Charge density distribution of API in crystals and ligand-receptor complexes

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Analysis of charge density distribution is a powerful method to recover information about non-covalent interactions in crystals and such important physical quantities as lattice energies. These quantities allow evaluation of the mutual stability of polymorphs and comparison of the strength of supramolecular associates in solids that is valuable for crystal engineering. Moreover, in the case of compounds that serve as active pharmaceutical ingredients (API) the energies of individual intermolecular interactions and lattice energies can be associated with the energies of ligand-receptor binding.

Herein we present the results of experimental charge density studies, quantum chemical calculations and Voronoi partitioning for several APIs (abiraterone acetate [1], bicalutamide [2] and lamivudine) used in common practice to treat tumors and HIV infection. As result the energies of individual interatomic interactions were evaluated for single crystals of API and simplified models describing ligand-receptor interaction constructed using PDB data as starting points. The characterization of intermolecular interactions was carried out with a variety of theoretical approaches including deformation electron density, QTAIM theory, NCI method, molecular electrostatic potential and solid bond angles (Fig. 1). The data on intermolecular interaction obtained for single crystals and models of ligand-receptor binding demonstrated the similarity of lattice energy values with those for the energies of interactions between API and receptor despite of conformational changes.

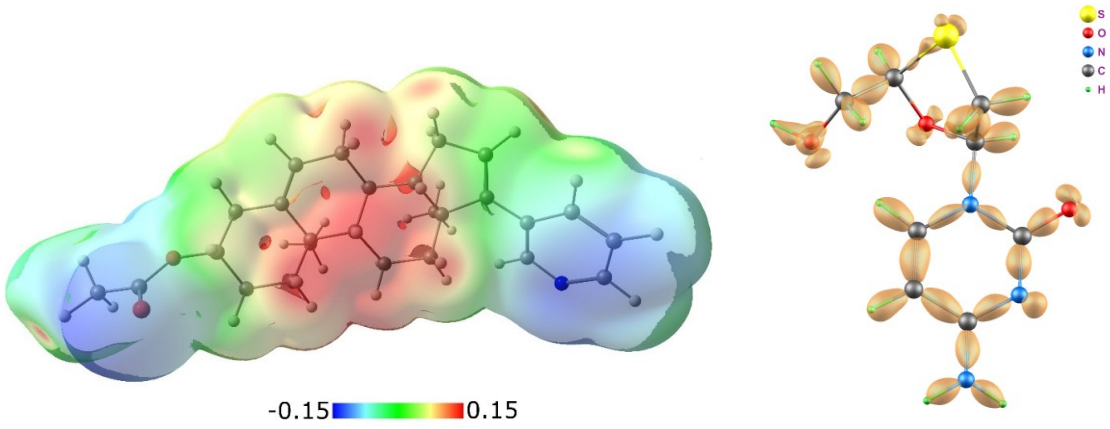

Figure 1. Molecular electrostatic potential of abiraterone acetate (left), 3D surface of experimental deformation electron density of lamivudine (right).

[1] Korlyukov, A. A., Vologzhanina, A. V., Trzybinski, D., Malinska, M., Wozniak, K. (2020), Acta Cryst. B76, 1018.

[2] Korlyukov, A. A., Malinska, M., Vologzhanina, A. V., Goizman, M. S., Trzybinski, D. & Wozniak, K. (2020). IUCRJ. 7, 71–82.

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