The use of supercritical CO_2 to develop liposomes encapsulating active pharmaceutical ingredients for pulmonary administration.

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Nanomedicines such as liposomes have many advantages over conventional treatments, for example, improving the therapeutic index of molecules by protecting them, increasing their half-life, and targeting specific tissues and cells. One of the limitations to the development of nanodrugs is the development of reproducible production methods that can be transposed to an industrial scale under GMP conditions [1].

For this purpose, the use of supercritical CO_2 has been investigated to produce liposomes. A production method using the PGSS process was developed for the production of liposomes using a "Quality By Design" approach. This process consisted of adding lipid materials and active ingredients in the high-pressure cell with aqueous buffer (1), regulate the temperature on 80°C and to pressurize the cell at 240 bar (2). The system was stirred at 500 rpm for 30 minutes and then the system was depressurized through a nozzle with ΔP decreasing without maintaining the pressure in the autoclave (3). A liposomes suspension was then recovery for physicochemical characteristics analysis (4) (Figure 1).

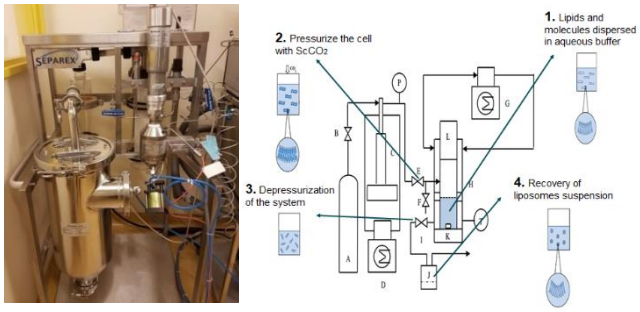

Figure 1. PGSS equipment and process to prepare liposomes.

Then, co-encapsulation tests of budesonide and salbutamol showed that the production method allowed to co-encapsulate both a hydrophilic and a hydrophobic active ingredient with high encapsulation efficiencies (EE) (89±7% for budesonide and 52±2% for salbutamol) identical or higher to that obtained with Thin Film Hydration method (TFH) at the same lipid concentration of 45 mM (85±2% for budesonide and 32±5% for salbutamol).

This versatile method, which uses only a single step production and no organic solvents, has been shown to produce liposomes of different lipid compositions suitable for different pharmaceutical applications with physicochemical characteristics suitable for drug delivery (size close to 200 nm and PdI between 0.2 and 0.4) [2].

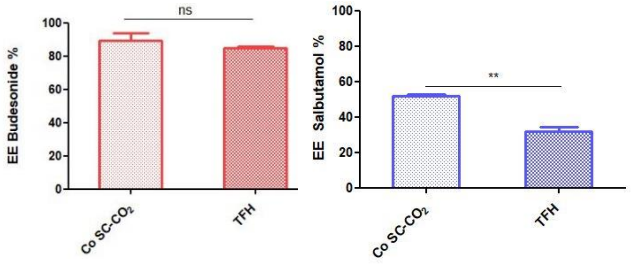

Figure 2. EE (%) of budesonide and salbutamol in liposomes produced by SC-CO_2 method or TFH method at 45 mM in lipids.

Regarding physicochemical properties, the size of liposomes prepared by SC-CO_2 is 181.8 ±15.3 nm with a PdI of 0.32±0.02. These values are significantly higher than those obtained with THF method but without any downstream processes such as extrusion step present in the TFH method [3]. The comparison of the supercritical CO_2 technology with the use TFH method, showed that the main advantages of this method are the absence of organic solvents, the production in a single step and the possibility to obtain a sterile finished product.

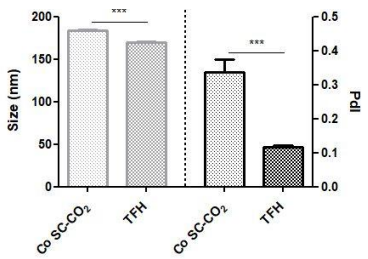

Figure 3. Size (nm) and PdI of liposomes produced by SC-CO_2 or TFH

References

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