PARTICLE FORMATION BY SUPERCRITICAL FLUID-ASSISTED PROCESSES

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Recent developments in biotechnology forecast a new generation of therapeutics. Yet, the increasing specificity of emerging drug candidates and its susceptibility to the classical administration routes raise new challenges to the Galenic pharmacology.

The pulmonary route is becoming an attractive alternative for the delivery of pharmaceutics[1], especially macromolecules like peptides, and proteins. However, it requires exquisite particles with specifications hard to achieve by most of the established technologies. Therefore, particle engineering using appropriate processes and excipients is required to produce particles of optimal size, morphology, and surface properties that would enhance drug target efficiency[2]. As a consequence, the preparation of drug micro and -nanoparticles with a controlled particle size distribution has become an important focus for the development of pharmaceutical delivery formulations[3].

Supercritical fluid-assisted technologies allow the generation of particles that are difficult or even impossible to obtain by traditional techniques such as milling, crystallization and spray drying which don't provide an efficient control of the particle size (a broad particle size distribution is normally obtained).

A novel method to produce fine dry powders (e.g. proteins, polymers, composites, cocrystals), making use of the properties of supercritical fluids, has been developed at IST. It consists of a concerted precipitation by two distinct mechanisms, the anti-solvent crystallization and the atomization and spray drying (A-SAIS process). Our results show that bioavailability issues can be overcome by accurate control of the particulate products properties, such as the crystalline form, morphology, size distribution, and the excipients composition and layering. Depending of the leading mechanism (atomization or anti-solvent) the morphology will vary from spheres to fibers (figure 1).

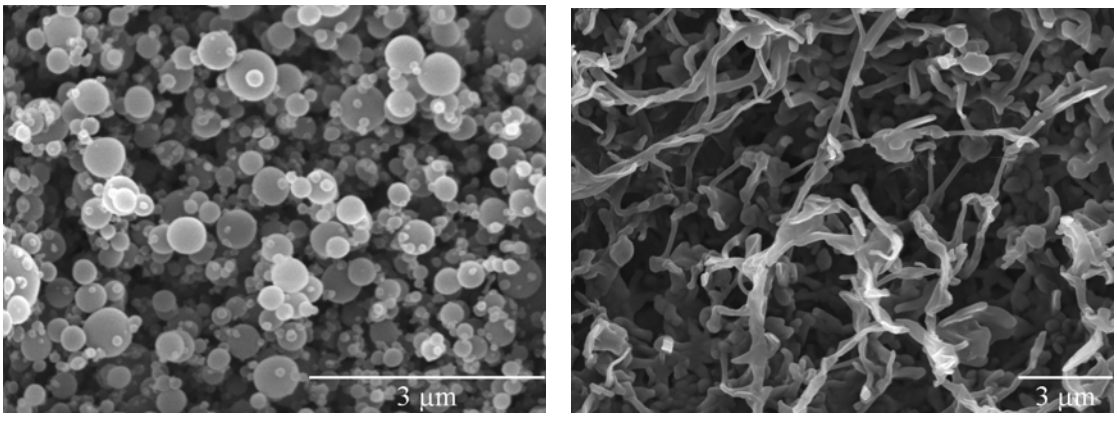

Figure 1 – Scanning Electron Microscopy images of lysozyme particles processed by the A-SAIS process: (a) spheres, and (b) fibers

The knowledge of the production process variables for the two precipitation mechanisms is the key to determine the precipitation sequence of drugs and excipients and then the degree of microencapsulation.

References

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