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CONTROLLING THE PARTICLE SIZE OF LIPID-CORE NANOCAPSULES PREPARED BY INTERFACIAL DEPOSITION OF POLYMER

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Introduction: The control of drug release has been the subject of numerous studies, those have being focused on the optimization of drug rate release and dosing regimen of substances using delivery carriers. Among these carriers, polymeric nanoparticles have attracted more attention, due to their potential to increase the therapeutic benefits of drugs. To ensure the nanotechnological characteristics of such formulations, the study of the influence of the parameters of formulation and process on the size and polydispersity of particles becomes very important.
Objective: Study the parameters of formulation and process influencing size and polydispersity of polymeric lipid core nanocapsules.
Materials and Methods: The formulations were prepared by interfacial deposition of preformed polymers, taking as a starting formulation that consisting of 0.1000 g of poly(epsilon-caprolcatone) (PCL), 0.0385 g of sorbitan monostearate (SM) and 0.1580 mL of capric/caprylic triglycerides (CCT) in organic phase and 0.0770 g of polysorbate 80 in aqueous phase. From this, the polymer amount in formulation was varied from 0.0100 to 0.3500 g (or 0.4-14 mg/mL of organic phase), accompanied by a linear increase in the concentration of all other components of the organic phase rendering constant the proportions of 1.00:0.38:1.35 of SM, CCT and PCL respectively. For comparisons and analysis, the concentration of polymer was used as a reference control. The viscosity of the organic phase was measured using a vibrational viscometer (SV-10, A&D Company, Japan). The surface tension of the different organic phases was determined by the Wilhelmy plate method using a tensiometer DCAT 11 (Dataphysics, Germany). Formulations were characterized in terms of size and polydispersity (Zetasizer and Mastersizer, Malvern).
Results and Discussion: Considering that the self-assembling to produce the nanocapsules is driven by the Marangony effect, the surface tension could be an important parameter to control the mean size of the particles. Despite the increase of the organic component concentrations in the organic phase, no changes were observed in the surface tension, in this way, the hypothesis formulated was refuted. On the other hand, a linear correlation was obtained plotting the final particle diameter and the concentration of the components in the different organic phases and plotting the viscosity values as a function of the particle diameter. These results corroborated the previous reports showing that the control of the mean particle size is a consequence of the viscosity of the organic phase. The size distributions for formulations prepared with polymer concentration of 0.4 to 4.0 $mg.mL^{-1}$ showed monomodal distributions, whereas the size distributions for formulations obtained with polymer concentrations of 10 and 14 $mg.mL^{-1}$ demonstrated micrometric population besides the nanometric range. Considering that the control of the mean diameter and polydispersity of the lipid-core nanocapsules could be related to the degree of aggregation in the organic phase, the viscosity of the organic phase was plotted as a function of the logarithm of the polymer concentration. The critical aggregation concentration in the organic phase was 4 $mg.mL^{-1}$. The results clearly showed for the first time that nanoparticles are formed in monomodal size distributions when the degree of aggregation is low in the organic phase before nanoprecipitation. The size distribution of lipid-core nanocapsules is control using the proportions of 1.00:0.38:1.35:0.77 of PCL, SM, CCT and polysorbate 80, respectively, in the organic and aqueous phase respecting concentrations below the critical aggregation concentration.
Conclusions: Polymer concentration higher than 4 $mg.mL^{-1}$ in the organic phase (above the critical molecular aggregate concentration) do not allow the control of the size of such formulations at the nanoscale. Furthermore, values below the critical aggregation concentration of the organic components, besides maintaining the nanoscale properties, also allow the control of the diameter range of nanoparticles.
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