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NONMONOTONICITY OF THE DEPENDENCE OF MEAN PARTICLE SIZE ON CONCENTRATION IN SUPERCRITICAL ANTISOLVENT PRECIPITATION

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Abstract

A variety of process parameters in Supercritical Anti-Solvent (SAS) method gives a possibility to obtain micro-, submicro- and nanoparticles with narrow size distribution. Deep understanding of parameters influence on particles size and morphology is necessary to carry out directional formation of particles with desired characteristics. One of important SAS processing parameters is initial concentration of micronized substance in the solution. For amorphous compounds the influence of concentration on particle size and morphology is well-understood. The increase in concentration leads to increase of particle size in the case of these substances. SAS precipitation of crystalline substances is more complicated and there is no qualitative description of it so far. There are examples when increase of concentration in the solution leads to increase, decrease or negligible changes of mean particle size of crystals. The aim of this work is to understand how concentration of substance in the solution influences crystalline particles size and morphology in SAS.

The influence of concentration on particles size and morphology is studied for different objects, namely oxalic, malonic and succinic acids, arbidol, moxifloxacin and levofloxacin, in a wide range of concentration in the solution. It is shown that, contrary to what's known for amorphous substances, the dependence of mean particle size on concentration of crystalline substances can be non-monotonous. The decrease, increase and negligible changes of particles size depending on concentration can be part of one concentration curve. This fact is observed for all studied objects for various solvents.

Qualitative interpretation of these results is given in terms of different crystallization mechanisms depending on supersaturation degree.

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