Preparation of inclusion complexes containing different active principles by supercritical antisolvent process

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The rate of absorption of orally-administered drugs is controlled by their rate of dissolution in water. However, most active principle ingredients (API) are poorly water-soluble, so high dosages are necessary to achieve a therapeutic concentration in the plasma, resulting in severe side effects on patient's health, mainly gastrointestinal ones. A common route to improve the bioavailability of poorly water-soluble drugs is to use a hydrophilic polymeric carrier to produce microcapsules, microspheres or inclusion complexes. In the pharmaceutical field, cyclodextrins (CDs) reveals to be particularly promising to enhance the drug dissolution rate thanks to the peculiar characteristics of CDs, characterized by a hydrophilic external surface and a hydrophobic internal cavity, which can hold drug molecules of proper size and hydrophobicity. In this way, *guest-host* inclusion complexes can be produced by non-covalent interactions (hydrophobic bonds, hydrogen bonds, van der Waals forces). In addition, CDs stabilize and protect the active principle incorporated in the cavity and also mask unpleasant odor and taste, so optimizing patient compliance.
In this work, inclusion complexes were prepared by coprecipitating two antinflammatory drugs, namely nimesulide (NIM) and ketoprofene (KET) and two antioxidants, namely rutin (RUT) and luteolin (LUT), with β-cyclodextrin (β-CD) by Supercritical AntiSolvent (SAS) technique. The effect of some operating conditions was investigated to ensure the attainment of composite microparticles with controlled dimensions. The formation of inclusion complexes with different API/β-CD molar ratios was demonstrated by Fourier transform infrared (FT-IR) spectroscopy and differential scanning calorimetry (DSC). The drug dissolution rate was definitely enhanced. SAS coprecipitation was effective to form inclusion complexes containing APIs for an accelerated release. These results are relevant since the pharmaceutical market requires new formulations to provide the best release profiles with a reduced amount of polymer, thus improving patients' compliance.