Impact of the efavirenz polymorphism on the mechanical properties and dissolution assays

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The Human Immunodeficiency Virus (HIV) infection is a complex disease of slow and uncertain course that leads the individual to develop the acquired immunodeficiency syndrome (AIDS). In view of the complexity of the disease and the need for a chronic treatment of it, the improvement in the properties of drugs for the treatment of patients is increasing. Efavirenz (EFV), a major antiretroviral therapy agent, is the most commonly used non-nucleoside reverse transcriptase inhibitor (NNRIT) in highly active antiretroviral therapy (HAART) for the treatment of adults[1]. And as part of efforts to simplify and optimize first-line treatment, the World Health Organization (WHO) has recommended EFV as the first choice[2]. EFV is a Class II drug under the Biopharmaceutical Classification System, which has a low solubility and high permeability[3], and is therefore interested in the development of strategies to increase solubility and / or dissolution, as well as to control manufacturing processes such as compression which could modify critical parameters in the dissolution as the polymorphism, the morphology among others. The crystallization is one of the manufacturing processes that has the greatest impact on the dissolution of a drug. During this process, some physical-chemical parameters such as crystalline or polymorphic structure, morphology and particle size, microstructure, etc. are modified. In this work, the EFV solvent crystallization was carried out, varying solvents, temperatures, and agitation. Thus, they obtained 27 crystallized samples and from them were made physical-chemical analyzes to evaluate the impact of these samples in relation to the polymorphism, particle size, Hausner factor, Carr index in the compression of the drug, and all samples compared to the raw material. Thus, it was found that the compression performed, given the axial force applied to the tabletting had better result for Polymorph I tablets, as well as the hardness was also higher for these tablets. And finally, it evaluated the dissolution efficiency of the tablets formed by the compressor and having the highest rate of dissolution reached was by a tablet of Polymorph II, which showed a smoother-looking surface on the particles.

Keywords: efavirenz; crystallization; compression; mechanical properties.

References

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