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Characterization and Evaluation of the Dissolution Increase of Molecular Solid Dispersions of Efavirenz

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Abstract : Efavirenz (EFV) is a drug used as first-line treatment of AIDS. However, it has poor aqueous solubility and wettability, presenting problems in the gastrointestinal tract absorption and bioavailability. One of the most promising strategies to improve the solubility is the use of solid dispersions (SD). Therefore, this study aimed to characterize SD EFZ with the polymers: PVP-K30, PVPVA 64 and SOLUPLUS in order to find an optimal formulation to compose a future pharmaceutical product for AIDS therapy. Initially, Physical Mixtures (PM) and SD with the polymers were obtained containing 10, 20, 50 and 80% of drug (w/w) by the solvent method. The best formulation obtained between the SD was selected by in vitro dissolution test. Finally, the drug-carrier system chosen, in all ratios obtained, were analyzed by the following techniques: Differential Scanning Calorimetry (DSC), polarization microscopy, Scanning Electron Microscopy (SEM) and spectrophotometry of absorption in the region of infrared (IR). From the dissolution profiles of EFV, PM and SD, the values of area Under The Curve (AUC) were calculated. The data showed that the AUC of all PM is greater than the isolated EFV, this result is derived from the hydrophilic properties of the polymers thus favoring a decrease in surface tension between the drug and the dissolution medium. In adittion, this ensures an increasing of wettability of the drug. In parallel, it was found that SD whom had higher AUC values, were those who have the greatest amount of polymer (with only 10% drug). As the amount of drug increases, it was noticed that these results either decrease or are statistically similar. The AUC values of the SD using the three different polymers, followed this decreasing order: SD PVPVA 64-EFV 10% > SD PVP-K30-EFV 10% > SD Soluplus®-EFV 10%. The DSC curves of SD's did not show the characteristic endothermic event of drug melt process, suggesting that the EFV was converted to its amorphous state. The analysis of polarized light microscopy showed significant birefringence of the PM's, but this was not observed in films of SD's, thus suggesting the conversion of the drug from the crystalline to the amorphous state. In electron micrographs of all PM, independently of the percentage of the drug, the crystal structure of EFV was clearly detectable. Moreover, electron micrographs of the SD with the two polymers in different ratios investigated, we observed the presence of particles with irregular size and morphology, also occurring an extensive change in the appearance of the polymer, not being possible to differentiate the two components. IR spectra of PM corresponds to the overlapping of polymer and EFV bands indicating thereby that there is no interaction between them, unlike the spectra of all SD that showed complete disappearance of the band related to the axial deformation of the NH group of EFV. Therefore, this study was able to obtain a suitable formulation to overcome the solubility limitations of the EFV, since SD PVPVA 64-EFZ 10% was chosen as the best system in delay crystallization of the prototype, reaching higher levels of super saturation.

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