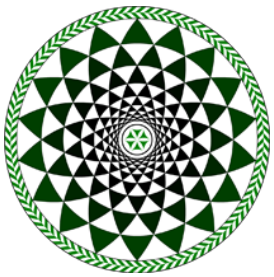

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Molecular reorientations in the crystalline and amorphous therapeutic drugs

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Recently, the phenomenon of polymorphism of therapeutic drugs has become the problem of increasing interest because of the common use of drugs in solid form, as tablets, powder inhalations, etc. The form of drug is sensitive to the effect of particular processes applied in drug production. Changes in the external conditions taking place in the process of drug production or storage can induce transformations in polymorphic forms. To ensure the proper therapeutic effect it is of vital importance to get the active pharmaceutical ingredient (API) and excipients in strictly defined chemically pure and stable form. Possible transformations in polymorphic forms can be manifested as changes in physicochemical properties, e.g. in solubility, hygroscopy, density, colour, hardness, compressibility, melting point, chemical stability and reactivity with the excipients, which affect bioavailability. It has been shown that the polymorphic forms differing in the rate of dissolution can be used by the organism to a different degree. It happens that one of the polymorphic form shows a declared pharmacological effect, while the other does not because e.g. it does not reach the therapeutically needed concentration in the blood for its low solubility.

Many active pharmaceutical ingredients and excipients are characterised by low solubility and thus inadequate bioavailability. Their amorphous forms usually are much better soluble than the crystalline forms and thus much more attractive.

Although many methods have been proposed for investigation of crystalline forms, characterisation of amorphous forms still remains a great analytical challenge. It is known that the properties of amorphous forms depend to a significant degree on molecular dynamics. It is generally believed that determination of molecular reorientations in amorphous forms may be of key importance for understanding of their physicochemical properties and for improvement in their physical stability.

The lecture presents results of the studies of molecular dynamics of the following active pharmaceutical ingredients: lovastatin, diazepam and nifedipine in the crystalline and amorphous forms.

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