

Vibrational Properties of an Anti-HIV Drug Abacavir: Experiment and Theory

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ABSTRACT

Abacavir (ABC) {(1S,4R)-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl] cyclopent-2-en-1-yl} methanol, is an antiretroviral medication which is used to prevent and treat HIV/AIDS. It belongs from nucleoside analog reverse transcriptase inhibitor (NRTI) a sub class of RTIs, which interrupt the virus to make copy of it. In this paper we reported the results of a systematic experimental IR and Raman study of Avacavir. Additionally the equilibrium geometry, harmonic vibrational frequency Raman and IR intensities were calculated using density function theory. Finally complete vibrational assignment of Abacavir is given for the observed Raman and Infrared spectra. The experimental and theoretical results are found to be in excellent agreement with each other. We believe that the results obtained herein will prove to be an excellent starting point for studying the detailed potential surface of the molecule which is needed to understand the drug receptor interactions.

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Introduction

Acquired immunodeficiency syndrome AIDS, is a disease in which body's immune system breaks down and is unable to fight off infection caused by human immune deficiency virus (HIV). HIV infects the human cells and uses the energy and nutrients provided by those cells to grow and reproduce. The highly active anti Retroviral therapy (HAART) (1) has largely reduced the morbidity and the mortality of HIV infected patients, but a serious metabolic syndrome combining insulin resistance, dyslipidemia, central adiposity and peripheral lipoatrophy has arisen in treated individuals. This highly active anti retroviral therapy includes protease inhibitors (PIs) and nucleoside reverse transcriptase inhibitors (NRTIs). RT is a multifunctional enzyme that catalyses RNA dependent DNA and DNA dependent DNA polymerases. These functions are required in the reproduction or replication of HIV, making RT central to the virus life cycle, thus providing a primary target for anti HIV drugs which are widely used in the treatment of AIDS(2-3).

Abacavir {(1S,4R)-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]cyclopent-2-en-1-yl}methanol is a synthetic nucleoside analog that is being increasingly used in the treatment of HIV infection (4-5). Abacavir after oral administration rapidly gets absorbed reducing the amount of HIV in blood which results in an increase in the number of CD4 cells or T-cells in the blood. Abacavir has activity in vitro against both HIV-1 and HIV-2 (6-7) cross resistance within the NRTI class of drugs Abacavir has important clinical consequence for the patient who are highly treatment experienced or for those patient in whom primary HIV infection is associated with the transmission of a resistant virus (8).

The application of Abacavir in health care requires its full characterization.

The survey of scientific literature reveals that to best of our knowledge neither the complete IR, Raman spectra nor the quantum chemical calculations for the molecular structure of Abacavir have been reported so far. In the present paper we report the experimental and theoretical IR and Raman spectra of Abacavir. It is important to note that a complete vibrational assignment of Abacavir is given in this study.

1. Experimental details

Abacavir is taken from Sigma Aldrich chemical company (US). Purity of the sample was greater than 99%. The sample was prepared from mixture of KBr in the ratio 99:1. Infrared spectra were recorded on a Shimadzu 8400 S-FT-IR spectrometer with a spectral resolution of 4 cm^{-1} in the region $400\text{-}4000\text{ cm}^{-1}$ at 300k. The FT-Raman spectra were recorded on a RENISHAW INVIA Raman Microscope attach with He-Ne laser of wavelength 633nm in the region $400\text{-}4000\text{ cm}^{-1}$ using 10mw power. The sample holder was consists of hemispherical bore of an aluminum.

2. Computational Model

A complete information about the structural characteristics and vibrational mode of Abacavir molecule is obtained by DFT (9) using Gaussian 03 (10). We apply DFT method with Becke's three parameter exchange function combined with gradient corrected correlated function (11-19) and split valance polarized 6-31 G basis set (20,21). Note that a fragment of Abacavir [Fig.1] was considered for calculations.

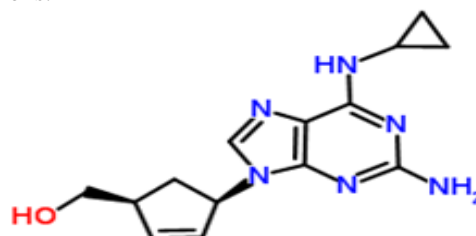


Fig 1. Abacavir Molecule.

In order to test the reliability of our modeling techniques we compare bond length and bond angle with the experimental values. Comparisons of experimental and theoretical values of bond length and bond angles are given in table 1 and table 2 respectively which were obtained from equilibrium configuration shown in fig2. The calculated B3LYP results are also compared with B3PW91 results showing an excellent agreement.

3. Result and Discussion

3.1 Structural Properties

We find that the calculated bond lengths and bond angles are slightly larger than the experimental values; this is because the calculations consider the isolated molecules in the gaseous state whereas the experimental results were obtained using crystalline Abacavir.

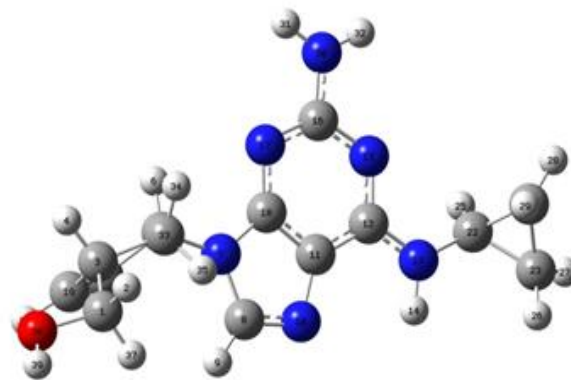


Fig 2. Optimized Geometry of Abacavir by DFT/ B3LYP 6-31G.

Table 1. Calculated and Experimental Bond Length.

Bond Length	This work (B3LYP/6-31G)	Experiment*
(C1H2) _{R1}	1.10	1.09
(C1H37) _{R1}	1.10	1.09
(C1O38) _{R1}	1.45	1.44
(O38H39) _{R1}	0.97	0.96
(C1C3) _{R1}	1.52	1.51
(C3C19) _{R1}	1.51	1.50
(C19H20) _{R1}	1.08	1.06
(C3H4) _{R1}	1.10	1.08
(C3C33) _{R1}	1.55	1.52
(C33H34) _{R1}	1.09	1.10
(C33H35) _{R1}	1.09	1.05
(C33C5) _{R1}	1.56	1.52
(C5C21) _{R1}	1.51	1.51
(C24H36) _{R1}	1.08	1.06
(C21C19) _{R1}	1.33	1.33
(C19H20) _{R1}	1.08	1.08
(C5N7) _{R1}	1.46	1.45
(N7C8) _{R2}	1.39	1.39
(C8H9) _{R2}	1.07	1.06
(C8N10) _{R2}	1.32	1.32
(N10C11) _{R2}	1.39	1.39
(C11C18) _{R3}	1.40	1.40
(C18N7) _{R3}	1.38	1.38
(C18N17) _{R3}	1.34	1.34
(N17C16) _{R3}	1.35	1.34
(C16N30) _{R3}	1.36	1.36
(N30H31) _{R3}	1.00	1.00
(N30H32) _{R3}	1.00	1.00
(C16N15) _{R3}	1.36	1.36
(N15C12) _{R3}	1.35	1.35
(C11C12) _{R3}	1.41	1.41
(C12N13) _{R3}	1.36	1.35
(N13H14) _{R3}	1.01	1.01
(N13H22) _{R4}	1.43	1.43
(C22H25) _{R4}	1.08	1.08
(C22C24) _{R4}	1.51	1.51
(C24H29) _{R4}	1.08	1.08
(C24H28) _{R4}	1.08	1.08
(C24C23) _{R4}	1.52	1.51
(C23H26) _{R4}	1.08	1.08
(C23H27) _{R4}	1.08	1.08

Table 2. Calculated and Experimental Bond Angles.

Bond Angle	B3LYP/6-31G	Experimental*
(H2C1H37) _{R1}	108.23	108.15
(H39O38C1) _{R1}	110.66	110.62
(H3C1O38) _{R1}	110.70	110.69
(C1C3H4) _{R1}	106.70	106.71
(C1C3C33) _{R1}	113.11	113.10
(C37C1C3) _{R1}	109.74	109.73
(C3C19H20) _{R1}	121.26	121.31
(C3C33H35) _{R1}	110.07	110.00
(C3C33H34) _{R1}	112.94	112.89
(H35C33C5) _{R1}	108.43	108.29
(H20C19C21) _{R1}	126.16	126.15
(C3C19C21) _{R1}	112.53	112.44
(C19C21H36) _{R1}	126.32	126.31
(C21C5C33) _{R1}	103.35	103.32
(C21C5H6) _{R1}	111.36	111.30
(H6C5N7) _{R1}	104.45	104.44
(C5N7C8) _{R1}	128.15	128.09
(H9C8N7) _{R2}	121.68	121.62
(N7C8N10) _{R2}	112.79	112.79
(C8N7C18) _{R2}	106.28	106.18
(N7C18C11) _{R2}	105.61	105.46
(C18C11N10) _{R2}	110.80	110.80
(C11N10C8) _{R2}	104.51	104.46
(N10C11C12) _{R3}	132.50	132.46
(C11C18N17) _{R3}	126.29	126.26
(C18N17C16) _{R3}	112.15	112.07
(N17C16N15) _{R3}	127.16	127.16
(C16N15C12) _{R3}	118.71	118.70
(N15C12C11) _{R3}	118.97	118.95
(N17C16N30) _{R3}	117.07	117.04
(N15C12N13) _{R3}	119.82	119.75
(C12N13H14) _{R3}	116.47	116.47
(C12N13C22) _{R4}	123.91	123.84
(N13N22H25) _{R4}	114.36	114.34
(H14N13C22) _{R4}	119.36	119.36
(H25C22C24) _{R4}	116.49	116.48
(C22C24H28) _{R4}	117.88	117.84
(C24C23H26) _{R4}	117.57	117.50
(C22C24H29) _{R4}	117.03	116.93
(H28C24C23) _{R4}	119.02	119.02
(C24C23H27) _{R4}	119.22	119.21
(C22C24C23) _{R4}	59.80	59.78
(C24C22C23) _{R4}	60.19	60.12
(C22C23C24) _{R4}	60.00	60.01

Reference 22

The calculated binding energy of molecule is

$$\text{B.E.} = (\text{T.E.})_{\text{molecule}} - [n_1 (\text{T.E.})_{\text{H}} + n_2 (\text{T.E.})_{\text{N}} + n_3 (\text{T.E.})_{\text{O}} + n_4 (\text{T.E.})_{\text{C}}] \quad \dots\dots\dots(1)$$

where n_1, n_2, n_3, n_4 are the numbers of hydrogen, nitrogen, oxygen and carbon atoms respectively. The calculated value of binding energy is -8.2 eV. B.E. per atom = B.E. / Number of atom, i.e., - 0.21 eV. Furthermore, the calculated dipole moment and HOMO-LUMO gap is 1.69 Debye and -5.0 eV respectively.

3.1. Vibrational analysis

The total number of atoms in Abacavir molecule is 39 giving total 111 (3N-6) normal modes. Since the molecule belongs to C1 point group symmetry, all the normal modes of vibration of the molecule are IR and Raman active. Note that DFT calculation gives the Raman scattering amplitude which cannot be taken directly as the Raman intensity. The Raman scattering cross-section, which are proportional to Raman intensity may be calculated from the Raman scattering amplitude and predicted wave number for each normal mode using the relationship (24, 25).

$$\frac{\partial \sigma_j}{\partial \Omega} = \left(\frac{2^4 \pi^4}{45} \right) \left(\frac{(v_0 - v_j)}{1 - \exp \left[\frac{-hcv_j}{kT} \right]} \right) \left(\frac{h}{8\pi^2 cv_j} \right) S_j \quad \dots\dots\dots(2)$$

where S_j and v_j are the scattering activities and the predicted wave numbers respectively of the j^{th} normal mode, v_0 is the wave number of the Raman excitation line and $h, c,$ and k are universal constants.

The Raman intensities obtained from this relation are in excellent agreement with the experimentally observed values which are shown in Fig 3. The calculated IR Raman intensities were used to predict the vibrational mode with Lorentzian line shape (full width at half maximum= 8 cm^{-1}) to produce simulated spectra. The vibration assignments for the different mode have been made on the basis of relative intensities, energies and line shape. All vibrational bands have been assigned satisfactorily after proper analysis. All the assigned wave numbers of different modes are shown in table.4. The R1, R2, R3 and R4 referred in the table below are R1 (Five membered ring) R2 (five membered ring with nitrogen) R3 (six membered ring) and R4 (three membered ring).

Table 3. Theoretical and experimental vibrational wave number (cm^{-1}) of Abacavir.

Unscaled	scaled	IR	Raman	Assignment
3794	3592	3740	3649	(C30H ₂) _{R1} Asymmetric stretching
3649	3463	3610	3640	(OH) _{R1} stretching
3626	3443	-	-	(N13H14) _{R3} stretching
3310	3160	-	3370	(C8H9) _{R2} stretching
3262	3116	3305	3310	(C24H ₂) _{R4} stretching + (C23H ₂) _{R4} Asymmetric stretching
3255	3110	-	-	(C19H) _{R1} stretching + (C21H) _{R4} stretching
3241	3097	3262	3255	(CH ₂) _{R4} Asymmetric stretching
3223	3081	3245	3240	(CH) _{R1} stretching
3171	3034	3176	3179	(CH ₂) _{R4} symmetric stretching + All CH stretching
3164	3028	-	-	(CH ₂) _{R4} symmetric stretching + All CH stretching
3157	3022	3150	3142	(CH ₂) _{R4} symmetric stretching + All CH stretching
3130	2997	3084	3095	(C33H ₂) _{R1} Symmetric stretching + (C5H6) _{R1} stretching
3068	2941	-	3065	(C33H ₂) _{R1} Symmetric stretching + (C5H6) _{R1} stretching
3061	2934	3040	3049	(C33H ₂) _{R1} Symmetric stretching + (C5H6) _{R1} stretching + (C1H ₂) _{R1} Asymmetric stretching
3046	2921	-	-	(C1H ₂) _{R1} Asymmetric stretching + (C3H4) _{R1} stretching + (C5H6) _{R1} stretching
3024	2901	3021	3029	(C3H4) _{R1} stretching + (C1H ₂) _{R1} Asymmetric stretching + (C33H ₂) _{R1} Asymmetric stretching
2997	2876	-	2991	(C1H ₂) _{R1} symmetric stretching
1693	1661	1675	1692	(C19C21) _{R1} stretching + (C19H20) _{R1} bending + (C21H36) _{R1} bending + R1 deforming
1678	1646	1652	1642	(N30H2) _{R3} scissoring + (N13H14) _{R3} bending + (N13C12) _{R3} stretching + R3 deforming + (N30C16) _{R3} stretching
1655	1624	1634	1630	(C11C12) _{R3} stretching + (N13H14) _{R3} bending + (N30H ₂) _{R3} scissoring + (N7C18) _{R3} stretching
1629	1599	1589	1590	(N17C18) _{R3} stretching + (C11C18) _{R3} stretching + (N15C12) _{R3} stretching + (N13C12) _{R3} stretching + (N30H ₂) _{R3} scissoring + (N13H14) _{R3} bending + R1 and R2 deforming
1560	1533	1527	-	(C1H ₂) _{R1} scissoring + (C33H ₂) _{R4} Scissoring + (C3H4) _{R1} bending + (N30H ₂) _{R3} scissoring + (N13H14) _{R3} bending
1558	1531	1538	1540	(N13C12) _{R3} stretching + (N13C22) _{R3} stretching + (N13H14) _{R3} bending + (N30H ₂) _{R3} scissoring + (N30C16) _{R3} stretching + (C18N7) _{R3} stretching + (N13H14) _{R3} bending + (C8H9) _{R1} bending + (C1H ₂) _{R1} Scissoring + R1, R2 deforming
1536	1510	-	-	(C33H ₂) _{R1} scissoring + (C1H ₂) _{R1} Scissoring
1532	1507	1509	1500	(C23H ₂) _{R4} scissoring + (C24H ₂) _{R4} Scissoring + (CN) _{R2} stretching + (C11C18) _{R3} stretching
1525	1500	-	1496	(N13H14) _{R3} bending + (N30H ₂) _{R3} scissoring + (N30C16) _{R3} stretching + (C24H ₂) _{R4} Scissoring
1512	1487	1476	1485	(C23H ₂) _{R4} Scissoring + (C24H ₂) _{R4} Scissoring + (C22H25) _{R4} bending + (N13H14) _{R3} bending + (N30H ₂) _{R3} rocking + (C18N17) _{R3} stretching + (C5H6) _{R1} bending
1506	1482	-	1476	(C22H ₂) _{R4} Scissoring + (C23H ₂) _{R4} Scissoring + (N13H14) _{R4} bending + R3 deforming
1482	1459	1450	1454	(C8H9) _{R2} bending + (C8N18) _{R2} stretching + (N30H31) _{R3} bending + (C16N15) _{R3} stretching + (N13H14) _{R3} bending + (C24H ₂) _{R4} Scissoring
1456	1434	1429	1437	(OH) _{R1} bending + (C1H2) _{R1} wagging
1439	1417	-	1422	(C5H6) _{R1} bending + (C33H ₂) _{R1} wagging + (C1H2) _{R1} wagging + (N30H2) _{R3} rocking + (N7C8) _{R1} stretching
1423	1402	1390	1395	(C22H25) _{R4} bending + (C23H ₂) _{R4} wagging + (C5H6) _{R1} bending + R2 and R3 deforming

1412	1391	-	-	(C22H25) _{R4} bending + (N13H14) _{R3} bending + (C11C12) _{R3} stretching + (C8N7) _{R2} stretching
1407	1386	1376	-	(C23H2) _{R4} wagging + (C1H2) _{R1} twisting + (C3H4) _{R1} bending + (C21H36) _{R1} bending + (C19H20) _{R1} bending + (C5H6) _{R1} bending
1375	1356	1370	1375	(N30H2) _{R3} rocking + (C12N15) _{R3} stretching + (C8H9) _{R2} bending
1373	1354	-	1360	(C19H20) _{R1} CH bending + (C1H2) _{R1} twisting + (C12N15 & C18N17) _{R3} stretching + (N30H2) _{R3} rocking
1339	1321	1338	1340	(C33H2) _{R1} wagging + all CH bending + (OH) _{R1} bending + (C-C) _{R1} stretching
1337	1319	-	1320	(C33H2) _{R1} twisting + (C1H2) _{R1} twisting + (CH) _{R1} bending
1329	1311	1309	-	(C33H2) _{R1} wagging + (OH) _{R1} bending + (CH) _{R1} bending + (N13H14) _{R3} bending + (N7C8) _{R2} stretching + all C=C stretching
1318	1307	-	1305	(OH) _{R1} bending + (C1H37) _{R1} bending + (CH2) _{R1} wagging + (CH) _{R1} bending + (C5N7) _{R1} stretching + (C8H9) _{R1} bending + all C-N stretching + (N17C18) _{R3} stretching + R3 (N17C16) _{R3} stretching + (N30H2) _{R3} rocking + (N13H14) _{R3} bending
1294	1277	1290	1292	(OH) _{R1} bending + (C1H37) _{R1} bending + (C33H2) _{R1} wagging + (CH) _{R1} bending + (C5N7) _{R1} stretching + (C8H9) _{R2} bending + all C=N stretching + (N15C12) _{R3} stretching + R3 (N30C16) _{R3} stretching + (N30H2) _{R3} rocking + (N13H14) _{R3} bending + (CH) _{R4} bending
1261	1246	1257	1255	(OH) _{R1} bending + (C1H37) _{R1} bending + (C-C) _{R1} stretching + (C33H2) _{R1} wagging + (C5H6) _{R1} bending + (C5N7) _{R1} stretching + R2 CN stretching + R3 deforming + (N30H2) _{R3} rocking + (CH) _{R4} bending
1255	1240	-	1247	(OH) _{R1} bending + (C1H37) _{R1} bending + (C33H24) _{R1} bending + (CH) _{R1} bending + (C5N7) _{R1} stretching + (CN) _{R2} stretching + (C=N) _{R2} stretching + (N30H2) _{R3} rocking + (C-C) _{R4} stretching + (C22H25) _{R4} bending
1242	1227	-	1237	(OH) _{R1} bending + (C1H2) _{R1} twisting + (C3H4) _{R1} bending + (C33H2) _{R1} twisting + (CH) _{R1} bending
1233	1218	-	-	(C1H2) _{R1} twisting + (C5N7) _{R1} stretching + (C8H9) _{R2} bending + R3 deforming + (N13H14) _{R3} bending
1221	1207	-	1205	(C33H2) _{R1} twisting + (NH) _{R1} bending + (N7C8) _{R1} stretching + (N7C18) _{R1} stretching + (C22H2) _{R4} rocking + (C23H2) _{R4} rocking + R4 deforming
1217	1203	-	1201	(C24H2) _{R4} rocking + (C23H2) _{R4} twisting + (C22H25) _{R4} bending + (CH) _{R1} bending
1206	1192	-	1189	(C33H2) _{R1} twisting + (OH) _{R1} bending + (CH) _{R1} bending + (C23H2) _{R4} twisting + (CN) _{R2} stretching + (C=N) _{R3} stretching + (N30H2) _{R3} rocking
1188	1175	1185	1179	(C33H2) _{R1} twisting + all CH bending + (C23H2) _{R4} twisting + (C24H2) _{R4} twisting + (CN) _{R2} stretching + all NH2 rocking
1167	1154	-	-	(C19H20) _{R1} bending + (C21H36) _{R1} bending + (C3C33) _{R1} stretching + all CH bending + (C8H9) _{R2} bending
1157	1145	1134	1135	(CH) _{R4} bending + (N30H2) _{R3} rocking
1127	1116	1130	-	(OH) _{R1} bending + (C1H2) _{R1} rocking + all CH bending + R1 (C-C) _{R1} stretching
1119	1108	1119	1121	(OH) _{R1} bending + (C1H2) _{R1} rocking + all CH bending + (N30H2) _{R3} rocking
1116	1105	1099	1088	(OH) _{R1} bending + (C1H2) _{R1} rocking + all CH bending + (N30H2) _{R3} rocking + (C23H2) _{R4} wagging
1098	1087	-	1081	(OH) _{R1} bending + (C1H2) _{R1} rocking + all CH bending + (N30H2) _{R3} rocking + (C=N) _{R3} stretching + (CH2) _{R4} wagging
1095	1085	-	-	(OH) _{R1} bending + (N30H2) _{R3} rocking + (CH2) _{R4} wagging
1076	1066	-	1076	(N30H2) _{R3} rocking + (C16N17) _{R3} stretching + (C24H2) _{R4} twisting + (C24H29) _{R4} bending + (N13H14) _{R3} bending + (N30H2) _{R3} rocking
1063	1053	1056	1057	(OH) _{R1} bending + (C33H2) _{R1} rocking + (C5H6) _{R1} bending + (C21H36) _{R1} bending + (C1H2) _{R1} rocking + (C3C19) _{R1} stretching + (N7C8) _{R2} stretching + (NH2) _{R3} rocking
1049	1040	1039	1040	(OH) _{R1} bending + (C33H2) _{R1} rocking + (CH) _{R1} bending + (C5N7) _{R1} stretching + (NC) _{R2} stretching + (C24H2) _{R4} twisting + (C22N13) _{R4} stretching
1037	1028	-	-1036	(OH) _{R1} bending + (C-O) _{R1} stretching + (C1C3) _{R1} bending
1013	1005	-	-	(CH) _{R1} bending
996	988	992	990	(C-O) _{R1} stretching + (C1H2) _{R1} rocking + (C5C21) _{R1} stretching + (C5H6) _{R1} bending + (C24H29) _{R4} bending
987	979	982	984	(C24H2) _{R4} rocking + (C22C23) _{R4} stretching + (N13C22) _{R4} stretching + (N17C16) _{R1} bending + (N15C16) _{R1} bending + (C33H2) _{R1} rocking + (C11N10) _{R2} bending + (C8H9) _{R2} bending + (C-C) _{R1} stretching + all CH bending
968	961	-	978	(C23H2) _{R4} twisting + (C24H2) _{R4} twisting + (N13H14) _{R4} bending + (N13C12) _{R4} stretching
965	958	970	967	(C-C) _{R1} stretching + (CH) _{R1} bending + (C23H2) _{R4} twisting + (C1H2) _{R1} rocking
918	912	-	-	(N7C5) _{R2} stretching + (CH) _{R1} bending + (C33C5) _{R1} stretching + (C23H2) _{R4} rocking + (CN) _{R2} bending
860	855	855	858	(C-C) _{R1} stretching + (C1H2) _{R1} rocking + all CH bending + (C23H2) _{R4} twisting
856	851	-	850	(C23H2) _{R4} twisting + all CH bending + all C-C stretching
853	848	847	848	(C24H2) _{R4} rocking + (C23H2) _{R4} rocking + all CH bending + (C22H2) _{R4} stretching
842	837	839	839	(C24H2) _{R4} rocking + (C23H2) _{R4} rocking + (C22H25) _{R4} bending + (C16N17C18) _{R4} bending + (N30H2) _{R3} rocking (CH) _{R1} bending + (C33H2) _{R3} rocking
835	830	-	835	C8H9 bending
809	805	802	805	(CH) _{R1} bending + (CH) _{R2} bending + (C8H9) _{R1} Bending + R2 and R3 CN out of plane bending + (CH) _{R1} out of plane bending
798	794	-	-	(CH) _{R1} out of plane bending + (CH) _{R1} stretching + (OH) _{R1} bending
789	785	790	789	(C23H2) _{R4} twisting + (C24H2) _{R4} twisting
756	753	-	779	R2 and R1 deforming + (CN) _{R2} bending + (CN) _{R3} bending + (C N3H2) _{R1} rocking
748	745	770	769	(C33H2) _{R3} twisting + all CH bending + (C16N17) _{R4} stretching + (N30H2) _{R3} rocking
747	744	-	760	(CN) _{R3} out of plane + (CH) _{R1} stretching
696	694	-	-	(CN) _{R3} out of plane + (CH) _{R4} bending + all CH bending
669	667	666	668	(CN) _{R2} out of plane + (CH) _{R2} out of plane + (CH) _{R1} bending
663	661	664	665	(CH) _{R3} rocking + (NH) _{R1} rocking

627	626	632	630	(CN) _{R3} bending + (CH) _{R1} bending
610	609	619	615	(CH) _{R1} bending + (CN) _{R3} bending + (N3OH ₂) _{R3} rocking
570	569	569	572	(N13H14) _{R2} bending
536	535	540	542	(N3OH ₂) _{R3} twisting
516	515	523	525	(CH) _{R2} bending + (NC) _{R2} stretching + (C=C) _{R3} stretching + (CH) _{R4} Bending + (NC) _{R2} bending
498	498	502	504	(CH) _{R1} bending + R2 and R3 deforming
471	471	-	490	(N3OH ₂) _{R3} wagging + (C-C) _{R4} bending + (CH) _{R1} bending
460	460	469	472	(N3OH ₂) _{R3} wagging + (C-C) _{R4} bending + (CH) _{R1} bending
457	457	467	465	(N3OH ₂) _{R3} wagging + (C-C) _{R4} bending + (CH) _{R4} bending
410	410	-	416	(N3OH ₂) _{R3} rocking + (C-C) _{R1} bending + (C5N7) _{R1} bending + (CN) _{R3} bending
383	383	-	-	(N3OH ₂) _{R3} rocking + all CH bending
340	341	-	345	(CH) _{R1} bending + (CN) _{R3} out of plane + (OH) _{R1} bending
318	319	-	-	(C16=NH ₂) _{R3} rocking + (CH) _{R4} bending
304	305	-	310	(CN) _{R2} out of plane bending + (CH) _{R1} bending + (CH) _{R4} bending
276	277	-	285	(OH) _{R1} bending
262	263	-	279	(CN) _{R2} out of plane bending + (CN) _{R3} out of plane bending + (OH) _{R1} bending
238	239	-	246	(CN) _{R2} out of plane bending + (CN) _{R3} out of plane bending + (N13H14) _{R2} bending
220	221	-	231	(CH) _{R1} bending + (OH) _{R1} bending
207	208	-	220	(CH) _{R1} bending + (CN) _{R2} out of plane bending + (CH) _{R4} bending
187	188	-	210	(CH) _{R1} bending + (CN) _{R2} out of plane bending + (CH) _{R4} bending
147	147	-	198	(N3OH ₂) _{R3} out of plane bending + (CN) _{R2} out of plane bending
126	126	-	135	All CH and NH rocking
115	115	-	-	(C1H ₂) _{R1} rocking + OH bending
89	89	-	90	All CH bending + R4 rocking
78	78	-	-	R2 and R3 rocking
45	45	-	-	(CH) _{R3} bending + (CH) _{R1} bending
35	35	-	-	(C22C24) _{R4} bending
24	24	-	-	(C1C3) _{R1} Bending
18	18	-	-	R3 bending + R4 bending + R1 rocking

Comparison of frequencies calculated by DFT/B3LYP with experimental values reveal an over estimation of the values of vibrational mode due to neglect of anharmonicity in system. Since the vibrational wave number obtained from the DFT calculations are higher than the experimental frequencies, they were scaled down by wave number linear scaling procedure (WLS) [$\mathbf{v}_{\text{obs}}/\mathbf{v}_{\text{cal}} = (1.0087 - 0.0000163 \times \mathbf{v}_{\text{cal}})$ cm⁻¹] also used as suggested by Yoshida et. Al. (26). The WLS method predicts the vibrational wave number with high accuracy and it is applicable to large number of molecule (compounds) except those where the effect of dispersion force is significant. The vibrational wave numbers calculated with approximate functions are often in good agreement with observed wave number when the calculated wave numbers are uniformly scaled with only one scaling factor. Experimental and theoretical Raman and FT-IR spectra are shown in Fig. 3 and Fig. 4. It is clear that theoretical and experimental FT-IR frequencies are in very good agreement with each other.

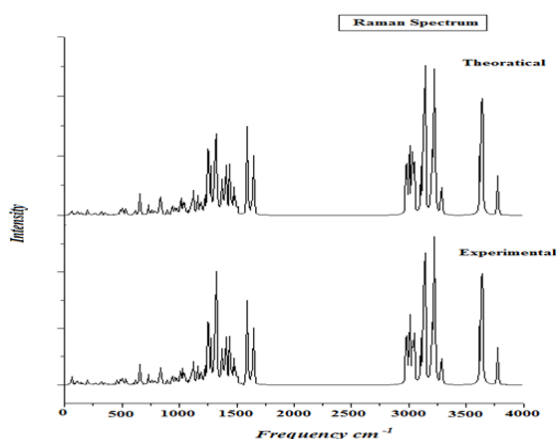


Fig 3. Calculated and experimental Raman spectra of Abacavir.

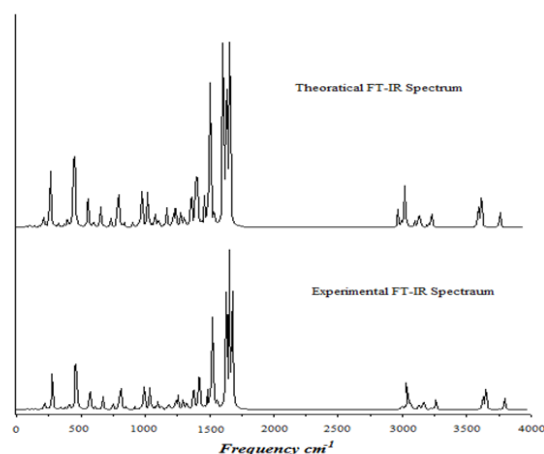


Fig 4. Calculated and experimental FT-IR spectra of Abacavir.

3.2.1 Ring1 (Five membered ring) Vibrations Stretching

The CH stretching vibrations give rise to multiple bands in the region 3000 cm⁻¹ to 3300 cm⁻¹. In IR spectra CH stretching is found at 3305 cm⁻¹, 3245 cm⁻¹, 3084 cm⁻¹ and 3021 cm⁻¹, in Raman spectra the CH stretching is found at 3240 cm⁻¹, 3142 cm⁻¹, 3095 cm⁻¹ and 3029 cm⁻¹ while it's theoretically observed values are 3110 cm⁻¹, 3081 cm⁻¹, and 2997 cm⁻¹. The CC stretching in ring-1 is found at 1130 cm⁻¹ in Raman spectra, at 1130 cm⁻¹ in IR spectra and its theoretically calculated values are 1154 cm⁻¹ and 1116 cm⁻¹. CN stretching in Raman spectra is found at 1040 cm⁻¹, in IR it is observed at 1039 cm⁻¹ while its calculated value is 1040 cm⁻¹ which are in excellent agreement with each other. The CO stretching is observed at 990 cm⁻¹ in Raman spectra, at 992 cm⁻¹ in IR spectra and its calculated value is found to be 996 cm⁻¹. The OH stretching is observed at 3640 cm⁻¹ in Raman spectra, at 3610 cm⁻¹ in IR spectra while its calculated value is found to be 3463 cm⁻¹.

Bending

CH bending is observed at 1692 cm^{-1} , 1540 cm^{-1} , 1485 cm^{-1} , 1422 cm^{-1} , 1395 cm^{-1} , 1360 cm^{-1} and 1320 cm^{-1} in Raman spectra, it is obtained at 1675 cm^{-1} , 1538 cm^{-1} , 1476 cm^{-1} , 1390 cm^{-1} , 1376 cm^{-1} , 1338 cm^{-1} in IR spectra and its theoretically calculated values are 1661 cm^{-1} , 1531 cm^{-1} , 1487 cm^{-1} , 1417 cm^{-1} , 1386 cm^{-1} , 1354 cm^{-1} and 1319 cm^{-1} . The OH bending vibrations in ring-1 are obtained in IR spectrum at 1429 cm^{-1} , 1290 cm^{-1} , 1257 cm^{-1} , and 1119 cm^{-1} while they are observed at 1437 cm^{-1} , 1292 cm^{-1} , 1255 cm^{-1} and 1121 cm^{-1} and theoretical calculated values of the same are 1434 cm^{-1} , 1277 cm^{-1} , 1246 cm^{-1} and 1145 cm^{-1} .

Scissoring

CH_2 scissoring is obtained at the frequency 1527 cm^{-1} and 1538 cm^{-1} in IR spectra where as its theoretically calculated value is 1531 cm^{-1} and 1533 cm^{-1} .

Rocking

CH rocking is observed at 1130 cm^{-1} , 1119 cm^{-1} , 1099 cm^{-1} , 1056 cm^{-1} , 1039 cm^{-1} in IR spectra the value for the same in Raman spectrum is found at 1121 cm^{-1} , 1088 cm^{-1} , 1057 cm^{-1} , 1040 cm^{-1} while theoretically calculated value for the same is 1116 cm^{-1} , 1108 cm^{-1} , 1105 cm^{-1} , 1053 cm^{-1} , 1040 cm^{-1} .

Twisting

Calculated value for CH_2 twisting is 1356 cm^{-1} and 1175 cm^{-1} , and the value of the same in Raman spectrum is observed are 1375 cm^{-1} and 1356 cm^{-1} while observed value in IR spectrum for CH_2 twisting is 1376 cm^{-1} and 1185 cm^{-1} .

Wagging

CH_2 wagging in IR spectrum is found at the frequency 1338 cm^{-1} , 1309 cm^{-1} , 1290 cm^{-1} which leads to multiple bands in this region and the value of CH_2 wagging frequency in Raman spectra is observed at 1340 cm^{-1} , 1305 cm^{-1} and 1292 cm^{-1} while their theoretically calculated values are 1321 cm^{-1} , 1311 cm^{-1} , 1307 cm^{-1} , 1277 cm^{-1} .

3.2.2 Ring2 (five membered ring with nitrogen) Vibrations**Stretching**

The wave number of the stretching mode is calculated to be 3160 cm^{-1} 1311 cm^{-1} and 1307 cm^{-1} and assigned at 1338 cm^{-1} , 1309 cm^{-1} in IR and at 1340 cm^{-1} and 1305 cm^{-1} in the Raman spectrum.

Bending

CH bending in the ring is calculated to be 1459 cm^{-1} , 1356 cm^{-1} and 979 cm^{-1} and corresponds to the observed peak at in 1454 cm^{-1} , 1375 cm^{-1} and 984 cm^{-1} in the Raman spectrum and at 1450 cm^{-1} , 1370 cm^{-1} and 982 cm^{-1} in IR spectrum. Out of plane bending is calculated at 667 cm^{-1} corresponding peaks are obtained at 666/ 668 cm^{-1} in IR and the Raman spectrum respectively.

3.2.3 Ring3 (six membered ring) Vibrations**Stretching**

CN stretching in the ring is calculated to be 1531 cm^{-1} , 1500 cm^{-1} , 1356 cm^{-1} and corresponding peaks are observed at 1538 cm^{-1} , 1370 cm^{-1} in IR spectrum and at 1540 cm^{-1} , 1496 cm^{-1} and 1356 cm^{-1} in the Raman Spectrum.

Bending

The NH bending in the ring is calculated to be at 1533 cm^{-1} , 1500 cm^{-1} and 1487 cm^{-1} which corresponding to the peaks at 1527 cm^{-1} and 1476 cm^{-1} in IR spectrum and at 1540 cm^{-1} and 1485 cm^{-1} in the Raman spectrum.

Scissoring

In the Ring NH_2 Scissoring is calculated to be 1533 cm^{-1} and 1500 cm^{-1} and the corresponding vibrations are observed

at 1527 cm^{-1} and 1538 cm^{-1} in IR spectrum and at 1540 cm^{-1} and 1496 cm^{-1} in the Raman spectrum.

Rocking

The wave number for NH_2 rocking is calculated to be 1487 cm^{-1} , 1356 cm^{-1} and 1246 cm^{-1} which corresponds to the peaks at 1476 cm^{-1} , 1375 cm^{-1} and 1257 cm^{-1} in IR spectrum and at 1485 cm^{-1} , 1375 cm^{-1} and 1255 cm^{-1} in the Raman spectrum.

3.2.4 Ring4 (three membered ring) Vibrations**Stretching**

CH stretching in the ring is calculated to be 3179 cm^{-1} , 3142 cm^{-1} and 1395 cm^{-1} and corresponding peaks are observed at 3176 cm^{-1} , 3150 cm^{-1} and 1390 cm^{-1} in IR spectrum and at 3034 cm^{-1} and 1402 cm^{-1} in the Raman Spectrum.

Bending

The NH bending in the ring is calculated to be at 1277 cm^{-1} , 1246 cm^{-1} and 988 cm^{-1} which corresponding to the peaks at 1292 cm^{-1} , 1255 cm^{-1} and 990 cm^{-1} in the Raman spectrum and at 1290 cm^{-1} , 1257 cm^{-1} and 992 cm^{-1} in the Raman spectrum.

Scissoring

In the Ring CH_2 Scissoring is calculated to be 1500 cm^{-1} and 1459 cm^{-1} and the corresponding vibrations are observed at 1509 cm^{-1} and 1450 cm^{-1} in IR spectrum and at 1500 cm^{-1} and 1459 cm^{-1} in the Raman spectrum.

Rocking

The wave number for CH_2 rocking is calculated to be 979 cm^{-1} , 848 cm^{-1} and 837 cm^{-1} which corresponds to the peaks at 982 cm^{-1} , 847 cm^{-1} and 839 cm^{-1} in IR spectrum and at 984 cm^{-1} , 848 cm^{-1} and 837 cm^{-1} in the Raman spectrum.

Twisting

Theoretically calculated value for CH_2 twisting is 1179 cm^{-1} and 1040 cm^{-1} , and the corresponding peaks in the Raman spectrum is observed at 1179 cm^{-1} and 1040 cm^{-1} and in IR it is observed at 1185 cm^{-1} and 1039 cm^{-1} .

Wagging

CH_2 wagging in IR spectrum is found at 1390 cm^{-1} and 1099 cm^{-1} and at 1395 cm^{-1} and 1088 cm^{-1} in Raman spectrum where as the theoretically calculated values for CH_2 wagging is 1402 cm^{-1} and 1105 cm^{-1} .

4. Summary

Vibrational spectroscopy measurement and density functional theory calculation have been applied to investigate Abacavir (27-28). The equilibrium geometry and vibrational wave numbers for all the mode of the molecule were determined and analyzed with DFT/B3LYP applying 6-31G basis set, giving allowance for the lone pair through the diffused functions. The comparison between theoretically and experimentally observed wave number from IR and Raman spectra reveals that the experimental and theoretical results are in excellent agreement.

A detailed normal coordinate analysis of all the normal modes clearly illustrates the composition of each normal mode in terms of internal coordinate. In the present study, the complete vibrational assignment along with all structural thermo dynamical and electronic parameters of Abacavir is presented and we believe that the results obtained herein will prove to be an excellent starting point for studying the detailed potential surface of the molecule which is needed to understand the drug receptor interactions.

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