



Determination of API polymorphism in Rabeprazole tablets

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ABSTRACT

Rabeprazole is a proton pump inhibitor that decreases intragastric acidity and used in the treatment of acid-peptic-related disorders. It exhibits polymorphism with 10 different crystalline forms and one amorphous [1]. The identification of the crystal form either in the raw Active Pharmaceutical Ingredient (API) or in a formulation is usually performed by XRD, DSC, TGA, IR or Raman Spectroscopy.

Rabeprazole tablets from a Greek pharmaceutical industry with an API concentration of 9.5 wt % and from the leading brand name Pariet that contains 12.26%wt Rabeprazole sodium were examined using the above mentioned techniques. No API was found in the XRPD patterns of both formulations leading to the conclusion that the API was in the amorphous state. The Greek producer claimed that the Gamma (monohydrate) polymorph was used. The absence of the Gamma polymorph from formulations was verified through the use of Raman spectroscopy. Characteristic Gamma polymorph peaks at 707, 1191, 1207, 1272 and 1289 cm^{-1} were absent from both formulations while the presence of the amorphous API Raman peaks at 712, 730 and 1197 cm^{-1} was observed.

In order to resolve the issue i.e. the apparent replacement of the Gamma form from the usually thermodynamically unstable amorphous form, pure Gamma crystalline powder was stressed by: a) anhydrous ethanol, b) pressure and c) heat. Ethanol was applied as stressing agent since often it is been used during the wet granulation process.

Application XRD, DSC and Raman Spectroscopy before and after the stressing has revealed that the API was transformed after the absolute ethanol stressing. This was verified by preparing artificial mixtures of Rabeprazole Gamma polymorph (9.5%wt) with placebo in order to simulate the production process. The presence of the Gamma polymorph was easily identified by all techniques. After the stressing of the artificial formulation with the monohydrate form with absolute ethanol the Gamma form was transformed to amorphous.

A plausible explanation of this behavior, which is under investigation, is that the monohydrate is stripped from its water in the presence of the anhydrous ethanol and thus it is transformed to an amorphous state material.

REFERENCES

[1] Tripathi, A., B. Joshi, and J. Joshi, *POLYMORPHISM IN RABEPRAZOLE SODIUM*. *Rasayan J. Chem*, 2010. **3**(4): p. 736-744.