TFC054

Solid dispersions containing Poloxamer 407 and Sodium Caprate as a strategy to produce amorphous Ursolic Acid

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Introduction: Ursolic acid (UA) is a natural triterpene that presents promissing pharmacological activities, such as antiinflammatory, anticancer and trypanocidal. However, this molecule presents poor water solubility, which is a limiting factor for the bioavailability. Among the strategies commonly employed to enhance water solubility of lipophilic drugs, solid dispersions have gained considerable attention lately and can be defined as crystalline, molecular or amorphous dispersion a lipophilic drug in a hydrophilic carrier, with resultant enhancement in solubility and dissolution profile of the drug. Therefore, it is of paramount importance to determine the organization of the drug in solid dispersion, if molecular, crystalline or amorphous, which has a very important contribution on water solubility. Compared to the crystalline state, amorphous particles are more soluble, because there is no crystal lattice to be broken during the dissolution process. Within this context, it also very important to choose carriers that may enhance the dissolution profile of the drug to a great extent, and surfactants such as Poloxamer 407 (P407) and Sodium Caprate (SC) are good candidates because of possible micellar solubilization. **Objective:** We aim to characterize solid dispersions (SDs) and physical mixtures (PMs) through Fourier Transform Infrared Spectroscopy (FTIR) and X-ray diffractometry (XRD) to determine if UA remains crystalline or was converted to the amorphous state in SDs. **Methods:** SDs prepared at the ratio 1:1:5, 1:2:5 and 1:5:5 (respectively, UA, P407 and SC, w/w) were produced employing the solvent method, where the raw materials were solubilized in methanol (1:10, w/v), evaporated under stirring at 40ºC, and the solid mass was ground with mortar and pestle to produce solid particles. PMs, containing the same ratio described for SDs, were obtained by simple mixture of drug and carriers. FTIR spectra were obtained by compressing potassium bromide and sample, followed by scanning, from 4000 to 400 cm^{-1}. XRD measurements of samples were performed with a copper anode operated at CuK radiation, = 1,5406nm, 40kV and 30mA, using a step width of 0,05°/s over a range of 2° and 50° at room temperature on a 2θ scale. **Results:** Among several distintic bands, UA FTIR espectrum revelead a band at approximetely 1700 cm^{-1}, which was broadened and less intense compared to pure UA or UA in PMs. This band is characteristic of a carbonyl stretching and was broadened because of possible conversion of UA to the amorphous state or because of intermolecular interaction by hydrogen bonding with the hydroxil of carriers. XRD showed the crystalline pattern of pure UA, presenting peaks at 4º, 8º and 14º on a 2θ scale. These peaks were preserved in PMs, but were considerably less intense in SDs, which is a clear indication of the conversion of UA from a crystal to an amorphous particle. **Conclusion:** The physicochemical characterization of UA in SDs and PMs clearly showed that the drug was converted to the amorphous state and remained crystalline in PMs. The impact of this change on water solubility will be investigated in further studies.

Keywords: Ursolic Acid, Poloxamer 407, Sodium Caprate, Solid Dispersions, Solubility, Amorphous State.

Financial support: CAPES (Coordenação de Aperfeiçoamento de Pessoal de Nível Técnico).