ISSN: 2582-4686 SJIF 2021-3.261,SJIF 2022-2.889,
2024-6.875 ResearchBib IF: 8.848 / 2024

THE MULTIDISCIPLINARY JOURNAL OF SCIENCE AND TECHNOLOGY

VOLUME-4, ISSUE-6

INTERMOLECULAR INTERACTION ENERGIES AND HIRSCHFELD SURFACE ANALYSIS OF ORGANIC SALT CRYSTAL FORMING NITRATE ION WITH NORFLOXACIN

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Abstract. In this article, the composition of a new organic salt complex of $HL+NO_3$ - composition formed by the nitric acid anion of norfloxacin (HL), molecular and crystal structures, studied using X-ray structure analysis (RTT), was found to have a molecular mass of 383.31 g/mol, a monoclinic, spatial form of singonia P21/N. Based on the data obtained in the RTT analysis of the synthesized organic salt, the Hirschfeld surface analysis of the comlex was carried out, as well as the energies of intermolecular interaction were calculated. According to the results of the Hirshfeld surface analysis, it was found that the main part of the effects is made up of H...O/O...H (45.6%), H...H (28.2%) bonds.

Keywords: *Norfloxacin, organic salt, nitrate anion, Hirshfeld, energy*

Introduction. Currently, various epidemiological situations in the world, climate changes and environmental pollution create favorable conditions for the survival and reproduction of viruses, bacteria and fungi. As a result of the activity of these harmful microorganisms, various diseases are increasing among the population. These situations impose very important tasks on the representatives of chemists, biologists, pharmaceuticals and medicine. It sets the task of creating new drugs that can have an effective effect against harmful microorganisms. As we know, creating a new drug takes a lot of time. Therefore, it is an important task to increase the range of action, reducing the amount of the acting substance in existing drugs. The antibacterial substance used as a medicine has a very low solubility in water. That's why there is a large amount of them in the composition of medicines.

Therefore, it is important to synthesize their soluble compounds: organic salts, complexes with biologically active metals.

Analysis of literature on the topic. In many cases, it has been found that the organic salts formed by individual drugs with inorganic or organic compounds increase their activity against the free ligand [1]. Norfloxacin (HL), which is being used as a drug in the group of fluoroquinolones with a broad spectrum of action, is one of the most effective fluoroquinolones [2]. The compound has an effective effect in medicine on digestive and biliary tract infections,

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skin, lung, prostate, and other infectious diseases [3,4]. The water solubility of HL is low, but the synthesis of its water solubility is good as well as biologically active compounds is important [5-6]. Organic salt state compounds of HL have been synthesized and studied by many scientists [7,8]. Taking into account the above cases, we aim to synthesize complex compounds of HL in the state of organic salt with good solubility with various organic and inorganic compounds, as well as to study the physicochemical properties of the complex obtained. In this study, the crystal and molecular structure of the complex in the organic salt state with the nitrate anion of HL was analyzed in the RTT method, with intermolecular interaction energies as well as Hirschfeld surface analysis.

Research methodology. The study used X-ray crystallography performed using an automatic Xcalibur R Oxford Diffraction diffractometer at room temperature as its primary methods. The intermolecular interaction energies in the crystal structure of the synthesized organic salt were determined using the UNI force fields [9] method included in the Mercury 2023.3.0 [10] program. Also, Hirschfeld surface analysis was performed using the Crystal Explorer 17.5 [11] program.

Analysis and results. The molecular and crystal structures of the organic salt complex were analyzed in the RTT method. Intermolecular interaction enegies as well as Hirschfeld surface analyses were also conducted based on RTT data from the complex compound obtained. In this new complex, the two compounds were observed to crystallize to form a mutual organic salt. The composition of the compound is an organic salt consisting of the $HL^{+}\cdot$ ($[C_{16}H_{19}FN_3O_3]^{+}$) cation in the svettir ion state as well as NO_3^- anions, whose crystal structure was analyzed in the RTT method. M=383.31, syngonia monoclinic, space group R21/n, It was found that V= 1598 $Å^3$.

The molecular structure of the $[HL]^+ \cdot [NO_3]^-$ containing organic salt as well as the internal molecular hydrogen bonds are shown in Figure 1.

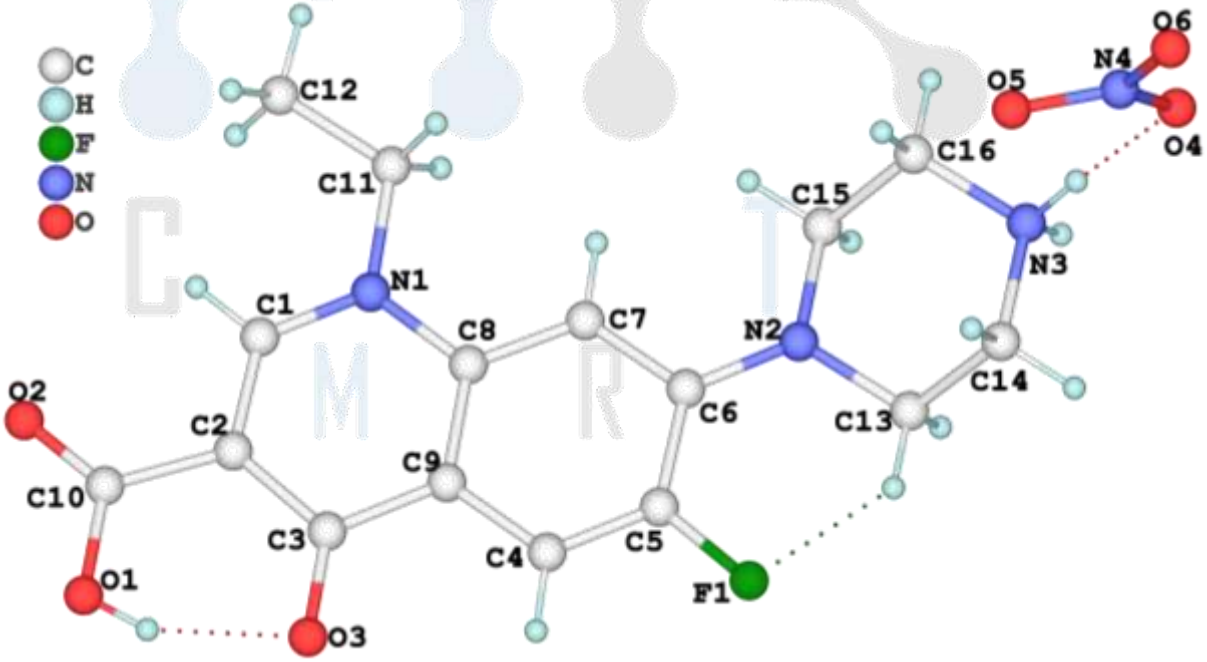

Figure 1. Molecular structure and internal hydrogen bonds of organic salt with $[HL]^+ \cdot [NO_3]^-$ content

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From the crystal structure of the organic salt, it can be seen that the internal molecular hydrogen bonding in the HL molecule is between O1–H1...O3 and C13–H13A...F and the Hydrogen of the Quaternary nitrogen atom in the HL molecule and the oxygen atoms in the nitrate anion are between N3HA...O4. Intermolecular hydrogen bonds are observed between N3-H3B...O6, C14-H14B...O2, C15-H15A...O4 atoms (Table 2).

Table 2

Geometry of the hydrogen bonds

Bond D*–H···A**	**Distance, Å**			**Angle D–H···A, grad**	**A atom cordination**
	D—H	**H…A**	**D…A**	**D—H…A**	
O1–H1…O3	0.8200	1.8000	2.5641(17)	154.00	-
N3–H3B...O6	0.8900	2.0800	2.937(2)	161.00	-1+x,y,z
N3–H3A…O4	0.8900	1.9700	2.8524(19)	169.00	-
C1–H1A…O2	0.9300	2.4600	2.7960(19)	101.00	-
C13–H13B…F1	0.9700	1.9600	2.726(2)	135.00	-
C14–H14B...O2	0.9700	2.5900	3.338(2)	134.00	x,y,-1+z
C15–H15A…O4	0.9700	2.4700	3.252(2)	138.00	-1/2+x,3/2-y,1/2+z

D*- electron donor; A**- acceptor atom

In this research work, the interaction energies of molecules predicted in the elementary cell of a new organic salt crystal synthesized were calculated through the Mercury 2023.3.0 program. In the crystal of the complex compound $[HL]^+[NO_3]^-$, molecules located at a distance of 5.52601, 5.9191, 6.88435 and 7.34863 Å interact with each other with energies of -103.007, -95.2232, -29.116 and -27.8706 kJ/mol (3-table). The total energy of formation of organic salt complex formed by HL with nitrate anion is -287.2 kJ/mol (Fig. 2).

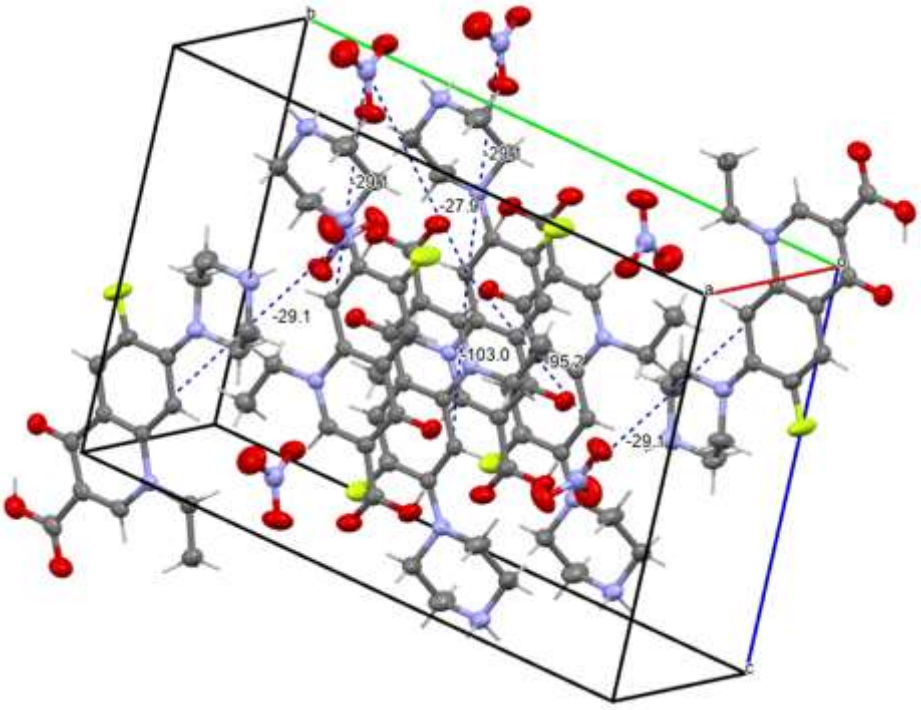

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Figure 2. $[HL]^{+}\cdot[NO_3]^{-}$ energy of interaction between molecules of the complex compound, kJ/mol.

Table-3.

Intermolecular interaction distances and energies of the $[HL]+[NO_3]^{-}$ complex

	The name of a pair of molecules	Intermolecular distance (Å)	Intermolecular interaction energy (E, kJ/mol)
	(HL^{+}) - (HL^{+})	5.52601	-103.007
	(HL^{+}) - (HL^{+})	5.9191	-95.2232
	(HL^{+}) - (NO_3^{-})	6.88435	-29.116
	(HL^{+}) - (NO_3^{-})	7.34863	-27.8706

Hirschfeld surface analysis is one of the widely used calculation methods for the quantitative expression of intermolecular interactions in the crystal structure of the complex. In order to visualize intermolecular interactions, Hirschfeld surface was analyzed using the CrstalExsplorer 17.5 program and two-dimensional fingerprint fields were calculated. Fingerprint fields allow us to identify the pairwise interactions of individual atoms and separate the contributions of various strong and weak interactions.

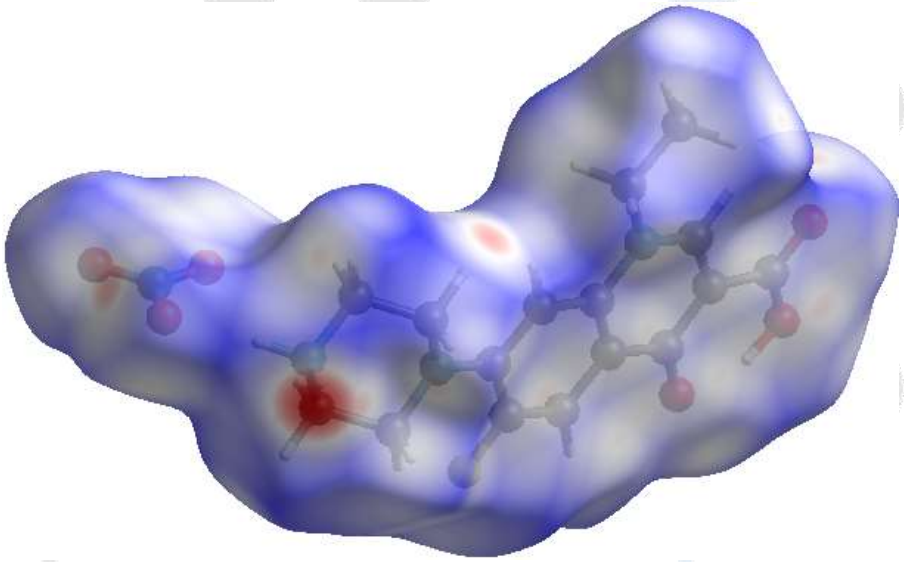

Figure 3. $[HL]^{+}\cdot[NO_3]^{-}$ complex content -0.4937 to 1.1433 a.m.b. is a three-dimensional Hirshfeld surface mapped by dnorm between

D_{norm} area volume is 392.65 3, surface is 341.55, dimensions are -0.4937 (red) 1.1433 a.m.b. (blue), and they are calculated by calculating the outside (de) and inner (di) distances to the nearest nucleus. locations with a low contribution are indicated in blue on the Hirshfeld surface, while locations with a high contribution are shown in red (Fig. 3). The two-dimensional fingerprint domain plot analysis revealed that the H...O/O...H interactions contribute the most to the Hirschfeld surface. It is 45.6% in the organic salt, 40.3% in the cation, and 89.2% in the anion (Figure 4), as would be predicted for molecules dominated by oxygen atoms.

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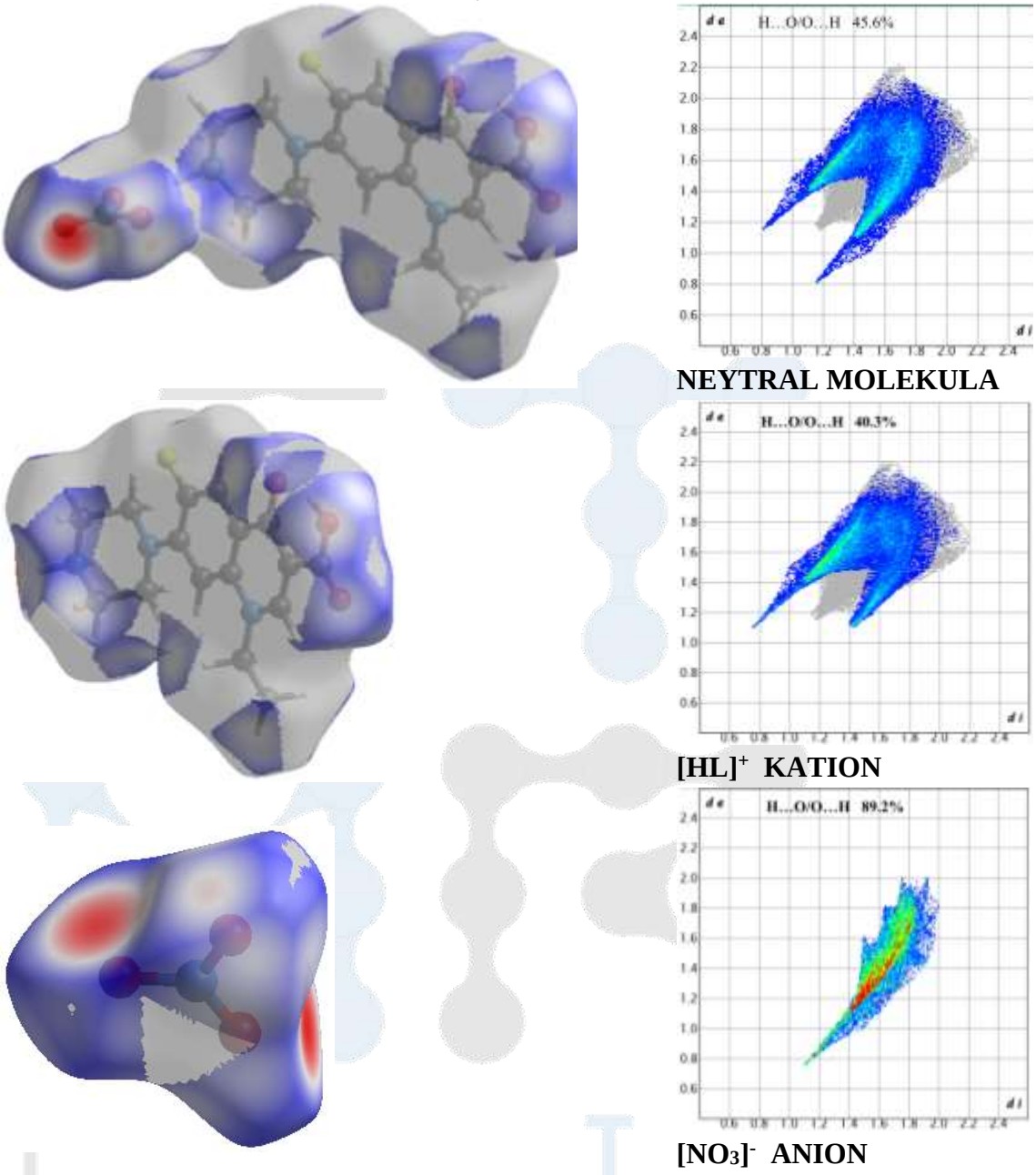

Figure 4: Three-dimensional Hirschfeld surface and two-dimensional fingerprint area mapped using the D_{norm} to show the organic salt's H...O/O...H interactions with its cations and anions.

The H...H reaction, which contributes 28.2% to organic salt, is one of the primary reactions. C...C (9.3%), H...F/F...H (4.6%), and H...C/C...H (3.4%) were significant, while N...C/C...N (2.1%), F...O/O...F(1.9%), O...C/C...O(1.5%), H...N/N...H(1.2%), F...N/N...F(1.0%), and N...O/O...N(0.8%) impacts contributed less (Fig.5)

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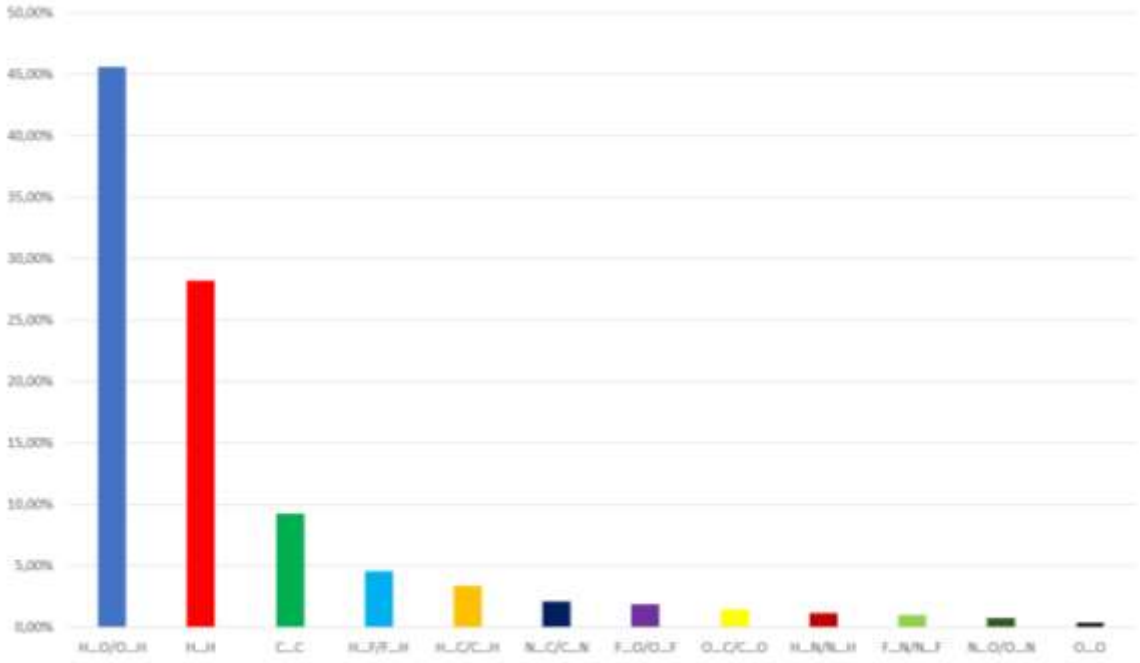

Figure 5. Hirschfeld fingerprint diagram of the $[HL]^{+}\cdot[NO_3]^{-}$ complex.

Conclusion: As a result of the conducted research, an organic salt complex of norfloxacin with nitrate ion was synthesized. The composition, molecular and crystal structures of the newly synthesized organic salt were determined using X-ray structure analysis (RTT). It was determined that the total value of the energy of mutual, intermolecular interaction of selected organic salt molecules in the crystal cell is equal to -287.2 kJ/mol. The Hirschfeld surface study revealed that the primary part of intermolecular interactions is H...O/O...H (45.6%), H...H (28.2%), C...C (9.3%), and H...F/F...H (4.6%).

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