524e Influence of Supersaturation and Growth on Particle Size and Morphology in High Pressure Co_2 Antisolvent Process

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Small particle synthesis using supercritical CO_2 as an antisolvent has been of interest in the pharmaceutical, cosmetic, and related industries. We are studying two different precipitation processes using supercritical CO_2 as an antisolvent to manipulate particle size and morphology. The first technique is called solution-enhanced dispersion by supercritical fluid or SEDS [1] to precipitate acetaminophen out of ethanol solution. SEDS utilizes a coaxial nozzle design where the liquid solution with the solute of interest is rapidly mixed with supercritical CO_2. The resulting mixture is then sprayed through an external nozzle into a high-pressure capture vessel maintained at constant temperature and pressure. Both experimental and theoretical studies show that particle size and morphology are strongly dependent on the time of the experimental runs as long as the supersaturation inside the collection vessel remains high. Since fresh solution is constantly fed into the vessel at high pressure for an antisolvent particle formation process, it is hard to stop particulate growth after precipitation and therefore it is hard to control particle size.

In order to control the acetaminophen particle size, a second technique is investigated. In this process, the solution and the antisolvent mix in a low volume tee to initiate nucleation. The precipitated drug then enters a stainless steel tube where the particles are allowed to grow in a controlled environment down the length of the tube. The growth can be slowed down or stopped somewhere inside the cylindrical tube by introducing pure CO_2 to dilute the existing solution in order to reduce the supersaturation. This technique offers the opportunity for manipulating the final particle size, shape, and uniformity.

1. Hanna, M. and P. York, *"Method and Apparatus for the Formation of Particles"*. World Intellectual Property Organization, 1994. **Patent WO95/01121**.