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THERMAL, SPECTROSCOPIC, X-RAY DIFFRACTION AND MICROSCOPIC INVESTIGATION OF GLASSY STATE OF DOXAZOSIN MESYLATE

[1] Marija Grèman, [1] Franc Vreèer, [2] Anton Meden

[1] Krka, d.d., Novo mesto. Research and Development Division, Novo mesto, Slovenia
[2] University of Ljubljana, Faculty of Chemistry and Chemical Technology, Ljubljana, Slovenia

Many pharmaceutical solids can exist in amorphous physical state. Amorphous drugs and excipients are very interesting in pharmaceutical development due to their properties i.e. significantly increased solubility and dissolution rate. It is known from the literature, that amorphization of substances results in theirs decreased physical and chemical stability [1-2]. Amorphous substances are generally hygroscopic, chemically less stable and they tend to transform into crystalline forms upon storage [3]. Some physico-chemical properties of glassy state of doxazosin mesylate were evaluated in the present study.

Amorphous form of doxazosin mesylate, which were prepared by fast cooling of the melt and by spray drying method, was investigated by FT-IR spectroscopy, Differential Scanning Calorimetry (DSC), X-Ray Powder Difractometry (XRPD), High Temperature XRPD and Hot Stage Microscopy coupled with Microphotography. The amorphous form was found to be stable at ambient conditions, but at temperatures above the glass transition, the transformation into crystalline forms was observed. The transformation was confirmed by DSC analysis and also by X-Ray diffraction obtained by variable temperature-dependent investigations. Individual thermal effects were observed under optical microscope and appropriate microphotographs have been taken. In the polymorphic mixture that was obtained by thermal crystallization of amorphous form in DSC, a new crystalline form of doxazosin mesylate was identified. It was found that the new polymorphic form is thermodynamically unstable. It undergoes irreversible polymorphic transition during heating to more stable form.

References:

1 K.J. Haleblian, J. Pharm. Sci., 64 (1975) 1269.

2 D.J.W. Grant, Theory and origin of polymorphism, in Polymorphism in pharmaceutical solids, (1999), p.1, H.G. Brittain (ed), Marcel Dekker.

3 D. Giron, J. Therm. Anal. Cal, 56 (1999) 1285.