

## **Master's Thesis in Pharmacy year 2016, Christoph Meier et al.**

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Titel:

Optimization of mixing homogeneity of Melatonin and Calcium glycerophosphate hard gelatine capsules

Abstract

The aim of this master thesis was to examine the influence of the spray dried mannitol on the content uniformity of a powder, used for the production of capsules. The hospital pharmacy of the University hospital Basel is responsible for the manufacture of different non - marketed dosage forms. Especially the capsules is a well - used form in the paediatrics. Based on the results of a previous master thesis, in which quetiapine fumarate as API in combination with the spray dried mannitol and Aerosil® showed the best result, this following work should prove, if the spray dried mannitol is compatible with other APIs like melatonin and calcium glycerophosphate, regarding the content uniformity as an important quality attribute. Melatonin has a very low dosage why it is a challenge in the manufacture. It can cause problems in the homogenous distribution during the blending process.

To observe the influence of the spray dried mannitol and try to reach a better content uniformity in the capsules, for each API different mixtures of powder have been produced with the spray dried and non - spray dried mannitol. The manufacture process has not been changed (exceptions are specified), to get a better understanding between the excipient and the API. For a statistical evidence, each variation mixture has been made three times. For every mixture, capsules were produced and in a following step verified on their mass and content uniformity.

Particle size analysis with different made mixtures and raw materials could be quantitative measure regarding the particle size and distribution. Further, the form, size and porosity has been observed by scanning electron microscopy.

The the spray dried excipient showed a very good flowability for the manufacture of capsules but a positive effect on the content uniformity could not be reached for

those two APIs. For melatonin, the addition of Aerosil® downgrade the content uniformity strongly. With calciumglycerophosphate, the deviation has been not so strong, but the combination of Aerosil® and spray dried mannitol gave better results, which can be lead back to the bigger particle size of calcium glycerophosphate than melatonin. Indifferent results could be observed in mixtures with and without the non - spray dried mannitol. For the manufacturing process of calcium glycerophosphate, there will be no changement. A liquid dosage form could be consider for melatonin.