Encenicline hydrochloride (Enc-HCl) is a partial, selective agonist of the α-7 nicotinic acetylcholine receptor. Previously, three monohydrates (I, II and X) were reported in the patent[1]. As described in the patent based on the solubility measurements, thermodynamic relationship between forms I and II is enantiotropy, but between forms I and X is monotropy, whereas there is no information regarding their crystal structures and phase transformations upon dehydration. Eight new polymorphs, one monohydrate and numerous solvates of EnC-HCl were obtained in crystal form screening. The properties of these various forms were characterized by powder X-ray diffraction, differential scanning calorimetry, and thermogravimetric analysis. The crystal structures have been determined either from single crystal or from powder diffraction data. Comparison of the thermodynamic stability of polymorphs were performed using total cell energy calculations, differential scanning calorimetry data and solvent mediated slurry-bridging experiments. Crystal structure information is used to explain and rationalize the relative stability of polymorphs and observed phase transformations.

Keywords: polymorphs, solvates, phase transition