Density functional theory study on the molecular structure of loganin

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Abstract. The computational Quantum Chemistry (QC) has been used for different types of problems, for example: structural biology, surface phenomena and liquid phase. In this paper we have employed the density functional method for the study of molecular structure of loganin. The equilibrium geometry, harmonic vibrational frequencies and infrared intensities were calculated by B3LYP/6-311G (d, p) method and basis set combinations. It was found that the optimized parameters obtained by the DFT/B3LYP method are very near to the experimental ones. A detailed conformational analysis was carried out. A detailed interpretation of the infrared spectra of loganin is also reported in the present work. The FT-IR spectra of loganin were recorded in solid phase. The thermodynamic calculations related to the title compound were also performed at B3LYP/6-311G (d, p) level of theory.

Keywords: FT-IR, molecular structure, conformer, vibrational spectra

1. Introduction

The traditional medicine used for the management of liver disorders has helped in the identification of the natural product responsible for the hepatoprotection [1,4,8]. One of the most important class of natural products found useful for the management of hepatic disorder is iridoid glycosides [30]. The monoterpene glucoside, loganin is a key intermediate in the biosynthesis of corynanthe, Aspidosperma, Iboga, Cinchona, Ipecacuanha and pyrolochinolin alkaloids [9] and of simple monoterpene glucoside [13]. It was first isolated from *strychnos nux vomica* [10]. Its structure [2] has been confirmed by the total synthesis [5]. Earlier we reported the immunostimulant and hepatoprotective activity of loganin and its modified analogues [36,42,43]. Here, in the present communication, the experimental FT-IR frequencies of the title molecule are compared with the theoretical frequencies obtained by Density Functional method. As a general approach to the vibrational problems of organic molecules, we have calculated harmonic frequencies of loganin and compared the results with the observed fundamental vibrational frequencies. This method is useful for obtaining a reliable assignment of the vibrational spectra. The purpose of this study assumes importance because of the further work on loganin, in which presumably, some modification by chemical reaction such as oxidation/reduction on polyfunctional bioactive

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natural product will generate new reactive sites in the molecule, which can be exploited for elaborating and appending pharmacophores to generate patentable compounds of biological interest. The aim of this study is to study and interpret the simulation of IR spectra of the title compound with the use of standard 6-311G (d, p) basis set. To the best of our knowledge quantum chemical calculations for loganin have not been reported so far in the literature.

2. Experimental section

Fresh fruit of plant *Strychnos nux-vomica* L (strychanaceae) (10 kg, collected from NBRI, Lucknow) were extracted with 95% ethanol (4×10 l) and was concentrated *in vacuo* at temperature below 50°C . It was diluted with water (0.5 l) and fractionated with n-hexane (3×300 ml), chloroform (3×300 ml) and n-butanol (3×200 ml), successively. On concentration, butanol fraction *in vacuo*, the crude loganin was precipitated out, which was filtered. This was crystallized with ethanol to give pure loganin (50 g), m.p. 223°C . The mother liquors were mixed and additional quantity of loganin (10 g) was isolated by column chromatography and it was identified from its spectral data (yield: 0.6%; m.p. 223°C); IR (KBr): 1714 cm^{-1} ($>\text{C}=\text{O}$); $^1\text{H-NMR}$ (400 MHz, D_2O): δ 7.42 (s, 1H, H-3), 5.41 (d, 1H, $J = 4$, H-1), 4.81 (d, 1H, $J = 8$, H-1'), 4.14 (bs, 1H, H-7), 3.92 (d, 1H, $J = 12$, H-6'), 3.31 (d, 1H, $J = 12$, H-6'), 3.73 (m, 1H, H-5'), 3.72 (s, 3H, OCH_3), 3.49 (t, 1H, $J = 8$, H-3'), 3.39 (t, 1H, $J = 8$, H-4'), 3.27 (t, 1H, $J = 8$, H-2'), 3.07 (m, 1H, H-5), 2.15 (m, 1H, H-6 α), 2.15 (m_e , 1H, H-9), 1.92 (m, 1H, H-8), 1.75 (m, 1H, H-6 β), 1.06 (d, 3H, $J = 6.6$, H-10); MS (FAB): m/z 391 ($\text{M}^+ + 1$), 413 ($\text{M}^+ + \text{Na}$); analysis calculated for $\text{C}_{17}\text{H}_{26}\text{O}_{16}$: C, 52.30; H, 6.66. Found: C, 52.26; H, 6.49%; $[\alpha]_{\text{D}}^{25} = -87.81$ ($C = 0.28$ in methanol) [35].

The above data is also supported by another work on loganin, in which anti-amnesic (cognitive enhancing) activity has been reported [26]. The FT-IR spectra of the sample of loganin have been recorded in CsI on a Perkin Elmer 1800 spectrophotometer. Spectroscopic preparation of the sample was carried out under an atmosphere of prepurified nitrogen. The FT-IR spectra of title molecule is recorded in the region $4000\text{--}500\text{ cm}^{-1}$ and is shown in Fig. 1.

Fig. 1. FT-IR spectrum of loganin.

3. Computational details

The DFT calculations were mainly carried out in the framework of the Becke–Lee–Yang–Parr (B3LYP) functionals, in which the exchange functional is a local spin density exchange with Becke gradient correction and the correlation functional is that of Lee, Yang and Parr with both local and nonlocal terms employing 6-31G (d, p) [3,16,17,25,31,44] as the basis set, using Gaussian 03 suite of programs [12], involving gradient optimized geometry [38]. The basis set 6-311G (d, p) augmented by d polarization functions on heavy atoms and p polarization functions on hydrogen atoms as well as diffuse functions for both hydrogen and heavy atoms were used. The Gauss View 3.0 [11] program has been employed to get a visual animation and also for the study of the normal modes description. It is well known that vibrational frequencies obtained by quantum chemistry calculation are typically larger than that of their experimental counterpart and thus experimental scaling factors are usually employed to have a better agreement with the experimental vibrational frequencies [14]. The scaling factor depends on both basis set and the method used in the calculation and is determined from the mean deviation between calculated and experimental value of the frequencies [37,39]. On the other hand B exchange functional have an advantage of standard frequency very close to unity so B based procedures can be often used without scaling [18,29,32]. The absolute infrared absorption intensities were calculated in the harmonic approximation, at the same level of theory as used for the optimized geometries, from the derivatives of the dipole moment and polarizability of each normal mode, respectively. The optimized structural parameters of loganin calculated by B3LYP method with the 6-311G (d, p) basis set are listed in Tables 1 and 2, in accordance with the atom numbering scheme as given in Fig. 2.

Table 1
Optimized bond lengths of loganin using B3LYP/6-311G (d, p) method

S. No.	Loganin parameter bond lengths	X-ray (Å)	Calculated B3LYP/6-311G (d, p) (Å)
1	C1–H2	–	1.101
2	C1–C3	1.511	1.536
3	C1–O14	1.346	1.402
4	C3–H4	–	1.100
5	C3–C5	1.515	1.525
6	C3–O15	1.419	1.414
7	C5–H6	–	1.107
8	C5–C7	1.529	1.536
9	C5–O17	1.414	1.412
10	C7–H8	–	1.095
11	C7–C9	1.530	1.532
12	C7–O19	1.415	1.429
13	C9–H10	–	1.105
14	C9–C11	1.507	1.524
15	C9–O23	1.442	1.434
16	C11–H12	–	1.101
17	C11–H13	–	1.092
18	C11–O21	1.418	1.414
19	O14–C24	–	1.415
20	O15–H16	–	0.968

Table 1
(Continued)

S. No.	Loganin parameter bond lengths	X-ray (Å)	Calculated B3LYP/6-311G (d, p) (Å)
21	O17–O18	–	0.969
22	O19–H20	–	0.969
23	O21–H22	–	0.967
24	C24–H25	–	1.095
25	C24–C26	1.432	1.437
25	C24–C52	1.509	1.517
26	O26–C27	1.357	1.358
27	C27–H28	–	1.083
28	C27–C29	1.333	1.346
29	C29–C30	1.482	1.475
30	C29–C37	1.510	1.513
31	C30–O31	1.341	1.358
32	C30–C36	1.119	1.218
33	O31–C32	1.449	1.435
34	C32–H33	–	1.089
35	C32–H34	–	1.093
36	C32–C35	–	1.092
37	C37–H38	–	1.093
38	C37–C39	1.553	1.567
39	C37–C52	1.549	1.559
40	C39–H40	–	1.094
41	C39–H41	–	1.093
42	C39–C42	1.522	1.536
43	C42–H43	–	1.100
44	C42–O44	1.439	1.430
45	C42–C46	1.522	1.537
46	O44–H45	–	0.965
47	C46–H47	–	1.099
48	C46–C48	1.528	1.529
49	C46–C52	1.535	1.547
50	C48–H49	–	1.095
51	C48–H50	–	1.092
52	C48–H51	–	1.095
53	C52–H53	–	1.094

4. Results and discussion

4.1. Geometry optimization

The conformer study was done by Monte Carlo Multiple Minimum method. Twenty three conformers were generated. Out of the 23 conformers, the minimum energy calculated by using HF/3-21G method and global minimum energy was found for the conformer number 19. In this conformer both hydrogen atoms attached with oxygen in R1 rotate by 180° to minimize the repulsion and other hydrogen attached to oxygen rotate nearly perpendicular to the plane of ring. All the 24 figures of the conformers

Table 2
Optimized bond angles of loganin using B3LYP/6-311G (d, p) method

S. No.	Loganin parameter bond angle	X-ray (in degree)	Calculated B3LYP/6-311G (d, p) (in degree)
1	H2–C1–C3	–	109
2	H2–C1–O14	–	110
3	H2–C1–O23	–	110
4	C3–C1–O14	109	107
5	C3–C1–O23	110	111
6	O14–C1–O23	107	108
7	C1–C3–H4	–	107
8	C1–C3–C5	108	109
9	C1–C3–O15	109	109
10	H4–C3–O5	–	108
11	C5–C3–O15	108	109
12	C5–C3–150	108	109
13	H6–C5–C7	–	109
14	C3–C5–H6	–	107
15	C3–C5–C7	111	110
16	C3–C5–O17	109	108
17	H6–C5–O17	–	110
18	C7–C5–O17	111	110
19	C5–C7–H8	–	108
20	C5–C7–C9	110	111
21	C5–C7–O19	111	109
22	H8–C7–C9	–	108
23	H8–C7–O19	–	105
24	C9–C7–O19	112	112
25	C7–C9–H10	–	109
26	C7–C9–C11	112	113
27	C7–C9–O23	108	108
28	H4–C3–O15	–	108
29	H10–C9–C11	–	108
30	H10–C9–O23	–	109
31	C11–C9–O23	107	106
32	C9–C11–H12	–	108
33	C9–C11–H13	–	109
34	C9–C11–O21	112	111
35	H12–C11–H13	–	107
36	H12–C11–O21	–	111
37	H13–C11–O21	–	107
38	C1–O14–C24	114	115
39	C3–O15–H16	–	106
40	C5–O17–H18	–	105
41	C7–O19–H20	–	107
42	C11–O21–H22	–	105
43	C1–O23–C9	111	112
44	O14–C24–H25	–	110

Table 2
(Continued)

S. No.	Loganin parameter bond angle	X-ray (in degree)	Calculated B3LYP/6-311G (d, p) (in degree)
45	O14–C24–O26	109	109
46	O14–C24–O52	106	107
47	H25–C24–O26	–	103
48	H25–C24–C52	–	112
49	O26–C24–H52	113	112
50	C24–O26–C27	115	115
51	O26–C27–H28	–	112
52	O26–C27–C29	124	124
53	H28–C27–C29	–	123
54	C27–C29–C30	120	120
55	C27–C29–C37	123	122
56	C30–C29–C37	116	117
57	C29–C30–O31	113	113
58	C29–C30–O36	123	123
59	31O–30C–36O	123	122
60	30C–31O–32C	115	115
61	31O–32C–33H	–	105
62	31O–32H–34H	–	110
63	31O–32C–35H	–	110
64	33H–32C–34H	–	110
65	33H–32C–35H	–	110
66	34H–32C–35H	–	108
67	29C–37C–38H	–	108
68	29C–37C–39C	112	111
69	29C–37C–52C	110	111
70	38H–37C–39C	–	109
71	38H–37C–52C	–	110
72	39C–37C–52C	104	104
73	37C–39C–40H	–	110
74	37C–39C–41H	–	111
75	37C–39C–42H	–	109
76	41H–39C–42C	–	112
77	39C–42C–43H	–	112
78	39C–42C–44O	111	111
79	39C–42C–46C	103	103
80	43H–42C–44O	–	110
81	43H–42C–46C	–	111
82	44O–42C–46C	106	106
83	42C–44O–45H	–	107
84	42C–46C–47H	–	106
85	24C–52C–53H	–	106
86	37C–52C–46C	103	105
87	37C–52C–53H	–	109
88	46C–52C–53H	–	107

Table 2
(Continued)

S. No.	Loganin parameter bond angle	X-ray (in degree)	Calculated B3LYP/6-311G (d, p) (in degree)
89	42C–46C–48C	114	115
90	42C–46C–52C	101	104
91	47H–46C–48C	–	109
92	47H–46C–52C	–	108
93	48C–46C–52C	115	115
94	46C–48C–49H	–	111
95	4C–48C–50H	–	110
96	46C–48C–51H	–	110
97	49H–48C–50H	–	108
98	49H–48C–51H	–	107
99	50H–48C–51H	–	107
100	24C–52C–37C	113	113
101	24C–52C–46C	114	114

Note: Experimental data is taken from [15].

and their corresponding energies (Table 6) have been given as the supplementary material. After finding out the most stable geometry the calculations were carried out by DFT method with a higher basis set. The calculations converged to optimized geometries, which correspond to the true energy minima, as also revealed by the lack of imaginary frequencies in the vibrational mode calculation. Subsequently, the local minimum energy obtained for loganin with 6-311G (d, p) basis set was found approximately to be -1415.690 A.U. In case of loganin molecule there is C_1 molecular symmetry. The dihydropyran ring is in sofa conformation with C_1 out of plane with the other atom. The torsion angles in the ring show a mean absolute deviation of 4° than the ideal sofa. The torsion angles in $C(1)–O(2)–C(3)–C(4)$ is negative and glucosyloxy group is in the quasiaxial position [6]. Experimental data is taken from the literature [15]. Nearly all the calculated bond lengths match well with the experimental values. For example, the optimized bond length of C–C in ring R3, falls in the range from 1.56 to 1.54 Å, which is in good agreement with those of the experimental bond length (1.550–1.520 Å). In the ring, carbon–carbon bond length is not the same (same type of hybridization) and this is due to the antibonding repulsion occurring between carbon and oxygen atom present in the ring and also the group attached to the ring. To achieve molecular stability, the strain was minimized and consequently, some bond length got enlarged and some bond lengths were contracted. The optimized bond length of C–O in ring R2 and R3 falls in the range from 1.358 to 1.437 Å, which is also in good agreement with the experimental bond lengths (1.357–1.442 Å). The other calculated bond length also show an excellent agreement with the experimental value. However, by allowing the relaxation of all parameters, some intermolecular interaction, and (hydrogen bonding) affects the bond angle and bond length so a comparison of calculated and experimental result gave important information about the intermolecular forces.

In case of loganin, there are four intermolecular hydrogen bonding interactions between $21O \dots 15O–16H$, $15O \dots 19O–20H$, $44O \dots 22H–21O$, $23O \dots 45H–44O$ which have been taken from the crystallographic data [15]. In general, bond between carbon and oxygen are overestimated but at the position where hydrogen bonding occurs, the bond between oxygen and carbon is underestimated, e.g., bond length where there is no hydrogen bonding are $C24–O26$, $O26–C27$, $C30–O31$, $C30–O36$ and is found to be 1.432, 1.357, 1.341 and 1.197 Å, respectively, and in case of experimental data corresponding

Fig. 2. Model molecular structure of loganin (conformer 19). (Colors are visible in the online version of the article; <http://dx.doi.org/10.3233/SPE-2011-0517>.)

calculated bond lengths are 1.437, 1.358, 1.358 and 1.218 Å (Table 5 of Supplementary material; see <http://www.mediafire.com/?mdls5a5nueyi74i>). Whereas, in places where hydrogen bonding occurs, the bond length between 23O–9C, 23O–1C, 15O–3C, 44O–42C, 21O–11C was found to be 1.442, 1.433, 1.419, 1.439, 1.418 Å and their corresponding calculated values are 1.434, 1.421, 1.414, 1.430 and 1.414 Å using B3LYP/DFT method. In experimental data refinement proceed to $R = 0.11$ (isotropic) and $R = 0.08$ (anisotropic), at which stage all H atom were revealed by different synthesis [15]. In final stages C–H distance were fixed at 0.96 Å and H–C–H angle at 109.5° [15]. As revealed by the Gauss view, no ring lies in plane and also, a single hydrogen atom of each methyl unit lies in the plane of adjacent ring while the other two are symmetrically positioned above and below the plane of adjacent ring. The methyl group is attached with the R3 ring and the C–H bond length which is in the plane and is smaller than the other which is nonplanar, e.g., bond length in between carbon and hydrogen which are nonplanar are 48C–49H, 48C–51H and it is 1.095 and 1.095 Å, respectively. While bond length between carbon and hydrogen (in case of CH₃ which is attached to ring R3), in plane is 1.092 Å. Since, there is a large deviation from the experimental bond length X–H, i.e, bond length arising from low scattering factor of hydrogen atom in X-ray diffraction experiment hence, we have not discussed the C–H bond

length. Several authors have reported that B3LYP method predicts bond length, which is systematically too large, particularly C–H bond lengths [24,27,28].

The angular changes in benzene ring geometry have also proved to be a sensitive indicator of the interaction between the substituent and the benzene ring [19]. The structural changes in the carbon skeleton involve both, the bond distances and bond angles. They are most pronounced at the place of substitution and depend on the electro negativity as well as on the σ/π donor/acceptor character of the substituent. The bond distances have already been discussed above and now the bond angles needs to be discussed.

The calculated substituent impact on the C–C–C bond angles of the benzene ring is summarized in Table 2. The data reflects the well-known trends observed for various substituents: groups with π -acceptor substituent tend to increase in α_{ipso} , decrease α_{ortho} and this results in a small increase in α_{para} , e.g., in the title molecule the bond angle between C37–C29–C27; C29–C37–C52; and C37–C52–C24 are 122.21°; 111.62° and 113.0° and their corresponding experimental data are at 123.2°; 112.3° and 113.1°, respectively, which are found to be in good agreement. Another feature concerning the bond angle between carbon and hydrogen in methyl group is that the bond angle which lies in a plane is different from the one which lies out of plane so methyl group gets distorted from the regular tetrahedral shape, e.g., bond angle between in plane carbon and hydrogen (34H–32C–35H, 50H–48C–49H) are 108.6°, 108.7° and the corresponding out of plane, 33H–32C–35H, 33H–32C–34H and 50H–48C–51H, 51H–48C–49H are 107.8°, 107.15° and 110.7°, 110.7° respectively calculated by B3LYP/6-311G (d, p).

4.2. Vibrational assignments

The molecule under study has 53 atoms and 153 normal modes of fundamental vibration. Out of 153 normal modes, $N - 1$ modes correspond to the stretching modes and remaining are bending modes. All the modes are divided into two parts: one corresponding to below 1000 cm^{-1} called the finger print region and the other corresponding to the above 1000 cm^{-1} called the functional group region. The assignments of the experimental wavenumbers are based on an animated view of normal mode description and a comparison with the theoretically scaled ones as listed in the Table 3. It needs to be emphasized that the calculated frequencies represent vibrational signatures of the molecules in its gas phase. Hence, the experimentally observed spectra of the solid/liquid samples may differ to some extent from the calculated spectrum. Moreover, the calculated harmonic force constants and frequencies are usually higher than the corresponding experimental quantities; due to combination of electron correlation effect [33] and basis set deficiencies. This is the reason for using scaling factors for theoretical calculations. Nevertheless, after applying the uniform scaling factor the theoretical calculation reproduce the experimental data well. The observed slight disagreement between the theory and the experiment could be a consequence of the anharmonicity [34] and of the general tendency of the quantum chemical methods to overestimate the force constants at the exact equilibrium geometry. The experimental FT-IR spectra are shown in Fig. 1. Vibrational frequencies at B3LYP/6-311G (d, p) level were scaled by 0.9682 above 800 cm^{-1} and 1.0119 below 800 cm^{-1} [29].

A good agreement between the theoretical and experimental wavenumbers for the majority of bands is evident. Some important modes of vibrations are discussed which are as follows.

4.3. Carbonyl absorption

Carbonyl absorptions are sensitive and both the carbon and oxygen atoms of the carbonyl group move during the vibration having nearly equal amplitude. In the present study a highly intense polarized IR

Table 3

Vibrational wavenumbers obtained for loganin at B3LYP/6-311G (d, p) in cm^{-1} , experimental frequencies from FT-IR spectra in cm^{-1} , IR intensities ($\text{K}_m \text{mol}^{-1}$) and assignment

S. No.	Wavenumber		Experimental	IR	Assignment
	Unscal.	Scal.	frequencies IR	intensity	
1	15	15		0.014	Twisting in Ring R1 and R2 with respect to 14O
2	20	20		0.031	Twisting in Ring R1 and R2 with respect to 14O
3	34	34		0.063	Twist ring R3 with respect R2
4	40	40		0.296	All ring bend
5	59	59		1.826	Twist(O-CH ₃)adjR2 + $\tau(\text{CC})\text{R1}$, R2&R3
6	63	63		0.216	Twist(O-CH ₃)adjR2
7	73	73		0.288	$\gamma(\text{CO})\text{adjR2R1}$ + $\tau(\text{CC})\text{R1}$, R2&R3
8	96	96		4.877	Twist(O-CH ₃)adjR2 + twist(CH ₃ OH)adjR1
9	106	107		1.697	R(C-O-C)R3 + R(CH ₂)R3 + $\gamma(\text{O-CH}_3)\text{adjR2}$ + $\gamma(\text{C-O})\text{adjR1}$ + $\gamma(\text{C-COH3})\text{adjR1}$
10	109	110		0.5748	Twist(O-CH ₃)adjR2 + $\gamma(\text{CCC})\text{R1}$ + $\gamma(\text{CO})\text{adjR1}$
11	118	119		3.131	Twist(O-CH ₃)adjR2 + (C-CH ₂ OH)adiR1
12	125	126		1.264	$\tau(\text{CC})\text{R1}$, R2&R3 + twist(O-CH ₃)adjR2
13	133	134		1.066	Twist(O-CH ₃)adjR2
14	151	152		0.179	R(CH ₂)R3 + $\gamma(\text{CCC})\text{R3}$ + $\gamma(\text{COC})\text{R1}$ + $\gamma(\text{C-CH}_3)\text{adjR3}$
15	173	175		1.035	Ring R1 breathing + Ring R2&R3 bending with respect to 14O
16	183	185		2.065	$\gamma(\text{C-O-CH}_3)\text{adjR2}$ + $\tau(\text{C-COH}_3)\text{adjR1}$
17	193	195		0.296	$\tau(\text{CO})\text{adjR3\&R2}$ + $\tau(\text{CC})\text{R2}$, R3&adjR2&R3 + $\gamma(\text{OH})\text{R1}$
18	205	207		2.071	Twist(C-CH ₃)R3 + $\gamma(\text{O-H})\text{adjR1}$
19	216	218		3.055	Twist(C-CH ₃)R3
20	254	257		8.740	S(C-C-O)R1 + $\gamma(\text{CCC})\text{R1}$
21	261	264		2.005	$\beta(\text{C-CH}_3)\text{adjR3}$ + $\beta(\text{O-H})\text{adjR3}$
22	265	268		17.59	$\gamma(\text{O-H})\text{R3}$ + S(CCC)R1
23	272	275		7.306	$\gamma(\text{C-O-C})\text{R2}$ + $\gamma(\text{O-H})\text{R3}$
24	289	292		86.22	$\gamma(\text{O-H})\text{R3}$
25	294	297		24.715	$\gamma(\text{C-CH}_3)\text{adjR3}$ + $\gamma(\text{C-O-C})\text{R1}$ + $\gamma(\text{OH})\text{R1}$ adjR3 + $\gamma(\text{CH})\text{R1}$
26	304	307		3.518	$\beta(\text{C-CH}_3)\text{adjR3}$ + $\gamma(\text{COC})\text{R1}$ + $\beta(\text{OH})\text{adjR1\&R3}$ + $\beta(\text{CH})\text{adjR1}$
27	321	324		9.321	Ring R3 breathing + $\gamma(\text{O-CH}_3)\text{R3}$
28	333	336		25.76	$\beta(\text{C-CH}_3)\text{adjR2}$ + $\beta(\text{C-C-O})\text{R2}$
29	345	349		13.835	Ring breathing R1 + $\gamma(\text{O-H})\text{R1}$
30	361	365		4.800	$\gamma(\text{O-H})\text{adjR1}$
31	383	387		34.437	$\gamma(\text{O-H})\text{adjR1}$ + R(CH ₂)R3 + $\gamma(\text{CCC})\text{R2}$
32	384	388		32.19	R(CH ₂)R3 + $\gamma(\text{OH})\text{R1}$ adjR1 + $\gamma(\text{CH})\text{R2}$
33	400	404		83.931	$\gamma(\text{C-H})\text{R1}$
34	418	422		59.959	Ring R1 breathing + $\beta(\text{O-H})\text{adjR1}$ + $\gamma(\text{CCC})\text{R2}$ + R(CH ₂)R3
35	420	424		35.999	$\gamma(\text{O-H})\text{adjR1}$ + R(CH ₂)R3 + $\beta(\text{CCC})\text{R1}$ + $\gamma(\text{CCC})\text{R2}$
36	427	432		61.548	$\gamma(\text{C-H})\text{R1}$ + ring R1 breathing
37	459	464		7.953	Ring R1, R2&R3 bend + $\beta(\text{O-H})\text{adjR1}$ + R(CH ₂)R3
38	465	470		3.867	oopring R2 bend + ring R1 breathing + $\gamma(\text{OH})\text{adjR1}$ + S(CCO)R2
39	473	478		72.049	Ring bend R1 + $\beta(\text{O-H})\text{R1}$
40	482	487		106.199	$\gamma(\text{O-H})\text{R1}$ + $\gamma(\text{C-H})\text{R1}$
41	521	527		14.315	Ring R1 breathing + ring R2 bend + $\beta(\text{C-CH}_3)\text{adjR3}$
42	536	542		3.393	Ring R2, R1&R3breathing + $\beta(\text{OH})\text{adjR1}$ + $\beta(\text{C-H})\text{adjR1}$

Table 3
(Continued)

S. No.	Wavenumber		Experimental frequencies	IR intensity	Assignment
	Unscal.	Scal.	IR		
43	546	552	550	0.450	$\gamma(\text{CCC})\text{R2} + \omega(\text{CH}_2)\text{adjR3}$
44	571	577	580	25.365	Ring breathing + $\omega(\text{CH}_3)\text{adjR2}$, R3
45	604	611	615	15.112	Ring R1 breathing + $\beta(\text{O-H})\text{adjR1} + \beta(\text{C-H})\text{adjR1}$
46	619	626		4.494	Ring R2 breathing + $\gamma(\text{CCC})\text{R2} + \text{R}(\text{CH}_2)\text{adjR1} + \beta(\text{C-H})\text{adjR1\&R2}$
47	634	641	630	7.140	Bending in R3 + $\text{R}(\text{CH}_2)\text{R3}$
48	648	655	645	24.447	Breathing in R1 + $\beta(\text{O-H})\text{adjR1} + \beta(\text{C-H})\text{adjR1}$
49	672	679	665	7.813	Ring R2\&R3 breathing + $\gamma(\text{CCC})\text{R3} + \beta(\text{O-H})\text{adjR1} + \beta(\text{C-H})\text{adjR1}$
50	701	709	720	0.317	$\beta(\text{CCC})\text{R2R3} + \text{R}(\text{CH}_2)\text{R3} + \beta(\text{CO})\text{adjR2}$
51	755	763	745	14.198	$\gamma(\text{C-CO}_2)\text{adjR2} + \text{Ring bend R2}$, R3
52	766	775		9.512	Ring bend R2 + $\gamma(\text{C-CO}_2)\text{adjR2}$
53	793	802		5.857	Ring R1, R2 bending + $\text{S}(\text{CO}_2)\text{adjR3}$
54	836	809	800	14.715	Bending R2, R3 + $\tau(\text{CH}_2)\text{R3}$
55	858	830		6.775	Ring R2, R3 bending + $\text{R}(\text{CH}_2)\text{R3} + \omega(\text{CH}_3)\text{R3}$
56	878	850	852	70.412	$\beta(\text{C-H})\text{R2\&R3} + \nu(\text{CO})\text{R2} + \nu(\text{CC})\text{R2R3} + \omega(\text{CH}_3)\text{R3} +$
57	897	868		13.258	$\beta(\text{C-H})\text{R1} + \text{R}(\text{CH}_2)\text{adjR1} + \gamma(\text{C-H-O})\text{R1}$
58	904	875		15.131	Ring R3 bend + $\text{R}(\text{CH}_3)\text{adjR1} + \tau(\text{CH}_2)\text{R3}$
59	912	882	890	85.186	$\gamma(\text{CCC})\text{R3} + \gamma(\text{C-H})\text{R3} + \text{R}(\text{CH}_3)\text{R3} + \text{R}(\text{CH}_2)\text{R3}$
60	939	909		12.226	$\gamma(\text{CH})\text{R2}$
61	973	942	943	51.100	$\nu(\text{CH}_3\text{-O})\text{adjR2} + \text{Ring breeding R2}$, R3
62	987	955		23.572	$\omega(\text{CH}_3)\text{R3} + \beta(\text{CCC})\text{R3} + \beta(\text{CH})\text{R3}$
63	996	964		120.111	Ring breathing R1
64	1005	973		20.279	$\nu(\text{O-CH}_3)\text{adjR1} + \text{ring bend} + \text{R}(\text{CH}_3)\text{R3}$
65	1017	984		41.175	$\beta(\text{CO})\text{adjR1} + \text{bending in R1}$
66	1031	998	990	98.574	$\nu(\text{CO})\text{R1} + \nu(\text{CC})\text{R1} + \beta(\text{O-H})\text{adjR1} + \beta(\text{C-H})\text{adjR1} + \gamma(\text{CCC})\text{R2\&R3} + \text{R}(\text{CH}_2)\text{R3}$
67	1040	1006		27.608	$\gamma(\text{CO})\text{R1} + \nu(\text{CC})\text{R3} + \gamma(\text{CH})\text{R1} + \gamma(\text{CC})\text{R1}$
68	1056	1022		75.666	$\gamma(\text{CC})\text{R3 R1} + \text{bending in R2}$
69	1063	1029		220.491	Ring breathing R2, R3 + $\nu(\text{O-CH}_2)\text{adjR1} + \text{bending R1}$
70	1069	1035		118.528	$\beta(\text{O-H})\text{adjR1} + \text{bending R1}$
71	1075	1040		77.439	$\beta(\text{O-H})\text{adjR1} + \nu(\text{CO})\text{R1} + \text{bending R1}$
72	1085	1050	1040	247.071	$\text{S}(\text{COC})\text{adjR1} + \text{R}(\text{CH}_2)\text{adjR1} + \gamma(\text{CH})\text{R3}$
73	1098	1063		104.792	$\gamma(\text{O-C-C})\text{R1} + \tau(\text{CH}_2)\text{R3} + \beta(\text{OH})\text{R2 R3}$
74	1101	1065		197.857	Ring breathing + $\nu(\text{C-CH}_3)\text{R3}$
75	1107	1071		9.0008	$\nu(\text{C-CH}_3)\text{R3} + \beta(\text{C-H})\text{R2\&R3} + \nu(\text{C-OH})\text{adjR1}$
76	1118	1082	1083	41.897	$\nu(\text{CO})\text{R1 adjR1} + \beta(\text{HO})\text{R1} + \nu(\text{CC})\text{R1}$
77	1122	1086		96.415	$\nu(\text{CC})\text{R1} + \nu(\text{C-CH}_3)\text{R3} + \nu(\text{O-CH}_3)\text{R1} + \beta(\text{CH})\text{R3} + \gamma(\text{CCC})\text{R3}$
78	1130	1094		80.320	$\nu(\text{O-CH}_3)\text{adjR2} + \nu(\text{CC})\text{R1} + \text{ring bend R2}$
79	1135	1098		92.081	$\nu(\text{CC})\text{R1} + \text{ring bending R1}$
80	1148	1111	1105	69.213	$\beta(\text{OH})\text{adjR1} + \nu(\text{CC})\text{R3} + \beta(\text{C-CH}_3)\text{R3}$
81	1151	1114		62.674	$\beta(\text{CH})\text{R3R2} + \text{ring R1 bend} + \nu(\text{C-CH}_3)\text{R2}$
82	1158	1121		11.173	$\beta(\text{CH})\text{R3R2} + \omega(\text{CH}_3)\text{adjR3} + \text{t}(\text{CH}_2)\text{R1}$
83	1172	1134	1122	67.610	Ring bend R1 + $\beta(\text{CH})\text{adjR3R2} + \gamma(\text{CH})\text{R3}$

Table 3
(Continued)

S. No.	Wavenumber		Experimental frequencies	IR intensity	Assignment
	Unscal.	Scal.	IR		
84	1178	1140		0.572	$\omega(\text{CH}_3)\text{adjR2}$
85	1192	1154	1150	18.220	$\beta(\text{CH})\text{adjR3R2}$ and $\text{R1R3} + \beta(\text{OH})\text{R1}$
86	1202	1163		10.924	$\beta(\text{CH})\text{adjR3R2}$ and $\text{R1R3} + \beta(\text{OH})\text{R1}$
87	1207	1168	1170	111.894	$\nu(\text{CO})\text{R2} + \omega(\text{CH}_3)\text{adjR2} + \beta(\text{CH})\text{adjR3}$, R2 and R1
88	1213	1174		3.331	$\omega(\text{CH}_3)\text{adjR2} + \text{t}(\text{CH}_2)\text{R3}$
89	1216	1177		29.455	$\omega(\text{CH}_3)\text{R2} + \text{t}(\text{CH}_2)\text{R3} + \beta(\text{CH})\text{adjR3}$, R2
90	1232	1192		15.816	$\beta(\text{CH})\text{R1} + \text{ring R1 bending} + \beta(\text{OH})\text{adjR1}$
91	1248	1208	1190	32.748	$\text{t}(\text{CH}_2)\text{adjR1} + \beta(\text{OH})\text{adjR1} + \beta(\text{CH})\text{R1}$
92	1277	1236		55.784	$\beta(\text{OH})\text{adjR1} + \beta(\text{CH})\text{R3}$
93	1280	1239		13.299	$\beta(\text{OH})\text{adjR1} + \beta(\text{CH})\text{R1 adjR1}$
94	1289	1248		1.455	$\beta(\text{CH})\text{adjR2}$, R3 and R3
95	1302	1260	1250	85.053	$\beta(\text{OH})\text{adjR1} + \beta(\text{CH})\text{R1}$
96	1310	1268		10.485	$\beta(\text{CH})\text{adjR2}$, $\text{R3} + \omega(\text{CH}_2)\text{R2}$
97	1314	1272		6.435	$\beta(\text{OH})\text{adjR1} + \beta(\text{CH})\text{R1}$
98	1320	1278		94.621	$\nu(\text{CC})\text{adjR2} + \text{ring bend R2}$, $\text{R3} + \gamma(\text{CH})\text{R3}$
99	1324	1281	1270	289.885	$\beta(\text{CH})\text{adjR3R2} + \text{bending R2} + \nu(\text{CC})\text{R2}$
100	1336	1293	1295	14.397	$\beta(\text{CH})\text{R1}$
101	1345	1302		13.893	$\beta(\text{CH})\text{R2}$ and R2 , R3
102	1352	1309		6.439	$\beta(\text{OH})\text{adjR} + \beta(\text{CH})\text{R1}$, R3 and R2 , R3 , R1
103	1367	1323		18.785	$\beta(\text{CH})\text{R1}$, $\text{R3 adjR1} + \beta(\text{OH})\text{adjR1} +$
104	1376	1332	1334	42.011	$\beta(\text{CH})\text{R1}$, R2 , $\text{R3 adjR1} + \beta(\text{OH})\text{adjR1}$
105	1385	1340		10.029	$\beta(\text{CH})\text{R1}$, $\text{R3} + \beta(\text{OH})\text{adjR1}$
106	1390	1345		4.716	$\beta(\text{CH})\text{R1} + \beta(\text{OH})\text{adjR1}$
107	1394	1349		21.453	$\beta(\text{CH})\text{R1 adjR1} + \beta(\text{OH})\text{R1}$
108	1397	1352		14.565	$\beta(\text{CH})\text{R1}$, $\text{R2 adjR1} + \beta(\text{OH})\text{adjR1}$
109	1399	1354		15.495	$\beta(\text{CH})\text{R1}$, $\text{R2 adjR1} + \beta(\text{OH})\text{adjR1}$
110	1407	1362		22.477	$\gamma(\text{CH})\text{R2} + \beta(\text{CH})\text{adjR1} + \text{S}(\text{OCH})\text{R2}$
111	1415	1370		3.630	$\gamma(\text{CH})\text{R2}$, R1 , $\text{R3} + \text{S}(\text{CH}_3)\text{R3}$
112	1419	1373	1373	33.415	$\gamma(\text{CH})\text{R1} + \nu(\text{C}-\text{CH}_3)\text{R3}$, R1
113	1427	1381		12.055	$\gamma(\text{CH})\text{R2}$, $\text{R1} + \nu(\text{CC})\text{R3}$, $\text{R1} + \nu(\text{C}-\text{CH}_3)\text{R3} +$
114	1429	1383		34.486	$\gamma(\text{CH})\text{R1} + \text{S}(\text{CH}_3)\text{adjR3}$
115	1430	1384		13.143	$\text{S}(\text{CH}_3)\text{adjR3} + \gamma(\text{CH})\text{R1} + \beta(\text{OH})\text{R1}$
116	1440	1394		33.696	$\omega(\text{CH}_2)\text{adjR1} + \beta(\text{OH})\text{adjR1} + \beta(\text{OH})\text{R2}$
117	1446	1400		2.664	$\gamma(\text{CH})\text{R1} + \beta(\text{CH})\text{R2}$
118	1472	1425	1410	8.021	$\beta(\text{CH}) + \beta(\text{CO})\text{R1}$
119	1482	1434	1425	24.256	$\text{S}(\text{CH}_3)\text{adjR2}$
120	1491	1443		3.592	$\text{S}(\text{CH}_2)\text{R3}$
121	1494	1446	1440	5.678	$\text{S}(\text{CH}_3)\text{adjR2}$
122	1509	1461		4.953	$\beta(\text{CH}_3)\text{adjR3}$
123	1511	1462		7.015	$\text{S}(\text{CH}_2)\text{adjR2}$
124	1515	1466		0.791	$\text{S}(\text{CH}_3)\text{adjR1}$
125	1517	1468		4.561	$\text{S}(\text{CH}_3)\text{adjR3}$
126	1603	1644	1600	142.5	$\nu(\text{CC})\text{R2}$
127	1783	1726	1710	250.7	$\nu(\text{CO})\text{adjR2}$

Table 3
(Continued)

S. No.	Wavenumber		Experimental frequencies IR	IR intensity	Assignment
	Unscal.	Scal.			
128	2927	2833		30.57	$\nu(\text{CH})\text{R1 adjR1}$
129	2960	2865		30.318	$\nu(\text{CH})\text{R1 adjR1}$
130	2999	2903		31.336	$\nu(\text{CH})\text{R1 adjR1}$
131	3000	2904		32.867	$\nu(\text{CH})\text{R1}$
132	3002	2906	2900	61.338	$\nu(\text{CH})\text{R3}$
133	3020	2923	2912	43.307	$\nu(\text{CH})\text{R1}$
134	3030	2933	2940	19.196	$\nu(\text{CH})\text{R3}$
135	3048	2951	2958	26.034	$\nu(\text{CH}_2)\text{adjR3}$
136	3062	2964		41.096	$\nu(\text{CH}_3)\text{adjR2}$
137	3072	2974		29.165	$\nu(\text{CH}_2)\text{R3}$
138	3080	2982		22.367	$\nu(\text{CH})\text{R1}$
139	3082	2983		4.570	$\nu(\text{CH})\text{R2}$
140	3096	2997		10.272	$\nu_{\text{as}}(\text{CH}_3)\text{adjR3} + \nu(\text{CH})\text{R2}$
141	3102	3003		28.561	$\nu_{\text{as}}(\text{CH}_3)\text{adjR3} + \nu(\text{CH})\text{R2}$
142	3109	3010		34.194	$\nu_{\text{as}}(\text{CH}_2)\text{R3} + \nu(\text{CH})\text{R2}$
143	3117	3017		22.469	$\nu_{\text{as}}(\text{CH}_2)\text{R3}$
144	3121	3021	3030	21.447	$\nu(\text{CH})\text{adjR1}$
145	3138	3038		20.707	$\nu(\text{CH})\text{adjR1}$
146	3139	3039		16.856	$\nu_{\text{as}}(\text{CH})\text{R3}$
147	3171	3070		16.372	$\nu_{\text{as}}(\text{CH}_3)\text{adjR2}$
148	3237	3134		02.022	$\nu(\text{CH})\text{R2}$
149	3773	3653	3520	39.715	$\nu(\text{OH})\text{R2}$
150	3776	3655		10.52	$\nu(\text{OH})\text{adjR1}$
151	3796	3675	3625	40.28	$\nu(\text{OH})\text{adjR1}$
152	3801	3680	3685	28.14	$\nu(\text{OH})\text{adjR1}$
153	3886	3699		18.89	$\nu(\text{OH})\text{R3}$

Notes: ν – stretching; ν_{s} – symmetric stretching; ν_{as} – asymmetric stretching; β – in-plane-bending; γ – out-of-plane bending; ω – wagging; R – rocking; t – twisting; τ – torsion, s – scissoring.

peak appears due to C=O stretching in the plane of the ring R2 and is observed at 1726 cm^{-1} , which is in good agreement with the experimental frequency obtained at 1710 cm^{-1} .

4.4. C–H vibrations

The change in the frequency also reflects the change in the geometry. Significant changes in frequency and intensity take place in the H–X stretching vibration. As the magnitude of the shift in H–X stretching vibrational frequency is known to represent a measure of the intermolecular interaction, the difference in frequency is in good agreement with the interaction energy. The hetero aromatic structure shows the presence of C–H stretching vibrations in the region $2800\text{--}3100\text{ cm}^{-1}$, which is the characteristic region for the ready identification of the C–H stretching vibration [41]. In the present study the C–H stretching vibration of the title compound is observed at 2923 and 2906 cm^{-1} , which are in good agreement with the calculated frequencies obtained at 2912 and 2900 cm^{-1} . Some other C–H stretching vibrations are also calculated at 2933 , 2904 , 2865 and 2833 cm^{-1} , which are also supported by the literature [22]. Some bending vibrations of C–H are also calculated and supported by literature. At lower frequency

region some significant intensity peaks of polarized IR due to out of plane bending in C–H are also observed.

4.5. Methylene group vibrations

The asymmetric CH₂ stretching vibrations are generally observed in the region 3100–3000 cm⁻¹, while the symmetric stretching vibrations are generally observed between 3000–2900 cm⁻¹ [22]. The CH₂ asymmetric stretching vibrations are calculated at 3010 and 3017 cm⁻¹, whereas CH₂ symmetric stretching vibrations are also calculated at 2951 and 2974 cm⁻¹. The bands corresponding to different bending vibrations of CH₂ group are summarized in Table 3 and are supported by the literature [22]. An intense IR band occurred at 1121, 1174, 1177 and 1208 cm⁻¹, due to the twisting of CH₂ in R3. Generally, twist occurs in the low frequency region but due to the hinging of ring R3 by R2 and also the spatial arrangement of molecule in plane which is disturbed by the twist in the planarity, it occurs in some higher region.

4.6. C–C vibrations

The C–C aromatic stretch known as semi-circle stretching, is calculated at 1644, 1281, 1278, 1114, 1111, 1098 cm⁻¹ etc., respectively, and is supported by the literature [23]. The theoretically calculated C–C–C bending modes and C–C torsional modes have also been found to be consistent with the recorded spectral values and the literature [23].

4.7. Methyl group vibrations

The asymmetric CH₃ stretching vibrations are calculated at 2997, 3003 and 3070 cm⁻¹, while symmetric CH₃ stretching vibrations are calculated at 2964 cm⁻¹. These assignments are also supported by the literature [40]. In the present study various bending vibrations of CH₃ group are also summarized in Table 3 and are supported by the literature [40].

4.8. C–O vibrations

In this study the C–O stretching vibrations are observed at 990, 1083 and 1170 cm⁻¹, which are in good agreement with the calculated frequencies obtained at 998, 1082 and 1168 cm⁻¹, respectively. The various bending and torsional vibrations assigned in this study are also supported by the literature [7]. A lot of discrepancies observed between experiment and theory are due to the intermolecular hydrogen bonding. Some mixing of different modes of vibration along with C=O plane and out of plane bending is also observed in the lower side of spectra.

4.9. O–H vibrations

In vibrational spectra, the strength of hydrogen bond determines the position of O–H band. Usually, the O–H stretching appears at high frequency ranging from 3600–3400 cm⁻¹ [20] because of lower reduced mass. In this study, loganin showed very strong absorption peaks at 3699, 3680, 3675, 3655 and 3653 cm⁻¹, which is due to the O–H stretching vibration. The observed frequency range is different from experimental one and probably this is due to the low scattering factor for hydrogen and also the intermolecular interaction occurring in the molecule which overestimates the stretching modes. The various bending vibrations of the hydroxyl groups are also found to be in good agreement with the observed spectra and literature [20].

4.10. C-group attached out of ring

Vibration belonging to the bond between ring and other groups are also important as mixing of vibration is possible due to the presence of heavy atom which shows lower absorption frequencies as compared to C–H, due to the increase reduced mass [21]. C–C stretching in (C–CH₃) is calculated at 1071 cm⁻¹ and 1086 cm⁻¹, in ring R3 and O–CH stretching is observed at some lower modes than the previous ones due to the higher reduced mass.

5. Conclusion

Equilibrium geometries and harmonic frequencies of loganin were determined and analyzed at DFT/B3LYP level of theory using 6-311G (d, p) basis set. The vibrational frequency calculations proved that the structure is stable (no imaginary frequencies). We found the geometry obtained by the B3LYP method to be very accurate. The difference between the observed and scaled wavenumbers values of most of the fundamentals is very small. Any discrepancy noted between the observed and the calculated frequencies may be due to the fact that the calculations have been actually done on a single molecule in the gaseous state contrary to the experimental values recorded in the presence of intermolecular interactions. Some intensity of lower modes do not match well and presumably, this is due to the inherent impurity of the sample, packing fraction (molecular–molecular interaction), modes of vibrations are so near that it is difficult task to identify these modes as they look like a band and also the basis set deficiencies, anharmonicity can be held responsible for it.

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