ISSN 2347-3487

Vibrational Spectra, Electronic Structure and Properties of the Molecules Aspirin and Ibuprofen.

Geh Wilson Ejuh[1], Nouemo Samuel[2], Chifu Ebenezar Ndikilar[3], Fridolin Tchangnwa Nya[4], and Ndjaka Jean Marie[5]
1 Univeristy of Dschang, I.U.T-FV Bandjoun, Department of General and Scientific Studies.
2 University of Yaoundé I, Faculty of science, Department of physics.
3 Federal University of Dutse, Nigeria, Faculty of Science, Department of Physics.
4 University of Maroua, Faculty of science, Department of physics.
5 University of Yaoundé I, Faculty of science, Department of physics.

ABSTRACT

The FT-IR Vibrational spectra analysis, electronic structures and properties of the anti-inflammatory drugs Aspirin and Ibuprofen in gas and water and ethanol have been studied by using ab initio and DFT computational calculation. The present investigation deals with the analysis of structural and bonding features responsible for biological activities, stability of the molecules, average polarizability, anisotropy, energies and the IR vibrational spectra of the molecules. The observed and the calculated vibrational frequencies are found to be in good agreement. The experimental FT-IR spectra also coincide satisfactorily with those of the theoretically constructed line spectra at the B3LYp/6-31+G* level of theory.

Indexing terms/Keywords

IR vibrational spectra; ab-initio; DFT; electronic structures; polarizability; Aspirin; Ibuprofen.

Academic Discipline And Sub-Disciplines

Physics and Chemistry, Biology

SUBJECT CLASSIFICATION

Physics Subject Classification

TYPE (METHOD/APPROACH)

Theoretical Studies

Council for Innovative Research
Peer Review Research Publishing System
Journal: JOURNAL OF ADVANCES IN PHYSICS
Vol. 10, No. 2
www.cirjap.com , japeditor@gmail.com

INTRODUCTION

Asprin (Acetylsalicylic acid) was first discovered and synthesized in 1897 and named as Aspirin in 1899. It is one of the most widely used therapeutic substances due to its analgesic, anti-inflammatory and antipyretic effect as is its action as an inhibitor of platelet aggregation. Salicin is enzymatically hydrolyzed to saligenin and glucose by β- glucosidase [1,2]. Saligenin is then slowly oxidized to salicylic acid in the blood and in the lever [3]. It was showed that Aspirin interferes with the biosynthesis of prostaglandins [4]. Its mechanism of action was discovered later by [5-7]. The crystal structure of Aspirin was first determined by [8] and was later on refined by [9]. Theoretical modeling of infrared spectra of Aspirin and its deuterated derivative have been studied in gas phase using DFT/B3LYP with the 6-31++G** basis set [10].

Ibuprofen [(RS)-2-(4-isobutylphenyl) propionic acid], is one of the most potent orally active antipyretic, analgesic and nonsteroidal anti-inflammatory drug (NSAID) used extensively in the treatment of acute and chronic pain, rheumatoid arthritis, osteoarthritis and alleviation of fever [11]. It was firstly synthesized by Adams with his colleagues in 1961 and called BTS 13621. It biological activity outstanding among substituted phenylalkane and alkene acids [12,13]. Ibuprofen molecule is flexible due to internal rotations of the propionic acid fragment and the isobutyl group. Ibuprofen contains a chiral carbon atom on the propionic acid side-chain, therefore it exists as two enantiomers. It is usually marketed as a 50:50 mixture of the S- and Renantiomers, even if it is known that the pharmacological activity is due almost exclusively to the S- enantiomer [13].

It was shown by [14] that the conformers' molecular structure and interactions between dissolved drug molecules determine pre-nucleation and nucleation processes. Information on distribution of conformers in a saturated solution might facilitate understanding of the mechanism of formation of one or another crystalline phase. However, in spite of the fact that ibuprofen has been thoroughly studied, information of this kind is absent in the literature. Presence of multiple conformations in fast mutual exchange issues a serious challenge to researchers and requires developing of new ways of analyzing experimental data.

Liu and Gao, 2012 [15] studied the molecular structure and vibrational spectra of ibuprofen using density function theory calculations. In 2014, Massimo et al carried out large-Scale B3LYP Simulations of Ibuprofen Adsorbed in MCM-41 Mesoporous Silica as Drug Delivery System [16]. The Conformational stability of ibuprofen using DFT calculations and optical vibrational spectroscopy was studied by Vueba et al, in 2008 [17].

Although some works have been done on these molecules, yet detail works are required to improve the understanding of their electronic structures, IR vibrational spectra and properties. Hence, the objective of this work is to decipher the molecular properties of the molecules Aspirin and Ibuprofen such as their structures, structural stabilities, dipole moments, polarizability tensors, average polarizability, anisotropy, thermodynamic properties, IR vibrational frequencies and spectra. We also intend to study the effect of different environments on the molecular properties of Aspirin and Ibuprofen since the gas phase results alone are inadequate to understand these properties. This is because in a living organism, these molecules are not in their neutral state, as the presence of solvent (water and ethanol) modifies their structures. Effect of solvation in water and ethanol (alcohol) on their structures need to be investigated.

1. Computational Methodology

The molecular structures and geometries of Aspirin and Ibuprofen were completely optimized by using ab- initio quantum mechanical calculations at the Restricted Hartree-Fock (RHF) level of theory without using any symmetry constraints. Initial geometry optimizations were performed using the ab-initio RHF method with 3-21G basis set. Final calculations were carried out with split valence 6-31+G* basis set with one set of diffuse sp-functions on heavy atoms only and a single d-type polarization function on heavy atoms. The structures were refined further using Density Functional Theory which is a cost effective method for inclusion of electron correlations with the three-parameter density functional generally known as Becke3LYP (B3LYP), which includes Becke's gradient exchange corrections (Becke, 1988) the Lee, Yang and Parr correlation functional [18] and the Vosko, Wilk and Nusair correlation functional [19] with a 6-31+G* basis set. At the first step, geometry optimizations were carried out then, the IR vibrational frequencies were calculated using the Hessian which is the matrix of second derivatives of the energy with respect to geometry.

Since the gas phase results are inadequate for describing the behavior of molecules in solutions, therefore the effect of solvating the molecule in bulk water and ethanol was investigated. For this purpose, the simplest Onsager reaction field model of the self-consistent reaction field (SCRF) theory [20] was used with the 6-31+G** basis set. In this calculation, the solute occupies a fixed spherical cavity within the solvent field. The electric dipole of the solute molecule induces a dipole in the medium and the electric field applied by the induced solvent dipole will interact with the molecular dipole and affect its stabilization.

The optimized molecular structures were tested by computing the second derivatives and checking that all the harmonic vibrational frequencies are found to be real at all level of calculations. All calculations in the present work were performed using Windows version of Gaussian 04 suit [21] of ab initio quantum mechanical program.

3. Results and Discussion

3.1 Optimized Geometric Properties of Aspirin

The geometric parameters of Aspirin molecule in gas phase, water and ethanol are listed in table 1 and its molecular structure is shown in figure 1. The calculated bond lengths and bond angles at RHF/6-31+G* level are slightly smaller than their corresponding values obtained at the B3LYP/6-31+G* level ranging from 0.01Å to 0.03Å and bond angles from 1 to 2 degree. It seems that inclusion of electrons correlation expand the molecules. There is little effect of salvation (water and ethanol) on the bond lengths and the bond angles at RHF/6-31+G* and at B3LYP/6-31+G* levels. The bond lengths and bond angles at the RHF/6-31+G* and at the B3LYP/6-31+G* are approximately equal to the experimental results given by [9]. The bond lengths at the B3LYP/6-31+G* level are in better accord with the experimental results [9] and with the theoretical results obtained by [10] while the bond angles at the RHF/6-31+G* level are in better accord with the experimental results [9] and with the theoretical results obtained by [10].

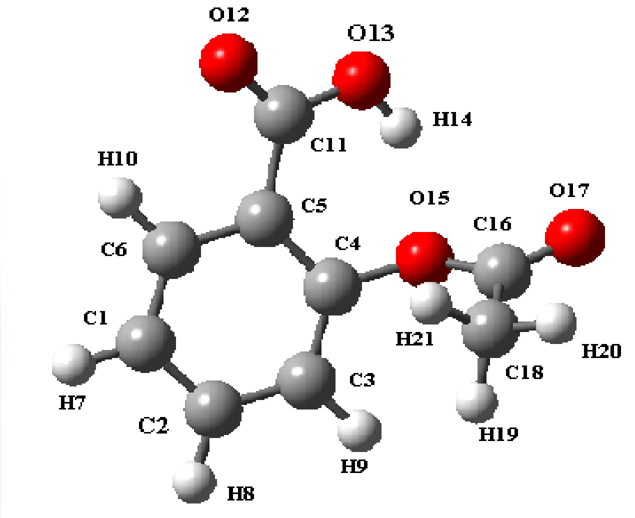

Figure 1: Aspirin

Table 1: Optimized geometrical parameters of Aspirin molecule in Gas phase, water and ethanol obtained at RHF and B3LYP methods by employing 6-31+G* basis sets. Bond Lengths are given in (Å) and Bond Angles are in (˚).

Geomet.		**RHF/6-31+G***			**B3LYP/6-31+G***		
Parameters	**Expt. [9]**	**Gas**	**Water**	**Ethanol**	**Gas**	**Water**	**Ethanol**
R(C1-C2)	1.397	1.388	1.388	1.388	1.399	1.398	1.398
R(C1-C6)	1.394	1.382	1.383	1.383	1.392	1.392	1.392
R(C2-C3)	1.378	1.384	1.385	1.385	1.395	1.396	1.396
R(C3-C4)	1.376	1.384	1.382	1.382	1.394	1.392	1.392
R(C4-C5)	1.376	1.391	1.393	1.393	1.405	1.408	1.408
R(C5-C6)	1.380	1.395	1.395	1.395	1.405	1.406	1.405
R(C5-C11)	1.487	1.509	1.507	1.507	1.511	1.506	1.506
R(C16-C18)	1.481	1.506	1.505	1.505	1.508	1.505	1.505
R(C18-H19)	0.956	1.079	1.083	1.083	1.091	1.091	1.090
R(C18-H20)	0.955	1.083	1.079	1.079	1.095	1.091	1.093
R(C18-H21)	0.952	1.083	1.083	1.083	1.096	1.095	1.095
R(C6-H10)	0.950	1.073	1.073	1.073	1.085	1.085	1.085
R(C2-H8)	0.961	1.075	1.075	1.075	1.086	1.085	1.086
R(C1-H7)	0.969	1.074	1.074	1.074	1.086	1.086	1.085
R(C3-H9)	0.965	1.075	1.074	1.074	1.086	1.085	1.085
R(C4-O15)	1.405	1.376	1.380	1.380	1.399	1.403	1.402

R(C11-O12)	1.239	1.186	1.189	1.188	1.211	1.215	1.214
R(C11-O13)	1.289	1.323	1.325	1.325	1.349	1.353	1.352
R(O15-C16)	1.361	1.364	1.362	1.362	1.401	1.399	1.399
R(C16-O17)	1.191	1.178	1.805	1.180	1.200	1.203	1.203
R(O13-H14)	0.989	0.951	0.952	0.952	0.978	0.981	0.980
R(H14-O15)		1.952	1.897	1.899	1.862	1.796	1.799
A(C2-C1-C6)	119.7	119.6	119.7	119.7	119.8	119.8	119.8
A(C1-C2-C3)	120.4	120.1	120.1	120.1	119.9	120.0	120.0
A(C3-C2-C8)	118.8	119.6	119.5	119.5	119.6	119.5	119.5
A(C2-C3-C4)	119.8	119.6	119.5	119.5	119.5	119.5	119.5
A(C3-C4-C5)	121.2	121.3	121.5	121.4	119.7	121.5	121.6
A(C4-C5-C6)	117.6	118.0	117.9	117.9	117.7	117.5	117.5
A(C4-C5-C11)	125.1	125.3	125.3	125.3	125.5	125.4	125.4
A(C6-C5-C11)	117.4	116.6	116.7	116.7	116.7	116.9	116.9
A(C1-C6-C5)	121.3	121.1	121.2	121.1	121.2	121.3	121.3
A(C2-C1-H7)	120.7	120.3	120.2	120.2	120.2	120.0	120.0
A(C6-C1-H7)	120.5	119.9	120.1	120.1	119.8	120.0	120.0
A(C1-C2-H8)	121.2	120.2	120.3	120.2	110.3	120.4	120.4
A(C2-C3-H9)	121.2	121.1	120.8	120.8	121.1	120.7	120.7
A(C4-C3-H9)	119.0	119.3	119.6	119.6	119.2	119.7	119.7
A(C1-C6-H10)	120.5	120.7	120.6	120.6	121.1	120.9	120.9
A(C5-C6-H10)	118.1	118.1	118.2	118.2	117.5	117.7	117.7
A(C16-C18-H19)		107.6	110.6	110.6	107.8	107.9	107.9
A(C16-C18-H20)		111.0	107.7	107.6	111.2	112.0	112.0
A(C16-C18-H21)		110.9	111.5	111.5	111.1	110.5	110.5
A(C3-C4-O15)	117.2	118.7	119.3	119.3	118.8	118.4	119.7
A(C5-C4-O15)	121.5	119.8	119.1	119.1	119.4	118.4	118.4
A(C5-C11-O12)	122.5	120.9	121.5	121.5	121.5	122.3	122.3
A(C5-C11-O13)	118.0	118.4	118.4	118.4	118.1	118.1	118.1
A(O15-C16-C18)		117.8	118.3	118.3	117.3	118.1	118.1
A(O17-C16-C18)		124.7	124.7	124.6	125.7	125.7	125.6
A(C11-O13-H14)	111.5	113.3	112.8	112.9	111.0	110.3	110.4
A(C4-O15-C16)	119.5	124.0	124.6	124.5	122.8	124.0	124.0
A(O15-C16-O17)	122.4	117.4	116.9	116.9	116.8	116.0	116.1
A(O12-C11-O13)	122.5	120.5	119.9	119.9	120.2	119.4	119.4
A(H19-C18-H20)		109.8	109.1	109.1	109.9	110.2	110.2
A(H19-C18-H21)		109.4	107.8	107.8	109.2	108.4	108.5
A(H20-C18-H21)		107.8	110.0	110.0	107.4	107.4	107.4

3.2 Optimized Geometric properties of Ibuprofen

The geometric parameters of the molecule Ibuprofen in gas phase, water and ethanol are listed in table

2 and its molecule structure is shown in figure 2. The calculated bond lengths and bond angles at RHF/6-31+G* level Are slightly smaller than their corresponding values obtained at the B3LYP/6-31+G* level ranging from 0.01Å to 0.03Å and bond angles from 1 to 2 degree. It seems that inclusion of electrons correlation expand the molecules. There is little effect of solvation (water and ethanol) on the bond lengths and the bond angles at RHF/6-31+G* and at B3LYP/6-31+G* levels. The bond lengths at the RHF/6-31+G* and at the B3LYP/6-31+G* are approximately equal to the experimental results given by [22]. The bond lengths at the RHF/6-31+G* level are in better accord with the experimental results [22].

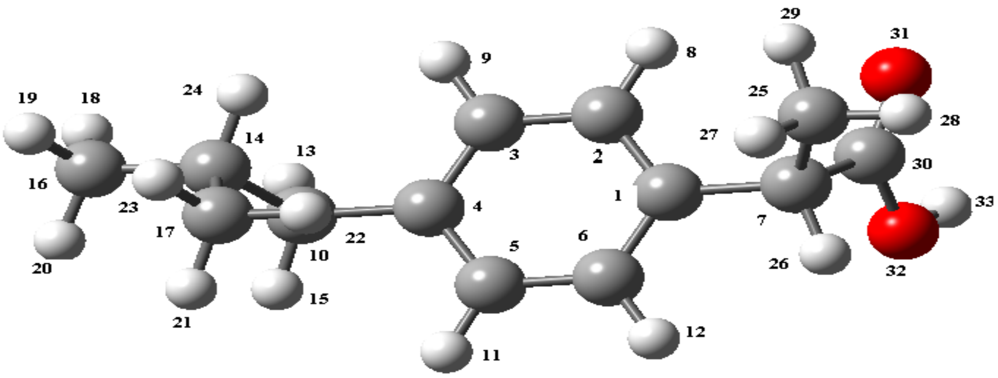

Figure 2- Ibuprofen

Table 2: Optimized geometrical parameters of Ibuprofen molecule in Gas phase, water and ethanol obtained at RHF and B3LYP methods by employing 6-31+G* basis sets. Bond Lengths are given in (Å) and Bond Angles are in (˚).

Geomet.		**RHF/6-31+G***			**B3LYP/6-31+G***		
Parameters	**Exp't. [22]**	**Gas**	**Water**	**Ethanol**	**Gas**	**Water**	**Ethanol**
R(C1-C2)		1.394	1.394	1.394	1.404	1.403	1.403
R(C1-C6)		1.387	1.387	1.387	1.399	1.399	1.399
R(C1-C7)	1.509	1.526	1.526	1.526	1.529	1.529	1.529
R(C2-C3)		1.384	1.384	1.384	1.395	1.395	1.394
R(C3-C4)		1.094	1.394	1.394	1.404	1.404	1.404
R(C4-C5)		1.388	1.388	1.388	1.401	1.401	1.401
R(C4-C10)	1.509	1.515	1.515	1.515	1.525	1.514	1.514
R(C7-C25)	1.509	1.532	1.532	1.532	1.539	1.538	1.538
R(C7-C30)	1.509	1.517	1.517	1.517	1.524	1.523	1.523
R(C10-C14)	1.509	1.542	1.542	1.542	1.551	1.551	1.551
R(C14-C16)	1.509	1.531	1.531	1.531	1.536	1.536	1.536
R(C14-C17)	1.519	1.531	1.531	1.531	1.535	1.535	1.535
R(C2-H8)		1.076	1.076	1.076	1.087	1.087	1.087
R(C3-H9)		1.077	1.077	1.077	1.088	1.088	1.088
R(C5-H6)		1.390	1.389	1.390	1.398	1.398	1.397

R(5-H11)		1.077	1.076	1.076	1.088	1.088	1.088
R(C6-H12)		1.076	1.076	1.076	1.088	1.088	1.088
R(7-H26)	1.092	1.083	1.084	1.084	1.095	1.095	1.095
R(C10-H13)		1.087	1.087	1.087	1.099	1.099	1.099
R(C10-H15)	1.092	1.087	1.087	1.087	1.099	1.099	1.099
R(C14-H24)	1.092	1.089	1.089	1.088	1.101	1.101	1.101
R(C16-H18)	1.092	1.086	1.087	1.086	1.097	1.097	1.097
R(C16-H19)		1.086	1.086	1.086	1.097	1.097	1.097
R(C16-H20)	1.092	1.088	1.087	1.087	1.098	1.098	1.098
R(C17-H21)		1.088	1.088	1.087	1.099	1.099	1.098
R(C17-H22)		1.084	1.084	1.084	1.096	1.095	1.096
R(C17-H23)		1.086	1.086	1.086	1.097	1.097	1.097
R(C25-H27)		1.084	1.084	1.084	1.095	1.095	1.095
R(C25-H28)		1.085	1.085	1.085	1.096	1.096	1.096
R(C25-H29)		1.082	1.082	1.082	1.093	1.093	1.093
R(C30-O31)	1.222	1.190	1.191	1.191	1.214	1.214	1.214
R(C30-O32)	1.305	1.329	1.329	1.329	1.358	1.357	1.357
R(O32-H33)	0.963	0.952	0.952	0.952	0.976	0.976	0.976
A(C2-C1-C6)		118.1	118.1	118.1	118.2	118.2	118.2
A(C2-C1-C7)		121.3	121.4	121.3	121.3	121.3	121.3
A(C6-C1-C7)		120.5	120.5	120.5	120.5	120.5	120.5
A(C1-C2-C3)		120.8	120.7	120.7	120.6	120.6	120.6
A(C1-C2-H8)		119.9	119.9	119.9	119.8	119.8	119.8
A(C3-C2-H8)		119.3	119.3	119.2	119.5	119.5	119.5
A(C2-C3-C4)		121.4	121.4	121.4	121.4	121.4	121.4
A(C2-C3-H9)		119.0	119.0	119.0	119.1	119.1	119.1
A(C4-C3-H9)		119.6	119.6	119.6	119.4	119.4	119.4
A(C3-C4-C5)		117.6	117.6	117.6	117.6	117.6	117.6
A(C3-C4-C10)		120.7	120.7	120.7	120.7	120.7	120.7
A(C5-C4-C10)		121.7	121.7	121.7	121.6	121.6	121.6
A(C4-C5-C6)		121.2	121.2	121.2	121.2	121.2	121.2
A(C4-C5-H11)		119.7	119.7	119.7	119.5	119.5	119.5
A(C6-C5-H11)		119.1	119.1	119.8	119.3	119.3	119.3
A(C1-C6-C5)		120.9	120.9	121.0	120.9	120.8	120.8
A(C1-C6-H12)		119.8	119.8	119.8	121.6	119.6	119.6
A(C5-C6-H12)		119.8	119.2	119.2	119.4	119.4	119.4
A(C1-C7-C25)		112.8	112.8	112.8	112.7	112.7	112.7
A(C1-C7-H26)		107.6	107.6	107.6	107.6	107.5	107.5
A(C1-C7-C30)		109.5	109.5	109.5	109.4	109.4	109.4

A(C25-C7-H26)		109.2	109.1	109.1	109.4	109.3	109.3
A(C25-C7-C30)		110.5	110.9	110.9	110.6	110.7	110.7
A(H26-C7-C30)		106.6	106.5	106.5	106.9	106.8	106.8
A(C4-C10-H13)		108.6	108.6	108.6	109.0	109.0	109.0
A(C4-C10-H14)		114.9	114.9	114.9	114.8	114.8	114.8
A(C4-C10-H15)		109.3	109.3	109.2	109.4	109.5	109.4
A(H13-C10-H14)		108.5	108.5	108.5	108.2	108.2	108.2
A(H13-C10-H15)		106.3	106.3	106.3	106.3	106.3	106.3
A(H14-C10-H15)		108.8	108.8	108.8	108.6	108.6	108.6
A(C10-H14-C16)		110.0	109.9	109.9	110.2	110.2	110.2
A(C10-H14-C17)		112.3	112.3	112.3	112.1	112.1	112.1
A(C10-H14-H24)		107.8	107.8	107.8	107.5	107.4	107.5
A(C16-H14-C17)		110.7	110.7	110.7	110.9	110.9	110.9
A(C16-H14-H24)		107.8	107.9	107.9	107.9	107.9	107.9
A(C17-H14-H24)		107.9	107.9	107.9	107.9	107.9	107.9
A(H14-C16-H18)		111.4	111.5	111.5	111.5	111.5	111.5
A(H14-C16-H19)		111.1	111.1	111.1	111.1	111.1	111.1
A(H14-C16-H20)		111.0	111.1	111.1	110.9	110.9	110.9
A(H18-C16-H19)		107.7	107.7	107.7	107.8	107.8	107.8
A(H18-C16-H20)		107.7	107.7	107.7	107.7	107.7	107.7
A(H19-C16-H20)		107.6	107.6	107.6	107.5	107.5	107.5
A(H14-C17-H21)		110.9	110.9	110.9	110.8	110.8	110.8
A(H14-C17-H22)		111.8	111.8	111.8	111.7	111.8	111.8
A(H14-C17-H23)		110.7	110.7	110.7	110.8	110.8	110.8
A(H21-C17-H22)		107.9	107.9	107.9	107.8	107.8	107.8
A(H21-C17-H23)		107.6	107.5	107.5	107.6	107.5	107.5
A(C7-C25-H28)		110.8	110.8	110.8	110.9	110.9	110.9
A(C30-O32-H33)		108.7	108.8	108.7	107.1	107.1	107.8

3.3 Energies and Dipole Moments

The dipole moments (in Debye) and total electronic energies (Kcal/mol) without zero point correction (E_1), with zero point correction (E_2), with thermal energy correction (E_3) and with enthalpy correction (E_4) for the two molecules both in gas phase and in different solvents are listed in Table 3 and 4 respectively. It is seen that Aspirin is slightly more stable in aqueous medium. The molecule is more stable in solvated phase than in the free state. The difference in total energies from gas phase to solvated phase is a bit larger when go from the uncorrelated to the electron correlation level of theory. This implies that the effect of electron correlation decrease the sum of electronic energy without zero point correction, the sum of electronic energy with zero point correction, the sum of electronic energy with thermal energies, the sum of electronic energy with enthalpies, and the sum of electronic energy with thermal free energies as we go from the uncorrelated method to correlated method.

We can compare the stability of the two molecules in different medium through their total energies. Aspirin molecule is found to be most stable by approximately 0.0056 a.u (3.50 Kcal/mol) at RHF/6-31+G* level and by nearly 0.0076 a.u (4.8 Kcal/mol) at B3LYP/6-31+G* in aqueous medium as compared to gas phase. The molecule Ibuprofen is found to be most stable by approximately 0.0052 a.u (3.20 Kcal/mol) at RHF/6-31+G* level and by nearly 0.00030 a.u (1.90 Kcal/mol) at B3LYP/6-31+G* in aqueous medium as compared to gas phase. Also at both RHF and B3LYP levels the stability of the molecules in ethanol is more pronounced than in gas phase. It implies that the order of stability of the molecule is greater in water than in ethanol and that of ethanol is greater than in gas. This shows that presence of alcohol tends to reduce the stability of Aspirin and Ibuprofen as compared to water, which may be of importance in their effectiveness in use. Our calculated energies values of Ibuprofen at the RHF level and B3LYP are approximately equal to those reported in literature [23].

The dipole moment of the molecule gives the strength of the polarity of the molecule. In case of Aspirin the magnitude of the dipole moment obtained at B3LYP/6-31+G* level is slightly lower in gas phase but is higher in solution phase (water methanol and ethanol) as compared to the corresponding values of the dipole moment at RHF/6-31+G* level. Oxygen atoms are having the largest electronegativity, in this molecule and the double bonded oxygen is seen to attract electrons more strongly than the single bonded one. The dipole moment at RHF level in gas is less than its value in water and ethanol by 2.11D and 2.01D respectively while that at the B3LYP level in gas phase is less than its value in water and ethanol by 3.68D and 3.48D respectively. The difference in the dipole moments between the two methods from the uncorrelated to the correlated level is -0.86D in gas phase, 0.71D in water and 0.61D in ethanol for Aspirin.

In the case of Ibuprofen, the magnitude of the dipole moment calculated at the B3LYP/6-31+G* level is slightly lower in value as compared to the corresponding value obtained at the RHF/6-31+G* level in gas phase, water and ethanol. The dipole moment at RHF level in gas is less than its value in water and ethanol by 0.52D and 0.49D respectively while that at the B3LYP level in gas phase is less than its value in water and ethanol by 0.45D and 0.42D respectively. The difference in the dipole moments between the two methods from the uncorrelated to correlated level is -0.22D in gas phase, -0.29D both in water and in ethanol for Ibuprofen. It is clear from Table 4 that there is some redistribution of charges which occurred in solvated phase which result in increase of the dipole moments. It means that for ethanol the impact on the charge distribution is similar to that of water.

Table 3: Dipole moments (µ) and Total electronic energies without and with zero point energy corrections, with thermal energy correction and with enthalpy correction of Aspirin molecule with respect to corresponding Gas phase energies in water and ethanol obtained using RHF and B3LYP methods by employing 6-31+G* basis sets. All energies are given in (a.u).

	RHF/6-31+G*			**B3LYP/6-31+G***		
	Gas	**Water**	**Ethanol**	**Gas**	**Water**	**Ethanol**
µ	5.61	7.72	7.62	4.75	8.43	8.23
E_1	-644.96430	-644.96991	-644.96965	-648.71131	-648.71899	-648.71853
E_2	-644.79487	-644.80040	-644.80010	-648.55421	-648.72622	-648.56120
E_3	-644.78393	-644.78955	-644.78924	-648.54262	-648.55021	-648.54975
E_4	-644.78298	-644.78861	-644.78829	-648.54168	-648.54927	-648.54881

E_1=Total Electronic Energy without Zero point correction, E_2=Total Electronic Energy with Zero point correction, E_3=Total Electronic Energy with Thermal energies, E_4=Total Electronic Energy with enthalpies.

Table 4: Dipole moments (µ) and Total electronic energies without and with zero point energy corrections, with thermal energy correction and with enthalpy correction of Ibuprofen molecule with respect to corresponding Gas phase energies in water and ethanol obtained using RHF and B3LYP methods by employing 6-31+G* basis sets. All energies are given in (a.u).

	RHF/6-31+G*			**B3LYP/6-31+G***		
	Gas	**Water**	**Ethanol**	**Gas**	**Water**	**Ethanol**
µ	1.83	2.35	2.32	1.61	2.06	2.03
E_1	-652.54414	-652.54837	-652.54815	-656.72924	-656.73211	-656.73199
E_2	-652.23902	-652.24396	-652.24347	-656.44437	-656.44748	-656.44731
E_3	-652.22419	-652.22907	-652.22858	-656.42860	-656.43177	-656.43163
E_4	-652.22325	-652.22811	-652.22763	-656.42766	-656.43083	-656.43069

3.4 Average Polarizability and Anisotropy of Aspirin and Ibuprofen

Polarizability gives information about the distribution of electrons in the molecule and play a fundamental role in determining the structural, orientational, dynamical and thermodynamical properties of a system [24]. The components of the diagonalized tensor and the associated average polarizability are very important in polarizability studies as shown by [25]. The polarizability tensor components, the average polarizability and the anisotropy of Aspirin and Ibuprofen obtained at RHF/6-31+G* and B3LYP/6-31+G* level of theories are listed in Table 3. All the six polarizability tensor components of Aspirin and Ibuprofen molecules α_{xx}, α_{xy}, α_{yy}, α_{xz} α_{yz} and α_{zz} components change significantly at both level of theory considered here. But they do not follow any regular pattern. The component α_{xz} is negative. From the Table 3, we can see that the tensor α_{xx} is responsible for the greatest contribution both in the average polarizability and the anisotropy for these molecules at all levels of theory. We can also see that the inclusion of electron correlation affects the average polarizability, <α>, and anisotropy. We equally observe that the effect of inclusion of electron correlation increases <α> by 39.10 percent in gas phase, 48.55 percent in water and by 48.05 percent in ethanol and increases anisotropy γ by 15.87 percent in gas phase, 34.12 percent in water and by 34.07 percent in ethanol for Aspirin molecule. In the case of Ibuprofen molecule, the effect of inclusion of electron correlation increases <α> by 37.43 percent in gas phase, 34.46 percent in water and by 34.64 percent in ethanol and increases anisotropy γ by 16.23 percent in gas phase, 14.83 percent in both water and ethanol.

Table 5: Polarizabilities of Aspirin and Ibuprofen in Gas phase, water and ethanol using RHF and B3LYP methods by employing 6-31+G* basis set.

	Aspirin			Ibuprofen		
Basis sets	**Gas**	**Water**	**Ethanol**	**Gas**	**Water**	**Ethanol**
RHF/6-31+G*						
α_{xx}	125.48	147.92	146.82	181.72	236.92	233.79
α_{xy}	3.97	7.10	7.00	6.94	8.24	12.33
α_{yy}	113.45	135.10	133.94	117.44	137.97	137.33
α_{xz}	-9.63	-11.52	-11.44	-4.08	-6.24	-6.10
α_{yz}	4.20	5.50	5.45	6.34	8.24	8.75
α_{zz}	72.00	77.69	77.46	133.31	160.94	159.22
< α >	103.64	120.24	119.41	144.16	178.61	176.78
γ	74.03	98.35	97.08	85.78	130.92	130.15
B3LYP/6-31+G*						
α_{xx}	142.84	184.03	181.81	206.15	266.90	263.56
α_{xy}	5.37	10.13	9.96	8.05	12.19	12.04
α_{yy}	128.71	168.68	166.36	129.02	150.24	148.99
α_{xz}	-9.85	-12.81	-12.66	-3.96	-5.93	-5.67
α_{yz}	3.16	4.18	4.11	7.13	9.33	8.93
α_{zz}	77.00	84.69	84.35	143.84	170.97	169.79
< α >	116.18	145.80	144.17	159.67	196.04	194.11
γ	89.57	137.32	134.61	104.11	157.69	154.57

3.5 Vibrational Frequencies, Assignments and Spectra

The vibrational frequencies and IR intensities for Aspirin and Ibuprofen molecule in gas phase as well as in different solutions (water, methanol and ethanol) at RHF and B3LYP levels with 6-31+G* basis sets have been calculated. This was done by calculating the matrix of second derivative of energy (the Hessian or Force constant matrix) which upon diagonalization yields the harmonics vibrational frequencies. The numerical computation of the Hessian requires minimum of 3N+1 energy and gradient evaluations (N is the number of atoms) and usually 6N+1 energy and gradient evaluations for acceptable accuracy.

Table 6 and 7 list the more prominent vibrational frequencies and their corresponding IR intensities for the two molecules. The frequencies reported are not scaled as is usually done in comparing the similar calculated frequency with observed frequency. The B3LYP results show a significant lowering of the magnitudes of the calculated frequencies decrease bringing them in better accord with experiment. The IR intensities do not show significant changes between different solvents, but these are usually larger as compared to their gas phase value.

Tentative assignments for modes of some IR intense vibrational frequencies of Aspirin and Ibuprofen molecule calculated at B3LYP level in the gas phase as well as in different medium (water and ethanol) are listed in Tables 8 and 9 respectively. These are made on the basis of the relative displacements of the atom associated with different calculated frequencies. The Calculated IR vibration line spectrum at the B3LYP for Aspirin in gas phase and different medium are shown in Figure 3(a), 3(b) and 3(c) while the calculated vibrational line spectrum for Ibuprofen are shown in Figure 4(a), 4(b) and 4(c). The calculated IR vibrational spectra assuming a line shape for the bands for Aspirin molecule both in gas phase and solvated medium are shown in figures (5 (a) to 5 (f) and for Ibuprofen are shown in figures 6(a) to 6(f)) at all level of calculations. The maximum IR intensity is associated with the C=O stretching in the COOH group is approximately at 1790 cm^{-1} for Aspirin. In case of Aspirin, the absorption for the hydroxyl (-OH) band is seen occurs at around 3600 cm^{-1}, whereas the CH stretching for the benzene ring appear in the 3000-3200 cm^{-1} region (Table 8). The agreement with experiment is within 5 to 10%. These deviations may be due to non-consideration of anharmonicity and use of a limited basis sets. No significant change in the position of the IR absorption is noticed in going from gas to solvated phase. For example, for the -OH group the absorption is at 3615 cm^{-1} in gas phase, 3556 cm^{-1} in water, 3558 cm^{-1} and 3559 cm^{-1} in ethanol while for C=O it is at 1862 cm^{-1} in gas phase, 1843 cm^{-1} in water, 1843 cm^{-1} in and 1843 cm^{-1} in ethanol. Experimentally the C=O IR absorption is found at 1754 cm^{-1} [9, 26, 27, 28, 29] which is slightly lower than our calculated value of frequency. Our calculated vibrational frequencies values and spectrum in gas phase and solvated phase were a in the same range with those reported in literature[9, 26, 27, 28, 29].

For Ibuprofen, the B3LYP results in gas phase, water and ethanol show significant lowering in magnitude of the calculated frequencies bringing them in better accord with experimental results [30, 31]. FT-IR spectrum of the molecule Ibuprofen have been reported [31] and presented some assignments for the observed spectrum in the region 400-4000 cm^{-1}. From table 9, it is clear that our theoretical values are closed to the experimental values of [31]. The agreement between our theoretical and experimental values is within 5-10 percent. The absorption for hydroxyl (-OH) and carbonyl (C=O) stretching occurs again at around 3600 cm^{-1} and 1800 cm^{-1} respectively, whereas for CH of benzene ring occurs at 3000-3200 cm^{-1} (Table 9). From table 8 and 9 it is clear that the results for Ibuprofen molecule are similar to those for Aspirin. The similarities of the vibrational frequencies confirm the similar behaviour of Aspirin and Ibuprofen molecules. The difference between experimental and calculated vibrational frequencies is that the experimental results given in literature were obtained using solid compounds of Aspirin and Ibuprofen while the theoretical results were obtained in gas phase, in water and in ethanol.

Table 6: Some IR intense vibrational frequencies of Aspirin molecule in Gas phase, water and ethanol obtained using RHF and B3LYP methods by employing 6-31+G* basis sets.

RHF/6-31+G*						B3LYP/6-31+G*					
Gas		Water		Ethanol		Gas		Water		Ethanol	
Vib. Freq.	IR Int.	Vib. Freq.	IR Int.	Vib. Freq.	IR Int.	Vib. Freq.	IR Int.	Vib. Freq.	IR Int.	Vib. Freq.	IR Int.
586	50	585	42	586	42	538	32	537	35	537	35
608	41	612	54	612	53	558	9	561	19	561	18
628	11	625	22	625	21	574	11	572	17	572	17
675	107	691	30	691	32	641	9	645	11	645	11
691	1	706	20	706	25	651	8	652	11	652	11
709	21	715	130	714	120	680	107	698	74	697	75
782	15	783	9	783	9	723	15	746	16	740	15
810	6	811	23	811	22	738	7	767	84	765	80
862	25	863	23	863	28	785	27	786	22	786	24
878	59	875	77	875	76	797	14	795	45	795	43
891	8	895	14	895	13	803	42	809	60	808	58
998	4	1004	8	1003	8	893	7	901	23	901	22
1009	33	1011	48	1010	47	915	79	915	151	915	146
1107	5	1112	24	1111	22	981	1	990	4	989	4
1120	70	1120	92	1120	91	1009	76	1010	174	1010	169
1133	9	1134	14	1134	13	1010	20	1019	0.7	1018	0.7
1138	1139	1140	1141	1142	1143	1144	1145	1146	1147	1148	1149
1174	8	1173	11	1173	11	1069	5	1068	9	1068	9
1195	2	1195	3	1195	2	1106	20	1103	33	1103	32
1221	37	1222	74	1222	71	1142	36	1141	122	1141	114
1239	8	1237	10	1237	10	1182	436	1173	740	1173	723
1323	298	1321	482	1321	470	1190	4	1195	7	1194	6

1332	8	1336	14	1336	14	1224	58	1220	45	1220	46
1350	30	1351	54	1351	41	1244	26	1245	82	1245	78
1363	290	1357	336	1357	344	1308	28	1310	100	1310	95
1422	4	1425	22	1425	20	1350	4	1350	11	1350	11
1504	580	1504	800	1503	788	1380	420	1393	596	1393	586
1559	50	1559	67	1559	66	1423	32	1424	45	1424	44
1306	12	1603	13	1603	13	1484	4	1484	5	1484	4
1617	103	1616	137	1616	136	1491	70	1491	120	1491	117
1619	18	1618	17	1618	17	1499	16	1499	23	1499	23
1654	62	1651	74	1651	73	1517	41	1514	47	1514	47
1771	26	1768	29	1769	29	1624	13	1621	16	1621	16
1802	72	1758	121	1758	117	1651	43	1647	102	1648	97
2007	608	1988	843	1989	831	1813	425	1791	734	1792	716
2047	470	2029	650	2030	640	1862	378	1842	597	1844	583
3238	2	3241	2	3240	2	3075	1	3078	2	3078	1
3304	4	3308	3	3308	3	3138	2	3142	1	3142	1
3346	8	3347	10	3347	10	3181	4	3182	6	3182	6
3371	2	3380	0.6	3379	0.7	3196	2	3207	0.1	3206	0.1
3384	10	3390	8	3390	8	3207	9	3215	6	3215	6
3395	9	3401	3	3401	4	3216	7	3224	0.6	3224	0.6
3418	2	3419	2	3419	2	3230	4	3232	3	3231	3
4060	185	4036	305	4038	298	3615	196	3556	439	3559	422

Table 7: Some IR intense vibrational frequencies with their IR intensities of Ibuprofen molecule in Gas phase, water and ethanol obtained using RHF and B3LYP methods by employing 6-31+G* basis sets.

RHF/6-31+G*						**B3LYP/6-31+G***					
Gas		**Water**		**Ethano**		**Gas**		**Water**		**Ethanol**	
Vib. Freq.	**IR Int.**	**Vib. Freq.**	**IR Int.**	**Vib. Freq.**	**IR Int.**	**Vib. Freq.**	**IR Int.**	**Vib. Freq..**	**IR Int.**	**Vib. Freq.**	**IR Int.**
632	68	627	115	630	109	589	45	586	65	586	64
655	79	651	126	653	129	621	65	618	118	618	114
689	23	687	36	688	33	640	29	638	38	638	38
762	45	759	72	761	72	710	45	708	70	708	68
863	17	863	25	863	25	792	19	791	29	791	28
958	14	956	22	956	22	870	19	869	27	869	27
1175	7	1175	12	1185	24	1087	46	1087	74	1087	72
1202	9	1184	25	1203	19	1110	47	1110	76	1110	74
1206	24	1206	38	1206	35	1138	4	1138	7	1138	7
1231	1	1232	30	1232	2	1153	33	1152	55	1153	55
1283	89	1281	141	1281	147	1168	186	1166	237	1166	234

1312	29	1311	94	1312	109	1223	6	1223	7	1223	7
1316	134	1314	114	1315	101	1233	2	1233	3	1233	3
1330	30	1330	30	1330	28	1254	3	1254	5	1254	5
1543	80	1542	110	1542	109	1398	52	1397	72	1397	71
1686	26	1686	43	1686	42	1554	23	1554	38	1554	37
1996	396	1987	614	1992	591	1809	288	1803	431	1804	422
3186	27	3188	43	3187	42	3023	27	3024	40	3024	40
3189	29	3191	47	3190	40	3028	42	3030	67	3030	65
3198	71	3199	102	3198	106	3035	50	3036	69	3036	68
3216	36	3215	55	3215	54	3057	29	3057	44	3057	44
3226	13	3228	19	3227	33	3060	21	3062	30	3062	29
3250	86	3250	91	3250	119	3095	66	3095	80	3095	79
3254	85	3255	128	3254	118	3100	51	3101	73	3101	72
3271	56	3269	107	3270	105	3113	40	3112	70	3112	68
3275	40	3274	57	3274	54	3122	30	3121	49	3121	48
3307	21	3305	32	3306	31	3144	14	3143	21	3143	20
3347	25	3346	29	3347	33	3169	18	3169	28	3169	28
3367	28	3368	48	3368	39	3186	24	3188	35	3188	34
4047	127	4050	180	4047	177	3677	59	3679	82	3679	80

Table 8: IR intense vibrational frequencies and their approximate description of Aspirin molecule in Gas phase, water and ethanol obtained using B3LYP methods by employing 6-31+G* basis sets.

	B3LYP/6-31+G*			
Exp't. [9, 26-29]	**Gas**	**Water**	**Ethanol**	**Approximate description**
Vib. Freq.	**Vib. Freq.**	**Vib. Freq.**	**Vib. Freq.**	
3600-3500	3615	3556	3559	O-H bond stretching in plane of COOH group.
3100-2850	3231	3231	3231	C-H bond symmetrical stretching of benzene ring in plane.
	3216	3224	3224	C-H bond asymmetrical stretching of benzene ring in plane.
	3207	3215	3215	C-H bond asymmetrical stretching of benzene ring in plane.
	3196	3207	3206	C-H bond asymmetrical stretching of benzene ring in plane.
	3182	3182	3182	C-H bond asymmetrical stretching of CH_3 group.
	3138	3142	3142	C-H bond asymmetrical stretching of CH_3 group.
3100-2850	3075	3078	3078	C-H bond symmetrical stretching of CH_3 group.
1754	1862	1843	1843	C-O bond stretching parallel to plane of benzene ring.
1754	1813	1791	1792	C-O bond stretching and C-O-H angle bending of COOH group in plane.
1605.2	1651	1648	1648	C=C bond symmetrical stretching of benzene ring.
1574.7	1624	1622	1621	C=C bond symmetrical stretching of benzene ring.
	1517	1514	1514	C=C-H angle bending of benzene ring.
1484.6	1499	1499	1499	H-C-H angle bending of benzene ring.

	1492	1491	1491	H-C-H angle and C-C-H angle bending of CH_3 and benzene ring respectively.
	1484	1484	1484	H-C-H angle bending of benzene ring.
	1424	1424	1424	Wagging motion in CH_3.
	1381	1394	1393	C-O-H angle bending in COOH group.
1400-1200	1350	1350	1350	C-C bond stretching of benzene ring.
1400-1200	1309	1310	1310	C-C bond stretching of benzene ring.
	1245	1245	1245	C-C bond stretching of benzene ring and C-O-H angle bending in COOH group.
1220-1190	1224	1220	1220	C=O bond stretching + C-C bond stretching.
	1190	1195	1194	C-C bond stretching of benzene ring and C-C-H angle bending.
1400-1200	1182	1173	1173	C-C bond stretching of benzene ring and C-C-H angle bending.
1400-1200	1142	1141	1141	C-C bond stretching of benzene ring.
	1106	1103	1103	Do same as above.
	1069	1069	1068	C-C bond stretching + C-C-H angle bending.
	1060	1060	1060	C-C bond stretching of benzene ring.
	1009	1010	1010	C-C-H angle bending of CH_3.
	981	990	989	Benzene ring distortion.
	915	915	915	Benzene ring breathing.
	893	901	901	Benzene ring distortion.
	803	809	808	Benzene ring distortion.
795	797	795	795	Benzene ring distortion.
	723	746	740	Benzene ring distortion and up and down motion in OH of COOH group along the Benzene ring plane.
	680	698	697	Do same as above.
648	651	652	652	CO_2 bending vibration.
	574	572	572	Benzene ring distortion + distortion of the CH_3 group.
540	558	561	561	CO_2 rocking vibrations.
465	538	537	537	Do same as above

.

Table 9: IR intense vibrational frequencies and their approximate description of Ibuprofen molecule in Gas phase, water and ethanol obtained using B3LYP methods by employing 6-31+G* basis sets.

	B3LYP/6-31+G*			
Exp't [30, 31]	**Gas**	**Water**	**Ethanol**	**Approximate description**
Vib. Freq.	**Vib. Freq.**	**Vib. Freq.**	**Vib. Freq.**	
3550-3350	3677	3679	3679	O-H bond stretching in plane of COOH group.
2950-2850	3186	3188	3188	C-H bond symmetrical stretching of benzene ring in plane.
	3169	3169	3169	C-H bond symmetrical stretching of benzene ring in plane.
3149	3144	3143	314 3	C-H bond symmetrical stretching of CH_3 group bind with C along COOH.

3149	3122	3121	3121	C-H bond symmetrical stretching of CH_3 group bind with C along COOH.
	3113	3112	3112	C-H bond asymmetrical stretching of CH_3 group.
	3100	3101	3101	C-H bond asymmetrical stretching of CH_3 group.
	3095	3095	3095	C-H bond asymmetrical stretching of CH_3 group.
	3060	3062	3062	C-H bond asymmetrical stretching of CH_2 group.
	3057	3057	3057	C-H bond asymmetrical stretching of CH_3 group.
2950-2850	3035	3036	3036	C-H bond asymmetrical stretching of CH_3 and CH_2 group.
2950-2850	3028	3030	3030	C-H bond asymmetrical stretching of CH_3 and CH_2 group.
2950-2850	3023	3024	3024	C-H bond asymmetrical stretching of CH_3 and CH_2 group.
1721	1809	1803	1804	C=O bond stretching parallel to plane of benzene ring.
	1554	1554	1554	C-C-H angle bending of benzene ring.
	1398	1397	1397	C-O-H angle bending in COOH group.
1400	1254	1254	1254	C-C bond stretching of benzene ring and C-O-H angle bending in COOH group.
	1233	1233	1233	C-C bond stretching of benzene ring and C-O-H angle bending in COOH group.
	1223	1223	1223	C-C bond stretching of benzene ring and C-O-H angle bending in COOH group
1294	1168	1166	1166	C-C-H angle bending of CH_3 group.
	1153	1152	1153	Do same as above.
	1138	1138	1138	C-C stretching of benzene ring and C-C-H angle bending.
	1110	1110	1110	C-C-H angle bending.
	1087	1087	1087	Do same as above.
900-460	870	869	869	Ring distortion and up and down motion in CH of COOH group along the Benzene ring plane.
790-460	792	791	791	Do same as above.
	710	708	708	Ring distortion + distortion in CH_3 group.
	640	638	638	Ring distortion + distortion in CH_3 group.
	621	618	618	Ring distortion + distortion in CH_3 group.
465	589	586	586	Ring distortion + distortion in CH_3 group.

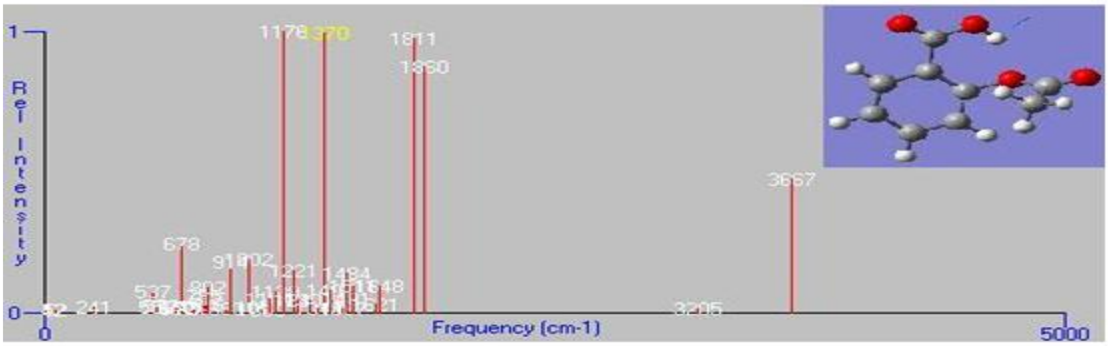

Figure 3 (a): IR Vibrational Spectrum of Aspirin in gas at the B3LYP/6-31+G*

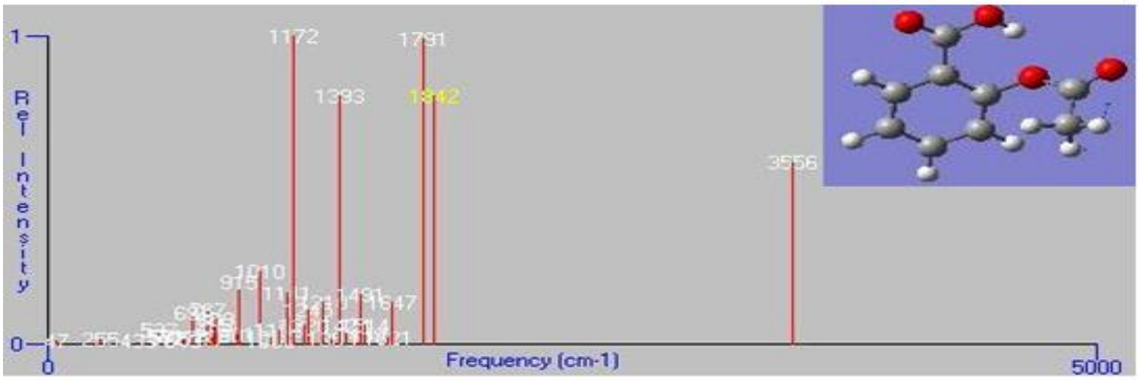

Figure 3 (b): IR Vibrational Spectrum of Aspirin in water at the B3LYP/6-31+G*

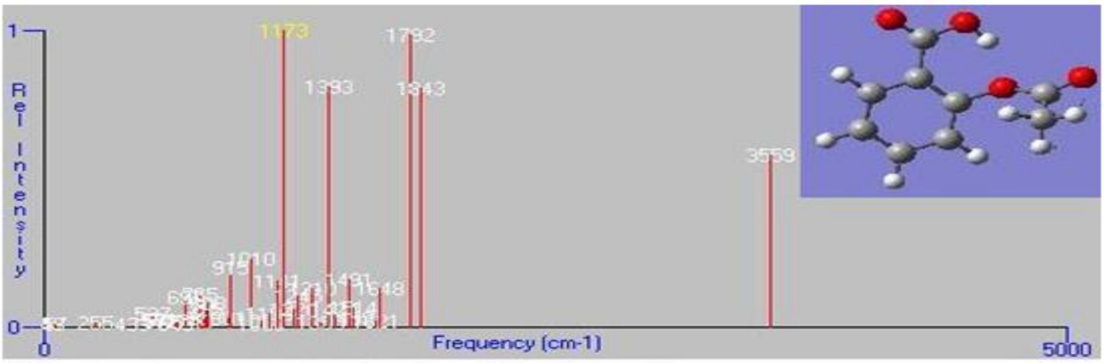

Figure 3 (c): IR Vibrational Spectrum of Aspirin in ethanol at the B3LYP/6-31+G*

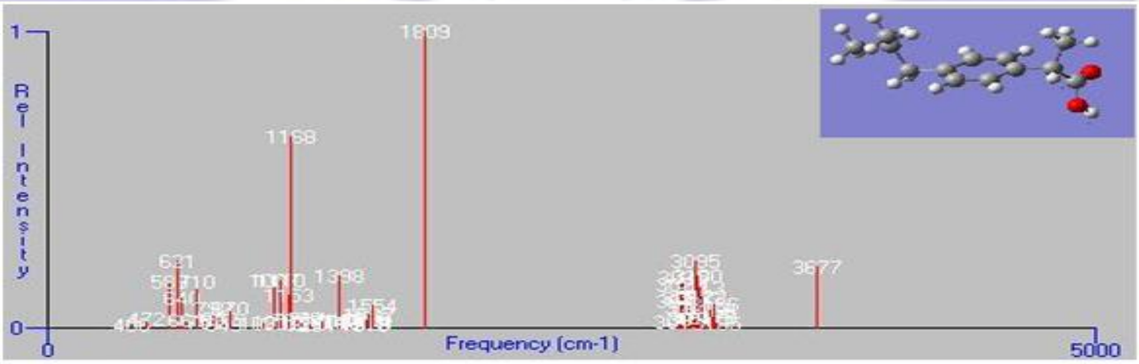

Figure 4 (a): IR Vibrational Spectrum of Ibuprofen in Gas at the B3LYP/6-31+G*

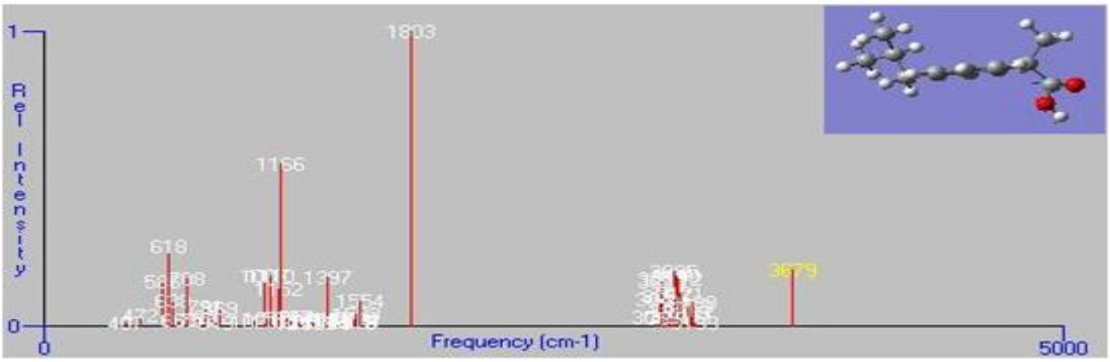

Figure 4 (b): IR Vibrational Spectrum of Ibuprofen in water at the B3LYP/6-31+G*

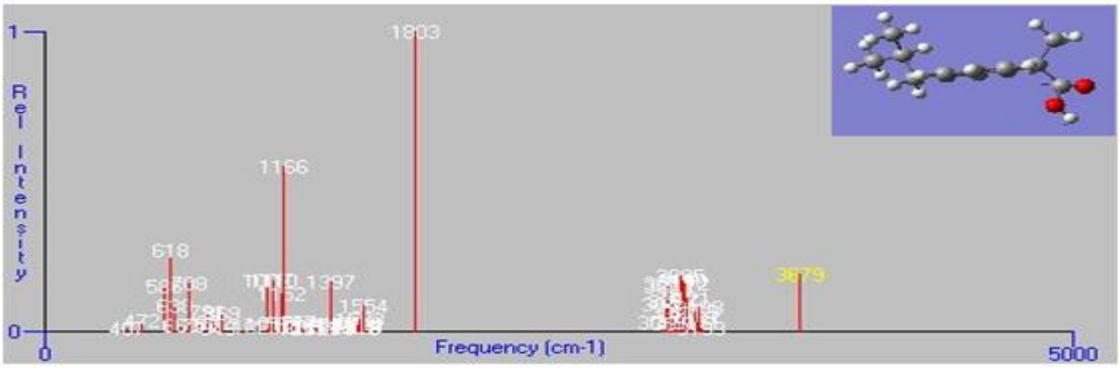

Figure 4 (c): IR Vibrational Spectrum of Ibuprofen in ethanol at the B3LYP/6-31+G*

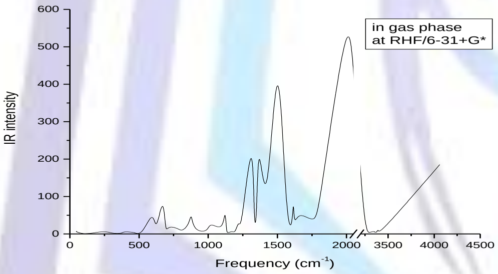	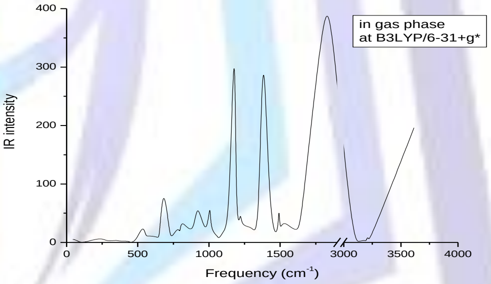
Figure 5 (a): Calculated IR vibration spectrum assuming a line shape for Aspirin in Gas phase at the RHF/6-31+G*.	**Figure 5 (d): Calculated IR vibration spectrum assuming a line shape for Aspirin in Gas phase at the B3LYP/6-31+G*.**
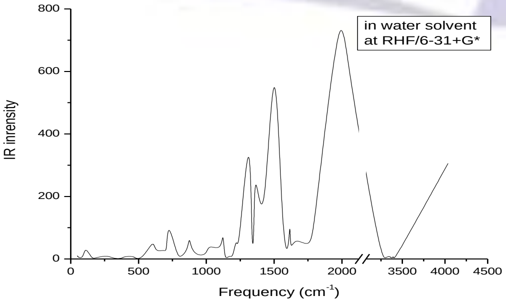	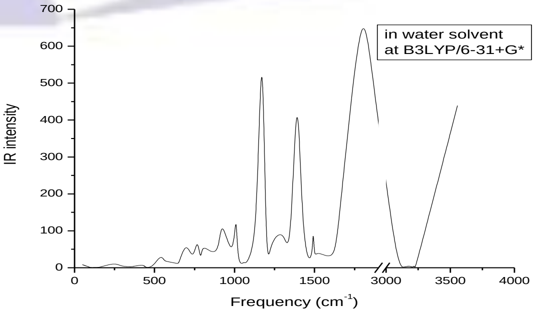
Figure 5 (b): Calculated IR vibration spectrum assuming a line shape for Aspirin in water at the RHF/6-31+G*.	**Figure 5 (e): Calculated IR vibration spectrum assuming a line shape for Aspirin in water at the B3LYP/6-31+G*.**

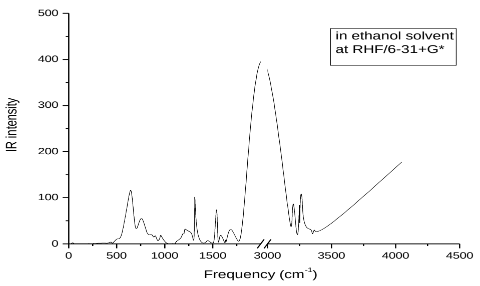

Figure 5 (c): Calculated IR vibration spectrum assuming a line shape for Aspirin in ethanol at the RHF/6-31+G*.

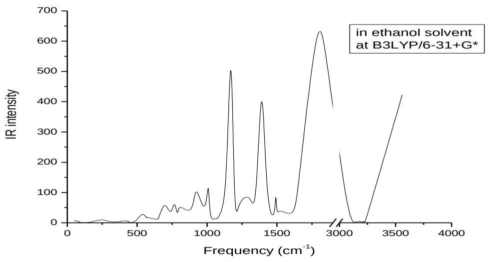

Figure 5 (f): Calculated IR vibration spectrum assuming a line shape for Aspirin in ethanol at the B3LYP/6-31+G*.

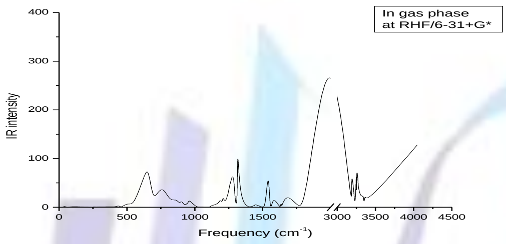

Figure 6 (a): Calculated IR vibration spectrum assuming a line shape for Ibuprofen in gas phase at the RHF/6-31+G*.

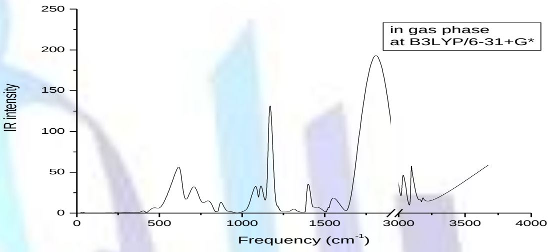

Figure 6 (d): Calculated IR vibration spectrum assuming a line shape for Ibuprofen in gas at the B3LYP/6-31+G*.

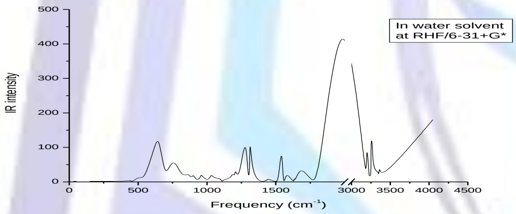

Figure 6 (b): Calculated IR vibration spectrum assuming a line shape for Ibuprofen in water at the RHF/6-31+G*.

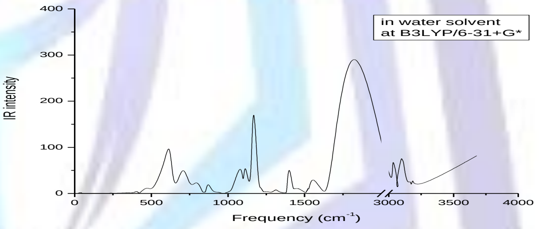

Figure 6 (e): Calculated IR vibration spectrum assuming a line shape for Ibuprofen in water at the B3LYP/6-31+G*.

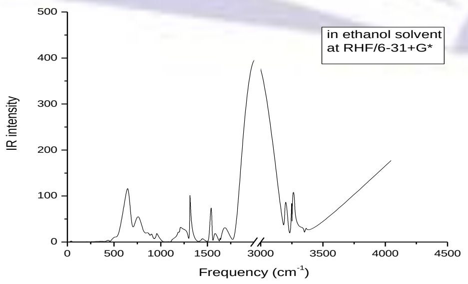

Figure 6 (c): Calculated IR vibration spectrum assuming a line shape for Ibuprofen in ethanol at the RHF/6-31+G*.

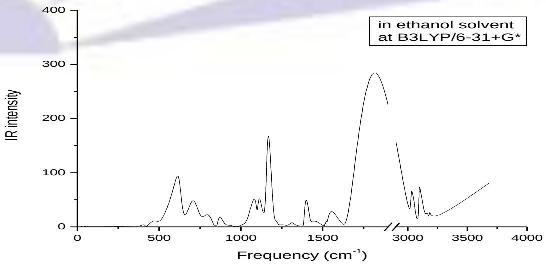

Figure 6 (f): Calculated IR vibration spectrum assuming a line shape for Ibuprofen in ethanol at the B3LYP/6-31+G*.

Conclusion

Geometric optimization and IR vibrational analysis of these molecules was performed using RHF/6-31+G* as well as B3LYP/6-31+G* methods. The most stable structure of these molecules in gas phase, water and ethanol, was obtained by using B3LYP/6-31+G* Method. The molecular structure of these molecules did not change appreciably in solvent medium, in comparison to gas phase geometry, at both levels of theory considered. Hence, there is no effect of water and ethanol (alcohol) on these molecules.

Our structural parameters (bond lengths and bond angles) are in good agreement with other theoretical and experimental values. The B3LYP/6-31+G* results for the molecule Aspirin are in good agreement with experimental and theoretical results given in literature while for Ibuprofen, the bond lengths at the RHF/6-31+G* level are in better accord with the experimental results due to the effect of electrons correlation.

The frequency calculations confirmed the stability of these molecules in gas phase as well as in different medium considered here. The theoretical IR spectra in gas phase for both Aspirin and Ibuprofen obtained by using the B3LYP/6-31+G* method are closer to the experimental spectra compared to RHF/6-31+G* method.

We observed that some charge transfer take place in going from gas phase to solvent medium both at the RHF and at the B3LYP levels. The dipole moments and polarizability of these molecules changed significantly following solvation in different media, in comparison to gas phase, at the RHF level of theory.

The high polarizability and dipole moment values of the molecules revealed that the electrostatic and dispersion contribution influence considerably the interaction of these molecules with other molecules. We also concluded that an appropriate treatment of the electron correlation is of fundamental importance, in order to obtain accurate estimates for the electrons contributions to the dipole moments and polarizabilities.

References

[1] Estrada, P., Mata, I., Dominguez, J.M., Castillon, M.P., Acebal, C., 1990. Kinetic mechanism of beta-glucosidase from Trichoderma reesei QM 9414, Biochim. Biophys. Acta 1033(3) (1990) 298-304.

[2] Julkunen-tiitto, R., and Meier M., 1992. The enzymatic decomposition of salicin and its derivatives obtained from Salicaceae species, J. Nat. Prod. 55(9); 1204-12.

[3] Chen, G., Fournier, R.L., Varanasi, S., 1997. Experimental demonstration of pH control for a sequential two-step enzymatic reaction, Enzyme Microb. Technol. 21; 491-495.

[4] Vane, J.R., and Bottling Eds, R.M., 1992. Aspirin and Other Salicylates, Chapman and Hall.

[5] Dewitt, D.L., 1999. Cox-2-selective inhibitors: the new super Aspirins, Mol. Pharm. 55; 625-31.

[6] Loll, P.J., Picot, D., Garavito, R.M., 1995. The structural basis of aspirin activity inferred from the crystal structure of inactivated prostaglandin H_2 synthase, Nature Struct, Biol. 2; 637-643.

[7] Picot, D., Loll, P.J., Garavito, R.M., 1994. The X-ray crystal structure of the membrane protein prostaglandin H_2 synthase-1, Nature 367, 243-249.

[8] Wheatley, P.J., 1964. The Crystal and Molecular Structure of Aspirin, J. Chem. Soc. 6036-6048.

[9] Kim, Y., Machida, K., Taga, T., Osaki, K., 1985. Structure redetermination and packing analysis of Aspirin crystal, Chem., Pharm. Bull. 33(7); 2641-2647.

[10] Boczar, M., Wójcik, M.J., Szczeponek, K., Jamróz, D., Zięba, A., Kawałek, B., 2003. Infrared Spectra of Aspirin and Its Deuterated Derivative. Chem. Phys. 286; 63.

[11] Adams, S., 1992.The propionic acids: a personal perspective. J. Clin. Pharmacol. 32; 317–323.

[12] Adams, S., Cliffe, E., Lessel, B., Nicholson, J., 1967. Some biological properties of 2-(4-isoburylphenyl)-propionic acid. J. Pharm. Sci. 1686.

[13] Khodov, I.A., Efimov, S.V., Klochkov, V.V., Alper, G.A., Batista de Carvalho, L.A.E., 2014. Determination of preferred conformations of ibuprofen in chloroform by 2D NOE spectroscopy. European J. Pharmaceutical Sciences, 65; 65-67.

[14] Mattei, A., and Li, T., 2012. Polymorph formation and nucleation mechanism of tolfenamic acid in solution: an investigation of pre-nucleation solute association. Pharm. Res. 29; 460–470.

[15] Liu L., and Gao, H., 2012. Molecular structure and vibrational spectra of Ibuprofen using density function theory calculations. Spectrochim Acta A Mol. Biomol. Spectroscopy, 89; 201-209.

[16] Massimo, D.P., Marta, C., Alfonso, P., Roberto, D., Piero, U., 2014. Large-Scale B3LYP Simulations of Ibuprofen Adsorbed in MCM-41 Mesoporous Silica as Drug Delivery System. J. Phys. Chem. C: 118(46); 26737–26749.

[17] Vueba, M.L., Pina, M.E., Bastista de Carvalho, L.A., 2008. Conformational stability of Ibuprofen: assessed by DFT calculations and optical vibrational spectroscopy. J.pharm. Sciences, 97(2); 845-59.

[18] Lee, C., Yang W., and Parr, R.G., 1988. Development of the Colle-Salvetti correlation-energy formula into a functional of the electron density, Phys. Rev. B. 37; 785-789.

[19] Vosko,S.H., Wilk L. and Nusair, M., 1980. Accurate spin-dependent electron liquid correlation energies for local spin density calculations: a critical analysis, Canadian J. Physics, 58(8); 1200-1211.

[20] Miertus, S., Scrocco, E., Tomasi, J., 1982. An Algorithm for the Location of Transition States

Chem. Phys. 65; 187

[21] Frisch, M.J., Trucks, G.W., Schlegel, H.B., Scuseria, G.E., Robb, M.A., Cheeseman, J.R., Montgomery, J.A., Vreven Jr, T., Kudin, K.N., Burant, J.C., Millam, J.M., Iyengar, S.S., Tomasi, J., Barone, V., Mennucci, B., Cossi, M. Scalmani, G., Rega, N., Petersson, G.A., Nakatsuji, H., Hada, M., Ehara, M., Toyota, K., Fukuda, R., Hasegawa, J., Ishida, M., Nakajima, T., Honda, Y., Kitao, O., Nakai, H., Klene, M., Li, X., Knox, J.E., Hratchian, H.P., Cross, J.B., Adamo, C., Jaramillo, R. Gomperts, R.E. Stratmann, O. Yazyev, A.J. Austin, R. Cammi, C. Pomelli, J.W. Ochterski, P.Y. Ayala, K. Morokuma, J., Voth, G.A., Salvador, P., Dannenberg, J.J., Zakrzewski, V.G., Dapprich, S., Danniels, A.D., Strain, M.C., Farkas, O., Malick, D.K., Rabuck, A.D., Raghavachari, K., Foresman, J.B., Ortiz, J.V., Cui, Q., Baboul, A.G., Clifford, S., Cioslowski, J., Stefanov, B.B., Liu, G., Liashenko, A., Piskorz, P., Komaromi, I., Martin, R.L., Fox, D.J., Keith, T., Al-Laham, M.A., Peng, C.Y., Nanayakkara, A., Challacombe, M., Gill, P.M.W., Johnson, B., Chen, W., Wong, M.W., Gonzalez, C., Pople, J.A. Gaussian, Inc., Wallingford CT, 2004.

[22] Perlovich, G.L., Kurkov, S.V., Hansen, L.K.R., Bauer-Brandl,A., 2004. Thermodynamics of Sublimation, Crystal Lattice Energies, and Crystal Structures of Racemates and Enantiomers: (+)- and (±)-Ibuprofen. J. Pharmaceutical Sciences, 93(3); 655-666.

[23] Betz, T., Zinnab, S., Schnell, M., 2015. The shape of Ibuprofen in the gas phase. J. Phys. Chem. Chem. Phys. 17(2015) 4538-4541.

[24] Andersson, M.P., and Uvdal, P., 2005. New Scale Factors for Harmonic Vibrational Frequencies Using the B3LYP Density Functional Method with the Triple-ζ Basis Set 6-311+G(d,p), J. Phys.Chem. A 109 (12); 2937.

[25] Costa M F, 2010. Ciencias Exatas e Tecnologicas, Londrina, 31(1) 31-36.

[26] Binev, I.B., Stamboliyaska, B.A., Y.I. Binev Y.I., 1996. Experimental and ab initio MO studies on the IR spectra and structure of pyridinium dicyanomethylide and trimethylammonium dicyanomethylide, J.Mol.Struct. 378; 189.

[27] Gabriela, M., and Aurel, P., 2014. Studies of different types of Aspirin by spectrophotometric methods. Acta Chemica IASI, 22(2); 155-164

[28] Pushpa, R., and Priya, P., 2013. Study of the spectral properties of inclusion complex of Aspirin with hydroxyl proppyl β- cyclodextrin. International J. Pharmaceutical and Clinical Science, 3(4); 24-28.

[29] Renganayaki, V., Srinivasan, S., Suriya, S., 2012. Vibrational Spectroscopy Investigation on Aspirin Using Semi-Empirical Calculations. International J. ChemTech Res., 4(3); 983-990.

[30] Barbara, S., Bill, G., and Peter, M., acol 2010. Modern Infrared Spectroscopy, John Wiley & Sons, New York.

[31] Ganesh M., and Lee, S.G., 2013. Synthesis, Characterization and Drug Release Capability of New Cost Effective Mesoporous Silica Nano Particle for Ibuprofen Drug Delivery. International J. Control and Automation, 6(5); 207-216.