**Influence of process and formulation parameters for the encapsulation of ibuprofen by the co-spray drying process**

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**Highlights**

* Co-spray drying process is used as an encapsulation tool.
* Operating parameters affect the loading of mesoporous silica nanoparticles.
* Ibuprofen is present in different states and location is revealed.

**1. Introduction**

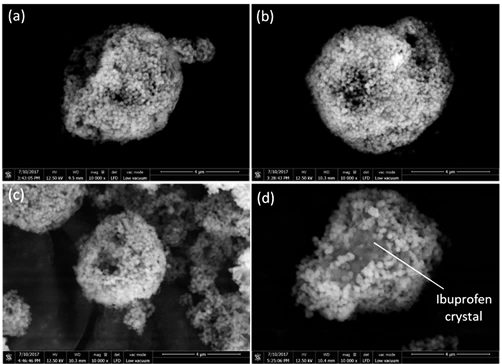
Nanosystems for biomedical applications present a great interest as therapeutic tools for the controlled release of active substances [1]. In this context, Mesoporous Silica Nanoparticles (MSN) are relevant drug carriers due to their biocompatibility [2] and high specific surface. Several processes may be used for drug loading [3]. Spray drying, currently used in the industry to dry a product, has a good potential for encapsulation [4], [5]. In this work, ibuprofen (poorly water-soluble molecule) is loaded inside the MSN by co-spray drying. Some properties after loading and their end-used properties can be modified depending on formulation parameters (Ibu/Si weight ratio (R=Ibu:Si), silica concentration, solvent) and process parameters (suspension flow rate, drying gas temperature, drying time, dispersion conditions, spray mesh size).

**2. Methods**

MSN with controlled properties (pore and particle diameter) were first synthesized with a semi-continuous sol-gel process. Then, the drug loading was performed using the Nano Spray Dryer B-90 (Büchi) [6]. An ultrasonic processor was used to facilitate the drug dissolution and the MSN dispersion. Several characterization techniques allowed improving the knowledge of the properties of the MSN and of the final carriers. Microscopic techniques (TEM, SEM) reveal the aspect of the material. The use of physico-chemical characterizations gives access to many information about the final product: DLS (MSN diameter), SAXS (porous organization), N2 adsorption (specific area, pore diameter). The combination of different solid-state (SS) techniques informs about the physical state and the drug-silica interactions (TGA, XRD, SS NMR). Complementary and multi-scale characterization techniques permit a real understanding of the parameters influence on loaded-particles properties.

**3. Results and discussion**

As an example, the results for the influence of the Ibu:Si weight ratio are presented here. The presence of crystalline ibuprofen on dried powder from R=40:60 to 100:0 was shown with XRD patterns and confirmed by TGA (which quantifies the amount of crystalline and amorphous solid). SS NMR revealed information about its mobility (solid or liquid-like) and its interaction with silica according to the Ibu:Si ratio. SEM and TEM observations suggested a conservation of the MSN matrix, but the MSN agglomerates did not have the same shape according to the Ibu:Si ratio, and the crystals shown by XRD seemed to be outside of the pores at R=75:25 (Figure 1). The pore and crystal sizes confirmed the impossibility for crystalline ibuprofen to be inside the pores [7]. SAXS and N2 adsorption gave a decreasing trend of peak intensities (SAXS), surface area, pore volume and pore diameter (N2 adsorption) as the Ibu:Si ratio increased, suggesting a loading of the active substance inside the pores of the MSN.



**Figure 1.** SEM images (x10k) of agglomerates with different R: 0:100 (a), 25:75 (b), 50:50 (c), 75:25 (d)

|  |  |  |  |
| --- | --- | --- | --- |
| **Sample (R=Ibu:Si)** | **Specific area (m2.g-1)** | **Pore volume (cm3.g-1)** | **Pore diameter (nm)** |
| **MSN** | 777 | 0.727 | 3.08 |
| **20:80** | 477 | 0.357 | 2.19 |
| **35:65** | 80 | 0.098 | 2.19 |

**Table 1.** Structural information determined by Nitrogen Adsorption

The combination of all these characterization techniques indicates links between the ibuprofen location (in or out of the pores) and its physical state (crystalline, amorphous, liquid-like). The other operating parameters had also an effect on the size of the particles and the ibuprofen loading.

**4. Conclusions**

The plentiful techniques permit to reveal that the drug is loaded firstly in the pores, and has been found in different states which are related to the localization inside the system (inside or outside the pores of the MSN). The Ibu:Si ratio influences drastically the agglomerate structure and the physical state of the substance. Afterwards, the effect of the parameters on the end-used properties like drug release kinetic will also be studied.

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