Study of Polymorphism of Carvedilol

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Polymorphism of pharmaceutical compounds must be considered as an important parameter to the drug development process. Different polymorphic forms often exhibit different biopharmauceutical and stability properties.

Literature data show that carvedilol can crystallize in different polymorphic and pseudopolymorphic forms [1-2].

In the present study we investigated the polymorphism of carvedilol by thermal methods (DSC and TGA analysis), by hot stage microscopy and by X-ray powder diffractometry at ambient conditions and also at elevated temperatures. Different crystalline forms of carvedilol were obtained either by crystallisation or by thermal method.

A new pseudopolymorphic form from ethylacetat and a new non-solvated form were identified.

The DSC curve of the pseudopolymorphic form suggests irreversible solid-liquid-solid phase transition which is also observed by hot stage microscopy. The X-ray powder diffraction pattern of the pseudopolymorphic form confirms that upon heating (up to 75°C), this form is transformed to the known form II.

DSC examinations revealed that the non-solvated form, which shows the DSC melting at about 75°C, undergoes irreversible phase transition to the known polymorphic form II. The polymorphic transition was confirmed by X-ray powder diffraction analysis.

X-ray diffraction pattern of the pseudopolymorphic form of carvedilol shows the most characteristic d-values at 16.81 and 12.21 and of the non-solvated form at 13.76 , 8.08 and 6.49 , respectively.

Reference

1. P. Beyer, E. Reinholz, EP 0 893 440 A1 (1999)
2. J. Hildesheim, S. Finogueev, J. et al., WO 02/00216 A1 (2002)