Comparative study of glycine co-crystallization with dicarboxylic acids by various technique.

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The multicomponent crystals present an extremely interesting, but insufficiently explored type of promising materials. The crystals to comprise several components in the unit cell could be applied in various fields of science and technology, and particularly in pharmaceutics. The usage of these compounds could improve the physicochemical properties of developed drugs such as solubility, rate of dissolution, stability on storage et al. Moreover, the components of this complex compound have ability to influence each other displaying synergetic effect that could increase the bioavailability.

The case study represents a comprehensive investigation of the crystallization process of glycine (the simplest amino acid used as individual medicine) in the presence of dicarboxylic acids by slow evaporation technique, mechanochemical co-grinding, antisolvent crystallization and spray drying. The dicarboxylic acids have been shown to favor crystallization of gamma-glycine [1], which has a higher biological activity as compared with alfa-glycine [2]. The only exception is glutaric acid, the role of which remains enigmatic. Another part of this work is related to the crystallization of glycine-dicarboxylic acid salts. A rare second polymorph of glycine semi-oxalate has been obtained by means of mechanical treatment and spray drying from aqueous solution. Five salts and one co-crystal have been isolated. The co-crystal of glycine with glutaric acid is the first known co-crystal (not a salt) of glycine [3]. Its formation is discussed in relation to the enigmatic absence of the effect of glutaric acid on the polymorphism of glycine.

The work was supported by grants from RFBR (10-03-00252; 11-03-00684; 11-03-12114), BRHE (RUX0-008-NO-06), FASI Grants P2529 and 16.740.11.0166.


Keywords: glycine; co-crystal; crystallization

Preparation and characterization of an anti-inflammatory drug etozemide co-crystals with dicarboxylic acids.

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Ethenzamide (2-ethoxybenamide) is an anti-inflammatory drug used to treat pain. A drawback for this drug is its poor solubility in water. Crystal engineering offers a solution by preparing molecular complexes of drugs with altered physicochemical properties. Cocrystals with an appropriate choice of formers can have a better bioavailability, stability and mechanical properties if compared to the parent drug. Some etozemide-cocrystals with carboxylic acids and saccharin have been reported previously.1,2 We have prepared two new etozemide-cocrystals with oxalic acid and fumaric acid. Crystal structures of both cocrystals were determined by single crystal X-ray diffraction analysis. Both cocrystal structures consist from planar etozemide-acid (2:1) trimers. Molecules are hydrogen bonded through N–H···O and O–H···O hydrogen bonds forming R_2^2(8) graph sets. Physicochemical properties and mechanochemical preparation possibilities of both cocrystals are characterized.


Keywords: etozemide, hydrogen bond, pharmaceutical cocrystal