MS05-P04

Co-crystal forms of the BCS class IV drug sulfamethoxazole

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Sulfamethoxazole, smz, is an antibiotic which is classified as a Biopharmaceutics Classification System (BCS) class IV, low solubility and low permeability drug. Co-crystal formation has been examined in an attempt to improve solubility. Both ball milling and crystallization from solution have been examined. Ball milling showed that thirteen co-formers gave new crystalline X-ray powder patterns and four gave X-ray amorphous patterns while crystallization from solution gave single crystals of four co-crystals and a salt. The co-formers which gave the co-crystals and the salt have better H-bond acceptors than the sulfonyl oxygens of smz. The 4,4-dipyridyl co-crystal has an interesting high Z'' structure. It crystallized in space group P1 with four smz and six 4,4'-dipyridyl molecules in the asymmetric unit.The lattice energies of smz and the co-crystals were estimated using the PIXEL program.The dissolution rates of the co-crystals are all lower than smz form I despite the fact that they have lower computed lattice energies than smz form I. It appears that the absence of any hydrogen bond in the smz form I structure with a D…A distance less than 3.2 Å and the presence of stronger hydrogen bonds in the co-crystals with D…A distances close to 2.8 Å is more important in determining dissolution rates than lattice energies.

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Co-crystals of fenamic acids with ethacridine

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It is expected that co-crystals of drug substances with different pharmaceutical properties and medical activities will be characterized by a wider spectrum of activity, new therapeutic properties and better bioavailability of the drug [1].

Although fenamic acids are very popular non-steroidal anti-inflammatory substances [2] used in therapy, their physical properties as solubility in water connected to the pharmaceutical dosage needs to be improved.

Ethacridine lactate is a drug used as an antiseptic agent therefore it can be expected that co-crystals of ethacridine with fenamic acids will combine pharmaceutical properties of both components and additionally will be characterized by improved bioavailability.

Organic complexes of fenamic acids (fenamic, mefenamic, flufenamic, tolfenamic)

and ethacridine have been obtained by formation of the network of intermolecular of N–H···O and C–H···O hydrogen bonds, occurring between the components of the co-crystal, as well as O–H···O and N–H···O hydrogen bonds generated by fenamate and ethacridine species along with water molecules. The crystal structure of fenamic acids with ethacridine will be presented and analysis of the hydrogen bonds will be performed.

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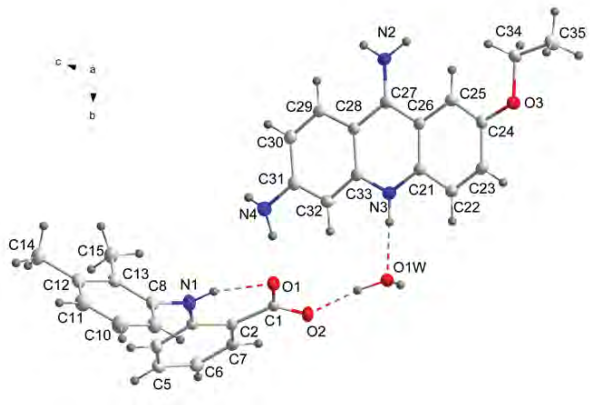
Figure. Structure of co-crystal of mefenamic acid with ethacridine.



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