

New Insights to Crystal Engineering

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Introduction

The in vivo pharmacokinetics of any drug molecule is depends on its physicochemical properties. The solubility and dissolution are the properties which majorly governs the in vivo absorption of drugs. There are various conventional approaches like cosolvency, solubilization using surfactant, salt formation etc. are used to enhance the solubility but limited with commercial adaptation. Crystal engineering is one of the emerging approaches for solubility enhancement with advantage of scale up possibilities.

Cocrystals

Cocrystal is the new solid form of drug with improved solubility along with stability and polymorphs also. The formation of hydrogen bonding between drug and cocrystal former is the mechanism behind improved physicochemical properties of drug after cocrystallization. This hydrogen bonding can be elaborated with supramolecular chemistry. The formation of hydrogen bond between two similar functional group is defined as 'homosynthon' and hydrogen bonding between two different functional group is defined as 'heterosynthon'. Generally the heterosynthons are more preferred and provide better results as compared to homosynthons. The advantage in cocrystallization is no breaking of old and no formation of new covalent bonds which results in retention of molecular and biological properties of drugs.

Techniques of Preparation of Cocrystals

Cocrystallization can be achieved by different solid based and solvent based techniques with good efficiency. The selection of technique is mostly depends compatibility of drug and cocrystal formers with the technique and subsequent results targeted.

Technique of Cocrystallization	Description
Neat grinding	In this technique drug and cocrystals are grinded together for definite period of time. Neat grinding is convenient technique at lab scale and large scale also.
Liquid assisted grinding	Drug and coformer are grinded with drop wise addition of liquid medium to improve the efficiency of cocrystallization. The selection of solvent is based on its safety and efficacy.
Extrusion	Hot melt extrusion technique is used for cocrystallization which involves application of high shear rate which leads to formation of agglomerates.
Cooling cocrystallization	Cocrystallization takes place between drug and coformer with the mechanism of cooling. This is one of the major solvent based technique used for cocrystallization.
Evaporative cocrystallization	Evaporation of solvent from both drug and conformers is the basic mechanism behind crystallization.
Reaction cocrystallization	Cocrystallization is takes place by mechanism of precipitation.
Super critical fluid technology	Use of supercritical fluid technology for cocrystallization.

Table 1: Techniques of cocrystallization.

Conclusion

Cocrystallization is the emerging technique across the globe in the domain crystal engineering. This approach is useful for the drugs with solubility and dissolution limited absorption and bioavailability. Additional advantage of cocrystallization along with solubility is improvement in flow property, compressability and stability. The future scope for the technique is drug-drug cocrystals of rational combination.