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DEVELOPMENT OF LIPID-CORE NANOCAPSULES CONTAINING RESVERATROL+CURCUMIN: AN INITIAL APPROACH

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Introduction: Phenolic compounds have attracted considerable interest for their beneficial effects for human health. In this context, resveratrol and curcumin exhibits various biological and pharmacological activities, including antioxidants and antitumoral activities, anti-inflammatory properties and cardiovascular protective effects[1,2]. Previous studies in the literature showed a synergic effect with the co-administration of resveratrol and curcumin[3]. However, their clinical application has been limited due to poor aqueous solubility, low bioavailability and susceptibility to the photodegradation[4,5]. In order to overcome these limitations, the association of resveratrol and curcumin to drug delivery systems represents an interesting strategy.
Objective: The aim of this study was to optimize lipid-core nanocapsule suspensions containing the association of resveratrol and curcumin, regarding the control of the particle size distribution at the nanoscale.
Materials and Methods: Lipid-core nanocapsules (LCNC) containing the association of resveratrol and curcumin (RC-LCNC) were prepared at different concentrations of each polyphenol (2.0, 1.0 and 0.5 mg mL^{-1}). The oily core was composed of caprylic/capric triglyceride mixture and sorbitan monostearate. Resveratrol-loaded lipid-core nanocapsules (R-LCNC) and curcumin-loaded lipid-core nanocapsules (C-LCNC) at 1.0 mg mL^{-1} of the polyphenol were prepared using the following oils: caprylic/capric triglyceride mixture (CCM), grape seed oil (GSO) and a mixture of grape seed oil and castor oil (GSO:CO 1:1 w/w). The aqueous phase (adjusted to pH 4.5-5.0 with 0.5% citric acid) of all formulations consisted of an aqueous dispersion of polysorbate 80. All formulations were prepared by the interfacial deposition of the preformed polymer method[6] using poly(ε-caprolactone) as a biodegradable polymer (1 %). Particle size distribution was determined by light diffraction considering the volume (%) of the particles. Formulations presenting the size distribution only at the nanoscale were further characterized by photon correlation spectroscopy (particle size and polydispersity index). In addition, the zeta potential was estimated for each formulation.
Results and Discussion: Although RC-LCNC prepared with CCM presented nanometric particle size distribution, its size distribution also presented particles at the microscale. This phenomenon could be related to presence of drug crystals due to the overconcentration of the drugs in the formulation. In order to determine if one of the substances presents a more contribution to these micrometric particles, we prepared lipid-core nanocapsules containing each substance separately. R-LCNC prepared with different oils did not show a micrometric population. These formulations presented a mean particle size between 209 and 256 nm, low polydispersity index (below 0.2) and negative zeta potential (-9.3 – -16.9 mV). On the other hand, C-LCNC presented micrometric particles, regardless of the type of the oil. Blank formulations prepared with CCM, GSO and the mixture of GSO:CO (1:1 w/w) presented mean particle size of 235 nm, 254 nm and 238 nm, respectively, polydispersity index lower than 0.2 and negative zeta potential (-9.9 – -14.2 mV).
Conclusions: Our study showed the need to optimize the concentration of both substances (resveratrol and curcumin) in lipid-core nanocapsules in order to obtain an adequate control of their particle size distribution. Curcumin showed a higher contribution to the presence of particles at the microscale. Studies are in progress to evaluate the loading of lower amount of curcumin in nanocapsules.

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