MAKING SCIENCE WORK

Nachrichten und Mitteilungen

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

05 · 2017

APV NEWS

The Galenus Technology Prize 2017 for innovative approaches to Nano Drug Delivery

For only the second time in the 12-year history of the Galenus Technology Prize, the award has been given to two different researchers, Dr Gregor Fuhrmann and Jun. Prof. Dr Peter Wich. Following the recommendations of Prof. Dr Bernhard Lippold, the foundation's scientific adviser, the board saw fit to honour both of their outstanding submissions.

Dr Fuhrmann is head of the ‚Biogenic Nano-Therapeutics' (BION) junior research group at the Helmholtz Institute for Pharmaceutical Research Saarland (HIPS), where his research focuses on extracellular vesicles as potential carriers in drug delivery systems. This is an area which has attracted considerable interest from the scientific community as this form of intercellular communication can not only be used to deliver drugs, but also direct them in a highly targeted manner.

Dr Peter Wich is the principal investigator at the WichLab of the Institute of Pharmacy and Biochemistry at the University of Mainz. Coming from a background in organic chemistry, his work capitalises on his knowledge in this area to complement his research interests in pharmaceutical technology. The award was given for the modification of the surfaces of biopolymer-based-nanomaterials, e.g. proteins, for use in drug delivery.

The prize-giving ceremony will be held on November 8th, 2017, at the Natural History Museum in Vienna. The Galenus Foundation wishes to congratulate both winners and looks forward to further ground-breaking work from these talented young researchers.

Lokale Gruppen

Mittwoch, 20. September 2017
Lokale APV-Gruppe Berlin um 19:00 Uhr bei der Bayer Pharma AG (Standort Berlin Wedding). Der genaue Treffpunkt wird noch bekannt gegeben.
Anmeldung erforderlich bis zum 13. September 2017 bei Dr. Andreas Sachse (andreas.sachse@cpl-sachse.de).

Mittwoch, 26. September 2017
Lokale APV-Gruppe Westfalen um 19:30 Uhr in der Hövels Hausbrauerei, Hoher Wall 5-7, 44137 Dortmund.
Anmeldung erforderlich bis zum 20. September bei Dr. Johanna Mosig (johanna.mosig@bayer.com).

Mittwoch, 27. September 2017
Lokale APV-Gruppe Basel um 19:30 Uhr im Gifthüttli Schneidergasse 11, 4051 Basel (www.gifthuettli.ch).
Anmeldung erforderlich bis zum 22. September 2017 bei Dr. Lars Restetzki (lars.restetzki@roche.com).

Montag, 16. Oktober 2017
Lokale APV-Gruppe Köln/Bonn/Aachen um 19:00 Uhr in Köln. Der genaue Veranstaltungsort wird noch bekanntgegeben.
Anmeldung erforderlich bis zum 25. August 2017 bei Dr. Heiko Spilgies (heiko@spilgies.de).

Dienstag, 28. November 2017
Lokale APV-Gruppe Mecklenburg-Vorpommern im Jack & Richies´s Steakhouse (An der Mühle 8, 17493 Greifswald-Wiek).
Anmeldung erforderlich bis zum 14. November 2017 bei Katharina Tietz (katharina.tietz@uni-greifswald.de).

Mittwoch, 29. November 2017
Lokale APV-Gruppe Rhein-Main ab 19:30 Uhr. Der Veranstaltungsort wird noch bekanntgegeben.
Weitere Informationen und Angaben zu den nächsten Terminen erhalten Sie bei Cathrin Pauly (pauly@aspiras.de).

Mittwoch, 06. Dezember 2017
Lokale APV-Gruppe Nord um 19:30 Uhr auf dem Fleetweihnachtsmarkt, Hamburg.
Weitere Informationen und Angaben zum Treffpunkt erhalten Sie bei bei Dr. Alexandra Steckel (alexandra.steckel@t-online.de).

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?

Christoph Marschall, Ludwig-Maximilians-Universität, D-München

J. I. Austerberry et al./European Journal of Pharmaceutics and Biopharmaceutics 115 (2017) 18–30

The effect of charge mutations on the stability and aggregation of a human single chain Fv fragment

James I. Austerberry, Rana Dajani, Stanislava Panova, Dorota Roberts, Alexander P. Golovanov, Alain Pluen, Christopher F. van der Walle, Shahid Uddin, Jim Warwicker, Jeremy P. Derrick, Robin Curtis

The aggregation propensities for a series of single-chain variable fragment (scFv) mutant proteins containing supercharged sequences, salt bridges and lysine/arginine-enriched motifs were characterised as a function of pH and ionic strength to isolate the electrostatic contributions. Recent improvements in aggregation predictors rely on using knowledge of native-state protein-protein interactions. Consistent with previous findings, electrostatic contributions to native protein-protein interactions correlate with aggregate growth pathway and rates. However, strong reversible self-association observed for selected mutants under native conditions did not correlate with aggregate growth, indicating 'sticky' surfaces that are exposed in the native monomeric state are inaccessible when aggregates grow. We find that even though similar native-state protein-protein interactions occur for the arginine and lysine-enriched mutants, aggregation propensity is increased for the former and decreased for the latter, providing evidence that lysine suppresses interactions between partially folded states under these conditions. The supercharged mutants follow the behaviour observed for basic proteins under acidic conditions; where excess net charge decreases conformational stability and increases nucleation rates, but conversely reduces aggregate growth rates due to increased intermolecular electrostatic repulsion. The results highlight the limitations of using conformational stability and native-state protein-protein interactions as predictors for aggregation propensity and provide guidance on how to engineer stabilizing charged mutations.

R. Meier et al./European Journal of Pharmaceutics and Biopharmaceutics 115 (2017) 102–112

Impact of fill-level in twin-screw granulation on critical quality attributes of granules and tablets

Robin Meier, Klaus-Peter Moll, Markus Krumme, Peter Kleinebudde

In a previous study a change of the fill-level in the barrel exerted a huge influence on the twin-screw granulation (TSG) process of a high drug loaded, simplified formulation. The present work investigated this influence systematically. The specific feed load (SFL) indicating the mass per revolution as surrogate parameter for the fill-level was applied and the correlation to the real volumetric fill level of an extruder could be demonstrated by a newly developed method. A design of experiments was conducted to examine the combined influence of SFL and screw speed on the process and on critical quality attributes of granules and tablets. The same formulation was granulated at constant liquid level with the same screw configuration and led to distinctively different results by only changing the fill-level and the screw speed. The power consumption of the extruder increased at higher SFLs with hardly any influence of screw speed. At low SFL the median residence time was mainly fill-level dependent and at higher SFL mainly screw speed dependent. Optimal values for the product characteristics were found at medium values for the SFL. Granule size distributions shifted from mono-modal and narrow shape to broader and even bimodal distributions of larger median granule sizes, when exceeding or falling below a certain fill-level. Deviating from the optimum fill-level, tensile strength of tablets decreased by about 25% and disintegration times of tablets increased for more than one third. At low fill-levels, material accumulation in front of the kneading zone was detected by pressure measurements and was assumed to be responsible for the unfavored product performance. At high fill-levels, granule consolidation due to higher propensity of contact with the result of higher material temperature was accounted for inferior product performance. The fill-level was found to be an important factor in assessment and development of twin-screw granulation processes as it impacted process and product attributes enormously.

A. Edlich et al./European Journal of Pharmaceutics and Biopharmaceutics 116 (2017) 155–163

Specific uptake mechanisms of well-tolerated thermoresponsive polyglycerol-based nanogels in antigen-presenting cells of the skin

Alexander Edlich, Christian Gerecke, Michael Giulbudagian, Falko Neumann, Sarah Hedtrich, Monika Schäfer-Korting, Nan Ma, Marcelo Calderon, Burkhard Kleuser

Engineered nanogels are of high value for a targeted and controlled transport of compounds due to the ability to change their chemical properties by external stimuli. As it has been indicated that nanogels possess a high ability to penetrate the stratum corneum, it cannot be excluded that nanogels interact with dermal dendritic cells, especially in diseased skin. In this study the potential crosstalk of the thermoresponsive nanogels (tNGs) with the dendritic cells of the skin was investigated with the aim

to determine the immunotoxicological properties of the nanogels. The investigated tNGs were made of dendritic polyglycerol (dPG) and poly(glycidyl methyl ether-co-ethyl glycidyl ether) (p(GME-co-EGE)), as polymer conferring thermoresponsive properties. Although the tNGs were taken up, they displayed neither cytotoxic and genotoxic effects nor any induction of reactive oxygen species in the tested cells. Interestingly, specific uptake mechanisms of the tNGs by the dendritic cells were depending on the nanogels cloud point temperature (Tcp), which determines the phase transition of the nanoparticle. The study points to caveolae-mediated endocytosis as being the major tNGs uptake mechanism at 37 °C, which is above the Tcp of the tNGs. Remarkably, an additional uptake mechanism, beside caveolae-mediated endocytosis, was observed at 29 °C, which is the Tcp of the tNGs. At this temperature, which is characterized by two different states of the tNGs, macropinocytosis was involved as well. In summary, our study highlights the impact of thermoresponsivity on the cellular uptake mechanisms which has to be taken into account if the tNGs are used as a drug delivery system.

Impressum:

Redaktion
Prof. Jörg Breitkreutz (Präsident der APV)
Dr. Martin Bornhöft (Leiter Geschäftsstelle der APV)

Vorstand der APV
Dr. Rainer Alex · Dr. Hermann Allgaier · Dr. Kathrin Bartscher · Prof. Dr. Jörg Breitkreutz · Prof. Dr. Heribert Häusler · Prof. Dr. Sandra Klein · Dr. Alexandra Steckel · Dr. Andreas Rummelt

Arbeitsgemeinschaft für Pharmazeutische Verfahrenstechnik e. V. (APV)
Kurfürstenstr. 59 · 55118 Mainz · Germany
Telefon +49 6131 9769-0
Telefax +49 6131 9769-69
email apv@apv-mainz.de
web www.apv-mainz.de

Verlag
ECV · Editio Cantor Verlag für Medizin und Naturwissenschaften GmbH
Baendelstockweg 20 · 88326 Aulendorf · Germany
Telefon +49 7525 940-0
Telefax +49 7525 940-180
email info@ecv.de
web www.ecv.de

Druck
Holzmann Druck GmbH & Co. KG
Gewerbestr. 2 · 86825 Bad Wörishofen · Germany

Satz
Anna-Maria Pötzl · APV e.V.

JETZT NEU: Leasing auch für andere Investitionsgüter

Leasing und Finanzierung von Investitionsgütern zu günstigen Konditionen:

- ✓ schont das Eigenkapital
- ✓ schafft Liquidität
- ✓ ist bilanzneutral
- ✓ erhöht die Eigenkapitalquote
- ✓ verbessert das Rating
- ✓ ermöglicht den Einsatz neuester Technologie
- ✓ auch „sale and lease back“ möglich

Sehr interessant auch für Nutzer von Maschinen für die Pharmaindustrie:

- ✓ niedrige Leasingraten statt hoher Kaufpreise
- ✓ Erweiterung der Dienstleistungspalette vom Verkäufer zum Full-Service-Anbieter
- ✓ erhöhte Kompetenz als „all in one“-Anbieter
- ✓ kein Bonitäts-/Ausfallrisiko für Hersteller/Händler
- ✓ Finanzierung von Neu- und Gebrauchtmaschinen
- ✓ Abdeckung der kompletten Produktpalette

Unser Kooperationspartner bietet Leasing von Neu- und Gebrauchtfahrzeugen zu Sonderkonditionen an. Alle Marken und Modelle sind lieferbar. Die nachfolgende Tabelle gibt nur wenige aktuelle Beispiele möglicher Modelle und Marken wieder.
NEU: Vorführwagen (VFW) aus dem Leasing-Pool und Dienst-/Werkswagen (DW) zu attraktiven Konditionen erhältlich.

Alle Preise in Euro zuzüglich gesetzlicher Mehrwertsteuer. Beschaffung durch die Leasing-Gesellschaft. 36 Monate Laufzeit, ohne Anzahlung, Laufleistung 15.000 km pro Jahr, Angebote freibleibend. Der Nachlass auf den Listenpreis ist in die ermäßigte Rate einkalkuliert. Sonderkonditionen für Fahrzeuge der Marke Toyota auch für Privatkunden!

Anfragen bitte an apv@apv-mainz.de, das Leasing-Unternehmen wird sich dann mit Ihnen in Verbindun g setzen.

Kfz-Leasing

Hersteller/Typ	Listenpreis	mtl. Rate
BMW 116i 5-Türer Advantage 80kW/109PS inkl. BusinessPackage, Navi, PDC, Klimaanlage, Durchladesystem, Sitzheizung vorne, Tempomat, 16" LM-Räder etc.	23.824,00 €	259,00 €
BMW 520d Touring 140kW/190PS inkl. BusinessPackage, Navigationssystem, Klimaautomatik, Sitzheizung vorne, PDC, Sport-Lederlenkrad, 17" LMR V-Speiche 618 etc	42.479,00 €	419,00 €
BMW X3 xDrive20d 140kW/190PS inkl. BusinessPackage, Klimaautomatik, Navigationssystem, Lordosenstütze, Sitzheizung vorne, PDC, Ablagenpaket, LM-Felgen etc.	42.479,00 €	439,00 €
Ford Mondeo Turnier Business Edition 118kW/160PS 6-G inkl. Navi, Sicht-Paket, Klimaautomatik, Sitzheizung vorne, Tempomat, PDC vorn + hinten, LM-Räder etc.	26.471,00 €	209,00 €
Ford S-MAX Business 1,5l EcoBoost 118kW/160PS 6-G inkl. Klimaautomatik, PDC vorn + hinten, Navigationssystem, Sitzheizung vorne, Tempomat, 17" LM-Räder etc.	28.067,00 €	219,00 €
Ford Edge Trend 2,0l TDCi 132kW/180PS 6-Gang inkl. Navi SYNC 3, Park-Assistent, Rückfahrkamera, Klimaautomatik, Frontscheibe/Lenkrad/Vordersitze beheizbar etc.	36.681,00 €	279,00 €
LandRover Range Rover Evoque TD4 Aut.HSE Dynamic 132kW/180PS inkl. Metallic, Navi, Klimaautomatik, Panoramaglasdach, BlackDesign, Winter-Paket, Assistenzsysteme etc.	55.294,00 €	679,00 €
MINI One 3-Türer 75kW/102PS inkl. Metallic, Klimaanlage, Lichtpaket, Sitzheizung, Ablagenpaket, Bordcomputer, Nebelscheinwerfer, 15" LM-Räder Heli Spoke etc.	16.378,00 €	179,00 €
Porsche 911Carrera 272kW/380PS inkl. PDK, Lederausstattung, Sitzheizung, Sportabgasanlage, BOSE Surround, ParkAssistent mit Rückfahrkamera, Schiebe-Hubdach etc.	115.854,00 €	1.359,00 €
Porsche Panamera 4 E-Hybrid 340kW/462PS inkl.PDK, ParkAssistent mit Rückfahrkamera, Panorama Dachsystem, Komfortsitze/Memory, BOSE Sound Spurhalteassist. etc.	100.156,00 €	1.459,00 €
SEAT Mii Chic 3-Türer 1.0 44kW/60PS inkl. Klimaanlage, PDC hinten, Tempomat, LM-Felgen, Sitzheizung Vordersitze, You&Mii Color Connection, Drive Mii App etc.	10.261,00 €	89,00 €
SEAT Ateca Excellence 1.4 EcoTSI DSG 110kW/150PS inkl. Metallic, Navi, Full Link, Connectivity Box, Klimaautomatik, GRA, Winterpaket, PDC/Kamera, LM-Räder etc.	26.676,00 €	249,00 €
VW Polo Comfortline 1,0l 48kW/65PS inkl. Klimaanlage, Radio Composition Colour, Müdigkeitserkennung, City-Notbremsfunktion, PDC vorn+hinten, Sitzheizung etc.	13.592,00 €	139,00 €

Vfw = Vorführwagen zu Sonderkonditionen, DW = Dienst-/Werkswagen (genannter Listenpreis = Kaufpreis)