Increasing Water Solubility of Drugs, the Prerequisite for Improvement of Bioavailability

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Abstract

Many of low water soluble drugs, from the group of small size molecules, once being administered as single therapeutic doses, not often may reach their plasma concentrations to associate to the therapeutics respond. Cyclodextrins (CD), the sugar's cyclized derivatives, that play a role as functionalized excipients in pharmaceutical formulations, enhance the drug solubility toward the formation of inclusion complexes by noncovalent intermolecular interactions between the molecules of CD and drug. The value of the binding affinity constant of inclusion complex formation imply to the steichiometric ratio of CD and drug in inclusion complex and its water solubility. The representative case study relates to binary and ternary solid systems formed of β-CD and anti epileptic drug carbamazepine (CBZ), and β-CD, CBZ and biopolymer HPMC, respectively. Both solid systems are formed by using each of two polymorphic form of CBZ, form I and form III, respectively. The dissolution profiles, gained by performing the test for the Intrinsic Dissolution rate (IDR), and contributes by the thermodynamic data from the thermal analyses, indicate that β-CD and HPMC influence the phase transition of metastable CBZ form I to stable CBZ form III. Though the CBZ form I exert higher water solubility then CBZ form III, both polymorphic forms in water medium undergo to transformation in CBZ dehydrate, that water solubility is lower comparing to solubility of a both anhydrous CBZ polymorphs.

Keywords: Solubility, inclusion complexes cyclodextrins, polymorphs, phase transition.