Journal of Theoretical and Applied Physics
a SpringerOpen Journal

RESEARCH Open Access

Molecular structure, vibrational spectra, UV–vis, NBO, and NMR analyses on nevirapine using *ab initio* DFT methods

Govindaswamy Ranganathan Ramkumaar[1*], Shanmugam Srinivasan[2], Thirumazhisai Jambulingam Bhoopathy[1], Sethu Gunasekaran[1], Julie Charles[3] and Jayaprakash Ramesh[4]

Abstract

Nevirapine is an anti-human immunodeficiency virus (HIV) agent that belongs to the class of the non-nucleoside inhibitors of the HIV-1 virus reverse transcriptase. Spectral characteristics of nevirapine have been probed into by methods of Fourier transform infrared (FTIR), FT-Raman, UV-visible, and quantum chemistry. The UV spectrum was measured in methanol. In order to gain some valuable insight into the recorded spectrum, the quantum mechanical calculations were performed for nevirapine using both ZINDO and time-dependent density functional theory at B3LYP/6-31G(d,p) level. The optimized molecular geometry, bond orders, natural bond order analysis, and harmonic vibrational wavenumbers of nevirapine were calculated by restricted Hartree-Fock and density functional B3LYP methods with the 6-31G(d,p) basis set using Gaussian 03 W program. The harmonic vibrational frequencies calculated have been compared with experimental FTIR and FT-Raman spectra. The restricted Hartree-Fock and density functional theory-based nuclear magnetic resonance (NMR) calculation procedure was also performed, and it was used for assigning the ^{13}C and ^{1}H NMR chemical shifts of nevirapine.

Keywords: FTIR; FT-Raman and UV spectra; *ab initio* DFT; Nevirapine; Chemical shift

Introduction

Nevirapine falls in the non-nucleoside reverse transcriptase inhibitor (NNRTI) class of antiretrovirals [1]. Both nucleoside and non-nucleoside RTIs inhibit the same target, the reverse transcriptase enzyme, an essential viral enzyme which transcribes viral RNA into DNA. Unlike nucleoside RTIs, which bind at the enzyme's active site, NNRTIs bind allosterically at a distinct site away from the active site termed the NNRTI pocket. Nevirapine is not effective against human immunodeficiency virus (HIV)-2, as the pocket of the HIV-2 reverse transcriptase has a different structure, which confers intrinsic resistance to the NNRTI class [2]. Resistance to nevirapine develops rapidly if viral replication is not completely suppressed [3]. The most common mutations observed after nevirapine treatment are Y181C and K103N, which are also observed with other NNRTIs [4]. Some clinical trials have demonstrated comparable HIV suppression with nevirapine-based regimens to that achieved with protease inhibitors [5,6]. Although concerns have been raised about nevirapine-based regimens in those starting therapy with high viral load or low CD4 count, some analyses suggest that nevirapine may be effective in these patients [7].

Literature survey reveals that there is no detailed study available on UV, natural bonding orbital (NBO), and nuclear magnetic resonance (NMR) and quantum mechanical work on nevirapine. This title of the compound with complete infrared (IR), Raman, and UV spectra includes quantum mechanical calculations with IR intensity for nevirapine. In the present communication, we reported detailed vibrational spectra of this molecule completely to identify the various normal modes with greater wavenumber accuracy. Band assignments were made by assuming C_1 point group symmetry. *Ab initio* Restricted Hartree-Fock (RHF) and density functional theory (DFT) calculations have been performed to support our wavenumber assignments.

* Correspondence: gr.ramkumaar@yahoo.com
[1]PG and Research Department of Physics, Pachaiyappa's College, Chennai, Tamil Nadu 600030, India
Full list of author information is available at the end of the article

Experimental

The compound nevirapine in pulverized form was purchased from reputed pharmaceutical company, Chennai, India with more than 98% purity and was used as such without further purification to record Fourier transform infrared (FTIR), FT-Raman, and UV spectra. The FTIR spectrum of the compound was recorded in the 4,000 to 400 cm^{-1} region in evacuation mode on Bruker IFS 66 V spectrophotometer (Ettlingen, Germany) using KBr pellet technique (solid phase) with 4.0 cm^{-1} resolution. The FT-Raman spectrum was recorded using 1,064-nm line of Nd:YAG laser as excitation wavelength in the 4,000 to 10 cm^{-1} region on Bruker IFS 66 V spectrometer equipped with FRA 106 Raman module which was used as an accessory. The UV-visible (UV–vis) spectral measurements were carried out using a Varian Cary 5E-UV-NIR spectrophotometer (Palo Alto, CA, USA). The spectral measurements were carried out at Sophisticated Instrumentation Analysis Facility, IIT Madras, India.

Computational details

All the theoretical computations were performed at restricted Hartree-Fock (RHF) and DFT-B3LYP levels on a Pentium IV/1.6-GHz personal computer using the Gaussian 03 W program package [8]. The geometries were first optimized at the RHF level of theory employing the 6-31G(d,p) basis set. DFT employed the B3LYP keyword, which invokes Becke's three-parameter hybrid method [9] using the correlation function of Lee et al. [10]. The optimized structural parameter was used in the vibrational frequency calculations at RHF and DFT levels to characterize all stationary points as minima. Then, vibrationally averaged nuclear positions of neviraprine were used for harmonic vibrational frequency calculations resulting in IR intensities and Raman depolarization ratios. Finally, the calculated normal mode vibrational frequencies provide thermodynamic properties by way of statistical mechanics. Besides, zero-point vibrational energy was also calculated in the present work. By combining the results of the Gauss view program [11] with symmetry considerations, vibrational frequency assignments were made with high degree of accuracy. Some ambiguity is necessary in defining internal coordination. However, we define coordinate form complete set and matches quite well with the motions observed using the Gauss view program. The ZINDO and time-dependent density functional theory (TD-DFT) methods at B3LYP/6-31G(d,p) level were used for the calculation of the UV–vis spectra. The IR and UV–vis spectra were calculated and visualized using the SWizard program [12]. The ^{13}C nuclear magnetic resonance (NMR) chemical shifts of the title compound were calculated using the keyword NMR in the RHF and DFT calculation at the B3LYP level with 6-31G(d,p) basis set.

Results and discussion

Molecular geometry

The calculated geometrical parameters (bond lengths and bond angles) were compared with available experimental data [13]. As the experimental values for nevirapine are known, the theoretically calculated values may supply an idea about the geometry of these molecules and also an idea of how the geometry of the molecule changes from the *ab initio* method of calculation and the DFT-B3LYP method of calculation. The optimized structural parameters of nevirapine from the RHF/6-31G(d,p) and B3LYP/6-31G(d,p) calculations and also the available experimental values are listed in Table 1, in accordance with the atom numbering scheme given in Figure 1. The B3LYP method leads to geometry parameters, which are close to available experimental data [13]. A statistical treatment of these data shows that, for the bond lengths, B3LYP/6-31G(d,p) is better than the RHF/6-31G(d,p) geometry. The correlation coefficients for bond lengths computed from the DFT and RHF methods with the experimental values were found to be 0.9958 and 0.9953, respectively. Similarly, the correlation coefficients for bond angles computed from the DFT and RHF methods with the experimental values were found to be 0.9222 and 0.9142, respectively. The agreement for bond angles is not as good as that for the bond distances. The slight variation with the experimental value is due to the fact that optimization is performed in an isolated condition, whereas the crystal environment affected the experimental X-ray structure.

Bond order analysis

The bond order of nevirapine is presented in Table 2. Bond order is related to bond strength, and the bonds with the higher bond order values have short bond length and vice versa. The analysis of bond order may predict that the weakest bonds may be cleaved preferentially, and they may possess a relatively low pi bond character. From Table 2, it is noted that the bond between N4 and C18 possesses relatively low pi bond character with low bond order values of 0.828 and 0.916 obtained from RHF and B3LYP methods, respectively. The C7-O16 bond order value is 1.968, which depicts the double bond character, while the C18-C20 and N4-C5 bond order values are approximately unity, which show the single bond character. It is also found that the optimized geometrical values are in support of the bond order analysis.

Electronic properties

The energies of four important molecular orbitals of nevirapine, the highest and second highest occupied molecular orbitals (MOs) (HOMO and HOMO – 1) and the lowest and the second lowest unoccupied MOs (LUMO

Table 1 Selected comparison between the calculated and experimental values of geometrical parameters of nevirapine

Parameters	Bond length (Å)			Parameters	Bond angle (deg)		
	RHF	DFT	[13]		RHF	DFT	[13]
N1-C2	1.4064	1.4082	1.4138	N1-C2-C8	119.9	119.2	118.2
N1-H21	0.9954	1.0123	1.0120	C3-C2-C8	118.8	116.8	116.7
C2-C3	1.3950	1.4098	1.4143	C2-C3-N11	122.6	122.4	122.2
C2-C8	1.3913	1.4062	1.4057	C3-N4-C18	114.9	114.2	114.7
C3-N4	1.4111	1.4216	1.3940	N4-C5-C6	120.4	121.9	122.3
N4-C5	1.0027	1.0073	1.0079	N4-C5-N15	118.0	116.8	115.7
N4-C18	1.0512	1.0621	1.0460	C6-C5-N15	121.6	121.3	122.0
C5-C6	1.4013	1.4169	1.3910	C5-C6-C12	118.1	118.0	118.6
C5-N15	1.3182	1.3410	1.3539	C2-C8-C17	121.4	121.1	119.5
C6-C7	1.4909	1.4920	1.4952	C9-C8-C17	121.0	121.2	119.5
C6-C12	1.3859	1.3980	1.4016	C8-C9-C10	119.0	118.2	117.8
C7-O16	1.9016	1.9263	1.9080	C8-C9-H22	120.6	120.3	121.1
C8-C9	1.3883	1.3977	1.3896	C10-C9-H22	120.4	120.5	121.1
C8-C17	1.5085	1.5082	1.4970	C9-C10-N11	123.2	123.2	123.6
C9-C10	1.3779	1.3896	1.3774	C3-N11-C10	118.8	118.7	118.5
C9-H22	1.0745	1.0855	1.1000	C6-C12-C13	120.0	120.4	119.7
C10-N11	1.3194	1.3359	1.3478	C6-C12-H24	118.6	117.8	120.1
C10-H23	1.0762	1.0879	1.1000	C13-C12-H24	121.5	121.8	120.1
C12-C13	1.3807	1.3890	1.3880	C12-C13-C14	117.1	117.2	117.8
C12-H24	1.0737	1.0846	1.1000	C12-C13-H25	121.9	121.7	121.1
C13-C14	1.3800	1.3926	1.3807	C14-C13-H25	121.1	121.1	121.1
C13-H25	1.0734	1.0843	1.1000	C13-C14-N15	123.8	123.7	123.8
C14-N15	1.3205	1.3349	1.3500	C13-C14-H26	120.5	120.6	118.1
C14-H26	1.0767	1.0886	1.1000	C5-N15-C14	119.5	119.4	118.1
C17-H27	1.0823	1.0920	1.1130	C8-C17-H27	110.6	110.7	109.5
C17-H28	1.0873	1.0983	1.1130	C8-C17-H28	111.4	111.9	109.4
C17-H29	1.0845	1.0953	1.1130	C8-C17-H29	111.2	111.5	109.5
C18-C19	1.4915	1.5023	1.5022	H27-C17-H29	108.4	108.2	109.5
C18-C20	1.0098	1.0042	1.0022	C20-C19-H31	119.0	119.4	120.0
C18-H30	1.0745	1.0845	1.0860				
C19-C20	1.5078	1.5187	1.5022				
C19-H31	1.0766	1.0864	1.0860				
C19-H32	1.0717	1.0820	1.0860				
C20-H33	1.0717	1.0818	1.0860				
C20-H34	1.0765	1.0862	1.0860				
CC	0.9953	0.9958		CC	0.914	0.9222	

and LUMO + 1) were calculated and are provided in Table 3. The lowest singlet → singlet spin-allowed excited states of nevirapine were taken into account for the ZINDO and TD-DFT at B3LYP/6-31G(d,p) level of calculation in order to investigate the properties of electronic absorption. The experimental and theoretical studies on the electronic absorption spectrum of nevirapine were made to explain each observed band, which was not done earlier. The experimental λ_{max} values are elicited from the UV-visible spectra recorded in methanol, and it should be declared which PCM model [14] has been used for simulating the solvent effect in the calculated UV spectra. The present experiment revealed three bands at 341.6, 360.2, and 452.5 nm

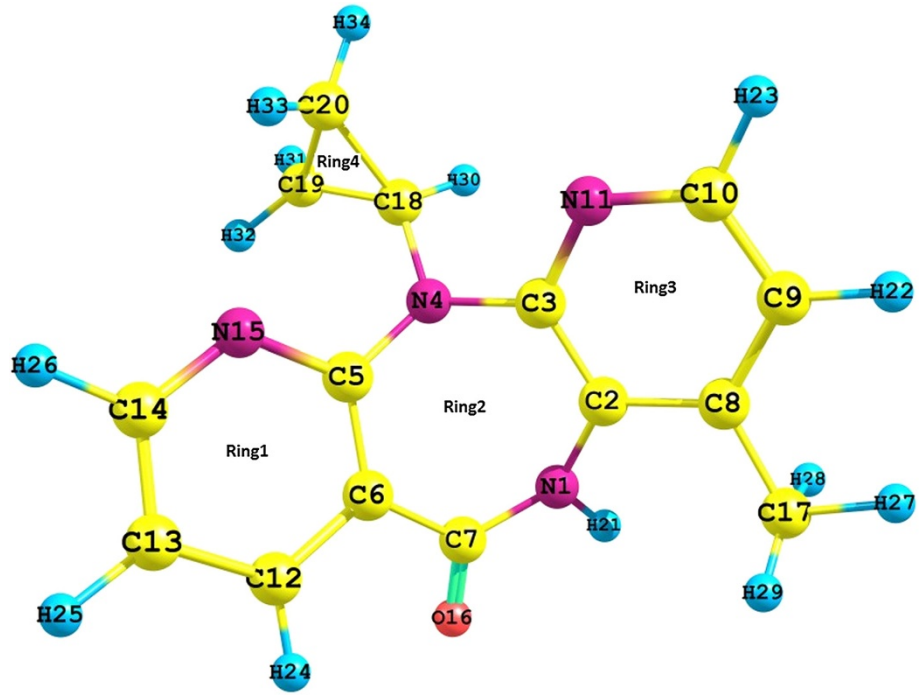

Figure 1 Atom numbering scheme of nevirapine.

in the UV region. Both the theoretical methods (ZINDO and TD-DFT) fairly estimate with the observed electronic band of nevirapine. The experimental electronic absorption bands were well predicted by both ZINDO and TD-DFT at B3LYP/6-31G(d,p) level of calculations. The calculated absorption wavelengths (λ_{max}), oscillator strength, excitation energies, and the experimental wavelengths are also given in Table 3. The energy gap between HOMO and LUMO is a critical parameter in determining molecular electrical transport properties [15]. In the electronic absorption spectrum of nevirapine, there are three absorption bands with a maximum of 452.5 nm. The strong absorption band at 452.5 nm is caused by the $n \rightarrow \pi^*$, and the other two calculated values of moderately intense bands are due to $\pi \rightarrow \pi^*$ transitions. The $\pi \rightarrow \pi^*$ transitions are expected to occur relatively at lower wavelength, due to the consequence of the extended aromaticity of the benzene ring. The HOMO and LUMO of nevirapine are represented in Figure 2.

Natural population analysis

The calculation of effective atomic charges plays a dominant role in the application of quantum mechanical calculations to molecular systems. Our interest here is in the comparison of different methods (RHF and DFT) to describe the electron distribution in nevirapine as broadly as possible and to assess the sensitivity of the calculated charges to change the choice of quantum chemical method. The calculated natural atomic charge values from the natural population analysis (NPA) and Mulliken population analysis (MPA) procedures using the RHF and DFT methods are listed in Table 4. According to Reed et al. [16], NPA scheme shows greater numerical stability and better describes the electron distribution in compounds of high ionic character. So, we also concluded that NPA from the NBO method is better than the MPA scheme. Table 4 compares the atomic charge site of nevirapine from both MPA and NPA methods. Moreover, we see that C18 has a positive value in MPA, whereas negative in NPA because the surrounding atoms, N4, C19 (negative), and H30 (positive), will not give a positive value for the C18 atom. This is one of the evidences that NPA is better than MPA. The NPA of nevirapine shows that the presence of four nitrogen atoms (N1 = −0.822 (RHF) and −0.741 (DFT), N4 = −0.554 (RHF) and −0.446 (DFT), N11 = −0.586 (RHF) and −0.510 (DFT), N15 = −0.565 (RHF) and −0.494 (DFT)) imposes large positive charges on the carbon atoms (C5 = 0.520 (RHF) and 0.427 (DFT), C7 = 0.871 (RHF) and 0.744 (DFT)). However, the nitrogen atoms N1 and N4 possess large negative charges, resulting in the positive charges on the carbon atoms C3, C5, and C7. Moreover, there is no difference in charge distribution observed on all hydrogen atoms except the H21 hydrogen atom (H21 = 0.453 in RHF and 0.444 in DFT).

Table 2 Bond orders of nevirapine

Bond order	RHF/6-31G(d,p)	B3LYP/6-31G(d,p)
N1-C2	1.463	1.493
N1-C7	0.915	0.924
N1-H21	0.869	0.877
C2-C3	1.331	1.278
C2-C8	1.446	1.410
C3-N4	1.325	1.362
C3-N11	1.297	1.248
N4-C5	0.944	1.001
N4-C18	0.828	0.916
C5-C6	1.380	1.347
C5-N15	1.315	1.273
C6-C7	1.315	1.264
C6-C12	1.445	1.435
C7-O16	1.968	2.016
C8-C9	1.409	1.415
C9-C10	1.435	1.422
C9-H22	0.953	0.933
C10-N11	1.363	1.381
C10-H23	0.966	0.944
C12-C13	1.420	1.407
C12-H24	0.952	0.938
C13-C14	1.427	1.428
C13-H25	0.955	0.938
C14-N15	1.360	1.385
C14-H26	0.964	0.941
C17-H27	0.976	0.957
C17-H28	0.957	0.942
C17-H29	0.962	0.941
C18-C19	1.450	1.461
C18-C20	0.967	0.980
C18-H30	0.908	0.869
C19-C20	1.429	1.455
C19-H31	0.968	0.951
C19-H32	0.958	0.942
C20-H33	0.934	0.899
C20-H34	0.965	0.940

The large positive charge on H21 is due to the large negative charge accumulated on the N1 atom.

Vibrational assignments

The experimental FTIR, FT-Raman, and calculated (RHF and DFT-B3LYP) vibrational spectra were shown in Figures 3, 4, 5 and 6. Since the calculated vibrational wavenumbers were known to be higher than the experimental ones, they were scaled down by the wavenumber linear scaling procedure of Yoshida et al. [17] using the following expression:

$$\nu_{\mathrm{obs}} = (1.0087 - 0.0000163\nu_{\mathrm{calc}})\nu_{\mathrm{calc}}$$

The above expression is used by Soni Mishra et al. [18], which really scaled the theoretical value to the observed values. Comparison of the frequencies calculated at RHF and DFT-B3LYP with experimental values (Table 5) reveals the overestimation of the calculated vibrational modes due to anharmonicity in real system which was neglected. Inclusion of electron correlation in DFT to a certain extent makes the frequency values smaller in comparison with the RHF frequency data. According to the theoretical calculations, nevirapine has a non-planar structure of C_1 point group symmetry. The molecule has 34 atoms and 96 normal modes of vibration active in both IR and Raman. The Chemcraft program was used to display the vibrational modes, and vibrational wavenumber assignments were made on the basis of combining the results of Chemcraft program with the symmetry and taking the atomic displacements into consideration based on the frequency calculation and also made in analogy with the structurally related molecules.

N-H vibrations

The Raman and infrared spectra of the nevirapine are presented in Figures 3 and 4. Table 5 lists the observed wavenumbers according to the main molecular groups of nevirapine. After scaling, the computed wavenumbers are in good agreement with the observed wavenumbers. The optimized and crystal geometries' agreement suggests that the crystal field is not intense enough to split the bands in the irreducible representation components predicted by the group theory. Furthermore, as it may be verified from Table 5, despite the changes in the intensity of the Raman and infrared bands, the corresponding energy differences are in general in the range of the experimental spectral resolution. In all the heterocyclic compounds, the N-H stretching vibrations occur in the 3,500 to 3,000 cm^{-1} region [19]. Figure 3 shows the high wavenumber region, where CH and NH stretching modes are expected to be observed. However, not all the observed bands are associated with fundamental vibrations, since some overtones and combinations of the low-energy modes originating in anharmonic effects are usually present in this region. Thus, the band placed around 3,300 cm^{-1} may be assigned to the worst overtone of the ν(C = O) band at 1,729 cm^{-1} in the calculated value. Some contribution of the bands around 1,589 cm^{-1} may be responsible for the structure observed in the broad band at 3,413 cm^{-1}, which is associated with the only ν(NH) mode expected in nevirapine. The broad

Table 3 Experimental and calculated absorption wavelength (λ), energies (*E*), oscillator strength (*f*), and frontier orbital energies of nevirapine

Method	λ (nm)	*E* (eV)	*f*	Assignment	E_{HOMO} (eV)	E_{LUMO} (eV)	E_{HOMO-1} (eV)	E_{LUMO+1} (eV)
Exp	341.6							
	360.2							
	452.5							
TD-DFT	349.4	3.5955	0.0301	$n \rightarrow \pi^*$	−5.0722	−1.4768	−5.8709	−0.8912
	355.4	4.3941	0.0628	$\pi \rightarrow \pi^{-*}$				
	465.7	4.9797	0.0014	$\pi \rightarrow \pi^*$				
ZINDO	343.9	7.5028	0.1160	$n \rightarrow \pi^*$	−7.7153	−0.2125	−8.3202	−0.04925
	345.1	8.1077	0.0143	$\pi \rightarrow \pi^{-*}$				
	439.6	8.2710	0.0190	$\pi \rightarrow \pi^*$				

appearance and the shift towards lower wavenumbers of the ν(NH) points out the involvement of this bond in the hydrogen bond pattern, in agreement with the reported structure. Hence, in the present investigation, the N-H stretching vibrations have been found at 3,413 cm^{-1} in IR, which are further supported by the RHF and DFT-B3LYP method.

C-H vibrations

The ν(CH) stretching bands are observed between 3,300 and 3,000 cm^{-1}. According to our DFT calculations, the bands above 3,000 cm^{-1} are associated with the corresponding ν(CH) of the cyclopropyl and pyridine moieties, which is supported by the comparison with the vibrational spectra of other cyclopropyl and pyridine molecules with similar substitutions [20,21]. The three low-energy ν(CH) bands correspond to the symmetric and antisymmetric stretching of the methyl group, as follows by comparing the vibrational spectra of nevirapine with the one of 4-methylpyridine [20,22]. Let us start considering the contribution of the cyclopropyl ring (R4), whose (CH_2) deformations are present in calculated values around 1,437 and 1,441 cm^{-1}. However, they are superimposed with the deformation vibrations of the CH_3 group and some stretching bands of the pyridine rings, which do not allow us to establish an unambiguous classification. The ring breathing and ring deformation fundamentals are found at 882 cm^{-1}. Finally, the deformations and torsions around the N4-C18 bond are observed, respectively, between 150 and 400 cm^{-1} and below 100 cm^{-1}, as it is verified in Table 5. Most of the normal modes associated with the pyridine rings (ring 1 and ring 3) may be best described in terms of Wilson's notation [23], since these vibrational modes are recognizable by showing characteristic group frequencies or systematic behaviors. The most important contributions to the vibrational spectra of these rings are the double bond stretching bands placed around 1,729 cm^{-1} with considerable intensity in both Raman and infrared spectra. Between 1,226 and 1,278 cm^{-1}, the vibrational bands are dominated by the CH deformations of both rings and the corresponding Kekule modes. Lowering the energy, other ring deformations, torsions, and out-of-plane deformations are mostly coupled with the vibrational modes of the central ring, as it is observed in Table 5 also. The heteroaromatic structure shows the presence of C-H stretching vibrations in the 3,100 to 3,000 cm^{-1} region which is the characteristic region for

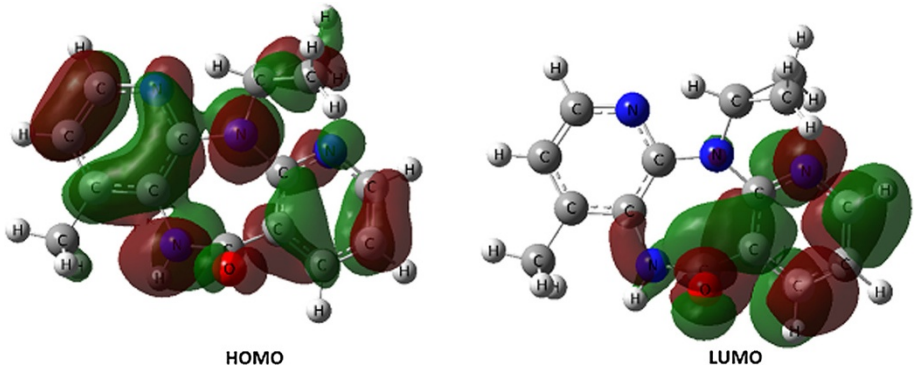

Figure 2 The HOMO and LUMO of nevirapine.

Table 4 Natural atomic charges of nevirapine

Numbered atom	MPA		NPA	
	RHF/6-31G (d,p)	B3LYP/6-31G (d,p)	RHF/6-31G (d,p)	B3LYP/6-31G (d,p)
N1	−0.837	−0.670	−0.822	−0.741
C2	0.244	0.289	0.097	0.107
C3	0.684	0.509	0.475	0.383
N4	−0.873	−0.602	−0.554	−0.446
C5	0.703	0.496	0.520	0.427
C6	−0.137	0.072	−0.243	−0.190
C7	0.660	0.408	0.871	0.744
C8	0.042	0.104	0.027	−0.012
C9	−0.236	−0.146	−0.329	−0.295
C10	0.161	0.099	0.098	0.028
N11	−0.695	−0.560	−0.586	−0.510
C12	−0.057	−0.078	−0.121	−0.175
C13	−0.236	−0.113	−0.338	−0.299
C14	0.183	0.119	0.110	0.044
N15	−0.671	−0.524	−0.565	−0.494
O16	−0.471	−0.372	−0.583	−0.484
C17	−0.364	−0.389	−0.671	−0.709
C18	0.107	0.085	−0.039	−0.071
C19	−0.281	−0.238	−0.512	−0.522
C20	−0.269	−0.203	−0.508	−0.515
H21	0.333	0.275	0.453	0.444
H22	0.157	0.085	0.242	0.244
H23	0.157	0.096	0.226	0.229
H24	0.179	0.107	0.248	0.251
H25	0.163	0.095	0.246	0.249
H26	0.158	0.100	0.224	0.227
H27	0.134	0.117	0.239	0.252
H28	0.157	0.140	0.251	0.259
H29	0.118	0.110	0.224	0.234
H30	0.216	0.146	0.298	0.292
H31	0.118	0.100	0.236	0.248
H32	0.129	0.101	0.247	0.252
H33	0.215	0.171	0.305	0.304
H34	0.108	0.070	0.235	0.244

the identification of such C-H stretching vibrations [24]. These vibrations are not found to be affected due to the nature and position of the substituents. Accordingly, in the present study, the band identified at 3,062 cm^{-1} in IR and 3,067 cm^{-1} in Raman for nevirapine has been designated to C-H stretching vibration. The observed C-H stretching modes show consistent agreement with the computed B3LYP and RHF results.

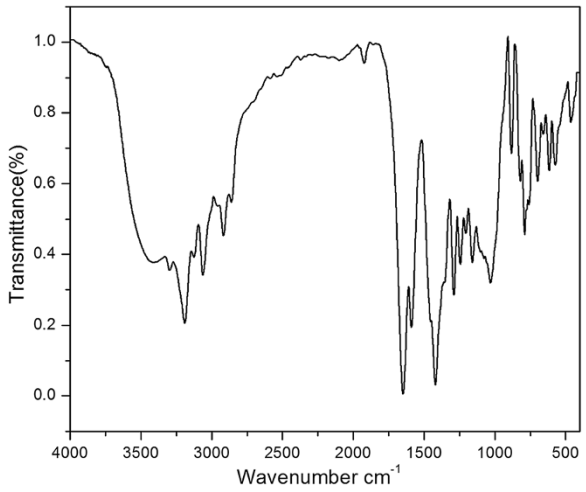

Figure 3 FTIR spectrum of nevirapine.

C-N vibrations

The C-N stretching frequency is a very difficult task since it falls in a complicated region of the vibrational spectrum, i.e., mixing of several bands are possible in this region [15] assigned C-N stretching absorption in the 1,386 to 1,266 cm^{-1} region for aromatic amines. The IR and Raman bands which appeared at 1,246 and 1,247 cm^{-1} have been assigned to C-N stretching vibration. The aromatic C-H vibrations calculated experimentally are in good agreement with that theoretically attained by DFT and RHF methods.

CH_2 scissoring, wagging, and rocking

As it was pointed out, the methyl group deformations are superimposed with the ones of the CH_2 groups and cannot be easily identified. A similar situation is observed with the ρ(CH3) rocking bands, which are

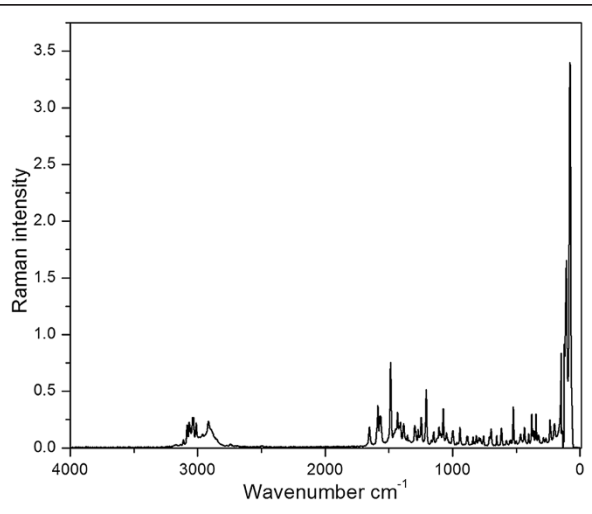

Figure 4 FT-Raman spectrum of nevirapine.

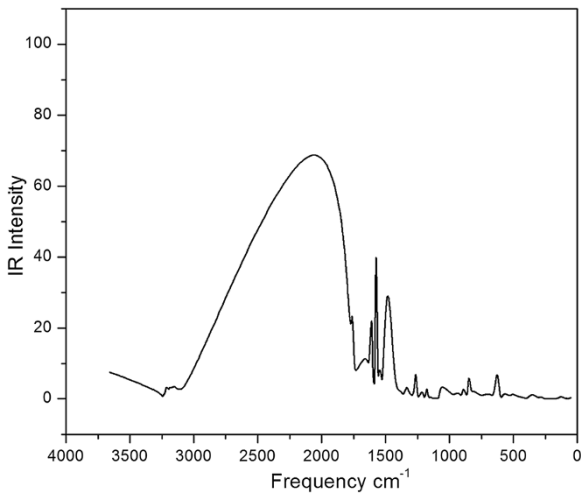

Figure 5 RHF-calculated IR spectrum of nevirapine.

predicted to exhibit a low intensity and/or to be coupled with other vibrational modes around 1,074 cm^{-1} in Raman spectra. In general, agreement can be traced between the scaled and experimental frequencies. However, some discrepancies are observed in the vibrational modes associated with the torsions (liberations) of the CH_3. For methyl-substituted benzene derivatives, deformation vibrations of methyl group normally appear in the 1,465 to 1,440 cm^{-1} and 1,390 to 1,370 cm^{-1} regions, respectively [25-27]. The bands at 1,462, 1,475, 1,478, and 1,487 cm^{-1} in DFT method and the bands at 1,585, 1,588, 1,602, and 1,606 cm^{-1} in RHF method are attributed to CH_3 scissoring vibrations. The wagging vibrations of the CH_3 group in nevirapine appear as independent vibrations. The torsional mode of CH_3 vibration is measured at 145 and 170 cm^{-1} in DFT method and 147 and 174 cm^{-1} in RHF method. As discussed previously, the conformation of the nevirapine molecule in the structure slightly differs from the conformation of the free molecule by a decrease in the butterfly angle due to a C7 = O16..HC19 hydrogen bond. This interaction, which is able to induce a deformation in the molecule, may also fix the methyl group by making its rotation around the threefold axis more difficult with the consequent hardening of the vibrational modes.

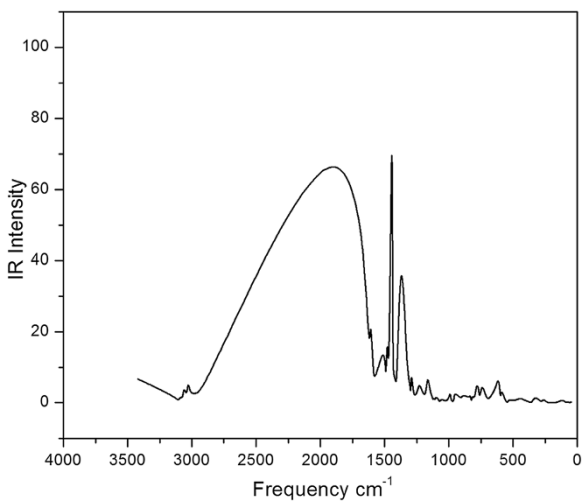

Figure 6 DFT-calculated IR spectrum of nevirapine.

The scissoring mode of the CH_2 group gives rise to a characteristic band near 1,465 cm^{-1} [28] in the IR and Raman spectra. In the present study, the band that appears at 1,420 cm^{-1} in IR and 1,432 cm^{-1} in Raman spectra is assigned to the scissoring mode of the CH_2 group. The calculated scaled values of 1,427 cm^{-1} in the DFT methods go in agreement with the experimental values of CH_2 scissoring vibrations of nevirapine. The CH_2 wagging, frequently combined with CH deformations, was assigned to the bands at 1,159 cm^{-1} in FTIR spectrum. The calculated scaled values of 1,150 cm^{-1} in DFT methods agree with the experimental values of CH_2 wagging vibrations of nevirapine. These modes exhibit almost no coupling with vibrations belonging to other moieties, but that is not the case for the CH_2 rocking, expected around 800 cm^{-1}, since the only band which is almost completely associated with a CH_2 rocking is the one at 819 cm^{-1} in FTIR spectrum.

^{13}C and ^{1}H NMR chemical shift assignment

The ^{13}C and ^{1}H NMR spectra theoretically with the aid of Gaussian and Facio software programs are shown in Figure 7a,b. Table 6 presents the predicted chemical shift values of nevirapine obtained by the RHF, DFT, and ChemDraw Ultra 8.0 software package and its assignment along with the shielding values. In general, highly shielded electrons appear downfield and vice versa. The predicted chemical shift values by the theoretical methods, both DFT and RHF, slightly deviates from the experimental values due to the theoretical calculations being carried out in the isolated gas phase. The carbon atom C7 appearing at much higher chemical shift value (181.5 ppm) is due to the double bond of oxygen atom. Similarly C3, C5, and C14 appearing at higher chemical shift values (150.1, 155.6, and 152.6 ppm) are due to nitrogen atoms N11, N4, and N15, respectively.

The carbon atoms C7, C3, C5, and C14 are highly electropositive and possess more positive charges than the other carbon atoms, and hence, the shielding is very small and appears upfield (see Table 6). In both the molecules, the DFT-calculated atomic charges revealed that the more electron-rich atoms are C17, C18, C19, and C20; they are highly shielded atoms and appear at downfield (lower chemical shift). The carbon atoms in the 2-pyridine are deshielded than the carbon atoms in the

Table 5 Observed and theoretical vibrational assignments of nevirapine

Experimental		Theoretical frequency						Vibrational assignments
FTIR	FT-Raman	B3LYP/6-31G(d,p)			RHF/6-31G(d,p)			
		Unscaled	Scaled	Intensity	Unscaled	Scaled	Intensity	
		44	44	0	50	50	0	τ(ring 1 + ring 2 + ring 4)
		58	58	0	66	67	0	τ(ring 2 + ring 3 + ring 4)
		74	75	0	80	81	0	τ(ring 1 + ring 2 + ring 3 + ring 4)
		88	89	0	95	96	0	τ(ring 1 + ring 2 + ring 3)
		113	114	1	124	125	1	τ(ring 1 + ring 2 + ring 3 + ring 4)
		144	145	0	146	147	0	$\tau(CH_3)$
		169	170	0	173	174	0	$\tau(CH_3)$
		184	185	0	189	190	0	τ(ring 1 + ring 2 + ring 3 + ring 4)
		221	222	0	241	242	0	τ(ring 1 + ring 2 + ring 3 + ring 4)
		240	241	0	258	259	0	δ(ring 1) + τ(ring 2 + ring 3 + ring 4)
		261	262	1	281	282	1	δ(ring 1) + τ(ring 2 + ring 3 + ring 4)
		279	280	0	304	305	0	δ(ring 1) + τ(ring 2 + ring 3 + ring 4)
		315	316	2	339	340	1	τ(ring 1 + ring 2 + ring 4)
		338	339	1	366	367	1	τ(ring 1 + ring 2 + ring 3 + ring 4)
		353	354	0	388	389	0	τ(ring 2 + ring 3 + ring 4)
	379	374	375	0	404	405	0	μ(ring 1 + ring 2 + ring 3 + ring 4)
	437	417	418	1	453	454	1	τ(ring 1 + ring 2 + ring 3)
464		442	443	1	480	480	1	τ(ring 1 + ring 2 + ring 3 + ring 4)
		466	467	1	507	507	1	μ(ring 1 + ring 2 + ring 3 + ring 4)
	523	486	486	1	525	525	1	μ(ring 1 + ring 2 + ring 3 + ring 4)
		536	536	1	573	573	2	δ(ring 1 + ring 2)
		538	538	0	588	587	0	δ(ring 1 + ring 2)
573		558	558	0	606	605	0	τ(ring 1 + ring 2 + ring 3 + ring4)
		593	592	4	626	625	9	τ(ring 1 + ring 2 + ring 3 + ring 4)
		596	595	0	646	645	3	τ(ring 1 + ring 2 + ring 3 + ring 4)
616	619	612	611	8	663	662	0	τ(ring 1 + ring 2 + ring 3 + ring 4)
659		633	632	5	681	679	1	δ(ring 1) + oop(NH) + δ(CO)
698	699	671	669	2	723	721	1	ν(ring 1 + ring 2 + ring 3 + ring 4)
		708	706	0	759	756	1	δ(ring 1 + ring 2 + ring 3 + ring 4)
		742	739	6	821	817	3	δ(ring 2)
		765	762	1	833	829	1	τ(ring 1 + ring 2 + ring 3)
		769	766	4	853	849	8	τ(ring 1 + ring 2 + ring 3)
789		788	785	5	861	856	2	τ(ring 1 + ring 2 + ring 3)
		801	798	1	871	866	0	oop(CO + NH) + τ(ring 2)
819		820	816	2	897	892	4	Ring 2(oop) + $\rho(CH_2)$
		828	824	0	908	902	1	ν(CH)
		837	833	2	929	923	1	ω(CH)
882		843	839	1	934	928	2	ω(CH)
		894	889	2	969	962	1	b(ring 1 + ring 2 + ring 3 + ring 4)
		909	903	1	984	977	1	b(ring 1 + ring 2 + ring 3 + ring 4)
		963	956	3	1,049	1,040	3	$\omega(C_2H_2)$
		966	959	0	1,081	1,071	3	$\omega(C_2H_2)$

Table 5 Observed and theoretical vibrational assignments of nevirapine *(Continued)*

		980	973	0	1,094	1,084	0	ν(CH)
		994	987	1	1,102	1,092	0	Ring 3(oop)
	999	995	988	3	1,110	1,100	0	Ring 2(ν(CH))
1,031		1,015	1,007	0	1,124	1,113	0	ρ(CH_2)
		1,060	1,051	1	1,148	1,137	0	ρ(CH_2)
		1,064	1,055	1	1,159	1,147	1	ω(CH_2)
	1,074	1,073	1,064	1	1,178	1,166	0	ρ(CH_3)
		1,084	1,074	0	1,190	1,177	4	ω(CH_2)
		1,105	1,095	2	1,193	1,180	2	δ(ring 1 + ring 2 + ring 3)
		1,119	1,108	1	1,210	1,197	0	δ(ring 1)
		1,129	1,118	2	1,212	1,199	1	ω(CH)
	1,149	1,132	1,121	0	1,228	1,214	3	ρ(CH_2)
1,159		1,162	1,150	4	1,256	1,241	0	ω(CH_2) + δ(CH)
		1,178	1,166	8	1,266	1,251	1	ρ(CH_2)
1,205	1,207	1,196	1,183	0	1,280	1,264	9	ρ(CH_2)
		1,240	1,226	6	1,288	1,272	3	Ring 2(δ(CH)) + δ(ring 1)
1,246	1,247	1,258	1,243	3	1,304	1,288	0	ν(ring 1) + ring 2(ν(CN))
		1,280	1,264	2	1,340	1,322	2	ν(ring 1) + ring 2(δ(CH))
1,290		1,294	1,278	3	1,351	1,333	4	δ(ring 1) + ring 2(ν(CN)) + ν(ring 3)
	1,297	1,308	1,291	9	1,383	1,364	0	Ring 2(ν(CN)) + ν(ring 1)
		1,313	1,296	2	1,398	1,378	3	ν(ring 3)
		1,320	1,303	6	1,435	1,414	2	Ring 3(δ(CH) + ν(CN))
		1,343	1,325	8	1,461	1,439	10	ν(ring 1 + ring 2 + ring 3 + ring 4)
	1,384	1,391	1,372	50	1,510	1,486	40	ν(ring 1+ ring 2 + ring 3 + ring 4)
		1,425	1,404	5	1,551	1,525	3	δ(CH_3)
1,420		1,436	1,415	6	1,556	1,530	6	Ring 2(δ(NH)) + ring 4(§(CH_2))
	1,432	1,449	1,427	8	1,578	1,551	10	§(CH_2)
		1,459	1,437	9	1,588	1,561	1	δ(CH_2)
		1,463	1,441	100	1,602	1,574	58	δ(CH_2)
		1,485	1,462	8	1,613	1,585	5	§(CH_3)
		1,499	1,475	14	1,617	1,588	4	§(CH_3)
		1,502	1,478	17	1,631	1,602	7	§(CH_3)
		1,511	1,487	11	1,635	1,606	30	§(CH_3)
		1,515	1,491	7	1,661	1,630	6	§(CH_2)
		1,526	1,501	17	1,673	1,642	14	ω(NH)
1,589	1,587	1,609	1,581	5	1,772	1,736	7	ν(ring 1 + ring 2 + ring 3)
		1,618	1,589	10	1,781	1,745	9	ν(ring 1 + ring 2 + ring 3)
		1,642	1,612	27	1,801	1,764	30	ν(ring 1 + ring 2 + ring 3)
1,649	1,652	1,645	1,615	7	1,808	1,770	9	ν(ring 1 + ring 2 + ring 3)
		1,764	1,729	97	1,944	1,899	100	ν(C = O)
2,917	2,916	3,030	2,907	4	3,183	3,046	3	as ν(CH_3)
		3,091	2,962	3	3,247	3,103	3	as ν(CH_3)
		3,139	3,006	3	3,284	3,137	3	as ν(CH_2)
		3,149	3,015	4	3,297	3,148	4	s ν(CH_2)
		3,152	3,017	4	3,304	3,155	3	s ν(CH_2)

Table 5 Observed and theoretical vibrational assignments of nevirapine *(Continued)*

		3,165	3,029	5	3,335	3,183	3	as ν(C_2H_2)
		3,169	3,033	4	3,345	3,192	3	as ν(C_2H_2)
		3,182	3,045	2	3,347	3,194	2	ν(CH)
3,062	3,067	3,201	3,062	5	3,373	3,217	4	ν(CH)
	3,081	3,212	3,072	1	3,381	3,224	1	ν(CH)
		3,226	3,084	2	3,397	3,238	1	ν(CH)
		3,253	3,109	0	3,407	3,247	0	as ν(CH_2)
3,125		3,263	3,118	2	3,417	3,256	2	as ν(CH_2)
3,413		3,602	3,422	7	3,868	3,658	8	ν(NH)

Types of vibrations: as ν, asymmetric stretching; s ν, symmetric stretching; δ, deformation; τ, torsion; ρ, rocking; b, breathing; §, scissoring; ω, wagging; μ, twisting; oop, out of plane.

cyclopropane so that the 2-pyridine carbon atoms appear at higher chemical shift values than the cyclopropane carbon atoms that were made by DFT method rather than RHF method. In this study, a good correlation between atomic charges and chemical shift was made. It is to be noted that ^{13}C NMR chemical shifts for nevirapine agree with the experimental values reported [29].

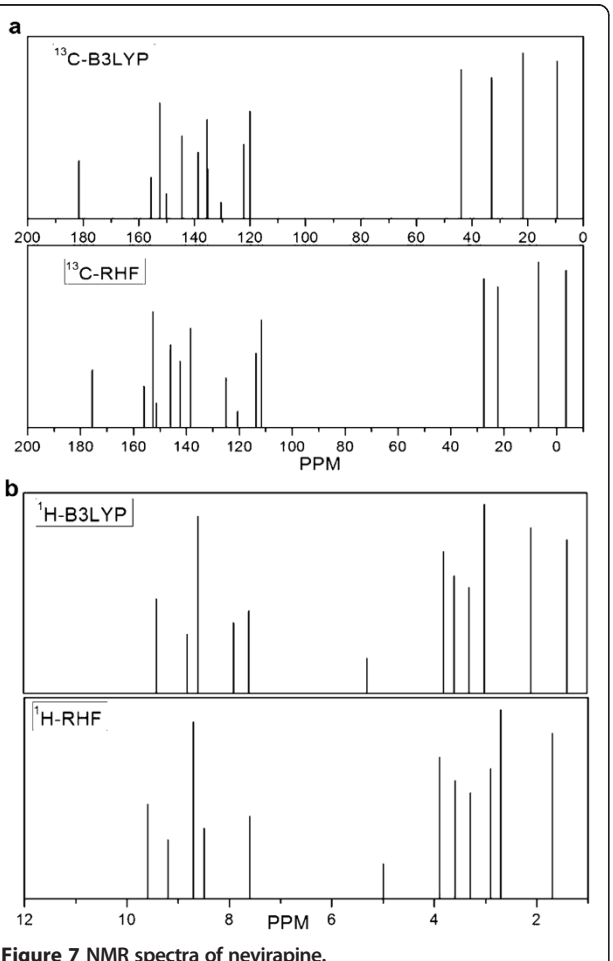

Figure 7 NMR spectra of nevirapine.

Table 6 gives the ^1H NMR predicted chemical shift values obtained by the DFT and RHF methods and ChemDraw Ultra 10.0 software program along with assignments. The predicted shielding values for each atom in the nevirapine molecule by B3LYP/6-31G(d,p) are given in Table 6. The predicted chemical shift values by the ChemDraw Ultra software program fairly agrees with the theoretical and experimental values.

The spectrum of nevirapine showed a singlet at 7.9 ppm for the proton of the 2-pyridine (H24) group, which is in good agreement with the experimental value. Triplet is predicted at 2.3, 2.3, and 2.3 ppm for the methyl group of hydrogen atoms (H25, H26, and H27). This higher absolute shielding for methyl group hydrogen is mainly due to the carbon atom (C17). The predicted value of singlet peak at higher chemical shift is at 9.6 ppm for 2-pyridine group of the indole proton (H26). Doublet is predicted at 0.3 ppm for the cyclopropane group of hydrogen atoms (H31 and H32). The hydrogen atoms of methylene group attached with C19 and C20 atoms show a multiplet at 0.3 to 0.9 ppm, which is due to the presence of C18 atom. In DFT and RHF methods, the hydrogen in cyclopropane group (H30, H31, H32, H33, and H34) is predicted. It contradicts to ChemDraw Ultra value and theoretical values, but other hydrogen fairly agrees with the experimental values.

Thermodynamic properties

The total energy of a molecule is the sum of translational, rotational, vibrational, and electronic energies, i.e., $E = Et + Er + Ev + Ee$. Thus, the molecular partition function is the product of the translational, rotational, vibrational, and electronic partition functions of the molecule [30]. The relations between partition functions and various thermodynamic functions were used to evaluate the latter due to translational, vibrational, and rotational degrees of freedom of molecular motions. The statistical thermochemical analysis of nevirapine is carried out considering the molecule to be at room

Table 6 The calculated ^{13}C and ^{1}H NMR chemical shifts of nevirapine

Atom position	B3LYP		RHF		ChemDraw Ultra	Expt[23]	Assignment
	Absolute shielding	Chemical shift	Absolute shielding	Chemical shift			
2	69.5	130.5	79.3	120.7	136.5	140.7	C2 in 2-pyridine
3	49.9	150.1	48.6	151.4	120.8	120.9	C3 in 2-pyridine
5	44.3	155.6	44.0	156.0	149.7	140.0	C5 in 2-pyridine
6	64.7	135.3	74.9	125.0	132.8	167.0	C6 in 2-pyridine
7	18.5	181.5	24.4	175.6	146.6	143.6	C7 in 1-amide
8	61.4	138.6	57.6	142.4	119.5	119.4	C8 in 2-pyridine
9	77.8	122.2	86.3	113.7	111.2	151.3	C9 in 2-pyridine
10	55.6	144.4	54.0	145.9	163.8	154.2	C10 in 2-pyridine
12	64.6	135.4	61.6	138.4	137.3	124.9	C11 in 2-pyridine
13	80.0	120.0	88.3	111.6	120.5	122.3	C13 in 2-pyridine
14	47.4	152.6	47.4	152.6	164.4	160.0	C14 in 2-pyridine
17	167.0	33.0	177.7	22.3	17.3	17.6	C17 in aliphatic
18	156.0	44.0	172.4	27.6	39.7	29.3	C18 in cyclopropane
19	190.6	9.4	203.5	5.5	5.5	8.5	C19 in cyclopropane
20	178.3	21.7	193.0	7.0	5.2	8.4	C20 in cyclopropane
21	27.3	5.3	27.6	5.0	4.5	8.0	H21 in secondary amide
22	25.0	7.6	25.0	7.6	6.9	7.0	H22 in 2-pyridine
23	23.8	8.8	23.4	9.2	7.9		H23 in 2-pyridine
24	24.7	7.9	24.1	8.5	7.6	8.0	H24 in 2-pyridine
25	25.0	7.6	25.0	7.6	6.7	7.2	H25 in 2-pyridine
26	23.2	9.4	23.0	9.6	8.0	8.5	H26 in 2-pyridine
27	29.2	3.3	29.3	3.3	2.1	2.3	H27 in methyl
28	29.0	3.6	29.0	3.6	2.1	2.3	H28 in methyl
29	29.6	3.0	29.7	2.9	2.1	2.3	H29 in methyl
30	22.0	3.8	22.1	3.9	8.3	3.6	H30 in cyclopropane
31	31.2	1.4	31.7	0.9	0.8	0.3	H31 in cyclopropane
32	30.5	2.1	30.9	1.7	1.4	0.3	H32 in cyclopropane
33	24.0	8.6	23.9	8.7	8.3	0.9	H33 in cyclopropane
34	29.6	3.0	29.9	2.7	2.1	0.9	H34 in cyclopropane

temperature of 298.15 K and 1 atm pressure. In the present analysis using B3LYP, the contributions due to internal rotations are not considered. The free energy of the molecule is calculated including zero-point vibrational energy. The values of zero-point energy of the molecule were 169.979 kcal/mol by DFT method and 182.400 kcal/mol by RHF method, respectively. Microscopically, the thermal energy is the kinetic energy of a system's constituent particles, which may be atoms, molecules, electrons, or particles in plasmas. Table 7 summarizes the calculated thermodynamic parameters, namely heat capacity, entropy, rotational constants, and dipole moments of nevirapine. Knowledge on permanent dipole moment of a molecule provides a wealth of information to determine the exact molecular conformation. The total dipole moment of nevirapine in DFT-B3LYP method is the lesser side of the dipole moment value of RHF method which was observed. In general, the LUMO becomes less bound, while the HOMO becomes more bound. From Table 7, it is concluded that the lowest energy gap was found at the DFT method. The variations in the entropy and zero-point vibrational energies seem to be insignificant.

Conclusion

Vibrational spectroscopy, restricted Hartree-Fock, and density functional calculations have been applied to the investigation of the NNRTI nevirapine. The theoretically calculated values of both bond lengths and bond angles of the structures of the minimum energy were then compared with available computed data. The data obtained during the course of this investigation show

Table 7 The calculated thermodynamic parameters of nevirapine

Parameters	RHF/6-31G(d,p)	B3LYP/6-31G(d,p)
Total energy (a.u.)	−868.55	−873.98
Zero-point energy (kcal/mol)	182.400	169.979
Rotational constants (GHz)	0.480	0.479
	0.351	0.342
	0.241	0.230
Rotational temperature (K)	0.02308	0.02301
	0.01685	0.01646
	0.01158	0.01107
Entropy (cal/mol K)		
Total	122.279	126.724
Translational	42.636	42.636
Rotational	33.333	33.404
Vibrational	46.31	50.684
Enthalpy (kcal/mol)		
Total	191.738	180.002
Translational	0.889	0.889
Rotational	0.889	0.889
Vibrational	189.961	178.225
Specific heat capacity (cal/mol K)		
Total	58.994	64.007
Translational	2.981	2.981
Rotational	2.981	2.981
Vibrational	53.033	58.045
Dipole moment (Debye)	2.8955	2.4883
HOMO (eV)	−8.36	−0.75
LUMO (eV)	2.65	−1.36
Energy gap (eV)	11.02	4.24

that a better agreement between the experimental and computed data is obtained using the DFT-B3LYP method with the basis set 6-31G(d,p). The bond order and atomic charges of the title molecule have been assessed by both RHF and DFT methods. The energies of important MOs, absorption wavelength (λ_{max}), oscillator strength, and excitation energies of the compound were also determined from TD-DFT and ZINDO methods and were compared with the experimental values. This study enlightens that the molecular geometry, vibrational wavenumbers, and ^{13}C NMR chemical shifts for nevirapine could be successfully elucidated by the RHF and DFT-B3LYP methods using the Gaussian program. The fitting between the calculated and measured vibrational wavenumbers was achieved by these methods, and the deviations between the calculated and experimental values are quite small after scaling the wavenumbers. Therefore, this study says beyond doubts that the theoretical calculation of the vibrational wavenumbers for nevirapine is quite useful for determining the vibrational assignment and for predicting new vibrational wavenumbers. The calculated normal mode vibrational wavenumbers provide thermodynamic properties by way of statistical mechanics.

Competing interests
The authors declare that they have no competing interests.

Authors' contributions
GRR, SS, and SG have developed the theoretical part and the simulation program; in addition, they had performed the calculations and also analyzed the data and respective results. TJB provided guidance at various stages of the study and reviewed the manuscript. JC participated in the editing of the manuscript. JR helped get the samples for our studies and also organized the manuscript in the journal format. All authors read and approved the final manuscript.

Authors' information
GRR is currently working as an assistant professor in the Department of Physics at the Pachaiyappa's College, Chennai, Tamil Nadu, India. He has completed Ph.D. from the University of Madras. His specialization includes quantum chemical computations using *ab initio* density functional theoretical methods for geometry optimization and vibrational spectral prediction of biomolecules for the analysis of experimental results.
SS is currently working as an assistant professor in the Department of Physics at the Presidency College, Chennai, Tamil Nadu, India. He is having more than 5 years of Ph.D. experience. His specialization includes vibrational spectral studies of natural product molecules with medicinal properties, and he has been involved in crystal growth and battery cell materials research. He is currently guiding ten Ph.D. students.
TJB is a head associate professor (Rtd.) in the Department of Physics at the Pachaiyappa's College, Chennai, Tamil Nadu, India. He is having more than 20 years of Ph.D. experience. He guided GRR, the first author of this manuscript, and he includes his experienced in ultrasonic measurements and theoretical work in vibrational spectral studies of antiviral drug molecules.
SG is a head associate professor (Rtd.) in the Department of Physics at the Pachaiyappa's College, Chennai, Tamil Nadu, India. He is currently acting as dean for Research & Development at St. Peter's University, Chennai, India and founding president of the Indian Spectrophysics Association. He has associated with this wonderful field of spectroscopy for the past 30 years. He has been guiding students since 1991 ever since the Department of Physics, Pachaiyappa's College has been upgraded as Research Department. He had so far guided 52 students for their Ph.D. degrees, and some more students are pursuing their research under his guidance. He has also guided more than 50 students for their M.Phil. degree. He had published more than 180 original research articles in reputed international and national journals having high impact factor.
JC is working as an assistant professor of Physics at the SSN College of Engineering, Kalavakkam, Tamil Nadu, India and has been involved in polymeric materials research.
JR is working as an assistant professor of Pharmaceutical Analysis at the JKK Munirajah Medical Research Foundation College of Pharmacy, Komarapalayam, Tamil Nadu, India and has been involved in pharmaceutical research work.

Acknowledgements
The authors thank the kind referees for their positive and invaluable suggestions, which improved this article greatly, and also to the editors for their valuable suggestions. The first author (GRR) sincerely acknowledges the language editor named Liezel A. Agor who greatly improved this article's quality. Finally, the first author (GRR) thanks the well-wishers from the Department of Physics, Pachaiyappa's College, Chennai and also the family who supported well by providing time to spend in finishing this article.

Author details
[1]PG and Research Department of Physics, Pachaiyappa's College, Chennai, Tamil Nadu 600030, India. [2]PG and Research Department of Physics, Presidency College, Chennai, Tamil Nadu 600005, India. [3]Department of

Physics, SSN College of Engineering, Kalavakkam, Kanchipuram District, Tamil Nadu 603110, India. [4]Department of Pharmaceutical Analysis, JKK Munirajah Medical Research Foundation College of Pharmacy, Komarapalayam, Namakkal (DT), Tamil Nadu 638183, India.

Received: 15 November 2012 Accepted: 2 September 2013
Published: 17 September 2013

References

1. Patel, SS, Benfield, P: New drug profile: nevirapine. Clinical. Immunotherapeutics **6**(4), 307 (1996)
2. Ren, J, Bird, LE, Chamberlain, PP, Stewart-Jones, GB, Stuart, DI, Stammers, DK: Structure of HIV-2 reverse transcriptase at 2.35-A resolution and the mechanism of resistance to non-nucleoside inhibitors. Proc Natl Acad Sci U S A **99**(22), 14410 (2002)
3. Montaner, JS, Reiss, P, Cooper, D, Vella, S, Harris, M, Conway, B, Wainberg, MA, Smith, D, Robinson, P, Hall, D, Myers, M, Lange, JM: A randomized, double-blind trial comparing combinations of nevirapine, didanosine, and zidovudine for HIV-infected patients: the INCAS Trial. Italy, The Netherlands, Canada and Australia Study. JAMA **279**(12), 930 (1998)
4. Conway, B, Wainberg, MA, Hall, D, Harris, M, Reiss, P, Cooper, D, Vella, S, Curry, R, Robinson, P, Lange, JM, Montaner, JS: Development of drug resistance in patients receiving combinations of zidovudine, didanosine and nevirapine. AIDS **15**(10), 1269 (2001)
5. Van Leeuwen, R, Katlama, C, Murphy, RL, Squires, K, Gatell, J, Horban, A, Clotet, B, Staszewski, S, van Eeden, A, Clumeck, N, Moroni, M, Pavia, AT, Schmidt, RE, Gonzalez-Lahoz, J, Montaner, J, Antunes, F, Gulick, R, Bánhegyi, D, van der Valk, M, Reiss, P, van Weert, L, van Leth, F, Johnson, VA, Sommadossi, JP, Lange, JM: A randomized trial to study first-line combination therapy with or without a protease inhibitor in HIV-1-infected patients. AIDS **17**(7), 987 (2003)
6. Podzamczer, D, Ferrer, E, Consiglio, E, Gatell, JM, Perez, P, Perez, JL, Luna, E, Gonzalez, A, Pedrol, E, Lozano, L, Ocana, I, Llibre, JM, Casiro, A, Aranda, M, Barrufet, P, Martinez-Lacasa, J, Miro, JM, Badia, X, Casado, A, Lupo, S, Cahn, P, Manos, M, Estela, J: A randomized clinical trial comparing nelfinavir or nevirapine associated to zidovudine/lamivudine in HIV-infected naive patients (the Combine Study). Antivir Ther **7**(2), 81 (2002)
7. Van Leth, F, Andrews, S, Grinsztejn, B, Wilkins, E, Lazanas, MK, Lange, JM, Montaner, J: The effect of baseline CD4 cell count and HIV-1 viral load on the efficacy and safety of nevirapine or efavirenz-based first-line HAART. AIDS **19**(5), 463 (2005)
8. Frisch, MJ, Trucks, GW, Schlegel, HB, Scuseria, GE, Robb, MA, Cheeseman, JR, Montgomery, JA, Jr Vreven, T, Kudin, KN, Burant, JC, Millam, JM, Iyengar, SS, Tomasi, J, Barone, V, Mennucci, B, Cossi, M, Scalmani, G, Rega, N, Petersson, GA, Nakatsuji, H, Hada, M, Ehara, M, Toyota, K, Fukuda, R, Hasegawa, J, Ishida, M, Nakajima, T, Honda, Y, Kitao, O, Nakai, H, et al.: Gaussian 03 Revision C.02. Gaussian Inc, Pittsburgh, PA (2003)
9. Becke, AD: Density-functional thermochemistry. III. The role of exact exchange. J Chem Phys **98**, 5648 (1993)
10. Lee, C, Yang, W, Parr, RG: Development of the Colle-Salvetti conelation energy formula into a functional of the electron density. Phys Rev B **37**, 785 (1988)
11. Frisch, A, Nielsen, AB, Holder, AJ: GAUSSVIEW User Manual. Gaussian Inc, Pittsburgh PA (2000)
12. Gorelsky, SI: SWizard program. http://www.sg-chem.net/. Accessed 4 February 2012
13. Sutton, LE: Tables of Interatomic Distances and Configuration in Molecules and Ions. Chemical Society, London (1965)
14. Sajan, D, Joseph, L, Vijayan, N, Karabacak, M: Natural bond orbital analysis, electronic structure, non-linear properties and vibrational spectral analysis of L-histidinium bromide monohydrate: a density functional theory. Spectrochimica Acta Part A **81**, 85 (2011)
15. Silverstein, RM, Bassler, GC, Morrill, TC: Spectrometric Identification of Organic Compounds, 5th edn. Wiley, New York (1981)
16. Reed, A, Weinstock, RB, Weinhold, F: Natural population analysis@f[a]@f[]. J Chem Phys **83**, 735 (1985)
17. Yoshida, H, Takeda, K, Okamura, J, Ehara, A, Matsuura, H: A new approach to vibrational analysis of large molecules by density functional theory: wavenumber-linear scaling method. J Phys Chem A **106**, 3580 (2002)
18. Mishra, S, Chaturvedi, D, Srivastava, A, Tandon, P, Ayala, AP, Siesler, HW: Quantum chemical and experimental studies on the structure and vibrational spectra of efavirenz. Vibrational Spectrosc **53**, 112 (2010)
19. Krishnakumar, V, Ramasamy, R: Density functional and experimental studies on the FT-IR and FT-Raman spectra and structure of 2,6-diamino purine and 6-methoxy purine. Spectrochim. Acta Part A **69**, 8 (2008)
20. Arenas, JF, López, T, Otero, JC, Marcos, JI: Vibrational spectra of methylpyridines. J Mol Struct **476**, 139 (1999)
21. Gounev, TK, Hur, SW, Dakkouri, M, GrunvogelHurst, A, Durig, JR: Infrared and Raman spectra, conformational stability, ab initio calculations, and vibrational assignments for cyclopropyldifluorosilane. Struct Chem **9**, 95 (1998)
22. Lopez, T, Woolley, MS, Otero, JC, Marcos, JI: Vibrational spectrum of 3-methyl and 4-methylpyridine. J Mol Struct **470**, 241 (1998)
23. Varsanyi, G: Vibrational Spectra of Benzene Derivatives. Academic Press, New York (1969)
24. Zwarich, R, Smolarek, J, Goodman, L: Assignment of out-of-plane vibrational modes in benzaldehyde. J Mol Spectrosc **38**(2), 336 (1971)
25. Reddy, BV, Rao, GR: Transferable valence force-fields for substituted benzenes.1. Monohalogenated anisoles. Vib Spectrosc **6**, 231 (1994)
26. Arenas, JF, Tocon, IL, Otero, JC, Marcos, JI: Vibrational spectrum of 2-methylpyridine. J Mol Struct **410**, 443 (1997)
27. Long, DA, George, WO: Spectroscopic and thermodynamic studies of pyridine compounds—V: Vibrational spectra and assignments for γ-Picoline and γ-picoline-d_7. Spectrochimica Acta **19**, 1777 (1963)
28. Vijayakumar, T, Hubert Joe, I, Reghunadhan Nair, CP, Jayakumar, VS: Vibrational spectral studies on charge transfer and ionic hydrogen-bonding interactions of nonlinear optical material L-arginine nitrate hemihydrate. J Raman Spectrosc **40**, 18 (2009)
29. Vailikhit, V, Bunsawansong, P, Leeprasert, T, Techasakul, S, Hannongbua, S: Conformational analysis of nevirapine in solutions, based on NMR spectroscopy and quantum chemical calculations. J Theo Comp Chem **5**(4), 913 (2006)
30. Srinivasan, S, Gunasekaran, S, Ponnambalam, U, Savarianandam, A, Gnanaprakasam, S, Natarajan, S: Spectroscopic and thermodynamic analysis of enolic form of 3-oxo-l-gulofuranolactone. Indian J Pure Appl Phys **43**, 459 (2005)

doi:10.1186/2251-7235-7-51
Cite this article as: Ramkumaar *et al.*: **Molecular structure, vibrational spectra, UV–vis, NBO, and NMR analyses on nevirapine using *ab initio* DFT methods.** *Journal of Theoretical and Applied Physics* 2013 **7**:51.