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Vibrational spectroscopic (FT-IR, FT-Raman), NMR and electronic structure calculations of metaxalone

M. Boopathi[1,2], P. Udhayakala[2*] and G. R. Ramkumaar[3]

[1]*Department of physics, Pachaiyappas College for Men, Kanchipuram- 631501, India*
[2]*Department of Chemistry, Dr.M.G.R Educational and Research Institute, Chennai -600095, India*
[3]*Department of Physics, C. Kandaswami Naidu College for Men, Chennai- 600102, India*

ABSTRACT

This work presents the characterization of 5-[(3,5-dimethylphenoxy)methyl]-1,3-oxazolidin-2-one (metaxalone) by DFT calculations and spectral techniques. The spectral analysis was carried out by using FT-IR and FT-Raman and ^{13}C and ^{1}H nuclear magnetic resonance (NMR) techniques. The FT-IR and FT-Raman spectrum were recorded in the range of 4000 to 400cm^{-1} and 4000 to 50cm^{-1} respectively. The over estimations of the calculated harmonic wavenumbers were efficiently corrected by the aid of a specific scaling procedure. ^{13}C and ^{1}H NMR chemical shifts of the molecule were calculated using gauge independent atomic orbital method (GIAO) and were compared with the experimental results. The molecular structure, fundamental vibrational frequencies and electronic structure calculations are carried out by density functional theory (DFT) method and B3LYP/ 6-311++G(d,p) basis set. Frontier molecular orbital energies, global reactivity descriptors and molecular electrostatic potential (MEP) were estimated. The thermodynamic properties at different temperatures were calculated revealing the correlations between standard heat capacities, entropy and enthalpy changes with temperatures.

Keywords: metaxalone, FT-IR and FT-Raman spectra, NMR, DFT calculations, MEP

INTRODUCTION

Oxazolidinone derivatives have been reported to possess various biological and pharmacological activities in the areas of drug development, antibacterials [1], sigmareceptors[2], psychotropics, antiallergy agents, antibiotics[3]. Metaxalone is one of the oxazolidinone derivative, commonly used in muscle relaxant therapies for acute low back pain [4]. It belongs to the Biopharmaceutics Classification System (BCS)class II of centrally acting skeletal muscle relaxant drug with antispasmodic effect [5] and also used to relieve pain caused by strain and sprains [6]. It is also used as an internal standard for few analytical methods [7].

In the present work, the combined solid phase FT-IR and FT-Raman vibrational spectroscopy and gas phase theoretical calculations with DFT method have been studied on the title molecule. DFT method has been favourite due to its great accuracy in reproducing the experimental values of molecular geometry, vibrational frequencies, atomic charges, thermodynamical properties etc.[8,9]. Among DFT calculation, Becke's three parameter hybrids functional combined with the Lee-Yang-Parr correlation functional (B3LYP) is the best predicting results for molecular geometry and vibrational wave numbers for moderately larger molecule [10,11]. It has been observed from the literature that there is no experimental and computational vibrational spectroscopic and electronic structure calculation study on metaxalone has been published yet. This inadequacy in the literature encouraged us to make this systematic study on the molecular structure and vibrational spectral analysis based on FT-IR, FT-Raman, NMR chemical shift, HOMO-LUMO analysis, global reactivity descriptors, molecular electrostatic potential map (MEP) and thermodynamical functions of the title molecule.

MATERIALS AND METHODS

The compound under investigation metaxalone on solid form was procured from a reputed pharmaceutical company, Chennai, India with more than 98% purity and was used as such without further purification to record FT-IR and FT-Raman spectra. FT-IR spectrum of the powder sample was recorded in KBr in the range 4000-400cm^{-1} using Perkin Elmer spectrometer with the resolution of ±1cm^{-1}. FT-Raman spectrum of the powder sample was recorded using 1064 nm line Nd:YAG laser as excitation wavelength in the region 4000-50cm^{-1} using Bruker RFS 27 spectrometer with 8 scans at a resolution of 2cm^{-1}. The ^{13}C and ^{1}H NMR was recorded on Bruker Avance III NMR 500 MHZ spectrometer using DMSO as a solvent. The spectral measurements were carried out at Sophisticated Analytical Instrument Facility, IIT Madras, India.

Computational Details

The entire set of calculations were performed by density functional theory(DFT) level three parameter hybrid model B3LYP method with the triple zeta extended 6-311++G(d,p) basis set. The geometry of the title compound, together with that of tetramethylsilane(TMS) is fully optimized with the Gaussion09 software package[12] and the vibrational frequency assignments were made with a high degree of accuracy with GaussView program [13]. ^{13}C and ^{1}H NMR chemical shifts were calculated with GIAO approach [14,15] by applying B3LYP method. The vibrational frequencies obtained by quantum chemical calculations are typically larger than the experimental counterparts so, an empirical uniform scaling factor 0.983 up to 1700cm^{-1} and 0.958 for greater than 1700cm^{-1} [16,17] have been used to counterbalance the systematic errors caused by the basic set incompleteness, neglect of electron correlation and vibrational unhormonicity[18]. The optimized structure of metaxalone is given in **Fig. 1.**

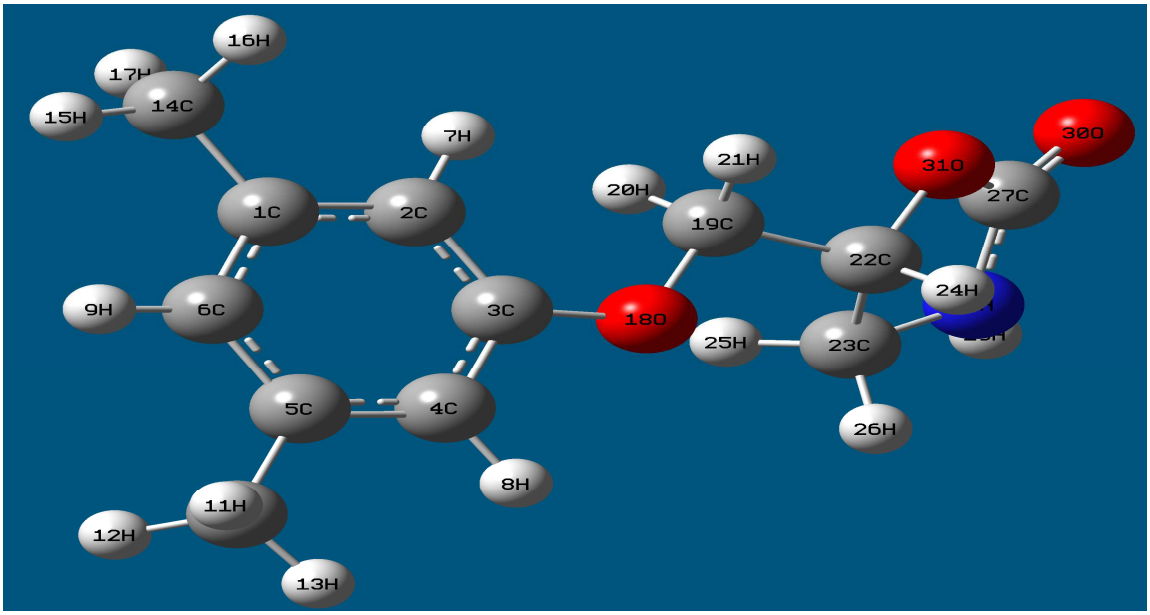


Fig.1 Optimized molecular structure with atom numbering of metaxalone

RESULTS AND DISCUSSION

Vibrational spectral analysis

The objective of the vibrational analysis of compound under study is to find vibrational modes connected with molecular structure. The vibrational analysis was done for the optimized structure of metaxalone, which has non-planar structure of C_1 point group symmetry. The vibrational spectral assignments have been performed by recorded FT-IR and FT-Raman spectra based on the theoretically predicted wavenumber by density functional B3LYP/6-311++G(d,p) method. The studied molecule consists of 31 atoms and 87 modes of vibration mostly active in both IR and Raman. The selected experimental and calculated frequencies and their assignments of the title compound are given in **table 1.** Observed and calculated FT-IR and FT-Raman spectra of metaxalone are given in **Fig. 2 and 3.**

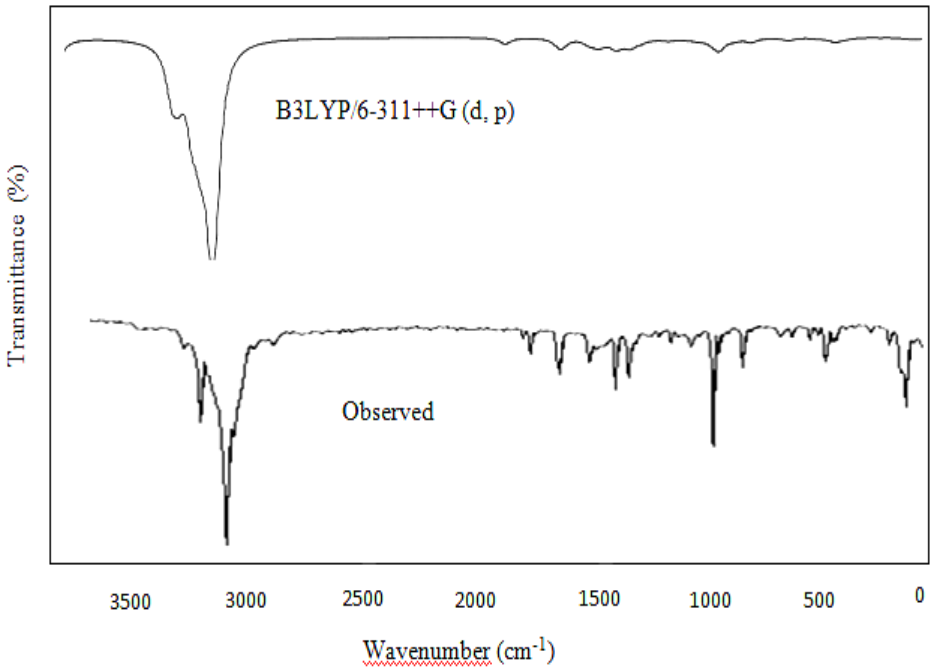


Fig. 2 Observed and calculated FT-IR spectra of metaxalone

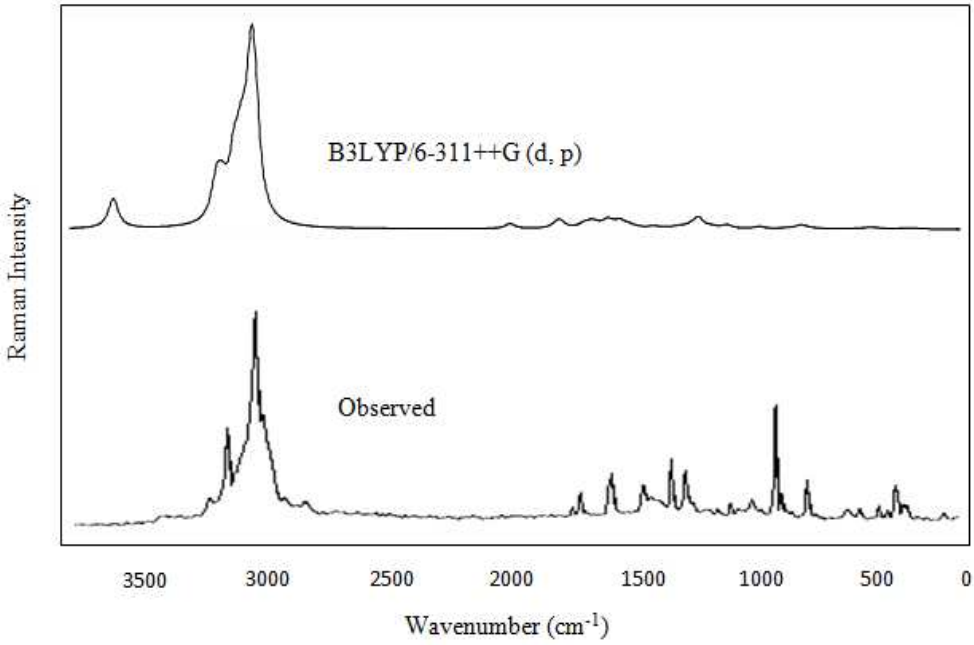


Fig. 3 Observed and calculated FT-Raman spectra of metaxalone.

C-H Vibrations

The hetero aromatic compounds commonly exhibit multiple weak bands in the region 3100–3000cm^{-1} [19] due to aromatic C–H stretching vibrations. The bands observed in the experimental FT-IR spectra at 3049 and 3013cm^{-1} and 3056, 3018cm^{-1} in FT-Raman spectra are assigned to C-H stretching vibration of the title compound and their theoretical counterpart appear in the range 3047,3024cm^{-1} . The C-H in-plane and out-of-plane bending vibrations generally lie in the range 1300-1000cm^{-1} and 1000 - 675cm^{-1}[20] respectively. The calculated wavenumbers at 1159, 1170 and 1295 cm^{-1} by B3LYP method of the target molecule is assigned to C-H in-plane-bending mode of vibration. These modes are in agreement with the experimental band at 1178, 1296cm^{-1} in FT-IR and 1159,1195 and 1299cm^{-1} in FT-Raman spectra. The C-H out- of-plane bending vibration in the calculated values are found in 933,843 and 683cm^{-1} is confirmed by the presence of strong band at 932,846,687cm^{-1} in FT-IR and 933,843,683cm^{-1} in FT-Raman spectra.

The asymmetric, symmetric stretching, scissoring and wagging vibration of CH_2 group appear in the regions 3000 ± 50, 2965 ± 30, 1455 ± 55 and 1350 ± 85 cm^{-1} , respectively[21,22]. The calculated modes at 2972, 2882 cm^{-1} is assigned to asymmetric and symmetric stretching vibration of CH_2 in oxazolidin-2-one ring of the title compound. The band observed at 2965cm^{-1} in FT-Raman and 2887 in FT-IR spectrum is assigned to these modes. The lowering of these modes are due to the attachment of phenoxy ring. The scissoring mode of CH_2 predicted by the presence of a wavenumber at 1494cm^{-1} by the DFT calculated value is confirmed by the presence of a band observed at 1481cm^{-1} in FT-Raman spectrum. A band observed at 1424cm^{-1} in FT-Raman spectrum is assigned to CH_2 wagging mode of vibration. The DFT calculation gives this mode at 1417cm^{-1}.

Methyl Group Vibrations

The compound under investigation posses two CH_3 groups in third and fifth position of the phenoxy ring. Usually, the C-H stretching vibrations of the methyl groups are expected in the range of 3000 – 2900cm^{-1}[23,24]. In the present molecule, the calculated frequency at 2974 cm^{-1} is in good agreement with the experimental FT-Raman at 2990cm^{-1} which is assigned to CH_3 asymmetric stretching vibration of methyl group present in the 5th position of the compound. The CH_3 symmetric stretching vibrations of the title molecule observed at 2916cm^{-1} in both FT-IR and FT-Raman spectra is supported by the calculated value at 2896cm^{-1}. The bands observed at 1093, 1082 cm^{-1} in FT-IR and 1095,1080 and 1048cm^{-1} in FT-Raman spectra is assigned to C-H in-plane bending vibrations. The calculated modes at 1078, 1072 and 1040cm^{-1} is well agreed with the experimental observations. The calculated modes at 863,824 and 683cm^{-1} is assigned to C–H out-of-plane bending vibrations which are confirmed by the presence of strong bands observed at 876,825 and 687cm^{-1} in FT-IR and 877,822and 683cm^{-1} in FT-Raman spectra. These assigned frequencies are in good agreement with the reported literature [25, 26]. The rocking mode of methyl groups are expected at 1045cm^{-1} [27]. The theoretically calculated value at 1040cm^{-1} is supported by the band observed at 1048cm^{-1} in FT-Raman spectra and is assigned to rocking mode of methyl group. The CH_3 torsional mode could be assigned at 28 cm^{-1} by theoretical method.

C-C vibrations

The C-C stretching vibrations are highly characteristic of the aromatic ring itself [28]. The C–C stretching vibrations are normally found in the region 1650–1200 cm^{-1}[29]. The C–C stretching mode is observed at 1609, 1452, 1433 and 1296cm^{-1} in FT-IR and at 1641,1454,1433 and 1299cm^{-1} in FT-Raman spectra. The corresponding calculated values by B3LYP method are at 1620,1603,1453,1432 and 1295cm^{-1} respectively. The theoretically computed values match well with the experimental observations.

C = O vibrations

The characteristic frequency of carbonyl group has been extensively used to study in wide range of compounds. A strong absorption band observed in these compounds in the region 1850-1550cm^{-1} due to C=O stretching vibration [30, 31]. For the title compound, the C=O stretching mode is seen as a strong band at 1737cm^{-1} in FT-IR, 1784cm^{-1} in FT-Raman and the DFT calculation give this mode at 1779 cm^{-1}.

C N Vibrations

The identification of C-N stretching vibration is rather difficult task since there are problem in identifying these frequencies from other vibrations. Mani *et al*. [32] assigned C-N stretching absorption in the region 1169cm^{-1} in FT-IR and 1120cm^{-1} in FT-Raman. Balachandran *et al.* [33] have reported the same vibration at 1245cm^{-1} both in FT-IR and FT-Raman. Hence, in the present work, the band observed at 1232cm^{-1} in FT-IR and 1236cm^{-1} in FT-Raman has been assigned to C-N stretching vibrations. The computed value at 1204cm^{-1} by B3LYP/6-311++G(d,p) is well agreed with the experimental observations. The band observed at 717, 726cm^{-1} in FT-IR and FT-Raman is assigned to C-N in-plane bending vibrations which are in accord with the calculated value at 711$cm^{-1.}$ The calculated frequency at 548cm^{-1} is in good agreement with the experimental observed band at 545cm^{-1} in FT-IR and 550cm^{-1} in FT-Raman spectrum and is assigned to the C-N out-of-plane bending mode of vibration.

Table 1. Comparison of selected experimental (FT-IR and FT-Raman) wavenumbers(cm^{-1}) with the calculated harmonic frequencies of metaxalone using B3LYP /6-311++G(d,p) basis set

S.No	Observed wave number (cm^{-1})		Calculated wave number (cm^{-1})	Vibrational Assignment
	FT-IR	FT-Raman	B3LYP	
1			28	$\tau(CH_3)$
2		73	86	t ring (oxazolidin-2-one)
3		118	129	lattice vibration
4		201	204	γ ring (phenoxy)
5		232	235	$\gamma (CH_2 + \gamma CH_3)$
6		297	281	$\omega (CH_3)$
7		371	358	$\omega (CH_3 + \gamma CH_2)$
8	459		464	$\rho (CH_2)$
9	474	477	474	γ (N-H)
10	495	509	495	γ (N-H) + βCH_3
11		508	508	ν ring (phenoxy)
12	526	522	520	$\rho (CH_3)$ +ring breathing (phenoxy)
13	545	550	548	γ (C-N)
14	579	581	577	γC-C(phenoxy ring)
15	611	612	605	ν (C-O)
16	687	683	683	γ (C-H)
17	717	726	711	β (C-N)
18	740	754	755	γ (N-H)
19	825	822	824	γ (C-H)
20	846	843	843	γ (C-H) + $\omega (CH_3)$
21	876	877	863	γ (C-H) + t (CH_2)
22	932	933	933	γ (C-H) + ν (C-O) + ν (C-H)
23	994	994	989	ν (ring)+ t (CH_2)+ ν (C-O)
24	1011		1008	$\gamma (CH_3)$ + ν(C-O)
25		1048	1040	$\rho (CH_3)$ + β(C-H)
26	1082	1080	1072	ν(C-O) + ω (N-H)+ β(C-H)
27	1093	1095	1078	β(C-H)+ ν(C-O)
28	1135	1103	1105	$\beta(CH_2)$ + β (N-H)
29	1158	1131	1127	$\beta (CH_2)$
30	1178	1159	1159	β(C-H)
31		1195	1170	β(C-H) + $\omega (CH_2)$
32	1232	1236	1204	ν(C-N) + $\omega (CH_2)$
33	1251	1263	1242	t (CH_2) + δ (N-H)
34	1296	1299	1295	β (C-H) + (νC-C)
35	1324	1327	1303	ν(N-H) + δ (CH_2)
36	1387	1379	1389	$\omega(CH_3)$
37		1424	1417	$\omega(CH_2)$ + γ (N-H)
38	1433	1433	1432	ν(C-C)+ $\omega(CH_3)$
39	1452	1454	1453	ν(C-C)
40		1481	1494	δ (CH_2)
41		1512	1506	δ (CH_2)
42	1609		1603	ν (C-C)
43		1641	1620	ν(C-C) +β(C-H)
44	1737	1784	1779	ν(C=O)
45	2887		2882	$\nu_s(CH_2)$
46	2916	2916	2896	$\nu_s (CH_3)$
47		2952	2935	$\nu_{as}(CH_2)$
48		2965	2972	$\nu_{as}(CH_2)$
49		2990	2974	$\nu_{as}(CH_3)$
50	3013	3018	3024	ν(C-H)
51	3049	3056	3047	ν(C-H)
52	3073	3083	3085	ν(C-H)
53	3465	3485	3485	ν(N-H)

υ– stretching; υ_s– symmetric stretching; υ_{as} – asymmetric stretching; β– in-plane bending; γ – out-of-plane bending; τ– torsion; ω- wagging; δ-scissoring and t-twisting

NMR CALCULATIONS

Nuclear magnetic resonance (NMR) is a research technique currently used for structure elucidation of complex molecules. The combined use of experimental and computational tools offers a powerful gadget to interpret and predict the structure of bulky molecules [34]. The experimental ^{13}C and ^{1}H NMR spectra of the metaxalone are shown in **fig.4** and **5** respectively. For reliable calculations of magnetic properties accurate predictions of molecular geometries are essential. Firstly, full geometry optimization of metaxalone was performed at the gradient corrected density functional level of theory using the hybrid B3LYP method. Then gauge- independent atomic orbital (GIAO) and ^{13}C and ^{1}H chemical shift calculations of the compound was done by same method using 6-311++G(d,p) basis set IEFPCM/DMSO solution [35]. Relative chemical shifts were estimated by using the corresponding TMS shielding calculated in advance at the same theoretical level as the reference. The isotropic shielding values were

used to calculate the isotropic chemical shifts with respect to the tetramethylsilane (TMS). The value of TMS are 182.46 and 31.88 ppm for ^{13}C and ^{1}H respectively.

In aromatic carbons, the range of ^{13}C NMR chemical shifts for a typical organic molecules occur larger than 100ppm [36]. The compound under investigation contains 12 carbon atoms of which eight carbon atoms are located in phenoxy ring and the remaining atoms are located in the oxazolidin-2-one ring. The chemical shift value of C3 is greater than other carbons due to the presence of the resonating effect of the neighbouring atom. The chemical shift value of C27 is the next higher due to the influence of a lone pair in oxygen and nitrogen atoms. The C10 and C14 atom has the smallest shift in all chemical shift localized on the methyl group. The observed and calculated chemical shift values show correlation with each other.

The proton chemical shift (^{1}H NMR) of organic molecules generally varies greatly with the electronic environment of the proton. Usually, hydrogen attached to or nearby electron withdrawing atom or group can decrease the shielding and move the resonance of attached protons towards a higher frequency, whereas electron donating atom or group increases the shielding and moves the resonance towards a lower frequency [37]. In the present study, the molecule contains fifteen hydrogen atoms. Among the fifteen, nine atoms are located in the phenoxy ring and the remaining six atoms are located in the oxazolidin-2-one ring. The chemical shifts of aromatic protons of organic molecules are usually observed in the range of 6.5 -8.2 ppm. In the title compound the signals of 3 theoretically calculated aromatic protons H7, H8 and H9 are 6.5, 6.7 and 6.9 ppm respectively. These chemical shift vales are higher than the methyl proton (H11,H12,H13,H15,H16 and H17) due to the electron withdrawing properties of attached groups and high symmetry of the molecule.

Naturally, the proton closer to the lone pair of electron is less shielded, and its signal appears at lower field. Among the six protons in the oxazolidin-2-one ring (^{1}H) of H24 and H21 are higher than the other protons due to the presence of lone pair of oxygen. The chemical shift (^{1}H) of H29 is higher than the (H20,H25 and H26) due to the lone pair of electrons on the nitrogen atom. The experimental and theoretical ^{13}C and ^{1}H isotropic chemical shift value of metaxalone are depicted in **table 2.**

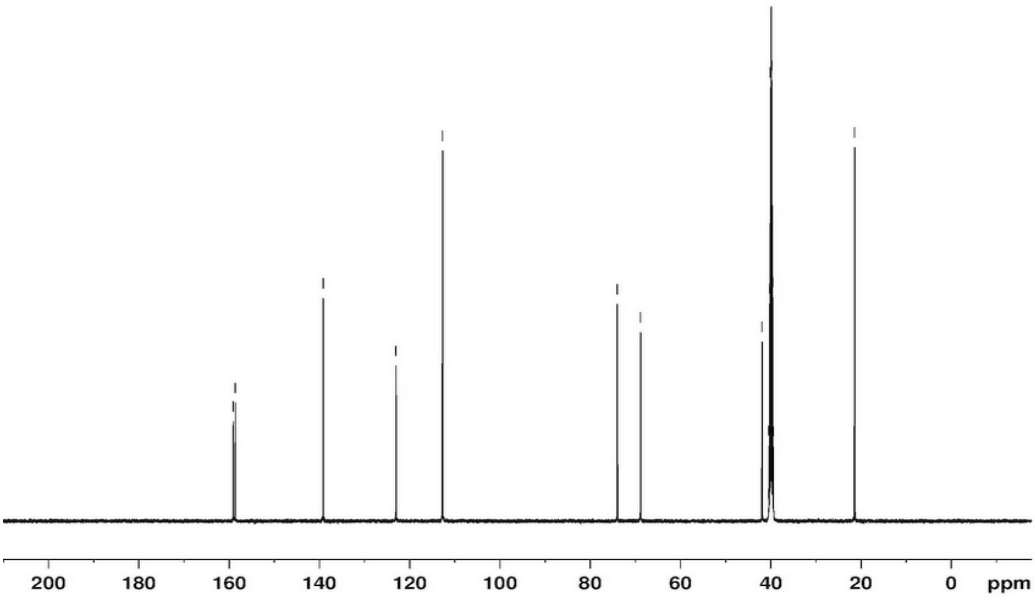


Fig. 4 Experimental ^{13}C NMR spectra of metaxalone

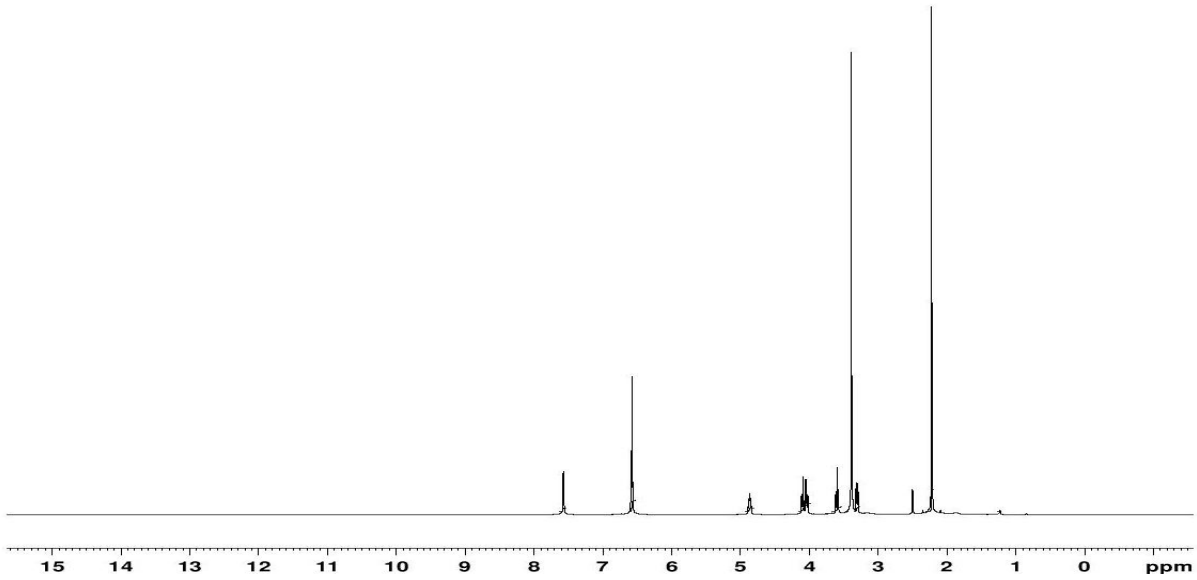


Fig. 5 Experimental ^{1}H NMR spectra of metaxalone

Table 2. Experimental and theoretical ^{13}C and ^{1}H isotropic chemical shift of metaxalone(with respect to TMS) in DMSO (all values in ppm)

Atoms	Carbon		Atoms	Hydrogen	
	Experimental	Calculated		Experimental	Calculated
C1	139	146	7H	6.57	6.5
C2	112	110	8H	6.6	6.7
C3	160	165	9H	7.5	6.9
C4	118	123	11H	2.5	2.5
C5	143	146	12H	2.5	2.47
C6	123	126	13H	1.23	1.78
C10	21	21	15H	2.2	1.95
C14	22	22	16H	2.52	2.47
C19	68	70	17H	2.5	2.53
C22	74	78	20H	3.62	3.79
C23	42	49	21H	4.84	4.34
C27	158	164	24H	4.89	4.99
			25H	3.32	3.46
			26H	3.62	3.82
			29H	4.11	4.16

Frontier molecular orbital analysis(FMO)

The frontier molecular orbitals play an important role in the electronic and chemical reactions[38]. According to FMO theory of chemical reactivity, transtition of electrons is due to interaction between highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) of reacting species [39]. E_{HOMO} is a quantum chemical parameter which is often associated with the electron donating ability of the molecule. High value of E_{HOMO} is likely to a tendency of the molecule to donate electrons to appropriate acceptor molecule of low empty molecular energy[40]. E_{LUMO} indicates the ability of the molecule to accept electrons. The gap between HOMO and LUMO characterizes the molecular chemical stability and explains the eventual charge transfer interactions taking place within the compound. A molecule with low energy gap is more polarizable and is generally assicoated with the high chemical activity and low kinetic stability[38]. The frontier molecular orbital energies of the title compound are shown in **fig. 6**.

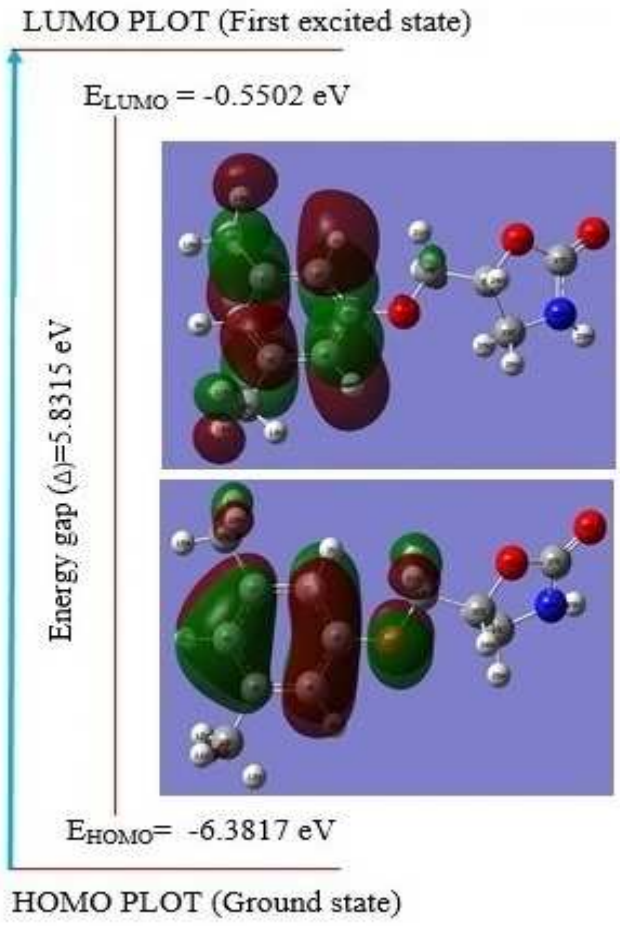


Fig. 6 The atomic orbital composition of the frontier molecular orbital for metaxalone.

Global Reactivity descriptors

Density Functional Theory (DFT), has become an atractive theoretical method because it gives exact basic vital parameters for even huge complex molecules at low cost[41]. Various qualitative chemical concepts like electronegativity(χ), chemical hardness (*η),* chemical softness (*S*), electrophilicity index (ω) and chemical potential(μ) have been calculated using the energies of the frontier orbital according to Koopman's theorem[42] and are given below.

Ionization potential (I) is related to the energy of the E_{HOMO} through the equation:
$I = -E_{HOMO}$

Electron affinity (A) is related to E_{LUMO} through the equation:
$A = -E_{LUMO}$

When the values of *I* and *A* are known, one can determine the electronegativity χ and the global hardness (η).

$$\chi = \frac{I + A}{2}$$

$$\eta = \frac{I - A}{2}$$

The absolute electrophilicity index (ω) [43] which is calculated by the equation

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

According to the definition, this index measures the propensity of chemical species to accept electrons. A high value of electrophilicity index describes a good electrophile while a small value of electrophilicity index describes a good nucleophile.

Chemical softness (*S*) is the measure of the capacity of an atom or group of atoms to receive electrons [44], it is estimated by using the equation:

$$S = \frac{1}{\eta}$$

The chemical potential(μ) which is negative of (χ), of a system is useful for describing phase transitions, the stratification of gases in a gravitational field, electric currents in semi conductor junctions and nuclear reactions[45]. HOMO–LUMO energy value, ionization potential, chemical hardness and electrophilicity index of metaxalone was calculated and depicted in **table 3.**

Table 3. Global reactivity descriptors of metaxalone

Parameter	Energy (eV)
E_{HOMO}	-6.381
E_{LUMO}	-0.5502
Electronegativity(χ),	3.466
Chemical hardness (*η*),	2.916
Chemical softness (*S*),	0.343
Electrophilicity index (ω)	2.060
Chemical potential(μ)	-3.466

Molecular Electrostatic Potential (MEP)

The molecular electrostatic potential(MEP), is a plot of electrostatic potential mapped on to the constant electron density surface. It may be used to predict reactive sites for electrophilic and nucleophilic attack. The MEPs surface simultaneously display molecular size , shape and electrostatic potential in term of colour grading and is very useful in the investigation of correlation between molecular structure and the physiochemcial property relationship of molecules including bio molecule and drugs [46-49]. The red and blue region refers to the electron rich and electron poor region while green region in the MEPs suggest almost neutral region. MEPs map of metaxalone generated at optimized geometry using Gaussview is shown in **Fig.7.** It is evident from the MEP map that the maximum negative region v(r) is associated with O30 atom having value of -0.6128a.u. due to the electronegative lone pair of oxygen. The maximum positive region localized on the H29 atom have the value of +0.02278a.u.

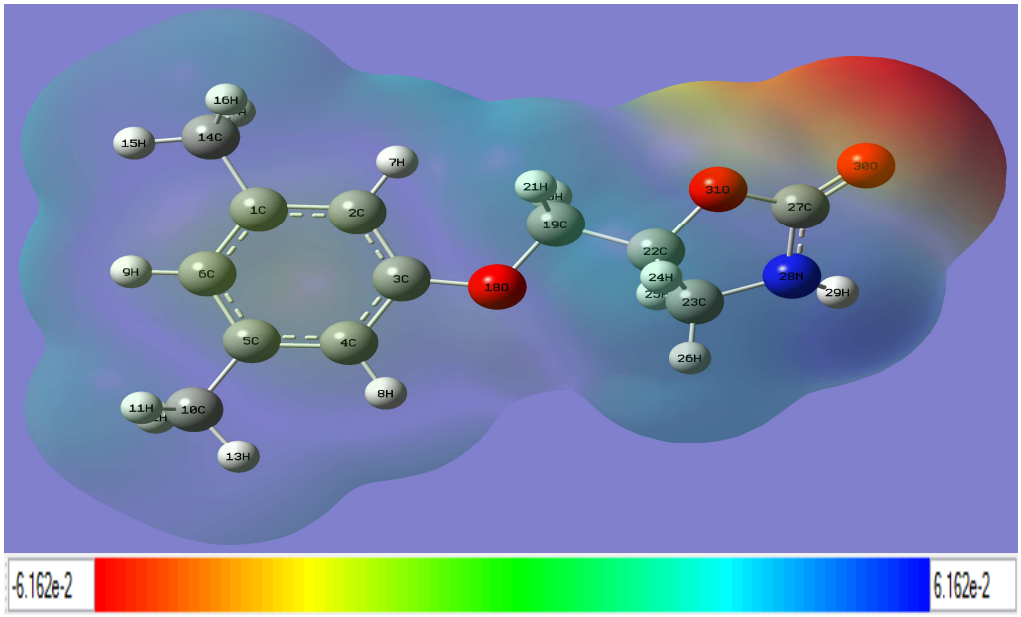


Fig.7 Molecular electrostatic potential map of metaxalone

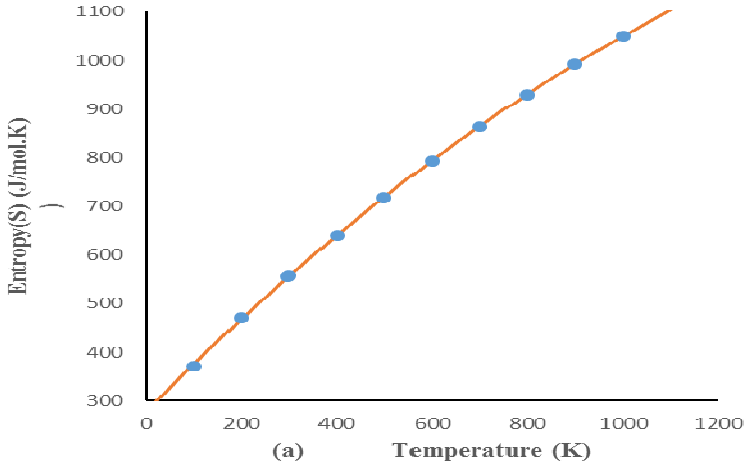
Thermodynamic properties

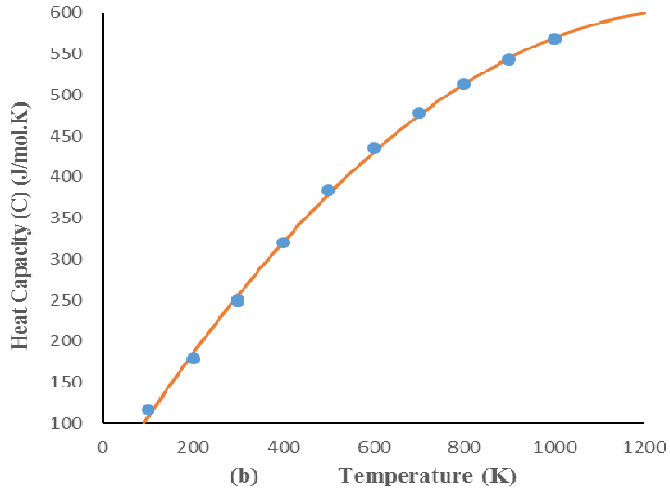
Calculation of thermodynamic properties of molecules is an important phenomenon for both chemical equilibrium and thermochemistry. On the basis of vibrational analysis at B3LYP/6-311++G(d,p) level. The standard statistical thermodynamic functions like heat capacity entropy and enthalpy changes of the title molecule have been calculated from the theoretical harmonic frequencies and tabulated in **table 4**. The molecule was considered to be at room temperature (298.15 K) and 1 atmospheric pressure at the time of performing the calculations. The calculated thermodynamical data can be used to compute the other thermodynamic energies according to relationships of thermodynamic functions and estimate directions of chemical reactions according to the second law of thermo dynamics [50]. It can be observed that the standard heat capacities, entropies and enthalpy changes are increasing with temperatures ranging from 100 to 1000 K due to the fact that the molecular vibrational intensities are increasing with temperature [51,52]. The correlation equations between temperature and entropy, heat capacity and enthalpy changes were fitted by quadratic formulas, and the corresponding fitting factors (R^2) for these thermodynamic properties are 0.9999, 0.9988 and 0.9996, respectively. The corresponding fitting equations are as follows and the correlation graph of those shown in **Fig 8.**

$S = 278.78605+0.99100T- 2.2x10^{-4} T^2$ ($R^2 = 0.9999$)
$C = 23.17624+0.87747T - 3.3x10^{-4} T^2$ ($R^2=0.9988$)
$H= -8.28679+0.104444T + 12.6x10^{-4} T^2$ ($R^2 = 0.9996$)

Table 4. Thermodynamic parameters of metaxalone at different temperatures at B3LYP/6-311++G(d,p) level

T(K)	S(J/mol.K)	C(J/mol.K)	dH (kJ/mol)
100	371.59	117.57	8.06
200	471.88	179.68	22.89
298.15	556.26	248.69	43.85
300	557.8	250.04	44.31
400	639.6	321.21	72.92
500	718.2	383.82	108.26
600	792.93	435.74	149.32
700	863.4	478.38	195.1
800	929.22	513.71	244.76
900	991.93	543.32	297.65
1000	1050.5	568.37	353.27





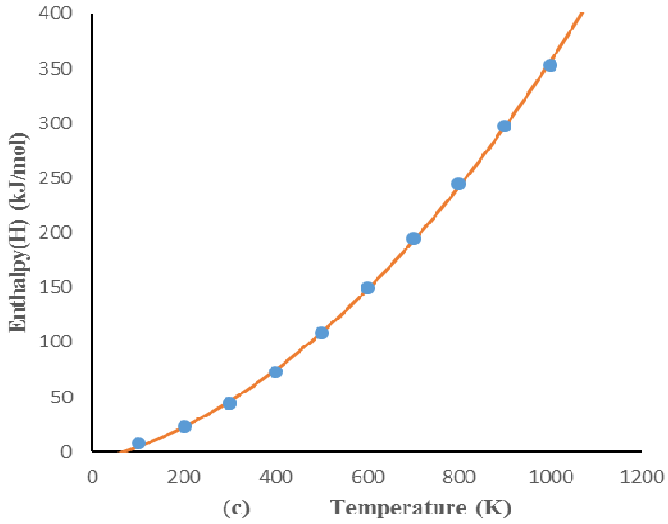


Fig. 8 Correlation graph between (a) Entropy, (b) Heat Capacity and (c) Enthalpy

CONCLUSION

In the present investigation, we have carried out the experimental and theoretical spectroscopic analysis of metaxalone using FT-IR, FT-Raman and NMR techniques. The vibrational and electronic properties of the title compound have been calculated by DFT method using 6-311++G(d,p) basis set. The theoretical chemical shifts of ^{13}C and ^{1}H NMR were compared with the experimental data, showing a very good agreement for both. The calculated HOMO, LUMO energy, energy gap and the global reactivity descriptors are used to analyze the chemical reactivity of the molecule. The MEP map shows the negative potential sites are on oxygen atom as well as the positive potential sites are around the hydrogen atoms. The correlations between the statistical thermodynamics and temperature implies that the heat capacities, entropies and enthalpies increase with the increasing temperature owing to the intensities of the molecular vibrations increase with increasing temperature.

REFERENCES

[1]W.A. Gregory, D.R. Brittelli, C.L.J. Wang,M.A. Wuonola, R.J. McRipley, D.C.Eustice, V. S. Eberly, P. T. Bartholomew,A.M. Slee, M. Forbes, *J. Med. Chem.*, **1989** 32, 1673.
[2] C. Gottschlich, H. Ruecker, *Bioorg. Med.Chem. Lett*., **1992,** 2, 165.
[3]D.R. Brittelli, D.C. Eustine, D.T. Batholomew,A.M. Slee, P.A. Feldmann, L.J. Braun, J. Borkowski, *J. Drugs Exp. Chim. Res.*, **1992** 16,14 .
[4] P.E.Toth and J.Urtis, *Clinical Therapeutics*, **2004**, 26(9), 1355.
[5] S.See, R.Giuzburg, *AmFam Physician*, **2008,** 78,365.
[6] M.N.Carrol, W.R.Luten,R.W.Southward, *Arch. Int. Pharmacodyn. Ther.*, **196**1, 130, 280.
[7] H. N. Mistri, A. G.Jangid, Pudage, N.Gomes, M.Sanyal and P.Shrivastav, *J Chromatogr B*, **2007**, 853(1), 320.

[8] M. Govindarajan, K. Ganasan, S. Periandy, M. Karabacak, *Spectrochim. Acta A*, **2011,** 79 646.
[9] S. Cradock, C. Purves, D.W.H. Rankin, *J. Mol. Struct.*, **1990,** 220, 193.
[10] Z. Zhengyu, Du. Dongmei, *J Mol Struct* ., **2000,** 505, 247.
[11] Z. Zhengyu, Fu. Aiping, Du. Dongmei, *Int J Quant Chem*., **2000,** 78, 186.
[12] M.J. Frisch et al., Gaussian, Inc., Wallingford, CT, **2009**.
[13] A. Frisch, A. B. Nielson, A. J. Holder, GAUSSVIEW User Manual, Gaussian Inc., Pittsburgh, PA **2000**.
[14] R. Ditchfield, *J. Chem. Phys.*, **1972,** 56, 5688.
[15] N. Azizi, A.A. Rostami, A. Godarzian, *J. Phys. Soc. Japan,* **1972,**74,1609.
[16] M. Karabacak, M. Kurt, M. Cinar, A. Coruh, *Mol. Phys.*, **2009,** 107, 253.
[17] N. Sundaraganesan, S. Ilakiamani, H. Saleem, P.M. Wojciechowski, D. Michalska, *Spectrochim. Acta A*, **2005,** 61, 2995.
[18] J.B. Foresman, A. Frisch, Exploring Chemistry with Electronic Structure methods, 2nd ed.,Gaussian Inc., Pittsburgh, PA, **1996.**
[19] D. N. Sathyanarayanan, *Vibrational Spectroscopy Theory and Application*, New Age International publishers, New Delhi,India, **1996.**
[20] A. Altun, K. Golcuk, M. Kumru, *J. Mol. Struct.*, **2003,** 155, 637.
[21] N.B. Colthup, L.H. Daly, S.E. Wiberly, *Introduction to Infrared and Raman Spectroscopy*, third ed. Academic Press, Boston, MA, **1990.**
[22] N.P.G. Roeges, *A Guide to the Complete Interpretation of Infrared Spectra of Organic Structures*, Wiley, New York **1994**.
[23] F. R. Dollish, W. G. Fateley, F. F. Bentely, charact.Raman freq. on Org. Comp., Wiley, New York **1997**.
[24] N. Sundaraganesan, C. Meganathan, Mustafa Kurt, *J Mol Struct.*, **2008,** 891, 284.
[25] A. Altun, K. GoIcuk, M. Kumru, *J Mol Struct.*, **2003**, 625,17.
[26] J.R. Durig, M.M. Bergana, H.V. Phan, J. Raman Spectros., **1991,**22,141.
[27] N. P. G. Roeges, A Guide to complete interpretation of IR spectra of organic structures, Wiley, New York, **1994**.
[28] G. Varsanyi, Vibrational spect benzene derivate, vol III, Academic kiaclo, Budapest, **1969**.
[29] L.J. Bellamy, The Infrared Spectra of Complex Molecule, third ed., Wiley, New York, **1975**.
[30] G. Socrates, Infrared Characteristic Group Frequencies, John wiley and Sons, New York **1981**.
[31] W.A. Seth Paul, A. Van Duyse, *Spectrochim. Acta A*, **1972,** *28*,211.
[32] P.Mani, H.Umamaheswari , B.Dominic Joshua, N.Sundaraganesan , *J. Mol. Struc.* **2008,** 863, 44.
[33] V. Balachandran and M. K. Murali, *Elixir Vib. Spec,*. **2011,** 40, 5105.
[34] S. Xavier, S Ramalingam and S Periandy, *J. Theor. Comput. Sci*., **2014**, 1,2.
[35] O.Alver, C. Parlak and M. Senyel, *Spectrochim. Acta A*, **2007**, 67, 793.
[36] K. Pihlajer, E. Kleinpeter (Eds,) Carbon-13 Chemical Shifts in structure and Spectro chemical analysis, VCH Publishers, Deerfield Beach, **1994**.
[37] R.M. Silverstein, G.C. Bassler, T.C. Morrill, Spectrometric Identification of Organic Compounds, 3rd ed., John Wiley & Sons, New York, NY, **1974**. 239
[38] I.Fleming, Frontier Orbitals and Organic Chemical Reactions Wiley, London, **1976**.
[39] A.Y. Musa, A.H. Kadhum, A.B. Mohamad, Rohoma, H.Mesmari *J Mol Struct,* **2010** 969,233.
[40] G .Gece, S.Bilgic,*Corros Sci.*, **2009**, 51,1876.
[41] S.Zor , F.Kandemirli, M.Bingul, *Prot. Met*, **2009**,45(1),46.
[42] T.Koopmans, *Physica*, **1933**, 1,104.
[43] R.G. Parr, L. Szentpaly and S. Liu , *J.Am.Chem.Soc*., **1999**, 121(9),1922.
[44] P. Senet, *Chem. Phys. Lett.*, **1997**, 275, 527.
[45] G. Frenking, A. Krapp, *J. Comput. Chem.*, **2007,** 28, 15.
[46] J.S. Murray, K. Sen, Molecular Electrostatic Potentials Concepts and Applications. Elsevier,Amsterdam, **1996.**
[47] E. Scrocco, J. Tomasi, in: P. Lowdin (Ed.), Advances in Quantum Chemistry, Academic Press, New York, **1978**.
[48] J. Sponer, P. Hobza, *Int. J. Quantum Chem.* **1996**,57, 959.
[49] M. Karabacak, L. Sinha, O. Prasad, Z. Cinar, M. Cinar, *Spectrochim. Acta A*, **2012**, 93-33.
[50] R. Zhang, B. Dub, G. Sun, Y. Sun, *Spectrochim. Acta A*, **2010,** 75, 1115.
[51] P.Singh, N.P. Singh, R.A. Yadav, *J. Chem. Pharm. Res*., **2010**, 2(6),199.
[52] J. Bevan Ott, J. Boerio-Goates, Calculations from Statistical Thermodynamics, Academic Press, **2000**.