RESEARCH PAPER

A Comparative DFT (B3LYP) Analysis of the Spectroscopic and Thermodynamic properties of Nitrofurantoin and Nitrofurazone antibiotic

Nidaa A. Jasim

Assistant Professor, Physical Chemistry, Ministry of Education /Karbala Directorate of Education/ IRAQ
nedaa.aljbory@gmail.com

Received: 12th Sep, 2025; Revised: 18th Oct 2025; Accepted: 6th Nov, 2025; Available Online: 1st December, 2025

ABSTRACT
The study examined a group of antibiotics called nitrofurans , Nitrofurantoin(NFT) and Nitrofurazone (NFZ) used to treat urinary and reproductive tract infections . A Gaussian mechanics program was used to arrive at theoretical information related to these compounds. The study relied on the use of density function theory (DFT, B3LYP) with the Gaussian program (09). It was applied to calculate the balanced geometric shape of nirofurazone e compound, as well as calculating the thermodynamic functions (E0, H0, A0, S0, CV), as well as some physical properties (EHOMO, ELUMO, IP). The vibrational spectra and frequencies were also studied. The aim of the study is to obtain theoretical information that will help researchers in the practical field to reach the most effective compounds of nitrofurans and those with the least harm to the human body.
Keywords: DFT, Nitrofurantoin, Nitrofurazone, Theoretical study
How to cite this article: Jasim NA; A Comparative DFT (B3LYP)Analysis of the Spectroscopic and Thermodynamic properties of Nitrofurantoin and Nitrofurazone antibiotic. Int J Drug Deliv Technol. 2026;16(1): 242-250. DOI: 10.25258/ijddt.16.1.26
Source of support: Nil.
Conflict of interest: None

INTRODUCTION

Nitrofurans are a class of antimicrobial drugs containing a furan ring with one or more nitro groups in their chemical structure [1]. The most clinically important and were used to treat bacterial infections in livestock representative of this drug class is nitrofurantoin [2]. Nitrofurans are widely used as antibiotics against various types of bacteria. They have been used to treat bacterial infections in cattle and a range of other animals [4]. The active component in their structure is the nitrofuran ring [5]. Nitrofurantoin belongs to the nitrofuran class and is used to treat uncomplicated urinary tract infections[6] . Nitrofurantoin's structure contains hydantoin ring [2,4-imidazolidinedione] associated with an imine group (N=CH) a to [5-nitofuran ring] with nitro group in 5th position[7] . Nitrofurantoin is produced by bacterial enzymes and intermediate electrophilic compounds are formed hindering metabolic processes within the bacterial cell such as inhibiting the citric acid cycle (Krebs cycle) and the synthesis of nuclic acids (DNA , RNA) as well as breaking down cell wall therefore [8] , it prevents bacterial proliferation and growth within the bladder . This drug is more resistant to the development of bacterial resistance because it acts on several targets simultaneously [9]. It is an antibiotic effective against various types of bacteria and has been widely available since 1953 [10]. Its effects are limited to treating urinary tract infections and do not affect other body systems[11]. Nitrofurantoin is one of the antibiotics that can cause liver problems . It can cause acute or chronic hepatitis syndrome, which can be severe and lead to cirrhosis and liver failure [12] .Nitrofurazone is a semi carbazone resulting from the formal condensation of semi carbazide with 5-nitrofuraldehyde. A broad spectrum antibacterial drug [13] . Although studies have shown it to be antibacterial, there are potential health risks associated with its use, particularly cancer (such as causing tumors in the breast, ovaries, and skin) and allergic reactions. Due to these concerns, it has been banned in many food-producing animals [14]. The main component of nitrofurazone is oxacillin, which has the ability to inhibit bacterial growth within the urinary tract. It prevents the formation of the bacterial cell wall, leading to bacterial death or inhibiting their growth and reproduction [15] . Previous studies have not shown that nitro causes chromosomal aberrations in rats or congenital malformations in sperm [16], while chromosomal aberrations have been recorded in mammals, with both positive and negative results obtained. While some studies have indicated an increase in breast fibroids whenNitrofurazone is taken orally in mammals, other studies have shown no evidence of such an increase[17].

Action of nitrofurans

The action of nitrofurans involves bacterial enzymes reactive intermediate compounds. These intermediate compounds bind nonspecifically to the ribonucleic acid (DNA) and ribonucleic acid (RNA) in bacteria lead to damage and inhibits their synthesis . The active ingredients also inhibit key bacterial enzymes involved in the citric acid cycle and protein synthesis [18]. The drug's

**Author for Correspondence: nedaa.aljbory@gmail.com*

effectiveness stems from this inhibition of bacterial enzyme activity, making it more difficult for bacteria to develop resistance . Bacterial cells can metabolize nitrofurantoin. Bacterial enzymes nitroeductases convert nitrofurantoin into highly active intermediate such as (nitro-anion-free radical) that damage and inhibits vital cellular processes such as protein synthesis, DNA and RNA synthesis, and cell wall synthesis . These enzymes then damage bacterial ribosomes, proteins, and other macromolecules, such as DNA, RNA, and cell wall components.. It also inhibits other metabolic prosses such as those involved in the citric acid cycle. As a result, this damage the bacteria's vital functions leading to cell death[19] . Some mutations in nitroreductase genes may lead to strong resistance against nitrofurans . Nitrofuran compound in particular, exhibit high activity against Gram-positive and Gram-negative bacteria, with narrow toxicity to human cells and indications of carcinogenic effects. Furthermore, the clear identification of nitrofurans using functional groups and molecules can enhance the efficacy of these compounds [20].

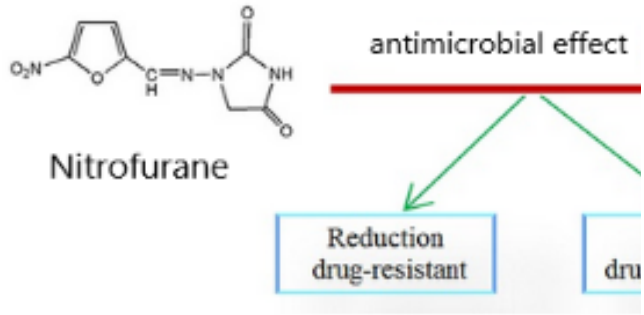

Fig 1: Action of nitrofurans

Density functional theory (DFT)

Theoretical chemistry is a discipline derived from theoretical physical chemistry, using computational programs and algorithms to develop a deep understanding of the molecular structure[21] and chemical reactions of certain complex compounds that are difficult to determine experimentally because they are costly and time-consuming It utilizes quantum mechanics and advanced computer applications to determine the[22]. properties of complex systems that are difficult to understand experimentally . The theoretical density function theory is considered one of the methods of quantum calculations in chemistry and physics, and one of the means of computer modeling for contemporary theoretical calculations[23] , This theoretical approach allows us to identify the intrinsic properties of relatively large, complex multi-particle systems; including the total energy of the system, the electron density of the orbitals, vibrational energies, and dynamical properties., physical and optical parameters of matter...). It is also one of the most widely used methods in quantum chemistry calculations because it can be applied to multi-particle systems at low cost and high speed[24]. Density Function Theory (DFT) in quantum mechanics is a method for calculating the quantum databases of complex particles, and its calculations rely on the density function of electrons ρ(r) instead of the wave function(ψ) . This simplifies the calculations because it transforms the problem from a multi-particle system to a single-particle system and relies on the Cohn-Sam potential. This simplifies the calculations because it transforms the problem from a multi-particle system to a single-particle system and relies on the Kohn - sham potential [25] .

Kohn–Sham equation for the electronic structure is given by

$$\nabla^2 \phi i(r) + V_{eff}(r) = E_i \phi_i(r) \qquad \frac{1}{2}$$

∇^2 Laplacian Operator ($\partial^2/\partial x^2 + \partial^2/\partial y^2 + \partial^2/\partial z^2$

ϕ (Phi): A scalar field, meaning it assigns a single value (like temperature or potential) to every point in space.

i: Often denotes the *i*-th component of a vector or field,

,

V_{eff}(r): The potential that affects a single electron and all other electron.

it is consist of **V_{ext}** (The external potential attracts the nucleus to the electron) and **V_H** (Hartree potential represents electrostatic repulsion

In density function theory calculations [26], the system and electronic structure are first determined, and then the appropriate exchange-Correlation functional, such as B3LYP(Slater[26] . Hartree -Fock , Bck s , and Lee- Yang -parr function) or GGA (Generalized Gradient Approximation) , LDA (Local Density A approximation) , The function is chosen based on the nature of the system and the electronic structure of the molecules being studied. To calculate thermodynamic functions using density function theory (DFT), the complex wave function is replaced by electron density as the underlying variable [27], where energies (e.g., total energy) and density are calculated and then used to evaluate thermodynamic properties [28]. These functions are calculated using functionals that describe chemical exchange and bonding , and VASP and Gaussian software are used to solve the Kohn-Sham equation in order to obtain the electron density and then the thermodynamic functions with high accuracy Gibbs energy , entropy , and total energy . One of the advantages of the density function theory method is dimensionality reduction by transforming the multi-body wave function problem into a three-dimensional electron density problem, thus reducing computational complexity [29], in addition to the method's efficiency, low cost, and accuracy . Density function theory (DFT) is commonly applied in computational chemistry to study chemical reactions, particularly organic reactions. Density function theory (DFT) is widely applied in computational chemistry to study many chemical reactions, especially organic reactions. DFT can also be used to calculate the electronic energies of various active compounds, making it easier for chemists to determine the thermal and kinetic properties of most chemical reactions with great accuracy[30].

RESULTS AND CALCULATIONS

Geometric Paramedic

In this theoretical study , the geometric shape has been calculated (bond lengths and bond angels) of nitrofurans compound using DFT method **(Fig 1 , Fig 2 , table 1 table 2**)

Nitrofurantion structure

Macrobid, Macrodantin and others

Chemical formula $C_8H_6N_4O_5$ (NFT)

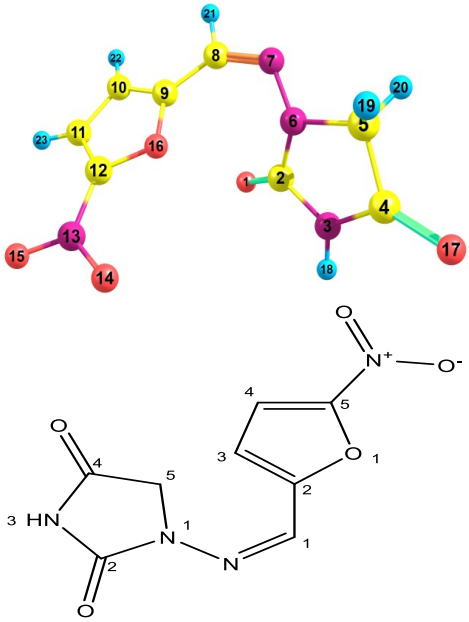

Fig 2: [(*E*)-(5-nitrofuran-2-yl)methylideneamino]imidazolidine-2,4-dione

Nitrofurazone structure

Chemical formula $C_6H_6N_4O_4$ (NFZ)

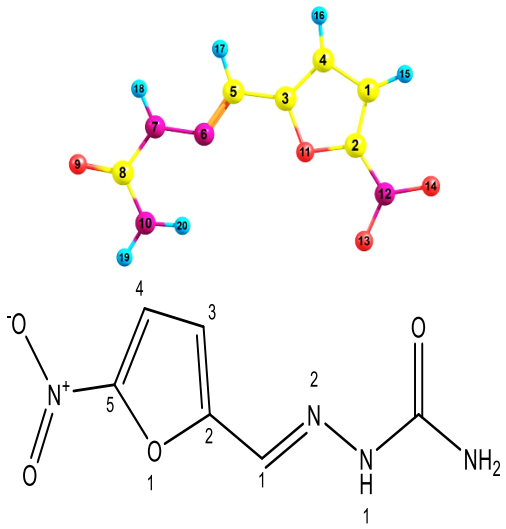

Fig 3: [(E)-(5-nitrofuran-2-yl)methylideneamino]urea

Bond lengths and angles:

In **table 1** and **table 2** we observe that there is a great similarity with a few differences , the bonds between C and NO_2 group in both compounds rang $1.418A^0$ - $1.415A^0$ ·the bonds in NO_2 group ranged $1.27A^0$- $1.26\ A^0$, the bonds in C=N group ranged $1.304A^0$-$1300\ A^0$ · and the bonds in C=O group $1.233A^0$- $1.246A^0$.

The bond lengths calculated from theoretical study by using DFT method help estimate the energy of diuretics Homo and Lumo , which may increase the drug's efficacy in inhibiting bacterial DNA . Knowing the bond energies allows us to determine the biological activity, chemical stability, and reactivity of the functional groups of both compounds. This explains the difference in the medical use of the two antibiotics, This explains the difference in the use of the two antibiotics in medicine, where is nitrofurantoin (NFT) is used to treat urinary tract infections while the nitrofurazone (NFZ) is used for localized infections. Even slight differences in angles, due to the presence of functional groups and hydrogen bonds, may alter the energy gap between the Homo and Lumo, affecting the stability of the antibiotic or potentially increasing its biological activity against bacteria. It may also influence the entropy value and its activity against bacterial enzymes.

Table 1: Geometric parameters (bond lengths, angles) in Angstrom for nitrofurantoin

bond lengths	Valu in Angstrom	*angles*	Value in Angstrom
R(1-2)	1.234	A(1-2-3)	126.9
R(2-3)	1.406	A(1-2-6)	127.8
R(2-6)	1.403	A(3-2-6)	105.2
R(3-4)	1.390	A(2-3-4)	114.0
R(3-18)	1.009	A(2-3-18)	121.9
R(4-5)	1.526	A(2-6-5)	111.8
R(4-17)	1.233	A(2-6-7)	125.7
R(5-6)	1.469	A(4-3-18)	124.1
R(5-19)	1.093	A(3-4-5)	105.6
R(5-20)	1.096	A(3-4-17)	126.9
R(6-7)	1.385	A(5-4-17)	127.5
R(7-8)	1.304	A(4-5-6)	102.9
R(8-9)	1.440	A(4-5-19)	110.9
R(8-21)	1.086	A(4-5-20)	111.4
R(9-10)	1.386	A(6-5-19)	111.6
R(9-16)	1.394	A(6-5-20)	111.0
R(10-11)	1.422	A(5-6-7)	117.5
R(10-22)	1.079	A(19-5-20)	108.9
R(11-12)	1.373	A(6-7-8)	120.9
R(11-23)	1.077	A(7-8-9)	132.6
R(12-13)	1.418	A(7-8-21)	112.9
R(12-16)	1.376	A(9-8-21)	114.3
R(13-14)	1.265	A(8-9-10)	130.5
R(13-15)	1.272	A(8-9-16)	120.3
angles	Value in Angstrom	angles	Value in Angstrom
A(10-9-16)	109.0	A(11-12-13)	131.1
A(9-10-11)	107.6	A(11-12-16)	111.2
A(9-10-22)	125.8	A(13-12-16)	117.7
A(9-16-12)	106.3	A(12-13-14)	118.7
A(11-10-22)	126.6	A(12-13-15)	116.0
A(10-11-12)	105.9	A(14-13-15)	125.3
A(10-11-23)	128.2	A(14-13-15)	125.3
A(12-11-23)	125.9		

Table 2: Geometric parameters (bond lengths, angles) in Angstrom for nitrofurazone

bond lengths	Valu in Angstrom	*angles*	Value in Angst
R(1-2)	1.373	A(2-1-4)	106.1
R(1-4)	1.423	A(2-1-15)	125.8
R(1-15)	1.077	A(1-2-11)	111.1
R(2-11)	1.383	A(1-2-12)	130.9
R(2-12)	1.415	A(4-1-15)	128.1
R(3-4)	1.386	A(1-4-3)	107.5
R(3-5)	1.434	A(1-4-16)	126.6
R(3-11)	1.393	A(11-2-12)	118.0
R(4-16)	1.078	A(2-11-3)	106.2
R(5-6)	1.300	A(2-12-13)	118.9
R(5-17)	1.092	A(2-12-14)	116.0
R(6-7)	1.348	A(4-3-5)	131.5
R(7-8)	1.414	A(4-3-11)	109.2
R(7-18)	1.017	A(3-4-16)	125.9
R(8-9)	1.246	A(5-3-11)	119.3
R(8-10)	1.357	A(3-5-6)	121.3
R(10-19)	1.006	A(3-5-17)	116.2
R(10-20)	1.009	A(6-5-17)	122.5
R(12-13)	1.265	A(5-6-7)	120.4
R(12-14)	1.274	A(6-7-8)	121.0
		A(6-7-18)	123.2
		A(8-7-18)	115.8
		A(7-8-9)	119.1
		A(7-8-10)	114.4
		A(9-8-10)	126.5
		A(8-10-19)	118.3
		A(8-10-20)	120.8
		A(19-10-20)	120.9
		A(13-12-14)	125.2

Charge and electronic density

In table 3,4 we observe that nitrogen and oxygen atoms have the highest electron density And high electronic cloud , which makes the carbon atoms bonded to them more positive and bond between them more polar . The oxygen atoms in the hydantoin ring (nitrofurantoin) more electronegative than the oxygen atoms in nitrofurazone) due to the double bond in C=O group in hydantoin ring . Therefore nitrofurantoin antibiotic more polar than nitrofurazone, as the electron density in nitrofurazone distribution along the side chain. this electron density distribution is the reason for difference in the effectiveness of the tow antibiotics and there ability to bind to bacterial proteins and enzyme.

Table 3: Charges and Electronic densities of nitrofurantoin NFT ($C_8H_6N_4O_5$)

Atom	Charge	Electronic Density	Atom	Charge
O1	-0.417	6.417	C12	0.565
C2	0.774	3.226	N13	0.028
N3	-0.685	5.685	O14	-0.274
C4	0.530	3.470	O15	-0.297
C5	-0.128	4.128	O16	-0.496
N6	-0.507	5.507	O17	-0.400
N7	-0.153	5.153	H18	0.363
C8	-0.008	4.008	H19	0.218
C9	0.338	3.662	H20	0.217
C10	-0.156	4.156	H21	0.178
C11	-0.073	4.073	H22	0.181
C12	0.565	3.435	H23	0.204

Table 4: Charges and Electronic densities of nitrofurazone NFZ ($C_6H_6N_4O_4$)

Atom	Charge	Electronic Density	Atom	Charge
C1	-0.076	4.076	O11	-0.485
C2	0.550	3.440	N12	0.024
C3	0.301	3.699	O13	-0.275
C4	-0.164	4.164	O14	-0.303
C5	0.018	3.981	H15	0.200
N6	-0.168	5.168	H16	0.175
N7	-0.519	5.518	H17	0.151
C8	-0.706	4.706	H18	0.323
O9	-0.452	6.452	H19	0.344
N10	-0.726	5.726	H20	0.365

Physical properties

Homo and Lumo are types of molecular orbital, Homo (highest occupied molecular orbital)

and Lumo (lowest unoccupied molecular orbital) , the energy difference ($_{LUMO\ -\ HOMO}$) reprecents to energy gap that can be used to determine the chemical stability and biological activity of the antibiotics against bacterial proteins and enzymes .The results in this study indicate that the energy gap in Nitrofurantoin equal 3.384 while the energy gap in Nitrofurazone equal 3.418 .

the energy gap reflected chemical stability and charge transfer capacity , which contributes to the antibiotic 's activity against bacteria. When the energy gap is small, the compound's activity increases, making it easier to oxidation-reduction reactions to generate free radicals that kill bacteria. Therefore, the results show that Nitrofurantoin is more effective than Nitrofurazone against bacteria.**(table 5)**

Table 5: E_{HOMO} , E_{lumo} and cap energy, (IP) of NFT and NFZ in (ev) unite

Comp.	E_{HOMO} (ev)	E_{LUMO} (ev)	E
Nitrofurantoin	-6.818	-3.434	
Nitrofurazone	-6.720	-3.302	

Thermodynamic Functions

The study showed higher thermodynamic values G(Gibbs free energy) , A (Helmholtz energy), H (Enthalpy) for NFT compared to NFZ due to NFT having additional sites for strong hydrogen bonds compared to the linear structure of NFT . Since these functions are indicators of chemical stability and activity so NFT is more active against bacteria . An increase in the entropy of nitrofurantoin compound may indicate multiple pathways through which the antibiotic weakens the bacterial cell. It targets vital pathways within the bacterial cell (protein synthesis, cell wall construction, DNA synthesis) , thus hindering bacterial growth and leading to bacterial death. In other words, the greater the entropy, the stronger the antibiotic's effect on bacteria **.(Table 6)**

Table 6: Standard Thermodynamic Function at 298.15K of the NFTand NFZ

Comp.	S^0 J /mol .K	E^0 KJ /mol	H^0 KJ /r
Nitrofurantoin	502.080	451.717	454.1
Nitrofurazoin	469.164	396.371	398.8

IR intensities

In (table 7), The study showed agreement between the values calculated theoretically using density function theory DFT and the experimental values, noting a slight difference in the theoretical calculations since they are performed at standard temperature and in the gaseous phase, while the experiments are carried out under laboratory conditions , in addition to the effect of hydrogen bonds which leads to a shift in the vibrations.

The measurement coefficient can be used to adjust the frequencies to accurately match the experimental results . The table 7 shows the most important infrared spectral values for compound NFT and compound NFZ, which reflect the unique structure of these two compounds. These spectra are used to confirm the identity of the antibiotic and compare them with experimental values.

Table 7: Comparison of the most Important infrared spectral values for NFT compound and NFZ compound experimentally and theoretically using DFT

Number	IR intensities	Frequency cm-1	Number	IR intensities
1	2.4998	34.6543	36	15.0441
2	1.1324	42.8208	37	10.1093
3	0.3758	62.1897	38	3.9379
4	2.0686	81.9543	39	24.4423
5	4.5797	104.2488	40	3.6409
6	3.6118	162.0054	41	1.45
7	1.6243	169.5338	42	23.2195
8	8.2442	202.2739	43	33.8593
9	5.604	214.6244	44	86.1833
10	5.6186	259.9099	45	143.5052
11	5.099	271.0215	46	55.6527
12	1.951	312.8648	47	160.5701
13	15.2035	383.0119	48	95.5545
14	2.4041	424.7305	49	219.1516
15	19.8789	515.9911	50	128.3344
16	10.354	528.183	51	143.4484
17	15.6476	550.1825	52	166.3096
18	23.5649	556.629	53	18.6776
19	6.8756	579.5639	54	52.2867
20	1.7023	594.5764	55	19.5273
21	7.2362	634.8223	56	134.4667
22	73.919	677.5923	57	67.5422
23	3.342	690.6002	58	23.5773
24	7.3337	708.0167	59	19.1334
25	19.884	715.5439	60	7.8126
26	83.9128	742.3111	61	548.5209
27	13.5536	780.8875	62	213.2207
28	31.7316	797.1592	63	13.3375
29	35.4353	842.642	64	2.2728
30	45.2395	852.1357	65	4.6916
31	83.9128	742.3111	66	0.3637
32	13.5536	780.8875	67	5.3783
33	31.7316	797.1592	68	81.8427
34	35.4353	842.642		
35	45.2395	852.1357		

Table 8: IR intensities and Frequency cm^{-1} of NFT

Nitrofurantoin	Theoretically	experimental	Nitrofuraz
	3670-3139	3281-3300	N-H (NH_2
N-H (hydantoin)	3300-3139	3400-3200	N-H (hydan
C-H	3139-3082	3100-2850	C-H
C=O	1797-1761	1808-1770	C=O
NO_2	1570-1323	1550-1340	NO_2
C-N (aliphatic)	1125-1070	1110-1000	C-N (aliph
C-N(aromatic)	1000-1250	1340-1250	C-N (aliph

Table 9: IR intensities and Frequency cm^{-1} of NFZ

Number	IR intensities	Frequency cm-1	Number	IR intensities
1	1.1395	48.7601	36	2.9971
2	2.4376	49.2391	37	394.6113
3	4.4309	60.9506	38	139.1498
4	0.3111	90.081	39	67.3541
5	0.6316	146.7887	40	85.5614
6	2.1511	160.2012	41	554.758
7	0.5973	203.571	42	90.8969
8	12.3217	253.2367	43	186.9444
9	17.688	281.9291	44	68.3674
10	4.2857	316.919	45	66.9143
11	3.1003	385.2936	46	234.0974
12	31.2082	426.3084	47	164.5592
13	8.1471	451.236	48	403.9004
14	4.6841	538.4386	49	31.9181
15	27.1061	558.4838	50	1.1653
16	74.1743	569.854	51	4.7686
17	1.545	591.8539	52	28.1857
18	268.6708	631.2222	53	37.5192
19	2.3477	642.8142	54	89.4957
20	23.4984	643.9157	55	1.1653
21	2.1748	691.4052	56	4.7686
22	7.5114	710.7811	57	28.1857
23	184.8345	758.3793	58	37.5192
24	13.5582	773.0892	59	89.4957
25	7.0221	815.2884	60	
26	39.2641	845.239	61	
27	13.4238	946.3236	62	
28	32.0669	960.4819	63	
29	35.4999	968.0725	64	
30	2.4522	970.2353	65	
31	3.1936	996.3919	66	
32	32.9333	1070.1918	67	
33	89.1136	1113.1781	68	
34	295.2471	1172.6026		
35	63.6459	1195.3194		

Studying the infrared absorption spectra of antibiotics is theoretically a powerful tool in pharmaceutical chemistry for investigating biological activity, monitoring antibiotic quality, detecting impurities, and saving time and effort in developing antibiotics.

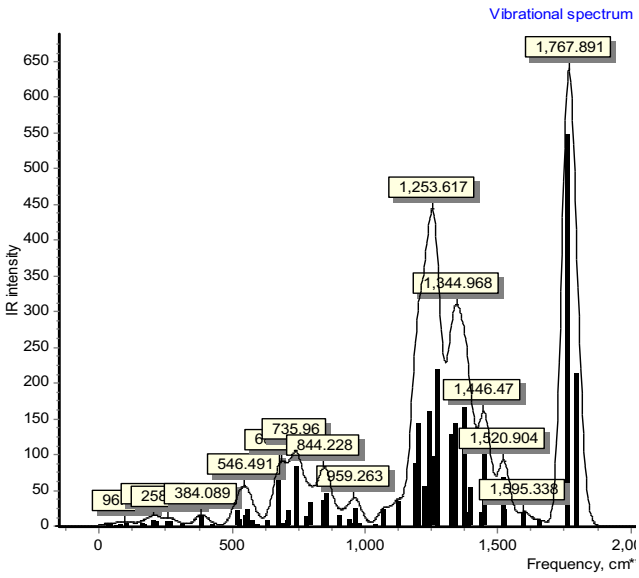

Fig 4: nitrofurantoin of IR Spectrum of Important values

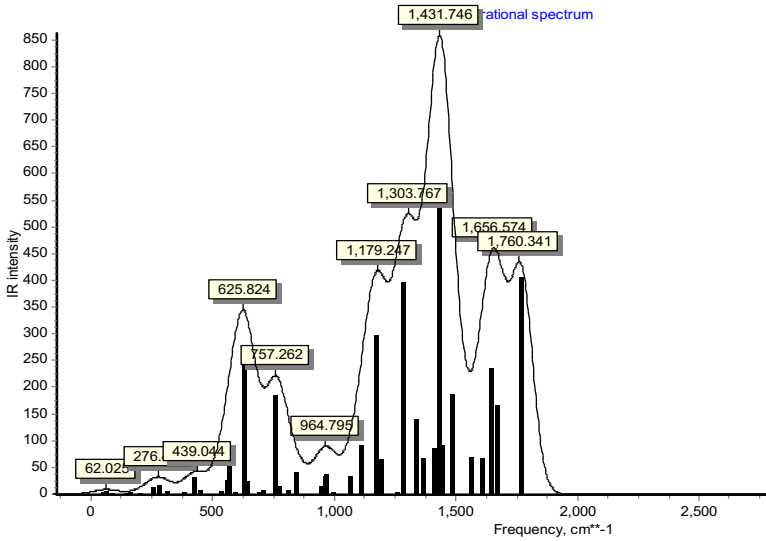

Fig 5: Nitrofurazone of IR Spectrum of Important values

AIM OF RESEARCH

The aim of theoretically studying furan compounds using DFT is to predict their properties, behavior, electronic structure, and physical characteristics without the need for costly and complex laboratory methods. It also helps in interpreting and analyzing laboratory results, which accelerates the development of nitrofuran derivatives and the design of more effective, less toxic, and less side-effect-producing derivatives..

RECOMMENDATIONS

In theoretical studies, density function theory is preferred with B3LYP due to its high ability to predict balanced geometric structures. Therefore, we recommend further theoretical studies of nitrofurans and comparing them with laboratory results to determine their biological activity and identify the antibiotic with the lowest toxicity, fewest side effects, and most effective targeting of bacteria.

REFERENCES

[1] Pedersen, JM., Matsson P., Bergstrom, CA., , 2013 , Early identification of clinically relevant drug interactions with the human bile salt export pump (BSEP/ABCB11). ***Toxicol Sci***. Dec ;136(2): 328-43.

[2] Liu, T., Hwang, L., Burley, SK., Nitsche, CI., Southan, C., 2025 , knowledgebase of protein-small molecule binding data. ***Nucleic Acids Res***. 6 ;53: 1633- 1644.

[3] Röschenthaler R., Kindler P., Herrlich P., Igbokwe J. 1970 , The action of nitrofurantoin: inhibition of growth of Escherichia coli K 12 and of IPTG-induced beta-galaotosidase synthesis. ***Zentralbl Bakteriol Orig*** ;215(2):203–211.

[4] Kettewll ,R., 2024 , lnsights into durability against resistance from the antibiotic nitrofurantoin, **npj Antimicrob Resist .,** 41 (2) : 1-6 .

[5] Nada ,F. K., Hannah, W., and Tomazo , J.K.,2025 , Long -term nitrofurantoin use :risks and alternatives in general practice , ***BRIT, J GEN PRACT*** , 75(756) : 334-335 .

[6] Christophr , L., ``Sabeel, P.V., Navaneethan , P., 2025 , Global prevalence of nitrofurantoin resistant uropathogenic Escherichia coil (UPEC)in human: systematic review and meta – analysis , ***J.Antimicrob. Chemother***., 20;80(10):2609-2621.

[7] Goodman, L.S. , and A. Gilman. (eds.), 1975, The Pharmacological Basis of Therapeutics. 5th ed. New York: ***Macmillan Publishing Co., Inc***., 1975., 1008-1019.

[8] Vass ,M., Hruska , K., Franek .M. , 2008 , Nitrofuran antibiotics **,** *Vet Med Czech*, 53(9): 469-500.

[9] Cooper, K.M., McCracken, R.J., Buurman, M., Kennedy, D.G., 2008: Residues of nitrofuran antibiotic parent compounds and metabolites in eyes of broiler chickens. ***Food Addit. Contam.*"**, 25 , 548-556.

[10] Calderaro A. , Maugeri A. , Laganà G., Magazù S., 2021 , Molecular Basis of Interactions between the Antibiotic Nitrofurantoin and Human Serum Albumin: A Mechanism for the Rapid Drug Blood Transportation. ***Int J Mol Sci***., 14 ;22(16).

[11] Wan, Y., Mills, E., Vieira, A., et al ., 2021, Alterations in chromosomal genes *nfsA*, *nfsB*, and *ribE* are associated with nitrofurantoin resistance in *Escherichia coli* from the United Kingdom. ***Microb Genom***.;7(12),100-105.

[12] Khamari, B., Bulagonda, E. P., 2024., Unlocking Nitrofurantoin: Understanding Molecular Mechanisms of Action and Resistance in Enterobacter ales. *Med Princ Pract***,** 34(2):121-137 .

[13] Guangxin, Y, Shuhai , D., et al ,2024 , Research progress on metabolites of nitrofurazone in aquatic products **,** ***Heliyon*** **,**10 (8) : 2405-8440**.**

[14] Mohammad, H. , Afshin, Z., Sara, F.,2003 , A Modified Method for the Synthesis of Nitrofurazone , ***Int. J. pharm . Res*** ., 2(2) : 67-69.

[15] Karapolat, S., et al , 2020 , The effective of nitrofurazone on wound healing in thoracoabdominal full thickness Skin defects ,***Wounds*** , 32 (5) :134-141 .

[16] Ali ,R., Elise , K., et al . 2011 , Activation of nitrofurazone by azomethanes :multiple activities in one enzyme , ***Sci . Rep*** , 1 (63) : 2045-2322 .

[17] Paul, R., Race, A. L. Lovering, R. M., 2005 , Structural and Mechanistic Studies of Escherichia coli Nitroreductase with the Antibiotic Nitrofurazone , ***J.Biol. Chem*** , 280(14) : 13256-13264.

[18] Calderaro, A., Maugeri, A. D., et al, 2021 , Molecular Basis of Interactions between the Antibiotic Nitrofurantoin and Human Serum Albumin: A Mechanism for the Rapid Drug Blood Transportation. ***Int J Mol Sci*** ,22(16): 23-28.

[19] Tan, IL., Polydefkis, M.J, Ebenezer, GJ.,2012 . Peripheral nerve toxic effects of nitrofurantoin. ***Arch Neurol*** , 69(2):265-268.

[20] Sepideh, R. , Sholeh, A., Farzad, R. , 2022, Nitrofurans as Potent Antibacterial Agents: A Systematic Review of Literature , ***Int. J. Adv. Biol. Biomed. Res*** 10(2): 126-138.

[21] Nidaa , A . Jasim ., 2020 ., Theoretical Study of Some Thermodynamic, Physical Properties and Spectra for Some Antihistamines by Using (DFT, B3LYP, 6-31G)., **Int. J. Pharm. Res.,** 12 (2) , 3378-3380.

[22] Davin , Thomas J., 2009, Computational chemistry of organometallic and inorganic species**,** ***PhD thesis*** , University of Glasgow **,** Glasgow , Scotland, 49-59 .

[23] Eram, K., Anuradha, S., et al , 2019 , Structural and Reactivity Analyses of Nitrofurantoin–4-dimethylaminopyridine Salt Using Spectroscopic and Density Functional Theory Calculations , ***Crystals*** , 9 (8): 413-423.

[24] Assadi , M. H .; et al ., 2013 "Theoretical study on copper's energetics and magnetism in TiO_2 polymorphs" , ***J. Appl. Phys.*** , 113 (23): 233913-233915.

[25] Jiashu , L., Martin, Gold H. G. **,** 2025 Standard Chemical Database 137 (GSCDB137): A Diverse Set of Accurate Energy Differences for Assessing and Developing Density Functionals **,** ***J. Chem. Theory Comput*** **,** 21 (24) :12601-1262.

[26] Drut . J.E., Furnstahl . R.J ., 2010 **,** Toward *ab initio* density functional theory for nuclei , ***Prog. Part. Nucl. Phys.,*** 64(1): 120-168.

[27] Nidaa, A. Jasim., 2020), Theoretical Study of Some Physical and Thermodynamic Properties for some Diclofenac Derivatives by using Semi-Empirical Calculations (PM3 Method) , ***Sys Rev Pharm*** ;11(12):1294-1304.

[28] Gabriella, G., 2017 , Quantum chemistry: DFT's midlife crisis, ***Nat. Rev. Chem,*** 1(2):0019.

[29] Andrew M.T., Trygve, H., 2022, FT Exchange: Sharing Perspectives on the Workhorse of Quantum Chemistry and Materials Science , 24 (47) : 28700-28781.

[30] Federico ,Z. and Mel,L.,2019 , Density and spin-density-functional theories through spin-free wave functions , ***Phys. Rev. A.,*** 100(6): 62507-62510. ·