Salbutamol spherical particles formation by supercritical antisolvent precipitation

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Aerosol drug administration is a widely-used approach in drug delivery, especially in treatment of respiratory tract diseases. A typical requirement to solid particles used in aerosol drug formulations is spherical morphology, because it minimizes mechanical damage to soft tissues due to the absence of razor edges. Particle morphology influences aerodynamic characteristics and absorption rate of API. It is often difficult or impossible to obtain particles with given morphology and size by conventional mechanical methods. Supercritical antisolvent (SAS) precipitation is a promising alternative for particle design, since it provides an opportunity to fine-tune morphology of particles precipitated by varying process parameters. In this work, we carried out SAS micronization of antiasthmatic drug salbutamol sulphate, which is commonly used in aerosol form. Despite SAS precipitation of salbutamol is described in literature, spherical particles were not obtained and micronization was carried out in a narrow range of process conditions. The aim of this work was to study SAS process of salbutamol and to obtain particles with spherical morphology.

The possibility to obtain nano-, submicro- and microparticles of salbutamol sulphate with spherical, plate- and needle-like morphology is demonstrated. At certain conditions particles precipitated by SAS are acceptable for aerosol formulations. Special attention is payed to the influence of solvent and concentration in the initial solution on particle size and morphology. Hexafluoroisopropanol seems to be the most promising solvent for this application. It dissolves salbutamol at significantly higher concentration than methanol and dimethylsulphoxide and allows obtaining particle with required morphology. Therefore, it is very attractive for future industrial application in SAS process. It is shown that the dependence of particle size on concentration can be non-monotonous.

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