The hypolipidemic agent acipimox has various potential hydrogen bonding donor and acceptor sites. A series of multi-component crystals can be formed owing to these moieties. Acipimox forms such structures with benzamide, isonicotinamide and urea. Each of these systems has a unique hydrogen bonding arrangement leading to changes in the physicochemical properties of acipimox. X-ray analysis of a hydrated co-crystal, acipimox•benzamide•0.5H2O (space group C2/c) revealed layers of dimeric acipimox-benzamide units, the layers being linked by hydrogen bonding from a bridging water molecule. A salt with formula (acipimox)- (isonicotinamide)+ (space group P2(1)/c) results from proton transfer from the carboxyl group of acipimox to the pyridyl nitrogen of isonicotinamide. The carboxyl group engages in an electrostatic interaction with the protonated pyridyl nitrogen. In addition, a hydrogen bond is formed between the donor amide and the acceptor carboxyl group of a second acipimox anion. These form a macrocyclic structure composed of two pairs of acipimox-isonicotinamide counterions in a R44(22) H-bonded motif, giving rise to interlaced layers. Acipimox and urea form two distinct systems, both crystallising in the space group P(-1). The kinetic crystallisation product is a co-crystal with 1:1 acipimox:urea stoichiometry (R22(8) motif), a second distinct urea molecule self-assembles forming infinite chains within channels formed by the packing arrangement. The thermodynamic form is an acetonitrile solvate in which the solvent molecules are included in isolated sites. The different H-bonding systems in each of these multi-component crystals give rise to differing physicochemical properties. For example the melting and degradation temperatures for each of these systems is distinct: that of the acipimox•benzamide co-crystal is lower than that of acipimox while the crystals containing isonicotinamide and urea have higher melting and degradation temperatures.


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