

01 . 2021



Nachrichten und Mitteilungen

APV NEWS

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



12th World Meeting on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology

VIRTUAL MEETING

LIVE event from 11 - 14 May 2021



in combination with



www.worldmeeting.org



Lokale Gruppen

Mittwoch, 31. März 2021

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).



Lokale APV-Gruppe Basel

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 Rhein-Neckar

Weitere Informationen und Angaben zu dem Veranstaltungsort sowie den nächsten Terminen erhalten Sie bei Dr. Viktoria Riedel (viktoria.riedel@schwabe.de).



Lokale APV-Gruppe Westfalen

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



Lokale APV-Gruppe Nordrhein

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



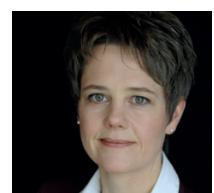
Lokale APV-Gruppe Mecklenburg-Vorpommern

Weitere Informationen und Angaben zu den nächsten 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?

Elena Richert, Ludwig-Maximilians-Universität, D-München

Silica particles incorporated into PLGA-based in situ-forming implants exploit the dual advantage of sustained release and particulate delivery

Stefanie Thalhauser, David Peterhoff, Ralf Wagner, Miriam Breunig

Poly (lactic-co-glycolic acid) (PLGA) in situ-forming implants are well-established drug delivery systems for controlled drug release over weeks up to months. To prevent initial burst release, which is still a major issue associated with PLGA-based implants, drugs attached to particulate carriers have been encapsulated. Unfortunately, former studies only investigated the resulting release of the soluble drugs and hence missed the potential offered by particulate drug release. In this study, we developed a system capable of releasing functional drug-carrying particles over a prolonged time. First, we evaluated the feasibility of our approach by encapsulating silica particles of different sizes (500 nm and 1 µm) and surface properties (OH or NH₂ groups) into in situ-forming PLGA implants. In this way, we achieved sustained release of particles over periods ranging from 30 to 70 days. OH-carrying particles were released much more quickly when compared to NH₂-modified particles. We demonstrated that the underlying release mechanisms involve size-dependent diffusion and polymer-particle interactions. Second, particles that carried covalently-attached ovalbumin (OVA) on their surfaces were incorporated into the implant. We demonstrated that OVA was released in association with the particles as functional entities over a period of 30 days. The released particle-drug conjugates maintained their colloidal stability and were efficiently taken up by antigen presenting cells. This system consisting of particles incorporated into PLGA-based in situ-forming implants offers the dual advantage of sustained and particulate release of drugs as a functional unit and has potential for future use in many applications, particularly in single-dose vaccines.

Formulating monoclonal antibodies as powders for reconstitution at high concentration using spray-drying: Trehalose/amino acid combinations as reconstitution time reducing and stability improving formulations

Jan Massant, Sabrina Fleurime, Maarten Batens, Heline Vanhaerents, Guy Van den Mooter

To increase their stability, therapeutic (or monoclonal) antibodies (mAbs) are often formulated as solids by using a variety of drying techniques, e.g. freeze-drying, spray-drying, or spray freeze-drying. The addition of excipients is required to preserve stability of the protein during the drying process and subsequent storage of the resulting solid form. The addition of low molecular weight excipients, such as amino acids, to sugar based spray- and freeze-dried formulations has been suggested to improve the storage stability of proteins in the dried state. In this study sugars (sucrose, trehalose), amino acids (Gly, Ala, Pro, Ser, Val, Leu,

Ile, Gln, His, Lys, Arg, Phe, Trp) and combinations thereof were investigated for their stabilizing effect during spray-drying and subsequent storage and for their reconstitution time reducing effect. Two IgG4 mAbs were used as model antibodies.

From an initial screening study, basic and small neutral amino acids, in combination with a sugar, such as sucrose or trehalose, showed reconstitution time reducing and stabilizing properties. Arg in particular displayed excellent reconstitution and stability enhancing properties. Moreover, Arg was the only amino acid providing stabilizing properties comparable to sucrose or trehalose. Previous work by the authors described a statistically substantiated comparison between the three basic amino acids in a sugar containing formulation, albeit limited to a single concentration level [5]. Therefore, a follow-up design of experiments (DoE) study was performed to determine the optimum trehalose/amino acid content required for an optimal protein stability and reconstitution time and to compare the effects of two basic amino acids, Lys and Arg, to those of two neutral amino acids, Gly and Pro. The conducted DoE covered a wide range of trehalose (30–120 mM) and amino acid (50–150 mM) concentrations. The concentration of trehalose was found to be the main contributor to a reduction in reconstitution time and an increase in stability. Here we show that the addition of amino acids such as Gly, Pro, and Lys does not improve stability, nor does it reduce the reconstitution time. Of the tested amino acids, only Arg showed a marked reduction in reconstitution time and improvement in stability compared to a trehalose. Moreover, the properties displayed by Arg could justify its application as the main stabilizer in spray-dried mAb formulations, eliminating the need for a sugar matrix altogether. But the weight ratio of stabilizer to protein was found the factor exerting the strongest overall influence on the formulation's reconstitution time and stability. More specifically, sufficient physical stability and an acceptable reconstitution time could be obtained with a protein to stabilizer weight ratio of at least 1:1.

Treatment of acute lung inflammation by pulmonary delivery of anti-TNF-α siRNA with PAMAM dendrimers in a murine model

Adam Bohr, Nicolas Tsapis, Camilla Foged, Ilaria Andreana, Mingshi Yang, Elias Fattal

To improve the efficacy of nucleic acid-based therapeutics, e.g., small interfering RNA (siRNA), transfection agents are needed for efficient delivery into cells. Several classes of dendrimers have been found useful as transfection agents for the delivery of siRNA because their surface can readily be functionalized, and the size of the dendriplexes they form with siRNA is within the range of conventional nanomedicine. In this study, commercially available generation 3 poly(amidoamine) (PAMAM) dendrimer was

investigated for pulmonary delivery of siRNA directed against tumor necrosis factor (TNF) α for the treatment of acute lung inflammation. Delivery efficiency was assessed in vitro in the RAW264.7 macrophage cell line activated with lipopolysaccharide (LPS), and efficacy was evaluated in vivo in a murine model of LPS-induced lung inflammation upon pre-treatment with TNF- α siRNA. The PAMAM dendrimer-siRNA complexes (dendriplexes) displayed strong siRNA condensation and high cellular uptake in macrophages compared with non-complexed siRNA. Q-PCR analyses showed that the dendriplexes mediated efficient and specific TNF- α silencing in vitro, as compared to non-complexed siRNA and dendriplexes with negative control siRNA. Also in vivo, the PAMAM dendriplexes induced efficacious TNF- α siRNA inhibition, as compared to non-complexed siRNA, upon pulmonary administration to mice with LPS-induced lung inflammation. Hence, these data suggest that PAMAM dendrimers are promising for the local delivery of TNF- α siRNA in the treatment of lung inflammation via pulmonary administration

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

Alle Rechte bei APV e.V. · All rights reserved ·
Printed in Germany · Jede Form des Nachdrucks verboten

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

Sehr interessant auch für Nutzer von Maschinen für die Pharmaindustrie:

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

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 10.000 km pro Jahr, gewerbliches Leasing, Angebote freibleibend. Der Nachlass auf den Listenpreis ist in die ermäßigte Rate einkalkuliert. Der jeweilige BAFA-Anteil ist bei den Plug-In-Hybrid Fahrzeugen und den reinen Elektrofahrzeugen (ZOE) bereits wie eine Anzahlung berücksichtigt. (* = Service inklusive).

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

Kfz-Leasing

 Alle Fahrzeuge mit der Abgasnorm Euro 6d-Temp

Hersteller/Typ	Listenpreis	mtl. Rate
Audi Q2 S line 35 TFSI 110kW/150PS S tronic inkl. Navigationspaket, Klimaautomatik, PDC/Kamera, Sitzheizung vorn, Lederlenkrad mit Multifkt., 17" LMR Ganzjahresreifen etc.	32.092,00 €	289,00 €
Audi Q3 Sportback 45 TFSI e 180kW/245PS S tronic inkl. MMI Navi plus, Klimaautomatik, Einparkhilfe plus, virtual cockpit, Geschwindigkeitsregelanlage, 18" LMR Ganzjahresreifen etc.	42.313,00 €	369,00 €
Audi e-tron 50 quattro 230kW inkl. MMI Navigation plus, 2-Zonen Klimaautomatik, LED-Scheinwerfer, Parkassistent mit Einparkhilfe plus, Sitzheizung vorn, 19" LMR etc.	58.777,00 €	399,00 €
BMW 330e Touring Sport Line 215kW/292PS inkl. Automatic, Business Paket Professional, Navi/Live Cockpit, Head-Up Display, Klimaautomatik, Parking Assistant, Sitzheizung vorn etc.	53.067,00 €	439,00 €
CUPRA Leon Sportstourer 1.4 e-Hybrid 180kW/245PS DSG inkl. Navigationssystem, 3-Zonen-Climatronic, Voll-LED-Scheinwerfer, Einparkhilfe, Geschwindigkeitsregelanlage, 19" LMR etc.	33.693,00 €	189,00 €
CUPRA Formentor VZ 2.0 TSI 4Drive 228kW/310PS DSG inkl. 3-Zonen-Climatronic, Navigationssystem, Parklenkassistent mit PDC und Rückfahrkamera, Sicherheitsassistenz, 19" LMR etc.	37.891,00 €	299,00 €
CUPRA Ateca 2.0 TSI 4Drive 221kW/300PS DSG inkl. Climatronic, Full Link, Parklenkassistent mit PDC, Top-View mit Rückfahrkamera, Voll-LED-Scheinwerfer, Tempomat, 19" LMR etc.	38.345,00 €	299,00 €
Mercedes CLA 250 e Shooting Brake 118kW/160PS inkl. Business Paket, MBUX Multimediasystem Advanced, LED High Performance Scheinwerfer, Park-Assistent Sitzheizung vorn, 17" LMR etc.	38.775,00 €	279,00 €
Mercedes 300 de T-Modell Avantgarde 9G-TRONIC 143kW/194PS inkl. Business-Paket, MBUX Augmented Reality für Navigation, Park-Assistent mit PDC/Kamera, Klimaautomatik, 18" LMR etc.	54.670,00 €	467,00 €
Mercedes GLC 300 de 4MATIC 143kW/194PS 9G-TRONIC inkl. Business-Paket, Festplatten-Navig., LED-High-Performance-Scheinw., Advanced Park-Paket, EASY-PACK Heckklappe, 18" LMR etc.	53.700,00 €	499,00 €
MINI Cooper 5-Türer 100kW/136PS inkl. Metallic, Connected Navigation, Klimaautomatik, Parkassistent, Classic Trim, Sportsitze + Sitzheiz. Fahrer/Beifahrer, Komfortpaket, 16" LMR etc.	24.958,00 €	259,00 €
Renault Megane Grandtour Tce 140 Business Edition 103kW/140PS inkl. Navigationssystem, Renault EASY LINK mit Smartphone-Integration, Einparkhilfe vorn + hinten, Ganzjahresreifen etc.	22.723,00 €	139,00 €
Skoda Karoq Ambition 1,0 TSI 81kW/110PS inkl. Klimaanlage, Musiksystem/DAB+, Parksensoren hinten, Sitzheizung Vordersitze, Außenspiegel abblendbar elektr. beheizbar, 17" LMR etc.	22.453,00 €	129,00 €
Skoda Octavia Combi Ambition 1,0 TSI 81kW/110PS inkl. Infotainmentsystem Bolero, 2-Zonen-Climatronic, Parksensoren hinten, Spurhalteassistent, Tempomat, 16" LMR AERO etc.	21.639,00 €	99,00 €
Skoda Superb Combi Ambition 1,4 TSI iV 160kW/218PS 6-Gang automat. inkl. Navigationssystem, PDC v+h/Kamera, LED-Scheinwerfer, beheizbare Vordersitze, 18" LMR Antares etc.	39.380,00 €	229,00 €