TFC029

Evaluation of emulsion solvent evaporation method as an approach to produce nanoparticles of Polycaprolactone containing ursolic acid

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Introduction: Preliminary studies have shown that ursolic acid (UA), a natural compound, presents important pharmacological properties, such as trypanocidal activity. However, it has low water solubility, which reduces its bioavailability. Among the existing drug delivery systems, polymeric nanoparticles (NPs) play a central role, due to their ability to sustain or control the release of drugs. Moreover, nanocoated systems are distinguished by high drug encapsulation efficiency, protection from degradation, and less likely to cause irritation due to their polymeric coating. **Objective:** To produce NPs containing UA and evaluate the process efficiency. **Methods:** NPs were prepared using an oil-in-water emulsion solvent evaporation technique (ESE). Briefly, 500mg of Polycaprolactone (PCL) were dissolved in 20mL of dichloromethane containing 10mg of UA (Solution 1). Solution of polyvinyl alcohol (PVA) was prepared in water (Solution 2). Solution 1 was added to 40 mL of solution 2. The resulting mixture was then placed in ice bath and emulsified using a ultra-turrax at 13,000 rpm at specific time. Another portion of 40 ml of solutions 2 was added to the emulsion. The final solution was stirred for 20 hours at 600 rpm on a magnetic stir plate to allow the solvent evaporation and formation of NP. The resulting suspension was centrifuged at 4800g for 20'. NPs were ressupended in water and submitted to three centrifuge cycles of 1220g for 20´each. NPs were collected and frozen at -20°C for at least 2 hours and then lyophilized for 24 hours. Two variables were analyzed in order to obtain a particle size in the nanometer range for intravenous administration, the stirring time and the PVA concentration. The obtained formulations were named: UAPC-01 (solution PVA 2% and stirring time of 30'), UAPC-02 (solution PVA 2% and stirring time of 1 hour), UAPC-03 (solution PVA 2% and stirring time of 2 hours), and UAPC-04 (solution PVA 2,25% and stirring time of 1 hour). The systems were evaluated by yield process and particle size distribution by light scattering. **Results:** The formulations UAPC-01, UAPC-02, UAPC-03, UAPC-04 presented a mean particle size, respectively, equivalent to 44,71 µm, 15,01 µm, 29,38 µm and 9,108 µm. These formulations presented, respectively, the following values of yield process: 63,21%, 63,21%, 37,60% and 63,80%. **Conclusion:** the emulsion solvent evaporation method with Polycaprolactone as carrier proved to be unable to produce nanoparticles containing ursolic acid. However, higher concentrations of the surfactant polyvinyl alcohol apparently decreased the particle size of the system. Moreover, higher stirring time did not decrease particle size, but resulted in decreased yield process values.

Keywords: Drug delivery systems, ursolic acid, Polycaprolactone, emulsion/solvent evaporation.

Financial support: FAPESP, CAPES