Poster Presentation

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Crystal structures of two molecules with small chemical structure difference

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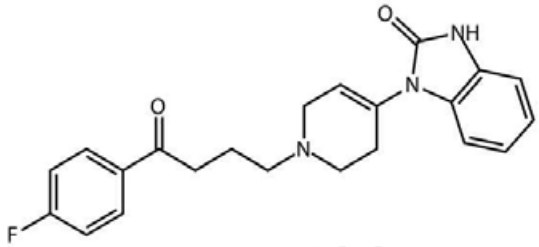
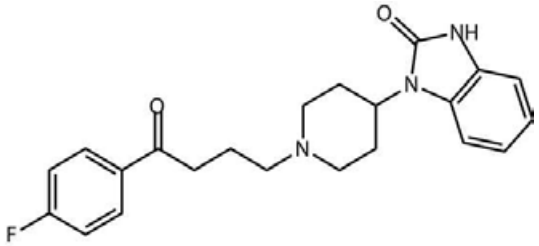
Droperidol and benperidol, neuroleptic pharmaceuticals, both are used as antipsychotics. The chemical structure of these two compounds differs only by one double bond in the middle of the molecule (see Scheme). It is known that both of these substances can form several polymorphs and solvates. Crystal structures of most of these phases are known [1, 2]. Despite the molecular structure similarities, there are no known droperidol polymorph or solvate isostructural to those of benperidol. Although there has been studies characterizing the crystal structures of chemically very similar compounds, general explanation to observed structural differences was not found (e.g. [3]). In this study we analyse the crystal structures of benperidol and droperidol by comparing the molecule conformation and packing in crystal structures of both of these compounds. Molecule conformation is compared and torsion angles which differ and therefore lead to different crystal structures are identified. Theoretical calculation of potential energy surfaces of these torsion angles are performed in Gaussian09. Intermolecular interactions and molecule packing in all crystal structures are compared by trying to understand the general differences between both molecules. Analysis of structures deposited in Cambridge Structural Database is performed to find conformations and intermolecular interactions characteristic for similar molecules by therefore trying to generalize structural formation possibilities for both pharmaceuticals and understand the reasons for crystallization of only observed structures. Theoretical calculations of benperidol and droperidol crystal structures where benperidol molecules are replaced by droperidol and vice versa are performed in CASTEP to compare the energy of experimentally observed crystal structure with that of theoretically possible structure isostructural to double-bond-different molecule.

[1] *A. Actins, R. Arajs, S. Belakovs et al., J. Chem. Crystallogr., 2008, 38, 169-174.,* ***[2]*** *N.M. Blaton, O.M. Peeters, C.J. De Ranter, Acta Crystallogr. Sect. B, 1980, 36, 2828-2830.,* ***[3]*** *T.A. Zeidan, J.T. Trotta, R.A. Chiarella et al., Cryst. Growth Des., 2013, 13, 2036-2046.*



Droperidol



Benperidol

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