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Title: Crystal Structures and Physicochemical Properties of Four New Lamotrigine Multicomponent

Forms

Authors: Khullar, S. (/jspui/browse?type=author&value=Khullar%2C+S.)

 $Mandal, S.K. \ (/jspui/browse?type=author\&value=Mandal\%2C+S.K.)$

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Abstract: In the present study, four new multicomponent forms of lamotrigine (LTG) with selected carboxylic

acids, viz. acetic acid, propionic acid, sorbic acid, and glutaric acid, have been identified. Preliminary solid-state characterization was done by differential scanning calorimetry/thermogravimetric, infrared, and powder X-ray diffraction techniques. X-ray single-crystal structure analysis confirmed the proton transfer, stoichiometry, and the molecular composition, revealing all of these to be a new salt/salt-cocrystal/salt monosolvate monohydrate of LTG. All four compounds exhibited both the aminopyridine dimer of LTG (motif 4) and cation—anion dimers between protonated LTG and the carboxylate anion in their crystal structures. Further, these new crystal forms were subjected to solubility studies in water, powder dissolution studies in 0.1 N HCl, and stability studies under humid conditions in comparison with pure LTG base. The solubility of these compounds in water is significantly enhanced compared with that of pure base, which is attributed to the type of packing motifs present in their crystal structures as well as to the lowering of the pH by the acidic coformers. Solid residues of all forms remaining after solubility and dissolution experiments were also assessed for any transformation in water

and acidic medium.

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