MS28-2-3 Piperazine scaffold in drugs –structural and pharmaceutical points of view
#MS28-2-3

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Abstract
Knowledge of the conformational stability of compounds with potential biological activity is essential for studying ligand-receptor interactions. Typically, such interactions are simulated computationally, which gives insight into both the nature of the ligand-receptor interactions and indicates the most efficiently interacting molecular fragment of the ligand. This knowledge, in turn, allows the design of new generic ligands that act more selectively, for example. Usually, the results of experimentally characterized ligand crystal structures are used as a starting point for such studies. It should be noted that the ligand rarely binds to the receptor with strong covalent bonds; rather, weak reversible non-covalent interactions such as hydrogen or halogen bonds, or aromatic interactions are involved. Hence, a detailed analysis of intermolecular interactions a given molecule can exhibit is often beneficial. What is more, a combined techniques approach, involving X-ray diffraction, spectroscopic, thermal, and computational studies, seems to be a value-adding methodology as well.
This contribution concerns ligands containing a piperazine fragment in their structure. Such scaffold is present in a variety of active pharmaceutical molecules (over 300 crystals in the CSD drug subset [1]), to mention only antibiotics (e.g. levofloxacin [2]), antidepressants (e.g. trazadone [3]), antifungal (e.g. posaconazole [4]) and anticancer drugs (e.g. imatinib [5]). Noteworthy is a variety of crystal forms determined so far, like polymorphs, co-crystals, salts and solvates.
We will show the intermolecular interactions analysis, and the basis for the discussion will be their hierarchy established on the analysis of large molecular synthons and estimated interaction energy. The data for the analysis will be retrieved from CSD database and supplemented with our own research results. Correlation to ligand activity and certain receptors affinity will be addressed. Particular attention will be paid to multi-component crystals, which may show better pharmaceutical properties than pure drugs.

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