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Polymorphism of Terfenadine studied by Polarised Light Microscopy and Differential Thermal Analysis

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Some polymorphic forms of organic pharmaceutical products have advantages relatively to others during the manufacturing and storage, as well as in their bioavailability. Thus, polymorphism in pharmaceutical industry is nowadays an important research field. The present paper deals with the identification of polymorphs of terfenadine, a drug used as a histamine H_1 receptor antagonist.

Generation of a variety of polymorphic modifications of terfenadine was achieved by crystallizing this substance in different solvents using different experimental conditions, Ethanol, methanol and ethanol/water cosolvent were used as crystallization media.

Slow or fast solvent evaporation rate, and solution temperature decreasing were the techniques employed for solid separation. Attempting to get better quality crystals, the solubility of terfenadine in methanol or ethanol solution was decreased by water vapor diffusion.

The solids obtained were studied by Polarised Light Microscopy, PLM, and by Differential Thermal Analysis, DTA, during heating/cooling cycles from ambient temperature to fusion. Detailed analysis of the optical images allows the identification of the phases observed.

The combination of PLM and DTA gives evidence for the components of the polymorphic mixtures arisen from each crystallization method. Three polymorphs were identified and two of them were isolated.

Most of the crystallization products are mixtures of crystalline phases often containing amorphous material. Structural disordered solid and low melting crystalline phases fuse at about 70 °C and recrystallizes at a temperature around 100 °C. Molten terfenadine gives rise by freezing to a vitreous state.