

TARGETED DRUG DELIVERY SYSTEMS BASED ON CHITOSAN OBTAINED BY SIMPLE AND DOUBLE EMULSIONS

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Abstract:

Drug carriers for pulmonary applications have become a popular topic and various polymer particulated systems have been investigated. This communication is focused on the preparation of two types of drug delivery systems, i.e. microspheres and microcapsules, obtained by using two different preparation methods, i.e simple W/O emulsion and double O/W/O emulsion.

The first part of this presentation is related to the preparation of peptides-functionalized microspheres (MSs), by the inverse emulsion (W/O) method, based on carboxymethyl chitosan (CMCS) and poly(vinyl alcohol) (PVA) and loaded with an anti-inflammatory model drug, Dexamethasone phosphate, as illustrated in Figure 1a.

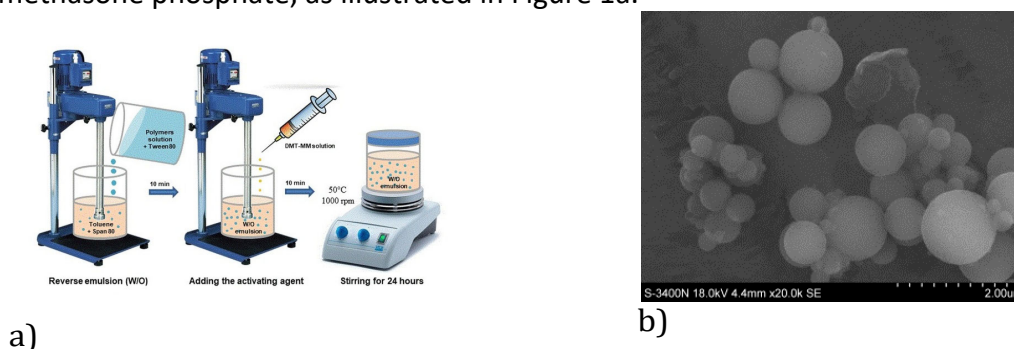
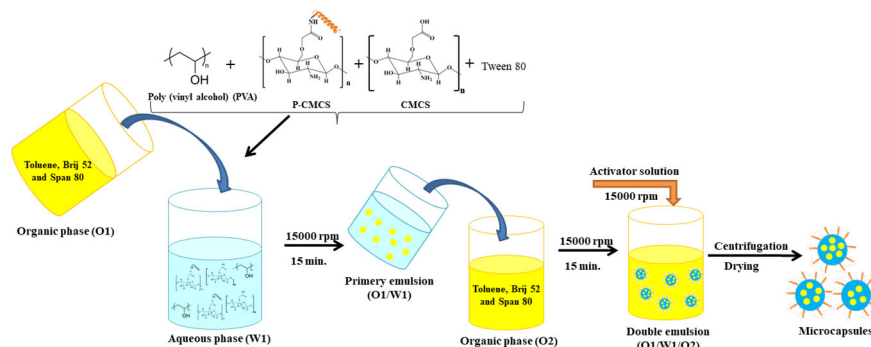


Figure 1. a) Schematic representation for the preparation method and b) SEM microscopy of MSs

The particles obtained were characterized by well-defined spherical shapes, and the average diameter was between 720 and 1150 nm, as shown in Figure 1b. Moreover, a direct correlation between the particle size and the initial amount of CMCS was established. Furthermore, the drug release in the weak alkaline environment that mimics the blood environment was influenced by the swelling degree of the particles. Finally, these peptides-functionalized MSs showed antibacterial properties against *Staphylococcus aureus* and *Escherichia Coli*.

In the second part of the communication, it will be presented the preparation of microcapsules (MCs), by a double O/W/O emulsion method (Figure 2), using as starting materials the

previously used polymers: poly(vinyl alcohol) (PVA), carboxymethyl chitosan (CMCS) and peptide-functionalized carboxymethyl chitosan. In view of their potential applications for the treatment of lung diseases, the same model drug, Dexamethasone, was used.



The colloidal properties of these microcapsules were highly influenced by the ratio between the two polymers. The sizes of obtained particles varied between 0.8 and 1.5 μm whereas the zeta potential values ranged from -16.9 mV to -24.8 mV, indicating a good stability in aqueous solutions. Moreover, it was demonstrated that the microcapsules show a high swelling degree in solutions that mimic the physiological environment (PBS, pH=7.4) and are hemocompatible. Evaluation of the impact of MCs on WI-38 normal human lung cells and RAW 264.7 mouse macrophages revealed a non-toxic or slightly cytotoxic effect. Internalization assay proved that microcapsules were localized at intracellular level.

These results demonstrate that the obtained drug delivery systems can be a safe alternative for the targeted treatment of pulmonary infections.

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