

INVESTIGATING CRYSTAL GROWTH IN AMBROXOL HYDROCHLORIDE SOLUTIONS WITH THE HELP OF FBRM TECHNIQUE IN CASE OF NON-TYPICAL SPHERICAL CRYSTALLIZATION METHODS

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Spherical crystallization is usually the last technological step in the production of solid form drugs. Not only purification can be achieved with it, but we can manufacture the optimal morphology of the crystals. Spherical morphology with suitable mean particle size is advantageous when direct tablet making technique is used. This way the amount of the additives can be reduced and smaller tablets can be produced. In our previous research [1] it was found that the spherical crystallization of ambroxol hydrochloride can be achieved by the non-typical methods, such as spherical agglomeration and cooling crystallization. Because of the spherical morphology, flowing and compaction properties of the powder have improved. In the present work the parameter optimization was further investigated with the help of an FBRM

probe, continuously observing the crystal growth in the non-typical crystallization systems. With this on line technique, it was possible to control the mean particle size and the optimal mixing time, and solvent-antisolvent ratio could also be determined. In case of the cooling crystallization, we applied an alternating temperature profile around the metastable zone in order to standardize the particle size. It was a heating-cooling cycle, so the smaller particles could dissolve when heating happened, then crystallize onto the surface of the larger crystals. With the FBRM probe, this process could be investigated and the exact, optimal length of the heating-cooling periods could be determined.

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