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THEORETICAL STUDY OF THE ELECTRONIC STRUCTURE OF THE COMPLEX $[Zn(CIP)Cl_2]\cdot 2H_2O$ OBTAINED BY THE INTERACTION OF CIPROFLOXACIN AND ZINC SULFATE

Abstract: *The DFT method was used to analyze some quantum-chemical parameters of the Zwitterionic form of Ciprofloxacin and its Zinc complex. And also an analysis of the surface of the electrostatic potential of them was carried out. The zwitterionic form of ciprofloxacin and the complex represent an ambifunctional system in which there are simultaneously two reaction centers for electrophilic and nucleophilic attacks.*

Key words: *Ciprofloxacin, Zwitterionic form, Zinc complex, DFT, QCP, HOMO, LUMO.*

Language: *English*

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Introduction

It is well known that ciprofloxacin is a quinolone type compound with high antibacterial activity [1]. Experiments have shown that the biological activity of metal complexes is higher than the biological activity of primary compounds [1-3]. Therefore, the electronic structure of the metal complex obtained by the interaction of ciprofloxacin hydrochloride and zinc sulfate (the reaction was carried out in the presence of HCl [4]) was studied by the B3LYP/6-31G(d) method using the ORCA 5.0 program package [5]. In addition, the zwitterionic form of ciprofloxacin was considered for comparison with the complex.

The frontier molecular orbitals (FMO) and electron densities on them (FED), as well as energy gap (ΔE), atomic charge distribution and electrostatic potential surface analysis are widely used in the study of the electronic structure of compounds [6-8]. The role of FMO in chemical reactions is known from the work of Fukui [9], and the parameters associated with frontier molecular orbitals are still fruitfully used in fields of chemistry and in QSAR [10]. The atomic charge distribution is one of theoretical parameter, which show total electron densities around an atom and electrophilic or nucleophilic centers.

Materials and methods.

The geometries of studied compounds (zwitterion form of ciprofloxacin and complex) were built using Avogadro program package [11], then they were fully optimized by the Pople basis set - RHF / 6-31G(d) using the ORCA 5.0 software [5]. The hybrid Becke method [12] with three parameters and correlation functions of Lee, Yang, and Parr [13] was chosen as the DFT (B3LYP) method.

The results of ORCA calculations (charges on atoms according to Mulliken and FMO) were visualized using the Avogadro program [11].

The electrostatic potential (ESP) analysis have been carried out using MultiWFN [14] and VMD [15] program packages.

Results and discussion.

According to the reference [1, 2, 4], many metal complexes of ciprofloxacin with different metals in different stoichiometric ratios have been obtained. The complex under consideration differs from others with a peculiar structure. The zinc atom is coordinated with two oxygen and two chlorine atoms. In the other part of the molecule has a quaternary nitrogen atom. The system is closed system, containing 42 atoms and 174 electrons. The ligand part of the complex is similar to the zwitterionic form of ciprofloxacin, in which the hydrogen of the OH group is transferred to the nitrogen in NH group, that is, the hydrogen atom is transferred from one side of the molecule to the other. On the other hand, it should be borne in mind that ciprofloxacin has been used as a hydrochloride salt. Any other way, ciprofloxacin has been used in the form of the hydrochloride salt and the transfer of the chlorine anion to the metal in solution is possible.

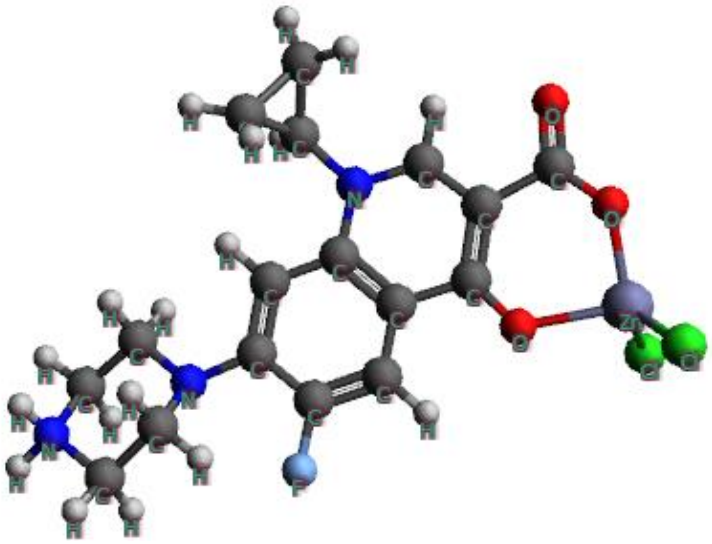

Fig.1. 3D geometry of the complex

Analysis of the atomic charge distribution of the complex illustrated that the largest negative charge is in the quaternary nitrogen atom of the piperazine ring, then in the oxygen and chlorine atoms. The largest positive charge is on the Zn atom. A large positive charge is also found on hydrogen atoms of the quaternary nitrogen atom.

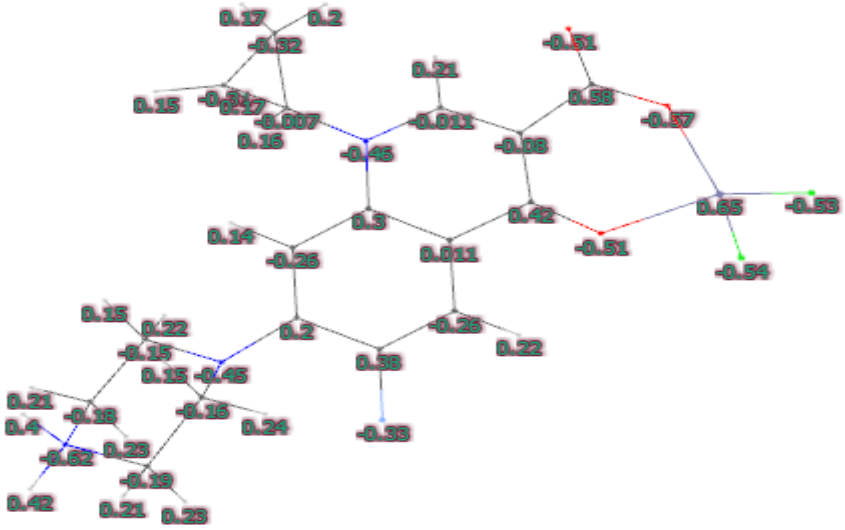

Fig. 2. Charge distribution on atoms of the complex

Almost the same picture is observed when comparing the charge distribution on the atoms of the zwitterionic form of ciprofloxacin and the ligand part of the complex (Fig.3). From the analysis of the charge distribution on atoms, it can be concluded that the zwitterionic form is an bifunctional system in which there are simultaneously two reaction centers for electrophilic and nucleophilic attacks. This conclusion is also relevant for the complex.

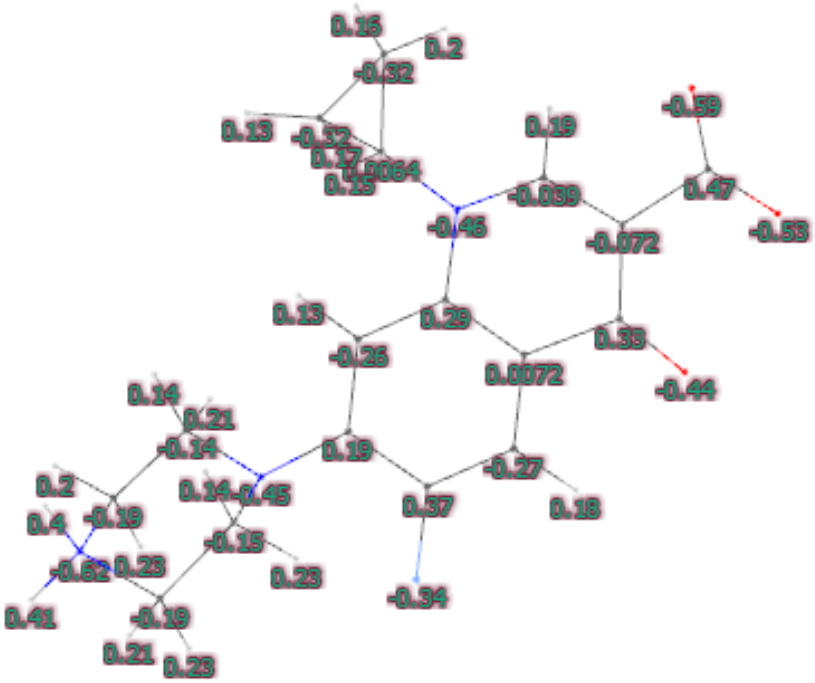

Fig.3. Charge distribution on atoms of the zwitterion form of ciprofloxacin

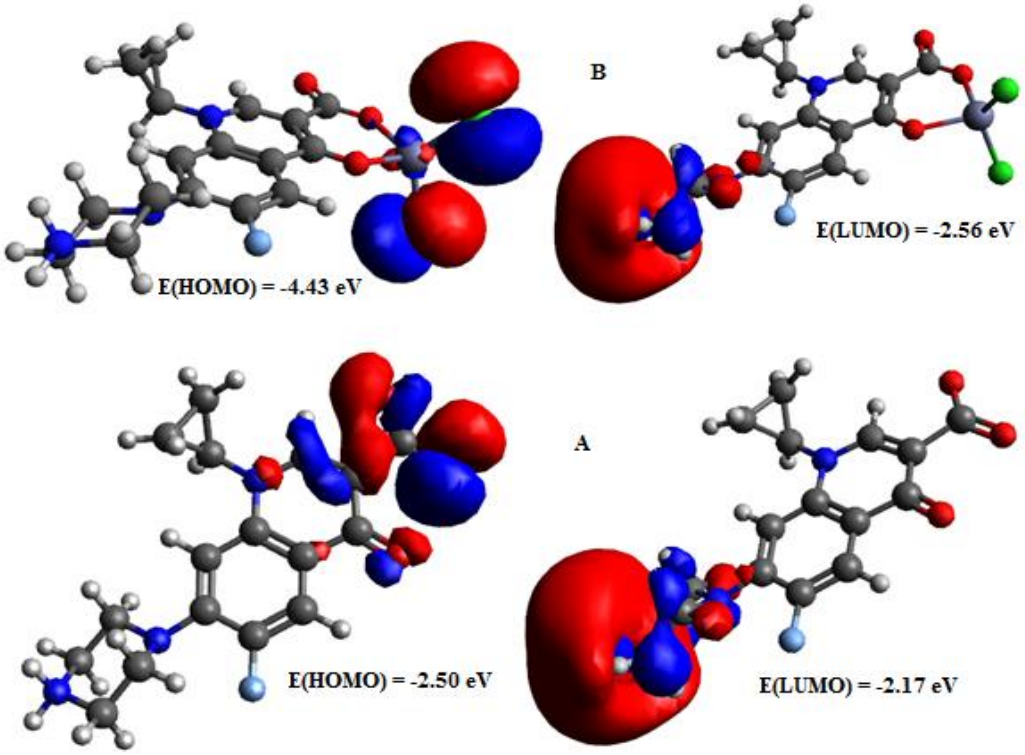

Fig. 4. Frontier electron densities (FED) on atoms of the zwitterion form (A) and complex (B)

The existence of two opposite reactive centers is also found in the frontier electron densities. Electron densities on LUMO of both compounds is localized in quaternary nitrogen atom of piperazine ring (Fig.4). At that time, oxygen atoms and zinc chloride make the largest contribution to HOMO.

Low-lying LUMO level and higher-lying HOMO level were determined for both compounds. Subsequently a very low band gap arose for the zwitterionic form (0.33 eV) and for the complex (1.87 eV), which indicates their highly reactivity.

Analysis of the surface of the electrostatic potential also described the presence of high and low electron density parts in both molecules. The largest maximum (electron-deficient center) is located around the hydrogen atoms of quaternary nitrogen atom, and the largest minimum is located around the chlorine atoms in the case of complex.

In the case of the zwitterionic form, the maximum is located in the vicinity of the hydrogen atoms of the quaternary nitrogen atom, and the minimum is located around the oxygen atoms.

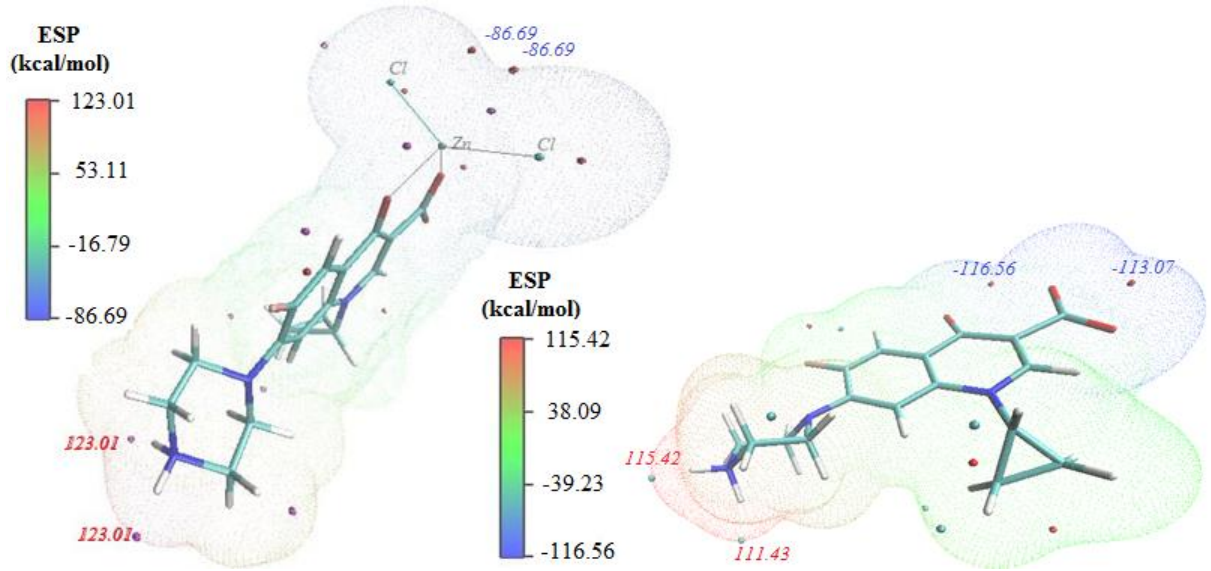

Fig. 5. The ESP minima and maxima for complex and zwitterionic form. The positive numbers represents the maximum, and the negative numbers represents the minimum.

Conclusion

Thus, the theoretical analysis of the electronic structure of the zwitterionic form of ciprofloxacin and the metal complex of ciprofloxacin with zinc was carried out by the B3LYP / 6-31G (d) method. All theoretical parameters calculated for both compounds visualized the presence of electron-donor and electron-accepting parts in the complex and zwitterion. Based on the parameter of the energy difference HOMO and LUMO (energy gap), a higher reactivity of the zwitter ion, as well as of the complex.

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