



# Excitation energies for anionic drugs predicted by PBE0, TPSS and $\tau$ HCTH density functionals

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## ABSTRACT

Numerous benchmarking studies dealing with TD-DFT calculated excitation energies for neutral molecules are reported in the scientific literature. However, charged species, both anionic and cationic, have received much less attention from this point of view. Against this background, here we report a comparative study of calculated excitation energies corresponding to the vertical singlet-singlet electronic transitions for a set of 96 anionic compounds containing basic well-known small-sized drugs and essential medicines. The objective of the work was to check the accuracy provided by one hybrid functional (PBE0), and two meta-GGA functionals (TPSS and  $\tau$ HCTH) in reproducing the experimental maximum absorption wavelengths. Computed data have been compared to available experimental data found in the literature. For the selected set of anions, it is shown that the two meta-GGA functionals performs similar to PBE0, with a slight advantage of TPSS density functional, which offers better values than PBE0 for mean signed-error and mean absolute error.

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## 1. Introduction

Molecular anions have different physical and chemical properties compared to their neutral and cationic forms. Such examples are the electronic affinity, electronic density, ionic potential, polarizability, valence electron binding energies or maximum absorption and fluorescent wavelengths [1]. Moreover, the deprotonation of neutral molecules in basic solutions affects the drugs' lipophilicity, solubility, their capacity to penetrate cellular membranes and their binding to biological targets. The maximum absorption wavelength of anion drugs can also impact their photolysis as well as their use in UV protection. In addition, some anions can change their color when they form metal complexes and thus, can be used in metal detection [2].

While the excitation energies of neutral molecules have been intensively studied by TD-DFT approaches [3–8], the anionic species have received much less attention from this point of view [3,9–11]. Quantum chemical calculations of the maximum absorption wavelength (MAW) for anions impose a careful analysis of all their possible conformers and tautomers, their Gibbs free energies and Boltzmann populations. Moreover, the properties of anion forms depend mainly on the enol or keto tautomerism, on the

possibility of the intramolecular hydrogen bonding and the type of the used (protic or polar) solvent.

For the reasons mentioned above we became interested in the molecules that change their maximum absorption wavelength by deprotonation. Thus, we studied 96 molecules with functional groups like carboxyl, hydroxyl, carboxamide, amine, sulfo that can form anions, focusing on the MAW value which can depend drastically on the used level of theory as well as on the relative contributions given by the possible tautomers of the investigated molecules. Our aim was to compare the accuracy of the computed experimental excitation energies for anionic drugs provided by the PBE0 hybrid functional [12–15], widely accepted as one of the best density functional for excitation energies, as well as two meta-GGA functionals (TPSS [16] and  $\tau$ HCTH [17]).

The non-empirical PBE0 functional was selected because it was used in many benchmarks [3,18] and, compared to other DFs, provides very good results, at least for the electronic vertical transitions [4,19]. Besides PBE0 DF we selected for this study one non-empirical (TPSS) and one empirical ( $\tau$ HCTH) meta-GGA functional.

The paper is organized in two parts. First, a comparison of the three used functionals is done followed by a detailed discussion of the computed and experimental excitation energies for representative molecules in the investigated set of anions.

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