

## Characterization of Polymorphic Forms of Rifaximin

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**Abstract :** Rifaximin is an oral antimicrobial, gut - selective and not systemic with adverse effects compared to placebo. It is used for the treatment of hepatic encephalopathy, travelers diarrhea, irritable bowel syndrome, *Clostridium difficile*, ulcerative colitis and acute diarrhea. The crystalline form present in the rifaximin with minimal systemic absorption is  $\alpha$ , being the amorphous form significantly different. Regulators are increasingly attention to polymorphisms. Polymorphs can change the form by altering the drug characteristics compromising the effectiveness and safety of the finished product. International Conference on Harmonization issued the ICH Guidance Q6A, which aim to improve the control of polymorphism in new and existing pharmaceuticals. The objective of this study was to obtain polymorphic forms of rifaximin employing recrystallization processes and characterize them by thermal analysis (thermogravimetry - TG and differential scanning calorimetry - DSC), X-ray diffraction, scanning electron microscopy and solubility test. Six polymorphic forms of rifaximin, designated I to VI were obtained by the crystallization process by evaporation of the solvent. The profiles of the TG curves obtained from polymorphic forms of rifaximin are similar to rifaximin and each other, however, the DTG are different, indicating different thermal behaviors. Melting temperature values of all the polymorphic forms were greater to that shown by the rifaximin, indicating the higher thermal stability of the obtained forms. The comparison of the diffractograms of the polymorphic forms of rifaximin with rifaximin  $\alpha$ ,  $\beta$  and  $\gamma$  constant in patent indicate that forms III, V and VI are formed by mixing polymorph  $\beta$  and  $\alpha$  and form III is formed by polymorph  $\beta$ . The polymorphic form I is formed by polymorph  $\beta$ , but with a significant amount of amorphous material. Already, the polymorphic form II consists of polymorph  $\gamma$ , amorphous. In scanning electron microscope is possible to observe the heterogeneity of morphological characteristics of crystals of polymorphic forms among themselves and with rifaximin. The solubility of forms I and II was greater than the solubility of rifaximin, already, forms III, IV and V presented lower solubility than of rifaximin. Similarly, the bioavailability of the amorphous form of rifaximin is considered significantly higher than the form  $\alpha$ , the polymorphic forms obtained in this work can not guarantee the excellent tolerability of the reference medicine. Therefore, studies like these are extremely important and they point to the need for greater requirements by the regulatory agencies competent about polymorphs analysis of the raw materials used in the manufacture of medicines marketed globally. These analyzes are not required in the majority of official compendia. Partnerships between industries, research centers and universities would be a viable way to consolidate researches in this area and contribute to improving the quality of solid drugs.

**Keywords :** electronic microscopy, polymorphism, rifaximin, solubility, X-ray diffraction

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