MAKING SCIENCE WORK

# Nachrichten und Mitteilungen

01 · 2020

# APV NEWS

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

# 6th Transatlantic Galenus Guest Professorship

Since 2014 the Galenus Foundation (Vienna, Austria) has been running a series of Transatlantic Galenus Guest Professorships. These started in Detroit (Wayne-State University) and have moved on to Florida, Harvard, MIT and Stanford. The next of these, slated for October 2020, will be hosted by Prof. Bill Williams III, College of Pharmacy at the University of Texas at Austin.

The position of the Galenus Guest Professor will be taken by Dr Sandra Klein, Professor at the University of Greifswald (Germany). Her research focuses on bio-predictive in vitro models and oral dosages for special patient groups. In addition, she works on enhancing the bioavailability of drugs which have poor solubility. As part of her Galenus Guest Professorship Prof. Klein will give a keynote lecture at Austin University which will be streamed live over the foundation`s website.

More information will be available on www.galenusprivatstiftung.at and on our Facebook account in due course.

Prof. Robert O. (Bill) Williams III

Prof. Sandra Klein

# Lokale Gruppen

Mittwoch, 25. März 2020

**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, 06. Mai 2020

**Lokale APV-Gruppe Basel** ab 18:30 Uhr im „Gifthüttli“, Schneidergasse 11, 4051 Basel (www.gifthuettli.ch/).

Anmeldung bis zum 01. Mai 2020 bei Dr. Lars Restetzki (lars.restetzki@roche.com).

## Lokale APV-Gruppe Westfalen

Weitere Informationen und Angaben zu den nächten Terminen erhalten Sie bei Dr. Johanna Anlahr (johanna.anlahr@bayer.com).

## Lokale APV-Gruppe Berlin

Weitere Informationen und Angaben zu den nächten Terminen erhalten Sie bei Dr. Andreas Sachse (andreas.sachse@cpl-sachse.de).

## Lokale APV-Gruppe Rhein-Neckar

Weitere Informationen und Angaben zu den nächten Terminen erhalten Sie bei Dr. Viktoria Riedel (viktoria.riedel@schwabe.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 Mecklenburg-Vorpommern

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

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

Eva Ramsay et al./ European Journal of Pharmaceutics and Biopharmaceutics 143 (2019) 18-23

**Role of retinal pigment epithelium permeability in drug transfer between posterior eye segment and systemic blood circulation**

Eva Ramsay, Marja Hagström, Kati-Sisko Vellonen, Susanna Boman, Elisa Toropainen, Eva M. del Amo, Heidi Kidron, Arto Urtti, Marika Ruponen

Retinal pigment epithelium (RPE) is a major part of blood-retinal barrier that affects drug elimination from the vitreous to the blood and drug distribution from blood circulation into the eye. Even though drug clearance from the vitreous has been well studied, the role of RPE in the process has not been quantified. The aim of this work was to study the role of RPE clearance (CLRPE) as part of drug elimination from the vitreous and ocular drug distribution from the systemic blood circulation. We determined the bidirectional permeability of eight small molecular weight drugs and bevacizumab antibody across isolated bovine RPE-choroid. Permeability of small molecules was 10–6–10–5 cm/s showing 13–15 fold range of outward and inward permeation, while permeability of bevacizumab was lower by 2–3 orders of magnitude. Most small molecular weight drugs showed comparable outward (vitreous-to-choroid) and inward (choroid-to-vitreous) permeability across the RPE-choroid, except ciprofloxacin and ketorolac that had an over 6 and 14-fold higher outward than inward permeability, respectively, possibly indicating active transport. Six of seven tested small molecular weight drugs had outward CLRPE values that were comparable with their intravitreal clearance (CLIVT) values (0.84–2.6 fold difference). On the contrary, bevacizumab had an outward CLRPE that was only 3.5% of the CLIVT, proving that its main route of elimination (after intravitreal injection) is not RPE permeation. Experimental values were used in pharmacokinetic simulations to assess the role of the RPE in drug transfer from the systemic blood circulation to the vitreous (CLBV). We conclude that for small molecular weight drugs the RPE is an important route in drug transfer between the vitreal cavity and blood, whereas it effectively hinders the movement of bevacizumab from the vitreous to the systemic circulation.

Pei T. Mah et al./ European Journal of Pharmaceutics and Biopharmaceutics 144 (2019) 139-153

**The use of hydrophobic amino acids in protecting spray dried trehalose formulations against moisture-induced changes**

Pei T. Mah, Peter O'Connell, Stefano Focaroli, Ross Lundy, Tom F. O'Mahony, Jayne E. Hastedt, Irina, Gitlin, Stefan Oscarson, John V Fahy, Anne Marie Healy

Trehalose is commonly used as a protein stabilizer in spray dried protein formulations delivered via the pulmonary route. Spray dried trehalose formulations are highly hygroscopic, which makes them prone to deliquescence and recrystallization when exposed to moisture, leading to impairment in aerosolization performance. The main aim of this study was to investigate and compare the effect of hydrophobic amino acids (i.e. L-leucine and L-isoleucine) in enhancing aerosolization performance and in mitigating moisture-induced changes in spray dried trehalose formulations. Trehalose was spray dried with 20–60% w/w of amino acid (i.e. L-leucine or L-isoleucine). The spray dried formulations were stored at 25 °C/50% RH for 28 days. Solid state characterization and in vitro aerosolization performance studies were performed on the spray dried formulations before and after storage. The addition of 20–60% w/w of amino acid (i.e. L-leucine or L-isoleucine) improved the emitted fractions of spray dried trehalose formulations from a dry powder inhaler. However, ≥ 40% w/w of L-leucine/L-isoleucine was needed to prevent recrystallization of trehalose in the formulations when exposed to 25 °C/50% RH for 28 days. X-ray photoelectron spectroscopy (XPS) demonstrated that samples with 40–60% w/w L-isoleucine had more amino acid on the surfaces of the particles compared to their L-leucine counterparts. This may explain the greater ability of the L-isoleucine (40–60% w/w) samples to cope with elevated humidity compared to L-leucine samples of the same concentrations, as observed in the dynamic vapour sorption (DVS) studies. In conclusion, this study demonstrated that both L-leucine and L-isoleucine were effective in enhancing aerosolization performance and mitigating moisture-induced reduction in aerosolization performance in spray dried trehalose formulations. L-isoleucine proved to be superior to L-leucine in terms of its moisture protectant effect when incorporated at the same concentration in the formulations.

Andreas Tosstorff et al./ European Journal of Pharmaceutics and Biopharmaceutics 144 (2019) 207-216

**Structure-based discovery of a new protein-aggregation breaking excipient**

Andreas Tosstorff, Hristo Svilenov, Günther H.J. Peters, Pernille Harris, Gerhard Winter

Reducing the aggregation of proteins is of utmost interest to the pharmaceutical industry. Aggregated proteins are often less active and can cause severe immune reactions in the patient upon administration. At the same time the biopharmaceutical market is pushing for high concentration formulations and products that do not require refrigerated storage conditions. For a given protein, the only solution pH, ionic strength and concentration of a very limited number of excipients are the only parameters that can be varied to obtain a stable formulation. In this work, we present a structure-based approach to discover new molecules that successfully reduce the aggregation of proteins and apply the approach to the model protein Interferon-alpha-2a.

Noritaka Odani et al./ European Journal of Pharmaceutics and Biopharmaceutics 145 (2019) 35-41

**Determining the effect of photodegradation on film coated nifedipine tablets with terahertz based coating thickness measurements**

Noritaka Odani, Shikhar Mohan, Eiji Kato, Hanzhou Feng, Yi Li, Md. Nayeem Hossain, James K. Drennen III, Carl A. Anderson

Film coating of nifedipine tablets is commonly performed to reduce photo-degradation. The coating thickness of these tablets is a primary dictating factor of photo-stability. Terahertz spectroscopy enables accurate measurement of coating thickness. This study identifies a method to determine an end-point of a photo-protective coating process by using coating thickness measurements from terahertz time of flight spectroscopy (THz-TOF). For this method, nifedipine tablets, at different coating thicknesses, were placed in a photostability chamber. The illumination conditions of the coated tablets were adjusted based on the time duration of these tablets inside the chamber. A multiple linear regression model was developed with the coating thickness estimates from THz-TOF and illumination conditions information to predict the amount of drug remaining after photo-degradation (percent label claim). The prediction error of this model was 1.03% label claim in the range of 88.4–100.6% label claim. According to this model, acceptable levels of photo-protection in illumination conditions of up to approximately 700,000 lx hours was achieved at the end of the coating process (approximately 50 μm coating thickness) performed in this study. These results suggest THz-TOF as a viable process analytical technology tool for process understanding and end-point determination of a photo-protective coating process.


## Impressum:

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Prof. Jörg Breitkreutz (Präsident der APV)
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**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

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| Skoda Scala "Style" 1,5 TSI 110kW/150PS "V" inkl. Klimaautomatik, Infotainmentsystem, DAB+, Freisprecheinrichtung, PDC hinten, Tempomat, 17" LM-Räder, Sitzheizung vorne etc. | 21.832,00 € | 119,00 € |
| Skoda Kamiq "Style" 1,5 TSI 110kW/150PS "V" inkl. Business Amundsen Navi, DAB+, Smartlink, Phonebox, Metallic, Klimaautomatik, PDC v+h, Tempomat, 17" LMR, Vorber. AHK etc. | 24.294,00 € | 139,00 € |
| Skoda Karoq "Sportline" 1,5 TSI 110kW/150PS "V" inkl. Metallic, Businesspaket Amundsen, Navi, DAB+, Heckklappe elektr., Climatronic, PDC v+h/Rückfahrkamera, Vorber. AHK, LMR etc. | 28.756,00 € | 159,00 € |
| Skoda Kodiaq "Sportline" 1,5 TSI 110kW/150PS DSG "V" inkl. Businesspaket, Navi, Abstandsassistent ACC, PDC v+h, Rückfahrkamera, LED-Scheinwerfer, AHK schwenkbar, 19" LMR etc. | 35.470,00 € | 199,00 € |
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| VW Tiguan IQ.DRIVE 2,0l TDI SCR 110kW/150PS "LW" inkl. Business Premium-Paket Navigation, Klimaautomatik, Parklenkassistent/Rückfahrkamera, LED, AHK, 18" LMR "Nizza" etc. | 36.311,00 € | 299,00 € |