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Polymorphic stability study: The influence of storage conditions on the Moxifloxacin hydrochloride.

Tamíris Amanda Júlio*; Igor Fernando Zâmara; Jerusa Simone Garcia; Marcello Garcia Trevisan.

LACFar, Institute of Chemistry, Federal University of Alfenas, Alfenas, Minas Gerais, Brazil.
*tamirisaj@hotmail.com

Introduction: Polymorphism is the ability of a crystalline compound has to present two or more different molecular arrangements. The polymorphic stability of a drug substance is a very important topic in the pharmaceutical industry. The polymorphs exhibit significantly different pharmaceutical properties which can alter the stability of formulation and even influence in its pharmacological activity. Moxifloxacin hydrochloride (MOX) is a fourth generation synthetic fluoroquinolone antibacterial agent. This medication generally is prescribed to the patient in high doses (about 400 mg daily). Therefore it is important to monitor and investigate the formation of polymorphs which can be potential toxics and change bioavailability. Consequently, these events affect the safety and efficacy of MOX solid formulations. **Objective:** The aim of this work was to investigate the influence of temperature and relative humidity (RH) on the structural changes of MOX. **Methods:** Samples of MOX were storage at 0% RH/ 20ºC (silica gel), 40% RH/ 20ºC (saturated solution of $Na_2Cr_2O_7.2H_2O$), 90% RH/ 20ºC (saturated solution of $Na_2C_2O_4$) and 75% RH/ 40ºC (satured solution of NaCl), and were analyzed at initial time and after one month by DSC (50 mL min^{-1} of N_2, 10ºC min^{-1}, 30-300ºC), TG (50 mL min^{-1} of N_2, 10ºC min^{-1}, 30-600ºC), XRPD (powder XRD method, in the range of 5-55 (2θ)) and FTIR (400-4000 cm^{-1}, 32 scans and spectral resolution of 4 cm^{-1}). **Results:** Thermal analysis (DSC and TG) showed modifications in the melting profile of MOX storage at 90% RH/ 20ºC and 75% RH/ 40ºC, and employed analysis of variance (Scot-Knott) with the enthalpies is possible to establish that there was an alteration in the drug. X-ray diffraction studies were then performed, in order to obtain more information and to support DSC and TG results. The XRPD patterns of the drug stored in the conditions mentioned above showed disappearance of the characteristic peaks of the MOX and the appearance of other new peaks, confirming the thermal results. The IR spectra corroborated with the results obtained by the other techniques. The most important changes occurred for the samples stored at 90% RH and 75% RH. One of the changes was detected in the region of O–H stretching vibrations involved in the hydrogen bonds region from approximately 3600-3150 cm^{-1}. The other alteration occurred in the 1705 cm^{-1}, region of C=O stretching vibrations. **Conclusion:** The storage conditions 90% RH/ 20ºC and 75% RH/ 40ºC have substantial influence on the MOX stability, contributing to the occurrence of polymorphic transition of moxifloxacin hydrochloride. Pharmacotechnical wet processes such as wet granulation, should not be recommended for producing this drug. Moreover, the association of thermal analysis results with XRPD technique and IR measurements ensure reliable interpretation of polymorphic stability studies.

Keywords: Fluoroquinolone, Stability, Polymorphism, Thermal Analysis.

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