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Biochemical Reactivity Optimized Geometry and Docking Study Gedatolisib by using DFT Method

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***Abstract*-- Gedatolisib is Cabazitaxel category of drugs which improved activity against preclinical tumor models resistant to chemotherapy including taxanes, In present communication geometry of Gedatolisib is optimized by using combination of DFT/B3LYP method and 6-311+G(d, p) basis set. The computed optimized geometry well matched with similar geometry. The electronic properties charge transport properties from donor to acceptor unit is discuss with help of highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) plot. Natural bond analysis (NBO) is used to discuss intermolecular interaction within title molecule. The chemical reactivity of title molecule are discussed with help of several reactivity parameter like global softness global hardness chemical potential electronegativity by using energies of frontier molecular orbital. Several transport properties regarding good drug like Log P Log S MR etc are also lies within oral drug range. The PASS online server are used discuss biological activity of title molecule. The docking of title molecule with 3IHY protein has been performed by using SWISS dock online server**

***Keyword*-- DFT. MR, NBO, HOMO, LUMO**

I. INTRODUCTION

A Healthy Mother makes foundation of healthy family via healthy child which grows our happiness of society but now days a biggest threat on our loving mother is that nearly one out of twenty eight mothers in india facing the same issue with severe mortality rates like every eight minute our one of facing women leaving her life just for the shake of it.it can cause due to hormonal change and disturbed lifestyle issue but in deep inside of it is due to changes DNA inside the cells in the breast tissue. To stop such issue we need develop an inhibitor or a pathways to repair the DNA damage response more specifically says that to slow the rates of changes in DNA cells cause breast cancer. Gedatolisib is not only slows the rate of the cause of growth of cancer cells but also plays important role to make pathways to correct the reason behind it too. when its been simply introduced through nano formulation its effectiveness increases drastically more. Gedatolisib is also a nangenration category element use in prevention breast cancer or more precisously says to stop the cancer cells growth in DNA cells.it belong to Cabazitaxel category of drugs which improved activity against preclinical tumor models resistant to chemotherapy including taxanes[1].

Gedatolisib showed better inhibitory activity toward PI3K/Akt/mTOR signalling than buparlisib[2].From last few decade fast growing computational machines provides tool for researchers to compute various hidden aspects of chemical system without experimental data[3-4]. The quantum chemical methods are utilized to compute structural spectroscopic electronic charge transport biochemical activity of any chemical without experimental data availability [5-6]. The quantum chemical methods provide stability reaction path and reaction mechanism to synthesize novel chemical molecule. In this present study. In present communication geometry optimization of Gedatolisib has been carried out by using DFT/B3LYP method and 6-311+G (d, p) basis set and optimized geometry of Gedatolisib is compared with observed results which established validity of quantum chemical method. The electronic property of title molecule is computed by several electronic parameters by using energies frontier molecular orbital. The nonlinear optical properties of title molecule are computed on optimized geometry which helps to understand intermolecular charge transfer within title molecule. The electronic transition from ground state to excited state by using TDDFT method. In best of our knowledge no such study has been carried out by any researcher.

II. COMPUTATIONAL METHOD

The initial geometry of title molecule is modelled by using Gaussian 6.0 program package[6-7]. The designed geometry of title molecule is optimized by using combination of DFT/B3LYP[8] and 6-311+G(d, p) basis set. The selected basis set contains 19 contracted orbitals in which valance level triple-split arrangement with d polarization function for C, O, N atoms and p polarization function for H atoms only however for better accuracy in computed result's additional diffuse function include for long range interactions. In present computation hybrid functional is utilized for correlation B3LYP. In B3LYP functional exchange functional provides by Becke's provides however correlation functional advanced by three scientist named Lee, Yang, and Parr. In B3LYP functional [9-10] exchange-correlation energy can be written as:

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$$E_{XC}^{B3LYP} = E_X^{LSDA} + a_0(E_X^{HF} - E_X^{LSDA}) + a_X(E_X^{B88} - E_X^{LSDA}) + E_C^{VWN} + a_C(E_C^{LYP} - E_C^{VWN})$$

In this expression E_X^{LSDA} termed as local spin density on exchange energy, E_X^{HF} stands Hartree–Fock exact exchange, E_X^{B88} stand as Becke's gradient-corrected exchange term, E_C^{VWN} is correlation energy, and E_C^{LYP} Lee–Yang–Parr correlation. The overall computation in present paper has been done by using G09 program package. The electronic properties and chemical reactivity parameters are computed by using highest occupied molecular energy (HOMO) and lowest unoccupied molecular orbital (LUMO) on optimized geometry. The HOMO LUMO and MESP picture of title molecule are plotted by using gauss View 6.0 program, The optical spectra (UV) of title has been performed on optimized geometry by same level theory. The docking of title molecule with suitable protein has been performed by using Swiss Dock online server, The docking picture of title molecule with suitable drug is plotted by using CHIMERA 4.0 program package.

III. Optimized Geometry

The optimized geometry of title molecule by using DFT/6-311+G(d, p) basis set are shown in fig-1. The optimized geometry of title molecule is completely unsymmetrical with group state energy -976.45 a.u.The animated geometry of central region title molecule having aromatic phenyl rings which improves π-conjugation so electron delocalization.

The computed C-C and C=N bond in aromatic phenyl rings are 1.38 A^0 -140A^0 and 1.35 A^0 -136A^0 respectively. The electron delocalization can affect electronic properties as well as intermolecular charge transfer. In title molecule presence of several nitrogen-rich in heterocyclic which acts electron-donating or electron-accepting centers also improves contribute intermolecular charge transfer within molecule. The computed C=N bond length in noncyclic rings are 1.41 A^0-1.50 A^0. The Oxygen-Oxygen atoms are part of cyclic ring are morpholine-type moieties which often increase molecular polarity however improves solubility. The computed C-O bond length in title molecule are ranging in between 1.42 A^0-1.44 A^0. In general Carbonyl groups contribute in nonbonding interactions which affect charge distribution. The computed C=O bond lengths are lies in between 1.21 A^0-1.22 A^0. In title molecule shown non-planar optimized geometry however twisting between aromatic cyclic part (1.89^0) reduces steric hindrance and stabilizes the structure. The one bond length of C-H which displace from plairity in methyl group is overestimated by 0.01 A^0. The ambiguity computed in bond length due to substitution of functional groups destroyed hybridization in between atoms just like in C_{19}-O_1 contribute orbitals 1 s (21.87%) p 3.57(78.13%) rather than SP^3 however in N_8 - C_{27} bonds nitrogen shows s(27.53%) p 2.63(72.47%) orbitals etc.

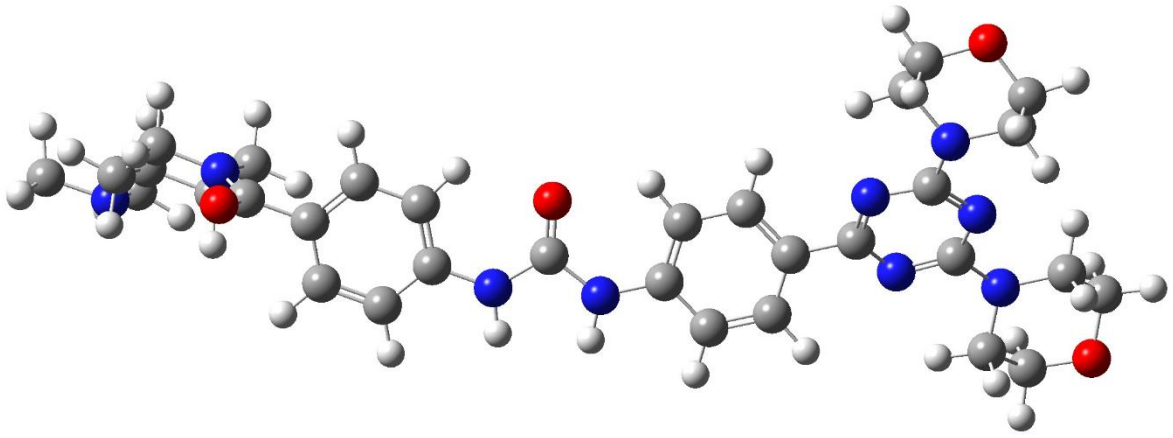

Fig-1 Optimized 3D geometry of title molecule

IV. Electronic Properties

The frontier molecular orbital play key role to determine reactivity of chemical systems. The highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) are important frontier orbitals. The energy required for transition electron from HOMO to LUMO orbital is termed as band gap. The band gap is important factor to describe reactivity of chemical system.

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A molecular system with lower energy gap less chemical stable more chemically reactive and vice versa[11-12]. The HOMO primarily acts donor however LUMO acts primarily acceptor. The HOMO (MO=164) is LP (1) N 13 is mixing of 13.28% of S orbital and 86.72% of P character however LUMO(MO=165) is σ* O1 - C19 in which occupancy of O1 is 41.93%) is mixing of 21.87% of s character however 78.13% of p character. In this bonding orbital occupancy of C19 is 58.07% having 33.42% of S nature and 66.58% of p character. The HOMO LUMO plot of title molecule is shown in Fig-2. The HOMO distributed or localized over the left side of title molecule specially around the electron-rich donor groups and conjugated π-system. The electron density of HOMO shown during the excitation process this part plays active part in electron donation. The orbital distribution shown electron delocalization over back bone within the title molecule. The LUMO is distributed over the central and right-side acceptor regions of the molecule. As we have discussed above HOMO delocalization orbital mean during excitation process electron transfer from this side in similar fashion LUMO localization shows electrons are transferred after excitation.

The extension of the LUMO across the conjugated pathway facilitates effective charge migration through the molecular framework. Several chemical reactivity parameters of title molecule are computed and listed in table-1 with help of HOMO and LUMO energies. The energy band gap (εLUMO $-\varepsilon$HOMO), electronegativity (χ), chemical potential (μ), global hardness (η), global softness (S), and global electrophilicity index (ω) of are calculated using formula as given below [13-16]

$\chi = -1/2(\varepsilon\text{LUMO} + \varepsilon\text{HOMO})$

$\mu = -\chi = 1/2\ (\varepsilon\text{LUMO} + \varepsilon\text{HOMO})$

$\eta = 1/2(\varepsilon\text{LUMO} - \varepsilon\text{HOMO})$

$S = 1/2\eta$

$\omega = \mu^{2}/2\eta$

The calculated frontier molecular orbital analysis revealed HOMO and LUMO energies of −6.560 eV and −5.142 eV, respectively. The HOMO–LUMO energy gap was found to be 1.417 eV, indicating comparatively high electronic delocalization and possible charge-transfer characteristics within the molecular system.

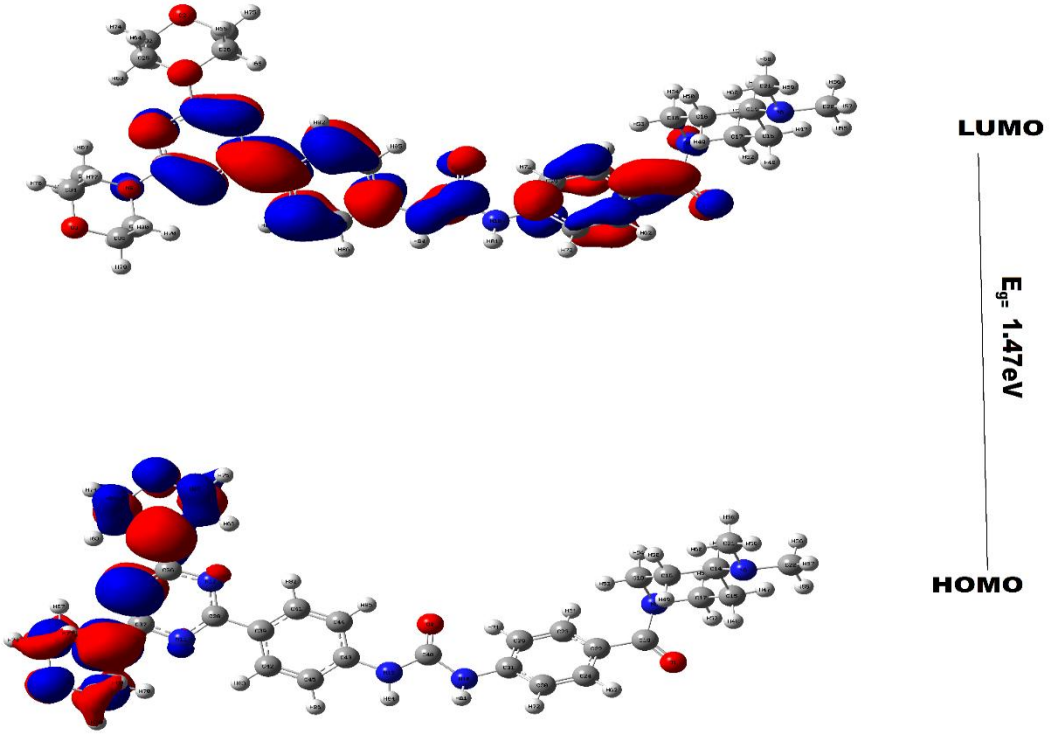

Fig-2 HOMO LUMO Plot of title molecule

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Table-1 Several Reactivity Parameters are of title molecule by using same level theory

S.N.	Parameters	Value
1	HOMO	−6.560 eV
2	LUMO	−5.142 eV
3	Band Gap(ELUMO−EHOMO)	1.417 eV
4	Electronegativity (χ)	5.851 eV
5	Chemical Potential(μ)	−5.851 eV
6	Chemical Softness	0.705 eV^{-1}
7	Chemical Hardness (η)	0.709 eV

V. NBO Analysis

The Natural bonding orbitals (NBO) analysis (table-2) is most significant technique to explore charge transfers or conjugative interactions in various systems. A Very strong ICT contribution occurs due to charge transfer from π (O_1–C_{19}) → π*(C_{22}–C_{24}) which stabilize title molecule up to 4.95kcal/mol. The strong charge transfer in between donor orbital σ(O1–C19) to acceptor orbital σ* (N_5–C_{19}) with contribution of 2.81kcal/mol.

The charge transport from donor orbital π (O_1–C_{19}) to acceptor orbital π* (O_1–C_{19}) creates Strong electron delocalization which stabilized title molecule upto 2.21kcal/mol. The π-electron transfer occurs due to σ(O_2–C_{32})to σ* (O_2–C_{33}) stabilize up to 1.99kcal/mol which decline up to 1.49kcal due to charge transfer from acceptor orbital to σ* (O_1–C_{22})improves Conjugative interaction upto 1.41 kcal/mol/ Some less significant contributor in Weak conjugation and Charge delocalization in between σ(O_1–C_{19}) to σ* (N_7–C_{25})and σ* (C_{22}–C_{23})stabilize up to 0.81-0.79kcal/mol.

Table-2 NBO analysis of title molecule using DFT/6-311+G(d,p) method

S.N.	**Donor NBO(i)**	**Acceptor NBO(j)**	**$E^{(2)}$**(kcal/mol)	**(Ej–Ei)**a.u	**F(i,j)** a.u
1	π (O_1–C_{19}	π*(C_{22}–C_{24})	4.95	0.42	0.042
2	σ(O_1–C_{19})	σ* (N_5–C_{19})	2.81	1.69	0.062
3	π (O_1–C_{19})	π* (O_1–C_{19})	2.21	1.78	0.055
4	σ(O_2–C_{32})	σ* (O_2–C_{33})	1.99	1.58	0.052
5	σ(O_1–C_{19})	σ* (O_1–C_{22})	1.49	1.76	0.045
6	σ(O_2–C_{32})	σ* (C_{25}–C_{24})	1.41	1.51	0.045
7	σ(O_2–C_{32})	σ* (N_7–C_{25})	1.32	1.10	0.037
8	σ(O1–C19)	σ* (C_{22}–C_{23})	0.87	0.95	0.031
9	σ(O_1–C_{19})	σ* (N_7–C_{25})	0.81	1.42	0.026
10	σ(O_1–C_{19})	σ* (C_{22}–C_{23})	0.79	1.43	0.024

VI. Biological Properties And Biological Activity

The electrotopological indices e.g. Log P and Log S of title molecule are computed by using ALOGPS 2.1 program [17-18]. The Log P shows how easily drug transport through cell membrane however Log S shown solubility of drug in cell membrane. The drug-likeness Lipinski's describe by five-rule method [19-20]. In this rule of suitable drug number of atoms lies in between 20-70 atoms, molecular weight lies within range180 – 500 and Log P >5. The computed molar refractive MR for lies in between 40-130 to become good oral drug. The molar refractive MR of any drug is calculated by below equation [21-22]

$$MR = \left[\frac{n^2-1}{n^2+2}\right]\left(\frac{MR}{\rho}\right) = 1.33\alpha\pi N$$

According to five rules for drug-likeness both title compound falls in category of, molecular weight of title molecule (615.7) nearly within range180 – 500 computed ionophilicity(3.23) Log S (-4.23) MR (86) fall within category of good drug except number of atoms(86) which are greater than beyond limit so our molecule have possibility to become good oral drug. because number of atoms in molecule A and B lies in between 20-70 atoms

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Several biological activities of title molecule is computed (table-3) by PASS inline server [23] for Pa>70%. The PASS on line server predicts several biological activities e.g. mutagenicity, teratogenicity and embryo toxicity etc of biological active molecules.

The title molecule shown activity against Prostate cancer treatment(o,559) CYP2H substrate (0.536) Phosphatidylinositol kinase inhibitor (0.374) Heat shock protein 27 antagonist (0,40$) neurodegenerative diseases treatment (0.334) etc

Table- 3 Several biological activities predicted by PASS for Pa>70%

S,N,	Biological Activity	Pa	Pi
1	**Prostate cancer treatment**	**0,559**	**0,005**
2	CYP2H substrate	0,536	0,100
3	Phosphatidylinositol kinase inhibitor	0,374	0,003
4	Histamine H1 receptor agonist	0,373	0,009
5	HMGCS2 expression enhancer	0,407	0,051
6	Heat shock protein 27 antagonist	0,411	0,056
7	Phosphatidylinositol3-kinase inhibitor	0,357	0,003
8	Orexin receptor 1 antagonist	0,346	0,009
9	Farnesoid X receptor antagonist	0,338	0,005
10	TRKB antagonist	0,340	0,014
11	Chloride channel blocker	0,359	0,041

VII. Molecular Docking

The molecular docking is used in drug discovery process. The molecular docking is design to mode of binding by affinity of ligand with a target protein. In docking procedures, one can evaluate binding affinity in between ligand-receptor complex on basis of Newtonian mechanics. The Swiss Dock [24] is online server used to predict target protein and binding of title molecule. Swiss dock shows 3IHY protein for docking. The 3IHY protein is mainly associated with cancer-related studies and enzyme inhibition research in molecular docking investigations however PASS already predict anticancer behaviour of title molecule.

For docking we upload mole 2 file of title molecule and pdb file protein on swiss dock server. The **molecular docking study** between a ligand and a protein target are shown in Fig-3. From this figure several number of **hydrogen bonds** with TYR495, ASN486 ligands and **hydrophobic interactions** shows good binding affinity (-10.0kcal/mol) and stability. The **Pi-cation** (LYS456) and **Pi-alkyl interactions** (TYR492, LEU394) shows electronic and hydrophobic stabilization. **Some weak van der Waals interactions** with nearby residues: LEU595. LEU573, SER487, THR488, ASP388, GLN461, GLN469, VAL472 etc. The docking score residue with title molecule of **−10 kcal/mol** shows strong intermolecular interactions, . high binding stability, favorable molecular recognition, and possible inhibitory potential toward the target protein.

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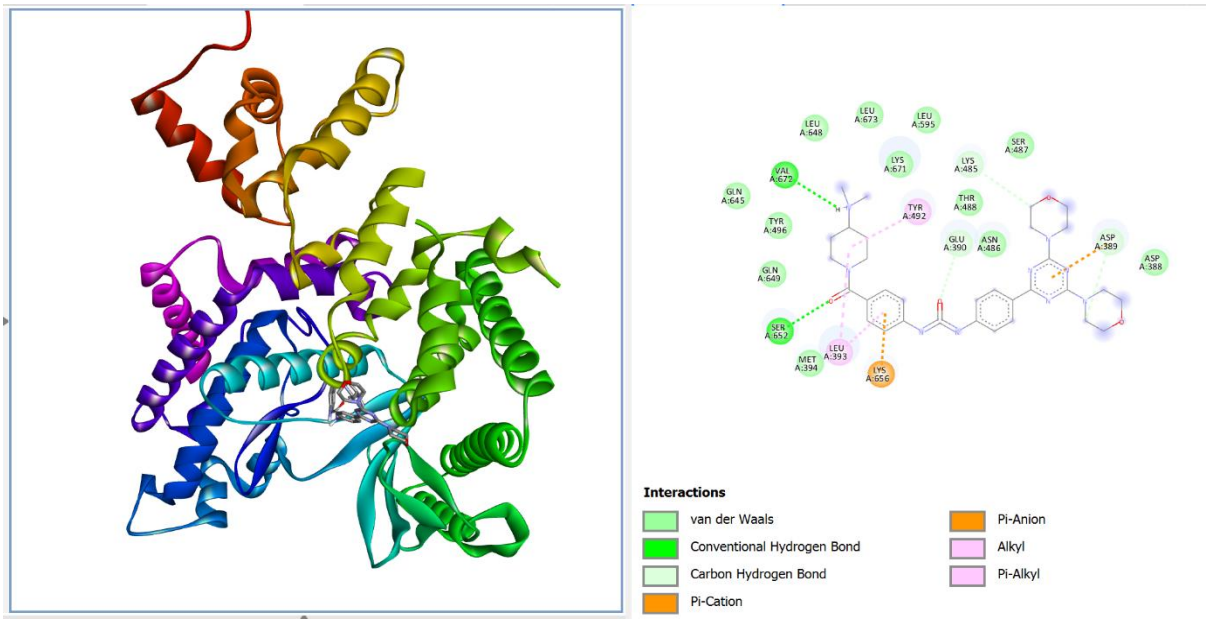

Fig-3 Molecular docking of title molecule with protein 3IHY

VIII. Conclusion

The geometry of title molecule is optimized by using DFT/6-311+G(d, p) basis set. The reactivity parameters are computed on optimized geometry by using same level theory. The computed HOMO–LUMO energy gap was found to be 1.417 eV, showing high electronic delocalization and possible charge-transfer characteristics within the molecular system. The ionization potential and electron affinity were estimated as 6.560 eV and 5.142 eV, electronegativity, chemical potential, and global hardness values were 5.851 eV, −5.851 eV, and 0.709 eV, respectively shown its better chemical reactivity. NBO analysis shows that very strong ICT contribution occurs due to charge transfer from π (O_1–C_{19}) → π*(C_{22}–C_{24}) which stabilize title molecule up to 4.95kcal/mol. The strong charge transfer in between donor orbital σ(O_1–C_{19}) to acceptor orbital σ* (N_5–C_{19}) with contribution of 2.81kcal/mol. All computed Lipinski's described five-rule method shows that title molecule has potential to become good oral drug. PASS online server predict title molecule has good anticancer potential however Swiss dock predict cancer protein 3IHY for docking. The docking score residue with title molecule of −10 kcal/mol shows strong intermolecular interactions, high binding stability, favourable molecular recognition, and possible inhibitory potential toward the target protein.

In this way title molecule has good Caliber to become anticancer drug specially Prostate cancer treatment as well as nonlinear optical behaviour due to good electron delocalization properties. All calculation has been performed on single molecule in gaseous phase so ignore molecular interaction and solvent effect in present calculation

REFERENCES

[1] "Androgen receptor variation affects prostate cancer progression and drug resistance" Edel McCrea , Tristan M. Sissung , Douglas K. Price , Cindy H. Chau , William D. Figg PharmD Volume 114, December 2016, Pages 152-162 Pharmacological Research.

[2] "Research progress of mTOR inhibitors" Yifan Chen, Xiaoping Zhou European Journal of Medicinal Chemistry Date: 15 December 2020 Article: 112820 Volume: Volume 208.

[3] A. K. Pandey, N. Misra, D. D. Dubey, K. K. Pandey, V. Singh, A. Dwivedi, Effect on nonlinear optical behaviors of p-butoxybenzylidene p-heptylaniline (BBHA) liquid crystal after doping of superhalogen (BO2) n, n= 1–2, by using density functional theory, Next Mat. 11, 101700.

[4] A. K. Pandey, A. Dwivedi, K.K. Pandey, D. D. Dubey, V. Singh, Study of electro-optical behavior of nematic liquid crystal p butoxybenzylidene, p-heptylaniline (BBHA) under applied electric field by using density functional theory Journal of Molecular Liquids 420 (2025) 126839

[5] Brown JS, Amend SR, Austin RH, Gatenby RA, Hammarlund EU, Pienta KJ. Updating the definition of cancer. Mol Cancer Res. 2023;21(11):1142–1147. doi: 10.1158/1541 7786.MCR-23-0411

[6] Frisch, M. J. et al Gaussian 09; Gaussian, Inc., Pittsburgh, PA, 2009.

[7] P.L.Fast, J.Corchado, M.L.Sanches, D.G.Truhlar, J.Phys.Chem A. 1999, 103, 3139.

[8] A.Frisch, A.B.Nelson, AJ.Holder, Gauss view, Inc.Pittsburgh PA, 2000.

[9] A.D. Becke, J. Chem. Phys, 1993, 98, 5648.

[10] C. Lee, W. Yang, R.G. Parr, Phys. Rev. 1988, B 37, 785.

[11] S.R. Ggadre and R.K. Pathak, Miximal and minimal characteristics of molecular electrostatic potentials, J. Chem. Phys. 93 (1990), pp. 1770–1774.

[12] 70. S.R. Ggadre and I.H. Shrivastava, Shapes and sizes of molecular anionsviatopographicalanalysisofelectrostaticpotential,J.Chem. Phys. 94 (1991), pp. 4384–4390.

[13] R. G Parr, R.G Pearson, J. Am. Chem. Soc. 105, 7512–7516(1983)

[14] P. Geerlings, F. D.Proft, W. Langenaeker, Chem. Rev.103, 1793–1874(2003)66.

[15] R.G. Parr, R.A. Donnelly, M. Levy, W.E. Palke, J. Chem. Phys. 68 (1978) 3801.

[16] R.G. Parr, R.G. Pearson, J. Am. Chem. Soc. 105 (1983) 751268.

[17] Tetk I. V.,Tanchuk V. Y., Kasheva T.A., Villa A. E., Estimation of aqueous solubility of chemical compounds using E-state indices, J Chem Inf Comput Sci; 41:1488–93 (2001).

[18] Tetk I. V., Tanchuk V. Y., Kasheva T. A., Villa A. E., Prediction of n-octanol/water partition coefficients from PHYSPROP database using artificial neural networks and E-state indices, J Chem Inf Comput Sci, 41:1407–21 (2001)

[19] R.P. Verma, C. Hansch, Bioorg. Med. Chem. 13 (2005) 2355–2372.,

[20] R.P. Verma, A. Kurup, C. Hansch, Bioorg. Med. Chem. 13 (2005) 237–255

[21] C.A. Lipinski, L. Franco, W.D. Beryl, J.F. Paul, Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings, Adv. Drug Deliv. Rev. 23 (1–3) (1997) 3–25, https://doi.org/10. 1016/S0169-409X(96)00423-1.

[22] H. Chow, H. Chen, T. Ng, P.Myrdal, S.H. Yalkowsky, Using backpropagation networks for the estimation of aqueous activity coefficients of aromatic organic compounds, J. Chem. Inf. Comput. Sci. 35 (4) (1995) 723–728, https://doi.org/10.1021/ ci00026a009.

[23] Jorgensen W.L.Duffy E. M., Prediction of drug solubility from Monte Carlo simulations Bioorg Med Chem Lett 10(11):1155–58 (2000).

[24] www.swissdock.ch