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## Large pore mesoporous silica (LPMS) suitable for therapy application in the drug delivery of unconventional large molecules

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Cancer is a leading cause of death worldwide, with 10 million deaths every year. The research dealing with its treatment is ever increasing.

The research has found in silica-based materials an interesting candidate in theranostic applications, due to silica biocompatibility and biosecurity [1].

The synthesis of mesoporous silica-based compounds, suitable for the encapsulation of theranostic substances and their delivery, has attracted a lot of interest in the last decades.

With respect to the classical silica-based materials [2], which present a porous structure in a dimension range between 2 and 5 nm, in this work we focus our effort on the synthesis of LPMSs with a porosity ranging from 30 to 60 nm (Figure 1). The aim of this work is to synthesize structures that present large pores, in order to insert inside them unconventional large therapeutic molecules (i.e. antitumoral proteins, antimicrobial, peptides).

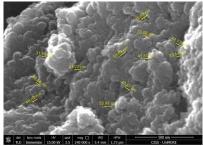


Figure 1: Pore dimensions in LPMS

The synthesis followed a hydrothermal mechanism, starting from an acidic water solution of TEOS (tetraethyl orthosilicate, the precursor of the silica structure), a surfactant (P123 or F127, precursors of the pore structure) and TMB (additive to the pore agent). The synthesis is MW assisted, and a time optimization has been performed.

Surfactants studied differ from the poly(ethylene oxide) lateral chain, that for F127 is fifth time longer.

Different ratios among TEOS and surfactants have been studied, finding a linear relationship between the amount of surfactant and pore dimensions (Figure 2), and confirming that F127 is a better surfactant for our scopes due to the higher average pore dimension obtained with the latter.

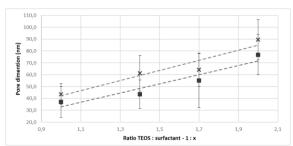


Figure 2: Relationship between pore dimensions and ratio TEOS: surfactant

In parallel, doped LPMS have been synthesized, including inside the structure different metal ions to achieve a synergic effect between the drug loaded inside the structure and the ions. Metal ions consider was: Ca<sup>2+</sup> that has an osteogenic activity and/or Ga<sup>3+</sup> that has an anticancer activity. Also in these cases, large pores have been achieved.

Loading tests have been performed using nisin as a reference molecule, a polycyclic antibacterial peptide. The dimensions of a non-hydrate molecule are in the range of 4-6 nm.

Comparing the loading efficiency of LPMSs instead of classical silica-based glasses, positive results have been reached; the loading efficiency of large molecules inside LPMS is far superior compared to classical structures.

<sup>[1]</sup> M. Gisbert-Garzarán, M. Vallet-Regí. Redox-Responsive Mesoporous Silica Nanoparticles for Cancer Treatment: Recent Updates. Nano. 2021, 11, 2222.

<sup>[2]</sup> V. Nicolini, G. Malavasi, G. Lusvardi, A. Zambon, F. Benedetti, G, Cerrato, S. Valeri, P. Luches. Mesoporous bioactive glasses doped with cerium: Investigation over enzymatic-like mimetic activities and bioactivity. Ceram. Int. 2019, 45, 20910-20920.