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Enhanced Kinetic Solubility Profile of Epiisopiloturine Solid Solution in Hipromellose Phthalate

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Abstract : Epiisopiloturine (EPI) is a drug candidate that is extracted from Pilocarpus microphyllus and isolated from the waste of Pilocarpine. EPI has demonstrated promising schistosomicidal, leishmanicide, anti-inflammatory and antinociceptive activities, according to in vitro studies that have been carried out since 2009. However, this molecule shows poor aqueous solubility, which represents a problem for the release of the drug candidate and its absorption by the organism. The purpose of the present study is to investigate the extent of enhancement of kinetic solubility of a solid solution (SS) of EPI in hipromellose phthalate HP-55 (HPMCP), an enteric polymer carrier. SS was obtained by the solvent evaporation methodology, using acetone/methanol (60:40) as solvent system. Both EPI and polymer (drug loading 10%) were dissolved in this solvent until a clear solution was obtained, and then dried in oven at 60ºC during 12 hours, followed by drying in a vacuum oven for 4 h. The results show a considerable modification in the crystalline structure of the drug candidate. For instance, X-ray diffraction (XRD) shows a crystalline behavior for the EPI, which becomes amorphous for the SS. Polarized light microscopy, a more sensitive technique than XRD, also shows completely absence of crystals in SS sample. Differential Scanning Calorimetric (DSC) curves show no signal of EPI melting point in SS curve, indicating, once more, no presence of crystal in this system. Interaction between the drug candidate and the polymer were found in Infrared microscopy, which shows a carbonyl 43.3 cm-1 band shift, indicating a moderate-strong interaction between them, probably one of the reasons to the SS formation. Under sink conditions (pH 6.8), EPI SS had its dissolution performance increased in 2.8 times when compared with the isolated drug candidate. EPI SS sample provided a release of more than 95% of the drug candidate in 15 min, whereas only 45% of EPI (alone) could be dissolved in 15 min and 70% in 90 min. Thus, HPMCP demonstrates to have a good potential to enhance the kinetic solubility profile of EPI. Future studies to evaluate the stability of SS are required to conclude the benefits of this system.

Keywords : epiisopiloturine, hipromellose phthalate HP-55, pharmaceuticaltechnology, solubility
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