

Inversion of population distribution of felodipine conformations at increased concentration in dimethyl sulfoxide is a prerequisite to crystal nucleation

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Abstract

Knowledge of the preferred conformations of biologically active compounds is of the utmost importance for a better understanding of the structure-activity relationships underlying their biological activity, as well as their mechanism of action. Moreover, investigating the mechanism of nucleation from a saturated solution can facilitate the discovery and preparation of new polymorphic forms. To search regularities in the crystal nucleation of biologically active compounds (drugs) from a saturated solution, we studied the conformational preference of felodipine in dilute and saturated solution in dimethyl sulfoxide. The inversion of conformation distribution at increased concentration occurs: conformers that dominate in a dilute solution become the least abundant in the saturated one. Conformers that dominate in the saturated solution are of the same type as revealed in crystalline state by X-ray. © 2014 Wiley Periodicals, Inc. and the American Pharmacists Association *J Pharm Sci* 103:392-394, 2014.

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Keywords

Crystallization, NMR spectroscopy, Nucleation, Polymorphism, Structure