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The use of Small and Wide Angle X-Ray Scattering (SWAXS) for the physico-chemical characterization of solid dispersions

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Introduction

Solid dispersions of active pharmaceutical ingredients (APIs) in freely water soluble carriers are often used in order to improve dissolution rate and/or solubility of poorly water soluble drugs in the aqueous gastro intestinal fluids [1]. In a solid solution the API is molecularly dispersed in the carrier. However, storage may lead to recrystallisation of the API in the carrier. These changes may substantially alter the dissolution profile/solubility of the drug in the aqueous dissolution media. We apply simultaneous small and wide-angle X-ray scattering (SWAXS), which is becoming more important for solid-state pharmaceutical analytics [2], in order to gain information of solid nano-structure and dispersions stability.

Material and Methods

Nimodipine (NI) was provided by Bayer Schering Pharma AG (D-Berlin) Polyethylene glycol 2000 (PEG 2000) was given by Clariant (CH-Basel).

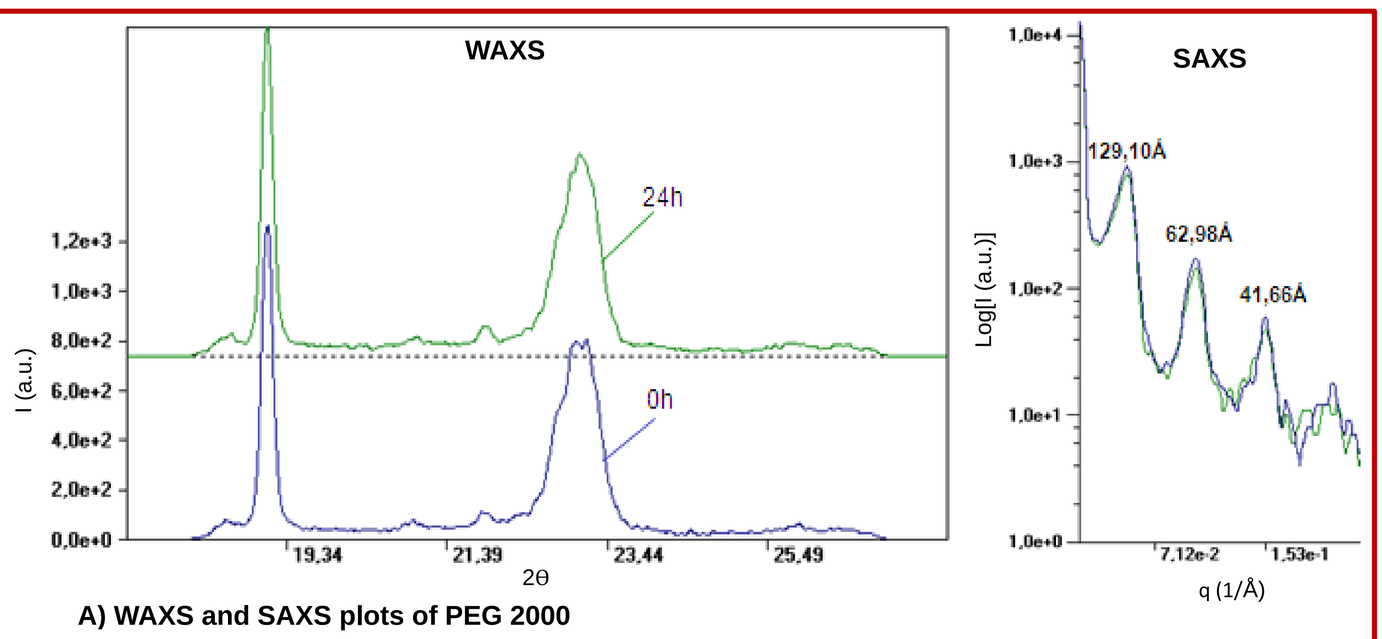
Solid dispersions of 20% NI and 80% PEG 2000 were prepared by melting PEG 2000 at 70 °C and dissolving NI in the melt. Subsequently the melt was cooled down to room temperature.

Hecus S3MICRO Workstation

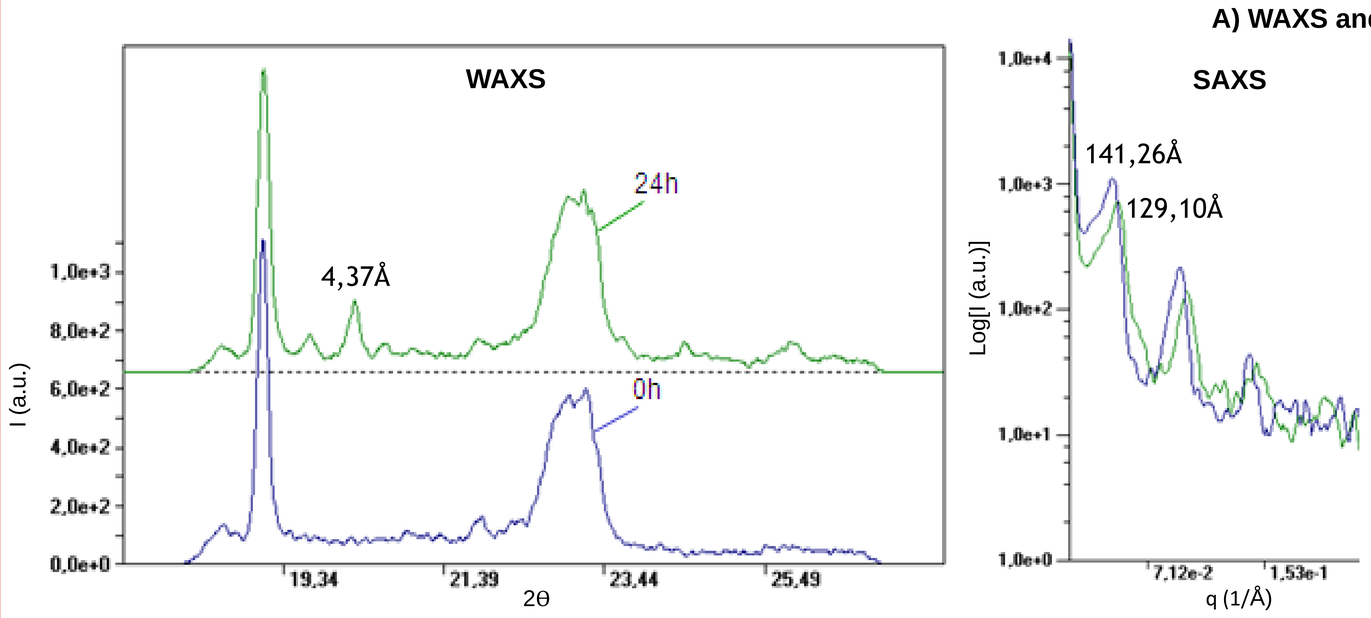
Simultaneous SAXS and WAXS was carried out using the S3MICRO (Hecus X-Ray systems, A-Graz). Operating conditions were 600s exposure time at room temperature.

Results and Discussion

While pure PEG 2000 (A) shows identical WAXS and SAXS plots for 0h (blue line) and 24h (green line), significant changes can be observed with 20% NI (B). At 0h the WAXS plot displays the typical PEG 2000 “fingerprint”, whereas after 24h, additional peaks (4.37Å) appear, indicating a recrystallisation of NI. When comparing the SAXS plot at 0h and 24h, it can be observed that the peak representing the



A) WAXS and SAXS plots of PEG 2000



B) WAXS and SAXS plots of PEG 2000 with 20% nimodipine

PEG 2000 lamellar structure at 129,10Å determined at 0h, is shifted towards 141,26Å at 24h. The peak positions observed at 24h perfectly correspond to the peak positions of pure PEG 2000, indicating that the presence of dissilved NI alters the lamellar structure of PEG 2000. Furthermore a decrease of the scattering intensity is observed possibly caused by the recrystallisation of NI.

Conclusion and Outlook

- The shift of the PEG lamellar structure and the decrease of scattering intensity indicate the recrystallisation of NI and highlight the importance of SAXS in the quality control of solid dispersions.
- Future Aims will be the evaluation of SAXS solid state analysis for providing an early indication of API recrystallisation i.e. aging behavior of solid dispersions.

References

[1] W.L. Chiou, S. Riegelmann. Pharmaceutical Applications of Solid Dispersion Systems. J. Pharm. Sci. 1971; 60: 1505-1510

[2] A. Hodzic, M. Kriechbaum, P. Laggner. Laboratory SWAXS for application in the pharmaceutical technology. Acta Cryst A. 2009; A65.

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