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Case Review

# Cocrystals: A New Form of Solid with Improved Physico-chemical Properties

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Co-crystals are defined as structurally homogeneous/ heterogeneous crystalline solids that include drug and coformer in specific stoichiometric proportions. The discrete neutral molecular reactants that make up co-crystals are solids at room temperature. According to this definition of co-crystals, a pharmaceutical co-crystal is a mixture in which one of the co-crystals' elements serves as an active medicinal ingredient and the other elements serve as coformers. An active drug hydrate is not a co-crystal, as is evident from the statement, but a solid-state drug hydrate is co-crystalline with a coformer to produce a co-crystal [1]. The pharmaceutical sector currently places a lot of attention on co-crystal methods. Pharmaceutical co-crystals can successfully enhance the drug substance's solubility, dissolving profile, bioavailability and physical stability, in addition to other crucial features such as flowability, chemical stability, compressibility and hygroscopicity [2].

**Figure 1:** Structure of Cocrystals.

For the creation of APIs, co-crystals' physicochemical characteristics are crucial. Adjusting the physicochemical parameters of pharmaceutical co-crystals during drug development improves the stability and efficacy of the dosage form [3]. Numerous studies have been conducted on physicochemical characteristics such as solubility, dissolution, crystallinity, melting point, bioavailability, and stability.

Numerous techniques are used for the formulation of co-crystals. The most general method is based on solution method and grinding method [4]. The solution method is of great significance for synthesis of co-crystals, which qualify for single X-ray diffraction testing can only be prepared through this method. Solution methods include evaporation of heterometric solution method, reaction crystallization method and cooling crystallization. Grinding method comprises solvent drop grinding and neat grinding. Apart from these methods, there are also lots of recently promising techniques, such as hot stage microscopy, ultrasound-assisted co-crystallization and co-crystallization using supercritical fluid [5].

Co-crystal characterization is an important constituent part within co-crystal research. The basic physicochemical properties of co-crystals can usually be characterized using scanning electron microscopy, Fourier transform infrared spectroscopy, differential scanning calorimetry, powder X-ray diffraction, Raman spectroscopy, solid-state nuclear magnetic resonance spectroscopy and terahertz spectroscopy [6].

## Applications of co-crystals

### Permeability enhancement

Co-crystals improve the penetration of drugs inside the biological membrane by changing their crystalline structure [7].

### Stability enhancement

Co-crystals avoid hydrate formation and improvement in the physical stability of the product [8].

Lowering the crystal lattice energy and increasing solvation are two mechanisms that increase the solubility of the API in a co-crystal. API solubility can be increased using either technique to varying degrees [9].

The pharmaceutical co-crystal approach enhanced the aqueous solubility and oral bioavailability of the product [10]. Meloxicamaspirin co-crystals showed better oral bioavailability as compared to pure drug and showed 12 times faster onset of action than a pure drug in rats [11].

Co-crystallization is used to modify the product's physicochemical properties, such as solubility and dissolution rate. The dissolution rate of the API in water or a buffer solution can be increased or decreased over time, depending on the coformer that co-crystallized with the API.

Multidrug co-crystals (MDCs) have an advantage over co-amorphous systems in terms of enhanced stability and reduced payload compared to mesoporous and cyclodextrin complexes.

Co-crystallization has also been studied as a technique for improving the chemical and physical properties of powders, such as mechanical strength and flow properties.

Co-crystallization could be a good strategy to improve dissolution rate using sugar-based coformers such as sucralose as coformer for preparing co-crystals with hydrochlorothiazide. The formed co-crystals provide the benefits of increased dissolution rate and taste masking of the product [12].

## Conclusion

Co-crystals enable a wide range of APIs to be used in pharmaceutical therapy. Some of the most appealing properties of co-crystallized APIs are increased solubility and chemical and physical stability. Overall, because of improved drug delivery performance, stability and an important intellectual property status, co-crystals are expected to play an important role in future drug development.

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