RESEARCH ARTICLE

Theoretical Study and Biological Activity of [Clotrimazole,7-[2-(Benzimidazolyl) AZO] 8- hydroxyl Quinoline] by Using (DFT) and (PM3) Method

Amar T. Musa[1*], Khalida Abaid[2], Faryal Majeed[3]

[1]*Industrial Research and Development Authority, Ministry of Industry and Minerals, Baghdad, Iraq*
[2] *Department of Chemistry, College of Sciences, Al-Nahrain University, Baghdad, Iraq*
[3] *Department of Veterinary Medicines, Industrial Research and Development Department, Ministry of Industry and Minerals, Baghdad, Iraq*

Received: 18th March, 2021; Revised: 09th April, 2021; Accepted: 20th May, 2021; Available Online: 25th June, 2021

ABSTRACT

Imidazole medications have broadened the spectrum of clinical narcotics to address different provisions. In the field of medicinal chemistry, numerous methods for the synthesis of imidazole and even their separate structure reactions give enormous scope. Medicinal chemistry is the science in which the effect of the chemical structure on

Biological activity is determined, and the practice of medicinal chemistry evolved from An observational one involving organic synthesis of new compounds is primarily focused on structural alteration and then defines their biological activity.[1,2] Functional and biological chemical activities of certain derivatives of benzimidazole [Clotrimazole (CTZ), 7-[2-(Benzimidazolyl) AZO] 8- hydroxyl quinoline (BIAHQ)] can be diagnosed using density functional theory DFT using Gaussian program 09, In addition, QSAR data has been used to develop relationships between biological activities and thermophysical properties of chemicals, through the HyperChem 8.0 program by using the semi-empirical (SE) method at the (PM3) level. In computational chemistry, new drugs and chemicals can be designed through numerous combinations of hypotheses for the start of every business, the theoretical the analysis is a valuable preliminary stage. Since it offers a theoretical explanation of the properties of substances (chemical, physical, and biological properties) without doing studies to find out about this and the lowest expense.

Keyword: Clotrimazole, BIAHQ, DFT, PM3, LOG P, QSAR, HOMO, LUMO, PIC50

International Journal of Drug Delivery Technology (2021); DOI: 10.25258/ijddt.11.2.21

How to cite this article: Musa AT, Abaid K, Majeed F. Theoretical Study and Biological Activity of [Clotrimazole,7-[2-(Benzimidazolyl) AZO] 8- hydroxyl Quinoline] by using (DFT) and (PM3) Method. International Journal of Drug Delivery Technology. 2021;11(2):358-364.

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

For the synthesis of pharmaceuticals and the treatment of different diseases, the value of the word 'Imidazole' and its derivatives have been popular for the past few years. In various natural compounds, the imidazole ring exists and is very commonly dispersed in essential amino acids. The incorporation of the imidazole nucleus is an important synthetic strategy in drug discovery. The high therapeutic properties of imidazole-related drugs have encouraged medicinal chemists to synthesize a large number of novel chemotherapeutic agents.[3,4] Numerous methods for the synthesis of imidazole and also their various structure reactions offer enormous scope in the field of medicinal chemistry.

Clotrimazole {1-[(2-chlorophenyl)- diphenylmethyl] imidazole}; The molecular formula of clotrimazole is $C_{22}H_{17}ClN_2$, and its molecular weight is 344.8 g/mol. It comprises four aromatic rings bound to a tetrahedral (sp3 hybridization) carbon atom, creating a steric encumbrance on this atom. Clotrimazole is known to be chemically unusual. An imidazole ring is one of the aromatic groups, and it mediates electron transfer reactions in biological processes. The remaining aromatic rings consist of triphenylmethyl systems that stabilize the radical intermediates. Chloro substituted at position C7 is one of these phenyl rings.[5]

In a recent analysis, researchers were able to prepare a compound 7-[2-(Benzimidazolyl) azo] 8-hydroxyl Quinoline (BIAHQ). The imidazole ring enters the replication reactions of the AZO compounds when it is reacted with the diazonium salt, which has electrophilic properties that allow it to be coupled with the dense electrophilic imidazole ring.[6] Where new

Author for Correspondence: Amartuma1975@gmail.com

types of azo dyes derived from the compound benzimidazole are prepared and used by artists and dyeing leather in leather tanning laboratories. Because they give them excellent coloring properties and their stability in color, it is necessary to know the toxicity of these dyes and their suitability for human use by applying the specifications of the pharmaceutical industry.[7]

Biological Activity

Pharmacological behavior is considered to characterize beneficial effects as a drug and bioactive, whether it has contact with or impacts some cell tissue in the human body. The impacts of prescription candidates as well as the toxicity of a substance. The beneficial or harmful effects of a drug on a living material are characterized by the biochemical reactions of living organisms, biological activity, or pharmacological activity. Through a wide range of physical and chemical parameters, the properties of biologically active molecules are determined. The parameters describing the biological activities are used as response variables and the physicochemical properties as predictor factors.[8]

Quantum Chemical

In relation to physio-chemical parameters and electronic characteristics considered for the design of a drug, it is a method of drug design:

1. Chemical changes in electronic characteristics modify the basis of the drug molecule's existence, which includes the fundamental physical properties of a particle. It includes electron, neutron, and proton characteristics; it's called quantum mechanics.
2. To alter the electronic property, the electrons in the molecules are aligned with the orbital electrons and hence the change in the properties that must be achieved is by the change of the orbitals.[9]
3. Some properties such as (shape and size of the molecule, the property of lipid susceptibility, electronic effects within the molecule, the distribution of charges) are believed to affect drug activity, so a measurable mathematical relationship was established, is the quantitative structure-activity relationship (QSAR).[10]

Optimized Structure

The reactive molecular diagram represents molecular structural optimization that contains the values of the reactivity indices. Figure 1 provides the optimized configurations of molecules. The outcome of the calculation revealed that the structural parameter data in Table 1 were coincidental with the available theoretical for clotrimazole molecule[11] utilizing the Gaussian 09 program for some benzimidazole derivatives {Clotrimazole (CTZ), (BIAHQ)}.

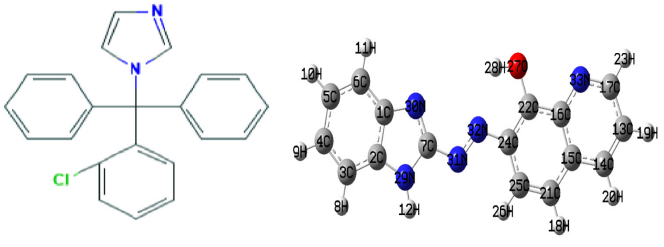


Figure 1: Optimized molecular structure for {Clotrimazole (CTZ), (BIAHQ)}

Molecular Orbital

The energy of the highest occupied molecular orbital (HOMO), also correlated with the electronic donation capacity of a molecule (negatively charged groups or red color atoms is represented as localized on nitrogen atoms in imidazole ring and oxygen atoms), attack lowest non-occupied molecular orbital (LUMO). And while LUMO's energy implies the molecule's ability to accept electrons (positive charge groups or green color atoms is represented as localized on the carbon and hydrogen atoms), attack HOMO. The electrons will be more likely accepted by the molecule[12,] as shown in Figure 2.

The theorem establishes a relationship between the energies of HOMO and LUMO and the potential for ionization and affinity of electrons. It is possible to determine the ionization potential (I) and affinity for electrons (A) using the Koopmans theorem,[13] as shown in equation (1).

$$E_{gap} = (E_{LUMO} - E_{HOMO})\ \ IP - EA \quad ...(1)$$

From the HOMO and LUMO energy values, the ionization potential (I) and electron

affinity (A) can be determined according to equations (2) and (3). Table 1 contains the

HOMO, LUMO distance, ionization potential, and electron affinity data.

$$IP = -E_{HOMO} \quad ...(2)$$

$$EA = -E_{LUMO} \quad ...(3)$$

To define universal reaction descriptors by means of HOMO and LUMO energies in order to define molecular or atomic properties of interest and chemical quantities. These chemical descriptors were defined by Koopman's theory.[13] And depicted by {electrophilicity (ω), chemical potential (μ),

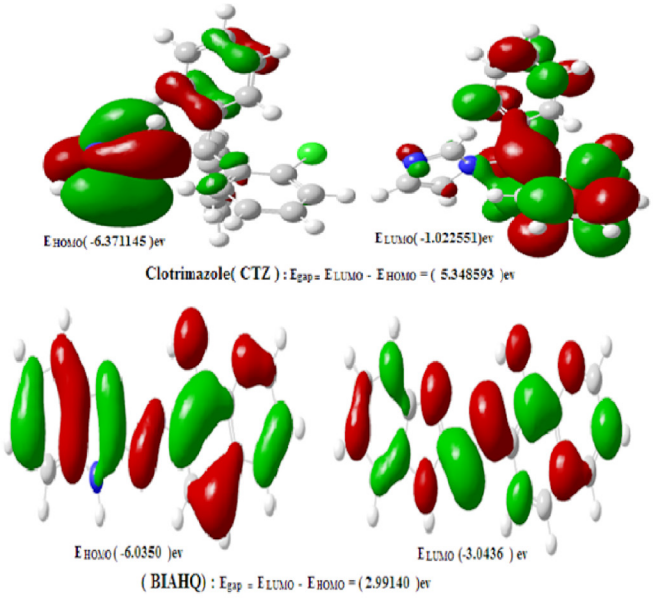


Figure 2: The energy values with molecular orbital geometry of {(CTZ), (BIAHQ)} molecules in gas phase

Table 1: The optimized geometry data of {(CTZ), (BIAHQ)} molecule for Bond length and Bond angle

Structural parameter	*DFT 6-311 G This work*	*DFT 6-311G other work [11]*	*Structural parameter*	*DFT 6-311 G This work*	*DFT 6-311G other work [11]*	*Structural parameter*	*DFT 6-311 G This work*	*Structural parameter*	*DFT 6-311-G This work*
Bond length in (A°) (CZM)			*Bond angle in Degree (CTZ)*			*Bond length in (A°) (BIAHQ)*		*Bond angle in Degree (BIAHQ)*	
$CL_1 – C_8$	1.808	1.764	$CL_1 - C_8 --- C_5$	122.46	122.7	$C_1 --- C_2$	1.42	C1--- C2 --- C3	122.01
$C_8 --- C_5$	1.40	1.408	$CL_1 - C_8 --- C_{17}$	114.71	115.4	C3-H8	1.08	C1--- C6 --- H11	119.81
$C_5 --- C_9$	1.40	1.408	$C_5 --- C_8 --- C_{17}$	122.81		C 1 - N 30	1.39	C3 --- C2 --- N29	133.28
$C_4 - C_5$	1.55	1.558	$C_8 --- C_{17} --- H_{34}$	119.35		C2 - N 29	1.38	C1 --- C2 --- N29	104.69
$C_6 - C_4$	1.55	1.558	$C_5 --- C_4 --- N_2$	109.16	109.6	C 7 - N 29	1.39	C2– N29– C7	107.43
$C_7 - C_4$	1.55	1.558	$C_6 - C_4 - C_7$	113.82		C 7 = N 30	1.33	N29 --- C7 – N30	112.41
$N_2 - C_4$	1.50	1.500	$C_6 --- C_4 --- N_2$	104.96		N29 – H12	1.00	C7 – N30 --- C1	105.02
$N_2 – C_{14}$	1.39	1.388	$C_7 --- C_4 --- N_2$	107.95		C 7-N 31	1.38	N30 --- C1 --- C2	110.42
$C_{16} = C_{14}$	1.37	1.368	$C_4– N_2– C_{14}$	128.77		N31 = N32	1.28	C2 –N29 - H12	128.41
$C_{16} - N_3$	1.39	1.375	$C_4– N_2– C_{15}$	124.92		N32 - C24	1.39	H12 - N29 - C7	124.14
$N_3 --- C_{15}$	1.32	1.314	$N_2 - C_{14} = C_{16}$	106.14	106.1	C13 --C14	1.37	C6 --- C1 --- N30	129.50
$N_2 - C_{15}$	1.38	1.376	$C_{14} = C_{16} - N_3$	110.39		C22 – O27	1.35	N29 - C7 – N31	116.51
$C_{16} – H_{33}$	1.07		$C_{16} – N_3 --- C_{15}$	105.49	105.5	O27 – H28	0.98	N30 --- C7 – N31	131.07
$C_{10} - C_6$	1.40		$N_3 --- C_{15} – N_2$	111.74	112.3			C7 – N31 --- N32	115.91
			$C_{15} – N_2 – C_{14}$	106.21				N31 --- N32 –C24	117.96
			$N_2 - C_{15} - H_{32}$	122.74				N32 – C24 ---C25	126.19
			$H_{32} - C_{15} - N_3$	125.51				C16---C22 --- O27	119.71
			$N_3 – C_{16} - H_{33}$	121.00				C22--- O 27 – H28	108.16
			$H_{33} - C_{16} = C_{14}$	128.59				O 27 - C22 --- C24	120.41
			$C_{16} = C_{14} – H_{31}$	131.40				C22 --- C16 ---N33	119.03
			$H_{31}– C_{14} - N_2$	122.42				C15 --- C16 ---N33	122.58
								C16 --- N 33 --C17	118.32
								N 33 --- C17---C13	123.20

electronegativity (χ), hardness (η), and softness (S)} in the Relationship Molecular Orbit System, expressed as follows: [(4), (5), (6), (7), (8)].

Chemical descriptor data for molecules of imidazole derivatives {Clotrimazole (CTZ), (BIAHQ)}, as seen in Table 2, 3.

$$\mu = - (I + A)/2 \quad ...(4)$$

$$\eta = (I – A)/2 \quad ...(5)$$

$$S = I / \eta \quad ...(6)$$

$$\chi = (I+A)/2 \quad ...(7)$$

$$\omega = \mu^2/2\eta \quad ...(8)$$

Vibrational analysis of Clotrimazole (CTZ)

Table 4 demonstrates the analysis of vibrational spectra and infrared intensities with their complete assignment of clotrimazole molecules. Clotrimazole has 42 atoms and 120 natural modes of vibration (120 A). As described by the table of symmetry characters, vibration results in the following modes:

$$\Gamma_{vibration} = \Gamma_{total} – (\Gamma_{rotation} + \Gamma_{translation}) = 3N–6 = (3 \times 42 \text{ atoms}) –6 = 120 \text{ A}$$

Under C1 symmetry, these modes are distributed into the irreducible representation. In the infrared, these usual vibrational modes are involved. The findings of this work showed strong alignment between the evidence on experimental and other theoretical frequencies.[14]

Table 2: Data of energetic values of the imidazole derivatives molecules Clotrimazole {(CTZ), (BIAHQ)}

Parameter	CTZ	BIAHQ
HOMO, (eV)	-6.37114	-6.0350
LUMO, (eV)	-1.02255	-3.0436
ΔE, (LUMO-HOMO	5.348593	2.99140
Ionization potential (IP), ev	6.371145	6.0350
Electron affinity (EA), ev	1.022551	3.0436

Table 3: Data of energetic values and data for Chemical reactivity of the imidazole derivatives molecules {(CTZ), (BIAHQ)}

Parameter	CTZ	BIAHQ
Hardness, (η)	2.674297	1.4957
Softness, (S)	0.37393	0.66858
Electrophilicity(ω)	2.55519	6.88816
Chemicalpotential(μ)	3.696848-	4.5393-
Electronegativity(χ)	3.696848	4.5393

Table 4: The theoretical vibrational frequencies (cm^{-1}), with its assignment for (CTZ)molecule

No.	Sym	*This Work DFT / 6-311 -G* Freq. (cm^{-1})	IR Intensity (Km mol^{-1})	*Other Work Freq.* (cm^{-1}) DFT 6-311 –G (14)	*EXP* (14)	Assignment
$_{1}\nu$	A	3158.20	0.20	3157	3167	C-H Str Sym(imidazol)
$_{2}\nu$	A	3094.38	4.68	3117	3116	C-H Str Sym(Phenyl)
$_{3}\nu$	A	3059.56	35.22	3084	3084	C-H Str aSym(Phenyl)
$_{4}\nu$	A	3047.61	9.66	3072	3061	C-H Str aSym(Phenyl)
$_{5}\nu$	A	1573.91	4.50	1589	1587	C-C-C Str (Phenyl)
$_{6}\nu$	A	1540.07	6.08	1557	1564	C-C-C Str (Phenyl)
$_{7}\nu$	A	1482.30	12.26	1493	1491	δ C-H (Phenyl)
$_{8}\nu$	A	1450.17	20.40	1453	1466	δ (imidazol)
$_{9}\nu$	A	1431.56	5.42	1434	1437	δ C-H (Phenyl)
$_{10}\nu$	A	1331.41	0.93	1322	1328	δ C-H (Phenyl)
$_{11}\nu$	A	1304.23	2.36	1317	1306	δ C-H (imidazol) + C=N Str. (imidazol.)
$_{12}\nu$	A	1271.52	7.11	1274	1276	C-C-C Str.(Phenyl)+ δC-H(Phenyl)
$_{13}\nu$	A	1234.86	8.35	1247	1210	δ C-H (imidazol) + δ (imidazol) + δC-H(Phenyl.)
$_{14}\nu$	A	1172.57	0.63	1177	1176	δC-H(Phenyl)
$_{15}\nu$	A	1112.860	2.49	1116	1115	δ (Phenyl)+ δC-H(Phenyl) + δ (imidazol)
$_{16}\nu$	A	1081.14	3.04	1082	1082	δ (Phenyl)+ δC-H(Phenyl)
$_{17}\nu$	A	1041.86	46.07	1063	1081	δ(imidazol)
$_{18}\nu$	A	1035.55	8.14	1044	1040	C-C-C Str.(Phenyl)+ δ C-H(Phenyl)
$_{19}\nu$	A	996.31	0.33	1000	996	ɣ C-H(Phenyl)
$_{20}\nu$	A	956.25	0.06	941	942	ɣ C-H (Phenyl)
$_{21}\nu$	A	903.96	5.10	903	902	ɣ C-H(Phenyl)+ δ(Phenyl) breathing
$_{22}\nu$	A	863.62	0.23	852	855	ɣ C-H(imidazol.) + ɣ C-H (Phenyl)
$_{23}\nu$	A	846.53	0.86	833	825	ɣ C-H (Phenyl) + ɣ C-H(imidazol.)
$_{24}\nu$	A	761.36	19.72	752	760	ɣ C-H (Phenyl)
$_{25}\nu$	A	709.44	27.78	702	705	ɣ C-H (Phenyl)
$_{26}\nu$	A	673.21	14.42	666	672	ɣ (imidazol.)+ δ (Phenyl)
$_{27}\nu$	A	640.32	8.85	633	634	ɣ (imidazol.)+ δ (Phenyl)
$_{28}\nu$	A	538.22	0.89	533	533	ɣ (Phenyl)
$_{29}\nu$	A	502.73	1.22	498	494	ɣ (Phenyl)
$_{30}\nu$	A	459.71	5.36	459	469	ɣ (Phenyl)
$_{31}\nu$	A	117.04	0.42	118	117	ɣ(Phenyl) + ɣ (imidazol.)
$_{32}\nu$	A	105.70	1.31	106	107	δ(Phenyl) + ɣ (imidazol.)
$_{33}\nu$	A	80.74	1.19	80	79	δ(Phenyl)+δ (imidazol.)+ ɣ(Phenyl)

Vibrational Analysis of 7-[2-(Benzimidazolyl) azo] 8-hydroxyl Quinoline (BIAHQ)

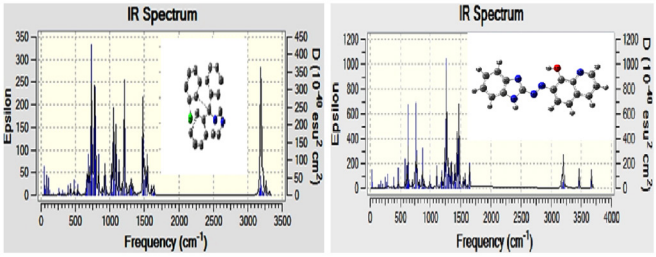
The measured Gaussian 5 software vibration frequencies using the DFT method are described in Table 5 for the BIAHQ molecule. The (BIAHQ) molecule comprises 33 atoms, so it has 63 natural modes of vibration. These modes are, under Cs symmetry, spread representation.

$$\Gamma vib = (3 \times 33 \text{ atoms}) - 6 = 93 = 30A'' + 63A'.$$

The IR spectrum of molecules {CLOTRIMAZOLE (CTZ), (BIAHQ)} are depicted as shown in Figure 3.

Table 5: The theoretical vibrational frequencies (cm^{-1}), with its assignment for (BIAHQ)molecule

		DFT / 6-311-G This Work		
No.	*Sym*	*Freq.(cm^{-1})*	*IR Intensity (Km mol^{-1})*	*Assignment*
$_1\nu$	A″	3602.40	56.31	N-H Str. (imidazol)
$_2\nu$	A″	3400.60	52.83	O-H Str.
$_3\nu$	A′	3153.89	7.87	C-H Sym.Str. (Quinoline)
$_4\nu$	A′	3145.59	31.56	C-H Sym. Str. (Benazimidazol)
$_5\nu$	A′	3131.92	46.58	C-H aSym Str.(Benazimidazol)
$_6\nu$	A′	3111.43	32.67	C-H aSym.Str. (Quinoline)
$_7\nu$	A′	1620.40	81.43	δ O-H
$_8\nu$	A′	1599.10	5.62	C--C--C Str. (Quinoline.),
$_9\nu$	A′	1584.06	8.95	δ N-H (imidazol), C-C-C Str. (Benazimidazol.)
$_{10}\nu$	A′	1546.10	40.40	C--C--C Str. (Quinoline.),
$_{11}\nu$	A′	1519.11	28.60	δC – H (Quinoline.)
$_{12}\nu$	A′	1512.30	2.06	δC-H(Benzimidazol),
$_{13}\nu$	A′	1451.30	17.95	N=N Str. (AZO)
$_{14}\nu$	A′	886.90	13.87	δ N=N (AZO)
$_{15}\nu$	A′	802.50	14.00	δ Benzimidazol (breathing)
$_{16}\nu$	A′	693.76	7.60	δ Quinoline (breathing)
$_{17}\nu$	A″	1008.70	0.04	ɣ C-H(Quinoline.)
$_{18}\nu$	A″	994.73	0.02	ɣC-H(Benzimidazol)
$_{19}\nu$	A″	846.10	0.48	ɣO-H
$_{20}\nu$	A″	391.92	0.05	ɣ N = N (AZO)



CTZ **BIAHQ**

Figure 3: The calculated Infrared spectrum of {CLOTRIMAZOLE (CTZ), (BIAHQ)} Molecules

Thermophysical Properties

The main parameter for use as a drug that can be used for drug development is binding energy. It is safer for medications to have a high negative value, where the value is more negative, which means that the compound is a healthy medicine. The lowest binding energy molecule would have the highest binding affinity. The semi-empirical PM3, the approach of the HyperChem 8.0 software, was used to test the thermo-physical properties of imidazole derivatives {(CTZ) (BIAHQ)}, as seen in Table 6, such as dipole moment, forming energy, binding energy, and nuclear energy.

Quantitative Structure-activity Relationships (QSAR)

To meet its target, a drug typically moves through a variety of biological membranes, so the movement of electrons in a drug molecule has a significant effect on drug activity and distribution, mediated by the electronic distribution in the drug structure. If it hits the action site, the type of bonds it forms with the target, which influences its biological activity. The most important characteristics (QSAR) that effects of biological activity is:

Table 6: Thermophysical properties

Properties	*CTZ*	*BIAHQ*
Total energy (kcal/mol)	-80870.5	-73042.1
Heat capacity, (kcal/moldeg)	0.0	0.0
Dipole moment (D)	4.062	4.65
Binding energy (kcal/mol)	-4775.5	-3838.4
Heat of Formation	124.754	93.461

LOG P

LOG P The metric to be used to measure the drug's passage across these membranes (a drug needs to migrate through a number of biological to meet its place of action) for the compounds used. The negative value of Log P reveals hydrophilicity, and the positive value of Log P shows hydrophobicity. Hydrophobic medicines tend to be more toxic because they have a wider distribution in the body. The optimal distribution coefficient for a substance is thus typically intermediate (not too hydrophobic nor too hydrophilic). LogP must be in the range ($0 < \log P < 3$) for good oral bioavailability.[15]

Table 7: QSAR properties

Properties	*CTZ*	*BIAHQ*
Gradient (kcal/mol/Ang)	0.075	0.099
Surface area (Grid) (A02)	534.5	508.47
Surface area (approx) (A02)	361.01	354.06
Volume (A03)	933.71	827.40
Refractivity(A03	98.89	72.21
Hydration Energy(Kcal/mol)	-4.70	-14.56
Partial Charges	0.0	0.0
Polarizability	40.34	32.70
Mass(amu)	344.84	289.30
Log P	5.11	3.33

Table 8: Data of PIC50 {value measures the effectiveness of compound inhibition towards biological or biochemical utility estimation}

Properties	*CTZ*	*BIAHQ*
PI C50	1.7044	-9.3602

Table 9: Data of electrostatic potential energy of imidazole derivatives molecules { (CTZ) , (BIAHQ) }

Parameter	*CTZ*	*BIAHQ*
E1	+0.490	+0.675
E2	-0.162	-0.143
ΔE= E2-E1	0.652-	-0.818

Hydration Energy

The lower energy of hydration is known to be the greater potential to dissolve in water in order to serve like the hydrophilic nature and anticipate the drug's most robust properties. When the material is immersed in water, the hydration energy is known as the energy consumed. A difference in the energy of hydration between (CTZ) and (BIAHQ) molecules, where (-4.70 kcal/mol), (-14.56 kcal/mol) respectively, as seen in Table 7.

Polarizability

Strongly polarizable molecules may be considered to have strong attractions. A molecule's polarizability can also improve aqueous solubility. We also note that, as seen in Table 7, the compounds (BIAHQ) (40.34) have the maximum polarizability more than (CTZ) (32.7).

Calculation of PIC50

Zineb Almi et al. 2014[16] establishes the correlation between biological activity and QSAR properties for the PIC50 value {value measures the effectiveness of the compound inhibition towards biological or biochemical utility estimation}estimation by applying the equation 8 to derive the QSAR property values described in Table 9 using the HyperChem 8 program.

PIC50 = 3.028 – 0.542 log p + 0.352 HE - 1.272 POL + 0.863 MR - 0.038 MV-0.024 MW + 19.120 q01 + 0.024 SAG ... (9)

Here, HE = hydration energy, Pol = polazibility, MR = molecular refractivity, LogP= Partition coefficient, MV= Molar Volume, MW= Molar Weight, SAG= Surface Area Grid, q01= atomic net charges. For biological properties measurement, if PIC50 is below -5, the PIC50 value is relevant, so the PIC50 value falls below 10000 ppm, which can be used as an appropriate ordinary antibiotic label. The PIC50 value for the molecule (BIAHQ) is shown to have a higher negative than the CTZ value (Table 8).

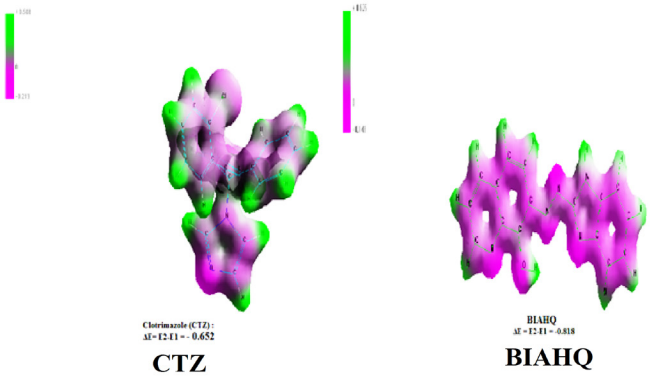


Figure 4: The 3D geometry of the electrostatic distribution potential for imidazole derivatives {[CTZ], [BIAHQ]}

The Distribution Electrostatic Potential due to 3D Mapped Structure

In a molecule's biological behavior, the surface area is known as the main parameter. The propagation of charged electrostatic potential is dependent on the surface area. A molecule's greater charging surface area will destroy more pathogens. The greater positive surface area of the charge indicates increased biological activity.

Given the 3D mapped structure, the values (ΔE) more negative suggest the electrostatic potential as the best method to estimate the parameters of biological activity,[17] based on the energy difference ΔE frontier orbital, the biological activity of a compound can be calculated. The molecular end of the positive charge is responsible for destroying the plasma membrane of Pathogens,[18] derived from the equation 9, as seen in Figure 4 has been included Data of electrostatic potential energy of imidazole derivatives molecules {(CTZ), (BIAHQ)} in Table 9.

$$\Delta E = E2 - E1 \quad ...(9)$$

E1=Electrostatic potential energy in a positive value, E2=Electrostatic the potential energy is negative, ΔE= Electrostatic potential energy difference of two-level.

CONCLUSIONS

The following points outline the most notable results of this research: The results of values P of the BIAHQ 3.3 are more acceptable than the values of the compound (CTZ) (5.11) and therefore are considered good bioavailability. The results showed that the surface area grid of the two components are Converging and acceptable, and (BIAHQ) has the highest negative value (-0.818) for the electrostatic (ΔE) values in light of the three-dimensional structure more than CTZ -0.652, so it is considered the most active. The BIAHQ 2.99 has the least gap {LUMO-HOMO gap is the most important parameter for the chemical reactivity} and, therefore, is considered more reactive than CTZ 5.348.

By comparison, the values of global reactivity between compounds were observed that (BIAHQ) more than CTZ.

For each of the parameters, softness (S), electronegativity (χ), electrophilicity (ω), and as well BIAHQ less than CTZ. For each of the parameters hardness (η), Chemical potential (μ), therefore, is considered BIAHQ the most reactive than (CTZ). The compound BIAHQ -9.36 has the PIC50 Highest negative value than (CTZ) (1.70), which can be used as an acceptable mark of standard antibiotic**.**

REFERENCES

1. Williams DA, Lemke TL. Foye's Principles of medicinal chemistry, Lippincott Williams and Wilkins, 2002; 5: 36.
2. Pandeya Nath SN. A Text Book of medicinal chemistry, SG publisher, 2004;1(3): 2-3.
3. Pozharskii AF, et al. Heterocycles in Life and Society. John Wiley & Sons, 1997.
4. Gilchrist TL. Heterocyclic Chemistry. Bath Press, 1985.
5. Crowley PD, Gallagher HC. J. Appl. Microbiol. Biotechnol. 2014;117(3):611–617.
6. A. Hassan. A. Habeeb, Khalid. J. Al – Adilee, Suadad. A.Jaber, " Chemistry and Martial Research ", 2014, Vol. 6 No. 8.
7. Klaus H, Muschke P, Rieper W, Raue R., Kunda K, Engel A. Azo Dyes, Inulmonns Encyclopia of industrial chemistry, 2005.
8. Gk. Etymology, bios, life; L, activus, with energy, Mosby's Medical Dictionary, 8th edition, 2009.
9. A. Kumer,W. Khan Proceeding of 8th international conference on green chemistry, 8th IUPAC Conference-2018, shangri-la hotel, bangkok, Thailand, 2018.
10. Tipker J, Verloop A. Use of STERIMOL, MTD, and MTD* Steric Parameters in Quantitative Structure-Activity Relationships. American Chemical Society.
11. Song H, Shin H.-S. The Antifungal Drug Clotrimazole, ActaCrystallogr. Sect. C Cryst.Struct. Commun., 1998;54: 1675–1677.
12. Popova A, Christov M, Deligeorigiev T. Corrosion, 2003;59 .
13. Koopmans T.C. Physica Amsterdam, 1934;1:104–113.
14. Socrates G. Infrared and Raman Characteristic Group Frequencies, 3rd ed. John Wiley, New York, 2004.
15. ACD/LogP/ Advanced Chemistry Development, Inc., Toronto, ON, Canada
16. ZinebAlmi SB, Lanez T, Tchouar N, Int. Lett. Chem. Phys. Astron, 2014;37:113-124.
17. Böhm M, Stürzebecher J, Klebe G. Three-dimensional quantitative structure− activity relationship analyses using comparative molecular field analysis and comparative molecular similarity indices analysis to elucidate selectivity differences of inhibitors binding to trypsin, thrombin, and factor Xa. Journal of medicinal chemistry, (1999), 42, 458-477.
18. Timofeeva, Kleshcheva N. L., Appl. Microbial. Biotechnol, 2011;89:475-492.