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Nachrichten und Mitteilungen

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

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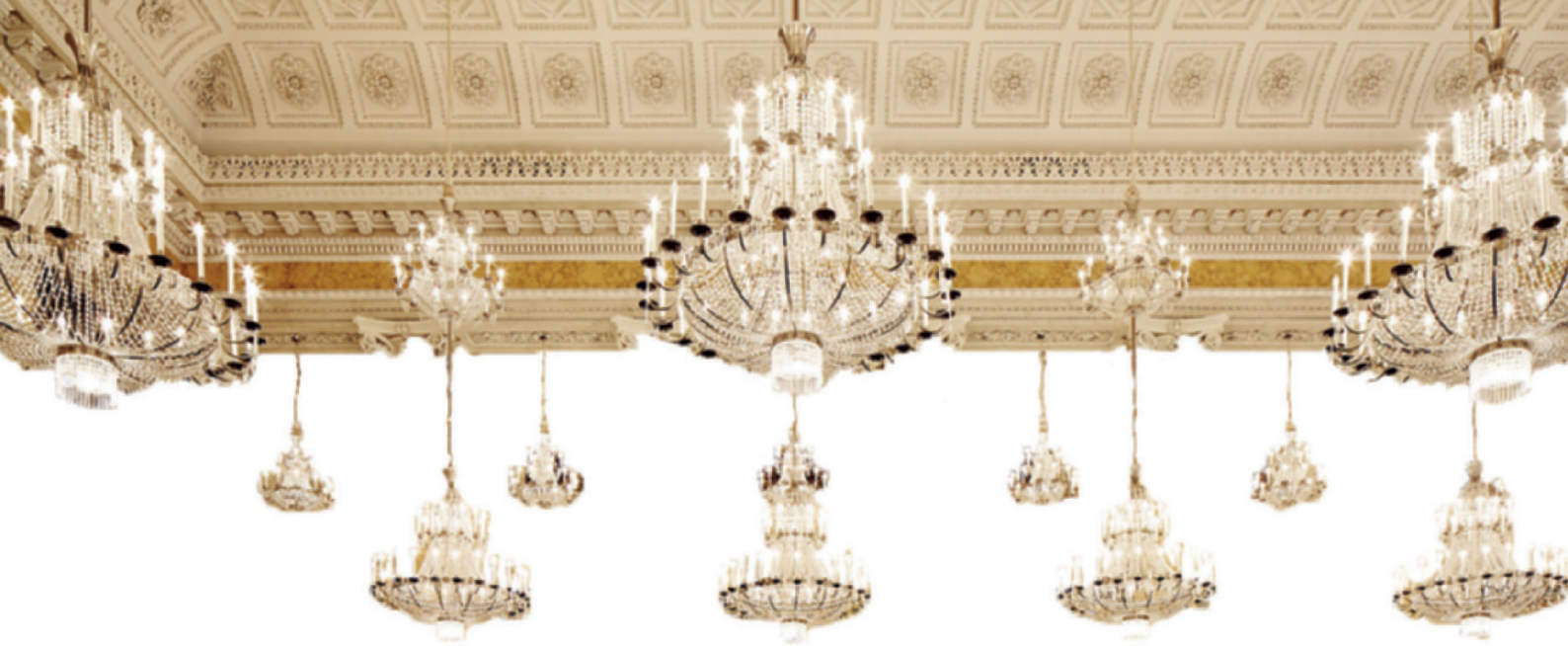
APV NEWS



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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 nächten Terminen erhalten Sie bei Dr. Lars Restetzki (lars.restetzki@roche.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 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 nächten Terminen erhalten Sie bei Dr. Johanna Anlahr (johanna.anlahr@bayer.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 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?

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

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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 €
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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 €
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