DISSOLUTION ENHANCEMENT OF MEFENAMIC ACID USING SOLID DISPERSIONS OBTAINED BY WET GRANULATION TECHNIQUE

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A significant number of active pharmaceutical ingredients, including anti-inflammatory ones, have low solubility in water, which negatively affects their bioavailability and therapeutic effectiveness. Therefore, many anti-inflammatory drugs have large dosages. One of the most promising options for overcoming this problem is the use of solid dispersion systems (SDS), in which pharmaceutically acceptable polymers can capture molecules of the active substance, forming certain chemical bonds with them and forming a new, more amorphous structure. An amorphous solid dispersion of the active substance and a hydrophilic polymer demonstrates better wettability, water absorption capacity and porosity, which results in enhancement drug dissolution. Mefenamic acid (MA), a BCS class II drug, displays high permeability and low solubility, thereby exhibiting a poor dissolution profile. Thepurpose of this research was to obtain enhancement of the dissolution profile using solid dispersion obtained by wet granulation technique. To obtain SDS, such methods as the solvent evaporation method, spray drying, hot melt extrusion, co-milling, co-grinding, high-energy mixing (KinetiSol) are generally accepted and the most widespread. At the same time, along with the above-mentioned methods, it is promising to study the possibility of using wet granulation methods common in the pharmaceutical industry, such as fluid bed granulation and high shear granulation. SDS were produced by wet granulation using GPCG 2 Lab Systems Fluid Bed Dryer, Glatt, Germany and Vertical Lab Granulator VG 65/10, Glatt, Germany. The ratio of MA to polyvinylpyrrolidone (PVP K17) and to hydroxypropylmethylcellulose (HPMC) is 1:20. The dissolution of SDS was determined by spectrophotometry as the amount of MA that passed into the solution in 30 minutes with stirring, wavelength 282 nm, purified water was used as a reference solution. The dissolution medium is water, temperature (37±0.5) °C. Differential Scanning Calorimetry (DSC), Fourier Transform Infrared Spectroscopy (FTIR) were performed to characterize the obtained solid dispersions and to identify the physicochemical interaction between drug and polymer carrier, hence its effect on dissolution. Also optical microscopy was performed to study the morphology of the obtained particles, including because the pharmaco-technological characteristics of SDS very important for the prospect of their further use for finished dosage form (tablets, capsules, granules, sachet). Wet granulation methods make it possible to obtain SDS with MA and significantly improve its dissolution. SDS of MA and HPMC produced by wet granulation using high shear technology and fluidized bed technology show an enhancement in dissolution by 8.60 and 9.46 times, respectively. At the same time, SDS with PVP K17 do not demonstrate improved dissolution compared to pure MA. Such results are promising for further more detailed discussion and research.

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