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International Association for Pharmaceutical Technology
Arbeitsgemeinschaft für Pharmazeutische Verfahrenstechnik e.V.
Gemeinnütziger wissenschaftlicher Verein

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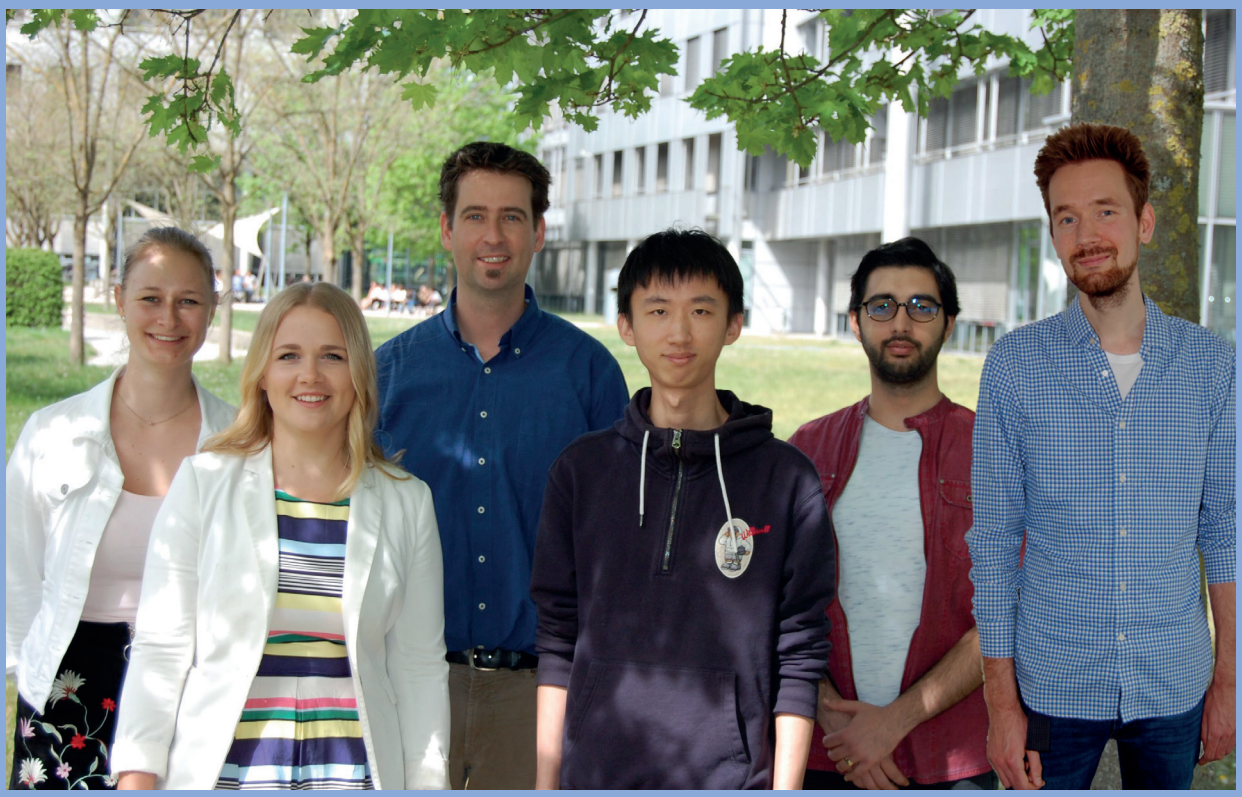
APV NEWS

Galenus Technology Prize 2019 for
New approaches to metal-organic nanoparticles

Dr Ulrich Laechelt has won the 2019 Galenus Technology Prize for his research into new approaches to metal-organic nanopharmaceuticals as drug delivery systems. Although currently based in Munich, Ulrich Laechelt comes from Saulgau/Germany and began his career at the Universities of Heidelberg and Munich, receiving his PhD in 2014.

The research for which he has been awarded the Galenus Technology Prize 2019 introduces two novel and incisive approaches to forming drug-metal nanopharmaceuticals. One the one hand, selected drugs can serve as organic linkers in coordination polymers and enable the formation of metal-based nanopharmaceuticals with very high drug loading capacity. On the other hand, Laechelt uses metal-organic frameworks (MOFs) with tuneable size and porosity as a very promising compound class for drug delivery.

The prize giving ceremony will be held on November 14th, 2019 at the Kunsthistorisches Museum Vienna (Austria). Further information will be available on www.galenusprivatstiftung.at/ 82.0.html.



Lokale Gruppen

Montag, 28. Oktober 2019

Lokale APV-Gruppe Westfalen um 19:30 Uhr in der Hövels-Hausbrauerei in Dortmund (Hoher Wall 5-7, 44137 Dortmund).
Anmeldung erforderlich bis zum 21. Oktober 2019 bei Dr. Johanna Anlahr (johanna.anlahr@bayer.com).

Mittwoch, 27. November 2019

Lokale APV-Gruppe Rhein-Main ab 19:30 Uhr. Der Veranstaltungsort wird noch bekanntgegeben.
Weitere Informationen und Angaben zu dem Veranstaltungsort sowie den nächsten Terminen erhalten Sie bei Cathrin Pauly (pauly@aspiras.de).

Mittwoch, 15. Januar 2020

Lokale APV-Gruppe Basel um 18:30 Uhr im Restaurant „Gifthüttli", Schneidergasse 11, 4051 Basel (www.gifthuettli.ch).
Anmeldung erforderlich bis zum 10. Januar 2020 bei Dr. Lars Restetzki (lars.restetzki@roche.com).

Donnerstag, 23. Januar 2020

Lokale APV-Gruppe Berlin um 19:00 Uhr bei der Chemisch-Pharmazeutisches Labor, Rolf Sachse GmbH (Stieffring 14, 13627 Berlin).
Anmeldung erforderlich bis zum 20. Dezember 2019 bei Dr. Andreas Sachse (andreas.sachse@cpl-sachse.de).

Lokale APV-Gruppe Mecklenburg-Vorpommern

Weitere Informationen und Angaben zu den nächten Terminen erhalten Sie bei Katharina Tietz (katharina.tietz@uni-greifswald.de).

Lokale APV-Gruppe Nordrhein

Weitere Informationen und Angaben zu den nächten Terminen erhalten Sie bei Klaus Wening (klaus.wening@grunenthal.com).

Lokale APV-Gruppe Oberbayern

Weitere Informationen und Angaben zu den nächsten Terminen erhalten Sie bei Dr. (USA) Julia Schulze-Nahrup (jsn@pharmoveo.de).

What´s hot in European Journal of Pharmaceutics and Biopharmaceutics?

Eduard Trenkenschuh, Ludwig-Maximilians-Universität, D-München

Victoria Pauli et al./ European Journal of Pharmaceutics and Biopharmaceutics 141 (2019) 90-99

Real-time monitoring of particle size distribution in a continuous granulation and drying process by near infrared spectroscopy

Victoria Pauli, Yves Roggo, Peter Kleinebudde, Markus Krumme

In continuous granulation, it can be important to control granules particle size distribution (PSD), as it may affect final product quality. Near infrared spectroscopy (NIRS) is already a routine analytical procedure within pharmaceutical continuous manufacturing for the in-line analysis of chemical material-characteristics. Consequently, the extraction of additional information related to granules' physical properties like particle size distribution is tempting, as it would enhance process knowledge without the need for new capital investments.

Three in-line NIRS methods were developed via partial least squares regression, to predict dried granules PSD-fractions X10, X50, and X90 within a GMP-qualified continuous twin-screw wet granulation and fluid-bed drying process. Methods were developed for the size range of 20–234 µm (X10), 98–1017 µm (X50), and 748–2297 µm (X90) and assessed with one internal and three external validation datasets in agreement with current guidelines on NIRS. Internal validation indicated root mean square error of predictions (RMSEPs) of 17 µm, 97 µm, and 174 µm, for PSD X10, X50, and X90 respectively, with acceptable linearity, slope, and bias. Furthermore, the ratio of prediction to deviation (RPD), the ratio of prediction error to laboratory error (PRL), and the range error ratio (RER) were evaluated, with all values within the acceptance range for adequate to good NIR methods ($1.75 > RPD < 3$, $PRL \leq 2$, $RER \geq 10$). Methods applicability to in-line processes and their robustness towards water content and active pharmaceutical ingredient content was further demonstrated with three independent in-line datasets in real-time, showing good agreement between predicted and reference values. In summary, methods demonstrated to be sufficient for their intended purpose to monitor trends and sudden changes in dried granules PSD during continuous granulation and drying. Because of their fast response time, they are unique tools to characterize the dynamic behavior and navigate the agglomeration state of the material in static and transient process conditions during continuous granulation and drying.

Michaela Breitsamer et al./ European Journal of Pharmaceutics and Biopharmaceutics 142 (2019) 61-69

Do interactions between protein and phospholipids influence the release behavior from lipid-based exenatide depot systems?

Michaela Breitsamer, Anja Stulz, Heiko H. Heerklotz, Gerhard Winter

The release mechanism for proteins and peptides from vesicular phospholipid gels (VPGs) is very complex. Drug release proceeds via a combination of erosion of the gel and diffusion of the drug out of it. This diffusion can be retarded by a slow permeation of the drug across the lipid bilayers in the gel as well as by its direct binding or adsorption to the lipid bilayers. Finally, the viscosity and homogeneity of the formulation may affect the release behavior. So far a direct correlation between one of these parameters and the release kinetics is not possible.

In the present study, we aimed to investigate the contribution of drug-membrane interactions to the release kinetics of exenatide from differently composed VPGs (POPC, POPG and mixtures of both). To this end, in vitro release of exenatide as well as in vitro release of the phospholipids was monitored. Binding affinities were determined by microscale thermophoresis (MST).

The sustained release behavior of exenatide could not simply be correlated to high viscosity of the VPG formulation. Release of exenatide from VPGs of anionic membranes containing POPG proceeded with a half-life of the order of 5 days and it seems to be controlled by the erosion of the gel. Its rate is unaffected by the initial pH inside the gel, independently of the strong impact of pH on exenatide binding to the membrane. At pH 4.5, exenatide is cationic and binds to membranes containing anionic POPG with a high affinity ($K_d \approx 10–30$ µM).

No high affinity membrane binding of exenatide is detected in this at pH 7.4, where exenatide is anionic, and to zwitterionic membranes composed of POPC. Exenatide release from the latter has a significantly longer half-life of 30 to 55 days. That means, these VPGs are much more resistant to erosion and show a very slow diffusional release. In this case, diffusion should be slowed down by the barrier function of the membranes rather than membrane affinity.

In conclusion, erosion of the VPG matrix and membrane permeability of the drug are the major parameters influencing the release of exenatide from VPGs of POPC-POPG, whereas drug binding to the membranes had a minor effect only.

Didier Clénet et al./ European Journal of Pharmaceutics and Biopharmaceutics 142 (2019) 334-343

A spray freeze dried micropellet based formulation proof-of-concept for a yellow fever vaccine candidate

Didier Clénet, Véronique Hourquet, Bertrand Woinet, Hervé Ponceblanc, Manuel Vangelisti

The stability of live-attenuated viruses is very challenging due to thermal sensitivity; therefore, solid form is usually required (often freeze-dried products). Micropellet technology is a lyophilization technology that has the potential to provide greater flexibility in the presentation of a given vaccine particularly in multi-dose format or in combination of different vaccines. As a novel vaccine alternative process, this spray freeze-dried (SFD) micropellet technology was evaluated using as a model a yellow fever virus produced in Vero cells (vYF).

Screening of excipients was performed in order to optimize physico-chemical properties of the micropellets. Sugar/polymer-based formulations induced high glass transition temperature (Tg), adequate breaking force and attrition resistance of the

SFD micropellets. These mechanical parameters and their stability are of considerable importance for the storage, the transport but also the filling process of the SFD micropellets. By adding excipients required to best preserve virus infectivity, an optimal sugar/polymer-based formulation was selected to build micropellets containing vYF. Monodisperse and dried micropellets with a diameter of about 530 µm were obtained, exhibiting similar potency to conventional freeze-dried product in terms of vYF infectious titer when both solid forms were kept under refrigerated conditions (2–8 °C). Comparable kinetics of degradation were observed for vYF formulated in micropellets or as conventional freeze-dried product during an accelerated stability study using incubations at 25 °C and 37 °C over several weeks. The results from this investigation demonstrate the ability to formulate live-attenuated viruses in micropellets. Pharmaceutical applications of this novel vaccine solid form are discussed.

C. Roos et al./ European Journal of Pharmaceutics and Biopharmaceutics 142 (2019) 387-395

Effects of absorption-modifying excipients on jejunal drug absorption in simulated fasted and fed luminal conditions

C. Roos, D. Dahlgren, E. Sjögren, M. Sjöblom, M. Hedeland, H. Lennernäs

Oral administration of drug products is the preferred administration route. In recent decades there has been an increase in drug candidates with low solubility and/or low permeability. To increase the possibility of oral administration for the poorly permeating drugs, the use of absorption modifying excipients (AMEs) has been proposed. These types of AMEs may also affect the regulatory assessment of a novel drug delivery system if they affect the absorption of a drug from any of the four BCS classes. The effects of AMEs have previously been investigated in various animal models, including the single-pass intestinal perfusion (SPIP) in rats. To further improve the biorelevance and the in vivo predictiveness of the SPIP model, four compounds (atenolol, enalaprilat, ketoprofen, metoprolol) were perfused in fasted or fed state simulated intestinal fluid (FaSSIF or FeSSIF) together with the AMEs N-acetyl-cysteine, caprate, or sodium dodecyl sulfate. For the highly soluble and poorly permeating compounds enalaprilat and atenolol (BCS class III), the flux was increased the most by the addition of SDS in both FaSSIF and FeSSIF. For ketoprofen (BCS class II), the flux decreased in the presence of all AMEs in at least one of the perfusion media. The flux of metoprolol (BCS class I) was not affected by any of the excipients in none of simulated prandial states. The changes in magnitude in the absorption of the compounds were in general smaller in FeSSIF than in FaSSIF. This may be explained by a reduced free concentration AMEs in FeSSIF. Further, the results in FeSSIF were similar to those from intrajejunal bolus administration in rat in a previous study. This suggests that the biorelevance of the SPIP method may be increased when investigating the effects of AMEs, by the addition of intraluminal constituents representative to fasted and/or fed state to the inlet perfusate.

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