Polymeric nanoparticles for encapsulation of lipophilic drugs by coacervation method

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INTRODUCTION AND OBJECTIVE

In coacervation method, or phase separation, the active is dissolved or dispersed in a solution of polymeric material and the polymer is induced to separate like a viscous liquid phase by addition of a non-solvent. In the simple coacervation, the phase separation is induced by temperature change, pH change or adding a non-solvent water-miscible that can compete with the polymer by the solvent and remove it. The point of formation of coacervate, or phase separation, is manifested as turbidity, due to the formation of polymer droplet. The phase more rich in polymer is the coacervate and the other phase is the equilibrium solution (Kissel 2006).

In the simple coacervation, the addition of a non-solvent for polymer solution containing active cause the diffusion of solvent from the rich polymer phase to the non-solvent, which induce the molecules of polymer to deposit and aggregate. In simple coacervation there is only a polymer and complex coacervation there are two polymer of opposite charge in which interactions electrostatics are formed, however, it must have stoichiometry of charge (Dong 2006; Prata 2008).

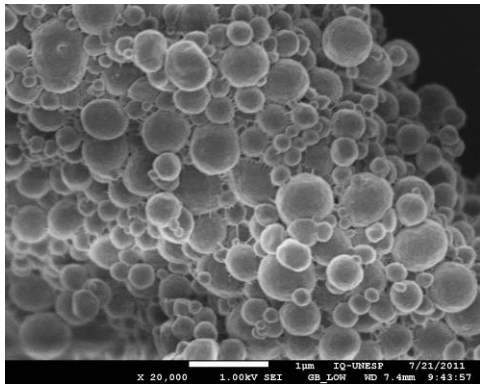
Coacervation is a method suitable for encapsulating lipophilic drugs, because it increases its low oral availability. The objective of this study was the synthesis of particles enteric from Eudragit® L-100 to encapsulate Ibuprofen (IBP) by simple coacervation method, varying the type and concentration of stabilizers polymer of droplets.

MATERIALS AND METHODS

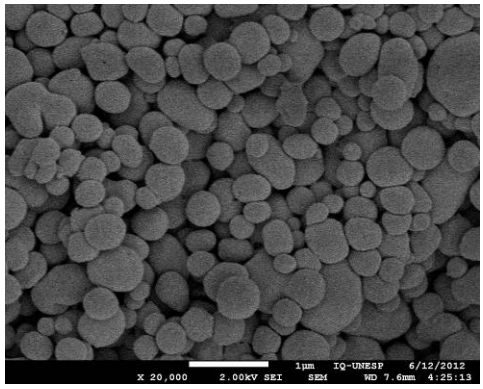
Nano and microparticles were obtained by the method of simple coacervation, according to Dong (Dong 2006) and adapted. Aqueous polymeric solutions are prepared by solubilization of hydrophilics polymer in water: HPMC in water (2% w/w) and systems CMC/HPMC (2% w/w 1:1) in water. An organic polymer phase is prepared by solubilization of Eudragit® L100 in ethanol (20% w/w). To synthesize nano and microparticles, the aqueous polymer is added dropwise into the organic polymer phase, with and without the drug, under magnetic stirring in 1000 rpm. IBP is previously dissolved in Eudragit® L100 organic polymer phase (30% w/w based on total dry mass). A turbid viscous solution containing the microparticles is formed and then it added water under stirring to phase separation and hardening of the particles. Water is a nonsolvent for the hydrophobic polymer, causing phase separation and formation of the coacervate. The particles formed are collected by centrifugation (3000 rpm, 15 min) and vaccum dried at 50°C for 72 h. The micro and nanoparticles were characterized by FEG-SEM and XRD.

RESULTS AND DISCUSSION

The micrographs show the morphology of the nanoparticles with HPMC as stabilizer, without IBP (Fig. 1a) and loaded with IBP (Fig. 1b) and microparticles with CMC/HPMC as stabilizer without IBP (Fig. 3a) and loaded with IBP (Fig. 3b).



(a)



(b)

Fig. 1 - Micrographs of nanoparticles with HPMC as stabilizer of droplets a) without IBP, b) loaded with IBP.

The stabilizers polymer type and concentration altered the morphology and size particle. Using only HPMC as a stabilizer in droplets, the particles were smaller and showed a more defined morphology and a size distribution clearly better than when was used HPMC/CMC.

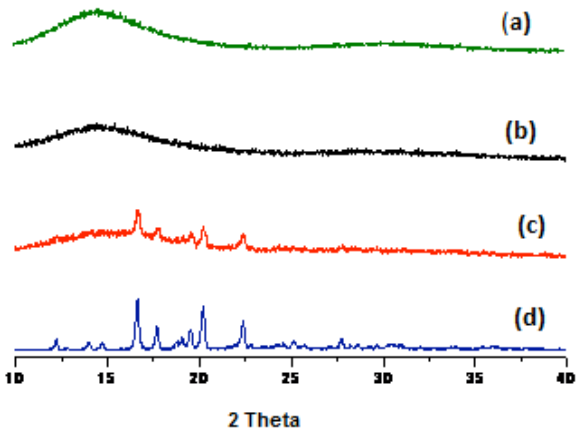
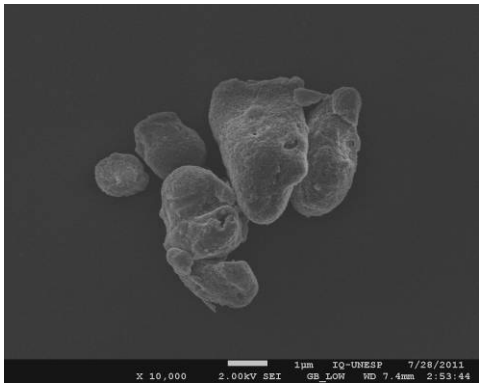
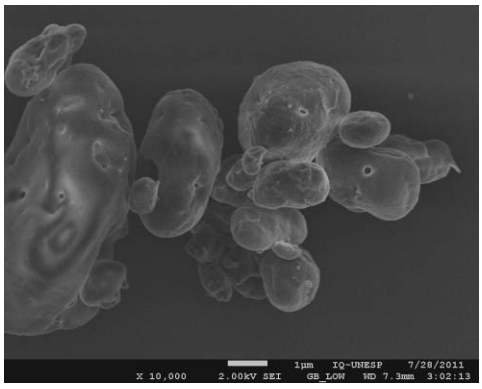


Fig. 2 – XRD curves of the microparticles with HPMC as stabilizer of droplets a) Eudragit® L100 b) Eudragit® L100 nanoparticles , c) Eudragit® L100 nanoparticles loaded with IBP, d) IBP pure.

The XRD results indicated that probably the IBP was encapsulated in a state crystalline in both, nano and microparticles (Fig. 2 curve c and Fig. 4 curve c). That was probably due to the limited solubility of IBP in Eudragit® L100 solution. If the solubility of the drugs in the polymer solution is low, the excess may be crystallized inside or outside the polymeric matrix. Tests with lower concentrations of drug are necessary to confirm.



(a)



(b)

Fig. 3 - Micrographs of microparticles with HPMC/CMC as stabilizer of droplets a) without IBP, b) loaded with IBP

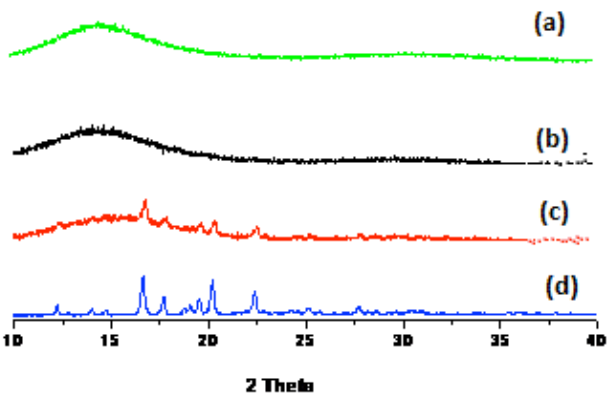


Fig. 4 – XRD curves of the microparticles with CMC/HPMC as stabilizer of droplets a) Eudragit® L100 pure b) Eudragit® L100 microparticles, c) Eudragit® L100 microparticles loaded with IBP, d) IBP pure.

CONCLUSIONS

Through these results, we concluded that enteric micro and nanoparticles can be obtained from Eudragit® L100 and to encapsulate drugs in them using the simple coacervation method The variation of parameters such as type and concentration of polymer stabilizers of droplets caused changes in morphology and particle size

ACKNOWLEDGMENTS

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