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Computational study of heterocyclic anticancer compounds through nbo method

Estudio computacional de compuestos heterocíclicos anticancerígenos mediante el método nbo

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ABSTRACT

In the present study NBO method contain the HOMO and the LUMO energies are calculated for 10 different heterocycles anticancer drug using B3LYP/6-31G(d,p). Frontier molecular orbitals (HOMO and LUMO) and Molecular Electrostatic Potential map of the compound was produced by using the π stacking of structures and anticancer activity of molecules. The NBO analysis was suggested that the molecular system contains π- π interaction, strong conjugative interactions and the molecule become more polarized owing to the movement of π-electron cloud from donor to acceptor. NBO, HOMO and LUMO energies, were investigated and Anticancer activity of Aromatic Heterocyclic compounds was investigated by NBO study and result was compared with our previous study about NICS and S-NICS of these 10 anticancer drug. the HOMO/LUMO gap of the heterocycle anticancer drug is significantly different from each other. The NBO method is used in both symmetric and asymmetric molecules and provides accurate information on the aromatics of the compound, especially the heterocyclic rings. It also provides accurate information in protected areas. Molecule 8 has the highest amount of HOMO and therefore aromaticity among the studied compounds which confirms the result of molecular orbital examination.

Keywords: Heterocyclic Compounds, Anticancer drug, Aromaticity, DFT, NBO study, HOMO-LUMO

RESUMEN

En el presente estudio, el método NBO contiene HOMO y las energías LUMO se calculan para 10 fármacos anticancerígenos heterociclos diferentes utilizando B3LYP/6-31G(d,p). Los orbitales moleculares fronterizos (HOMO y LUMO) y el mapa de potencial electrostático molecular del compuesto se produjeron utilizando el apilamiento π de estructuras y la actividad anticancerígena de las moléculas. El análisis NBO sugirió que el sistema molecular contiene interacción π-π, fuertes interacciones conjugativas y que la molécula se vuelve más polarizada debido al movimiento de la nube de electrones π del donante al aceptor. Se investigaron las energías NBO, HOMO y LUMO y se investigó la actividad anticancerígena de los compuestos heterocíclicos aromáticos mediante el estudio NBO y se comparó el resultado con nuestro

estudio anterior sobre NICS y S-NICS de estos 10 fármacos anticancerígenos. la brecha HOMO/LUMO del fármaco anticanceroso heterociclo es significativamente diferente entre sí. El método NBO se usa tanto en moléculas simétricas como asimétricas y proporciona información precisa sobre los aromáticos del compuesto, especialmente los anillos heterocíclicos. También proporciona información precisa en las áreas protegidas. La molécula 8 tiene la mayor cantidad de HOMO y, por lo tanto, aromaticidad entre los compuestos estudiados, lo que confirma el resultado del examen de orbitales moleculares.

Palabras clave: compuestos heterocíclicos, fármaco contra el cáncer, aromaticidad, DFT, estudio NBO, HOMO-LUMO.

1. INTRODUCTION

Computational chemistry is showing an increasingly important role in the fields of biological, material and chemical sciences. (Kerru et al., 2019) Aromatic Heterocyclic compounds (HCs) have drawn much attention in the fields of medicinal chemistry, and cancer therapy, as different molecules have exhibited varied biological activities, such as antioxidant and 18, antiviral19, anticancer20. (Bashiz et al., 2016; Shekarkhand, Zare, Monajjemi, Tazikeh-Lemeski, & Sayadian, 2020)

Aromatic Heterocyclic compounds (HCs) are applicants for anticancer drug and have significant biological activities. Heterocyclic compounds are known as anticancer drugs due they have targeted DNA and causing cancer cell demise. (Najafi, 2020; Yalazan et al., 2020) Recently, drug developers focused on designing and synthesizing small molecules as anticancer agents. A lot of heterocyclic compounds have been studied in order to develop new chemical agents in the drug discovery industry. (Mıhçıokur & Özpozan, 2017) The world health organization alerts that, nearly 1 in 6 deaths is because of cancer disease. There are more than 200 different types of cancers found so far. (Murugavel, Ravikumar, Jaabil, & Alagusundaram, 2019) Literature review also exposes that a minor change in the structure of anticancer drugs can lead to quantitative and qualitative variations in biological action. (Hokmabady, Raissi, & Khanmohammadi, 2016; Mohammadian, Zare, & Monajjemi, 2017)

Heterocyclic compound because of the played a vital action in the metabolism of all cells; 6 (or sometimes 5) membered hetero-cycles including one to three heteroatoms. Recently, imidazole fragment has been attracting much concentration because of its role as attractive scaffold for biochemical active heterocyclic drugs(Awad, Abdel-Aal, Atlam, & Hekal, 2019). In recent years the DFT calculations attracted several research group to evaluation the anticancer drug activity. (Joshi & Ghanty, 2019; Miar, Shiroudi, Pourshamsian, Oliaey, & Hatamjafari, 2020; Mumit et al., 2020) Sunusi Y. Hussaini and coworkers done DFT calculations and antitumor studies Nitrile functionalized silver(I) N-heterocyclic carbons complexes. Density functional theory was used to model the structures of the The benzimidazolium salts and their complexes and were screened for cytotoxicity against a breast cancer cell line (MCF-7), using the MTT assay. All the Ag(I)-(Hussaini et al., 2018) Hashemzadeh and Heidar Raissi in 2018, used DFT calculations and molecular dynamics simulation study for Covalent organic framework as smart and high efficient carrier for anticancer drug delivery.(Hashemzadeh & Raissi, 2018; Zare, Shadmani, & Pournamdari, 2013) Safdari and coworkers in 2017 used DFT Calculations and Molecular Dynamics Simulation Study on the Adsorption of 5-Fluorouracil Anticancer Drug on Graphene Oxide Nanosheet as a Drug Delivery Vehicle.. molecular dynamics simulation results show that 5-fluorouracil drugs are strongly adsorbed on the Graphene oxide surface by increasing the temperature from 250 to 400 K, as reflected by the most negative van der Waals (vdW) interaction energy and a high number of hydrogen bonds between GONS and drug molecules (Safdari, Raissi, Shahabi, & Zaboli, 2017). Jeyaseelan and coworkers in 2019 studied Spectroscopic, quantum chemical, molecular docking and in vitro anticancer activity studies on 5-Methoxyindole-3-carboxaldehyde. The natural bond orbital (NBO) analysis was carried out to evaluate the intramolecular stabilization interactions of the molecule, which are responsible for the bio-activity of the molecule. (Jeyaseelan, Premkumar, Kaviyarasu, & Benial, 2019; Miar et al., 2020)

Anticancer property of Heterocycles structures is due to nucleophilic centers i.e. mercapto and amino and hydroxyl and acidic groups, several heterocyclic compound, have been reported to have antimicrobial activity mainly due to heteroatom in the skeleton of them and also possess anticancer activity (Fathima, Meeran, & Nagarajan, 2019; Malik, Dar, Gull, Wani, & Hashmi, 2018; Martins et al., 2015; Sun et al., 2011) Subsequently, the study of complexes contain heterocyclic ligand with DNA has gained increasing interest, owing to its use in tumor treatment and molecular biology due to high interaction of heterocycle compounds with DNA. DNA is the key component of the antitumor agent and stacking interaction with metal complexes is used to identify drug interaction strategy. (Ali, Nadeem Lone, A Al-Othman, Al-Warthan, & Marsin Sanagi, 2015; Sathyadevi, Krishnamoorthy, Butorac, Cowley, & Dharmaraj, 2012) Schiff base metal complexes liking with DNA by cleavage or binding mechanism. In common, the ternary compounds can be bonded to the nucleic acid via the groove and electrostatic binding mode, leading to intercalation. (Ali, Lone, Alothman, & Alwarthan, 2017; Fathima et al., 2019; Sathyadevi et al., 2012)

The basis in DNA or RNA as Cytosine, thymine, and uracil, the basal are contain heterocyclic compound and also contain many consecutive hydrogen bond-donor and acceptor groups, which makes it ideal for studying of interaction of heterocyclic drug with them (Godzieba & Ciesielski, 2020). Structurally, pyrimidines are heterocyclic, aromatic organic compounds with two nitrogen containing carbon ring structures at positions 1 and 3 of the six membered ring.

The investigation of the drug–DNA bases interactions is essential and will recovered regarding the action mechanism of antitumor, antiviral drugs, and some carcinogenic compounds.(Galbiati et al., 2011) A range of techniques have been engaged for the interactions study of some anticancer drugs with DNA. The antitumor activity of a drug is related to its molecular properties as well as to its interactions with different targets in cells (Spiegel & Magistrato, 2006).

A large number of the important heterocyclic compounds are used in the medical activities. It is notable pyridoxine, folic acid, thiamine, riboflavin B12 and E families of the vitamins are included of heterocyclic structures. The majority of heterocycle compounds and typically common heterocycle fragments present in most pharmaceuticals currently marketed, alongside with their intrinsic versatility and unique physicochemical properties, have poised them as true cornerstones of medicinal chemistry. (Jia, Bonaventura, Bonaventura, & Stamler, 1996; Martins et al., 2015; Omar, 2020)

To date, a new generation of molecularly targeted drugs is eagerly expected whose rational for suggestion new structure for anticancer drug or other type of drugs to investigate the activity to binding DNA or cancer cell. In recent years Computation study in biological field specially on drugs and interaction with DNA attract the research attention (Kruszewski & Krygowski, 1972)

.in our previous report we have optimized and discussed about several active compounds which are shoed anticancer activity through NMR study and NICS and S-NICS study. (Mohammadian et al., 2017; SamieiSoofi, Zare, & Monajjemi, 2018; Soofi et al., 2016)

The HOMO, LUMO and the HOMO–LUMO gap are very essential for studying the electronic properties, reactivity and stability of structures. (Arivazhagan M & Meenakshi R, 2011; Lavallo, 2006) The ability of a donor electron is related to the energy of the HUMO (EHOMO) while the accept of an electron implies the energy of the LUMO (ELUMO) (Felegari & Monajjemi, 2015; Ghiasi & Parseh, 2014; Mıhçıokur & Özpozan, 2017; Mumit et al., 2020). Consequently, an effective interaction process is involved if the value of EHOMO increases and the value of ELUMO decreases. The energy gap between the HOMO and the LUMO is correlated with the molecule reactivity. In general, the lower the energy gap, the better the electron transfer process (Mohamed, Abdel-Aal, Mahmoud, Faten, & Hend, 2018)

Therefore, here we report herein DFT calculations involving NBO analysis, electronic spectra, highest occupied molecular orbital (HOMO)-lowest unoccupied molecular orbital (LUMO) energy. study on geometric, charge transfer, HOMO/LUMO gap and electronic properties of selected heterocycle anticancer drug. A t last the aromaticity was used as parameter for anticancer activity.

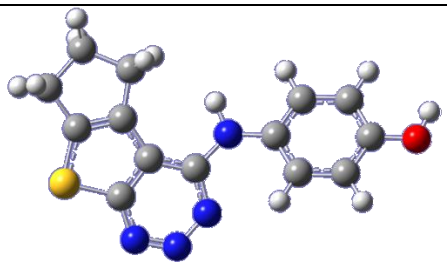
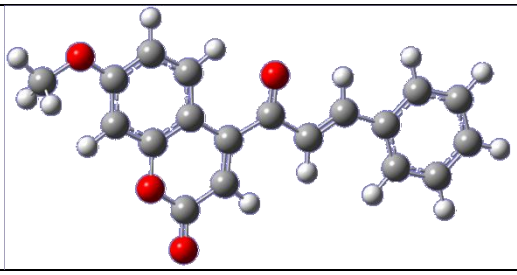
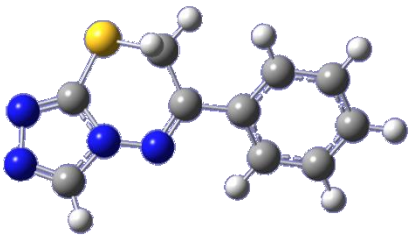
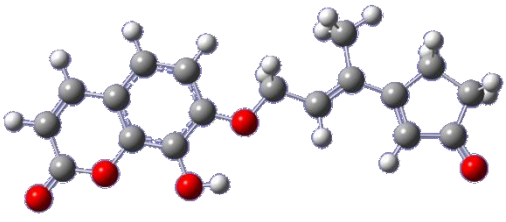
2. THEORETICAL BACKGROUND

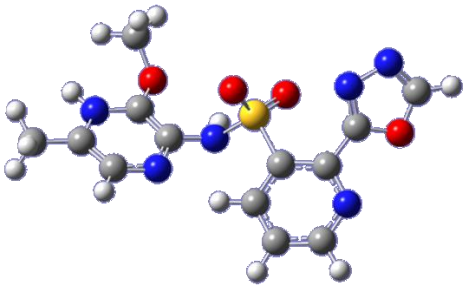
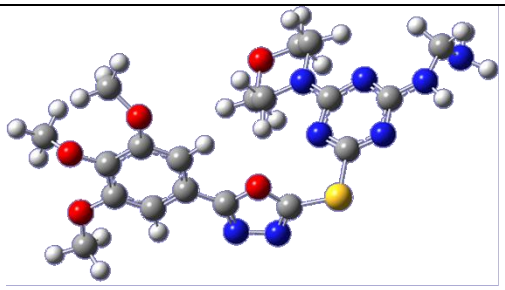
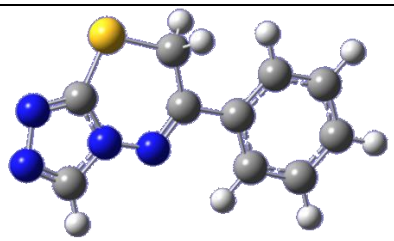
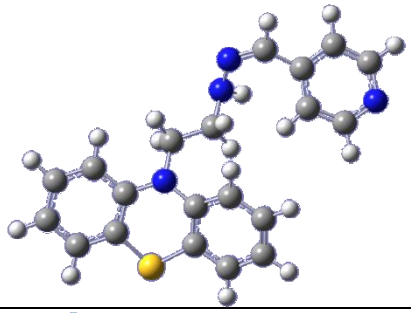
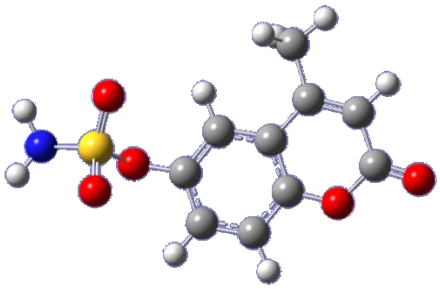
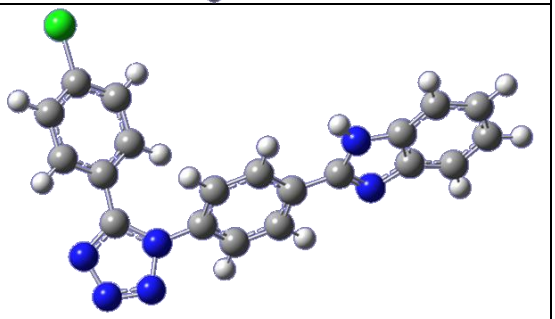
The molecular structure was drawn using Gauss View 6.0.16 software and then optimized. The full molecular geometry optimization of the compound was carried out by employing the density functional theory at B3LYP level(Monajjemi & Mohammadian, 2015; Safdari et al., 2017) and 6-31G+(d,p) basis set with the help of Gaussian 09W software package .The optimized structure of the compound 1 (table 1) has been used to calculate the molecular electrostatic potential, highest occupied molecular orbital and lowest unoccupied molecular orbital energy by Gaussian 09W software. The total energy (kcal .mol-1), highest occupied molecular NBO were calculated after fully optimization of all the structures.

3. RESULTS AND DISCUSSION

The HOMO, LUMO and the HOMO–LUMO gap are very crucial for studying the electronic belongings, reactivity and stability of structures. Optimized structures with atoms numbering of heterocyclic compounds are showed in table 1. The capability of a donor electron is related to the energy of the HUMO (EHOMO) while the accept of an electron implies the energy of the LUMO (ELUMO).32,33 Consequently, an e®ective interaction process is involved if the value of EHOMO increases and the value of ELUMO decreases. The energy gap among the HOMO and the LUMO is correlated with the molecule reactivity.

Table 1: optimized structures with atoms numbering of heterocyclic compounds

molecule	Chemical structure	Molecule	Chemical structure
M1		M6	
M2		M7	

M		M8	
M4		M9	
M5		M10	

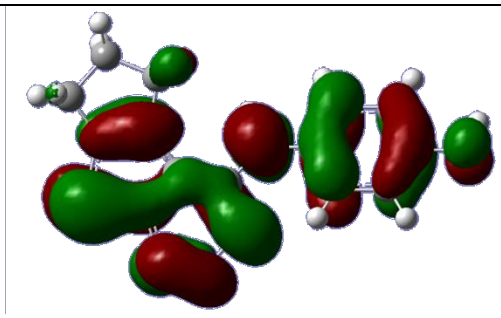
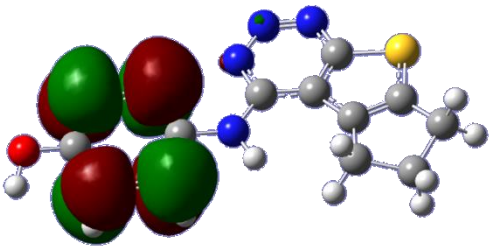
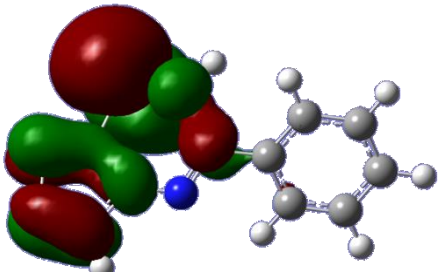
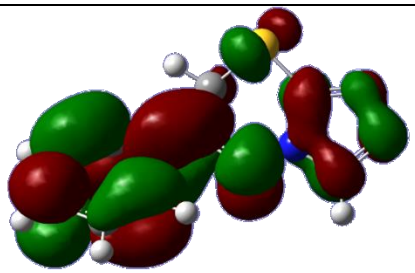
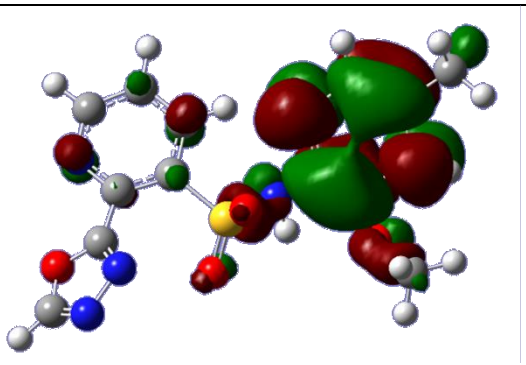
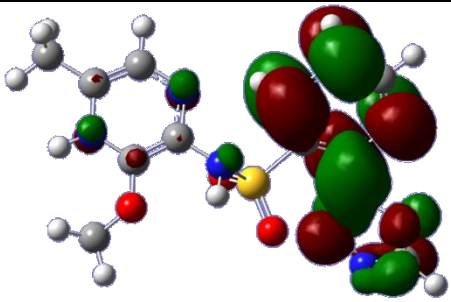
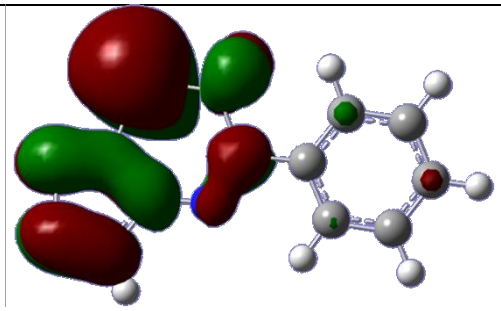
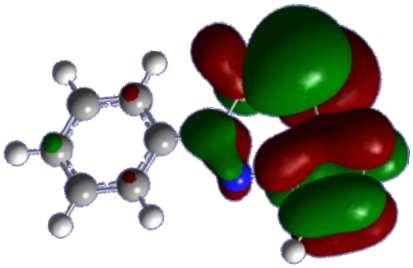
All calculations were carried out by using Gaussian program. Among various functional for DFT calculation, Becke's three parameter hybrid functional combined with Lee–Yang–Parr correlation functional designated B3LYP was used. were optimized at the B3LYP/6-311+G* level of theory. Geometry optimizations and frequency calculations were carried out at B3LYP/6-311+G.

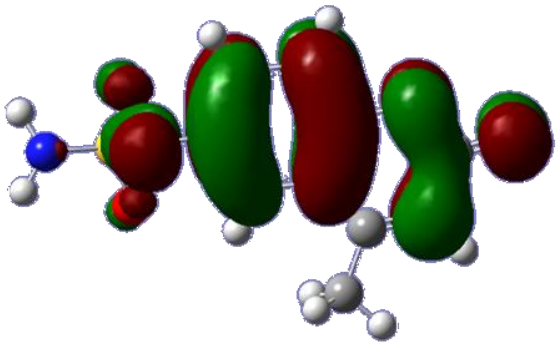
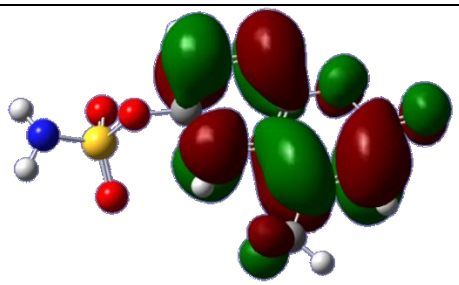
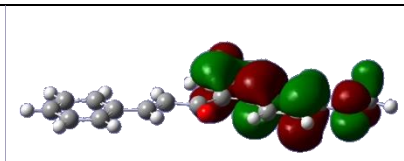
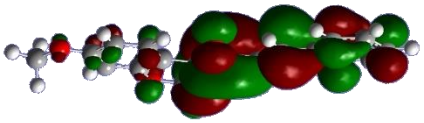
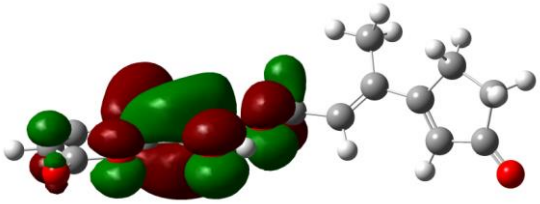
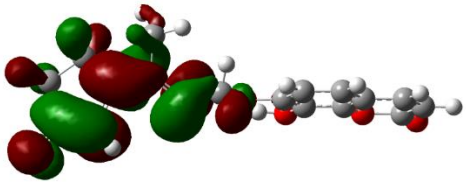
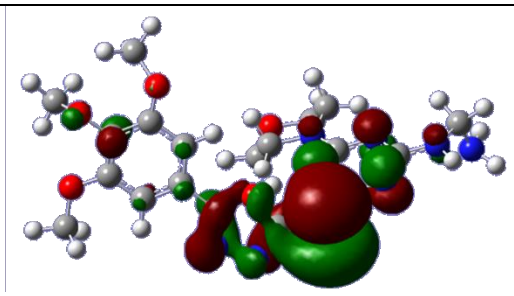
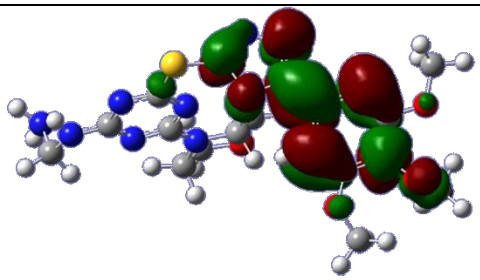
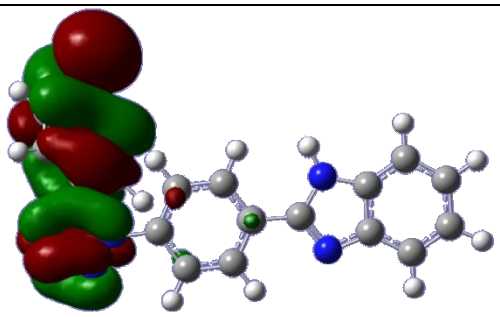
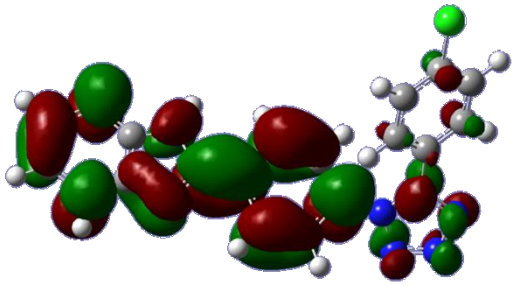
The NBO study were calculated at the B3LYP/6–31G* level with B3LYP/6–311G* geometries using the Gaussian 94 program.

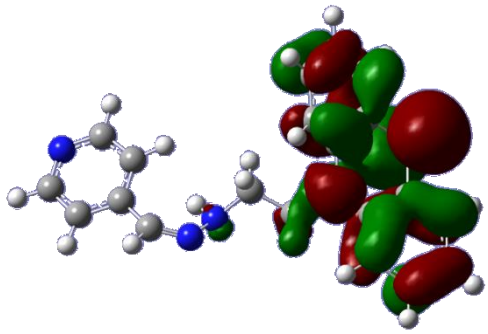
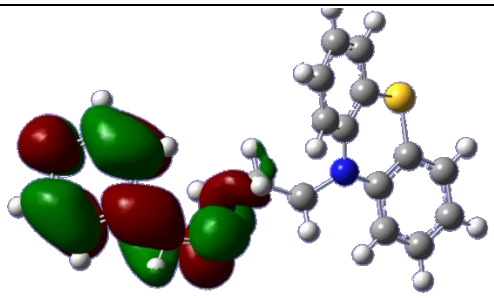
In previous our research As declared NMR parameters mainly depend on the local chemical bonding environment for heterocycle anticancer drug (Shekarkhand et al., 2020) Optimization and NMR shielding constants with orientations of the principal data such as standard components. The electron donating and receiving ability of a molecule can be defined using the value of HOMO and LUMO energy. The frontier molecular orbital's (i.e., FMO's) energy gap supports to indicate the stability of structure. Besides, FMO's also informs about the kinetic stability and chemical reactivity of a molecule. Furthermore, the FMO's helps for predicting the most reactive position of a studied molecule. The calculated energy value of HOMO and LUMO orbitals are -0.26751 and -0.18094 eV, respectively. The FMO's energy gap (ΔEHOMO-LUMO) of the mentioned organic molecule was found to be -0.08657 eV. The lower value of HOMO and LUMO energy gap showed that the studied molecule has high chemical reactivity, biological activity and polarizability.(Demir, Tinmaz, Dege, & Ilhan, 2016; Fazal et al., 2015) The frontier molecular orbital distribution of the compound was depicted in Fig. 6. Moreover, the chemical reactivity parameters of the studied molecule such as chemical softness (S), chemical potential (μ), electrophilicity index (ω) and

chemical hardness (η) were calculated (table 3.) in our previous study also carried out with the help of energy of HOMO and LUMO orbitals. (Bashiz et al., 2016)

Table 2: HOMO and LUMO plot of compound

molecule	HOMO	LUMO
M		
M2		
M3		
M4		

M5		
M6		
M7		
M8		
M9		

M10		

electrophilicity index of a molecule informs about the binding ability of a compound with biomolecules. The higher value of electrophilicity index of mentioned molecule showed that it has higher binding capacity with biomolecules and can act as an electrophilic species. While, the lower value of chemical hardness with high negative value of chemical potential means that the studied molecule is a soft molecule with high polarizibility.

Table 3. nucleus-independent chemical shifts (NICS, and Anisotropy) properties related to aromaticity for. Studied anticancer drugs.

Molecule	χ (aniso)	NICS (0.0)
1	3.3011 22.8291 1.5534	7.3089 11.2267 11.0180
2	2.061 10.868	8.7939 9.4343
3	6.8668 33.2676 12.1921	9.9182 -5.6579 9.5627
4	2.0619 10.8680	8.739 9.4343
5	18.5042 1.7318	0.7274 11.0327
6	3.0295 3.4972 15.2492	10.356 8.9144 1.6786
7	1.1257 15.2066 33.0340	12.3185 -1.5720 1.61169
8	14.9072 8.7459 19.8843	3.5817 0.6561 2.8910

Contributions perpendicular to the ring plane. NBO of molecules showed it would have high interaction with cancer cell and DNA and its pyridine and purine bases. In molecule 7 there is 3ring one ring contain

hydroxyl group has NICs negative and has aromaticity and other rings with oxygen and ketone group has a few antiaromaticity and other ring with 5 Carbone has high antiaromaticity Molecule 8 has weakly antiaromaticy and has high ability to interact with DNA bases.

In our previous report on 10 selected heterocycles anticancer drug we have developed a steady method based on NMR performance of the magnetic components, by the NICS and S-NICS method, The isotropy in all NMR calculations are positive which indicates negative values for aromaticity. It is obvious that the isotropies for NICS data can explain the quantity and quality of the aromaticity for some molecules, but those are not able for expressing the mechanism as well as S-NICS.

Although NBO method is a simple method compared to NICS and S-NICS method, it has many benefits, such as it could show the shape and structure of the molecular orbitals and help to understand to aromaticity of molecules. It is, more logically, dependent on inspection of the shielding area around each molecule or bio-molecule. Not only does this method work as a new criterion of aromaticity, but also it is potentially very useful in understanding the mechanism of other fields such as nano-biotechnology, including protein folding, protein structure determination, DNA pairing mechanism, and t-RNA-amino acid binding, that are sensitive to proton chemical shifts from structural and conformational changes. Molecule 3 and 7 showed more aromaticity then other molecules and expect have extra interaction with DNA and genome of cancer cells. High interaction and aromaticity of heterocyclic rings results the high interaction of anticancer drug with DNA and cancer cell. The charge density as aromaticity of bioactive atoms in anticancer drugs. decreases the amount of such a significant interaction and then the pharmacological characteristics of these drugs would be decreased. Charge and aromaticity have an important role in determining the binding affinity and then reactivity of these ligands with the cancer cell receptor or mutant DNA of cancer cell genetics.
The NBO method is used in both symmetric and asymmetric molecules and provides accurate information on the aromatics of the compound, especially the heterocyclic rings. It also provides accurate information in protected areas.

The presence of sulfur as a heterocyclic atom in the ring due to the difference in atomic diameter and the difference in orbital surfaces with carbon atoms has caused its atomic orbitals to interact with carbon less than atoms such as nitrogen and oxygen and thus reduce the amplitude of molecular electron cloud The current in the electron mass of the pie and finally the flow of the aromaticity of the ring, so the presence of heterocyclic atoms of oxygen and nitrogen in the rings of anticancer compounds is preferable. .
The aromatic nature of the compounds containing external oxygen is slightly weakened due to the oxygen groups outside the ring and the aromatic nature is lower compared to the compounds containing nitrogen and nitrogen-containing compounds are expected to show more antitumor ability. And show better interaction with the DNA and genome sequences of tumor and cancer cells. The results of this study are in line with the results of anti-cancer properties performed by experimental researchers Natural Bond Orbital (NBO) analysis result such as Energy gap of HOMO and LUMO were don and result is showed in table 4.

Table 4: Energy gap of HOMO and LUMO

Molecule			Energy gap(eV)	Molecule			Energy gap(eV)
M1	**HOMO**	-0.25409	0.06678	M6	**HOMO**	-0.31372	0.08504
	LUMO	-0.18731			**LUMO**	-0.22868	
M2	**HOMO**	-0.26322	0.0738	M7	**HOMO**	-0.29139	0.08548
	LUMO	-0.18940			**LUMO**	-0.20591	
M3	**HOMO**	-0.18712	0.01075	M8	**HOMO**	-0.27858	0.10907

	LUMO	-0.17637			**LUMO**	-0.16951	
M4	**HOMO**	-0.25425	0.06627	M9	**HOMO**	-0.29077	0.09973
	LUMO	-0.18798			**LUMO**	-0.19104	
M5	**HOMO**	-0.31400	0.11343	M10	**HOMO**	-0.25409	0.06678
	LUMO	-0.20057			**LUMO**	-0.18731	

Aromatic heterocyclic compounds have great potential in the treatment of cancer. Aromaticity is highly sensitive to chemical changes in the logic under study, and many thesis factors, including the electronegativity of atoms and functional groups, the hydrogen bond, and the magnetic anisotropy of the system, will change under its influence. The highest occupied orbitals of this compound play a very important role in how this compound interacts with other molecules because they are able to interact with the empty orbitals of other adjacent molecules. By examining the HOMO and LUMO orbitals and the energy level of the molecule, important information about the molecule and how it interacts with other molecules can be obtained.

The presence of sulfur as a heterocyclic atom in the ring due to the difference in atomic diameter and the difference in orbital surfaces with carbon atoms has caused its atomic orbitals to interact with carbon less than atoms such as nitrogen and oxygen and thus reduce the amplitude of molecular electron cloud and thus reduce The current in the electron mass of the pie and finally the aromaticity of the ring becomes ring, so the presence of heterocyclic oxygen and nitrogen atoms in the rings of anticancer compounds is preferable, and of course the presence of sulfur outside the ring contributes to the cloud electron flow of the pie and improves aromaticity. The aromatic properties of external oxygen-containing compounds are slightly attenuated due to oxygen groups outside the ring, and the aromatic properties are lower than those of nitrogen-containing compounds, and nitrogen-containing compounds are expected to be more anti-tumor. And show better interaction with the DNA and genome sequences of tumor and cancer cells. Molecule 8 has the highest amount of aromatics among the studied compounds which confirms the result of molecular orbital examination and is expected to show the highest anti-tumor properties. Because the wide aromatics and flat structure of the compound increase the ability to combine with the genome of tumor and cancer cells, and significantly reduce the rate of cancer cells and help control their growth and proliferation. The accurate measure of the aromatics of the compound were done by NICS and S-NICS study in our previous study. (Shekarkhand et al., 2020) will be outside the plane and these values can be considered under the influence of the system Å a measure of the aromaticity of the compounds?

Aromaticity is highly sensitive to chemical changes in the logic under study, and many thesis factors, including the electronegativity of atoms and functional groups, the hydrogen bond, and the magnetic anisotropy of the system, will change under its influence. The presence of oxygen outside the heterocyclic ring in the anticancer compound causes the electron super-electrons of the foot to be pulled out of the heterocyclic ring and weakens the aromatic nature of the ring. And improves the electron flow of the pie electron cloud and thus improves the aromatization properties. The presence of sulfur as a heterocyclic atom in the ring due to the difference in atomic diameter and the difference in orbital surfaces with carbon atoms has caused its atomic orbitals to interact with carbon less than atoms such as nitrogen and oxygen and thus reduce the amplitude of molecular electron cloud and thus reduce The current in the electron mass of the pie and finally the flow of the aromaticity of the ring, so the presence of heterocyclic atoms of oxygen and nitrogen in the rings of anticancer compounds is preferable.

The following table contains data from the calculations of chemical shift and asymmetry parameters. Sufi and astronomical relations presented in 2016 were used to calculate these parameters.

Table 5: of chemical shift and asymmetry parameters

Molecule	Asymmetry parameter	Chemical shift
M1	**-4/01929** **-1/22619** **-0/38445**	**7.3089** **11.6711** **11.9654**
M2	**0/434769** **1/081052**	**8.7939** **9.4343**
M3	**-0/12484** **0/287273** **0/570596**	**9.9182** **-5.6579** **9.5627**
M4	**-0/44659** **0/143749** **0/295094**	**7.8119** **8.9993** **-1.052**
M5	**-0/4025** **7/914309**	**0.7274** **11.0327**
M6	**0/169707** **0/057107**	**10.1356** **1.6786**
M7	**-4/49613** **0/171378**	**12.3185** **1.572**
M8	**2.2053** **11.7567**	**2.2053** **11.7567**
M9	**-0/70116** **10/08911**	**10.8887** **10.551**
M10	**-0/60893** **-2/57131**	**7.7846** **-3.600**

In molecule m5,: HOMO electron cloud confirms the aromaticity of molecules especially rings containing 3 nitrogens. HOMO electron cloud confirms the aromatization of the molecule. Especially oxygen-containing rings. In m7, Low HOMO electron cloud confirms the lack of aromatics of the molecule. And the large distance between HOMO and LUMO also confirms the lack of aromatization of the molecule. A weak and discontinuous electron cloud that indicates non-aromatic. The distance between the two levels is equal to 0.08548. in molecule m9: Has a strong aromaticity. HOMO electron cloud confirms molecule aromatization. and HOMO-LUMO misalignment also confirm the molecular aromatization

4. CONCLUSION

Density functional theory (DFT), quantum theory of atom in molecule (QTAIM), and natural bond orbital (NBO) have been performed for geometry optimization, energy, electronic properties, for 10 heterocycles anticancer drug. Furthermore, NBO analysis indicated a stronger donor– acceptor interactions DNA with drug. Moreover, the HOMO, LUMO and NBO analyses are used to elucidate the nature of electron and aromaticity of 10 selected drug. Molecule 8 has the highest amount of HOMO and therefore aromaticity among the studied compounds which confirms the result of molecular orbital examination. The result shoed molecules have good and expanded HOMO and could interact with DNA's LUMO and would have good anticancer properties. The HOMO and LUMO gap showed the molecules some molecules could interact with DNA and cancer cell more easily than other.

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