Lipid-composite particles by liquid-CO_2 cryospraying technology: advantages, challenges and pharmaceutical applications

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In recent years, a new generation of CO_2-based technologies has gained considerable interest in pharmaceutical and biotech industries, offering innovative, organic solvent-free, scaleable and economically viable solutions to address critical issues related to biopharmaceutical properties and drug product development.

Dense or liquid CO_2 has been applied in several processes as an atomization medium for the production of micro- and nanoparticles systems, by exploiting the thermal and mechanical properties of carbon dioxide rapid phase changes [1,2]. Variosol® cryospraying is one of these processes, based on the dynamic interaction between two sprayed fluids in different thermodynamic conditions. A liquid or pasty fluid can be converted into a micro or nano sized solid by the combined thermodynamical (Joule-Thomson effect) and mechanical (atomization) actions resulting from liquid-CO_2 rapid expansion. These properties can be advantageously applied to several classes of excipients, especially lipids or lipids-polymers composite, facilitating in some cases the formation of eutectic blends at low temperatures. Applying appropriate operating conditions, CO_2 expansion allows to eliminate water during spraying at low Tº [3], thus making it possible to spray disperse systems, such as emulsions or microemulsions, to obtain very fine dry particles combining hydrophilic and hydrophobic materials in the same matrix.

Lipid-based formulations (LBF) offer nowadays a wide range of possibilities, from e.g. enabling drugs intestinal solubilization and absorption of oral products [4], to controlling drug release, or improving efficacy in dermal products, facilitating drug interaction with skin components. However, most LBF are liquid or semisolid at room temperature, which may present a disadvantage in terms of stability, processability, product dosing (e.g. necessity of soft gel capsules) and high production costs. In fact, the development of solid forms (especially micro- or nanoparticulates) has been the focus of recent innovation in the field of LBF [4].

The cryogenic effect obtained during liquid-CO_2 expansion can be used to process composites, containing excipients or active molecules in liquid form, and still obtain LBF as fine, solid microparticles. The appropriate choice of materials and processing conditions are key factors to develop micronized and possibly nanosized LBFs for specific application such as improved drug solubilization and bioavailability, controlled or delayed release, drug stabilization, helping to address specific patients needs and targeting different routes of administration.

References

[1] Foster et al. , Ind. Eng.Chem. Res, (2003), 42, 6476-6493
[2] Danan H., Esposito P. , Ther. Delivery (2014), 5 (2) 205-232
[3] Danan H., Esposito P. et al. , European Patent, EP 2298286 B1 (2009)
[4] Feeney et al., Adv. Drug Delivery Revs., (2016), 101, 167-194

Figures

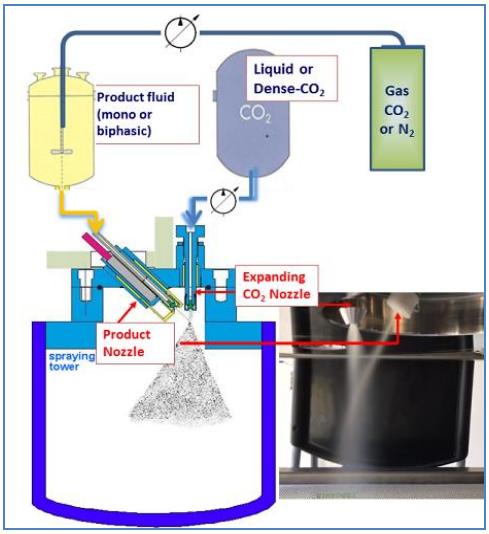

Figure 1. Scheme of CO_2 cryospraying technology

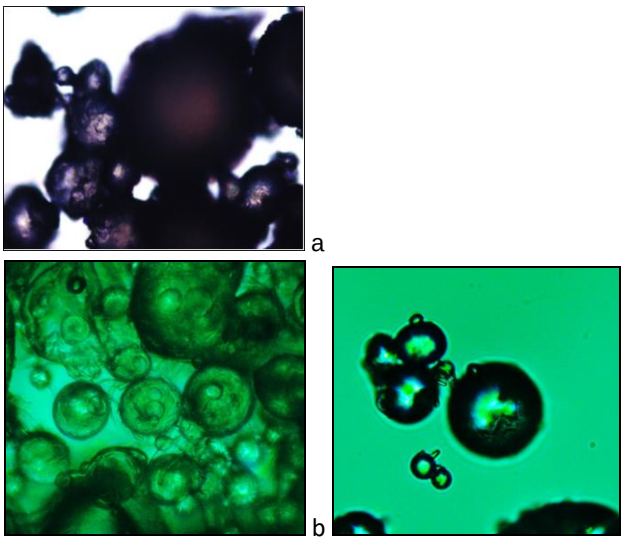

Figure 2. Optical Microscopy Images of dry (a) and water-suspended (b) drug- containing microspheres