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Development and Obtaining of Solid Dispersions to Increase the Solubility of Efavirenz in Anti-HIV Therapy

Authors : Salvana P. M. Costa, Tarcyla A. Gomes, Giovanna C. R. M. Schver, Leslie R. M. Ferraz, Cristovão R. Silva, Magaly A. M. Lyra, Danilo A. F. Fonte, Larissa A. Rolim, Amanda C. Q. M. Vieira, Miracy M. Albuquerque, Pedro J. Rolim-neto

Abstract : Efavirenz (EFV) is considered one of the most widely used anti-HIV drugs. However, it is classified as a drug class II (poorly soluble, highly permeable) according to the biopharmaceutical classification system, presenting problems of absorption in the gastrointestinal tract and thereby inadequate bioavailability for its therapeutic action. This study aimed to overcome these barriers by developing and obtaining solid dispersions (SD) in order to increase the EFZ bioavailability. For the development of SD with EFV, theoretical and practical studies were initially performed. Thus, there was a choice of a carrier to be used. For this, it was analyzed the various criteria such as glass transition temperature of the polymer, intra- and intermolecular interactions of hydrogen bonds between drug and polymer, the miscibility between the polymer and EFV. The choice of the obtainment method of the SD came from the analysis of which method is the most consolidated in both industry and literature. Subsequently, the choice of drug and carrier concentrations in the dispersions was carried out. In order to obtain DS to present the drug in its amorphous form, as the DS were obtained, they were analyzed by X-ray diffraction (XRD). SD are more stable the higher the amount of polymer present in the formulation. With this assumption, a SD containing 10% of drug was initially prepared and then this proportion was increased until the XRD showed the presence of EFV in its crystalline form. From this point, it was not produced SD with a higher concentration of drug. Thus, it was allowed to select PVP-K30, PVPVA 64 and the SOLUPLUS formulation as carriers, once it was possible the formation of hydrogen bond between EFV and polymers since these have hydrogen acceptor groups capable of interacting with the donor group of the drug hydrogen. It is worth mentioning also that the films obtained, independent of concentration used, were presented homogeneous and transparent. Thus, it can be said that the EFV is miscible in the three polymers used in the study. The SD and Physical Mixtures (PM) with these polymers were prepared by the solvent method. The EFV diffraction profile showed main peaks at around 2θ of 6,24°, in addition to other minor peaks at 14,34°, 17,08°, 20,3°, 21,36° and 25,06°, evidencing its crystalline character. Furthermore, the polymers showed amorphous nature, as evidenced by the absence of peaks in their XRD patterns. The XRD patterns showed the PM overlapping profile of the drug with the polymer, indicating the presence of EFV in its crystalline form. Regardless the proportion of drug used in SD, all the samples showed the same characteristics with no diffraction peaks EFV, demonstrating the behavior amorphous products. Thus, the polymers enabled, effectively, the formation of amorphous SD, probably due to the potential hydrogen bonds between them and the drug. Moreover, the XRD analysis showed that the polymers were able to maintain its amorphous form in a concentration of up to 80% drug.

Keywords : amorphous form, Efavirenz, solid dispersions, solubility
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