APV – Arbeitsgemeinschaft für Pharmazeutische Verfahrenstechnik e. V.

APV NEWS

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Nachrichten und Mitteilungen

MAKING SCIENCE WORK

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

Lokale Gruppen

Mittwoch, 14. September 2016

Lokale APV-Gruppe Berlin um 19:00 Uhr. Ort wird noch bekanntgegeben.

Anmeldung erforderlich bis zum 05. September 2016 bei Dr. Andreas Sachse (andreas.sachse@cpl-sachse.de).

Mittwoch, 12. Oktober 2016

Lokale APV-Gruppe Rhein-Main ab 19:30 Uhr. Der Ort wird noch bekanntgegeben.

Weitere Informationen erhalten Sie bei Cathrin Pauly (pauly@aspiras.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. Mangal et al./European Journal of Pharmaceutics and Biopharmaceutics 102 (2016) 168–177

Relationship between the cohesion of guest particles on the flow behaviour of interactive mixtures

Sharad Mangal, Thomas Gengenbach, Doug Millington-Smith, Brian Armstrong, David A.V. Morton, Ian Larson

In this study, we aimed to investigate the effects cohesion of small surface-engineered guest binder particles on the flow behaviour of interactive mixtures. Polyvinylpyrrolidone (PVP) – a model pharmaceutical binder – was spray-dried with varying L-leucine feed concentrations to create small surface-engineered binder particles with varying cohesion. These spray-dried formulations were characterised by their particle size distribution, morphology and cohesion. Interactive mixtures were produced by blending these spray-dried formulations with paracetamol. The resultant blends were visualised under scanning electron microscope to confirm formation of interactive mixtures. Surface coverage of paracetamol by guest particles as well as the flow behaviour of these mixtures were examined. The flow performance of interactive mixtures was evaluated using measurements of conditioned bulk density, basic flowability energy, aeration energy and compressibility. With higher feed l-leucine concentrations, the surface roughness of small binder particles increased, while their cohesion decreased. Visual inspection of the SEM images of the blends indicated that the guest particles adhered to the surface of paracetamol resulting in effective formation of interactive mixtures. These images also showed that the low-cohesion guest particles were better de-agglomerated that consequently formed a more homogeneous interactive mixture with paracetamol compared with high-cohesion formulations. The flow performance of interactive mixtures changed as a function of the cohesion of the guest particles. Interactive mixtures with low-cohesion guest binder particles showed notably improved bulk flow performance compared with those containing high-cohesion guest binder particles. Thus, our study suggests that the cohesion of guest particles dictates the flow performance of interactive mixtures.

D. Molnar et al./European Journal of Pharmaceutics and Biopharmaceutics 103 (2016) 51–61

Insertion stability of poly(ethylene glycol)-cholesteryl-based lipid anchors in liposome membranes

Daniel Molnar, Jürgen Linders, Christian Mayer, Rolf Schubert

Liposomes consist of a hydrophilic core surrounded by a phospholipid (PL) bilayer. In human blood, the half-life of such artificial vesicles is limited. To prolong their stability in the circulation, liposomal bilayers can be modified by inserting poly(ethylene glycol) (PEG) molecules using either PL or sterols as membrane anchors. This establishes a hydrophilic steric barrier, reducing the adsorption of serum proteins, recognition and elimination by cells of the immune system. In addition, targeting ligands (such as antibodies) are frequently coupled to the distal end of the PEG chains to direct the vesicles (then called 'immuno-liposomes') to specific cell types, such as tumor cells. To our knowledge, experiments on the stability of ligand anchoring have so far only been conducted with PL-based PEGs and not with sterol-based PEGs after insertion via the sterol-based post-insertion technique (SPIT). Therefore, our study examines the insertion stability of PEG-cholesteryl ester (Chol-PEG) molecules with PEG chains of 1000, 1500 and 2000 Da molecular mass which have been inserted into the membranes of liposomes using SPIT. For this study we used different acceptor media and multiple analytical techniques, including pulsed-field-gradient nuclear magnetic resonance (PFG-NMR), free-flow electrophoresis, size exclusion chromatography and ultracentrifugation. The obtained data consistently showed that a higher molar mass of PEG chains positively correlates with higher release from the liposome membranes. Furthermore, we could detect and quantify the migration of Chol-PEG molecules from radioactively double-labeled surface-modified liposomes to negatively charged acceptor liposomes via free-flow electrophoresis. Insertion of Chol-PEG molecules into the membrane of preformed liposomes using SPIT is an essential step for the functionalization of liposomes with the aim of specific targeting. For the first time, we present a kinetic analysis of this insertion process using PFG-NMR, showing that insertion into the liposomal membranes takes place within 90 s for Chol-PEG1000 molecules.

S. T. F. C. Mortier et al./European Journal of Pharmaceutics and Biopharmaceutics 103 (2016) 71–83

Uncertainty analysis as essential step in the establishment of the dynamic Design Space of primary drying during freeze-drying

Séverine Thérèse F.C. Mortier, Pieter-Jan Van Bockstal, Jos Corver, Ingmar Nopens, Krist V. Gernaey, Thomas De Beer

Large molecules, such as biopharmaceuticals, are considered the key driver of growth for the pharmaceutical industry. Freeze-drying is the preferred way to stabilise these products when needed. However, it is an expensive, inefficient, time- and energy-consuming process. During freeze-drying, there are only two main process variables to be set, i.e. the shelf temperature and the chamber pressure, however preferably in a dynamic way. This manuscript focuses on the essential use of uncertainty analysis for the determination and experimental verification of the dynamic primary drying Design Space for pharmaceutical freeze-drying. Traditionally, the chamber pressure and shelf temperature are kept constant during primary drying, leading to less optimal process conditions. In this paper it is demonstrated how a mechanistic model of the primary drying step gives the opportunity to determine the optimal dynamic values for both process variables during processing, resulting in a dynamic Design Space with a well-known risk of failure. This allows running the primary drying process step as time efficient as possible, hereby guaranteeing that the temperature at the sublimation front does not exceed the collapse temperature. The Design Space is the multidimensional combination and interaction of input variables and process parameters leading to the expected product specifications with a controlled (i.e., high) probability. Therefore, inclusion of parameter uncertainty is an essential part in the definition of the Design Space, although it is often neglected. To quantitatively assess the inherent uncertainty on the parameters of the mechanistic model, an uncertainty analysis was performed to establish the borders of the dynamic Design Space, i.e. a time-varying shelf temperature and chamber pressure, associated with a specific risk of failure. A risk of failure acceptance level of 0.01%, i.e. a 'zero-failure' situation, results in an increased primary drying process time compared to the deterministic dynamic Design Space; however, the risk of failure is under control. Experimental verification revealed that only a risk of failure acceptance level of 0.01% yielded a guaranteed zero-defect quality end-product. The computed process settings with a risk of failure acceptance level of 0.01% resulted in a decrease of more than half of the primary drying time in comparison with a regular, conservative cycle with fixed settings.

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APV NEWS – Leasing-Highlights zu Sonderkonditionen

Kfz-Leasing: Vorteile für APV-Mitglieder

Leasing und Finanzierung von Investitionsgütern zu günstigen Konditionen für APV-Mitglieder:

- ✔ 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 Hersteller von Maschinen für die Pharmaindustrie:

- ✔ niedrige Leasingraten statt hoher Kaufpreis
- ✔ 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

Die APV hat für ihre Mitglieder einen Rahmenvertrag mit einem bekannten Leasing-Unternehmen geschlossen. Als Kooperationspartner der APV bietet das Unternehmen Leasing von Neu- und Gebrauchtfahrzeugen zu Sonderkonditionen. 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, 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.

JETZT NEU: Leasing auch für andere Investitionsgüter

Hersteller/Typ	Listenpreis	mtl. Rate
Audi Q5 3.0 TDI quattro S tronic 190kW/258PS inkl. Metallic, Designpaket Leder Milano, Sportsitze, MMI Navi plus, Komfortpaket, 18"LM-Felgen, PDC/Kamera etc.	51.504,00 €	569,00 €
Audi Q7 3.0 TDI quattro tiptronic 200kW/272PS inkl. MMI Navigation plus, Metallic, Lederausstattung, PDC/Kamera, Matrix-LED-Scheinwerfer, Vordersitze elektr. etc.	61.017,00 €	659,00 €
BMW 320d Touring Advantage Automatic 140kW/190PS inkl. BusinessPackage mit Navi Connected Drive, Metallic, Klimaautomatik, LM-Felgen, PDC, Tempomat etc.	40.328,00 €	379,00 €
BMW X5 xDrive30d 190kW/258PS inkl. Automatik, Metallic, Lederausstattung, Klimaautomatik, Navigations-Paket ConnectedDrive, PDC/Kamera, LM-Räder etc.	57.655,50 €	655,00 €
Mercedes CLA 220d Shooting Brake "Urban" 130kW/177PS inkl. Automatik, Navi, Klimaautomatik, PDC mit Rückfahrkamera, LED-Scheinwerfer, Sitzheizung vorne etc.	37.075,00 €	389,00 €
Mercedes GLC SUV 250d 4MATIC Diesel 9G-TRONIC 150kW/204PS inkl. Metallic, Lederpolster, Navi COMAND Online, Park-Assistent mit Kamera, EXCLUSIVE Interieur etc.	47.175,00 €	559,00 €
MINI Cooper Clubman 100kW/136PS inkl. Klimaautomatik, Metallic, PDC hinten, Ablagenpaket, Nebelscheinwerfer, Lichtpaket, LM-Felgen, Bluetooth etc.	21.798,00 €	199,00 €
VW Tiguan Comfortline 1,4l TSI DSG 110kW/150PS inkl. Business Premium Paket mit Navigation, Metallic, Klimaanlage, Sitzheizung vorne, PDC, 17" LM-Felgen etc.	29.328,00 €	319,00 €

Vfw = Vorführwagen zu Sonderkonditionen, DW = Dienst-/Werkswagen (genannter Listenpreis=Kaufpreis)