DETECTION OF PHASE TRANSITIONS IN THE STUDIES OF ACTIVE SUBSTANES AND SOLID DOSAGE FORMS

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Polymorphism is the ability of a compound in the solid state to exist in different crystalline forms. Molecules, having the same chemical composition, exhibit different spatial arrangements and/or exist in different configurations and conformations [1]. In pseudopolymorphs (solvates) molecules of solvents are incorporated into the crystal lattice. Contrary to the crystalline forms of polymorphs, amorphous forms are characterized by the lack of long-range molecule arrangements. The spatial arrangement of molecules in an active substance determines its physical properties and influences the bioavailability and stability of a drug product. The most frequent phase transitions that can be present in an active substance include: polymorphic transition, hydration, dehydration, amorphisation and crystallization. The knowledge about the phase transitions which can arise during the active substance manufacturing, formulation process and stability studies is very important. Phase transitions may lead to the formation of an undesirable phase of the active substance with different properties than its desirable form. Studies of phase transitions in an active substance contained in a solid dosage form are very complicated, because there are many additional factors to consider, including a small concentration of the active substance, the presence of crystalline and amorphous placebo constituents, as well as the interactions between the active substance and the excipients.

There are a number of methods used to characterize crystalline and amorphous forms of the active substance. A definitive evidence of polymorphism or pseudopolymorphism is the demonstration of a nonequivalent structure by single crystal X-ray diffraction. X-ray powder diffraction (XRPD) and variable temperature X-ray powder diffraction (VT-XRPD) can also be used to provide an unequivocal proof of polymorphism and pseudopolymorphism. Other methods, including e.g. differential scanning calorimetry (DSC), thermogravimetric analysis (TGA) as well as Raman (RS) and infrared spectroscopes (IR), help to further characterize the crystalline and amorphous forms.

In this presentation, a few examples of phase transition studies in the active substances and solid dosage forms will be discussed: structural and physicochemical studies of olopatadine hydrochloride conformational polymorphs, phase transitions of dutasteride performed by the VT-XRPD method [2], erlotynib polymorphism studies performed by means of RS and the evaluation of analytical methods for the detection of phase transitions in tablets containing aripiprazole [3] and imatinib [4].

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