Molecular Structure, Vibrational Spectra, UV-Visible and NMR Spectral Analysis on Ranitidine Hydrochloride using AB Initio and DFT Methods

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A B S T R A C T

A systematic approach has been adopted for structural analysis of Ranitidine Hydrochloride by using FTIR, FT Raman and UV-Vis and NMR spectroscopic techniques. The vibrational analysis are aided by electronic structure calculations HF method and density functional methods (B3LYP) performed with 6-31G(d,p) basis set, with the observed FTIR and FT Raman data, complete vibrational band assignments and analysis of the fundamental modes of the compound are carried out. The UV absorption spectra of the title compound dissolved in methanol. Natural Bond Orbital analysis has been carried out to explain the charge transfer (or) delocalization of change due to the intra molecular interactions. The first order Hyperpolarizability (βo) of this novel molecular system and related properties (β, α_o, Δx) of Ranitidine hydrochloride are calculated using HF and DFT(B3LYP/61-31G(d,p)) methods . In addition the molecular electrostatic potential (MEP) have been investigated using theoretical calculations, the calculated HOMO, LUMO energies and $\square_{max}$ were determined by time- dependent DFT (TD DFT) method. ^{1}H and ^{13}C NMR theoretical shifts of the molecule were calculated. The thermodynamic functions of the title molecule are also performed using DFT method. Thermodynamics properties and atomic charges were calculated using both Hartee Fock and density functional method using above the basis set and compared.

Introduction

Ranitidine hydrochloride is in a group of drugs called histamine-2 blockers. Ranitidine works by reducing the amount of acid our stomach producers. Ranitidine hydrochloride Chemically N[2-[[[- (dimethylamino) methyl]-2furanyl] metgyl] thiyo]ethyl]-N'-methyl-2-nitro-1,1-,HCl (Ranitidine hydrochloride) is H_2 receptor antagonist indicated for duodenal ulcer

(Keith G.T,2000). It is used to treat and present ulcers in the stomach and intestine. It is also treats conditions in which the stomach too much acid such as Zollinger Ellison Syndrome, gastro esophageal, reflex disease and erosive esophagitis [International Journal of Pharm Tech Research, 2010; Martindale, 1973).

Ranitidine is mainly used to treatment of Peptic Ulcers Diseases (or) PUD is an ulcer is defined as the mucosal erosion equal to (or) greater than 0.5cm of an area of the gastrointestinal tract exposed to the acid and pepsin secretion. The recommended adult oral dosage of ranitidine is 150 mg twice daily or 300 mg once daily. The effective treatment of erosive esophagitis requires administration of 150 mg of ranitidine 4 times a day. A conventional dose of 150 mg can inhabit gastric acid secretion up to 5 hours but not up to 10 hours. An alternative dose of 300 mg leads to plasma fluctuations; thus a sustained release dosage form of Ranitidine hydrochloride is desirable (Dave, B.S, 2004). Hence the present investigation was undertaken to study the vibrational spectra of this molecule completely and to identify the various normal modes with greater wave number accuracy. The band assignments have been made by assuming c_1 point group symmetry. DFT calculations have been performed to support our wave number assignments and HOMO – LUMO values are calculated.

Experimental

The compound under the investigation namely Ranitidine hydrochloride $C_{13}H_{22}N_4O_3S.HCl$ is monoclinic. A projection of N[2-[[[5-(dimethylamino) methyl]-2furanyl] methyl] thiyo]ethyl]-N'-methyl-2-nitro-1,1-, HCl (Ranitidine hydrochloride) is shown in the Fig.1 was procured from the reputed pharmaceutical company Chennai, Tamil Nadu, INDIA and which was used without further purification. The FTIR spectrum of the compound was recorded in the 4000-400cm^{-1} region in evacuation mode on Bruker IFS 66v model spectrometer using KBr pellet technique solid phase 4.0 cm^{-1} resolution. The FT-Raman accessory in the region 4000-500cm^{-1} using a Nd:YAG laser operating at 100mw power. The UV-Vis spectrum of Ranitidine hydrochloride was recorded in the region 200-600nm. The spectral measurements were carried out at the Indian Institute of Technology (IIT) Madras (Tamil Nadu) India. ^1H and ^{13}C NMR spectra have been recorded using BRUKER AVANCE III 500 MHZ NMR at SAIF, IIT, and Madras, India.

Computational Method

In the present work, quantum chemical methods like Hartee Fock (HF) and Density Functional B3LYP method with the 6-31G(d,p) basis set are employed to study the complete vibrational spectra of the title compound and to identify the various normal modes with greater accuracy. The present investigation was under taken to study the vibrational spectra of this molecule completely. These calculations have been performed to support our wave number assignments.

The calculations are performed by Gaussian 09W program package on the personal computer. The optimized molecular structure, vibrational frequencies, Thermodynamic properties, hyperpolarizability, NBO analysis, UV-Vis and NMR spectra of the entitled compound were performed using the Gaussian 09W package program which is the modern computational chemistry software package with gauss view molecular visualization program on the pc at B3LYP/6-31G(d,p) method.

Results and Discussion

Molecular Geometry

The molecules Ranitidine hydrochloride has 45 atoms with 129 normal modes of vibrations. It belongs to C_1 point group symmetry. Fig. 1 shows the optimized geometry of the title compound and Table 1. Presents the optimized values obtained for band length and bond angle. The various bond length and bond angle are found to be almost same at B3LYP/31-G(d,p) and HF methods. The bond length between C_1-C_2 in B3LYP and HF methods are found to be 1.3901 and 1.3713 respectively which are in good agreement with the experimental value.

The bond length between C_{10}-H_{30} in B3LYP and HF methods are found to be 1.0942 and 1.0839 respectively which are in good agreement with the experimental value 1.09. The bond lengths between O_{13}-C_{14} and C_{18}-N_{19} in B3LYP and HF methods are found to be 1.3794 and 1.3564, 1.45 and 1.44 respectively which are in good agreement with the experimental 1.37 and 1.46. The bond angle between C_1-C_2-N_5 in B3LYP and HF methods are 124.43°, 124.82° are good agreement with the experimental value 124.43°. The bond angle N_3-C_9-H_{29} in B3LYP and HF methods are 109.44° and 109.71° which are in good agreement with the experimental value 109.44°. The bond angle C_{10}-C_9-H_{29} in B3LYP and HF method are 110.05°, 109.82° which are in good agreement with the experimental value 109.44°. The bond angle C_{14}-C_{12}-H_{33} in B3LYP and HF methods are 110.71° and 109.95° which are in good in agreement with the experimental value 109.52°. The calculated geometrical parameters of Ranitidine hydrochloride. The optimized bond length are (longer than or smaller than) the experimental values as the theoretical calculations result from isolated molecules in gaseous state where as the experimental results were from molecule in solid state (Gunasekaran et al, 2003). Bond angle and dihedral angles were referred from (C.N. Rao, 1964, C.N.Rao,1963).

Vibrational Band Assignment

The observed and calculated frequencies using RHF/cc-PVDZ., B3LYP/6-31G(d,p) methods and their IR intensities and assignments are listed in Table 2. Experimental and Theoretical FTIR spectra of Ranitidine hydrochloride are shown in Fig. 2. Experimental and theoretical FT-Raman spectra of Ranitidine hydrochloride are presented in Fig. 3. The description of the various band assignments are as follows.

N-H Vibration

Primary aliphatic amines absorb in the region 3450-3250cm^{-1} in solids or liquids and they are broad and of medium intensity. In solid and liquid phase, a band of medium intensity is observed at 3400-3300cm^{-1} for secondary aromatic amines. In general the vibrational bands due to the N-H stretching are sharp and weak than those of O-H stretching vibrations by virtue of which they can easily identified (R.Huey, 2007). Hetero aromatic containing in the N-H group has a stretching absorption (Sagdine, 2007) in the region 3500-3220cm^{-1}. The bands of moderate intensity found in the region 1430-1330cm^{-1} may be due to interaction between C-N stretching and N-H bending group (Varsanyi, 1973). The N-H stretching vibration give rise to a weak band at 3500-3300cm^{-1}. The band appear at 3414cm^{-1} in the FTIR spectrum of 2-amino-4.6-dimethoxy pyrimidine molecule was assigned to NH_2 stretching vibration (Wilson B.E, 1995). Bayari et al [12] assigned the band at 3364cm^{-1}, which corresponds to N-H stretching in methylphenidate. Based on this the

symmetric and asymmetric N-H stretching vibrations of the molecule Ranitidine hydrochloride are assigned to 3570cm^{-1} FT-Raman are respectively.

C-H Vibration

The hetero aromatic structure shows the presence of C-H stretching vibrations in the region 3250-3000cm^{-1} which is characteristic region for the ready identification of C-H stretching vibrations (D.Becke, 1993). Hetero cyclic compound C-H vibration absorption bands are usually weak, in many is too weak for detection. In this region, the bands are not affected, appreciably by the nature of substituents. In the Present work, the FTIR and FT Raman bands observed at 3191cm^{-1} and 3188cm^{-1} have been assigned to C-H stretching vibration.

The B3LYP level at 6-31G(d,p) gives the frequency values 3148cm^{-1} and 3200cm^{-1} in HF as shown in Table 2. In general the aromatic C-H stretching vibrations calculated theoretically are in good agreement with the experimentally reported values (Y.Uesugi, 1997) for trisubstituted benzene in the region 3250-3000cm^{-1}. The title molecule Ranitidine Hydrochloride has out- of- plane and in-plane aromatic C-H bending vibrations. The out of plane bending mode of C-H is found well with experimentally predicted in the region 900-800 cm^{-1} at B3LYP/6-31G(d,p). The observed FTIR value of 879-859cm^{-1} is in agreement with 878 and 857cm^{-1} of B3LYP/6-31G(d,p) results. The C-H in plane bending vibrations assigned in the region 980-1260 cm^{-1} even though found to be contaminated by C-CH$_3$ stretch are found in literatures. (S.Gunasekaran, 1993), while the experimentally observed values are at 1074 and 1263cm^{-1}.

C-N Vibration

The identification of C-N stretching frequency is a very difficult task since, the mixing of bands are possible in this region (S.Gunasekaran, 2005). The C-N stretching band is assigned at 1319cm^{-1} in 2,6-dibromo-4-nitroanilineby Krishnakumar et al (2005) and Xavier Jesu Raja et al (1994) have identified the FT-IR band at due to C-N 1342cm^{-1} in Theophylline. Gunasekaran et al (2008) have observed C-N stretching band at 1312cm^{-1} in benzocaine. Seshdri et al (2009) have observed the C-N stretching band at 1305cm^{-1} in FTIR and 1307cm^{-1} in FT Raman spectra of 7-chloro-3-methyl-2H-1, 2, 4-benzothiadiazine 1,1-dioxide. (Silverstein et al,1981) assigned C-N stretching vibrations in the region 1342-1266cm^{-1} for aromatic amines. Hence in the present investigation, the FTIR bands observed at 1304, 1263cm^{-1} and the bands at 1263, 1248, 1228 cm^{-1} in the FT Raman spectrum of Ranitidine hydrochloride are assigned to the C-N stretching mode of vibrations. The Calculated value 1263,1231,1308cm^{-1} In B3LYP and 1280, 1246, 1219cm^{-1} in HF method are excellent agreement with the experimental observation of both in FTIR and FT Raman spectra.

C=C and C-C Vibration

The C=C aromatic stretching vibrations gives rise to characteristic bands in both the observed IR and Raman spectra, covering the spectral range from 1650-1430cm[-1](S. Gunasekaran2003). In our study the C=C stretching vibrations of the title compound observed at 1618 and 1590cm^{-1} in FT-IR and 1600 and 1587cm-1 in FT-Raman are assigned to C=C stretching vibrations respectively. The calculated values are 1600, 1584cm^{-1} and 1606, 1584cm^{-1} in B3LYP method with 6-31G (d,p) and HF method

respectively. The ring 1590-1430cm^{-1} (C.S. Hsu,1974) The present investigation C-C stretching vibrations have been observed at 1417cm^{-1} in FT-IR and 1450, 1437, 1408cm^{-1} in FT-Raman is due to C-C stretching vibrations. The calculated wave numbers are 1454 and 1440, 1400cm^{-1} in B3LYP method with 6-31G(d,p) and 1447, 1442cm^{-1} in HF method respectively. The C=C and C-C stretching vibrations predicted by B3LYP and HF methods values are in good agreement with the experimental value are presented in Table 2. The bands are observed 1045, 1021cm^{-1} in FT-IR and 1023, 1007, 802cm^{-1} in FT-Raman have been assigned to C-C in plane bending vibrations.

C-O Vibrations

Generally the C-O stretching vibrations occur in the region1320-1210cm^{-1} (Barbara.H 2010). In the present study, the medium bands observed at 1304 and 1263cm-1in FT-IR and the weak band observed at 1306 and 1263, 1248cm^{-1} in FT-Raman are assigned to C-O stretching vibration. The calculated bands observed at 1308, 1263 and 1256cm^{-1} in B3LYP level with 6-31G(d,p) and 1311, 1280, 1246cm^{-1} in HF method respectively are in excellent agreement with experimental frequency. From the data available in literature, it is found that the intensities of the carbonyl bands of aldehyde vary with structural features. In alcoholic solution, there is a distinct fall in the intensity of aldehyde due to carbonyl absorption. Ashdown and Keltz (1948) have reported number of such cases and the range of frequencies 1020-1110cm^{-1} to be associated with the C-O linkage. The experimental frequencies at 1164, 1133, 1133, 1122, 1074, 1021 and 925 cm-1 in FTIR and 1164, 1135, 1102, 1073, 1046, 1023, 1007 and 955 cm^{-1} in FT-Raman spectrum of Ranitidine hydrochloride are

assigned to C-O stretching vibrations. This is in excellent agreement with B3LYP/6-31G(d,p) and HF method.

C-S Vibrations

In general, the assignment of the band due to C-S stretching vibrations in different compounds is difficult. Both aliphatic and aromatic sulphides have weak-to-medium bands due to C-S stretching vibration in the region 780-510cm^{-1} (Venkataramana Rao, 2002 Krishnakumar V , 1998). Double band conjugation with C-S band like vinyl or phenyl lowers the C-S stretching vibration and increase the intensity. In view of this the medium intense bands present at 761, 698, 660 641cm^{-1} in FT-IR and 756, 720, 661cm^{-1} in FT-Raman spectrum of ranitidine hydrochloride are assigned due to C-S stretching modes of vibration.

NO$_2$ (Nitro group Vibration)

The NO$_2$ stretching vibrations are very useful group vibration because of their spectral position and strong intensity. The NO$_2$ asymmetrical stretching vibrations in nitro alkenes occur in the range 1560-1530cm^{-1} and the symmetric vibration lie in the range 1390-1370cm^{-1}, the asymmetrical stretching being their stronger than the symmetrical stretching. In aromatic compounds the NO$_2$ stretching bands shift down to slightly lower than wave numbers in the range 1540-1500cm^{-1} and 1370-1330cm^{-1} (L.E Sutton,1958). Aromatic nitro compounds have strong vibrations of the NO$_2$ groups at 1570-1485cm^{-1} and 1370-1320cm^{-1} due to asymmetric stretching vibrations respectively (S. Muthu,2012 and Jone Pradeepa,2014). In Ranitidine hydrochloride the FTIR spectrum1379cm^{-1} and FT Raman 1554cm^{-1},1533cm^{-1} which are due to NO$_2$ stretching vibration.

UV-Vis Spectral Analysis

The UV-Vis electronic spectrum of Compund in Methanol solvent was recorded with 200-600nm range is shown in Fig 4. To support experimental observations, the theoritical electronic excitation energies, absorption, obsorption weavelength and oscillator strength were calculated by TD-DFT with GAUSSIAN 09W program. All Calculations were performed asssuming the title compound was in the Liquid phase and Methonal solvent. The experimental and calculated result of UV-Vis spectral data were compared in Table 3. The experimentally measure UV-Vis data 325nm, 228nm and 198nm showed good agreement with theoritically computed data 287.31nm, 259.48nm and 257.51nm respectively which was obtained by TD-DFT B3LYP/631-G(d,p) method. The analysis of the wave function indicates that the electron absorption corresonds to the transition from the ground to the first excited state. It is mainly described by an electron excitation from highest occupied molecular orbital (HOMO) to the lowest unoccupied molecular orbital (LUMO). The HOMO energy characterizes the abiity of electron donating , LUMO characterizes the ability of electron accepting and the gap between HOMO and LUMO characterizes the molecular chemical stability (K. Sarojini,2013). The HOMO is located over the entire Carbon chain and LUMO transudation implies and electron density transfer to the electronegative hydroxyl group from carbon chain. The HOMO and LUMO surfaces are sketched in Fig.5 According to the B3LYP calculation the energy gap (ΔE) between HOMO (-6.01240302eV) and LUMO (-.014176332) of the molecules is about 4.998226688 eV. This energy gap between HOMO and LUMO explains the ultimate charge transfer interactions within the molecule.

HUMO and LUMO Analysis

Many organic molecule that contain conjugated π electrons are characterized by hyperpolarizabilities have been analyzed by means of vibrational spectroscopy (R. S, Mulliken 1958). In most of the cases, even in the absence of inversion symmetry, the strongest bands in the Raman spectrum are weak in the IR spectrum vice versa. But the intra molecular charge transfer from the donor to acceptor group through a single-double bond conjugated path can induce large vibrations of both the molecular dipole moment and the molecular polarizibility, making IR and Raman activity strong at the same time. It is also observed in Ranitidine hydrochloride. The analysis of the wave function indicates that the electron absorption corresponds to the transition from the ground to the first excited state and is mainly described by one-electron excitation from the highest occupied Molecular Orbital (HOMO) to the Lowest Unoccupied Molecular Orbital (LUMO). The atomic orbital compositions of the Frontier Molecular Orbital are sketched in fig 5. The HOMO and LUMO energy gap of Ranitidine hydrochloride has been calculated by using DFT/B3LYP/6-31G(d,p) basis sets Table 3, reveals that the energy gap reflects the chemical activity of the molecule. LUMO as an electron acceptor represents the ability to donate and electron. The HOMO and LUMO energy gap (ΔE) (transition from HOMO to LUMO) of the molecule is explains the fact that eventual transfer interaction is taking place with the molecule.

HOMO energy (B3LYP/6-31G(d,p)) = -6.01240302
LUMO energy (B3LYP/6-31G(d,p)) = -1.014176332

HOMO-LUMO energy (B3LYP/6-31G(d,p)) = 4.998226688

Mulliken's Population Analysis

The total atomic charges of Ranitidine hydrochloride obtained by Mullikan's population analysis by HF and B3LYP method, with 6-3G(d,p) basis set were listed in Table 4. The atomic charges affect dipole moment, polarizability, electronic structure and more a lot of properties of molecular systems. The charge distribution of the title compound shows that the Carbon atoms (C_1, C_{14}, and C_{17}) attached with Nitrogen, Carbon and Oxygen is positive [0.335504, 0.324143] remain Carbon atoms are negatively charged. H_{24} has the maximum positive charge of 0.30893e and H_{23} has the next maximum charge of 0.272443e Hence the Nitrogen atoms attract the Carbon N_3 and the hydrogen atom H_{23}. N_3 atom has highly negative charge of -0.553581 and H_{23} attached to it has positive charge 0.272443 in B3LYP method. The other Carbon atoms C_2, C_8, C_9, C_{10}, C_{12}, C_{15}, C_{16}, C_{20}, C_{21} and Cl_{44} have negative atomic charges. All the hydrogen atoms exhibit positive charge Both HF and B3LYP method. From the result it is clear that the substitution of aromatic ring leads to a redistribution of electron density. The charge distribution on the molecule has an important influence on the vibrational spectra (Y. Ataly,2008). The corresponding plot of Mullikan's charges obtained by B3LYP/6-3G(d,p) are shown in Fig 6. respectively.

First Order Hyperpolarizability

The polarizability α, the Hyperpolarizability β and electric dipole moment μ of the Ranitidine hydrochloride are calculated by finite field method, using B3LYP/6-31G (d,p) basis set available in DFT methods. To calculate all the electric dipole moments and the first Hyperpolarizability for the isolated molecule the origin of the Cartesian Co-ordinate system was chosen at own canter of mass of Ranitidine hydrochloride. The first Hyperpolarizability ($β_0$) of this novel molecular system and related properties (β, $α_0$ and Δα) of Ranitidine hydrochloride are calculated and it is based on the finite field approach. In the presence of an applied electronic field, the energy of a system is a function of the electric field. First hyper polarizability is a third rank tensor that can be described by 3x3x3 matrixes is a tetrahedral. The 27 components of the 3D matrix can be reduced to 10 components due to the Kelinman Symmetry (T. Vijakumar, I.H. Joe, 2008). The components of β are defined as the coefficients in the Taylor series expansion of the energy in the external electric field. When the external electric field is weak and homogeneous this expansion becomes:

$$E = E0 - \mu_\alpha F_\alpha - 1/2_{\alpha\beta}F_\alpha F_\beta + 1/6\beta_{\alpha\beta\gamma}F_\alpha F_\beta F_\gamma$$

E^0 is the energy of unperturbed molecules Fα is the field at the origin μ_x, $\alpha_{\alpha\beta}$ and $\beta\alpha\beta\gamma$ is the components of dipole moment, polarizability and the first Hyperpolarizability respectively. A the anisotropy of the polarizability Δα and the mean first Hyperpolarizability βo using the x,y,z components they are defined as

$$\mu = (\mu x^2 + \mu y^2 + \mu z^2)^{1/2}$$

$$\alpha_o = \alpha_{xx} + \alpha_{yy} + \alpha_{zz}/3$$

$$\Delta\alpha = 2^{-1/2}[(\alpha_{xx}-\alpha_{yy})^2 + (\alpha_{yy}-\alpha_{zz})^2 + (\alpha_{zz}-\alpha_{xx})2 + 6\alpha^2_{xx}]^{1/2}$$

$$\beta_o = (\beta^2x + \beta^2y + \beta^2z)^{1/2} \text{ and}$$
$$\beta_x = \beta_{xxx} + \beta_{xyy} + \beta_{xzz}$$

$$\beta_y = \beta_{yyy} + \beta_{xxy} + \beta_{yzz}$$

$\beta_z = \beta_{zzz} + \beta_{xxz} + \beta_{yyz}$

since the values of the polarizabilities (α) and Hyperpolarizability (β) are reported in atomic units (a.u.) , the calculated values have been converted into electrostatic units (esu) (α: 1a.u. = 0.1482 X10^{-24}esu: 1 a.u. = 8.639X10^{-33}esu). The first orders Hyperpolarizability (β) of the molecule along with related properties were calculated using RHF and B3LYPmethods are presented in Table 5. Urea is one of the molecules which has good non-linear comparative studies, (μ = 1.3732 debye and β = 0.3728X10^{-30}esu). In RHF method, dipole moment (μ) is nearly 4.0 times greater than urea and hyperpolarizability is 15 times greater than urea. In B3LYP method, the dipole moment is 3.5 times greater than urea and hyperpolarizability is 11 times greater than urea. Hence the title compound has good non-linear property.

NBO Analysis

NBO (Natural Bond Orbital) analysis provide an efficient method for studying intra and inter molecular bonding and interaction among bonds, and also provides a convenient basis for investigation charge transfer or conjugative interactions in molecular system. (Kosar,2011) Another useful aspect of NBO method is that it gives information about interactions in both filled and virtual orbital spaces that could enhance the analysis of intra and intermolecular interactions. The second order Fock matrix was carried out to evaluate the donor – acceptor interactions in the NBO analysis (D.A. Kelinman, 1962). For each donor NBO (i) and acceptor (j), the stabilization energy associated with i→j delocalization can be estimated as,

$E(2) = \Delta E_{ij} = q_i \, F(i,j)2/\Box j - \Box i$

Where q_i is the donor orbital occupancy, $\Box i$, $\Box j$ are diagonal elements (orbital energies) and F_{ij} is the off-diagonal NBO Fock matrix element. In Table 6. The perturbation energies of significant donor-acceptor interactions are presented. The larger the E(2) value , the intensive is the interaction between electron donors and electron acceptors. In Ranitidine hydrochloride, the interactions between the first lone pair LP(3) of O_7 with σ^* (N_5-O_6) have the highest E(2) value around 136.79 kcal/mol. The other significant interactions giving stronger stabilization energy value of 58.34kcal/mol to the structure are the interactions between anti bonding of C_1-C_2 between the same lone pair LP(1) of nitrogen. The intermolecular hyper conjugative interaction of σ (C_1-C_2) and σ^* (N_5-O_6) leading to strong stabilization of 30.57kcal/mol. The intra molecular hyper conjugative interaction of σ (C_{14}-C_{15}) to σ^* (C_{16}-C_{17}) and σ (C_{16}-C_{17}) to σ^*(C_{14}-C15) leads to 12.95 and 14.63 kcal/mol respectively. These interactions are observed as increase in electron density in anti bonding orbital that weakens the responsible for biological properties. Hence Ranitidine hydrochloride structure stabilized by these orbital's interactions. In ranitidine hydrochloride oxygen larger percentage of NBO and gives the larger polarization co-efficient because it has the higher electro negativity. The calculated values of E(2) are given in Table 6.

Thermodynamic Properties

The Variation in Zero-point Vibrational Energies (ZPVEs) seems to be important. The value of some thermodynamic parameters such as Zero-point vibrational energy, thermal energy, specific heat capacity, rotational constant, entropy of Ranitidine hydrochloride but HF and DFT/B3lYP with 6-31G(d,p) basis sets are listed in the Table 7. The statistical thermo

chemical analysis of Ranitidine hydrochloride was performed considering the molecule to be at room temperature 298K and one atmospheric pressure.

All the thermodynamic data supply helpful information for further study of the title molecule. The can be used to compute the other thermo-dynamic energies according to relationships of thermodynamic functions and estimate directions of chemical reactions according to the second law of thermo dynamical field (S. Subashchandrabose, 2010). The ZPVEs, energy is lower in the B3LYP method at 6-31G (d,p) basis set than by HF method. The biggest value of ZPVEs of Ranitidine hydrochloride is 247.0806 KJ mol^{-1} obtained at HF method. However, specific heat capacity and entropy were calculated the smallest values for HF but the highest values were obtained B3LYP method. The minimum value of thermal energy are calculated in246.640 at B3LYP/6-31G(d,p) whereas the maximum one was calculated 263.023 at HF Method in Ranitidine hydrochloride molecule. The thermodynamic functions such as heat capacity at constant pressure (Cp), entropy (S) and enthalpy change (ddH) for the title compound were evaluated from the theoretical harmonic frequencies obtained from B3LYP method in the temperature range 100-1000 K and are listed in Table 8.

From this table it is evident that the properties increase with the increases in temperature due to the fact that the vibrational intensities of molecules increase with temperature. The correlation between these thermodynamic properties and temperatures are fitted by quadratic formulae as follows and corresponding fitting factor (R^2) for these thermodynamic

properties were found to 0.99958, 0.99941 and 0.99954. The temperature dependent correlation graphs are shown in Fig 7.

$$C^0_{pm} = 355.22896 + 1.28893T - 5.1641 \times 10^{-4} T^2 \quad (R^2 = 0.99958)$$

$$S^0_m = 71.25293 + 1.66492T - 4.54469 \times 10^{-4} T^2 \quad (R^2 = 0.99941)$$

$$\Delta H^0_m = -15.90805 + 0.20217T - 3.61844 \times 10^{-4} T^2 \quad (R^2 = 0.99954)$$

NMR Spectral Analysis

In this study, ^{1}H and ^{13}C NMR chemical shifts of Ranitidine hydrochloride were calculated and depicted in Table 9. These calculations obtained at B3LYP/6-31G(d,p) and HF methods for the optimized geometry were observed to be in good agreement with experimental results. The ^{1}H isotropic chemical shift values were obtained from 2.034 to 5.183ppm while these values were calculated from 2.454 to 10.414ppm at B3LYP/6-31G(d,p) and 2.039 to 10.334 ppm in HF method, as seen from table, all computations are in good agreement with experimental data. The Proton H(32), observed to be about 4.842ppm was found to be 4.780ppm at B3LYP/6-31G(d,p) and 4.224ppm at HF method, calculation level of theory. In addition ^{13}C isotropic chemical shifts with regard to TMS calculated at the same basis set are given in the same Table 9. ^{13}C chemical shift values were obtained from 38.512 to 158.524ppm where as these values were experimentally observed from 39.996 to 155.049 ppm. The chemical shifts of C_{14} and C_{17} connected with oxygen O_{13} was observed to be 151.054, 159.164ppm and 146.163, 155.662ppm by the B3LYP/6-31G (d,p) and HF method.

Table.1 Optimized Geometrical Parameters (bond lengths, bond angles)
of the Ranitidine Hydrochloride

Parameters	Ranitidine hydrochloride		
Bond Length (A)	B3LYP/6-31G(d,p)	HF/6-31G(d,p)	Experimental
C_1-C_2	1.3901	1.3713	1.39
C_1-N_4	1.3888	1.3802	1.37
C_1-N_4	1.3500	1.3392	1.37
C_2-N_5	1.3986	1.3987	1.39
C_2-H_{22}	1.0786	1.0665	1.08
N_3-C_9	1.4701	1.4601	1.46
N_3-H_{23}	1.0129	0.9964	1.01
N_4-C_8	1.4555	1.4528	1.46
N_4-H_{24}	1.023	0.9962	-
N_5-O_6	1.2389	1.1985	1.23
N_5-O_7	1.2633	1.2159	1.23
O_7-H_{24}	1.8145	1.9438	-
C_8-H_{25}	1.0931	1.0827	1.09
C_8-H_{26}	1.0928	1.0803	1.09
C_8-H_{27}	1.0967	1.0846	1.09
C_9-C_{10}	1.5346	1.5299	1.53
C_9-H_{28}	1.0937	1.0828	1.09
C_9-H_{29}	1.0911	1.0791	1.09
C_{10}-S_{11}	1.8384	1.8169	1.81
C_{10}-H_{30}	1.0942	1.0839	1.09
C_{10}-H_{31}	1.0954	1.0849	1.09
S_{11}-C_{12}	1.8614	1.8281	1.81
C_{12}-C_{14}	1.4813	1.4870	1.48
C_{12}-H_{32}	1.0919	1.0814	1.09
C_{12}-H_{33}	1.0948	1.0840	1.09
O_{12}-H_{45}	-	3.2661	-
O_{13}-C_{14}	1.3794	1.3564	1.37
O_{13}-C_{17}	1.3755	1.5410	1.37
O_{12}-H_{45}	1.9893	2.2164	-
C_{14}-C_{15}	1.3621	1.3379	1.39
C_{15}-C_{16}	1.4337	1.4416	1.39
C_{15}-H_{34}	1.0807	1.0708	1.09
C_{16}-C_{17}	1.3611	1.3385	1.36
C_{16}-H_{35}	1.0794	1.0690	1.09
C_{17}-C_{18}	1.4971	1.4981	1.49
C_{18}-N_{19}	1.4597	1.4471	1.46
C_{18}-H_{36}	1.0982	1.0860	1.09
C_{18}-H_{37}	1.1079	1.0937	1.09
N_{19}-C_{21}	1.4600	1.4500	1.46
C_{20}-H_{38}	1.4583	1.4484	1.46
C_{20}-H_{39}	1.0941	1.0840	1.09
C_{20}-H_{40}	1.1065	1.0941	1.09
C_{21}-H_{41}	1.0927	1.0821	1.09
C_{21}-H_{42}	1.0941	1.0838	1.09
C_{21}-H_{43}	1.1065	1.0941	1.09
H_{21}-H_{43}	1.0944	1.0839	1.09
H_{35}-H_{45}	-	2.9278	-
Cl_{44}-H_{45}	1.2991	1.2708	-
Bond angle(degree)			
C_2-C_1-N_3	118.4154	117.4768	119.11

$C_2-C_1-N_4$	123.0839	125.1815	119.11
$N_3-C_1-N_4$	118.4924	117.3416	115.90
$C_1-C_2-N_5$	124.4323	124.8236	124.43
$C_1-C_2-H_{22}$	121.9211	122.0252	-
$N_5-C_2-H_{22}$	113.6184	113.1335	-
$C_1-N_3-C_9$	121.5155	120.9690	-
$C_1-N_3-H_{23}$	111.5491	111.8755	110.00
$C_9-N_3-H_{23}$	112.1218	112.3712	110.00
$C_1-N_4-C_8$	125.1630	125.0850	125.03
$C_1-N_4-H_{24}$	110.4457	112.8836	110.00
$C_8-N_4-H_{24}$	118.7809	116.6753	110.00
$C_2-N_5-O_6$	117.8601	117.1744	117.17
$C_2-N_5-O_7$	120.0803	120.1574	117.17
$O_6-N_5-O_7$	122.0539	122.6657	-
$N_4-C_8-H_{25}$	108.7819	108.6456	109.48
$N_4-C_8-H_{26}$	110.5495	110.6743	109.48
$N_4-C_8-H_{27}$	112.2318	111.7167	109.48
$H_{25}-C_8-H_{26}$	108.5211	108.427	109.00
$H_{25}-C_8-H_{27}$	107.8541	108.1871	109.00
$H_{26}-C_8-H_{27}$	108.7998	109.1004	109.00
$N_3-C_9-C_{10}$	113.0907	113.0405	120.20
$N_3-C_9-H_{28}$	107.1546	106.9286	109.00
$N_3-C_9-H_{29}$	109.4461	109.7174	109.44
$C_{10}-C_9-H_{28}$	109.883	109.961	109.44
$C_{10}-C_9-H_{29}$	110.0599	109.8253	109.44
$H_{28}-C_9-H_{29}$	106.9888	107.167	109.52
$C_9-C_{10}-S_{11}$	109.0667	109.5211	-
$C_9-C_{10}-H_{30}$	110.1587	110.0955	109.52
$C_9-C_{10}-H_{31}$	109.8973	109.9448	109.52
$S_{11}-C_{10}-H_{30}$	110.2585	109.7627	-
$S_{11}-C_{10}-H_{31}$	108.5317	109.0905	-
$H_{30}-C_{10}-H_{31}$	108.9053	108.4048	109.00
$C_{10}-S_{11}-C_{12}$	99.9229	99.9055	-
$S_{11}-C_{12}-C_{14}$	111.4601	111.0513	-
$S_{11}-C_{12}-H_{32}$	109.5588	109.6513	-
$S_{11}-C_{12}-H_{33}$	107.2345	108.4048	-
$S_{11}-C_{12}-H_{45}$	-	78.5279	-
$C_{14}-C_{12}-H_{32}$	109.3878	109.2113	109.21
$C_{14}-C_{12}-H_{33}$	110.7167	109.9503	109.52
$C_{14}-C_{12}-H_{45}$	-	72.5861	-
$H_{32}-C_{12}-H_{33}$	108.4126	108.5075	108.50
$H_{32}-C_{12}-H_{45}$	-	169.4803	-
$H_{33}-C_{12}-H_{45}$	-	61.7781	-
$C_{14}-O_{13}-C_{17}$	107.7264	107.8006	-
$C_{14}-O_{13}-H_{45}$	122.3262	122.3736	-
$C_{17}-O_{13}-H_{45}$	129.884	129.6233	-
$C_{12}-C_{14}-O_{13}$	116.9300	116.9549	-
$C_{12}-C_{14}-C_{15}$	133.9878	133.2882	-
$O_{13}-C_{14}-C_{15}$	109.0793	109.7559	109.00
$C_4-C_{15}-C_{16}$	107.0218	106.3712	-
$C_{14}-C_{15}-H_{34}$	125.7696	126.2153	-
$C_{16}-C_{15}-H_{34}$	127.2083	127.4135	127.50
$C_{15}-C_{16}-H_{17}$	106.7599	106.1059	-
$C_{15}-C_{16}-H_{35}$	127.9659	127.9851	127.50
$C_{17}-C_{16}-H_{35}$	125.2741	125.9085	127.50
$O_{13}-C_{17}-C_{16}$	109.4125	109.9664	109.50

O_{13}-C_{17}-C_{18}	116.7275	116.1595	109.50
C_{16}-C_{17}-C_{18}	133.8257	133.8328	-
C_{17}-C_{18}-N_{19}	111.5908	109.4996	-
C_{17}-C_{18}-H_{36}	109.1477	109.4415	-
C_{17}-C_{18}-H_{37}	108.9221	109.4618	-
N_{19}-C_{18}-H_{36}	107.8622	109.4419	109.46
N_{19}-C_{18}-H_{37}	113.0426	109.4623	109.46
H_{36}-C_{18}-H_{37}	106.0654	109.5204	109.00
C_{18}-N_{19}-C_{20}	112.1605	120.0001	-
C_{18}-N_{19}-C_{21}	111.9604	119.9996	-
C_{20}-N_{19}-C_{21}	111.2485	120.0003	-
N_{19}-C_{20}-H_{38}	109.4921	109.4995	109.50
N_{19}-C_{20}-H_{39}	112.8509	109.442	109.50
N_{19}-C_{20}-H_{40}	109.9046	109.4619	109.50
H_{38}-C_{20}-H_{39}	108.1121	109.4421	109.44
H_{38}-C_{20}-H_{40}	108.1059	109.462	109.44
H_{39}-C_{20}-H_{40}	108.2477	109.5199	109.44
N_{19}-C_{21}-H_{41}	109.3509	109.5000	109.50
N_{19}-C_{21}-H_{42}	113.3977	109.4413	109.46
N_{19}-C_{21}-H_{43}	109.9561	109.4623	109.46
H_{41}-C_{21}-H_{42}	107.8124	109.5199	-
H_{41}-C_{21}-H_{43}	108.0158	132.0854	-
H_{42}-C_{21}-H_{43}	108.1503	109.5199	-
C_{16}-H_{35}-H_{40}	-	36.7166	-
C_{20}-H_{40}-H_{35}	-	151.0333	-
C_{12}-H_{45}-H_{43}	-	166.8127	-
C_{12}-H_{45}-Cl_{44}	-	-	-
O_{13}-H_{45}-Cl_{44}	170.7082	-	-
N_{19}-C_{21}-H_{41}	-	-	-
N_{19}-C_{21}-H_{42}	-	-	-
N_{19}-C_{21}-H_{43}	-	-	-
H_{41}-C_{21}-H_{42}	-	-	-
H_{41}-C_{21}-H_{43}	-	-	-
H_{42}-C_{21}-H_{43}	-	-	-
C_{16}-H_{35}-H_{40}	-	-	-
C_{20}-H_{40}-H_{35}	-	-	-
C_{12}-H_{45}-H_{43}	-	-	-
C_{12}-H_{45}-Cl_{44}	-	-	-
O_{13}-H_{45}-Cl_{44}	170.7082	166.8127	-

Fig.1 Atom Numbering Scheme of Ranitidine Hydrochloride
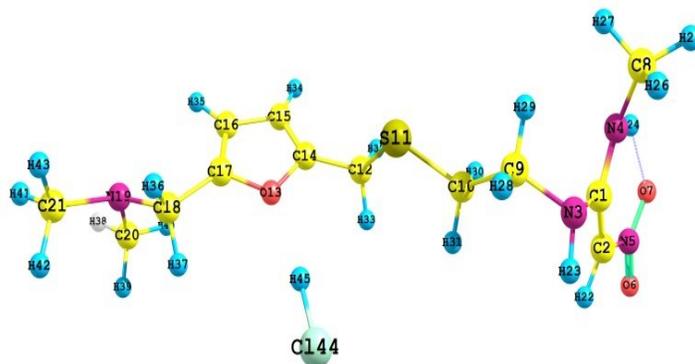
Table.2 Vibrational Band Assignments

| Experimental		Computed wave number				Vibrational assignment
FT-IR	FT-Raman	B3LYP/6-31G(d,p)	IR intensity	HF/6-31Gd,p)	IR intensity	
3570	-	3589	0.59	3454	7.21	N-H stretching
3254	-	3285	0.66	3284	6.88	C-H stretching
3191	3188	3140	0.34	3200	53.88	CH$_2$ asym stretching
-	3177	3110	0.84	3125	158.55	CH$_2$ sym stretching
3097	3097	3035	0.66	3114	88.75	CH$_2$/CH asym stretching
3014	3014	-	0.73	3019	33.28	CH$_2$/CH sym stretching
2982	-	2948	-	-	-	CH$_3$/CH$_2$/CH stretching
2973	2961	2939	2.32	-	-	CH$_3$/CH$_2$/CH stretching
2944	2943	2925	3.69	-	-	C-H stretching
-	2920	-	0.38	-	-	C-H stretching
-	2863	-	-	-	-	C-H stretching
2775	2813	2775	-	-	-	C-H stretching
1715	-	1695	1.19	1764	25.89	C=C stretching
1618	-	1600	0.36	1606	177.06	C=C stretching
1590	1600	1584	0.90	1584	219.17	C-C stretching
-	1587	1551	10.16	1569	40.85	NO$_2$ asym stretching
-	1554	1530	0.54	1533	26.98	NO$_2$ sym stretching
1498	1537	1499	42.57	1481	486.40	H-C-H sym stretching
1417	1483	1454	43.10	1447	37.40	C-N sym stretching
-	1450	1440	4.42	1442	15.37	C-C sym stretching
-	1437	1400	8.77	1391	57.03	C-C-H out of plane bending
1379	1408	1382	5.75	1380	128.03	NO$_2$ sym stretching
1304	1376	1308	4.02	1311	11.42	C-N sym stretching
1263	1306	1263	.069	1280	27.94	C-H in plane bending
-	1263	1256	10.69	1246	8.99	C-H out of plane bending
1221	1248	1231	1.52	1219	8.32	C-H out of plane bending
1194	1228	1184	2.67	1183	27.88	C-H in plane bending
1164	1186	1173	16.46	1159	37.11	C-H in plane bending
1133	1164	1144	39.26	1134	25.31	C-H deformation
1122	1135	1127	53.83	1116	9.14	C-C stretching
1074	1102	1092	7.10	1112	51.77	C-H in plane deformation
1045	1073	1065	2630	1074	6.31	C-C stretching
1021	1046	1034	186.68	1061	11.71	C-N stretching
1005	1023	1011	18.45	988	1.31	C-C-C bending
991	1007	996	7.91	973	3.98	C-O asym stretching
956	975	975	26.84	938	23.20	H-C-C bending
925	955	886	12.64	894	24.87	C-C stretching
879	-	878	3.05	873	17.61	C-C stretching
859	880	857	48.14	845	38.48	C-C stretching
799	863	789	12.78	812	2.06	C-H out of plane bending
761	802	762	9.27	743	56.30	C-C-C bending
698	756	726	28.25	703	0.86	H-C-C bending
660	720	680	3.70	680	5.30	C-C-C bending
641	661	638	72.22	-	-	C-H out of plane bending
523	522	495	10.37	517	0.32	C-H out of plane bending

Table.3 Experimental and Calculated Absorption Wavelength Oscillator Strength and Transition of Ranitidine Hydrochloride by DFT Method

Excitation	Singlet A	Energy (eV)	$\square_{max}$	Experimental	Oscillator strength	Transition
Excited State 1	0.63280	4.3154	287.03nm	325.05nm	0.0257	HOMO-4→LUMO
	0.23847					HOMO-LUMO
89 - 94						
93 – 94						
Excited State 2						
89-94	-0.18571	4.7782	259.48 nm	228.50nm	0.2545	HOMO-4→LUMO
91-94	0.20362					HOMO-2→LUMO
92-94	0.32139					HOMO-1→LUMO
93-94	0.50541					HOMO-LUMO
Excited State 3						
89-94	0.15122	4.8147	257.51nm	198.00nm	0.1341	HOMO-4→LUMO
90-94	-0.15881					HOMO-3→LUMO
91-94	0.22810					HOMO-2→LUMO
92-94	0.51900					HOMO-1→LUMO
93-94	-0.25897					HOMO-LUMO

**Fig.2** FTIR Spectrum of Ranitidine Hydrochloride
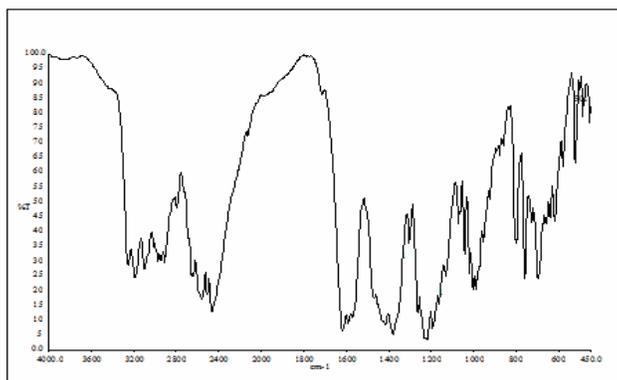
Fig.3 FT-Raman Spectrum of Ranitidine Hydrochloride
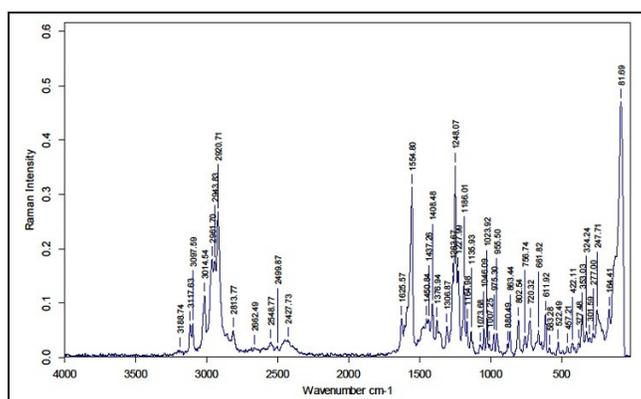
Table.4 Mullikan Atomic Charges of Ranitidine Hydrochloride at HF, B3LYP Methods with 6-31G(d,p) Basis Set

Atoms	B3LYP/631G(d,p)	HF/6-31G(d,p)
C_1	0.686027	0.530046
C_2	-0.157582	-0.029443
N_3	-0.705524	-0.553581
N_4	-0.723149	-0.542816
N_5	0.555955	0.049252
O_6	-0.487634	-0.429087
O_7	-0.566328	-0.486974
C_8	-0.153029	-0.189678
C_9	-0.049428	-0.082027
C_{10}	-0.390170	-0.340209
S_{11}	0.142775	0.098112
C_{12}	-0.407371	-0.415912
O_{13}	-0.643034	-0.502179
C_{14}	0.336944	0.335504
C_{15}	-0.217259	-0.148682
C_{16}	-0.212575	-0.141055
C_{17}	0.343299	0.324143
C_{18}	-0.033360	-0.094587
N_{19}	-0.592079	-0.407572
C_{20}	-0.137952	-0.167514
C_{21}	-0.131337	-0.158340
H_{22}	0.175319	0.108692
H_{23}	0.312305	0.272443
H_{24}	0.368397	0.308937
H_{25}	0.146574	0.133811
H_{26}	0.155953	0.142761
H_{27}	0.134204	0.129060
H_{28}	0.161340	0.141566
H_{29}	0.153683	0.134891
H_{30}	0.160462	0.148159
H_{31}	0.149868	0.142596
H_{32}	0.170493	0.156007
H_{33}	0.170275	0.154547
H_{34}	0.169233	0.104358
H_{35}	0.179252	0.111891
H_{36}	0.147701	0.126075
H_{37}	0.121820	0.097455
H_{38}	0.122978	0.111561
H_{39}	0.092269	0.085636
H_{40}	0.129332	0.116907
H_{41}	0.123291	0.110754
H_{42}	0.092285	0.086285
H_{43}	0.123485	0.110742
Cl_{44}	- 0.228775	-0.231230
H_{45}	0.211064	0.188694

Fig.4 UV-V is Spectrum of Ranitidine Hydrochloride
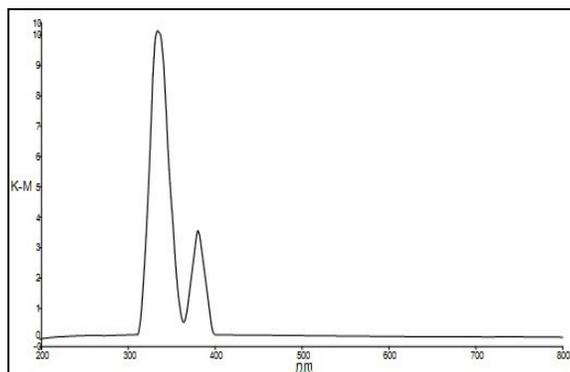
Table.5 The Electric Dipole Moment (µ), Polarizability (α), and First hHyperpolarizability (β) of Ranitidine Hydrochloride

	RHF-cc-PVDZ					B3LYP/cc-PVDZ				
	a.u	esu x(10^{-24})		a.u	esu x(10^{-33})		a.u	esu x(10^{-24})		a.u
μ_x	-2.868	-0.0425	β_{xxx}	465.239	4019.19	μ_x	-2.675	-0.3965	β_{xxx}	708.733
μ_y	-1.166	-0.1728	β_{xxy}	-36.336	-313.91	μ_y	-1.133	-0.1680	β_{xxy}	-62.594
μ_z	-1.199	-0.1776	β_{xyy}	163.487	-1412.38	μ_z	-1.092	-0.1619	β_{xyy}	105.878
μ	5.513	0.0817	β_{yyy}	-8.222	-71.03	μ	4.819	0.7142	β_{yyy}	53.165
α_{xx}	259.907	38.518	β_{xxz}	173.373	1497.76	α_{xx}	291.412	43.1872	β_{xxz}	153.119
α_{xy}	9.901	1.467	β_{xyz}	-43.877	-379.06	α_{xy}	8.018	1.1882	β_{xyz}	-24.525
α_{yy}	189.859	28.137	β_{yyz}	-93.575	-808.40	α_{yy}	197.777	29.3105	β_{yyz}	-37.133
α_{xz}	16.303	2.416	β_{xzz}	54.488	470.72	α_{xz}	20.083	2.9764	β_{xzz}	53.998
α_{yz}	7.041	1.043	β_{yzz}	-89.708	-774.98	α_{yz}	7.703	1.1416	β_{yzz}	-37.389
α_{zz}	163.183	24.183	β_{zzz}	-59.740	-516.09	α_{zz}	170.693	25.2967	β_{zzz}	-61.555
α_{tot}	204.316	30.279	β_{tot}(esu)	660.76	5708.30	α_{tot}	219.959	32.5979	β_{tot}(esu)	495.385
$\Delta\alpha$	516.510	76.546				$\Delta\alpha$	273.921	40.595		

Table.6 Significant Donor −Acceptor Interactions of Ranitidine Hydrochloride and their Second Order Perturbation Energies

Donor NBO(i)	Acceptor (NBO j)	E(2)[a] Kcal/mol	Ej - Ei[b] (a.u)	F(i,j)[c] (a.u)
	BD*(2) N5-O6	30.57	0.19	0.078
	BD*(2) N5-O6	8.78	0.34	0.059
	BD*(2) C16-C17	12.95	0.32	0.060
	BD*(2) C14-C15	14.63	0.31	0.063
	BD*(2) C1-C2	27.45	0.31	0.086
	BD*(2) C1-C2	58.34	0.28	0.116
	BD*(1) C2-N5	11.68	0.64	0.078
	BD*(1) N5-O7	22.12	0.73	0.115
	BD*(1) N5-O6	20.58	0.79	0.115
	BD*(1) N5-O6	136.79	0.16	0.141
	BD*(1) C14-C15	27.54	0.38	0.092
	BD*(2) C16-C17	28.13	0.39	0.094
	BD*(1) C21-H42	8.24	0.72	0.070
	BD*(2) C1-C2	26.37	0.10	0.063

a E(2) means energy of hyper conjugative interaction(stabilization energy)
b Energy difference between donor and acceptor i and j NBO orbitals
c F(i,j) is the fock matrix element between i and j NBO orbitals

Table.7 The Calculated Thermodynamic Parameters of Ranitidine Hydrochloride

| Parameters	HF	B3LYP
Total Energy (a.u)	1804.49553	-1811.803
Zero point Vibrational Energy (Lcal/mol)	247.08061	230
Rotational Temperature (K)	0.02364	0.02390
	0.00316	0.00325
	0.00308	0.00314
Rotational constants (GHz)	0.49258	0.49794
	0.06577	0.06782
	0.06412	0.06540
Entropy (cal/mol/-kelvin)		
Total	189.625	191.621
Translational	43.453	43.453
Rotational	36.291	36.230
Vibrational	109.881	111.938
Heat Capacity (cal/mol-kelvin)		
Total	86.878	92.025
Translational	2.981	2.981
Rotational	2.981	2.981
Vibrational	80.916	80.064
Energy (kal/mol)		
Total	263.023	246.640
Translational	0.889	0.889
Rotational	0.889	0.889
Vibrational	261.245	244.862

Table.8 Thermodynamic properties for the Ranitidine hydrochloride obtained by B3LYP/6-31G (d,p) DFT calculations

T(K)	S (J/molK)	Cp (J/molK)	ddH (KJ/Mol)
100	503.71	201.02	13.07
200	675.55	304.22	38.45
298	825.64	404.76	73.21
300	818.15	406.67	73.96
400	948.97	505.93	119.68
500	1071.37	591.75	174.69
600	1185.74	662.59	237.52
700	1292.40	720.93	306.79
800	1391.93	769.51	381.38
900	1484.99	810.42	460.44
1000	1572.23	845.15	543.26

Table.9 The Calculated 13C and 1H NMR chemical shifts of Ranitidine hydrochloride

Atom position	B3LYP		HF		Exp
	Absolute sheilding	Chemical shift	Absolute shielding	Chemical shift	
C_1	41.460	158.524	33.807	166.177	155.049
C_2	89.790	110.194	99.385	100.599	113.677
C_8	161.473	38.512	172.320	27.664	39.996
C_9	147.603	52.381	161.834	38.150	39.996
C_{10}	152.358	47.627	168.668	31.316	46.469
C_{12}	156.581	43.404	172.311	27.673	45.618
C_{14}	48.930	151.054	53.821	146.163	142.128
C_{15}	84.226	115.758	89.822	110.163	113.128
C_{16}	87.418	112.567	94.210	105.774	107.389
C_{17}	40.820	159.164	44.322	155.662	155.049
C_{18}	135.788	64.196	151.028	48.957	51.075
C_{20}	150.077	49.907	162.855	37.130	46.640
C_{21}	146.174	53.810	159.495	40.489	51.075
C_{44}	946.912	-746.927	981.334	-781.349	-
H_{22}	25.677	6.920	25.589	7.008	5.183
H_{23}	29.171	3.426	29.492	3.105	3.329
H_{24}	22.182	10.414	22.263	10.334	-
H_{25}	28.978	3.618	29.209	3.388	-
H_{26}	28.816	3.780	29.132	3.465	-
H_{27}	28.956	3.641	29.263	3.334	-
H_{28}	28.850	3.747	29.238	3.359	-
H_{29}	28.743	3.853	29.189	3.408	-
H_{30}	28.912	3.685	29.609	2.988	-
H_{31}	29.294	3.303	29.867	2.730	2.847
H_{32}	27.817	4.780	28.373	4.224	2.847
H_{33}	28.507	4.090	29.145	3.452	4.842
H_{34}	25.560	7.036	25.686	6.910	-
H_{35}	25.339	7.257	25.525	7.072	-
H_{36}	28.147	4.450	28.697	3.900	-
H_{37}	28.607	3.990	29.183	3.414	-
H_{38}	29.655	2.942	29.989	2.608	3.329
H_{39}	30.143	2.454	30.558	2.039	2.847
H_{40}	29.226	3.370	29.651	2.946	2.304
H_{41}	29.417	3.179	29.736	2.861	2.847
H_{42}	29.628	2.968	30.114	2.483	-2.304
H_{43}	29.380	3.217	29.751	2.845	-
H_{45}	27.239	5.358	23.297	6.300	-

Fig.5 HUMO and LUMO of Ranitidine Hydrochloride
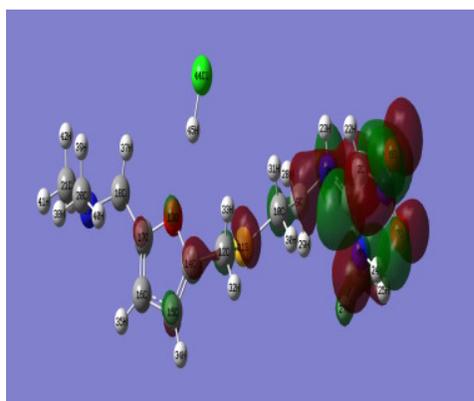
LUMO (First Excited State); ELUMO= -01240302
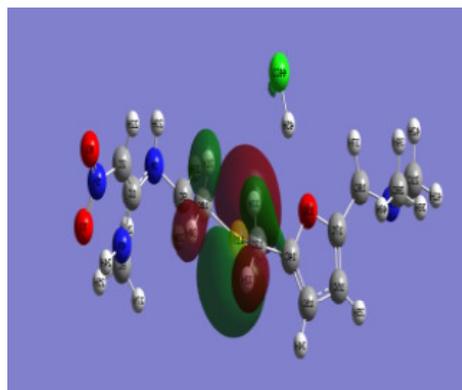
HOMO (ground State); EHOMO = -01417632

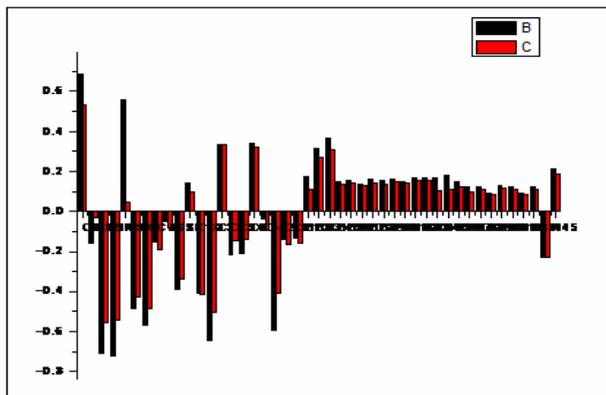**Fig.6** Mulliken Charge Distribution in Ranitidine Hydrochloride

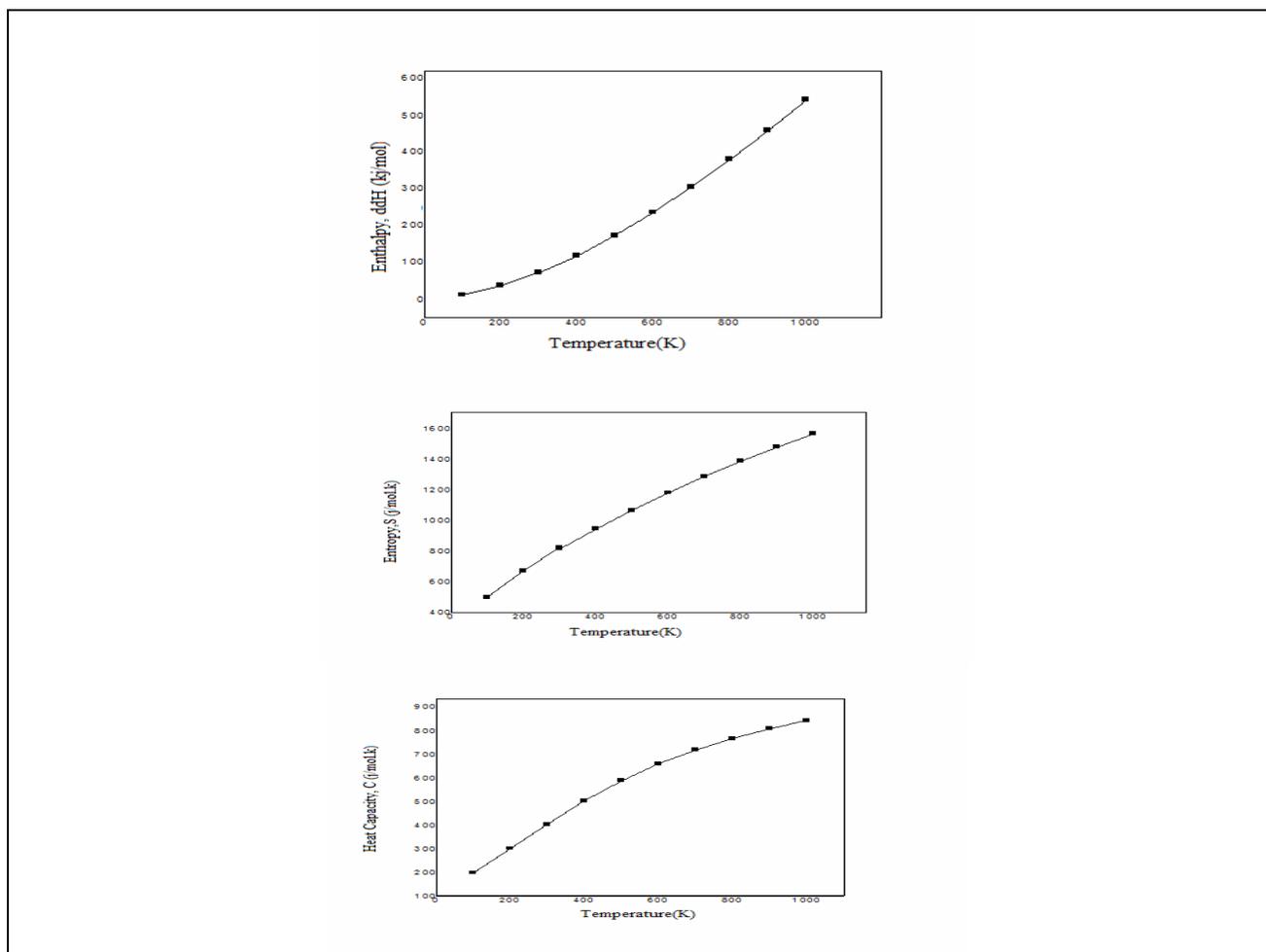**Fig.7** Thermodynamic properties of Ranitidine hydrochloride
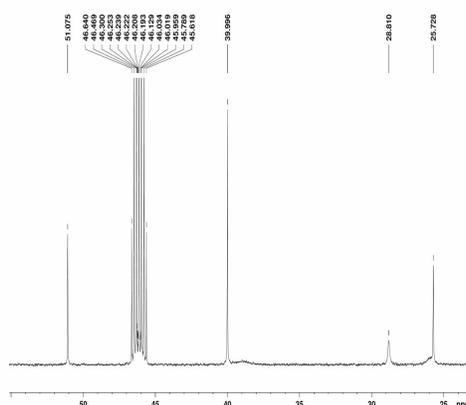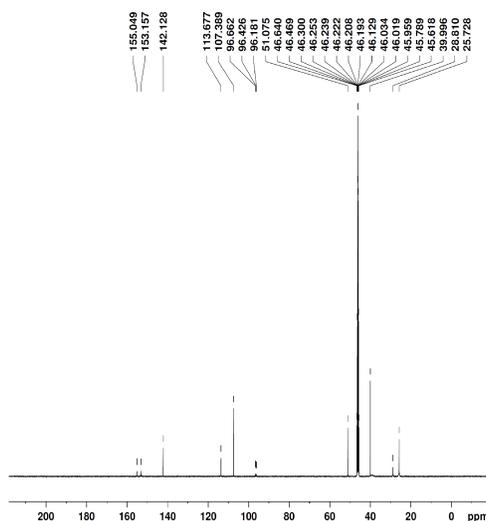
Fig.8(a) 13C NMR Spectrum of Ranitidine Hydrochloride

Fig.8(b) 1H NMR Spectrum of Ranitidine Hydrochloride

The carbon atom C_{17} appearing at very higher chemical shift value (159.164ppm) than the other carbon atoms and hence the shielding is very small (Table.9). The more electron rich atoms are C_8, C_9, C_{10}, C_{12}, C_{18}, C_{20}, C_{21}, and Cl_{44}. These are highly shielded atoms and hence appear at downfield (lower chemical shift). For visual comparison, the observed and calculated ^{13}C and ^{1}H NMR spectra of the titled compound were presented in Fig.8a and Fig.8b. Apart from that deviations are due to the theoretical calculations belong to isolated molecules in gaseous phase and experimental results belong to molecules in solid state.

Conclusion

The molecular geometry of Ranitidine hydrochloride was optimized by both DFT-B3LYP and HF methods using 6-31G(d,p) as basis set. A B3LYP method treat the electronic energy as a function of the electron density of all electrons simultaneously and thus includes electron correlation effect. The complete molecular

structural parameters and thermodynamic properties of the compound have been obtained. The vibrational frequencies are compared both experimentally as well as theoretically. The energies of Molecular orbital's, absorption wavelength (λ_{max}), oscillator strength excitation energies of the compound were determined and compared with the experimental values. The dipole moment, polarizability and the Hyperpolarizability of the compound studied have been calculated by B3LYP method with 6-31G(d,p) basis set. NBO population analysis is suitable for the estimation of atomic charges. The HOMO-LUMO energy explains the eventual charge transfer interactions taking place within the molecule. The FT-IR, FT-Raman and MNR (^{1}H and ^{13}C) spectral studies were carried out both DFT-B3LYP and HF methods using 6-31G(d,p). The UV spectrum was measured in methanol solvent. To sum up, this study not only shows the way to the identification of the molecules but also the researchers for the future studies in both the fundamental researchers and applications in technology and industry.

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