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

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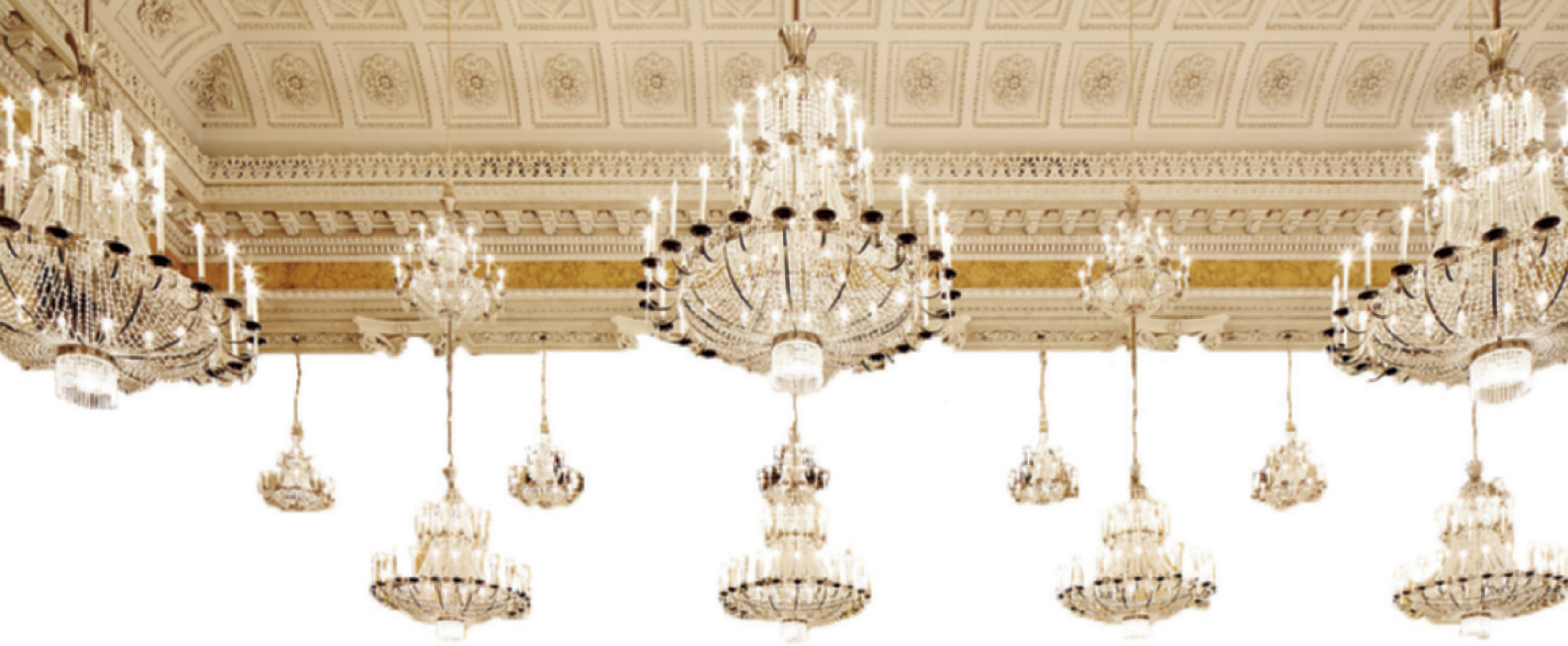
APV NEWS



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Mittwoch, 02. Dezember 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).

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).

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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).

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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

F. Sahnen et al./ European Journal of Pharmaceutics and Biopharmaceutics 154 (2020) 89-97

Conversion of indomethacin nanosuspensions into solid dosage forms via fluid bed granulation and compaction

F. Sahnen, J.P. Kamps, K. Langer

Preparation of pharmaceutical nanosuspensions is a popular technique to increase the dissolution velocity of poorly water-soluble drugs. Subsequent drying into a compaction-ready powder or granule is a critical process due to possible adverse solid characteristics and the risk of growth of nanoparticles. This work evaluated the drying of nanosuspensions via fluid bed granulation with focus on the binder selection and used concentrations, as well as the parameters spray rate and atomization pressure. Design of experiments was used to identify significant parameters. Indomethacin nanosuspensions were prepared by wet media milling and dried on a carrier consisting of lactose, microcrystalline cellulose, and crospovidone with and without additional binder during granulation. Resulting granules were compacted into tablets and their in vitro dissolution performances were characterized. A higher content of binder PVP and a higher spray rate led to less growth of resuspended nanoparticles. Finally, indomethacin nanoparticle tablets showed a superior dissolution performance in contrast to raw indomethacin tablets.

Karsten Flügel et al./ European Journal of Pharmaceutics and Biopharmaceutics 154 (2020) 214-221

Impact of structural relaxation on mechanical properties of amorphous polymers

Karsten Flügel, Robert Hennig, Markus Thommes

Fusion based methods, such as hot-melt extrusion, are a common way of preparing amorphous solid dispersions. Since the amorphous glass, however, is not in a configurational equilibrium, the molecular arrangement of the obtained material can differ in dependence of the preparation conditions. Although the changes in the configuration of an amorphous material, which are commonly referred to as structural relaxation or physical aging, are well investigated, the impact on mechanical properties of amorphous solid dispersions have widely been neglected so far. The presented study investigated copovidone as a model polymer commonly used in amorphous solid dispersions and revealed that structural relaxation was already introduced into the polymer during hot-melt extrusion while its degree was cooling rate dependent. The degree of structural relaxation significantly affected the mechanical properties of copovidone as assessed by diametral compression tests, macroindentation and nanoindentation. An increase in Young's modulus and indentation hardness was observable with a higher degree of structural relaxation, which, during tablet compression, translated into tablets with significantly lower tensile strength. Furthermore, evaluation of the force-displacement curves during tablet compression revealed a decreased proportion of irreversible deformation with higher degree of structural relaxation correlating well with the increased indentation hardness during macroindentation. Thus, understanding structural relaxation and its impact on material properties is of utmost importance to assess the processability and compaction performance of amorphous solid dispersions in dependence of their preparation conditions and thermal history.

Rebecca Chamberlain e al./ European Journal of Pharmaceutics and Biopharmaceutics 154 (2020) 309-316

Freeze-drying in protective bags: Characterization of heat and mass transfer

Rebecca Chamberlain, Jonas Schlauersbach, Matthias Erber

During lyophilisation of highly potent Active Pharmaceutical Ingredients (APIs) potential contamination of the freeze-drier is an important safety issue. Since the stoppers are in semistoppered position during the lyophilization process, API may contaminate the chamber and cross-contamination may occur as well. In this study two protective bags, which enclose each tray and their influence on heat and mass transfer during freeze-drying were investigated. Sublimation tests were performed using either purified water or solutions containing trehalose as well as hydroxypropyl-β-cyclodextrin (HPbCD) as bulking agents. During sublimation tests with purified water both bags clearly influenced heat and mass transfer compared to unpacked reference vials. The bag, which was originally designed to be used for steam sterilization, had a massive impact on drying characteristics. The bag membrane becomes the rate limiting factor, generating a separate compartment within the bag. In this compartment vapor pressure is much higher compared to the chamber pressure during primary drying, leading to altered drying conditions. However, drying was still possible. The other bag, which was specifically designed for lyophilization, also had an impact on drying behavior which could be assigned to the foil between shelf and bottom of the vials. This was detectable as differences in Kv values. Membrane resistance, however, becomes negligible when 10% (w/w) trehalose or HPbCD solutions were dried using the later bag as containment. The data reported in this work demonstrate the relevance and value of sublimation tests

to understand the lyophilization process, especially when new components are implemented. The data should be considered, when freeze-drying shall be performed using such bags.

Tuomas Kilpeläinen et al./ European Journal of Pharmaceutics and Biopharmaceutics 155 (2020) 49-54

Raman imaging of amorphous-amorphous phase separation in small molecule co-amorphous systems

Tuomas Kilpeläinen, Katja Pajula, Tuomas Ervasti, Emilia Uurasjärvi, Arto Koistinen, Ossi Korhonen

Many new active pharmaceutical ingredients (API) undergoing development have low permeabilities or low aqueous solubilities. However, the amorphous state is usually more soluble than its crystalline counterpart. The amorphous state has a higher Gibb's free energy, which can improve the apparent solubility but decrease the stability since the amorphous state tends to transform to the more stable crystalline form. Before recrystallization, a co-amorphous binary mixture's ingredients have to undergo a phase separation. The aim of this study was to obtain a better understanding of the amorphous-amorphous phase separation in co-amorphous binary mixtures and test the suitability of imaging Raman spectroscopy for detecting this phenomenon. To study the phase separation, we prepared three different 50:50 mass ratio binary mixtures of APIs: paracetamol-terfenadine, (PAR-TRF), paracetamol-indomethacin (PAR-IMC) and terfenadine-indomethacin (TRF-IMC). The binary mixtures were amorphized with melt-quenching and stored above their glass transition temperature (Tg) to monitor their phase separation. Thermal degradation was determined with a high performance liquid chromatography (HPLC) method to ensure that melt-quenching did not cause any thermal degradation of the molecules. Thermodynamic attributes (crystallization tendency, melting point (Tm) and Tg) were measured with differential scanning calorimetry (DSC) to ensure that the co-amorphous systems transformed to the amorphous state and remained amorphous after cooling and reheating. Phase separation was studied from the surface and cross-section (CS) with Raman imaging to examine if it occurred more on the surface than in the bulk. The Raman spectra were analyzed with principal component analysis (PCA) and Contour plots were produced from the PCA-score values to visualize concentration differences in the mixtures. The results showed that API vs API concentrations increased as a function of time in both surface and CS images before crystallization. This suggests that Raman imaging is a suitable technique to detect the phase separation phenomena in small molecule co-amorphous binary mixtures.

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