

Optimizing Famotidine Solubility by Co-amorphization with Succinic Acid †

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Abstract: Famotidine (FMT) is a histamine H₂-receptor antagonist that competitively inhibits the action of histamine on parietal cells reducing gastric acid secretion. FMT is the 2019 125th most prescribed drug in the USA. Since it belongs to class IV (low solubility–low permeability) in the Biopharmaceutical Classification System, different strategies have been performed to overcome this issue. Among these, co-amorphous systems exhibit a significant increase in drug dissolution and improved physical stability compared to single amorphous phases. In this work, we report an FMT – succinic acid (1:1 molar relationship) co-amorphous of improving FMT solubility. High-energy mechanical activation for 60 minutes was employed for its preparation. The diffraction powder pattern and differential scanning calorimetry curves account for its amorphous nature. The interactions involving the main functional groups of FMT and the co-former were revealed by Fourier transform infrared spectroscopy and supported by density functional theory and quantum theory of atoms in molecules analysis. Solubility measurements in distilled water and simulated gastric fluid and stability assays were conducted. The results are compared with those obtained for the previously reported FMT – malic acid co-amorphous. The vitreous phase, prepared by a green method, presents increased solubility and, therefore, optimized pharmacokinetics than the parental drug.

Keywords: Famotidine; low solubility; co-amorphous

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Conflicts of Interest

The authors declare no conflict of interest.