MAKING SCIENCE WORK

Nachrichten und Mitteilungen

01 · 2018

APV NEWS

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

Drug Delivery Innovation Center started at INVITE Research Center

Martin G. Müller, INVITE GmbH, Lverkusen, Germany

The development of today's innovative medicines often requires substantial efforts to overcome challenges like low solubility and bioavailability of new APIs. Advanced manufacturing concepts like continuous manufacturing or drug printing of individualized medicines are of growing importance and mark a paradigm shift in the way how drugs are being made in the 21st century. Regulatory authorities like the EMA or the FDA are open to interact with the pharmaceutical industry and offer advice on these topics.

Since these trends pose common challenges to the pharmaceutical industry and require major research efforts to address fundamental process understanding, it makes sense to team up and join forces of all stakeholders. This thought has led to the foundation of the Drug Delivery Innovation Center (DDIC), an open consortium focusing on pre-competitive joint research in pharmaceutical sciences. Founding Tier 1 members of the open consortium are the companies Bayer AG, LB Bohle GmbH, Merck KGaA (all Germany) and UCB S.A. (Belgium), together with the university partners TU Dortmund University and HHU Düsseldorf. The research center INVITE* leads the consortium and builds the legal frame. The official start of the DDIC consortium was on September 1st, 2017.

The DDIC will foster international, multi-disciplinary networks in the area of research to advance pharmaceutical sciences in the area of drug delivery in close collaboration with academia and pharmaceutical industry along the entire value chain. Besides pharmaceutical companies the developing network of the DDIC will include equipment manufacturers and excipient suppliers.

Precompetitive research at DDIC will focus on seven research clusters:

1) Low solubility /poor bioavailability of oral drugs
2) Drug delivery forms for special patient groups/ personalized medicines
3) Continuous manufacturing (incl. advanced process control, modelling and prediction)
4) Fundamental process understanding / PAT
5) Models for predicting biopharmaceutical properties
6) Drug formulations for biomolecules
7) Nanomedicines / nanotechnologies

DDiC
Drug Delivery innovation Center

In addition to the Professors J. Breitkreutz and P. Kleinbudde (HHU Düsseldorf) and G. Sadowski, M. Thommes and G. Schembecker (TU Dortmund University), also Professor W. Weitscheis (University Greifswald) and Professor G. Winter (LMU München) agreed to be members of the scientific board of the DDIC.

DDIC not only stands for cutting-edge research in the fields of pharmaceutical and process technologies. To generate a highly skilled talent pool for our partners, the DDIC will establish a Master of "Industrial Pharmacy" and a unique PhD training program.

The concept of the DDIC is based on privileged memberships with different access to the research program and the results. We are looking forward to discuss with you a possible participation in the DDIC consortium. For more details please contact Armin Schweiger, Managing Director of INVITE: Schweiger@invite-research.com

*The INVITE GmbH, which is located at the CHEMPARK Leverkusen (Germany), is a private public partnership between Bayer AG and the universities TU Dortmund University and HHU Düsseldorf.

Lokale Gruppen

Dienstag, 27. Februar 2018
Lokale APV-Gruppe Westfalen ab 19:30 in der Hövelsbrauerei (Hoher Wall 5-7, 44137 Dortmund).
Weitere Informationen und Angaben zu den nächsten Terminen erhalten Sie bei Dr. Johanna Mosig (johanna.mosig@bayer.com).

Donnerstag, 01. März 2018
Lokale APV-Gruppe Köln/Bonn/Aachen um 19:30 Uhr im Füchschen (Ratinger Str. 28, 40213 Düsseldorf).
Anmeldung erforderlich bis zum 22. Februar 2018 bei Dr. Heiko Spilgies (heiko@spilgies.de).

Mittwoch, 28. März 2018
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)

Donnerstag, 05. April 2018
Lokale APV-Gruppe Mecklenburg-Vorpommern um 19:30 Uhr in der Goldmarie (Fischstraße 11, 17489 Greifswald).
Anmeldung erforderlich bis zum 23. März 2018 bei Katharina Tietz (katharina.tietz@uni-greifswald.de).

Mittwoch, 25. April 2018
Lokale APV-Gruppe Basel um 19:30 Uhr im Restaurant „Gifthüttli“ (Schneidergasse 11, 4051 Basel (www.gifthuettli.ch/)).
Weitere Informationen und Angaben zu den nächsten Terminen erhalten Sie bei Dr. Lars Restetzki (lars.restetzki@roche.com).

Lokale APV-Gruppe Berlin
Weitere Informationen und Angaben zu den nächsten Terminen erhalten Sie bei Dr. Andreas Sachse (andreas.sachse@cpl-sachse.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

S. Barimani et al./European Journal of Pharmaceutics and Biopharmaceutics 119 (2017) 28–35

Evaluation of in–line Raman data for end-point determination of a coating process: Comparison of Science–Based Calibration, PLS-regression and univariate data analysis

Shirin Barimani, Peter Kleinebudde

A multivariate analysis method, Science–Based Calibration (SBC), was used for the first time for endpoint determination of a tablet coating process using Raman data. Two types of tablet cores, placebo and caffeine cores, received a coating suspension comprising a polyvinyl alcohol–polyethylene glycol graft–copolymer and titanium dioxide to a maximum coating thickness of 80 µm. Raman spectroscopy was used as in–line PAT tool. The spectra were acquired every minute and correlated to the amount of applied aqueous coating suspension. SBC was compared to another well–known multivariate analysis method, Partial Least Squares-regression (PLS) and a simpler approach, Univariate Data Analysis (UVDA). All developed calibration models had coefficient of determination values (R2) higher than 0.99. The coating endpoints could be predicted with root mean square errors (RMSEP) less than 3.1% of the applied coating suspensions. Compared to PLS and UVDA, SBC proved to be an alternative multivariate calibration method with high predictive power.

J. Mittag et al./European Journal of Pharmaceutics and Biopharmaceutics 119 (2017) 215–223

Impact of plasma protein binding on cargo release by thermosensitive liposomes probed by fluorescence correlation spectroscopy

Judith J. Mittag, Barbara Kneidl, Tobias Preiß, Martin Hossann, Gerhard Winter, Stefan Wuttke, Hanna Engelke, Joachim O. Rädler

Thermosensitive liposomes (TSLs) whose phase-transition temperature (Tm) lies slightly above body temperature are ideal candidates for controlled drug release via local hyperthermia. Recent studies, however, have revealed disruptive shifts in the release temperature Tr in mouse plasma, which are attributed to undefined interactions with blood proteins. Here, we study the effects of four major plasma proteins – serum albumin (SA), transferrin (Tf), apolipoprotein A1 (ApoA1) and fibrinogen (Fib) – on the temperature-dependent release of fluorescein di-ß-D-galactopyranoside (FDG) from TSLs. The amount of fluorescein released was quantified by fluorescence correlation spectroscopy (FCS) after hydrolysis of FDG with ß-galactosidase (ß-Gal). This approach is more sensitive and thus superior to previous release assays, as it is impervious to the confounding effects of Triton on conventional fluorescence measurements. The assay determines the molar release ratio, i.e. the number of molecules released per liposome. We show that shifts in the Tr of release do not reflect protein affinities for the liposomes derived from adsorption isotherms. We confirm a remarkable shift in induced release towards lower temperatures in the presence of mouse plasma. In contrast, exposure to rat or human plasma, or fetal bovine serum (FBS), has no effect on the release profile.

J. Yu et al./European Journal of Pharmaceutics and Biopharmaceutics 119 (2017) 224–234

Protection of hydrophobic amino acids against moisture-induced deterioration in the aerosolization performance of highly hygroscopic spray-dried powders

Jiaqi Yu, Hak-Kim Chan, Thomas Gengenbach, John A. Denman

Background

Inhalable particles containing amorphous form of drugs or excipients may absorb atmospheric moisture, causing powder aggregation and recrystallization, adversely affecting powder dispersion and lung deposition. The present study aims to explore hydrophobic amino acids for protection against moisture in spray-dried amorphous powders, using disodium cromoglycate (DSCG) as a model drug.

Materials and methods

DSCG powders were produced by co-spray drying with isoleucine (Ile), valine (Val) and methionine (Met) in various concentrations (10, 20 and 40% w/w). Particle size distribution and morphology were measured by laser diffraction and scanning electron microscopy (SEM). Physiochemical properties of the powders were characterized by X-ray powder diffraction (XRPD), differential scanning calorimetry (DSC), thermogravimetric analysis (TGA) and dynamic vapor sorption (DVS). Particle surface chemistry was analyzed by X-ray photoelectron spectroscopy (XPS) and time-of-flight secondary ion mass spectrometry (ToF-SIMS). In vitro aerosolization performance was evaluated by a next generation impactor (NGI) after the powders were stored at 60% or 75% relative humidity (RH) for one month and three months.

Results and discussion

Ile, Val and Met significantly reduced the deleterious effect of moisture on aerosol performance, depending on the amount of amino acids in the formulation. Formulations containing 10% or 20% of Ile, Val and Met showed notable deterioration in aerosol performance, with fine particle fraction (FPF) reduced by 6–15% after one-month storage at both 60% and 75% RH. However, 40% Ile was able to maintain the aerosol performance of DSCG stored at 75% RH for one month, while the FPF dropped by 7.5% after three months of storage. In contrast, 40% Val or Met were able to maintain the aerosol performance at 60% RH storage

but not at 75% RH. At 40% w/w ratio, these formulations had particle surface coverage of 94.5% (molar percent) of Ile, 87.1% of Val and 84.6% of Met, respectively, which may explain their moisture protection effects.
Conclusion
Ile, Val and Met showed promising moisture protection effect on aerosol performance. The results broaden the understanding on the use of hydrophobic amino acids as an excipient for long-term storage of inhalation powders formulations that are hygroscopic.

E. Koepf et al./European Journal of Pharmaceutics and Biopharmaceutics 119 (2017) 396–407

The film tells the story: Physical-chemical characteristics of IgG at the liquid-air interface

Ellen Koepf, Rudolf Schroeder, Gerald Brezesinski, Wolfgang Friess

The presence of liquid–air interfaces in protein pharmaceuticals is known to negatively impact product stability. Nevertheless, the mechanisms behind interface-related protein aggregation are not yet fully understood. Little is known about the physical–chemical behavior of proteins adsorbed to the interface. Therefore, the combinatorial use of appropriate surface-sensitive analytical methods such as Langmuir trough experiments, Infrared Reflection-Absorption Spectroscopy (IRRAS), Brewster Angle Microscopy (BAM), and Atomic Force Microscopy (AFM) is highly expedient to uncover structures and events at the liquid–air interface directly. Concentration-dependent adsorption of a human immunoglobulin G (IgG) and characteristic surface-pressure/area isotherms substantiated the amphiphilic nature of the protein molecules as well as the formation of a compressible protein film at the liquid–air interface. Upon compression, the IgG molecules do not readily desorb but form a highly compressible interfacial film.
IRRA spectra proved not only the presence of the protein at the interface, but also showed that the secondary structure does not change considerably during adsorption or compression. IRRAS experiments at different angles of incidence indicated that the film thickness and/or packing density increases upon compression. Furthermore, BAM images exposed the presence of a coherent but heterogeneous distribution of the protein at the interface. Topographical differences within the protein film after adsorption, compression and decompression were revealed using underwater AFM.
The combinatorial use of physical–chemical, spectroscopic and microscopic methods provided useful insights into the liquid–air interfacial protein behavior and revealed the formation of a continuous but inhomogeneous film of native-like protein molecules whose topographical appearance is affected by compressive forces.

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 Verbindung setzen.

Kfz-Leasing

Hersteller/Typ	Listenpreis	mtl. Rate
Audi A5 Sportback 2.0 TDI 110kW/150PS inkl. MMI Navigation, Komfortklimaautomatik, PDC vorne + hinten, Sitzheizung vorne, Rücksitzanlage 3-sitzig, 17" LM-Felgen etc.	35.025,00 €	339,00 €
Audi Q5 2.0 TDI 110kW/150PS inkl. Komfortklimaautomatik, MMI Navigation, Sitzheizung vorne, PDC vorne + hinten, Xenon Plus, Rücksitzbank plus, 18" LM-Felgen etc.	36.756,00 €	379,00 €
BMW 216i Active Tourer Advantage 75kW/102PS inkl. Klimaautomatik, Nebelscheinwerfer, Sitzheizung vorn, PDC hinten, LM-Felgen, Licht-/Regensensor, Ablagenpaket etc.	24.857,00 €	199,00 €
BMW X1 sDrive18i 103kW/140PS inkl. Klimaanlage, Navigation, Sitzheizung vorne, Lordosenstütze Fahrer/ Beifahrer, PDC hinten, 17" LM-Räder, Ablagenpaket etc.	28.563,00 €	299,00 €
BMW 520i Limousine 135kW/184PS Automatic inkl. Navigationssystem, Klimaautomatik, PDC, Sitzheizung vorne, Durchladesystem, Sport-Lederlenkrad, 17" LM-Räder etc.	40.924,00 €	379,00 €
Ford ECOSPORT Cool & Connect 1.0 92kW/125PS inkl. Navi Ford SYNC3, Klimaanlage, PDC hinten, Tempomat, Frontscheibe/Vordersitze/Lenkrad beheizbar, Technik-Service etc.	17.429,00 €	179,00 €
Ford Edge 2.0 TDCi 4x4 Trend 132kW/180PS inkl. Navi SYNC 3, Klimaautom., Rückfahrkamera, Frontscheibe/ Lederlenkrad/Vordersitze beheizb., 19"LM-Räder, TechnikService etc.	36.008,00 €	329,00 €
Jaguar XJ Premium Luxury 3.0 L V6 Diesel 221kW/300PS inkl. Fahrerassistenz-/Parkhilfe-Paket, 4Zonen Klimautom., Frontscheibe+Lenkrad beheizbar, Klangsystem, LM-Felgen etc.	80.400,00 €	909,00 €
Kia Picanto 1.0 EDITION 7 49kW/67PS inkl. Radio RDS/MP3, Zentralverriegelung mit Funkfernbedienung, Fensterheber elektrisch vorn, Fahrersitz höhenverstellbar etc.	9.655,00 €	99,00 €
Kia Sportage DREAM-TEAM Edition Premium+ 97kW/132PS inkl. Navi, JBL Soundsystem, DAB+, Lederpolster, PDC vorn+hinten, Tempomat, Assistenzsysteme, Sitzheizung etc.	24.151,00 €	199,00 €
Mini One Countryman "Pepper" 75kW/102PS inkl. Metallic, Klimaautom., PDC hinten, Lichtpaket, Sitzheizung, Ablagenpaket, Nebelscheinwerfer, 17" LM-Räder Imprint Spoke etc.	23.462,00 €	189,00 €
Skoda Fabia 1.0 MPI COOL PLUS 55kW/75PS inkl. Klimaanlage, Musiksystem Swing mit DAB, getönte Scheiben, Außenspiegel elektrisch einstell- und beheizbar etc.	11.118,00 €	75,00 €
Skoda Octavia Combi "DRIVE" 85kW/115PS inkl. Klimaautomatik, Müdigkeitserkennung, Parksensoren hinten, Sitzheizung vorne, Tempomat, 17" LM-Felgen, etc.	20.782,00 €	159,00 €
Skoda Karoq 1.0 TSI Style 85kW/115PS inkl. Klimaautomatik, PDC vorne+hinten, Infotainmentsystem Bolero 8“ Display, DAB+, 18“ LM-Felgen, Tempomat, Frontradarassist etc.	21.756,00 €	189,00 €
VW Golf "JOIN" 1,0l TSI 63kW/85PS inkl. Navigationssystem, 2-Zonen-Klimaautomatik, PDC v+h, Müdig-keitserkennung, 16" LM-Räder "Woodstock", Sitzheizung Vordersitze etc.	18.340,00 €	169,00 €
VW Arteon 1,5l TSI ACT 110kW/150PS inkl. 3-Zonen Klimaautomatik, Navigationssystem, LED-Scheinwerfer, Tempomat, Müdigkeitserkennung, Spurhalteassistent etc.	30.824,00 €	269,00 €