Wissenschaftliche Posterausstellung: Poster 15

Ultra fine cyclosporin A nanocrystals produced in a super small scale

Romero, G. B. (1), Keck C. M. (2) and Müller R. H. (1)

(1) Freie Universität Berlin - Institute of Pharmaceutics, Biopharmaceutics & NutriCosmetics, Berlin, Germany
(2) PharmaSol GmbH, Berlin, Germany

Cyclosporin A (CyA) is a potent imunosupressor used in case of organ transplants and also for dermal diseases such as psoriasis. Its administration via oral has many drawbacks, including toxicity, systemic effects and low bioavailability. In case of dermal diseases, the topic route would be recommended. However, cyclosporin A has very low skin penetration and consequently, low dermal bioavailability and bioactivity. One approach to overcome these problems is formulating it as nanocrystals [1]. Size below 100 nm is essential, because it has the highest increase in saturation solubility. This creates largest penetration-enhancing concentration gradient between dermal formulation and skin. Therefore, in order to increase the topical performance of this drug, ultra fine CyA nanocrystals in the lower nanorange (<100 nm) were produced in a super small scale (0.5 g batch).

The production principle was a top-down approach, in this case, wet bead milling in a super reduced scale. The milling chamber consisted of a 1 mL glass vial filled with 50% (v/v) grinding media and 50% (v/v) CyA coarse suspension. It was processed in a magnetic stirrer at 1,200 rpm and 5°C for 5 days. Particle size was assessed by photon correlation spectroscopy (PCS) and light microscopy. Samples were drawn after 1hour, 6 hours, 1 day, 2 days, 3 days and 5 days.

Up to 3 days milling, particle size gradually reduced as a function of time. The smallest PCS diameter was 93 nm and polydispersity index was 0.138. Such super small scale production is meaningful for the development of formulations of high costly drugs and new chemical entities which are not available at large amounts. For instance, the batch size of a traditionally used bead mill such as the PML-2 (Bühler AG, Switzerland) is normally around 150 g for the discontinuous mode. In the super small scale investigated in this study, the batch size is reduced by a factor of 300 fold.

CyA nanocrystals <100 nm for enhanced skin penetration were successfully produced and a super small scale approach for production of nanocrystals was established. This is meaningful for the R&D of formulations of new and/or high costly molecules e.g., radiolabeled drugs for pharmacokinetics studies.

[1] Shegokar, R., Müller, R. H., Int. J. Pharm. 399, 129-139, (2010)