Poster Presentation

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Reversible De-/Rehydration Process in Paroxetine Hydrobromide

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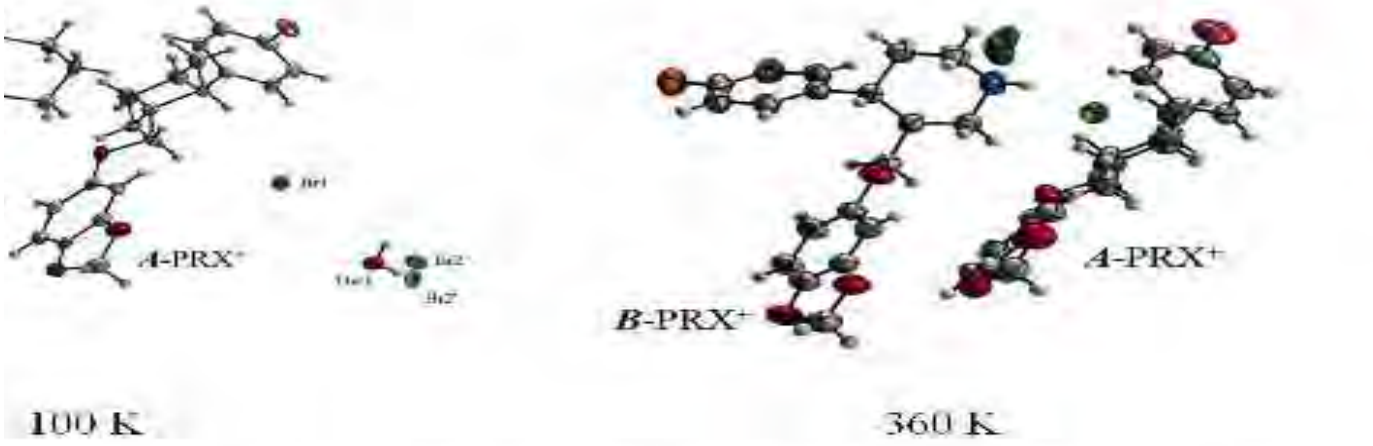
Paroxetine (PRX) is an antidepressant widely used in depression treatment for decades. The anhydrous and hemidrate chloride forms have been used in pharmaceutical formulations. During their developing a discussion associated with its physical forms and the complex hydration/dehydration behavior involving these phases were established. To improve our understanding of this issue we investigate the crystal structure of paroxetine bromide hemidrate, (PRX+.Br-).H2O, as a model for understanding the stability anhydrous/hemihydrate paroxetine arrangements and the nature of the intermolecular interaction of water within the crystal lattice by single crystal X-ray diffraction experiments. A combination of complementary characterization techniques were also used including Differential Scanning Calorimetry (DSC), thermogravimetric analysis (TGA), Hot Stage microscopy and solubility measurements. As expected the paroxetine bromide hemidrate, (PRX+.Br-).H2O, is isostructural with the paroxetine chloride hemidrate, (PRX+.Cl-).H2O. As in that case, the crystal packing of (PRX+.Br-).H2O is stabilized by strong NH2+...O and NH2+...Br hydrogen bonds which forms infinite channels along the b axis. The water and bromide anions are located along these channels. The DSC/TGA analysis for (PRX+.Br-).H2O show an endothermic desolvation process with an onset temperature of 77.09 ºC, that is not present in the paroxetine chloride hemidrate DSC curve. This process leaves to a paroxetine anhydrous bromide crystal structure that is isomorphic to the anhydrous chloride one. However, this structure is spontaneously rehydrated at ambient atmosphere. This rehydration phenomenon probe the stability of paroxetine hemihydrate arrangement, since (PRX+.Br-) is slightly more soluble that its hydrate form. As opposed to chloride hemidrate, the rehydration of paroxetine bromide only involves a rearrangement of the water molecule within the cavities.



type view of the asymmetric units of (a) (PRX+.Br-).H2O and (b) (PRX+.Br-). are disordered in two positions with a maximum occupation of 0.70.

Keywords: Paroxetine, Active Pharmaceutical Ingredient, Desolvation Process