of Catalonia, Barcelona, Spain) in 2002. He decided after to stay in Barcelona and carried out a master at the International Center for Numerical Methods in Engineering (CIMNE) in Finite Elements Method. In parallel he studied a DEA in Applied Physic in UPC (University polytechnic of Catalonia, Barcelona, Spain) with Prof. Jose-Manuel Redondo. To validate both diplomas, he made six months internship in EDF Paris (Electricity of France) in CFD and turbulence modeling. One year later he joined the newly created Barcelona Supercomputing Center-Centro Nacional de Supercomputación (BSC-CNS) to make the CFD pre and post-processing tasks of the Department of Computer Applications in Science and Engineering. Since then he has done engineering and biomedical research such as the respiratory system. Therefore, all issues related to big data, such as massive data I/O and visualization of large data sets are part of his main interests.

Numerical evaluation of exhalation through the nose treatment for eosinophilic chronic rhinosinusitis using computational fluid dynamics

Takahisa Yamamoto[1]*, Yoshiki Kobayashi[2]
[1]National Institute of Technology, Gifu College, Japan
[2]Kansai Medical University, Japan

Background and Objective: Recently patients who suffer Eosinophilic Chronic Rhinosinusitis with asthma (ECRS) have significantly increased in Asia. This disease has been recognized as an incurable disease, and its symptoms are multiple nasal polyps, excessive rhinorrhea, rhinostenosis and asthma. The difficulties to cure this disease arise from that any conventional medications are not effective and ECRS is not only nasal disease but also whole airway disease. Nose operations have been conducted for ECRS patients to improve patient's QOL, however, almost of the patients suffer the recurrences. The authors have developed new medication technique, aerosol medicine exhalation through the nose (ETN). In this treatment, the patient inhales aerosol of inhaled corticosteroid (ICS) medicine from mouth using portable inhaler. Then some of the aerosol particles still float and remain in upper airway. When the patient exhales inhaled air through the nose, the aerosol particles are effectively transported on the walls of middle meatus and olfactory fissure. Although the effectiveness of this treatment has been confirmed in clinical practice study, the magnitude of the effectiveness strongly depends on each patient. This study performed Computational Fluid Dynamics (CFD) analysis for ETN treatment. Two of the advantages in this study are that this study focuses on computer-aimed medication for clinical application and the CFD analysis elucidates the aerosol transportation during not only inhalation but also exhalation periods.

Method: Several patients, who had ECRS with asthma and endoscopic sinus surgery, ware selected in this study. 3D anatomically accurate patient-specific models were reconstructed from the data obtained using multidetector CT scanner. This study performed conjugation of Euler-Lagrange particle transport model for aerosol transport and a Large Eddy Simulation model for complex intranasal turbulent flow. This analysis is able to take transient fluid flow and transport of aerosol particles into account, and consequently, providing highly accurate predictions of aerosol deposition on upper airway wall.

Results and Discussion: ETN formed impinging flow toward upper wall of nasopharynx, subsequently complex swirl and circulation flow in the nasopharynx region during exhalation period. In addition, main flow of ETN passed upper region of nasal cavity. Such the tendencies affected on aerosol medicine transport characteristics; a part of medicinal particles moved into ethmoidal sinuses. Total amount of the aerosol deposition during ETN depends on flow rate of inhalation and exhalation. This tendency is more remarkable on the upper wall of nasopharynx. On the other hand, deposition rate of aerosol on the ethmoidal sinuses did not appear strong correlation with flow rate of exhalation. These results imply that there is an optimum inhalation and exhalation condition in each the patient, and CFD analysis is able to elucidate such the condition easily.

Audience Take Away:

- This paper describes newly developed treatment method, we call "Exhalation through the nose (ETN for shorten)" method, for Eosinophilic Chronic Rhinosinusitis (ECRS) which is one of intractable nasal diseases.
- In ETN method, steroid aerosol is transported inside nasal cavity from nasopharynx to nostril, and then the aerosol is able to reach ethmoid sinuses effectively.
- This paper elucidates transport characteristics of the aerosol during the exhalation as well as relationship between exhalation conditions (flow rate and duration time) and aerosol deposition distribution.

Biography

T. Yamamoto (corresponding author) is working several medical-engineering cooperative researches in medical institutes; visiting lecturer at Fujita Health University, visiting researcher at Nagoya University, and visiting associate professor at IJN-UTM Cardiovascular engineering centre. This study has been supported by Japan Grants-in-aid for Scientific Research fund since 2016. In this conference, the author is going to present not only transport phenomena in airways but also how enhance medical treatment using CFD analysis (the authors call it "Computer-aimed Medication").

Case presentation: Patient with metastatic pancreatic adenocarcinoma treated with nanoliposomal irinotecan combination therapy

Matej Dobravc Verbic*, MSc Pharm; Borut Stabuc, MD, Ph.D.
University Medical Centre Ljubljana, Slovenia

Pancreatic cancer is the fourth most fatal cancer in both men and women. Patients usually remain asymptomatic until advanced stages of disease, and prognosis has not improved over the past 20 years. However, new treatment options for locally advanced and metastatic disease have emerged in the last years, including newer nanoparticle formulations of previously existing active substances. In 2013, after showing superiority to gemcitabine monotherapy, albumin-bound paclitaxel (in combination with gemcitabine) emerged as a 1st line treatment option for patients with metastatic disease and with good performance status. More recently, nanoliposomal irinotecan (in combination with 5-fluorouracil and leucovorin) was introduced as a 2nd line option for metastatic pancreatic cancer in adult patients with disease progression following gemcitabine based therapy. We present the first case of treatment with nanoliposomal irinotecan in Slovenia.

A 69-year old female patient was first diagnosed with metastatic pancreatic adenocarcinoma in August 2015. Computer tomography (CT) demonstrated a tumor in the transition body/tail region of the pancreas with encasement of splenic vein. Multiple metastatic lesions were seen in 6th and 8th liver segments. Serum CEA and CA 19-9 levels were grossly elevated. Diagnosis was confirmed with ultrasound-guided biopsy. In the following two years, several chemotherapy regimens, including gemcitabine-nab-paclitaxel combination therapy, FOLFIRINOX (5 fluorouracil, leucovorin, irinotecan and oxaliplatin combination therapy), gemcitabine monotherapy, and transarterial chemoembolization with doxorubicin drug-eluting beads for liver metastases, showed good responses with disease regression and localized pain reduction. Switches in regimens were performed due to various toxicities. Grade III peripheral neuropathy with paresthesias in fingers and toes, and alopecia universalis appeared during gemcitabine-nab-paclitaxel regimen. Persistent grade III neurotoxicity with formication, and grade II/III nausea and vomiting required discontinuation of FOLFIRINOX regimen. After seeing disease progression with gemcitabine monotherapy, a new treatment regimen with nanoliposomal irinotecan (in combination with 5-fluorouracil and leucovorin) was introduced in September 2017. There was a partial remission seen after 6 cycles, but a quick disease progression with increase in laboratory markers followed after a short pause in the treatment. However, CT scan showed no progression of the disease, and therefore, chemotherapy was reinstituted. Low grade adverse events of this regimen included diarrhea, nausea and fatigue. Thus far, patient received 11 cycles of nanoliposomal irinotecan, and remained in good condition after over 2.5 years of receiving chemotherapy. According to last CT scan, there has been a progression in size of one of the liver metastases, while the primary tumor and other liver metastases remained stable. New nanoparticle chemotherapy formulations played a significant role in the treatment success of presented patient.

Audience Take Away:

- New nanoliposomal technologies are changing the clinical practice and are becoming commonly used as a treatment strategy for metastatic pancreatic cancer.
- Nanoliposomal irinotecan in combination with 5-fluorouracil and leucovorin is a promising second line option for the treatment of metastatic pancreatic cancer.
- With a careful selection of treatment strategies in patients with good performance status in metastatic pancreatic disease, quality and duration of life may be significantly increased.
- The audience will be presented with a real case example of a patient with metastatic pancreatic adenocarcinoma, in whom various chemotherapy regimens have been used over a period of 2.5 years. An insight into the nanoparticle formulations used in actual clinical practice with its benefits and risks will be given.
- Case presentation from the clinical practice could bring a broader understanding of the role and importance of new drug-delivery systems in cancer treatment.

Biography

Matej Dobravc Verbic graduated at the Faculty of pharmacy, University of Ljubljana in 2010. Since then, he works as a hospital and clinical pharmacist at the University Medical Centre Ljubljana (UMCL), Slovenia. In 2012, he was awarded best student at the MSc program in Clinical Pharmacy, International practice and policy at UCL, London. From 2013 to 2016, he was coordinating clinical pharmacy activities at the UMCL Pharmacy. During 2016 and 2017, he was working for non-governmental organization Medecins sans frontieres in Africa. Since the return, he continues his clinical work at the Department for gastroenterology at UMCL.

Nanostructured biomaterials and technologies for bone regeneration

Marcelo Nacucchio
University of Buenos Aires, Argentina

New scaffolds and biomaterials will be presented with pharmaceutical characterization as well biological evaluation. For one bioceramic/polymeric new product clinical trials results will be presented. Prospectives technologies associated with this field of bone regeneration will be presented and discussed regarding your advantages and potentials under a risk management assessment.

Audience Take Away:

- Useful for academic as well industrial colleagues for new research projects related to regenerative medicine.
- As well pharmaceutical technology mainly regarding to drug delivery systems.

Biography

Marcelo Nacucchio is Professor of Pharmaceutical Technology, School of Pharmacy and Biochemistry, University of Buenos Aires, Argentina. Member of National Academy of Pharmacy and Biochemistry of Argentina, Real National Academy of Pharmacy of Spain (Madrid), Real Acadèmia de Farmàcia de Catalunya (Barcelona), Peruvian Academy of Pharmacy (Lima, Perú) and the Iberoamerican Academy of Pharmacy (Seville/Granada-Spain).

He has published more than 40 peer review papers, co-authored 5 books chapters, Editor of book Topics in Pharmaceutical Technology (Editorial Universitaria de Buenos Aires-in press), as well more than 100 presentations in international events. He is or has been Member of the editorial board of several scientific journals like Journal of Controlled Release (Elsevier), Journal of Drug Delivery Science and Technology (Elsevier former Ed. De la Santé)), Latin American Journal of Pharmacy (Argentina), Annals of the National Academy of Pharmacy and Biochemistry (Argentina), etc. Member of the scientific board of the Argentine National Pharmacopeia (Ministry of Health, Argentina). Organizer and Member of several scientific committees of meetings in Argentina, USA, France, Brazil, México, Perú, Germany, Spain, Chile, Uruguay, Colombia, Hungary, UK, etc. President of Science and Technology dept. Argentinian Pharmaceutical Laboratories Chamber. Founder and Scientific secretary of Controlled Release Society, Argentinian Chapter.

Awarded 8 times for your contributions in the Science and Technology (Ministry of Science and Technology, National, Academy of Pharmaceutical Sciences, University of Buenos Aires) as well Entrepreneurial activities (Fundación Invertir, BBVA, MAPFRE Foundation, FUNPRECIT Foundation, Presidency of the Argentine Nation).

CONTENTS

Brain targeted nanotherapeutics: An enticing journey from ideation to product realization

Vandana B. Patravale Ph.D.
Institute of Chemical Technology, India

Dementia (neurodegenerative ailments) accounts for over 50 million cases worldwide with estimated new 7.7 million cases every year. Neurodegenerative ailments associated progressive decline in clinical condition mainly results from poor transport of therapeutic actives across blood brain barrier (BBB) and oxidative stress induced disease progression. To overcome this challenge, we developed smart targeted micellar nanocarriers (t-micelles) comprising a novel lipid bioconjugate (t-ligand) with an inherent ability to circumvent BBB via active transport pathway (patented technology). The t-ligand was designed using in silico glide molecular docking on BBB active transport receptor crystal structure. Designed t-ligand exhibited selective affinity binding at the BBB active transport receptor site and was synthesized successfully. The t-ligand exhibited self-assembling property and the resulting micellar geometry was optimized using SANS tool.

For therapeutic application, t-micelles of donepezil (first line drug for treatment of dementia) were developed and incorporated in gel for microneedle assisted transdermal delivery. t-Micelles showed 1.6 fold higher brain permeation in zebra fish model as competed to plain micelles. The Draize patch test confirmed suitability of proposed treatment regimen and showed 4 fold increment in skin permeability flux as compared to treatment without microneedle patch. In vivo pharmacokinetic and biodistribution studies demonstrated 3 fold rise in bioavailability with significantly high donepezil brain uptake when given as microneedle pretreated transdermal t-micellar gel in contrast to marketed oral formulation. As second application, t-micelles of curcumin (antioxidant-neuroprotective drug for treatment of neurodegenerative disorders) were also developed and incorporated into a nasal spray for nose-to-brain delivery. In vivo pharmacokinetic and biodistribution studies demonstrated enhanced brain transport of curcumin with t-micelles mainly in the dementia sensitive areas of brain viz. olfactory region, hippocampus and cerebellum. The studies confirmed the potential of t-micelles as a platform Trojan Horse strategy to improve the brain delivery of therapeutic actives and confirmed its suitability towards effective delivery via multiple routes of administration.

Key features:

- Next generation novel, targeted and efficacious strategy to treat neurological ailments
- Industrially feasible and scalable platform technology
- Patented technology

Audience Take Away:

- A scientific and rationale thought process for innovative targeted nanoformulation development
- Step by step approach towards in-depth planning and execution from ideation to product realization

Biography

Vandana Patravale is a Professor of Pharmaceutics at Department of Pharmaceutical Sciences and Technology of the Institute of Chemical Technology, India. She has over 100 refereed publications, 250 research presentations, 2 books, 11 book chapters, 9 granted patents, 24 patents in pipeline and 2 trademark registries to her credit. Her areas of expertise include development of novel nanocarriers for treatment, diagnosis and prevention of various ailments, fabrication of medical device viz. coronary stents, intrauterine devices etc. She is a recipient of prestigious Bill and Melinda Gates Foundation grant to develop the first ever eco-friendly nanovaccine for nasal immunization.

Investigations on the cytotoxic effect of gold nanoparticles synthesized using Ferulic acid on human epidermoid carcinoma (A431) cells

Lonchin Suguna*, Ph.D., Indra Rajendran, M.Sc., Rama Rajaram , Ph.D., Rajaram Anantanarayanan, Ph.D.
Central Leather Research Institute, India

Nowadays, gold nanoparticles (AuNPs) are gaining wide attention in several areas including research and development and medical fields. Certain polyphenols have the property of converting the Au3+ solution into AuNPs at an appropriate pH and at the same time binding to them. One such polyphenol, ferulic acid, (fa) has been used to synthesize gold nanoparticles. Ferulic acid (4-hydroxy-3-methoxycinnamic acid) is a polyphenol found in coffee, rice, fruits (citrus fruits, banana, and orange juice) vegetables (eggplant, bamboo shoots, beetroot, cabbage, spinach and broccoli) and beverages. It has been used in the treatment of diabetes, cardiovascular diseases, neurodegenerative disorder, Alzheimer's disease, skin diseases, melanoma and non-melanoma skin cancers. In this study, stable gold nanoparticles (AuNPs) have been formed by reacting ferulic acid with $HAuCl_4$ at room temperature. Ferulic acid also acts as the stabilizing agent. Optimal formation of fa-AuNPs was obtained when the pH of ferulic acid was 9.5 and MR for ferulic acid to $HAuCl_4$ was 1:4. The synthesized fa-AuNPs have been characterized using UV- Visible spectroscopy, HR-TEM, DLS and FTIR analyses. The average size of fa-AuNPs was found to be 34.2 ± 1.3 nm as measured by DLS. fa-AuNPs were found to induce cytotoxicity to human epidermoid carcinoma cells (A431) in a concentration and time dependent manner. Further, the mode of cell death was via apoptosis, as evidenced through sub-G1 population. The loss of mitochondrial membrane potential (MMP) was observed with increase in ROS levels and caspase -3 activity. From these results, it could be concluded that fa-AuNPs induced cell death of A431 cells via apoptosis through mitochondria dependent pathways. Hence, fa-AuNPs can be considered as a promising candidate for use in skin cancer treatment.

Audience Take Away:

- Will learn the techniques for the synthesis of ferulic acid reduced gold nanoparticles
- Can try these nanoparticles in any other cancer cell lines and observe whether they have similar cytotoxic effect

Biography

Lonchin Suguna has completed her Ph.D at 27 from the University of Madras. She did her postdoctoral studies at ETH-Zentrum, Switzerland. She is working as a Scientist in the Department of Biochemistry, Central Leather Research Institute, India. She has published 60 papers in reputed journals and serving as a reviewer, Editorial board member for many journals. She was awarded Mr.V.V.Swaminathan Diamond Jubilee Research Endowment award for the outstanding contribution in the scientific evaluation of medicinal properties of plants, by Indian Association of Biomedical Scientists, 2012 (Gold Medal). She received Fellow of International Medical Sciences Academy (FIMSA) in the year 2014.

magnus Group

DAY 2

WORKSHOP

2ND EDITION OF GLOBAL CONFERENCE ON

Pharmaceutics and Drug Delivery Systems

JUNE 04-06, 2018
ROME, ITALY

CONTENTS

Biography

Mario Jug, Ph.D. is an associate professor at the Department of Pharmaceutical Technology at Faculty of Pharmacy and Biochemistry, University of Zagreb. He received a Ph.D. degree in Pharmacy at the University of Zagreb in 2006. He was trained at several prestigious institutions abroad, including the PostDoc research at the University of Florence under the supervision of Professor Paula Mura and several shorter visits to East NMR Center at University of Debrecen. His scientific and teaching activities are focused in the field of Pharmaceutical Technology and Advanced Drug Delivery System. He was active researcher in several scientific projects funded by Ministry of Science and Education of Republic of Croatia, Croatian Science Foundation and one project granted by BICRO. Until now, Mario Jug has published 37 scientific papers of which 28 are listed in Current Content Database, that received more than 400 quotations in Scopus database.

Challenges of *in vitro* drug release testing in case of advanced mucosal formulations

Mario Jug
University of Zagreb, Croatia

Mucosal route of drug delivery is recognised as suitable alternative to conventional drug administration routes (i.e. oral and parenteral), providing the possibility of more efficient local therapy with reduced systemic drug exposure as well as alternative application route for drugs that undergo extensive biotransformation in liver that leads to low and variable oral bioavailability. Nowadays, nanotechnology has been introduced to such delivery systems in order to improve their efficiency and safety. All this brings new challenges in evaluation of such formulations, prompting us to critically revise and upgrade the currently used methodology. *In vitro* release test is an important assay both in product development phase as well as in its quality control assurance. However, considering the diversity in formulations design, physicochemical and release characteristics of mucosal delivery systems, it is not possible to devise a single method which would be suitable for such purpose. This presentation is aimed to offer an extensive overview of currently available methodologies, both compendial and noncompendial, for *in vitro* drug release testing of mucosal delivery systems aimed for ocular, nasal, oromucosal, vaginal and rectal application. Critical parameters of such assays and instrumental setups will be discussed in details with a special focus on the evaluation of nanodelivery systems. In order to avoid unnecessary proliferation of equipment and method design, compendial apparatuses and methods should be used as a first approach in method development when applicable. Equipment set up, the selection of dissolution media type and volume, membrane characteristics, agitation speed, temperature, and assay analysis technique need to be carefully selected based on the properties of mucosal drug delivery system. The final goal of the method development is to obtain adequate simulation of conditions present *in vivo* at the application site. This would lead to development of novel biorelevant *in vitro* dissolution/release methods should that would enable better prediction of formulation performance *in vivo* and, preferably, the establishment of an *in vitro/in vivo* correlation.

Audience Take Away:

- The audience will get useful guidelines how to perform in vitro release testing of specific formulation aimed for mucosal delivery, that could be readily applicable in their laboratory
- Some practical, ready to use solution to the problems present in the field of drug release testing will be given, in relation to the apparatus setup, media preparation and selection, sampling etc.
- Critical analysis of the currently available methodology will allow the audience to avoid some of the common mistakes and obtain more accurate data
- This presentation might initiate new research lines

magnus Group

DAY 2

POSTERS

2ND EDITION OF GLOBAL CONFERENCE ON

Pharmaceutics and Drug Delivery Systems

JUNE 04-06, 2018
ROME, ITALY

Discovering multiple drug binding sites and modes with Wrap 'n' Shake

Mónika Bálint[1]*, Csaba Hetényi[1], PhD, Gabriella Schilli[1], István Horváth[2]
[1]Department of Pharmacology and Pharmacotherapy, Medical School, University of Pécs, Szigeti út 12, 7624 Pécs, Hungary.
[2]Chemistry Doctoral School, University of Szeged, Dugonics tér 13, 6720 Szeged, Hungary.

Blind docking has been widely used for fast mapping of binding sites on the entire surface of drug targets. Reliability of blind docking is limited by approximations of hydration models, simplified handling of molecular flexibility, and imperfect search algorithms. Wrap 'n' Shake (WnS)[1,2] a systematic, atomic resolution method was developed to overcome such limitations of blind docking. The poster presentation features how WnS systematically "wraps" the entire target into a monolayer of ligand molecules and extracts functional binding sites by rapid molecular dynamics shakers. WnS was validated on biologically important systems such as mitogen-activated protein, tyrosine-protein kinases, key players of cellular signaling, and farnesyl pyrophosphate synthase, a target of antitumor agents.

Audience Take Away:

- WnS is a systematic method which predicts stable positions of ligands on the target surface. WnS combines the advantages of a fast docking, with the precision of explicit solvent molecular dynamics. WnS is freely available, and automatized. WnS works is synergy with popular open source program packages AutoDock and Gromacs. We envision that WnS can become the tool of choice for systematic exploration of multiple binding sites and modes of ligands in drug design and structural biology.

Biography

Mónika Enikő Bálint is an Assistant Lecturer in Pharmacology. Her main area of current research is focused on the development of pharmacoinformatics tools and investigation of molecular pathomechanisms of diseases. Mónika started her PhD studies in 2013, after winning a PhD scholarship from Balassi Institute in Budapest, Hungary. Currently she is the first author in two, and the co-author of other seven scientific articles finalizing her PhD Thesis. Mónika works in the research group of Assoc. Prof. Csaba Hetényi, at the Department of Pharmacology and Pharmacotherapy, Medical School, University of Pécs, Hungary.

Thermoresponsive nanocarriers for doxorubicin delivery combined with hyperthermia

Ilya Yakavets[1,2,4*], M.Sc.; Aigul Kulmukhamedova[1,2,3], M.D.; Zied Ferjaoui[5,6], M.Sc.; Halima Alem[5], Ph.D.; Lina Bezdetnaya[1,2] M.D., Ph.D.; Sophie Marchal[1,2], Ph.D.

[1] CRAN, CNRS UMR 7039, Université de Lorraine, Nancy, France
[2] Institut de Cancérologie de Lorraine, Vandoeuvre-lès-Nancy, France
[3] Department of Radiology, Medical Company Sunkar, Almaty, Kazakhstan
[4] Belarussian State University, Minsk, Belarus
[5] Institut Jean Lamour, CNRS UMR 7198, Université de Lorraine, Nancy, France
[6] Unite Nanomatériaux et Photonique, Faculté des sciences de Tunis El Manar, Tunis, Tunisia

Due to their ability to carry anticancer drugs and generate localized heat when exposed to an alternating magnetic field, superparamagnetic iron oxide (SPIO) nanoparticles (NPs) can be used as multimodal cancer therapy agent by combining chemotherapy and hyperthermia. Fe3O4 nanoparticles were synthesized with covalent grafting of a biocompatible responsive copolymer based on 2-(2-methoxy) ethyl methacrylate (MEO2MA) and oligo (ethyleneglycol) methacrylate (OEGMA) on a ferromagnetic core. Lower critical solution temperature (LCST) of the core/shell NPs was tuned in physiological media in order to release the cancer drug at controlled temperatures. The 41-42°C LCST was obtained with a copolymer composed with 60% MEO2MA and 40% OEGMA. The second step consisted to functionalize the same core/shell by grafting folic acid (FA), a biological cancer targeting molecule at the end of the MEO2MA60-co-OEGMA40 copolymer. Both types of NPs (NP and NP-FA) were loaded with the anticancer agent doxorubicin (DOX). *In vitro*, DOX release kinetics was investigated at 42°c: 25% at 5h, 50% at 24h and 100% at 56h of DOX release were measured for both types of NP. At 37°C, NPs were found stable until 24h (<10% DOX release).

Further, the viability of human ovarian cancer cells (Skov3) exposed to NPs, free DOX or DOX-NPs for 24h at 41°C or 37°C for control cells, was assessed by measuring cell metabolic activity (MTT test). Results showed that NPs (without DOX) preserved cell viability (> 78.44 ± 9.48 %) irrespective of the temperature and the NP concentration. DOX-NPs at 41°C strongly decrease cell viability (32.97 ± 4.31 % cell viability vs 66.03 ± 5.15 % at 37°C). Compared with free DOX, DOX-NPs at 37°C were significantly less cytotoxic (66.03 ± 5.15 % vs 32.97 ± 4.31 % cell viability for 20 µg/ml DOX). At 41°C, cell viabilities were 32.97 ± 4.31 % and 17.25 ± 1.80 % cell for respectively DOX-NPs and free DOX. Considering that the release of DOX from NPS during 24h at 41°C was only 50%, DOX-NP cytotoxicity (32.97 ± 4.31 %) was found comparable to that (25.84 ± 6.82 %) obtained for 10 µg/ml free DOX.

The last step of the study concerned FA functionalized DOX-NPs (DOX-NP-FA). Skov3 cells highly express FA receptors on the external surface of their plasmatic membrane and need to be maintained in FA-free medium to favor the binding of NPs to the receptors. Because the lack of FA at 41°C during 24h is detrimental for cell viability, experiments were carried out at 37°C and at 41°C for 5h. Preliminary results showed that DOX-NP-FA were slightly less cytotoxic than free DOX at 37°C (59.47±6.63% vs 47.33±6.63% cell viability). At 41°C, the loss of cell viability was found equivalent for both agents.

This study demonstrates the potential of Fe3O4@P(MEO2MA60-co-OEGMA40) nanoparticles for cancer treatment combining chemotherapy and hyperthermia.

Acknowledgements: This work was supported by the JCS «Center for International Programs», Kazakhstan.

Audience Take Away:

- This presentation establishes the potential of supermagnetic iron oxide nanoparticles in the treatment of ovarian cancers combining chemotherapy and hyperthermia.
- This work opens the way to the development of core/shell nanomaterials for drug delivery.

Biography

Ilya Yakavets is a co-directed PhD student in Université de Lorraine (Nancy, France) and in Belarussian State University (Minsk, Belarus). He defended his Master degree in Belarussian State University (Minsk, Belarus) in 2016 in the field of Biophysics.

Presently, his PhD research focuses on the application of hybrid nanosized photosensitizer carriers based on liposomes and cyclodextrins in photodynamic therapy. The current abstract describes PhD study results of development and application of drug-in-cyclodextrin-in-liposome nanoparticles to improved delivery of porphyrin photosensitizer to the tumor targets. The presentation this PhD project at BioSE Doctoral School (Nancy, France) was awarded by the first prize in 2017.

In vivo siRNA delivery in whitefish: siRNA uptake and the efficacy of gene expression silencing

Pawel Brzuzan[1*], Ph.D., Maciej Woźny[1], Ph.D., Maciej Florczyk[1], M.Sc., Paulina Budzińska[1], Bogdan Lewczuk[2], Ph.D., Piotr Gomułka[3], Ph.D., Ph.D., Stefan Dobosz[4]

[1]Department of Environmental Biotechnology, Faculty of Environmental Sciences, University of Warmia and Mazury in Olsztyn, ul. Słoneczna 45G, 10-709 Olsztyn, Poland

[2]Department of Histology and Embryology, Faculty of Veterinary Medicine, University of Warmia and Mazury in Olsztyn, ul. M. Oczapowskiego 13, 10-713 Olsztyn, Poland

[3]Department of Ichthyology, Faculty of Environmental Sciences, University of Warmia and Mazury in Olsztyn, ul. M. Oczapowskiego 5, 10-719 Olsztyn, Poland

[4]Department of the Salmonid Research in Rutki, Inland Fisheries Institute in Olsztyn, Rutki, 83-330 Żukowo, Poland

The delivery of therapeutic snippets of RNA (mainly siRNA) to the right cells at the right time is an essential step in the RNA mediated therapeutics, that in fish has not been studied in sufficient detail. Here we report an efficient in vivo delivery of MiRNA92b-3p mimic to whitefish, a Teleost fish with commercial importance. To address this issue, juvenile individuals of whitefish were exposed to synthetic miRNA, miR92b-3p mimic through intraperitoneal injection. After 24 and 48 h of the treatment, blood and livers of the fish were collected to tract uptake of the synthetic miRNA and to assess its specific and off-side effects. qPCR indicated that, within the first 24 h of the treatment, miR92b-3p levels were markedly elevated in the plasma and the liver of the injected fish compared to control fish injected with vehicle solvent only. Furthermore, 48 h after the injection, the mimic abrogated mRNA expression of several genes in the liver, including p53 tumor suppressor and its downstream effector, cdkn1a. Finally, histopathological and ultrastructural analyses did not show any major changes in the livers of the exposed fish, as well as no differences were found in biochemical measurements of the fishes blood between the experimental groups. Together, these results indicate that the miR92b-3p mimic was effectively delivered into the liver of the injected fish, and that the treatment did not cause any distinct off-side effects. The described methodology of miRNA mimic delivery has utility for the study of miRNA-dependent silencing mechanisms and the development of both miRNA diagnostic marker and therapeutic target in fish liver injury.

The study was funded by the National Science Centre of Poland (decision number: DEC-2016/21/B/NZ9/03566)

Audience Take Away:

- The described methodology of miRNA mimic delivery has utility for the study of miRNA-dependent silencing mechanisms in cold-blooded fish

Biography

Brzuzan leads a team that focuses on the role of microRNA in biology and medicine with a special emphasis on toxicology. The team has skills in using both experimental fish (whitefish, rainbow trout) and cell cultures to study perturbations of molecular responses to environmental pollutants. His present interest is in disease states featuring microRNA in drug induced liver toxicity as well as current understanding of microRNAs as therapeutic targets in cancer. He looks also if bioactive cyanobacterial metabolites have molecular abilities to modulate regulatory elements of cell processes (RNA, protein), thus becoming important tools for clarifying the mechanisms of these cell processes and serving as lead structures for the development of new therapeutic agents.

Unnatural amino acids derived peptidomimetics with potent anti-biofilm activity

Jeong Kyu Bang Ph.D
Korea Basic Science Institute, Republic of Korea

We present on the first chemical synthesis of ultra-short pyrazole-arginine based antimicrobial peptidomimetics derived from the newly synthesized N-alkyl/aryl-pyrazole amino acids. Through systematic tuning of hydrophobicity, charge, and peptide length, we can obtain the shortest peptide Py11 with the most potent antimicrobial activity. Py11 displayed greater antimicrobial activity against antibiotic-resistant bacteria, including MRSA, MDRPA and VREF and was approximately 2-4 times higher than that of melittin. Besides its higher selectivity (therapeutic index) toward bacterial cells than LL-37, Py11 showed highly increased proteolytic stability against trypsin digestion, and maintained its antimicrobial activity in the presence of physiological salts. Interestingly, Py11 exhibited higher anti-biofilm activity against MDRPA compared to LL-37. The results from fluorescence spectroscopy, and transmission electron microscopy (TEM) suggested that Py11 kills bacterial cells possibly by integrity disruption damaging the cell membrane, leading to the cytosol leakage and eventual cell lysis. Furthermore, Py11 displayed significant anti-inflammatory (endotoxin-neutralizing) activity by inhibiting LPS-induced production of nitric oxide (NO) and TNF-alpha. Collectively, our results suggest that Py11 can serve a new class of antimicrobial and antisepsis agents.

Audience Take Away:

- Synthesis of Fmoc-pyrazole amino acids for the first time
- Ultra short peptidomimetics showed broad-spectrum of antimicrobial activity including MRSA, VREF, and MDRPA
- Ultra short peptidomimetics also showed potent anti-biofilm activity

Biography

Jeong Kyu Bang has been working as a medicinal chemist at Korea Basic Science Institute, Korea since 2007, where he is currently involving in the synthesis of small molecule and peptidomimetics inhibitors for antimicrobial and anti-cancer targets. After completion of his PhD from Osaka University Japan, he moved to NIH, USA for post-doc. His research is mainly focused on the synthesis of unnatural amino acid and small molecules for the antibacterial drug development, and also actively engaged on developing the inhibitors for PLK1PBD.

Poly(glycolide-ε-caprolactone) and poly (glycolide-ε-caprolactone-D,L-lactide) coatings enriched with ciprofloxacin formed on metallic implants

J.Jaworska[1]* Ph.D., K.Jelonek[1] Ph.D., W.Kajzer[2] Ph.D., J.Szewczenko[2] Ph.D., J.Kasperczyk[1]
[1]Polish Academy of Sciences, Poland
[2]Silesian University of Technology, Poland

Caprolactone-based polymers are willingly used as a biodegradable materials with desirable properties. They are frequently used as a drug delivery systems for controlled release of different active substances like: antibiotics, growth factors, and hormones. They are mostly copolymers composed of L,L or D,L-lactide and **ε**-caprolactone. Titanium (Ti) is widely used as a biomedical material since it has extraordinary mechanical properties, high corrosion resistance and satisfactory inherent osseointegration ability. It is used in orthopedic and dental applications. Its biomedical applications are connected with their good biocompatibility and corrosion resistance. From the other hand, the use of metallic implants for medical applications is associated with some complications, such as: bone infection, pain, metallic staining of the surrounding tissue, device failure, muscular necrosis, periprosthetic fibrosis and loosening of prosthesis. Metallic implants are constantly modified in order to overcome these difficulties.

Biodegradable coatings containing caprolactone units additionally enriched with ciprofloxacin formed on Ti6Al4V alloys have been developed. The polymer coatings were investigated as a carrier for ciprofloxacin-antibacterial drug. Coatings have been obtained according to the dip-coating method. Two kinds of polymers containing caprolactone units have been used: poly(glycolide-**ε**-caprolactone) and poly(glycolide-**ε**-caprolactone-D,L-lactide). The properties of the layered metal/polymer+drug system have been presented and the influence of the kind of polymer on the drug release has been evaluated. Different types of drug release profile depend on the type of used system. The CFX release from poly(glycolide-**ε**-caprolactone) is uniform with one stage, contrary to poly(glycolide-**ε**-caprolactone-D,L-lactide). The mechanism of ciprofloxacin release from GCap and GCapL matrices is different.

The objective of presented study was the comparison of ciprofloxacin releasing bioresorbable coatings made of copolymer and terpolymer: poly(glycolide-**ε**-caprolactone) and poly(glycolide-**ε**-caprolactone-D,L-lactide) on titanium-based prototype forms of the implants.

The work is the result of the research project No. 2015/19/B/ST5/03431 funded by the National Science Centre

Audience Take Away:

- The audience will know which factors influence the release mechanism of the drug from biodegradable coatings on metallic implants
- The audience will know what should be taken into an account during designing of metallic implants with biodegradable coatings
- The audience will know how to extend the function of metallic implants- to provide the therapeutic function
- The research provide practical solution to a problem which concern medical implants like complications connected e.g. with bone infection

Biography

Joanna Jaworska have finished Silesian University, faculty of Chemistry in 2004, then I started my scientific work in Centre of Polymer and Carbon Materials of Polish Academy of Sciences. During my PhD work I have analyzed the degradation process of different aliphatic polyesters used in medicine by means Nuclear Magnetic Resonance Spectroscopy. After PhD (in 2011) I focused on designing and developing various drug delivery systems where I incorporated different active substances like: anti-inflammatory drugs, cytostatics, antirestenotic drugs. Currently, my research concern biodegradable coatings on medical implants with ability to release the drug.

Dual-targeted biodegradable micelles for anticancer drug delivery

Katarzyna Jelonek[1]*, Alicja Zajdel[2], Adam Wilczok[2], Małgorzata Latocha[3], Monika Musiał-Kulik[1], Aleksander Foryś[1], Janusz Kasperczyk[1,2]

[1]Centre of Polymer and Carbon Materials, Polish Academy of Sciences, Curie-Sklodowska 34 St., 41-819 Zabrze, Poland

[2]School of Pharmacy with the Division of Laboratory Medicine in Sosnowiec, Medical University of Silesia, Katowice, Poland, Chair and Department of Biopharmacy, Jedności 8, Sosnowiec, Poland

[3]Medical University of Silesia, School of Pharmacy with the Division of Laboratory Medicine in Sosnowiec, Department of Cell Biology, Sosnowiec, Poland

Polymeric micelles have been widely studied and developed as drug carrier for targeting solid tumors. They are able to incorporate drugs of poor water solubility in the hydrophobic core while the hydrophilic corona provides biocompatibility and prolonged circulation in blood after intravenous administration. The effectiveness of nano drug delivery may be increased by using active targeting ligands. Folate-targeted drug delivery systems can improve the tumor uptake by folate receptor-mediated endocytosis and avoid their non-specific attacks to normal tissues. Folic acid (FA) has been known to target FA receptors (FAR) that are overexpressed in several human carcinomas including breast, ovary, endometrium, kidney, lung, head and neck, brain, colon and myeloid cancers while only minimally distributed in normal tissues. Biotin receptors are often overexpressed on the surface of rapidly proliferating cancer cells. It has been found that cells that over-express folate receptors also show over-expression of biotin receptors. Moreover, tumors are heterogenous and tumor cells are substantially different from each other. Therefore, it was hypothesized that the tumor – targeting efficiency would be enhanced if the drug delivery system is decorated by both targeting molecules, which can target both vitamin receptors. Additionally, it is beneficial to incorporate more than one active agent into nanoparticles, because combination therapy is recognized as more efficient compared to conventional therapy based on a single therapeutic agent. The aim of the study was to obtain biodegradable poly(L-lactide)-co-poly(ethylene glycol) (PLA-PEG) micelles functionalized with folic acid and biotin. Paclitaxel or paclitaxel and curcumin were loaded into micelles. Encapsulation efficiency and *in vitro* drug delivery was studied. Finally, the *in vitro* cytotoxicity against Ovcar-3 cell line was studied.

The work is the result of the research project No. 2017/01/X/NZ7/00276 funded by the National Science Centre.

Biography

Katarzyna Jelonek is an assistant professor at the Centre of Polymer and Carbon Materials, Polish Academy of Sciences. Her research interests focus on the medical and pharmaceutical application of biodegradable polymers, especially in the field of controlled drug delivery systems. Currently she works on anticancer delivery systems (e.g. targeted single- and multidrug micelles) and anti-restenotic systems (drug-eluting coatings of vascular scaffolds).

PLGA nanoparticles co-delivering MDR1 and BCL2 siRNA for overcoming resistance of paclitaxel and cisplatin in recurrent or advanced ovarian cancer

Hyung Jun Ahn, Ph.D.,
Korea Institute of Science and Technology, South Korea

The inherent or acquired resistance to paclitaxel and cisplatin, which are commonly used chemotherapeutic agents for ovarian cancer treatment, remains an important issue in chemotherapy of multidrug resistant ovarian cancer. Currently, it is still challenging to deal with the recurrent or advanced stage ovarian cancer. When drug efflux and anti-apoptotic pathways are highly interdependent and also involved in developing the resistance of multidrug resistant ovarian cancer, simultaneous inhibition of both pathways represents the potential targets to enhance the efficacy of chemotherapy. Herein, we introduce PLGA nanoparticles system as a "dual RNAi delivery system" to contain both MDR1 and BCL2 siRNA, which is designed for simultaneous inhibition of drug efflux and cell death defense pathways. In the present studies, siRNA-loaded PLGA nanoparticles efficiently elicit the simultaneous suppression of both genes, which consequently shows more enhanced drug-sensitivity than sole suppression of drug efflux or anti-apoptosis in the resistant ovarian cancer cells, owing to the interdependence of both pathways. Our siRNA-loaded PLGA nanoparticles for co-delivering MDR1 and BCL2 siRNA provide an efficient combination therapy strategy to overcome the chemoresistance of paclitaxel and cisplatin on the paclitaxel-resistant SKOV3-TR and cisplatin-resistant A2780-CP20 ovarian cancer respectively, as well as to expand the use of traditional chemotherapeutics to the treatment of recurrent or advanced ovarian cancer.

Audience Take Away:

- When drug efflux and anti-apoptotic pathways are highly interdependent and also involved in developing the resistance of multidrug resistant ovarian cancer, simultaneous inhibition of both pathways represents the potential targets to enhance the efficacy of chemotherapy.
- Our siRNA@PLGA nanoparticles, as a dual RNAi suppressor system on the MDR ovarian cancer cells, provide a combination therapy strategy to overcome the chomoresistance of paclitaxel and cisplatin on MDR SKOV3-TR and A2780-CP20 ovarian cancer.
- Our studies also suggest an efficient means to expand the use of traditional chemotherapeutics to the treatment of recurrent or advanced ovarian cancer.

Biography

Hyung Jun Ahn is a Principal Research Scientist of Biomedical Research Institute at Korea Institute of Science and Technology (KIST). He received his BS, MS, and PhD degrees from Seoul National University (Chemistry). After postdoctoral training under the supervision of Prof. Yigong Shi at the Department of Molecular Biology, Princeton University, Dr. Ahn joined a Senior Research Scientist, KIST in 2006. Dr. Ahn has been an Adjunct Professor at the Department of Biomedical Engineering in University of Science and Technology since 2010. Dr. Ahn's research is concerned with biomaterials-based drug delivery, siRNA delivery, and molecular imaging technology.

Non-invasive method for screening drug penetration in skin using different dermal drug delivery systems by Raman microscopy

Attila Gácsi*, Ph.D., Mónika Bakonyi, Szilvia Berkó, Ph.D., Anita Kovács, Ph.D., Mária Budai-Szűcs, Ph.D., Erzsébet Csányi, Ph.D.
University of Szeged, Hungary

Dermal drug delivery systems are getting more attention nowadays because their application is beneficial in many conditions. Dermal application is advantageous due to a decrease in potential adverse reactions and the avoidance of first pass metabolism. However, the skin penetration of drugs is a really complex process because many factors have an impact on it.

The exact knowledge of drug distribution in the skin would be necessary for the optimization of dermal formulations by locate their penetration pathways. Spectroscopic methods can provide molecular information about the structure of skin specimens. Raman spectroscopy is a modern spectroscopic technique based on detecting the characteristic vibrational energy levels of a molecule. This technique is suitable for detecting changes in the structure of skin components and also for following-up the penetration of drug components.

The poster presentation will show the advantage of Raman microscopy on the screening of drug penetration in different skin layers. We used four different drug delivery systems (hydrogel, oleogel, lyotropic liquid crystal (LLC) and nanostructured lipid carrier (NLC)) for screening drug penetration in skin. The model drug component was lidocaine.

Producing proper and spectacular images for the presenting the drug component presences in different skin regions, some other observations need to be done. Firstly, checking the Raman sensitivity of the chosen drug is necessary. In our work the lidocaine is suitable model component for the observation. The next step is the checking of different drug carriers' spectral characteristics combining the drug component, placebo and drug containing dermal carrier systems spectra.

For the investigation the surface of human abdominal skin samples were coated with the different dermal carrier systems. After 6 hours treatment, the carrier systems were removed from the skin surface, and tissue samples were performed by using cryomicrotome. The specimens have been observed with Raman microscope, a distribution map of skin samples have been recorded (0.4 mm^2 area, 205 spectra altogether). The Raman distribution maps can be prepared by evaluating the all recorded spectra. The results showed increased drug penetration in the following order: hydrogel, oleogel, LLC and NLC systems. In case of NLC system, lidocaine showed enrichment in lower dermis region.

This research was supported by the project nr. EFOP-3.6.2-16-2017-00009, titled Establishing and Internationalizing the Thematic Network for Clinical Research. The project has been supported by the European Union, co-financed by the European Social Fund and the budget of Hungary.

Audience Take Away:

- Effective and non-destructive method of screening drug penetration in skin.
- Efficiency of Raman spectroscopy on pharmaceutical use.
- Different dermal drug delivery systems' effect on skin penetration.

Biography

Attila Gácsi is research fellow at the University of Szeged, Institute of Pharmaceutical Technology and Regulatory Affairs. He has got the M.Sc. degree in 2012 as chemist and got the Ph.D degree in 2017. He joined to the Dermal and Semisolid Research Group in 2016. The scope of the research group is the development and investigation of different dermal carrier systems and explores the influence on skin of these carriers systems, such as diffusion and penetration studies using diffusion cell and spectroscopic experiments. In this field many publications have been published.

Eucommia ulmoides ameliorates glucotoxicity by suppressing advanced glycation end-products in diabetic mice kidney

Sang Keun Ha* Ph.D., Moon Ho Do, Jinyoung Hur, and Yoonsook
Korea Food Research Institute, South Korea

In this study, we evaluated the effects of EU on AGEs-induced renal disease and explored the possible underlying mechanisms using streptozotocin (STZ)-induced diabetic mice. STZ-induced diabetic mice received EU extract (200 mg/kg) orally for 6 weeks. EU treatment did not change blood glucose and glycated hemoglobin (HbA1c) levels in diabetic mice. However, the EU-treated group showed a significant increase in the protein expression and activity of glyoxalase 1 (Glo1), which detoxifies the AGE precursor, methylglyoxal (MGO). EU significantly upregulated nuclear factor erythroid 2-related factor 2 (Nrf2) expression but downregulated that of receptor for AGE (RAGE). Furthermore, histological and immunohistochemical analyses of kidney tissue showed that EU reduced periodic acid–Schiff (PAS)-positive staining, AGEs, and MGO accumulation in diabetic mice.

Audience Take Away:

- Pharmacuticals, glucotoxicity; advanced glycation end-product

Biography

Korea Food Research Institute, 2011-present.

Study of penetration and analgesic and antiinflamatory effects of indomethacin nanoemulsion

Anayanti Arianto*, Hakim Bangun, and Septania Romauli
University of Sumatera Utara, Indonesia

Background: Indomethacin is a potential nonsteroidal antiinflamatory drugs (NSIDs), but it can cause gasrtointestinal irritation if it is given orally. The delivery system of indomethacin through skin can avoid the side effect, but the skin has a major barrier that is stratum corneum which causes low drug penetration. Therefore, nanoemulsion preparation is made to enhance drug penetration and to avoid the side effects.

Purpose: The purpose of this study was to prepare indomethacin nanoemulsion preparation and to determine the analgesic and antiinflammatory effect in rats.

Method: The nanoemulsion preparations containing 1 % indomethacin was prepared with menthol as enhancer, Tween 80 as surfactant, and sorbitol as co-surfactant by spontaneous emulsification method. The the particle size of nanoemulsion was measured by using Particle Size Analyzer. *In vitro* penetration study was determined with diffusion cell using rabbit's skin. Analgesic effect was measured by using plantar test infrared method in mice and anti-inflammatory effects by using paw edema method in mice.

Results: The average particle size of indomethacin nanoemulsion without menthol was 313.16 nm and nanoemulsion containing 4% menthol was 816.71 nm. The surface tension of indomethacin nanoemulsion and indomethacin nanoemulsion containing 4% menthol were 47.70 and 46.2 dyne/cm, respectively. The addition of menthol increased the penetration of indomethacin and the analgesic and antiinflamatory effects. The penetration of indomethacin and analgesic and antiinflamatory effects of Indomethacin nanoemulsion containing 4 % menthol were higher compared to commercial 1% indomethacin gel.

Conclusion: From the results of the study it can be concluded that the indomethacin can be formulated into nanoemulsion preparation with menthol as enhancer. Indomethacin nanoemulsion with the addition of mentol gives the higher penetration and the analgesic and anti-inflammatory effects.

Biography

Anayanti Arianto is a professor of Department of Pharmaceutical Technology, Faculty of Pharmacy, University of Sumatera Utara. Since 1986 she has been working as academic staff of Faculty Pharmacy, University of Sumatera Utara. She finished her doctoral course on 2015 from Faculty of Pharmacy, University of Sumatera Utara and she became professor of pharmaceutical technology on 2017. Her research interest is about transdermal drug delivery system, gastroretentive drug delivery system; sustained release, and cosmetic preparations. She has published about 15 papers in reputed journals.

Quality evaluation of rifaximin tablets by an eco-friendly spectrophotometric method in the ultraviolet region

Ana Carolina Kogawa, Ph.D.
Universidade Estadual Paulista – UNESP, Brazil

Rifaximin, an oral antimicrobial, acts locally in the gastrointestinal tract with minimal systemic adverse effects. It is mainly used for the treatment of hepatic encephalopathy, but also in cases of ulcerative colitis, irritable bowel syndrome, travelers' diarrhea and acute diarrhea. Rifaximin tablets do not present an ecologically correct method by spectrophotometry in the ultraviolet region neither in official compendiums nor in literature. The analytical techniques for determination of rifaximin reported in the literature require large amount of time to release results and are significantly onerous. Furthermore, they use toxic reagents both for the operator and environment and, therefore, can not be considered environmentally friendly analytical techniques. The objective of this work was to develop and validate an eco-friendly spectrophotometric method in the ultraviolet region to quantify rifaximin in tablets. The method was validated by linearity, selectivity, precision, accuracy and robustness. It was linear over the concentration range of 10-30 mg mL^{-1} with correlation coefficients greater than 0.9999 and limits of detection and quantification of 1.39 and 4.22 mg mL^{-1}, respectively. The validated method is useful and applied for the routine quality control of rifaximin in tablets, since it is effective, low cost and fast in the release of results, it optimizes analysts and equipment and uses environmentally friendly solvents. The quality of a pharmaceutical product is directly related to the health of patients and a practical analysis method and reliable can be the first step in the rational use of pharmaceuticals. In this context, universities have executed a fundamental role serving as research centers for the development and validation of analytical methods.

Audience Take Away:

- The audience will take away from my presentation a useful and applied method for the routine quality control of rifaximin tablets.
- It showed linearity, selectivity, accuracy, precision, robustness and adequate detection and quantification limits in the range 10 to 30 μg mL^{-1}.
- The developed and validated method is effective, fast in the release of results, low cost, it optimizes analysts and equipment, uses environmentally friendly solvents, being considered a green method, which does not prejudice either the operator or the environment.
- The quality of a pharmaceutical product is directly related to the health of patients and a practical analysis method and accurate can be the first step in the rational use of pharmaceuticals.

Biography

Ana Carolina Kogawa graduated in Pharmacy-Biochemistry in 2008, received her Master's in 2012 and PhD in Pharmaceutical Sciences in 2015 from the Universidade Estadual Paulista – UNESP, Brazil. She has experience in managing people, lectures, quality tools and activities of the pharmaceutical industry with emphasis on Quality Ccontrol. She has published more than 40 papers in renowned journals and has been serving as a reviewer of manuscripts in more than 15 international journals. Currently she develops her postdoctoral research at the School of Pharmaceutical Sciences of Araraquara, Brazil, funded by Fundação de Amparo à Pesquisa do Estado de São Paulo (Fapesp).

Radiolabeled drug/ligand loaded Micelles: Exploring diagnostic and therapeutic potentials for glioma through the intranasal route

Prashant G. Upadhaya[1]*, Ph.D. (Tech.) Research Fellow; Swapna J. Nabar[2], Ph.D.; Rajesh Chinagandham[2], Ph.D.; Ankit A. Agrawal[1], Ph.D. (Tech.) Research Fellow, Sharmila Banerjee[2], Ph.D., Vandana B. Patravale[1], Ph.D. (Tech.)
[1]Department of Pharmaceutical Sciences and Technology, Institute of Chemical Technology, India
[2]Radiation Medicine Centre, Bhabha Atomic Research Centre, India

Developing effective methods for drug delivery into the brain is one of the major challenges faced today. In the current arena the research fraternity is mostly involved in the drug discovery and chemical modification of pre-existing molecules which certainly do not facilitate enhanced uptake for most of the systemically administered chemotherapeutic agents. The reason being the complex structure of the blood brain barrier (BBB).

Malignant gliomas are the most common primary tumors that occur in the human brain. The 5-year survival rate for patients with glioblastoma is less than 5% even with surgery followed by radiation and chemotherapy. According to the recent reports, brain cancer is on the rise in geriatric population, also, there are disturbing reports of the brain tumor in younger age groups. Currently, on the diagnosis front, invasive biopsy is the preferred method to confirm the diagnosis of cancer. Some modern brain imaging techniques such as PET, PET-CT, SPECT and SPECT-CT are the various modalities for the detection of tumors and cancers, however, the delivery of contrast/imaging agents when given systematically as an aid for brain imaging is inefficient, due to the complex structure of BBB. On the therapy front, standard treatment consists of maximal surgical resection, radiotherapy, and concomitant and adjuvant chemotherapy with Temozolomide or other anti-cancer drugs either given orally, intrathecally or through the convection enhanced delivery (through skull). Thus, harnessing the potential advantage of BBB bypassing non-invasive route for preferential delivery of diagnostic and therapeutic agents to glioma becomes the prime requirement in the current arena.

Previous studies undertaken in our lab (Jain et. al., 2010) have proved the potential of drug loaded micellar nanocarriers for higher brain uptake through the olfactory axonal pathway. Keeping this in mind we further developed safe, stable, economic and industrially feasible micellar nanocarriers for diagnostic and therapeutic usage to be delivered using non-invasive intranasal route. In order to explore the diagnostic and therapeutic potentials, we radiolabeled the chemotherapeutic drug Methotrexate and the targeting ligand Folic acid with 99mTc (Technetium) using the Design of Experiments approach. The radiolabeled moieties were found to be stable upon evaluation under various nasal and cerebrospinal fluid mimicked conditions. Further, the same were encapsulated into micelles for intranasal administration. The radiolabeled drug loaded micelles were also found to be stable when evaluated under nasal and cerebrospinal fluid mimicked conditions.

Audience Take Away:

- The fabrication of micellar nano-carrier systems
- Radiolabeling of Drugs and Ligands
- Use of diagnostic and therapeutic potentials of nanocarriers and radionuclides
- These insights could further be used by the audience to explore the area of specific targeting of drug/diagnostic agent with the aid of nano formulations.

Biography

Prashant G. Upadhaya is a Ph.D. (Tech.) Research student at the Department of Pharmaceutical Sciences and Technology, Institute of Chemical Technology, Mumbai, India. His research is focused on the development of colloidal formulations for non-invasive treatment of glioma. He has published 9 research articles and 2 book chapters (communicated). He has also delivered several poster and oral presentations at various national and international symposiums.

The most sensitive neurodevelopmental period for the effects of methamphetamine on creating predisposition to drug addiction in adulthood

Ivana Hrebíčková*, Ševčíková Mária, Šlamberová Romana Ph.D.
Charles University, Czech Republic

Psychostimulants, including methamphetamine (MA), have neurotoxic effect, especially, if they are targeting CNS during its critical periods of development. Prenatal/neonatal MA exposure (5 mg/ml/kg) during gestation and/or lactation makes adult rats more sensitive to acute injection to the drug with the same mechanism of action. However, it is still not known which of gestation/lactation stage is the most sensitive to this effect. This study could clarify which of the gestational stage during human pregnancy is the most suited for the treatment of drug-addicted pregnant women. Drug-seeking behavior of adult male and female rats was tested in Conditioned Place Preference (CPP) test. Eight groups of male and eight groups of female rats were tested in adulthood: rats, whose mothers were exposed to MA (5 mg/ml/kg) or saline (SA, 1 ml/kg) during the first half of gestation period (GD 1-11), the second half of gestation period (GD 12-22) and neonatal period (PD 1-11) simulating 1st, 2nd and 3rd trimester, respectively. In order to do so, we compared indirect neonatal applications via the exposed dams with the group of rat pups that received MA or SA directly by injections. Our data demonstrated that application of MA in dose 5 mg/ml/kg during conditioning resulted in increased drug-seeking behavior, but this effect was not affected by prenatal drug exposure. Only neonatal MA exposure influenced creating drug addiction in adulthood. Exposure during early lactation period caused the most significant changes in number of entries and the time spent in the chambers associated with drug administration. Finally, stage of later gestation and early neonatal development seems to be crucial for administration of MA. In conclusion, results suggest that the most significant neurotoxic effects of MA were precisely within the second and third trimester when underway development of monoaminergic nerve terminals in structures responsible for drug-induced alterations in drug-seeking behavior.

Audience Take Away:

- Correlations in human and rat neuro-ontogeny
- Effects of psychostimulants drugs on neurodevelopment
- Model of creating drug-seeking behavior in experimental studies
- Sex differences in drug abuse and drug-seeking behavior
- Sex differences in pharmacokinetics and pharmacodynamics of psychostimulants

Biography

Ivana Hrebickova is a postgraduate student at Charles University in Prague, 3rd Faculty of Medicine. Since 2012 she has been working in Department of Normal, Pathological and Clinical Physiology as a scientific researcher in the field of Biomedicine and also working as a lecturer of Structure and function of human body at Faculty of Medicine. She is currently preparing for the dissertation defense. She is the first author of six scientific publications, and also a co-author of many other publications with impact factor.

magnus Group

DAY 3

KEYNOTE FORUM

2ND EDITION OF GLOBAL CONFERENCE ON

Pharmaceutics and Drug Delivery Systems

June 04-06, 2018
Rome, Italy

Biography

El Hassane Larhrib was educated at the University of Sciences and Technology, Lille I and the faculty of Pharmacy, Lille II, France where he obtained an MSc Biochem, DU Pharm, DESS Pharm. Tech., a certificate in Pharm. Chemistry and. He moved to the UK to do a PhD in Pharmaceutical technology at Liverpool John Moores University, using high speed compaction simulator to fundamentally study the mechanism of compaction of pharmaceutical powders under the supervision of Dr. James Wells and Prof. Mike Rubinstein (1994-1998). Following his PhD, Dr Larhrib worked for 4 years (1998-2002) as Senior Research Fellow in Pharmaceutics at the Department of Pharmacy, King's College London. He worked at Liverpool John Moores University as a Senior lecturer in Pharmaceutics for 6 years (2002-2007) before joining the industry; Solid Solution Limited, Liverpool (2007-2010). He was involved in cosmetic products development and manufacture. He moved to Medway school of Pharmacy before joining the University of Huddersfield as a Senior lecturer in Pharmaceutics in July 2011. Dr. Larhrib is a regular reviewer for many international Pharmaceutical journals and member of editorial board of journal of International Research in Medical and Pharmaceutical Sciences and British Journal of Pharmaceutical Research. He is an academic member of Royal Pharmaceutical Society of Great Britain and Fellow of HEA.

Drug delivery to the lungs from dry powder inhalers: Impact of the inhaler device and patient inhalation manoeuvre

El Hassane Larhrib Ph.D.

University of Huddersfield, UK

Inhaled therapy plays an important role in the management of airway diseases such as, asthma and chronic obstructive pulmonary disease (COPD). Peak inhalation flow has been considered for so many years by the inhalation scientists as the most important parameter governing drug delivery to the lungs from DPIs, however, many patients especially those with low lung capacity are unable to generate sufficient inhalation flow to deaggregate the powder formulation to get most of the dose into their lungs. In addition to the peak inhalation flow (MIF), this presentation will focus on other inhalation parameters such the inhaled volume (Vin) and the acceleration rate of the air flow at the start of the inhalation manoeuvre (ACIM) and to investigate their impact on the dose emission and aerodynamic characteristics from two inhaler devices (low resistance: Ombrez Breezhaler and high resistance device: Easyhaler).

Traditionally, the in-vitro total emitted dose (TED) and its particle size distribution via a DPI is measured using standard pharmacopoeial methods and is widely accepted by the regulatory authorities. The method involves simulating an inhalation profile through a dry powder inhaler (DPI) using a vacuum pump to emit a dose and collect it into a cascade impactor. The measured particle size distributions represent particle deposition into different zones of the lungs. Humans cannot replicate the square wave generated by a vacuum pump; nor can the majority of patients achieve the pharmacopoeia-recommended inhalation parameters (4 KPa pressure drop and 4 Litres inhaled volume). These limitations are becoming more problematic as the use of DPIs are extended to, for example: paediatric, who do not have the lung capacity of a healthy adult. In this presentation we will discuss an Ex-vivo method that replaces the vacuum pump used in pharmacopoeia methods with a patient inhalation profile to provide information on the TED that the patient would have inhaled in real life.

Audience Take Away:

- The difference between different dry powder inhalers (DPIs) and how the design of a DPI device affects drug delivery to the lungs.
- Should we look for a threshold inhalation flow to deaggregate the powder formulation or the peak inhalation flow when choosing an inhaler device?
- Understand the important inhalation manoeuvre parameters to maximize drug delivery to the lungs, especially for patients with low lung capacity.
- Understand how to use a DPI more efficiently to get most of the inhaled dose into the lungs.

- In case patient cannot generate a high flow rate, they should be encouraged to prolong their inhalation time or inhale twice to empty the dose.
- Introducing the audience to an Ex-vivo method using patient inhalation profile that replaces the vacuum pump used in pharmacopoeia methods.
- Drug delivery to the lungs has attracted several advantages compared to other routes of drug delivery, because it allows direct delivery to site of action, quick onset of action, requires small doses when compared to other routes and limits systemic side effects. It avoids the first pass metabolism and this makes it suitable for delivering large and fragile molecules such as proteins and peptides. The advantages of the inhalation therapy over other routes will help the audience to have a better understanding of the inhalation therapy and this may encourage some of the scientists to use it in the future for delivering small and large molecules for both local and systemic effect.
- Make the audience aware of the most important inhalation manoeuvre parameters that affect drug delivery to the lungs and hence clinical outcome.
- Learn how the design of the inhalers can affect the drug delivery to the lungs and hence the clinical outcome.
- The audience will be aware of the latest techniques in delivering drug to the lungs in-vitro and Ex-vivo.
- This presentation includes the latest techniques in inhaled aerosols, which can be used both in research and also in teaching the inhaled aerosols and drug delivery.
- Inhaled aerosol is complex because of the interaction involved between patient, inhaler device and the formulation. In this presentation we focused on the inhalation manoeuvre and the inhaler device and by understanding the importance of these factors will lead us to the right direction to educate patients on how to use their inhaler device correctly to improve their adherence to their inhaled medication. Drug delivery to the lungs can be improved by choosing the right device for a right patient and by inhaling fast and hard from the start of the inhalation manoeuvre and by inhaling for as long as he could.
- There is no ideal inhaler device and more work is needed to make them easy for use by the patient and to enhance drug delivery to the lungs. Most currently marketed DPIs are flow rate dependent, ideally, an inhaler device should provide the same dose to the lungs of a patient irrespective of the flow rate or disease state.

Biography

Michal Abrahamowicz is a James McGill Professor of Biostatistics at McGill University, in Montreal, Canada. He develops new, flexible statistical methodology for survival analyses and bias control in prognostic and pharmaco-epidemiological studies of different drugs and treatments. His collaborative research includes arthritis, cardiovascular, and cancer epidemiology. He is the Nominated Principal Investigator on 2 major grants from the Drug Safety & Effectiveness Network (DSEN) of the Canadian Institutes for Health Research for enhancing methodology of population-based longitudinal studies of drug safety and comparative effectiveness. He published >340 papers, and was invited speaker at > 40 major international conferences on 6 continents. He is the co-chair of the international STRATOS initiative for improving the analyses of observational studies of health.

Flexible analyses of population-based pharmaco-epidemiological studies of comparative effectiveness and safety of drugs

Michal Abrahamowicz, Ph.D.

McGill University, Canada

Recent large governmental initiatives e.g. Canadian Drug Safety and Effectiveness Network or the US Sentinel program, emphasize the need to assess the real-life effectiveness and safety of drugs in population-based studies. Increasing availability of large databases, generated through electronic health records makes such studies more and more popular, and enhances their impact on the policy makers decisions regarding which drugs are withdrawn from the market, as well as on clinicians decisions regarding how and to whom the specific drugs are prescribed. Whereas such large database studies ensure adequate statistical power, they typically rely on conventional statistical models, and use simplistic metrics of drug use, e.g. current dose, or any use in the past 3 months. Yet, these metrics ignore important variation in the patterns of drug use in real-life clinical practice, where daily doses, treatment duration, frequency of treatment interruptions, all vary substantially between subjects and within-subjects over time. We present both simulation-based and real-life data illustrating how the above limitations of the models used in comparative effectiveness and safety studies seriously hamper the ability to detect the important benefits or adverse effects of a drug. We then demonstrate how our new, flexible statistical methodology, that accounts for variation in drug use patterns and for cumulative effects of past drug use, helps assessing accurately the causal effects of drugs in population-based studies and produces results consistent with the drug pharmaco-dynamics/-kinetics characteristics. The advantages of our new methodology are illustrated with empirical pharmacoepidemiological studies of the associations between: (1) benzodiazepines and fractures, (2) oral glucocorticoids and infections, (3) thiazide diuretics and cardiovascular disease.

Audience Take Away:

- This talk will help the audience understand the analytical challenges involved in assessing real-life safety and effectiveness of drugs and, as a consequence, improve the accuracy and validity of their own studies.
- By becoming more aware of the methodological issues arising in post-marketing studies of the drugs, the audience will be able to critically assessed the methods and conclusions of published studies.
- For those conference participants that may be (now or in future) actively involved in post-marketing studies, I will provide concrete information that will allow them to both (a) better design their analyses, and (b) use the user-friendly, publicly available software that implements our new state-of-the-art methods.

magnus Group

DAY 3

SPEAKERS

2ND EDITION OF GLOBAL CONFERENCE ON

Pharmaceutics and Drug Delivery Systems

June 04-06, 2018
Rome, Italy

HEA-HEMA hydrogels: Composition effect on physicochemical and pharmaceutical properties

I. Ermolina[1]*, PhD, E. V. Hackl[2], PhD, V.V. Khutoryanskiy[3], PhD
[1]De Montfort University School of Pharmacy, Leicester, UK
[2]University of Reading, School of Pharmacy, Reading, UK
[3]University of Reading, School of Pharmacy, Reading, UK

Hydrogels have attracted considerable attention due to their capability to be used for numerous pharmaceutical and biomedical applications (i.e. drug delivery systems, contact lenses and wound dressings). Hydrogels are swellable polymeric materias capable of imbibing a large amount of liquid and, therefore, a large amount of drug. Recently we have described novel cross-linked 2-hydroxyethylacrylate-co-2-hydroxyethylmethacrylate (HEA-HEMA) hydrogels with different co-polymer compositions synthesized by three-dimensional free-radical copolymerisation. The aim of the present work is to characterize the physicochemical and pharmaceutical properties of HEA-HEMA hydrogels, which potentially can be used as sustain drug delivery systems. The effects of the hydrogel composition (HEA/HEMA ratios) and liquid medium (aqueous PEG and glycerol solutions) on morphology, swelling and mechanical properties were examined using different analytical techniques. The molecular dynamics results for hydrogels were obtained by Broadband Dielectric Spectroscopy. The current study has been specifically focused on the analysis of the free/bound water redistribution in the hydrogels using thermoanalytical techniques. Also the effect of different methods of sterilization was studied with respect to the stability of hydrogels. The pramaceutical aspect of this study included the analysis of drug loading and release for the cases of low molecular weigth drugs (riboflavin) and proteins (lysozyme). The results show that HEA-HEMA hydrogels can be used as a sustain drug delivery system for both small drugs and biomacromolecules. The variation of the HEA-HEMA composition as well as liquid medium permits controlling the properties of hydrogels allowing producing the hydrogels with the drug release rate desired.

Biography

Irina Ermolina gained her PhD degree in 1995 in molecular physics at Kazan Institute of Biochemistry and Biophysics, Russian Academy of Sciences, following by postdoctoral studies at Hebrew University of Jerusalem, Glasgow University and Southhampton University. Currently, she is a senior lecturer at De Montfort University, Leicester, UK, teaching the pharmaceutical technology, pharmaceutical material sciences and analytical techniques. She specializes in pharmaceutical and biopharmaceutical materials science; drug delivery systems (hydrogels and nanoparticles); PAT; formulation development and stability study of freeze-dried pharmaceuticals; dynamic structure of proteins in solutions and membrane films. She has published 49 peer reviewed articles.

Cyclic GMP-AMP: A new hope for metabolic disease?

Chaodong Wu*, MD, Ph.D., Honggui Li
Texas A&M University, USA

Obesity is an ongoing pandemic which serves a causal factor of a wide range of metabolic diseases such as type 2 diabetes, non-alcoholic fatty liver disease, and atherosclerotic cardiovascular diseases. Accumulating evidence has suggested inflammation as a factor underlying the pathogenesis of obesity-associated metabolic diseases. To date, however, there is no reliable anti-inflammation-based therapy for metabolic diseases. Given this, there is a critical need to develop new and effective therapies for treatment of obesity-associated metabolic diseases. Over the past several years, cyclic GMP-AMP (cGAMP) has been identified as a dinucleotide that critically regulates innate immunity. Additionally, mitochondrial dysfunction pertinent to oxidation stress is shown to increase intracellular (endogenous) levels of cGAMP, which, in turn contributes to the development and progression of inflammation that causes insulin resistance and metabolic dysregulation. In contrast, treatment of obese mice with exogenous cGAMP results in amelioration of obesity-associated inflammation and improvement of systemic insulin resistance and aspects of diet-induced fatty liver disease. Specifically, in response to cGAMP treatment, high-fat diet (HFD)-fed C57BL/6J mice revealed a significant decrease in adipose tissue inflammation, evidenced by decreases in the phosphorylation states of JNK1 p46 and NFkB p65 and in the mRNA levels of proinflammatory cytokines. Moreover, treatment with exogenous cGAMP brought about significant improvement of systemic glucose homeostasis. These in vivo results were recapitulated by the results from cultured adipocytes, in which treatment with exogenous cGAMP decreased the proinflammatory responses and increased insulin signaling. Similarly, treatment with exogenous cGAMP significantly ameliorated HFD-induced hepatic fat deposition, through reducing the expression of lipogenesis-related genes, and decreased inflammation in the liver. In cultured primary mouse hepatocytes, treatment with exogenous cGAMP significantly increased the effect of insulin on inducing Akt phosphorylation and decreased the effect of palmitate on inducing fat deposition. In addition, treatment with exogenous cGAMP decreased the effect of lipopolysaccharides on stimulating proinflammatory signaling pathway through JNK in mouse primary hepatocytes. Taken together, these findings validate that exogenous cGAMP exerts anti-inflammatory effects, which is different from endogenous cGAMP. Additionally, exogenous cGAMP is capable of enhancing systemic insulin sensitivity and metabolic homeostasis, which is attributable to improving inflammatory and metabolic responses of adipose and liver tissues. As such, the anti-inflammatory, anti-steatotic, and insulin-sensitizing effects of exogenous cGAMP warrant future studies to develop cGAMP mimic(s) as novel therapy for obesity- associated metabolic diseases.

Audience Take Away:

- The presentation will share new knowledge on how inflammation is regulated in the context of the pathogenesis of obesity-associated metabolic diseases. It also helps promote the development of new and effective drugs for metabolic diseases.
- The presentation shares methodology for analysis inflammation and inflammatory disease, which will benefit general audience.

Biography

Chaodong Wu, MD and PhD, is a tenured associate professor of nutrition in the department of Nutrition and Food Science of Texas A&M University (TAMU). Previously, he was an assistant professor of nutrition at TAMU, and a research assistant professor of biochemistry at the University of Minnesota (Minneapolis, Minnesota). He has authored and co-authored over 67 research articles. He has also served as editor and/or reviewer for a number of scientific journals, and served on several NIH study sections. In 2015, he was selected as Faculty Fellow of AgriLife Research.

Computational blind docking of ligands to drug targets: Methodology and applications

Csaba Hetényi[1],*, PhD, Mónika Bálint[1], Gabriella Schilli[1], István Horváth[2]

[1]Department of Pharmacology and Pharmacotherapy, Medical School, University of Pécs, Szigeti út 12, 7624 Pécs, Hungary.
[2]Chemistry Doctoral School, University of Szeged, Dugonics tér 13, 6720 Szeged, Hungary.

Originally, computational blind docking (BD) was introduced as a fast approach for finding binding positions and conformations of ligand molecules via scanning the entire surface of target molecules. BD can find not only primary binding sites but also allosteric or prerequisite ones. Since the introduction of BD in 2002, it has gained numerous applications in drug design. A combination of advanced molecular dynamics techniques with BD has yielded new, systematic methods for prediction of structures of target-ligand complexes at atomic resolution. Molecular dynamics also allows the use of explicit hydration models and helps distinguishing between binding modes of different target-ligand binding affinities. The present lecture features new results in method development and applications of BD in comparison with experimental structure determination methods.

Audience Take Away:

- Computational docking is a key technique of target-based drug design at numerous pharmaceutical companies and research institutions. Besides routine docking applications in high throughput screening, blind docking can also detect allosteric binding sites which play an important role in e.g. anti-cancer drug discovery. This approach is also useful for understanding dynamics of target-ligand interactions and mapping of drug binding pathways at atomic resolution.

Biography

Csaba Hetényi is an Associate Professor in Pharmacology. He has co-authored research articles in prestigious journals J Am Chem Soc, PNAS, EMBO Reports, Bioinformatics, and is also a co-inventor of US patents. He has received more than 1600 independent citations for his research results, has a Hirsch-index of 19 and his works were favorably evaluated by several review articles and research papers. In 2011, Dr. Hetényi won a Talentum Academy Award for his research achievements. His present research interest is focused on the development of pharmacoinformatics tools and investigation of molecular pathomechanisms of diseases. Dr. Hetényi collaborates with researchers in Sweden, Estonia, Spain, and the USA.

The competitive binding Studies of CMP Inhibitor and polysialic Acid (polySia) to the polybasic polysialyl-transferase domain (PSTD) in the polysialyltransferase

Guo-Ping Zhou[1,3]*, Li-Xin Peng[1], Xue-Hui Liu[2], Bo Lu[1], Ji-Ming Huang[1], Si-Ming Liao[1], Dong Chen[1], and Ri-Bo Huang[1]

[1]Engineering Research Center for Non-food Biorefinery, Guangxi Academy of Sciences, 98 Daling Road, Nanning, Guangxi 530007, China
[2]Institute of Biophysics, Chinese Academy of Sciences, Beijing, P. R. China
[3]Gordon Life Science Institute, Boston, MA, 02478 USA

Polysialic acid (polySia) is a novel glycan that posttranslationally modifies neural cell adhesion molecules (NCAMs) in mammalian cells. Up-regulation of polySia-NCAM expression is associated with tumor progression in many metastatic cancers. Both members of the ST8Sia family of α2,8-polysialyltransferase (polyST), ST8Sia II (STX) and ST8Sia IV (PST), utilize CMP-Neu5Ac as the activated sugar nucleotide donor to catalyze polysialylation of NCAM. The previous immunoblotting studies suggested that heparin and cyclic monophosphate (CMP) are possible polysialyltransferase inhibitors, which can modulate migration in ST8SiaII-expressing tumour cells. In this study, we further found that the interaction between polySia and the polybasic polysialyltransferase domain (PSTD) in the polyST was inhibited is due to the formations of the PSTD-heparin or PSTD-CMP complex by using the methods of the circular dichroism (CD) spectroscopy, the Isothermal titration calorimetry (ITC) and NMR spectroscopy. Our findings indicate the competitive bindings exist between heparin or CMP and the PSTD, and between polySia and the PSTD. Incorporating the previous NMR results and the molecular modeling analysis into the current data of CD spectra and ITC data, we propose that an α-helix within ST8 Sia IV is a major contributor in modulating bindings of polySia to the PSTD or CMP inhibitor to the PSTD. These biophysical studies provide the insight for drug design of the inhibitors of neural cell adhesion molecule (NCAM) polysialylation.

Audience Take Away:

- Help the audience to use much simpler and less time consuming methods to identify potential inhibitors.

Biography

Guo-Ping Zhou is currently a Distinguished Professor of Gordon Life Science Institute, USA. He is also an Adjunct Professor of several academics in the United States and China. He received his Ph.D in Bio-physics from University of California at Davis, and completed his postdoctoral training at Stanford Univer-sity and Harvard University, respectively. He determined the 3D NMR structures of some proteins, protein-DNA complexes, super lipids such as dolichol and other polyisoprenyls, as well as polyisoprenol recognition sequences. He has successfully introduced the elegant wenxiang diagrams to elucidate the mechanisms of the coiled-coil proteins, protein-lipids, protein-DNA interactions, and prion protein mis-folding observed by NMR. Meanwhile, he has also published many papers in Bioinformatics. His current research is focused on investigation into the relationship between the functions and structures of polysialyltransferases. In addition, as Editorial Board Member, Guest Editor and Bentham Brand Ambassa-dor, Zhou has edited some special issues on structural biology for several influential scientific journals.

The main trends in the developing novel therapeutics for Alzheimer's disease treatment

Sergey Bachurin
Russian Academy of Sciences, Russia

Alzheimer's disease (AD) is characterized by a chronic and progressive neurodegenerative process resulting from the intracellular and extracellular accumulation of fibrillary proteins: beta-amyloid and hyperphosphorylated Tau. Over accumulation of these aggregates leads to synaptic dysfunction and subsequent neuronal loss. The precise molecular mechanisms of AD are still not fully understood but it is clear that AD is a multifactorial disorder and that advanced age is the main risk factor. Over the last decade more than 50 drug candidates have successfully passed phase II clinical trials, but none have passed phase III. Here, we summarize data on current "anti-Alzheimer's" agents currently in clinical trials based on findings available in the Thomson Reuters «Integrity» database, on the public website www.clinicaltrials.gov, and on database of the website Alzforum.org. As a result, it was possible to outline some major trends in AD drug discovery: 1) the development of compounds acting on the main stages of the pathogenesis of the disease – the so-called "disease-modifying agents". These drugs could potentially slow the development of structural and functional abnormalities in the CNS providing sustainable improvements of cognitive functions, which persist even after drug withdrawal. 2) Focused design of multitargeted drugs acting on multiple molecular targets involved in the pathogenesis of the disease. 3) Finally, the repositioning of old drugs for new ("anti-Alzheimer's") application, offers a very attractive approach to facilitate the completion of clinical trials [Bachurin S. et al., Med.Res.Rev.,(2017). 37(5):1186-1225].

Audience Take Away:

- The recent date about the main approaches for the developing novel pharmaceuticals for Alzheimer's disease treatment
- The copy of the recent review of the author on the same topic in hogh-ranking scientific journal
- The information about experimental facilities for the primary testing for neuroprotective activity that provides the Institution where the author work (IPAC ARS)

Biography

Bachurin Sergey has completed his PhD and Dr. Sci. Degree in Moscow State University, Russia. In 1992 and in 1995 he had been working in the University San Francisco and in Taft's University (USA). Since 2006 he is a director of the Institute of Physiologically Active Compounds, Russian Academy of Science in Chernogolovka, Russia, and the Head of Department of Medicinal and Biological Chemistry. He has published more than 220 papers in reputed journals and about 40 patents, and has been serving as an editorial board member of repute.

Casein-based nanovehicles for oral delivery of chemotherapeutic combinations to overcome multidrug resistance in gastric cancer

Maya Bar-Zeev*, M.Sc., Yehuda G. Assaraf, Ph.D. and Yoav D. Livney, Ph.D.
Technion – Israel Institute of Technology, Israel

Gastrointestinal cancers are the third leading cause of cancer-related deaths worldwide. Moreover, multidrug resistance (MDR) mediated by ATP-dependent efflux transporters remains a dominant obstacle toward curative cancer therapy. Furthermore, most chemotherapeutic agents are lipid-soluble, administered intravenously using harmful solvents and surfactants. An effective and selective oral delivery system would significantly contribute to patients' quality of life, reduce hospitalization costs and circumvent infection with antibiotic-resistant pathogens prevalent in hospitals.

Bovine milk is comprised of 80% phosphoproteins known as Caseins. Their amphiphilic structure enables them to naturally self-assemble into casein micelles (CM). In previous studies we have demonstrated the potential of β-CN micelles (β-CM) and re-assembled casein micelles (rCM) to serve as nanovehicles for oral delivery and target-activated release of hydrophobic cargo, including nutraceuticals and chemotherapeutic agents, in the stomach.

Herein we compared the rCM- and the β-CM- based oral delivery platforms. Each comprised an individually encapsulated synergistic duo of a chemotherapeutic drug along with its corresponding chemosensitizer, which counteract ATP-driven MDR efflux pumps (e.g. p-glycoprotein (P-gp)/ ABCB1, breast cancer resistance protein/ ABCG2), that expel a spectrum of anticancer drugs from cancer cells and therefore markedly suppresses the efficacy of numerous hydrophobic chemotherapeutics. Hence, the rationally designed encapsulated pair is expected to display enhanced efficacy and synergy in overcoming MDR phenomena in gastric cancer. This novel treatment strategy, can allow less painful treatment at the comfort of the patient's home. The target-activated release mechanism, aimed to locally treat gastric cancer, can diminish untoward toxicity to the upper gastro-intestinal tract and minimize toxic side effects caused by systemic chemotherapy. This nanosystem could also be applied for the treatment of various non-malignant gastric disorders and tailored to individual drug combinations for personalized medicine.

Audience Take Away:

- Casein-based nanovehicles are an efficient platform for oral delivery and target-activated release of synergistic hydrophobic drug combinations in the stomach.
- Casein-based delivery systems can release synergistic drug combinations to overcome two modalities of ATP-dependent MDR in gastric cancer.
- Casein based delivery systems may enable treatment at home, thus avoiding exposure of immunocompromised cancer patients to antibiotics-resistant bacteria prevalent in hospitals.

Biography

Maya received her B.Sc. (Summa Cum Laude) in Pharmaceutical Engineering from the Jerusalem College of Engineering in 2011. She is currently a PhD direct track student of the Norman Seiden international multidisciplinary graduate program in Nanoscience and Nanotechnology at the Technion - Israel Institute of Technology. Her PhD research main focus is on the development of milk protein based nanovehicles for oral delivery of chemotherapeutic drug combinations to overcome multidrug resistance in cancer. Currently, she is the first author in three articles and has participated in several international forums presenting her PhD study results.

Use of an inflating agent to engineer novel lactose carrier for inhalation and drug deposition in-vitro using three model drugs: salbutamol, beclomethasone and fluticasone

Ursula Thevarajah, BSc, MSc
University of Huddersfield, UK

The aim of this study was to engineer a novel lactose carrier in the presence of an inflating agent in the crystallisation medium to produce large hollow spherical carrier particles for inhalation. Hollow spherical Engineered carrier and tomahawk shaped commercial carrier (control) were characterised using various analytical techniques such as scanning electron microscopy (SEM), X-Ray powder diffraction (X-RPD), differential scanning calorimetry (DSC). Both carriers were assessed for pulmonary drug deposition in-vitro with Andersen Cascade Impactor (ACI) using various drugs: salbutamol sulphate (SS), beclomethasone di-propionate (BDP) and fluticasone propionate (FP). Engineered lactose performed better than commercial lactose for both hydrophobic corticosteroids BDP and FP and showed less performance than commercial lactose for hydrophilic water-soluble SS. Our study showed that morphological features of lactose carrier affects drug deposition, therefore carriers with different morphological features are not interchangeable. Drugs for inhalation have different physic-chemical properties and a lactose carrier may not perform equally well with all drugs, therefore finding a universal carrier for all drugs remains a challenge for DPIs.

Audience Take Away:

- This work is novel.
- The use of various analytical techniques which can benefit scientists working within the pharmaceutical, biological and chemical sectors.
- Obtain an understanding of the influence of the physico-chemical properties of DPI formulations on aerosol performance.

Biography

Ursula Thevarajah is a PhD researcher at the University of Huddersfield working under the supervision of Dr El Hassane Larhrib. Prior to this, she obtained her masters in pharmaceutical and analytical science also at the University of Huddersfield. During her masters, she undertook her research project in formulation and delivery of dry powder inhalers to the lungs, which sparked her passion to further her studies with a PhD in the inhalation field. She worked on engineering a lactose carrier which could be used as a carrier in dry powder inhaler formulations.

Characterization of lactose carrier for dry powder inhaler formulations

Faiza Naseer BSc, MSc
University of Huddersfield, UK

Most dry powder inhalers are formulated by mixing micronized drugs with lactose as a carrier. Lactose is the major element in terms of weights in a dry powder inhaler formulation therefore, any changes in its physicochemical properties can affect drug detachment from the surface of the carrier hence, affect the performance of the dry powder inhaler. The aim of this study was to characterize the carrier using various analytical techniques such as atomic force microscopy, differential scanning calorimetry, thermogravimetric analysis, scanning electron microscopy, freeze fracturing and laser diffraction. This was carried out to ascertain the suitability of lactose as a carrier for dry powder inhalers.

Audience Take Away:

- This work is novel.
- The use of interesting analytical techniques which can benefit scientists working within the pharmaceutical, biological and chemical sectors.
- Obtain an understanding of how aerosols are formulated.
- To give an insight into the therapeutic aerosol.

Biography

Faiza Naseer is a PhD researcher at the University of Huddersfield working under the supervision of Dr El Hassane Larhrib. Prior to this, she completed her masters in pharmaceutical and analytical science also at the University of Huddersfield. During her masters, she gained the opportunity to carry out her research project within the inhalation field, where the passion to undertake a PhD in inhalation arose. She is currently working on engineering a lactose carrier which could be employed as a carrier in dry powder inhaler formulations.

EAAT3 proteins as a pharmacological target for the design of new antiepileptic drugs

Lourdes Amable Vega Rasgado[1]*, M en C Verónica Alcántara Farfán[2]

[1]Lab. de Neuroquímica del Depto. de Bioquímica de la Escuela Nacional de Ciencias Biológicas del Instituto Politécnico Nacional, México

[2]Lab. de Bioquímica Farmacológica del Depto. de Bioquímica de la Escuela Nacional de Ciencias Biológicas del Instituto Politécnico Nacional, México

About 50 millions of people suffer from epilepsy, and 30% of them do not respond with traditional antiepileptic drugs. Thus, different strategies for seizures control in such patients are required. Seizures are the result of an imbalance between excitatory and inhibitory impulses on the central nervous system, being glutamate (GLU) the major excitatory neurotransmitter. GLU participates in several physiological but also pathological processes, including epilepsy. For recycling, to avoid neurotoxicity of ammonium generated during its metabolism and to finish its excitatory effect as neurotransmitter, GLU is removed from the synaptic cleft to the glia and back to neurons by GLU transporters, a family of proteins called EAATs. In neurons EAAT3 is highly expressed, which dysfunction has been implicated in epilepsy. EAATs activity is regulated by external GLU levels, and coupling GLU transportation by EAATs with the activity of enzymes related to its metabolism would improve the efficiency of the process. Here we study EAAT3 as a mechanism to counteract glutamatergic overstimulation that occurs in seizures.

Audience Take Away:

- Clarify a little bit more the roll of EAAT3 in seizures mechanism.
- To explore the coupling of GLU transportation through EAAT3 with its oxidative deamination.
- Study the possibility of controlling seizures through modulations of EAAT3 activity.
- Evaluate the possibility of EAAT3 as a pharmacological target for the development of new antiepileptic drugs.

Biography

Lourdes Amable Vega Rasgado on Mexico City, Mexico. Graduated as chemist, bacteriologist and parasitologist by Escuela Nacional de Ciencias Biológicas (ENCB) of Instituto Politécnico Nacional (IPN) México, with master's degree on pharmacology by Escuela Superior de Medicina of IPN. Master,s degree and PHD on neurosciences by Universidad de Salamanca, Spain. Professor of general and clinical biochemistry; head of clinical biochemistry academy and of neucrochemistry laboratory at biochemistry department from ENCB of IPN. Author of papers on different journals of neurobiochemistry and neuropharmacology. Main research lines: Alterations of brain biochemistry associated with epilepsy, schizophrenia, Parkinson's and Alzheimer's diseases; new drugs and diagnostic methods design.

Hard alginate capsules shell as enteric capsules

Hakim Bangun, Ph.D.
University of Sumatera Utara, Indonesia

Most pharmaceutical capsules are made from gelatine. These material dissolve in the low pH gastric juices in the stomach. But, for certain purposes capsules are designed to pass through the stomach and into the intestine before dissolving, such products are described by a variety of terms, including gastric resistant, entero soluble, delayed release, and enteric capsules. Enteric capsules are used when the drug may irritate the gastric mucosa. Enteric capsules also used when the drug is inactivated by gastric fluid (such as stomach acid).

In this sesion it will be discussed about the hard alginate capsule shell. Hard alginate capsules are made from sodium alginate. Sodium alginate is a sodium salt of alginic acid. Alginic acid is a polysaccharide that is derived from seaweed (brown algae) and it is non-toxic, biodegradable, and biocompatible.

In this sesion it will be discussed the preparation, physical properties, and the application of hard alginate capsules shell as enteric capsules. The physical properties of hard alginate capsules shell such gastric resistance *in vitro* and *in vivo*, disintegration *in vitro*, britleness, equilibrium moisture content, water vapour permeability, and drug release will be discussed. Furthermore, drug biovailability and the safety to the stomach in animal experiment will be also discussed. As drugs model are used that drugs are irritating the gastric mucosa, namely nonsteroidal antiinflamatory drugs (aspirin, indomethacin, mefenamic acid) and $FeSO_4$ antianemic drug.

Biography

Hakim Bangun obtained Ph.D. degree from Faculty of Pharmaceutical Sciences, The University of Tokushima, Japan on 1990. Since 1980 he has been working as academic staf at Faculty of Pharmacy, University of Sumatera Utara. He became Professor of Pharmaceutical Technolog/Physical Pharmacy on 1999. His research interest is about the application of alginate in pharmaceutical preparation, such as enteric capsules, gastroretentive drug delivery system, drug encapsulation, gastric delivery system, sustained release, nano capsules, peridental gel etc. He also interests about the biological activities of alginate.

Synthesis and cytotoxicity studies on novel piperazinylacetamides

Enise Ece Gurdal[1]*, Eman Bobtaina[2], Rengul Cetin Atalay[3], Irem Durmaz[3], Mine Yarim[1]

[1]Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Yeditepe University, 34755, Kayisdagi, Istanbul, Turkey
[2]Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Benghazi University, Belooan, Benghazi, Libya
[3]Bioinformatics Department, Graduate School of Informatics, Middle East Technical University, Ankara, Turkey

Cancer, characterized by uncontrolled cell growth, causes the death of about 7 million patients each year. Malignant cells can spread all over the body through the lymphatic and the circulatory systems. Side effects of chemotherapeutic drugs being used for cancer treatment affect patients' quality of life negatively. In addition, resistance to cancer chemotherapy often develops. Therefore, the need for new therapeutic agents is increasing day by day (Deng et al., 2015).

In this study, novel compounds, bearing N-[2-(4-substitutedpiperazine-1-yl)acetyl]-N'-[bis-(4-fluorophenyl)methyl] piperazine structures were synthesized. *In vitro* cytotoxic activities were screened in comparison with camptothecin (positive control) and 5-fluorouracil (reference).

To obtain starting compound, 1-[4-bis(4-fluorophenyl)methyl]piperazine was N-acetylated with chloroacetyl chloride. Target compounds were gained after substitution of N-acetyl chloride group by various piperazine derivatives.

Physical properties of the synthesized compounds were determined and their structures were confirmed by using spectral methods (UV, IR, 1H-NMR, 13C-NMR, Mass spectrometry) and elemental analyses. In addition, their cytotoxic properties were evaluated *in vitro* by NCI-60 Sulforhodamine B (SRB) assay against human cancer cell lines, Huh7 (hepatocellular), MCF7 (breast) and HCT116 (colorectal).

According to the activity data, most of the compounds are more cytotoxic than 5-fluorouracil against hepatocellular (Huh7) and colorectal (HCT116) cancer cell lines. However, in breast (MCF-7) cancer cell line, all benzhydrylpiperazine derivatives are less cytotoxic than 5-fluorouracil (5-FU). The most active compound for Huh7 cell line is m-methoxyphenyl derivative (compound 5; GI_{50} = 7.04 μM), and the most active compound against colorectal (HCT-116) cancer cell line is p-chlorophenyl derivative (compound 1; GI_{50} = 4.36 μM).

Audience Take Away:

- Piperazine is an extensively studied heterocycle in drug discovery studies. By this presentation, it is aimed to share current research on benzhydrylpiperazine derivatives.
- The audience is expected to use the information on drug discovery studies for cancer.

Biography

Enise Ece Gurdal graduated from Faculty of Pharmacy, Yeditepe University, Turkey in 2007. Afterwards, she became a Teaching Assistant in the same Faculty and was registered to Medicinal Chemistry Ph.D. program under the Institute of Health Sciences. After she completed her thesis under supervision of Prof. Mine Yarim in 2012, she remained in Yeditepe University as an Assistant Professor. She has been the Vice Dean since 2015. During summer 2017, she performed in silico target prediction studies in Martin Luther University, Halle as a DAAD scholar under supervision of Prof. Wolfgang Sippl. Her research interest is development of novel anticancer agents.

Stability studies on the formulations of inclusion complex of tenoxicam in SBE_7 β cyclodextrin and beta cyclodextrin

K.V.R.N.S.Ramesh
RAK Medical & Health Sciences University, United Arab Emirates

The present study was carried out to evaluate the usefulness of sulfobutyl ether β-cyclodextrin (SBE7-β-CD), [captisol], in increasing the dissolution rate of tenoxicam. The efficacy of captisol in increasing the dissolution when compared with beta cyclodextrin is investigated. The approach employed to prepare the inclusion complexes of the drug with captisol and beta cyclodextrin is by freeze-drying and kneading methods. The phase solubility studies indicated that a 1:1 M complex was formed between tenoxicam and the two complexing agents. The complex in captisol showed a much higher dissolution rate compared to the complex prepared in beta cyclodextrin and pure drug tenoxicam. In between the kneaded and freeze-dried complexes, the freeze-dried complex showed higher dissolution efficiency and rate. At the end of 30 minutes, the pure drug showed less than 20% dissolution, the kneaded and freeze dried complexes exhibited 75% and 94% dissolution respectively. The inclusion complexes were evaluated by differential scanning calorimetry (DSC), X-ray diffraction (XRD), and Fourier transform infrared spectroscopy (FT-IR). The drug is found to exist in amorphous state in the complexes. The efficacy of hydrophilic polymers, gelucire and hydroxypropyl cellulose in stabilizing the high dissolving amorphous forms of tenoxicam in the tablet formulations was studied and the findings of the investigation suggested that the hydrophilic polymers were able to offer protection in preventing the transformation of the amorphous drug during compression and storage. It is observed that after storage, there is a significant decrease in the dissolution of drug in formulations prepared by beta cyclodextrin whereas such an adverse effect is not seen in tablets that had complexes made of captiosl. The post compression properties of the tablets formulated were evaluated. The hardness of tablets of all formulations was in the range of 2.71 to 3.27 kg/cm^2. The friability of tablets of all formulations was less than 1 %. The tablet formulations in all the prepared batches contained tenoxicam within 100 ± 5% of expected content. It can be concluded from the results of the present study that careful formulation is essential to stabilize the high dissolving forms of drugs to retain their physical stability and high dissolution characteristics.

Audience Take Away:

- The audience will be able to use the results and findings of the study in developing fast dissolving dosage forms and take appropriate measures in stabilizing the dosage forms.
- The methods employed will help in exploring newer hydrophilic polymers in evaluating their utility in stabilizing the fast dissolving forms.
- The investigators in this field will be able to design new projects and expand the studies into carrying out studies on various therapeutic categories of drugs.
- A more rationalistic and optimal tablet formulation can be developed and the findings of the study should help in thoroughly carrying out evaluations of the drug and various excipients used in the tablet dosage forms.

Biography

K.V.R.N.S. Ramesh is a post graduate in pharmaceutical sciences and obtained his doctoral degree in Pharmaceutics specialization from Andhra University, India. His broad area of interest is in the development of controlled release dosage forms and investigations on the stabilization of fast dissolving dosage forms. He has 30 years of teaching and research experience. He has published about 35 research papers in National & International Journals. He has delivered lectures in different seminars and conferences organized in the area of Pharmaceutics and Drug Product Development. He has worked in Addis Ababa University under the United Nations Development Project. He presently is Associate Dean and Professor at RAK College of Pharmaceutical Sciences, RAK Medical & Health Sciences University, United Arab Emirates.

CONTENTS

Development and evaluation of self micro emulsifying drug delivery systems of itraconazole

Hemant K. S. Yadav
RAK Medical & Health Science University, UAE

During the presentation the presenter will be talking about the formulation and evaluation of self microemulsifying system of a poorly water soluble drug. The talk will include what are self microemulsifying systems and how to prepare them along with their advantages. Approaches of choosing surfactant and co-surfactant for the formulation. How these systems can increase the bioavailability of a drug? The talk will also cover the various characterization and evaluation methods for the prepared formulation.

Audience Take Away:

- Audience will have a good exposure of a formulation system which can be useful to improve solubility of a poorly water soluble drug.
- If an audience is working professional in a pharmaceutical industry it will be great exposure for them to use the technology in manufacturing as it can be easily scaled up.
- This will be highly useful for a teacher to pass the information to a group of students that this technique is highly useful for increasing bioavailability of a poorly water soluble drug.

Biography

Hemant Yadav is currently working as Associate professor in RAK College of pharmaceutical sciences, RAK Medical & Health Science University, UAE, he has total of 13 years of teaching experience and 2 years of industrial experience. He has published around 35 articles in reputed journals and authored 8 chapters in books published from Elsevier, Taylor and Francis, nova science publishers, etc. He has guided 20 post graduate students. He is currently working in drug delivery area by formulating various novel drug delivery systems.

Microbiological pharmaceutical analysis: Better safe than sorry

Ana Carolina Kogawa*, Hérida Regina Nunes Salgado
Universidade Estadual Paulista – UNESP, Brazil

Rifaximin, an oral antimicrobial, is mainly used for the treatment of hepatic encephalopathy, but also in cases of ulcerative colitis, irritable bowel syndrome, *Clostridium difficile*, travelers' diarrhea and acute diarrhea. Rifaximin does not present microbiological methods described in official compendiums and they are extremely important and necessary in the evaluation of power of antimicrobials. So, a microbiological method by turbidimetry was developed and validated to evaluate the power of rifaximin in tablets and its degradation products (acidic, basic, neutral and photolytic), as well as rifaximin raw material recrystallized from different solvents. The results were compared with analyzes by HPLC. The method used *Escherichia coli* and was linear over the concentration range of 50-98 μg mL^{-1}, precise with values of relative standard deviation less than 5 %, exact by the recovery test and robust against small and deliberate variations in the method. The potency, by turbidimetric method, of rifaximin in tablets after degradation in basic and photolytic media was different from that revealed by the HPLC method. The potency, by turbidimetric method, of rifaximin in raw material after treatment with different solvents also showed different results from the HPLC method. In these cases, the physico-chemical method showed much higher contents than the potencies revealed by the microbiological method. Production of rifaximin involves the use of different solvents and the performance of these solvents can affect the activity of the antimicrobial, which is not always correctly revealed by physico-chemical methods. This is an alert to the production of pharmaceutical inputs and the presence of microbiological analyzes throughout the industrial process. The process of obtaining raw material must be standardized, aiming not only the quality of the medicine, but also, aiming the consequences of the use of non-quality medicines that generate a vicious cycle in the public health system. Antimicrobials should be analyzed by microbiological methods in conjunction with physico-chemical methods. The quality of a pharmaceutical product is directly related to the health of patients and a reliable analysis method can be the first step in the rational use of pharmaceuticals.

Audience Take Away:

- The audience will take away from my presentation a reliable, effective, practical, simple, fast and low cost option for microbiological analyzes.
- The turbidimetric method is ideal for dynamic logistics of Quality Control of antimicrobials and can be easily applied in laboratories and pharmaceutical industries.
- The turbidimetric method reveals the true activity of the antimicrobial often not detected by physicochemical methods.
- The turbidimetric method can be and should be expanded and applied by laboratories, industries and research centers around the world. The use of microbiological methods should be encouraged concomitantly with physicochemical methods with the objective of take care of the quality of drugs and medicines that arrive to patients.
- The quality of a pharmaceutical product is directly related to the health of patients and a practical analysis method and accurate can be the first step in the rational use of pharmaceuticals.

Biography

Ana Carolina Kogawa graduated in Pharmacy-Biochemistry in 2008, received her Master's in 2012 and PhD in Pharmaceutical Sciences in 2015 from the Universidade Estadual Paulista – UNESP, Brazil. She has experience in managing people, lectures, quality tools and activities of the pharmaceutical industry with emphasis on Quality Ccontrol. She has published more than 40 papers in renowned journals and has been serving as a reviewer of manuscripts in more than 15 international journals. Currently she develops her postdoctoral research at the School of Pharmaceutical Sciences of Araraquara, Brazil, funded by Fundação de Amparo à Pesquisa do Estado de São Paulo (Fapesp).

Nature of Naproxen enantiomers medicinal activity difference. Study by using model systems and modern physical methods.

Tatyana V. Leshina[1]*, Aleksandra A. Ageeva[1], Ekaterina A. Khramtsova[1,2], Miguel A. Miranda[3]

[1]Laboratory of Magnetic Phenomena, Voevodsky Institute of Chemichal Kinetics and Combustion SB RAS, Novosibirsk, Russia

[2] Novosibirsk State University, Novosibirsk, Russia

[3]Departamento de Química/Instituto de Tecnología Química UPV-CSIC, Valencia, Spain

The difference in the medical properties of the enantiomers of many chiral drugs is a well-known fact. This is a big problem, since most drugs are still used in the form of racemates. The latter is connected with the difficulties of separation. One of the most prominent representatives of drugs in which enantiomers differ not only in degree but also in the directions of therapeutic activity are nonsteroidal anti-inflammatory drugs (NSAIDs). Naproxen is one of the NSAIDs that is available in the form of S isomer only. His R analogue does not exhibit anti-inflammatory properties but has a therapeutic activity in other directions. To understand the reasons of the difference in naproxen (NPX) enantiomers medical activity in this work original approach has been developed. The interaction of (S)- and (R)-NPX with chiral donors in linked systems – dyads have been investigated. These model systems are believed to simulate NPX enantiomers binding with chiral amino acid residues located in active sites of COXs enzymes. Idea is that upon binding some kind of diastereomers analogs are formed. In diastereomers, as it is known, enantiomers may exhibit different reactivities. Spin chemistry and photochemistry study of photoinduced charge transfer (CT) between (S)- and (R)-NPX and (S)-tryptophan and (S)-N-methylpyrrolidine linked by different bridges has shown the stereoselectivity of partial and full CT. The exciplex quantum yields and the rates of its formation are larger for the dyads containing (R)-NPX that let us suggest the greater contribution from CT processes with (R)-optical isomer. This is consistent with fact that (R)-NPX is more active in the processes of the chiral metabolism by the action of cytochrome P450 known to involve electron transfer. Really, (R)-NPX is slightly more active in oxidative metabolism. However, in the enzymatic chiral inversion of NPX-CoA esters by AMACR and other transferases (R)-isomer demonstrates appreciably greater activity than the (S)-analog. (S)-isomer - drug naproxen, according to above results, has to exhibit a more reversible binding with the amino acid donors that is an agreement with the results of biochemical research. In order to establish the nature of abovementioned stereoselectivity in processes with participation of S and R NPX another physical method - spin chemistry was used. The comparison of spin chemistry experimental results with calculation has shown that the reason of difference in R and S reactivity in ET is the distinction of spin density distribution in paramagnetic form of (R,S)- and (S,S)-diastereomers. This result is directly related to the reactivity of the enantiomers since the spin density and the electron density distributions correlate with each other. For example, the formation of hydrogen bonds between naproxen and amino acid residues in the active site of COX can be dependent on the electron density distribution of the enantiomers. Thus, it is worth noting that developed approach can apply to study other NSAIDs which have enantiomers of different activity.

Audience Take Away:

- The potential practical significance of these results is the realization of why the enantiomers of naproxen differ from each other. The lack of such knowledge is a big problem for pharmacology.
- Taking into account that the scope of the NSAIDs is constantly expanding, one can hope that the knowledge of the nature of the differences between the enantiomers will serve to search for new areas of their activity.
- In addition, this report will serve as a source of new knowledge, since the foregoing approach to studying the properties of chiral drugs is completely original.

Biography

Tatyana V. Leshina is Professor of Physical Chemistry in the Institute of Chemical Kinetics and Combustion Siberian Branch of the Russian Academy of Sciences. She works in the area of spin chemistry and is the author of the discovery "A new pattern of radical reactions in solution" (1998), devoted to the observation and explanation of the nature of the influence of inner and external magnetic fields on radical reactions in solutions. Today she applies the spin chemistry and photochemistry methods to study the chemical nature of the difference in medical activity of chiral drugs enantiomers on the examples of model processes.

Nanoparticles in receptor-mediated drug delivery to brain parenchyma

Mehrdad Azarmi Aghajan[1*], Hadi Maleki[1], Nader Nikkam[1], Hassan Malekinejad[2]

[1]Faculty of Life Science and Biotechnology, Shahid Beheshti University, Tehran, Iran

[2]Faculty of Pharmacy, Urmia University of Medical Science, Urmia, Iran

In RMT route, NPs are designed to target specific cells and cause cell death or induce a significant change in cellular behavior. Receptor-targeted therapeutics are developed to restrict the distribution of toxic drugs to only the pathologic cells, thus diminishing collateral side effects to healthy ones. Note worthly, receptor-mediated drug delivery by NPs not only can enable membrane-impermeable drugs to enter target cells by receptor-mediated endocytosis, but it can induce remarkable changes in cell fate by activating a receptor's natural signaling cascade. Endocytosis encompass the route by which extracellular substrate is carried into a cell by membrane invagination. Almost all eukaryotic cells experience endocytosis, and can take part in processes as hormone signaling , vitamin and mineral uptake, extracellular solute uptake, pathogen removal, and even simple membrane turnover. Indeed, endocytosis is an active phenomenon in some cells that the entire plasma membrane is internalized and replaced in less than 30 minutes. Three sub categories are considerable in endocytosis process which include Phagocytosis, Fluid-phase pinocytosis and receptor-mediated endocytosis. Receptors belong to a class of proteins with extracellular domain which interact to specific exogenous ligand and carry the receptor/ligand (R/L) complex in to the cell by vesiculation. Interestingly, some specific receptors overexpressed under pathological condition which can be exploited for targeted drug delivery by NPs, e.g. diphtheria toxin receptor in inflammatory disease. RMT pathway also known as the molecular Trojan horse strategy due to its capability in transporting of ligand associated cargoes. Endocytosis after ligand/receptor complex formation which follow by transport through endothelial cytoplasm and exocytosis at basolateral side of the BBB are the three important steps of the RMT. Nanoparticles as drug or drug vehicles may be threatened by degradation in second step due to lysosomal system which isn't considerable in brain drug delivery. Over all, RMT route is so considerable to drug delivery by nanoparticles due to low side effect and targeted drug delivery.

Audience Take Away:

- Advantages and disadvantage of nanoparticles as drug or drug delivery vehicles (DDV)
- Importance of Drug delivery to central nerve system
- RMT route to cross the Blood-Brain Barrier (BBB)
- RMT importance in CNS drug delivery

Biography

Mehrdad Azarmi Aghajan is the M.Sc. student of Biotechnology at Shahid Beheshti University, Tehran, Iran. His prior project was about diabetes and herbal based drugs with cooperation of specialist from biology, biochemistry, medicinal plant and pharmacognosy. He got the first rank in first stage of Iran 21th student Olympiad and selected in the last stage. Now he is working on transcellular brain drug delivery by nanoparticles. He has published some papers in reputed journals in pharmacology field.

CONTENTS

Methotrexate induced liver and renal toxicity management by cornus mas: Back to nature antioxidants in fighting drug side effects

Hassan Saeiahan[1*], Mehrdad Azarmi Aghajan[2], Homeira Hatami[3], Ph.D, Gholareza Dehghan[3], Ph.D.

[1]Faculty of Medicine, Department of Medical genetics and Molecular Biology, Iran University of Medical science, Tehran, Iran
[2]Faculty of Life Science and Biotechnology, Department of Plant Science and Biotechnology, Shahid Beheshti University /G.C./ Tehran, Iran
[3]Faculty of Natural science, Department of Animal Biology, University of Tabriz, Tabriz, Iran

Methotrexate, abbreviated MTX and formerly known as amethopterin, is an antineoplastic, antimetabolite and antifulate drug. It is used in treatment of cancer, autoimmune diseases, ectopic pregnancy, and for the induction of medical abortions. Disturbances in the normal redox state of cells can cause toxic effects through the production of peroxides and free radicals that damage all components of the cell, including proteins, lipids, and DNA. Natural antioxidants such as fruits and vegetables, which provide protection against free radicals, can decrease the incidence and mortality rates of cancer and heart diseases, in addition to their other health benefits. Cornus mas fruits have anthocyanins, flavonoids, and plenty of oxalic acid content. It also contains antioxidant substances including butyrate hydroxyanisole and butylated hydroxytoluene, and has the potential to fight cancer. The present study indicated the hepatoprotective and Nephroprotective effects of cornus mas fruit extract in methotrexate induced renal and liver injury in rat model.

Audience Take Away:

- They will know the Cornus Mas fruit extract benefits and antioxidant capacity.
- This study may show a new way for studying the Cornus mas fruit active components.
- This study illustrated that cornus mas can be used as anti-side effect natural drug, beside cytotoxic drugs.
- Audience can reach out to the ingredients and active molecules of this natural drug.

Biography

Hassan Saeiahan is the Medical Genetics master student at Iran University of medical science, Tehran, Iran. Hassan Saei received the B.Sc. degree in Animal biology from the University of Tabriz, Iran in 2017. He has the honor of 1st grade and highest G.P.A in the field and obtained Silver medal at National Biology Olympiad 2017. He also got 9th rank in cellular and molecular biology master entrance exam over 13086 participants. He also done several researches about natural drugs and drug side effects and published a book and several papers at renowned journals.

About PDDS 2019

3rd Edition of Global Conference on

PHARMACEUTICS & DRUG DELIVERY SYSTEMS

June 27-29, 2019, Paris, France

https://pharmaceuticsconference.com