MAKING SCIENCE WORK

Nachrichten und Mitteilungen

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

03 · 2019

APV NEWS

PBP WORLD MEETING

in combination with

ResearchPharm®
International Exhibition for R&D

12th World Meeting

on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology

Vienna, Austria
23 - 26 March 2020

www.worldmeeting.org

Lokale Gruppen

Mittwoch, 29. Mai 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).

Dienstag, 10. September 2019
Lokale APV-Gruppe Berlin um 19:00 Uhr in den Firmenräumen der Bayer Pharma AG (Standort Berlin Wedding) statt.
Anmeldung erforderlich bis zum 05. August 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 Westfalen
Weitere Informationen und Angaben zu den nächten Terminen erhalten Sie bei Dr. Johanna Anlahr (johanna.anlahr@bayer.com).

Lokale APV-Gruppe Basel
Weitere Informationen und Angaben zu den nächten Terminen erhalten Sie bei Dr. Lars Restetzki (lars.restetzki@roche.com).

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

Nobuhiro Nagai et al./ European Journal of Pharmaceutics and Biopharmaceutics 136 (2019) 184-191

A drug refillable device for transscleral sustained drug delivery to the retina

Nobuhiro Nagai, Saaya Saijo, Yuanhui Song, Hirokazu Kaji, Toshiaki Abe

Continuous drug administration with better adherence to treatment and less invasive procedures is important in treating retinal diseases such as age-related macular disease. In this study, we report a drug-refillable device consisting of a silicone reservoir and an injectable gelatin/chitosan gel (iGel). The silicone reservoir was fabricated with polydimethylsiloxane (PDMS) using a computer-aided design and manufacturing to have micropores at a releasing side for uniaxial release to the sclera. A stainless steel wire and sheet were combined in the side and bottom of the reservoir to ensure flexibility and to fit on the curvature of the eyeball and prevent irritation to the sclera through the bottom of the reservoir. The drug was injected and formulated in the reservoir by in situ crosslinking of gelatin/chitosan gel with the crosslinker; 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride. The in vitro release study using fluorescein molecules showed that the release rate from encapsulated iGel in the reservoir was slower than that from the original iGel. After reinjecting the iGel into the reservoir, the same release profile as the first injection was observed. The reservoir containing iGel was placed on the sclera of a rabbit and the distribution of 150 kDa fluorescein isothiocyanate-dextran (FD150) in the retina and choroid/retinal pigment epithelium (choroid/RPE) was studied. The cryosections showed that FD150 was observed in the choroid/RPE. Homogenates of the retina and choroid/RPE showed fluorescence during 12 weeks implantation, indicating the drug could be delivered to the retina by using the device. The drug filling was successful into the reservoir implanted on the sclera through the conjunctiva by using a needle. In conclusion, the refillable drug delivery device is a promising tool to administer drugs long-term by reinjection with less invasiveness to intraocular tissues.

Michael Hofmann et al./ European Journal of Pharmaceutics and Biopharmaceutics 136 (2019) 192-202

A novel technique for intraduodenal administration of drug suspensions/solutions with concurrent pH monitoring applied to ibuprofen formulations

Michael Hofmann, Florian Thieringer, Mai Ahn Nguyen, Wiking Månsson, Peter Robert Galle, Peter Langguth

Characterization of dissolution of solid suspended drug particles in vivo is important for developing biopredictive in vitro tests. Therefore, methods to gain deeper insights into particle dissolution in vivo are needed. The soft Bioperm intubation method, a well established tool for investigation of permeability, absorption, metabolism, and drug interactions at predefined locations in the gastroinstinal tract, was modified. The novel intubation method involved pump-controlled infusion of pharmaceutical suspensions as well as simultaneous pH monitoring. This technique was used in a proof of concept study in healthy humans. Plasma sampling and non-compartmental analysis allowed comparison of three different ibuprofen drug products, a solution and two suspensions with different particle size distribution, as well as two different infusion rates. Both a particle size effect and an effect of altering infusion rates on pharmacokinetic parameters were shown. Moreover, it was possible to monitor intestinal pH changes after intestinal infusion. Infusion of ibuprofen resulted in a pH drop that was quantified by the concept of Area Between Curves (ABC).

Hristo Svilenov et al./ European Journal of Pharmaceutics and Biopharmaceutics 137 (2019) 131-139

The ReFOLD assay for protein formulation studies and prediction of protein aggregation during long-term storage

Hristo Svilenov, Gerhard Winter

The formulation of novel therapeutic proteins is a challenging task which aims at finding formulation conditions that will minimize protein degradation during long-term storage. One particularly important and difficult-to-predict protein degradation pathway is the so-called non-native aggregation. The qualitative and quantitative prediction of the latter has been a subject of extensive research over the past two decades. An increasing body of evidence shows that the widely-used short-term biophysical techniques cannot accurately rank formulation conditions in order of their effect on the aggregation during long-term storage of some therapeutic proteins, e.g. monoclonal antibodies. Here we suggest a novel approach for the selection of formulation conditions that will suppress the formation of protein aggregates during long-term storage. We postulate that conditions (i.e. pH, buffer type, ionic strength) that reduce the isothermal aggregation of various denaturant-induced partially folded protein species will be conditions that impede protein aggregation during long-term storage. To test our hypothesis, we developed an isothermal microdialysis-based unfolding/refolding assay, named ReFOLD, which we use to induce moderate aggregation of partially folded proteins. Next, we assessed

the relative monomer yield after isothermal unfolding/ refolding of two monoclonal antibodies, each formulated in 12 different conditions. Using the proposed approach, we were able to accurately rank the formulations in order of their effect on the amount of protein aggregates detected after storage for 12 months at 4 °C and 25 °C, while widely-used stability-indicating parameters like protein melting and aggregation onset temperatures failed to provide accurate predictive formulation rankings.

Fabian J. Simons et al./ European Journal of Pharmaceutics and Biopharmaceutics 137 (2019) 196-208

Modeling, design and manufacture of innovative floating gastroretentive drug delivery systems based on hot-melt extruded tubes

Fabian J. Simons, Karl G. Wagner

The problem of many gastroretentive systems is the mechanistic connection of drug release and gastric retention control. This connection could be successfully separated by formulating hollow tubes via hot-melt extrusion and sealing both tube ends, which led to immediately floating devices. The tube wall consisted of metformin crystals embedded in an inert polymer matrix of Eudragit® RS PO and E PO. Very high drug loadings of up to 80% (w/w) were used without generating a 'burst release'. Sustained release profiles from four to more than twelve hours were achieved by varying the polymer proportions without affecting the floatability. Buoyancy was found to mainly depend on the cylinder design, i.e. the outer to inner diameter ratio. This allowed the polymer/metformin composition to be changed without affecting buoyancy, i.e. a separation of floatability and release control was achieved. A prediction model was implemented that allowed for the buoyancy force to be determined with high accuracy by selecting a suitable ratio of outer to inner diameter of the modular tube die. Wall thickness and mass normalized surface area were identified as geometric parameters that mainly influenced the release properties. Conclusively, this study offers a highly flexible and rational manufacturing approach for the development of gastroretentive floating drug delivery systems.

Impressum:

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

Vorstand der APV
Prof. Dr. Johannes Bartholomäus · Dr. Kathrin Bartscher · Dr. Karoline Bechthold-Peters · Prof. Dr. Jörg Breitkreutz · Prof. Dr. Heribert Häusler · Prof. Dr. Sandra Klein · Dr. Hans Lindner · Dr. Martin Lück

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.

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, gewerbliches Leasing, Angebote freibleibend. Der Nachlass auf den Listenpreis ist in die ermäßigte Rate einkalkuliert.

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

Kfz-Leasing

NEU: Alle Fahrzeuge mit der Abgasnorm Euro 6d-Temp

Hersteller/Typ	Listenpreis	mtl. Rate
Audi A3 Sportback sport 35 TFSI 110kW/150PS S tronic inkl. MMI Navigation, Klimaautomatik, PDC hinten, Tempomat, Xenon plus, Sitzheizung vorn, 17" LM-Räder etc.	29.181,00 €	269,00 €
Audi Q5 35 TDI quattro 120kW/163PS S tronic inkl. Klimaautomatik, MMI Navigation, Audi side assist, PDC v+h, Rückfahrkamera, Sitzheizung vorn, Xenon, 17" LM-Räder etc.	41.748,00 €	369,00 €
BMW 220d Active Tourer M-Sport 140kW/190PS inkl. Business Paket, Navi Plus, Klimaautomatik, PDC hinten, LED-Scheinwerfer, Tempomat, Sitzheizung vorn, 17" LM-Räder etc.	41.966,00 €	269,00 €
BMW 520i Touring 135kW/184PS inkl. Automatic, Klimaautomatik, Navigationsystem, Parking Assistant, Sitzheizung Fahrer/Beifahrer, Innen- und Außenspiegelpaket, 17" LM-Räder etc.	46.176,00 €	419,00 €
BMW X1 sDrive18i Advantage 103kW/140PS inkl. Navigationssystem, Klimaautomatik, PDC hinten, Tempomat, Lordosenstütze Fahrer/Beifahrer, Sitzheizung vorn, 17" LM-Räder etc.	29.908,00 €	239,00 €
BMW i3S 120AH 1,5l 88kW/120PS inkl. Navi Professional, Klimaautomatik, Interieurdesign Loft, Tempomat, Comfort Paket, Wireless Charging, 20" LM-Räder Doppelspeiche 431, etc.	38.126,00 €	339,00 €
Mercedes A 220d Kompakt-Limous. "Style" 140kW/190PS inkl. Automatik, Navigations-Paket/ MBUX, Klimaautomatik, Sitzheizung vorn, aktiver Park-Assistent, 17" LM-Räder, Tempomat etc.	33.460,00 €	369,00 €
Mercedes C 220 d Lim. "Avantgarde" 118kW/160PS inkl. Automatik, Navi, volldig. Instrumenten-Display, Rückfahrkamera, aktiver Parkassistent/PDC, Sitzheizung vorn, LED-Scheinwerfer etc.	39.725,00 €	399,00 €
MINI One 3-Türer "Blackyard" 75kW/102PS inkl. Midnight Black metallic, Klimaanlage, PDC hinten, Lichtpaket, Ablagenpaket, Sitzheizung vorne, 16" LM-Räder Victory Spoke black etc.	18.697,00 €	159,00 €
Skoda Karoq 1.6 TDI Style "LW" 85kW/115PS DSG inkl. Metallic, Businesspaket, Navi, DAB+, Klimaautomatik, LED-Scheinwerfer, PDC v+h, Rückfahrkamera, GRA, 18" LM-Räder etc.	29.395,00 €	199,00 €
Skoda Superb Combi 2.0 TDI Ambition SCR 110kW/150PS DSG inkl. Businesspaket Amundsen, Navi, Smartlink+, Climatronic, PDC v+h, Sitzheizung vorn, GRA, 16" LM-Räder etc.	32.269,00 €	249,00 €
Toyota Aygo 1.0l x-play 3-Türer 53kW/72PS 5-Gang inkl. Klimaanlage, Audiosystem, USB-Schnittstelle, Bluetooth Freisprecheinrichtung, Memory Funktion für Fahrersitz etc.	10.353,00 €	110,00 €
Toyota Yaris 1,0l VVT-i 3-Türer 53kW/72PS 5-Gang inkl. Cool & Sound-Paket, Audiosystem, Klimaanlage, Zentralverriegelung mit Funkfernbed., USB-Schnittstelle, Bluetooth-Freispr. etc.	12.176,00 €	125,00 €
VW T-Roc "IQ.DRIVE" 1.5 TSI OPF 110kW/150PS DSG inkl. Navigationssystem Discover Media, 2-Zonen Climatronic, Autom. Distanzregelung ACC, Parklenkassist, 17" LM-Räder etc.	26.332,00 €	245,00 €
VW Golf "IQ.DRIVE" 1,6l TDI SCR 85kW/115PS DSG inkl. 2-Zonen Climatronic, Navi Discover Media, Parklenkassist, Lane Assist, Blind Spot-Sensor, Sitzheizung vorn, LM-Räder etc.	26.479,00 €	229,00 €