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Pharmaceutical salts of antidiabetic drugs: mechanochemical synthesis, solid state characterization and solubility evaluation

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The interest in multicomponent solid forms has increased in the last years within the pharmaceutical industry and also the solid-state community due to the possibility of obtaining materials with improved properties[1,2]. Crystallization strategies, supported by solvent- and solid-based[3] techniques, have also received attention in the search and development of efficient methodologies for the screening of multicomponent crystals.

In this work, two antidiabetic drugs with limited aqueous solubility, chlorpropamide and tolbutamide, were selected to develop multicomponent forms on the basis of the synthon types using a series of coformers. Liquid Assisted Grinding (LAG) was used as a mechanochemical synthetic tool. Attempts to produce salts by LAG led to the formation of polycrystalline material. These solids were then characterized by powder X-ray diffraction as well as by spectroscopic and thermal methods. Recrystallization by slow solvent evaporation was carried out when the above-referred techniques strongly suggest the formation of a new solid form. In those cases where suitable crystals were obtained, single crystal X-ray diffraction experiments were performed. Solubility determination of the selected solid forms has proved the advantage they offer over their corresponding parent APIs.

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