APV FOCUS GROUP DRUG DELIVERY

COMBINING SCIENCE & TECHNOLOGY TO CREATE ADVANCED DRUG DELIVERY SYSTEMS

INTERNATIONAL ASSOCIATION FOR PHARMACEUTICAL TECHNOLOGY

NEWSLETTER **ISSUE 3/2019 - December**

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Suggest a meeting to be announced!

MEETING REPORT (I)

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Provided by Peter van Hoogevest, PhD

6th International Symposium on Phospholipids in Pharmaceutical Research - September 9th–10th, 2019

Phospholipid Research Center, Heidelberg, Germany

The Phospholipid Research Center Heidelberg (www.phospholipid-institute.com) organised its "6th International Symposium on Phospholipids in Pharmaceutical Research" from 9th–10th September 2019 at the Chester Hotel, Conference Center, Heidelberg, Germany. 164 researchers from all over the world attended the meeting. International experts from academia and industry presented in their seminars innovative and new applications of phospholipids, categorised in five topics: Introduction to Phospholipids, Advances in Oral and Topical Use of Phospholipids, Phospholipids in Industry, Special Seminar: Phospholipid Research in South Korea; and Phospholipids in Academia.

The first day started with a general introduction to phospholipids. Prof. Alfred Blume (University Halle (Saale) Germany), President of the Phospholipid Research Center, highlighted the physicochemical properties of phospholipids. Prof. Gerald Brezesinski (Max-Planck-Institute of Colloids and Interfaces, Potsdam, Germany) discussed the use of modern analytical methods like GIXD (grazing incidence x-ray diffraction) and TRXF (total-reflection x-ray fluorescence) to study structures in (phospho)lipid monolayers and their interaction with ions.

In the following section on "Advances in Oral and Topical Use of Phospholipids", Prof. Paola Luciani (University Bern, Switzerland) showed new avenues for diagnosis and treatment of liver fibrosis. Her research team uses a human immortalized hepatic stellate cell (HSC) line in vitro model for studying the progression of liver fibrosis and the positive effect of soybean lecithin on liver fibrosis; an excellent example showing that phospholipids can be used as technical and bioactive excipients. The following seminar on "Phospholipid-Based Tablets: A New Dimension to Formulation of Antimalarials", by Prof. Athony Attama (University of Nigeria, Nsukka/Nigeria) discussed the use of lipid matrices as solidified reverse micellar solutions containing PHOSPHOLIPON ® 90 H prepared by fusion for the antimalarial compounds artemether and lumefantrine. The seminar shows that the combination of excellent science and straightforward preparation methods (addressing the situation in Africa) results in valuable formulation concepts. In the final seminar of this section, PD Dr. Dominique Lunter (University Tübingen, Germany) gave an interesting review on the use of phospholipid in dermal formulations with emphasis on discussing the potential of phospholipids to replace synthetic emulsifiers in dermal preparations.

In the afternoon section on "Phospholipids in Industry" representatives from the pharmaceutical industry gave lectures on their R&D work with phospholipids. The first, Dr. Christian Klose (Lipotype GmbH, Dresden, Germany), showed the use of "shotgun lipidomics" to analyse the lipid profile of the skin as a tool to assess the baseline of the lipid composition (and its biological variability) and effects of lipid based formulations on the skin for cosmetics and dermatological applications. In the second seminar Dr. Hannah Han (Heron Therapeutics Inc., San Diego/USA) informed on the development activities of a parenteral emulsion with egg PC as emulsifier for the lipophilic aprepitant (antiemetic) drug product (CINVANTI® Injectable Emulsion). This is an excellent demonstration that emulsions with egg PC, as a biocompatible, non-toxic emulsifier, can be used in solubilising formulations, avoiding the use of synthetic detergents as solubilisers. Dr. Gerard Jensen (Gilead Sciences Inc., Foster City, USA) reviewed experiences from Gilead's clinical and commercial use of liposomal therapeutics with a focus on carrier vehicle toxicity. He gave as examples the commercial products AmBisome® and DaunoXome®, and clinical lipid systems including those for simple solubilisation of poorly water-soluble compounds.

The scientific part of the first day was concluded by a seminar given by Ass. Prof. Jun-Pil Jee (Chosun University, Gwangju, Rep. of Korea) on "Phospholipids: The Versatile Component in Development of Drug Delivery Systems". His research area comprises interests in using polyethyleneglycol-phospholipids for solubilisation of hydrophobic drugs and to increase the stability of such systems in blood by exploring ABC triblock fluorous copolymer based on PEG-1,2-distearoyl-sn-glycero-3-phosphoethanolamine (DSPE). The first day finished with a conference Dinner for the participants at the Schwetzingen Palace.

At the beginning of the second day, six students, whose posters were pre-nominated by the Scientific Advisory Council from the 62 posters presented, were invited to give a 10-min presentation about their research as part of the "Young Session" chaired by Prof. Dr. Christel Müller-Goymann (University of Braunschweig, DE). Later three of them were selected as the Poster Award winners.

The day continued with a section on "Phospholipids in Academia". First speaker was Dr. Gero Leneweit (Carl Gustav Carus Institute, Niefern-Öschelbronn; Germany). His interesting research focuses on a novel industrial production method for asymmetric liposomes with high encapsulation efficiencies especially for macromolecular drugs (e.g. proteins and nucleotides) by means of centrifugation of nano-emulsions. Prof. Elias Fattal (University Paris Sud, Châtenay-Malabry, France) showed two impressive examples of his research: physicochemical and biopharmaceutical properties of nanoparticles with dexamethasone palmitate and DSPE-PEG2000 and siRNA against luciferase loaded in neutral liposomes after complexation with protamine and coupling of an aptamer against CD44 to DSPE-PEG2000. An inspiring seminar was given by Prof. Avi Schroeder (Technion Research and Development Foundation Ltd., Haifa, Israel). He discussed the use of 'barcoded liposomes' that target sites of cancer where they perform a programmed therapeutic task. Specifically, liposomes that diagnose the tumor and metastasis for their sensitivity to different medications, providing patient-specific drug activity information that can be used to improve the medication.

After lunch, Prof. Heiko Heerklotz (Albert Ludwigs University, Freiburg i. Br., Germany) presented his detailed physicochemical research on the release mechanism and the influence of phospholipids on the release characteristics of thermosensitive liposomes. The final seminar was dedicated to "What Theoretical Modelling Tells Us About the Mechanical Stability of Lipid Membranes in the Presence of Drug Molecules" presented by Rachel Downing, a PhD student of Prof. Sylvio May (North Dakota State University, Fargo, USA) who replaced her supervisor as presenter when he could not attend. She showed that their mathematical model predicts stability guidelines for inserting drug molecules into lipid bilayers: membranes with larger head-groups are more suitable for more hydrophobic drugs that penetrate deeper into the hydrocarbon core.

Most of the projects funded by the Phospholipid Research Center were represented. The Scientific Advisory Council selected the following three posters which were awarded with a 500 € poster prize:

- Near-Infrared Light Triggered-Release in Deep Brain Regions Using Ultra-Photosensitive Nanovesicles, Hejian Xiong, Xiuying Li, Peiyuan Kang, John Perish, Frederik Neuhaus, Andreas Zumbuehl, Zhenpeng Qin.
- Liposomes as Drug Delivery Systems for the Treatment of Infectious Diseases, Maria Manuela Gaspar, Maria Eugénia M. Cruz.
- Stairway to Asymmetry: 5-Step Approach to Asymmetric Proteoliposomes, Maria Markones, A. Fippel, M. Kaiser, C. Drechsler, C. Hunte, H. Heerklotz.

Figure 1 shows the winners from left to right: Prof. Andreas Zumbühl (National Centre of Competence in Research in Chemical Biology, Geneva, Switzerland and Acthera Therapeutics Ltd., Basel, Switzerland) accepting on behalf of Mr. Hejian Xiong (Departments of Mechanical Engineering and Bioengineering, University of Texas at Dallas, USA), Ms. Maria Markones (Albert Ludwigs University, Freiburg i. Br., Germany) and Dr. Manuela Gaspar (Universidade de Lisboa, Research Institute

for Medicines (iMed.U, Lisboa), Faculty of Pharmacy, Lisbon, Portugal). The awards were presented by Prof. Christel Müller-Goymann, Vice-President of the Phospholipid Research Center.

Fig. 1: The Poster Award Winners of the Sixth International Symposium on Phospholipids in Research. From left to right: Andreas Zumbühl, Maria Markones and Manuela Gaspar.

The symposium concluded with the announcement of the Thudichum-Award winners 2019. The Phospholipid Research Center awards the "Thudichum Award" to Young Scientists based on their outstanding publications on phospholipid research and the Life Award to a reputed scientist to honour his/her lifelong achievements in phospholipid research. The award is named after the famous German/English physician and biochemist Johann Ludwig Wilhelm Thudichum (1829-1901), who was first to isolate and characterise numerous brain compounds including phospholipids and related species, and recognise the physiological importance of phospholipids.

This year, the members of the scientific committee awarded two researchers for the Thudichum Young Scientist Award: Dr. Philipp Uhl (Heidelberg University Hospital, Heidelberg, Germany) for his publications in pharmaceutical phospholipid research related to cell penetrating liposomes enabling oral delivery of peptide drugs, and Dr. Dominik Witzigmann (Nano-Medicines Research Group, UBC Vancouver; Canada) for his papers in pharmaceutical phospholipid research on the use of a zebrafish model to assess the body distribution of nanoparticles and RNA delivery by means of lipidic particles. The Award (with 2500 € for each winner) was presented by the first winner of the Thudichum Life Award in 2017, Prof. Daan Crommelin (Utrecht University, The Netherlands) (Fig. 2.).

Fig. 2: The Winners of Thudichum Young Scientist Award of the Sixth International Symposium on Phospholipids in Research: Dr. Dominik Witzigmann (l) and Dr. Philipp Uhl (r) with Prof. Daan Crommelin.

For the second time the "Thudichum Life Award" has been awarded. Dr. Herbert Rebmann (Honorary President of the Phospholipid Research Center) congratulated Prof Yechezkel (Chezy) Barenholz for his lifelong outstanding achievements in the field of phospholipid research (Fig 3.).

Fig. 3: Prof. Dr. Yechezkel (Chezy) Barenholz (r), Winner of Thudichum Life Award of the Sixth International Symposium on Phospholipids in Research, congratulated by Dr. Herbert Rebmann (l), Honorary President of the Phospholipid Research Center.

Prof. Barenholz is famous for the development of one of the first liposome products with targeted drug delivery properties (Doxil®). In addition, he has an outstanding record of accomplishments in the biophysics, biochemistry, analysis, synthesis etc. of phospholipids and related dosage forms and is a role model for a generation of phospholipid researchers.

The success of the Sixth International Symposium on Phospholipids in Pharmaceutical Research 2019 was based on the many creative minds and inspiring scientists who demonstrated the numerous applications of phospholipids in pharmaceutical research and development. The author would like to acknowledge the speakers, poster authors, chairmen, scientific advisory council and the University Heidelberg (students of Prof. Gert Fricker) for their support. Special thanks go to Ms. Britta Merz, Dr. Dorothea Gutekunst and Ms. Ina von Jeinsen for their contributions to the outstanding organisation and coordination of the symposium. Finally, we would also thank all participants for their enthusiastic contributions. The next International Symposium on Phospholipids in Pharmaceutical Research will be held on September 13th – 14th, 2021.

MEETING REPORT (II)

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Provided by Prof. Regina Scherließ

First meeting of the International Nasal Focus Group - Unmet needs in nasal drug delivery

Nasal drug delivery presents many distinct and different challenges compared to pulmonary drug delivery (alongside which it is often considered) and many aspects are not yet fully understood. Hence the identification of those challenges and the design of strategies to overcome them are key to innovation in this field.

On May 15th 2019, an international group of experts in nasal drug delivery met to ascertain and codify unmet needs and unknowns in nasal delivery. The meeting was hosted by Prof. Regina Scherließ in Kiel, Germany, and it was attended by academic colleagues from the University of Parma, Italy, King's College London, UK, The Free University of Brussels in Belgium, University of Tours in France and Kiel University, as well as from several industrial partners interested in nasal delivery. The purpose of the meeting was to establish an "International nasal focus group" and build the basis for future research and collaboration within the topic of the development of innovative nasal products. In a workshop format, a broad collection of research questions and ideas was discussed within the framework of the following three main topics: 1. Formulation and device needs, 2. Meaningful product characterisation and modelling and 3. Influencing absorption and clearance.

1. Formulation and device needs

Since the nasal drug delivery market is expanding, more challenging drug candidates and targets will enter the field, requiring more sophisticated formulation and delivery strategies. Key challenges are a targeted deposition in the nose to reach the systemic circulation or the brain specifically and an improved absorption. A potential strategy is the use of functional excipients like permeation enhancers. Can a better understanding of local effects of such augment and extend their use? Not to neglect the sensory effects of a nasal formulation since they strongly affect patient compliance. Can they be modified or masked? Aims may also be reached using optimised devices. Easy-to-use but nevertheless sophisticated devices are desired which may help to target specific regions in the nose or are adapted for special groups of patients like children.

2. Meaningful product characterisation

To assess the formulations, critical quality attributes need to be defined and meaningful prediction models have to be used. How significant is the use of different nasal cast for the estimation of deposition and do we need further models for prediction of dissolution and absorption or are the current models fitting the expectations?

3. Influencing absorption and clearance

Another important question is the consideration of in-vitro in-vivo correlations, since the different regions of the nose have very different properties not only in terms of absorption and clearance. But also, the differences between the various species and/or individuals as well as pathological differences are remarkable. However, it is interesting to examine whether this leads to a change in pharmacokinetics and which test systems are best suited for such experiments?
These questions, which were collected in the course of the workshop, are designed to stimulate research and develop new collaborations in order to gain a better understanding of nasal application and to further optimise innovative nasal products.

DRUG DELIVERY PRODUCTS

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Provided by Dr. Louise Rosenmayr-Templeton

RYBELSUS®

On 20 Sep 2019 the FDA approved Rybelsus®, an oral formulation of semaglutide, a glucagon-like peptide-1 (GLP-1) analog developed by Novo Nordisk (Bagsværd, Denmark) for the treatment of Type 2 diabetes in adults in conjunction with diet and exercise [1-3]. Its therapeutic effect is due to its ability to reduce blood glucose by stimulating insulin secretion and lowering glucagon secretion in a glucose-dependent manner. Semaglutide is already licensed in a formulation for once weekly subcutaneous injection under the tradename, Ozempic®. Rybelsus® is the first GLP-1 agonist licensed for oral administration, and its approval opens up GLP-1 agonist treatment as an option to sufferers of Type 2 diabetes who are reluctant to inject drugs.

The tablets are available in three strengths, 3mg, 7 mg and 14 mg for once daily dosing. The 3 mg dose is a starter dose for the first 30 days after which the dose is increased to 7 mg. After at least 30 days the dose can be increased to 14 mg if required.

Semaglutide has a 94% sequence homology to human GLP-1 and a molecular weight of 4113.58 g/mol. Its circulation in blood is prolonged due to albumin binding, promoted by the attachment of a C_{18} fatty diacid at the position 26 lysine bound through a hydrophilic linker. Albumin binding reduces its renal clearance and protects against metabolic degradation, as does a modification at position 8 which inhibits its metabolism by the enzyme, dipeptidyl-peptidase 4. Oral bioavailability of semaglutide is low and variable as would be expected given its chemical composition and high molecular weight, with an estimated population-PK absolute bioavailability of around 0.4%-1% [2, 4]. Its oral absorption occurs predominately in the stomach [5] and is facilitated by the co-delivery of salcaprozate sodium (SNAC), a permeation enhancer, which is co-formulated with semaglutide in Rybelsus® tablets. SNAC has been shown to improve the delivery of semaglutide across gastric mucosa via transepithelial pathways in a concentration-dependent manner [6]. Other excipients in Rybelsus® tablets include povidone, microcrystalline cellulose and magnesium stearate [2].

Semaglutide absorption from the gastro-intestinal tract is sensitive to the volume and nature of liquid administered and the presence of food. For this reason, patients must swallow Rybelsus® whole with no more than 4 ounces (approx. 120 mL) water at least 30 minutes before imbibing any other food, beverage, or oral medication [2, 7]. Not adhering to this regimen e.g., taking Rybelsus® with food or eating shortly after taking the medication reduces semaglutide bioavailability, while waiting more than 30 minutes may increase it. Following oral administration, T_{max} is achieved one hour post-dose with steady-state plasma levels being attained following 4 to 5 weeks administration. In Type 2 diabetes patients, the mean population-PK estimated steady-state concentrations after daily oral administration of 7 and 14 mg semaglutide were around 6.7 nmol/L and 14.6 nmol/L, respectively.

Approval was granted based on the outcome of 10 PIONEER clinical trials, involving 9,543 individuals and included head-to-head studies of Rybelsus® and sitagliptin, empagliflozin and liraglutide 1.8 mg [2, 8-10]. In the trials, Rybelsus® reduced A1C levels (= % glycated haemoglobin levels in blood which is a key indicator of blood sugar control), and resulted in weight loss. The most common side-effects were nausea, abdominal pain, diarrhea, decreased appetite, vomiting and constipation. Like other GLP-1 agonists, Rybelsus is contraindicated in patients affected by or with a family history of medullary thyroid cancer or in those with Multiple Endocrine Neoplasia syndrome type 2. This is due to thyroid C-cell tumors have been shown to occur in rodents with semaglutide [2].

The US market launch is planned for Q4 2019 with initial supplies being manufactured in Denmark, while manufacturing at a purpose-built facility in Clayton, NC and at a recently purchased tabletting and packaging facility in Durham, NC comes on line [1].

Novo Nordisk has also applied to extend Rybelsus' approval to an additional indication to reduce the risk of major adverse cardiovascular events (MACE) such as heart attack, stroke, or cardiovascular death in adults with type 2 diabetes and established cardiovascular disease (CVD). A decision from the FDA is expected in Q1 2020.

Rybelsus® is also being reviewed by other regulatory agencies including the European Medicines Agency and the Japanese Pharmaceuticals and Medical Devices Agency.

SECUADO®

The Secuado® transdermal patch from Noven Pharmaceuticals, part of the Hisamitsu Group, became the first patch to be approved by the FDA for the treatment of schizophrenia in adults [11-12] on 11 Oct 2019. This transdermal delivery system contains the atypical anti-psychotic, asenapine. It has been developed in three dosage strengths: 3.8 mg/24 hours, 5.7 mg/24 hours and 7.6 mg/24 hours with the lowest dose being the starting dose that can be increased as required after one week. The 3.8 mg/24 hr strength is equivalent based on AUC to 5 mg twice daily of the previously licensed sublingual formulation of asenapine, while Secuado 7.6 mg/24 hrs equates to 10 mg dosed twice daily sublingually. The mechanism of action of asenapine is not entirely understood but it is thought to act through antagonist activity at dopamine, D2, and 5-HT 2A receptors.

Each dosage strength has an identical composition per unit area with the patch size varying from 20 cm^2 (containing a total of 6.4 mg asenapine) for the 3.8 mg/24 hrs dose and 40 cm^2 (containing a total of 12.8 mg asenapine) for the 7.6 mg/ 24 hrs dose. The patch system is composed of alicyclic saturated hydrocarbon resin, butylated hydroxytoluene, isopropyl palmitate, maleate salts (monosodium maleate and disodium maleate), mineral oil, polyester film backing, polyisobutylene, silicone-treated polyester release liner, sodium acetate anhydrous, and styrene-isoprene-styrene block copolymer.

Drug release from the patch over a 24-hour period is approximately 60% of the total drug loading. In general, maximum asenapine blood conditions are attained between 12 and 24 hours, with steady-state asenapine plasma levels being achieved in around 72 hours. The apparent elimination half-life is 30 hours after patch removal.

Approval was partially based on clinical data generated on the sublingual formulation of asenapine, and additional efficacy data obtained on the patch formulation in a 6-week, Phase 3 randomized, double-blind, and placebo-controlled trial of adult patients with schizophrenia. In this study involving 616 patients, Secuado® achieved the primary endpoint of a statistically significant improvement from baseline in the total Positive and Negative Syndrome Scale (PANSS) compared to placebo at Week 6. This scale is a 30-item scale that measures positive and negative symptoms of schizophrenia (7 items each) and general psychopathology (16 items), each rated on a scale of 1 (absent) to 7 (extreme). It also achieved the key secondary end-point of improvements in the validated clinician-related Clinical Global Impression scale (CGI-S). The most common side-effects reported were extrapyramidal disorder, application site reaction, and weight gain.

References and Further Information

[1] FDA approves Rybelsus® (semaglutide), the first GLP-1 analog treatment available in a pill for adults with type 2 diabetes. https://www.novonordisk-us.com/media/news-releases.html?122973.

[2] Entry for Rybelsus® on Drugs@FDA https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=BasicSearch.process.

[3] FDA approves first oral GLP-1 treatment for type 2 diabetes. https://www.fda.gov/news-events/press-announcements/fda-approves-first-oral-glp-1-treatment-type-2-diabetes.

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[6] Buckley S.T., S.G. Schléele, R.K. Kirk and L.B. Knudsen. SNAC-mediated absorption mechanism of action in an oral formulation of semaglutide. ePoster #786, 53rd Annual Meeting, European Association for the Study of Diabetes, Lisbon, Portugal 11-15 Sep 2017.

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[10] Pratley R, Amod A, Hoff ST, et al. Oral semaglutide versus subcutaneous liraglutide and placebo in type 2 diabetes (PIONEER 4): A randomised, double-blind, phase 3a trial. *Lancet*. 394(10192):39-50.

[11] U.S. FDA Approves SECUADO® (asenapine) Transdermal System, the First-and-Only Transdermal Patch for the Treatment of Adults with Schizophrenia. http://www.noven.com/PR101519.php.

[12] Entry for Secuado® on Drugs@FDA. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/212268s000lbl.pdf.

ACADEMIC GROUPS WITH FORMULATION CAPABILITIES FOR PHARMACEUTICAL 3D PRINTING

This newsletter section is intended to give a brief overview of academic groups working on pharmaceutical 3D printing. The printing technologies the groups are focusing on are listed under "Research Focus". It is part of an occasional series giving brief details of European research teams exploring different aspects of drug delivery research. It is not intended to be a comprehensive list of those involved in the area. As it is a living document, our readers are most welcome to suggest other research teams they are aware of for inclusion in our next edition.

The contact person given is the head of the department or working group.

BELGIUM

Research Focus	Fused deposition modeling
Institution	Ghent University
Address	Laboratory of Pharmaceutical Technology, Campus Heymans, Ottergemsesteenweg 460, 9000 Ghent
Contact	Chris Vervaet
eMail	chris.vervaet@ugent.be
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DENMARK

Research Focus	Fused deposition modeling
Institution	University of Copenhagen
Address	Department of Pharmacy, Universitetsparken 2, 2100 København
Contact	Jukka Rantanen
eMail	jukka.rantanen@sund.ku.dk
Web site	https://pharmacy.ku.dk/research/manufacturing-materials/

FINLAND

Research Focus	Fused deposition modeling
Institution	Abo Akademi University
Address	Pharmaceutical Sciences Laboratory, Abo Akademi University, Artillerigatan 6A, FI 20520 Turku
Contact	Niklas Sandler
eMail	niklas.sandler@abo.fi
Web site	https://gbiomed.kuleuven.be/english/research/50000715/50000716/

GERMANY

Research Focus	Fused deposition modeling, micro/semi-solid extrusion
Institution	Heinrich Heine University Düsseldorf
Address	Institute of Pharmaceutics and Biopharmaceutics, Universitätsstr. 1, 40225 Düsseldorf
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eMail	joerg.breitkreutz@uni-duesseldorf.de
Web site	http://www.pharmazie.hhu.de/en/institutes/ptb.html

Research Focus	Fused deposition modeling
Institution	Technical University (TU) Dortmund
Address	Laboratory of Solids Process, Emil-Figge-Str. 68, 44227 Dortmund
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Web site	http://www.fsv.bci.tu-dortmund.de/cms/en/home/index.html

Research Focus	Fused deposition modeling
Institution	Universität Greifswald
Address	Department of Biopharmaceutics and Pharmaceutical Technology, Felix-Hausdorff-Straße 3, 17489 Greifswald
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Web site	https://pharmazie.uni-greifswald.de/institut/abteilungen/biopharmazie-und-pharm-technologie/

ITALY

Research Focus	Fused deposition modeling
Institution	University of Milan
Address	Laboratorio di Biofarmaceutica e Tecnologia Farmaceutica, Via Giuseppe Colombo 71, 20133 Milan
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UNITED KINGDOM

Research Focus	Micro/semi-solid extrusion, fused deposition modeling
Institution	University of Nottingham
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Web site	https://www.nottingham.ac.uk/pharmacy/index.aspx

Research Focus	Fused deposition modeling, stereolithography, selective laser sintering
Institution	University College London
Address	UCL School of Pharmacy, 23/39 Brunswick Square, London, WC1N 1AX
Contact	Simon Gaisford
eMail	s.gaisford@ucl.ac.uk
Web site	https://www.ucl.ac.uk/pharmacy/

Research Focus	Fused deposition modeling
Institution	King's College London
Address	School of Cancer & Pharmaceutical Sciences, Franklin-Wilkins Building, Stamford Street London, SE1 9NH
Contact	Mohamed A. Alhnan, formerly University of Central Lancashire
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Web site	https://www.kcl.ac.uk/scps

Technologies

General: 3D-printing is the automated construction of a three-dimensional object from thin layers. While this concept is true for almost all 3D-printing techniques, the mode of layer creation/solidification varies greatly. In the following, a very brief description of the main principles is given.

Fused deposition modeling: A (via hot melt extrusion) pre-manufactured, drug-containing polymer filament is molten in the print head and deposited on a print bed.

Micro/semi-solid extrusion: Similar to fused deposition modeling but the stock formulation is not a filament but a semi-solid mass that is extruded and deposited from the print head via pressurized air.

Stereolithography: A laser is used to crosslink a drug-containing photopolymer/photo initiator solution to build up the desi-red structure.

Selective laser sintering: A layer of given powder mixture is solidified by fusing it together with a laser.

DRUG DELIVERY LITERATURE

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Provided by Dr. Carsten Timpe

Peptide, Protein-based Drug Delivery

Nanoparticles: Oral Delivery for Protein and Peptide Drugs

Cao SJ, Xu S, Wang HM, Ling Y, Dong J, Xia RD, Sun XH., AAPS PharmSciTech. 2019 May 20;20(5):190

The strategies for improving the bioavailability of protein and peptides are reviewed, including chemical modification of nanocarriers, absorption enhancers and mucous adhesion systems. The status, advantages, and disadvantages of various strategies are systematically analyzed. The systematic and personalized design of various factors affecting the release and absorption of drugs based on nanoparticles is pointed out. It is expected to design a protein peptide oral delivery system that can be applied in the clinic.

Dermal and Transdermal Drug Delivery

Pharmaceutical Topical Delivery of Poorly Soluble Polyphenols: Potential Role in Prevention and Treatment of Melanoma

Heenatigala Palliyage G, Singh S, Ashby CR Jr, Tiwari AK, Chauhan H., AAPS PharmSciTech. 2019 Jul 11;20(6):250

This review will provide an overview of poorly soluble polyphenols that have been reported to have antimetastatic efficacy in melanomas.

Microneedles as a perspective for transdermal therapeutic systems

Wolaschka T., Ceska Slov Farm. 2019 Spring;68(1):12-26

Microneedles (MI) by their painless application appear to increase drug permeation when applied transdermally. In this review work, various types of MI (solid, coated, hollow, matrix, hydrogel forming) their size, shape, grouping, but also materials and technologies used in MI production are described. Finally, the work is focused on current clinical trials in which MI have been tested.

Gene Drug Delivery, Gene Therapy, siRNAs

Stimulus-responsive vesicular polymer nano-integrators for drug and gene delivery

Mu X, Gan S, Wang Y, Li H, Zhou G., Int J Nanomedicine. 2019 Jul 18;14:5415-5434

This review summarizes the latest advances in stimulus-responsive polymeric nanovesicles for biomedical applications. Different functionalized polymers are in development to construct more complex multiple responsive nanovesicles in delivery systems, medical imaging, biosensors and so on.

Chitosan for gene delivery: Methods for improvement and applications

Chuan D, Jin T, Fan R, Zhou L, Guo G., Adv Colloid Interface Sci. 2019 Jun;268:25-38

This review introduces the features of chitosan in gene delivery, summarizes current progress toward methods promoting the properties of chitosan related to gene delivery, and presents different applications of chitosan in gene delivery vectors. Finally, future prospects of gene vectors based on chitosan are discussed.

Nanosystem-based Drug Delivery

Targeted Nanoparticle Drug Delivery System for the Enhancement of Cancer Immunotherapy

Zhang H, Wu Y, Hu Y, Li X, Zhao M, Lv Z., J Biomed Nanotechnol. 2019 Sep 1;15(9):1839-1866

In this review, the five main classes of immunotherapy will be introduced, and then extensively covered are advanced biomaterials and novel strategies of nanotechnology intervention and detailed how these approaches function to enhance immunotherapeutic and combinational combination therapeutic efficacy.

Cell membrane camouflaged nanoparticles: a new biomimetic platform for cancer photothermal therapy

Wu M, Le W, Mei T, Wang Y, Chen B, Liu Z, Xue C., Int J. Nanomedicine. 2019 Jun 17;14:4431-4448

In this review, the recent development of cell membrane-coated NPs in the application of photothermal therapy and cancer targeting is discussed. The underlying biomarkers of cell membrane-coated nanoparticles (CMNPs) are discussed, and future research directions are suggested.

Advanced biomedical applications of carbon nanotube

Raphey VR, Henna TK, Nivitha KP, Mufeedha P, Sabu C, Pramod K., Mater Sci Eng C Mater Biol Appl. 2019 Jul;100:616-630

The review focuses on the characteristic properties of carbon nanotubes (CNTs) which make them the most selective candidate for various multi-functional applications. The greater surface area of the CNTs in addition to the capability to manipulate the surfaces and dimensions has provided greater potential for this nanomaterial. The CNTs possess greater potential for applications in biomedicine due to their vital electrical, chemical, thermal, and mechanical properties. The unique properties of CNT are exploited for numerous applications in the biomedical field.

Ocular Drug Delivery

Pharmaceutical Formulation Methods for Improving Retinal Drug Delivery

Stryjewski TP, Stefater JA, Eliott D., Semin Ophthalmol. 2019;34(4):218-222

This review focuses on the formulation methods used in commonly prescribed retina drug products.

Intranasal Drug Delivery

Evaluation of intranasal delivery route of drug administration for brain targeting

Erdő F, Bors LA, Farkas D, Bajza Á, Gizurarson S., rain Res Bull. 2018 Oct;143:155-170

In this review the focus is on giving an overview on the anatomical and cellular structure of nasal cavity and absorption surface. It presents some possibilities to enhance the drug penetration through the nasal barrier and summarizes some in vitro, ex vivo and in vivo technologies to test the drug delivery across the nasal epithelium into the brain. Finally, the authors give a critical evaluation of the nasal route of administration showing its main advantages and limitations of this delivery route for CNS drug targeting.

Oral Drug Delivery

Innovations in Oral Therapies for Inflammatory Bowel Disease

Ma C, Battat R, Dulai PS, Parker CE, Sandborn WJ, Feagan BG, Jairath V., Drugs. 2019 Aug;79(12):1321-1335

In this review, different mechanisms of oral drug delivery to the gastrointestinal tract are summarized, key findings from phase II and III randomized trials of novel oral SMDs highlighted, and discussed how oral SMDs are likely to be integrated into future IBD treatment paradigms.

Oral delivery of non-viral nucleic acid-based therapeutics - do we have the guts for this?

O'Driscoll CM, Bernkop-Schnürch A, Friedl JD, Préat V, Jannin V., Eur J Pharm Sci. 2019 May 15;133:190-204

This review will focus on the barriers to the oral delivery of nucleic acids and the strategies, in particular formulation strategies, which have been developed to overcome these barriers.

Pulmonary drug delivery

Interactions between microbiome and lungs: Paving new paths for microbiome based bio-engineered drug delivery systems in chronic respiratory diseases

Chellappan DK, Sze Ning QL, Su Min SK, Bin SY, Chern PJ, Shi TP, Ee Mei SW, Yee TH, Qi OJ, Thangavelu L, Rajeshkumar S, Negi P, Chellian J, Wadhwa R, Gupta G, Collet T, Hansbro PM, Dua K., Chem Biol Interact. 2019 Sep 1;310:108732

This review highlights the relationships between microbiota and different types of respiratory diseases, the importance of microbiota towards human health and diseases, including the role of novel microbiome drug delivery systems in targeting various respiratory diseases.

Emerging trends in the novel drug delivery approaches for the treatment of lung cancer

Sharma P, Mehta M, Dhanjal DS, Kaur S, Gupta G, Singh H, Thangavelu L, Rajeshkumar S, Tambuwala M, Bakshi HA, Chellappan DK, Dua K, Satija S., Chem Biol Interact. 2019 Aug 25;309:108720

In this review, various modes of nano drug delivery options like liposomes, dendrimers, quantum dots, carbon nanotubes and metallic nanoparticles have been discussed. Nano-carrier drug delivery systems emerge as a promising approach and thus is expected to provide newer and advanced avenues in cancer therapeutics.

Oligonucleotide therapy: An emerging focus area for drug delivery in chronic inflammatory respiratory diseases

Mehta M, Deeksha, Tewari D, Gupta G, Awasthi R, Singh H, Pandey P, Chellappan DK, Wadhwa R, Collet T, Hansbro PM, Kumar SR, Thangavelu L, Negi P, Dua K, Satija, Chem Biol Interact. 2019 Aug 1;308:206-215

The current review focuses on various novel dosage forms like nanoparticles, liposomes that can be used efficiently for the delivery of various oligonucleotides such as siRNA and miRNA. The future perspectives and targets for oligonucleotides in the management of respiratory diseases are also discussed.

Subunit-based mucosal vaccine delivery systems for pulmonary delivery - Are they feasible?

Marasini N, Kaminskas LM., Drug Dev Ind Pharm. 2019 Jun;45(6):882-894

This review will discuss our current understanding of pulmonary immunology and developments in fabricating particle characteristics that may evoke potent and durable pulmonary immunity.

The APV Drug Delivery Focus Group (APV DD) is a section of the APV (Arbeitsgemeinschaft für Pharmazeutische Verfahrenstechnik e.V. / International Association for Pharmaceutical Technology), a major European society for those sharing a professional interest in pharmaceutical sciences. The Focus Group was established in 2003 in response to the increasing importance of drug delivery within modern pharmaceutics.

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COMBINING SCIENCE AND TECHNOLOGY TO CREATE ADVANCED DRUG DELIVERY SYSTEMS

OUR MISSION STATEMENT:

Modern drug delivery research and development is a truly multidisciplinary approach and must combine all relevant scientific, technical, medical and regulatory aspects required for the design, preparation, testing, manufacturing and registration of drug delivery systems and their components. It is the mission of the APV Drug Delivery Working Group to foster and promote all aspects of research and development required to transform drug molecules into safe, applicable and acceptable drug delivery systems, which provide therapeutic benefit, convenience to the patient and improve patient compliance.

Our mission includes in particular the following tasks:

- Thoroughly understanding the physical-chemical and biopharmaceutical properties of the drug substance to be delivered and the components of the drug delivery system
- Understanding the biological barriers and the interactions of the drug molecule and its delivery system with the biological environment and the biological target including PK/PD and PK/safety relationships
- Research on excipients, materials and technologies required for the design, preparation and manufacturing of drug delivery systems for a selected route of administration
- Development and understanding of methods for in vitro and in vivo evaluation of drug delivery systems and their components
- Knowledge of regulatory requirements for clinical testing, manufacturing and registration of drug delivery systems

All disciplines relevant to the above-mentioned areas of drug delivery R&D are invited to contribute to the APV Drug Delivery Group:

Pharmaceutics, Biopharmaceutics, Analytics, Biology, Physical Chemistry, Biochemistry, Physics, Engineering Sciences, Nano Technology, Material Sciences, Polymer Science, Toxicology, Drug Safety, Clinical Research, Drug Regulatory Affairs, etc.

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