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Computational and spectroscopy study of melatonin

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Hartree-Fock (HF) and Density Functional Theory (DFT) play an important role in computational quantum theory especially in physical chemistry. Melatonin is a hormone produced naturally by the pineal gland that prevents the production of melanin. It is believed to be involved in regulating the reproductive cycle. The energy bandgaps for melatonin structure have been calculated using DFT and HF method at different basis sets. The bond length, bond angle, and dihedral angles for the melatonin compound have been described. The atomic orbital (GIAO), ^{1}H and ^{13}C NMR chemical shifts of the title compound in the ground state have been calculated using the density functional method (B3LYP) with the 6-31G(d,p) basis set. Using the PCM model, the electronic absorption spectra have been determined using the TD-DFT method based on the B3LYP/6-311G(d,p) level optimized structure in different solvents (DMSO, ethanol, aniline, chloroform, THF, and diethyl ether), the maximum wavelength has been observed in DMSO solvent. Frontier molecular orbitals (FMOs), Molecular electrostatic potential (MEP) surfaces, and thermodynamic parameters have been described for melatonin molecule.

Keywords: Melatonin, Density Functional Theory (DFT), Hartree-Fock (HF), UV-Vis, ESP, thermodynamic

Melatonin or 5-methoxy-*N*-acetyltryptamin (Figure 1) was found and isolated by Aaron Lerner in 1958. Melatonin is a neurohormone primarily formed from bovine pineal located in the third ventricle in the brain. The pineal gland is an organ shape similar to a pine cone (its hence name)[1]. Extra pineal of melatonin was reported in the marrow bone cells, retina, skin, harderian gland, platelets, cerebellum, lymphocytes, and gastrointestinal tract of species vertebrate [2-5]. Melatonin was found in the plant such as bananas, tomatoes, wheat, cucumber, beets, rice, fruits, and vegetable. It is present in smaller organisms for instance algae, bacteria, and fungi[6]. It is also found in human milk, vertebrates, and insects[7]. Melatonin is memory related, and its association with body posture and balance control has been shown[8]. Melatonin controls memory formation by influencing the hippocampal neurons directly[9]. It has anti-depressant, anti-nociceptive, anti-neophobic, anxiolytic, and effects on activity with regulating locomotor[10]. Melatonin effects on anti-inflammatory, anti-oxidant, anti-tumor, pain-modulating, vascular, retinal, seasonal reproductive, reducing blood pressure, ovarian physiology, and osteoblast differentiations[11]. Melatonin adversely affects dopamine release, the rise in cAMPassociated with melatonin receptors in the mesolimbic dopaminergic system suggests that the role of melatonin may be addictive behaviour control[8, 10]. With aging, specific diseases, Alzheimer's disease, senile dementia, pineal calcification, melatonin production is decreased[12]. Other disorders with a reduced level of melatonin include stress, pain, endocrine and metabolic disorders, particularly type 2 DM and acute intermittent porphyria[13]. The synthesis of melatonin continues 24 hours a day. Nevertheless,

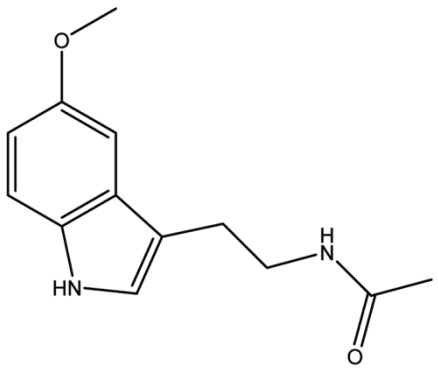

Figure 1 — Stature of Melatonin

at night, more is produced and released into the blood. Approximately 30 µg of melatonin is synthesized every day in an adult person and at the mid-dark time, the average concentration in the blood is reached. Melatonin is not retained in the pineal gland; it is released into the bloodstream and then processed easily in the liver[14]. Under cytochrome P450 monooxygenases A2 and 1A, the liver hydroxylates melatonin in the C6 position, which is then converted into the sulfate derivative, a6-sulfatoxymelatonin, which is extracted from the body *via* urine[15, 16]. This study analyses the structure of melatonin using a quantum chemical calculation.

Computational methods

Both Density Functional Theory (DFT) and Hartree-Fock (HF)[17, 18]have optimized the structure of melatonin. Different basis sets were applied to the Melatonin structure to find the approximated energy band gap. The reason we use different base sets is that each base set includes certain unique characteristics as different from another[19]. The HOMO & LUMO energy level and energy band gap (ΔE) for specific basis sets carryout by DFT and HF methods Table I. The B3LYP method at the 6-31G(d,p) basis set has been chosen for all calculations of the melatonin molecule[20]. At the same stage of the theory, the harmonic vibrational frequencies for the optimized structure were measured and the frequencies obtained were scaled by 35.47[21,22]. NMR data were produced in different references at some methods. The molecular electrostatic potentials were evaluated using the B3LYP/6-31G(d,p) method to investigate the reactive sites of melatonin structure. Furthermore, TD-DFT, MEP, frontier molecular orbital and thermodynamic parameters for the title compound were done with B3LYP/6 31G(d,p).

Result and Discussion

Energy bandgaps

The first step of the computational research is to find the optimized molecular structure usingthe Gaussian program 09. Table I identified the energy of the HOMO & LUMO and the energy bandgaps within the various basis sets (3-21G, 6-31G(d,p), 6-311G(d,p), cc-pVDZ, LanL2DZG, SDD, and DGDZVP) at both methods (DFT and HF). The results show that all values are very close to each other, But we select the 6-31G(d,p) basis set, for the reason that it contains more parameters[23].

Molecular geometry

The optimized structure of the title compound is shown in Figure 2 for both DFT and HF methods

Table I — HF and DFT methods, HOMO & LUMO energy level and energy bandgaps of different basis are set.

	DFT			HF		
Basis sets	HOMO energy level (ev)	LUMO energy level (ev)	Energy band gaps (ev)	HOMO energy level (ev)	LUMO energy level (ev)	Energy band gaps
3-21G	-0.202	-0.013	5.137	-0.292	-0.125	4.538
6-31G	-0.197	-0.016	4.914	-0.291	-0.119	4.667
6-311G	-0.205	-0.026	4.863	-0.294	-0.110	5.016
cc-pVDZ	-0.198	-0.021	4.799	-0.289	-0.116	4.717
LanL2DZG	-0.203	-0.027	4.779	-0.291	-0.106	5.040
SDD	-0.203	-0.027	4.778	-0.296	-0.104	5.221
DGDZVP	-0.205	-0.029	4.774	-0.296	-0.104	5.221

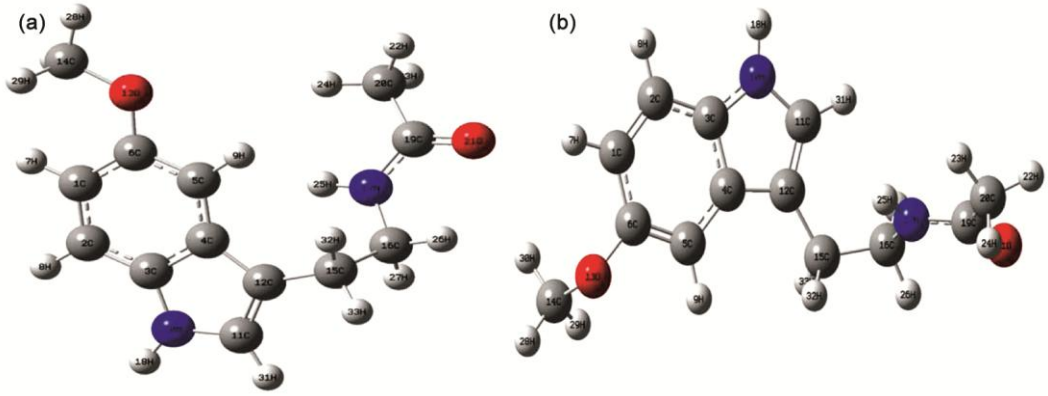

Figure 2 — Molecular Geometry of Melatonin a) DFT/6-31G(p,d) b) HF/6-31G(p,d)

at basis set 6-31G(d,p). Geometric parameters (bondlengths, bondangles, and dihedral angles) were calculated by B3LYP/6-31G(d,p).The aromatic ring in melatonin structure was distorted from the natural hexagon, the length of the bond for C-C and C=C was equal to 1.396Å and 1.429Å, but in the benzene ring the actual bond length between C-C and C=C was equal to 1.341Å and 1.543Å respectively, this is because of the steric effect of the two different groups attached to the benzene ring in melatonin. The bond length between C-N, C-O, and C=O equal to 1.392, 1.399, and 1.252Å respectively, but the experimentally bond length for C-N, C-O, and C=O equal to 1.472, 1.355, and 1.223 Å[24]. All result bond length, bond angles, and dihedral angles for melatonin were present in Table II.

Vibrational Assignments

The vibrational frequency was measured at 6-31G(d,p) basis sets using the DFT method. IR was observed in Figure 3. with specific vibrations have been present in Table III. The key functional group that has been vibrated is discussed below.

C-C /C=C vibrations

The carbon-carbon vibration stretching in a ring typically occurs in a 1400-1600 cm^{-1} region[25-27]. Aromatic such as benzene ring carbon-carbon vibration occurred in area 1420-1625 cm^{-1}. In the benzene ring, two or more vibration occurs, the strong vibration began at 1500 cm^{-1}. Also if the ring is conjugated with other atoms the vibration has occurred at 1580 cm^{-1}. In melatonin compounds, the carbon-carbon vibration was stated at 1409.85 cm^{-1} to 1605.31cm^{-1}. Moreover, melatonin was conjugated to the more groups, the strong vibration for carbon in the benzene ring was observed at 1690.25 cm^{-1}. The intense vibration in both rings of melatonin was observed between 1605.31-1690.25 cm^{-1}. The carbon-carbon single bond was vibrated at a reign of 1363.06-1471.72cm^{-1}. The stout vibration for C-C in the benzene ring was detected at 1471.72cm^{-1}, it is symmetrical vibration. The carbon out of the ring was vibrated symmetrically at 1329.76-1363.06 cm^{-1}. In the reign 524.22, 688.05, 773.67, and 825.79 cm^{-1} symmetrically vibrated for both C=C and C-C in the plane. The vibration ofthe carbon-carbon single bond out of the plant occurred at 909.46cm^{-1}.

C-H Vibrations

Commonly C-H stretching vibration for aromatic compounds was observed in the area 3000-3100 cm^{-1}due to weak bonds of C-H. The C-H bonding vibration in the plane was found in the 990-1390 cm-1

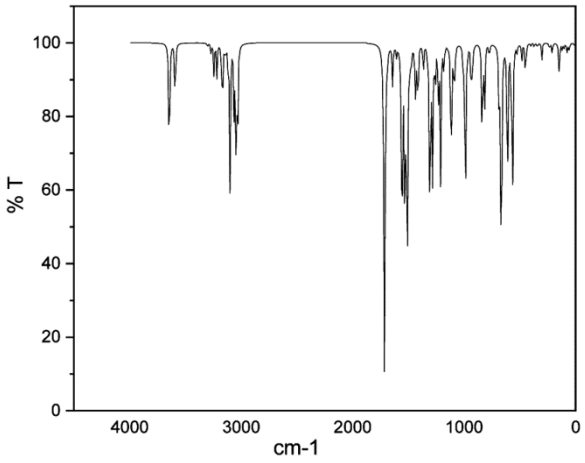

Figure 3 — IR Spectra for Melatonin at DFT/6-31G(p,d)

Table II — Molecular structure parameters (Bond Lengths, Bond angles and Dihedral angles) for title compounds.

Symbol	Bond Length	Symbol	Bond angles	Symbol	Dihedral angles
C2-C1	1.396	C3-C2-C1	118.296	C4-C3-C2-C1	-0.016
C3-C2	1.396	C4-C3-C2	121.836	C5-C4-C3-C2	0.367
C4-C3	1.429	C5-C4-C3	119.059	N10-C3-C2-C1	179.649
C5-C4	1.405	N10-C3-C2	131.047	C11-N10-C3-C2	-179.621
N10-C3	1.391	C11-N10-C3	109.044	C12-C11-N10-C2	-0.173
C11-N10	1.392	C12-C11-N10	110.157	O13-C6-C5-C4	-179.657
C12-C11	1.378	O13-C6-C5	115.197	C14-O13-C6-C5	-177.958
O13-C6	1.399	C14-O13-C6	118.925	C15-C12-C11-N10	-178.213
C14-O13	1.448	C15-C12-C11	126.347	C16-C15-C12-C11	94.064
C15-C12	1.505	C16-C15-C12	114.218	N17-C16-C15-C12	62.919
C16-C15	1.547	N17-C16-C15	112.692	C19-N17-C3-C15	124.760
N17-C16	1.462	C19-N17-C3	122.689	C20-C19-N17-C16	-179.903
C19-N17	1.372	C20-C19-N17	115.458	O21-C19-N17-C16	1.247
C20-C19	1.517	O21-C19-N17	122.632		
O21-C19	1.252				

Table III — Specific atom vibrations measured using DFT (6-31 G*).

	vibrationassignments	frequency (cm^{-1})	St. NO	vibration assignments	frequency (cm^{-1})
1	(NH17-C16-C17) Be,ro	8.13	47	(O13-C14)sy,st	1143.00
2	(O13-C14)Be,ro	55.05	48	(C1-H7,C2-H8)Be,sc	1171.26
3	(C,H,N,O)Out, sy.st	73.55	49	(C14-H28,29,30)An,st	1184.23
4	(All atom) Moves	89.45	50	(C6-O13)sy,st	1210.02
5	(C25-H22,23,24)Be,ro	104.23	51	(Benzene ring)sy,st	1230,47
6	(All atom) moves	119.95	52	(C11-N10-C3)An,st	1258.46
7	(All atoms) moves	145.79	53	(C19-N17)An,st	1282.15
8	(C14-H28,29,30)Be,ro	159.21	54	(H in aring)Be,ro	1297.93
9	(C12-C15)sy,st	208.93	55	(C out of the ring)sy,st	1329.76
10	(All atom)sy,st	228.52	56	(C out of the ring)sy,st	1363.06
11	(O13-C14)sy,st	233.82	57	(C15-H32)Be,ro	1371.70
12	(C16-H25,27)Be,ro	301.73	58	(C-C in Benzene ring)An,st	1409.85
13	(All atom)sy,st	341.82	59	(C-C in Benzene ring)An,st	1419.86
14	(All atom)sy.st	370.63	60	(C20-H22,23,24) Be,sc	1437.65
15	(All atom)sy.st	400.15	61	(C-C in Benzene ring) sy,st	1471.72
16	(C19-C20-N17)Be,sc	440.51	62	(C14-H28,29,30)Be,ro	1485.13
17	(C19-C20-N17)Be,sc	450.77	63	(C=C in Benzene ring)An,st	1507.28
18	(C6-C13-C14)Be,sc	481.42	64	(C20-H23,24,C15-H26,26)Be,sc	1508,73
19	(C15-H32,33)Be,ro	493.65	65	(C16-H26,27)Be,sc	1516.98
20	(Benzene ring)sy.st	524.22	66	(C15-H32,33)Be,sc	1517.84
21	(N10-H18)Be,ro	564.69	67	(C14-H28,29,39)Be,sc	1518.46
22	(C16-H26,27)Be,ro	578.19	68	(C20-H22,23,24)Be,sc	1527.39
23	(O21=C19-N17)sy,st	607.28	69	(All C in Benzene ring)sy,st	1531.00
24	(All atom)sy,st	612.52	70	(C14-H29)sy,st	1533.30
25	(All atom)Be,sc	625.78	71	(N17-H25)Be,ro	1556.44
26	(N17-H25)Be,ro	666.23	72	(N10-H18)sy,st	1605.31
27	(All atom)sy,st	681.67	73	(All C in both rings)sy,st	1640.44
28	(C1=C6)sy,st	688.05	74	(C5=C6, C2=C3)An,st	1690.25
29	(Benzene ring)sy.st	767.63	75	(C19=O)sy,st	1713.57
30	(C3=C4)sy,st	773.67	76	(C14-H28,29,30)sy,st	3031.00
31	(C11-H31)Be,ro	813.67	77	(C10-H32,33)sy,st	3047.22
32	(C4=C5)sy,st	825.79	78	(C20-H22,23,24)sy,st	3048.42
33	(C2-H8,C1-H7)Be,ro	836.02	79	(C16-H25,26)sy,st	3062.94
34	(C15-C15-C12)sy,st	840.10	80	(C15-H32,33)An,st	3098.69
35	(C15-C16)sy,st	909.46	81	(C14-H29,H30)An,st	3101.06
36	(C5-H9)sy.st	922.73	82	(C20-H23,24)An,st	3117.21
37	(C5-H9)sy,st	935.56	83	(C16-H26,27)An,st	3140.61
38	(C2-H8,C1-H7)An,st	969.45	84	(C14-H28,29,30)An,st	3166.64
39	(C12=C11-N10)sy,st	971.07	85	(C20-H22,23,24)An,st	3175.84
40	(Benzene ring)sy,st	988.16	86	(C1-H7,C2-H8)An,st	3216.47
41	(C20-H22,23,24)Be,ro	1007.44	87	(C1-H7, C2-H8)sy,st	3242.98
42	(C15-C16-N17)An,st	1080.79	88	(C5-H9)sy,st	3269.04
43	(C20-H23,23,24)Be,ro	1086.04	89	(C11-H31)sy,st	3301.48
44	(C=C Benzene ring)An, st	1094.89	90	(N17-H25)sy,st	3591.38
45	(C11-N10)sy,st	1114.12	91	(N10-H18)sy,st	3644.83
46	(C16-N17)sy,st	1118.60	92		

Abbreviation: sy: symmetrical, An: anti-symmetrical st: starching, ro: rocking, sc: Scissoring, Be: binding.

range, it is low intensity[28,29]. To identify the characterization of the compounds, the C-H bond is very useful[30]. The vibration of the interaction between carbon and hydrogen in the plane occurs above 1200 cm^{-1}[31,32].The peak of vibration of carbon-hydrogen out of the plane is usually observed in the range 700-1000 cm^{-1}[33-35]. In this study the peak of C-H out of the plane of melatonin was discovered in the range 813.67-1184.23 cm^{-1}, this is in agreement with the previous literature. Also, the symmetrical

vibration of C-H out of the plan was observed at 3031-3062.94 cm^{-1}, moreover, the anti-symmetric vibration of C-H out of the plane was observed in the range 3098.69-3242.98 cm^{-1}. The carbon-hydrogen bond in the benzene ring was vibrated in the reign 1297.93 cm^{-1}, this is in complete agreement with is literature [22].

O-H vibrations

The vibration of C=O was observed in the area 1700-1750 cm^{-1} according to most literature surveys[36-38]. According to the information of this study, the strong vibration peak for C=O has been observed at 1713.57cm^{-1} it is symmetrical stretching.

N-H vibrations

The stretching vibration peaks of nitrogen and hydrogen were observed in 3500-3350 cm^{-1} and 1650 to 1550 cm^{-1}[39]. In our Melatonin structure has two nitrogen atoms that mean two peaks were observed one for (N17-H25) and the other for (N10-H18). The peaks occurred in the range 1556.44, 3591.38 $cm^{-1,}$ and1605.31, 3644.83 cm^{-1} respectively.

C-N vibration

In Melatonin structure, the vibration of C-N was symmetrically stretching in the region 114.12 cm^{-1} and118.6 $cm^{-1}$for both (C11-N10)sy,st and (C16-N17)sy,st respectively.

NMR analysis

The Chemical Shifts ^{13}C NMR is used to describe chemical compounds[40]. Gauge Including Atomic Orbital (GIAO) is the fastest measurement technique based on the set of parameters used. For several aspects of the subject state, a GIAO approach was preferable. NMR on the referencesTMSHF/6-31G(d)GIAO, TMS B3LYP/6-311+G(d,p)GIAO, and CH4 HF/6-31G(d)GIAO have been calculated carbon chemical shifts of the title compound. Whereas hydrogen and nitrogen on such references TMS B3LYP/6-311+G(2d, P)GIAO and TMS HF/6-31G(d)GIAO have been measured. But oxygen on the references H_2O B3LYP/6-311+G(2d,P)GIAO and H_2O HF/6-31G(d)GIAO were calculated chemical shifts.

The results of the ^{13}C NMR were showing in Table IV. Melatonin compound have thirteen carbon atoms; the carbon was ordered from higher chemical shifts to lower chemical shifts (ppm) according to TMS HF/6-31G(d) referenceC20>C15>C16>C14>C2>C5>C1>C12>C11>C4>C3>C6>C19,but according to TMS B3LYP/6-3+G(2d,p) reference the carbon chemical shit was ordered from C20>C15>C16>C6>C14>C2>C5>C1>C12>C11>C4>C3>C19. Moreover, according to the reference CH4 HF/6-31G(d) the carbon was well-arranged from C20>C15>C16>C14>C2>C1>C12>C11>C4>C3>C5>C6>C19. The carbon NMR result showed that the C19 was observed in higher ppm (lower filed), but C20 was observed in lower ppm (higher filed) for three of the references.

Table IV — ^{13}C NMR chemical shifts in ppm for melatonin with different references.

^{13}C. NO	NONE ppm	TMS HF/6-31 G(d) GIAO ppm	TMS B3LYP/6-311+G(2d,P) GIAO ppm	CH4 HF/6-31 G(d) GIAO ppm
C1	80	120	103	119.8
C2	88	111	94	111
C3	64	134	118	135
C4	66	133	116	133
C5	82	117	100	117
C6	42	157	140	157
C11	76	123.5	106.2	122.3
C12	77	123	106	122.2
C14	128	72	54	71
C15	165	35	17	34
C16	150	50	32	49
C19	28	172	155	171
C20	170	30	13	29

Melatonin has sixteen hydrogen atoms, for both references, the hydrogen chemical shift was ordered from higher ppm (lower filed) to lower ppm (higher filed) and starts from H9 to lower ppm H22,H9>H7>H8>H31>H18>H26>H25>H28>H29>H30>H32>H24>H27>H33>H23>H22. For nitrogen NMR analysis, melatonin has two nitrogen atoms. TMS HF/6-31G(d) reference for N10 was observed at 124 ppm but N17 was observed at 131 ppm. While according to TMS B3LYP/6-311+G(2d,p) N10 was identified at 121.8 ppm, and N17 was detected at 128 ppm as in Table V.

Meanwhile, melatonin has two oxygen atoms. Oxygen NMR for melatonin gives two peaks according to H_2O HF/6-31 G(d)GIAO reference for O13 and O21 that occurred at 80ppm and 410ppm respectively. But for H_2O B3LYP/6-311+G(2d, P) GIAO reference, the two peaks for O13 and O21were observed at 78 ppm and 405 ppm respectively, as listed in Table VI.

UV- Vis spectroscopy analysis

UV-Vis spectroscopy is a quite easy tool for the analysis of the chemical structure and complex

Table V — ^{13}C NMR chemical shifts in ppm for melatonin with different reference.

H. NO	NONE ppm	TMS HF/6-31 G(d) GIAOppm	TMS B3LYP/6-311+G(2d,P) GIAOppm
H9	25.45	7.20	6.45
H7	25.70	6.95	6.2
H8	25.80	6.85	6.12
H31	25.90	6.70	5.98
H18	26.20	6.40	5.70
H26	27.73	4.90	4.15
H25	27.75	4.86	4.13
H28	28.35	4.25	3.52
H29	28.80	3.75	3.02
H30	28.90	3.70	2.98
H32	29.45	3.15	2.42
H24	29.60	3.00	2.27
H27	30.05	2.55	1.85
H33	30.15	2.45	1.72
H23	30.75	1.83	1.10
H22	30.85	1.75	1.00

Table VI — Nitrogen and Oxygen NMR chemical shifts in ppm for melatonin with different references.

N. NO	NONE ppm	TMS HF/6-31 G(d) GIAOppm	TMS B3LYP/6-311+G(2d,P) GIAOppm
N10	137.15	124	121.8
N17	130.42	131	128
O. NO	NONEppm	H2O HF/6-31 G(d) GIAO	H2O B3LYP/6-311+G(2d,P) GIAO
O13	240.20	80	78
O21	-85	410	405

formation[41].To obtain UV-Vis spectra for the melatonin molecule, the time-dependent (TD) B3LYP method with a 6-31 G(d,p) basis set was used. For n=6, 12, 18, and 30 the absorption spectrum was represented as shown in Figure 4. From the charts, the x-axis is the wavelength in the nanometer and the absorbance was displayed at the y-axis. According to the graphs, there is a similarity between graphs n=18 and n= 30; that means the convergence state was observed at state 18 (n=18). The maximum wavelength for both (n=18 and n=30) is equal to 215.8 nm.

Solvation Model of UV-Vis spectroscopy

Figure 5 showed the melatonin UV-Vis spectra using some solvents (DMSO, Ethanol, Aniline, Chloroform, THF, and Diethyl ether) respectively. Dimethyl sulfoxide (DMSO) solvent has the greatest value in a wavelength (218.2 nm). Ethanol and diethyl ether was obtained the smallest wavelength which is equal to 198 nm. Both chloroform and tetrahydrofuran (THF) have the same wavelength of maximum peaks which is equal to 199 nm. While the wavelength for aniline solvent equals 201 nm.

Frontier molecular orbitals (FMOs)

One of the most important orbitals in a molecule are frontier molecular orbitals named highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO).Frontier Molecular orbitals are very useful parameters for quantum chemistry and their properties[42,43]. In the

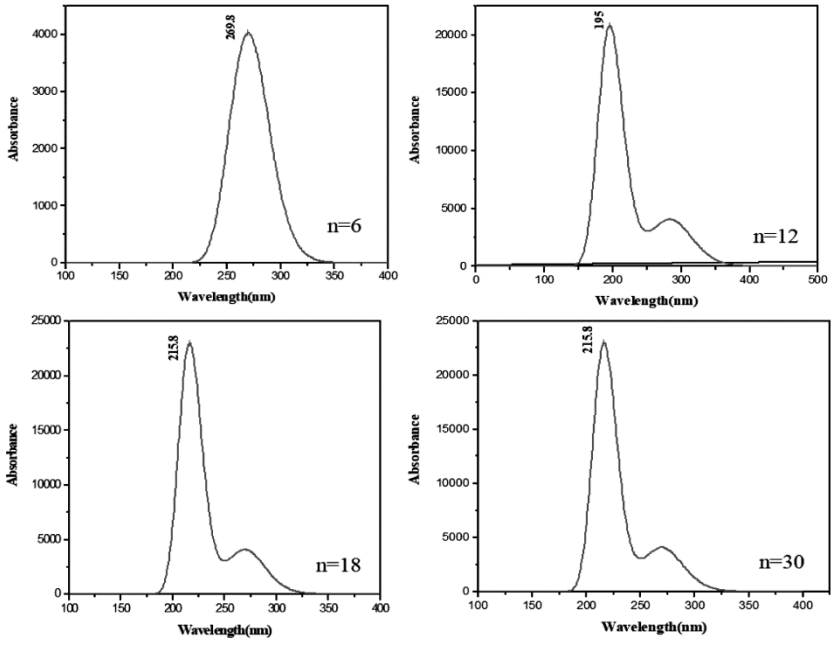

Figure 4 — Absorption spectrum according to the (n)

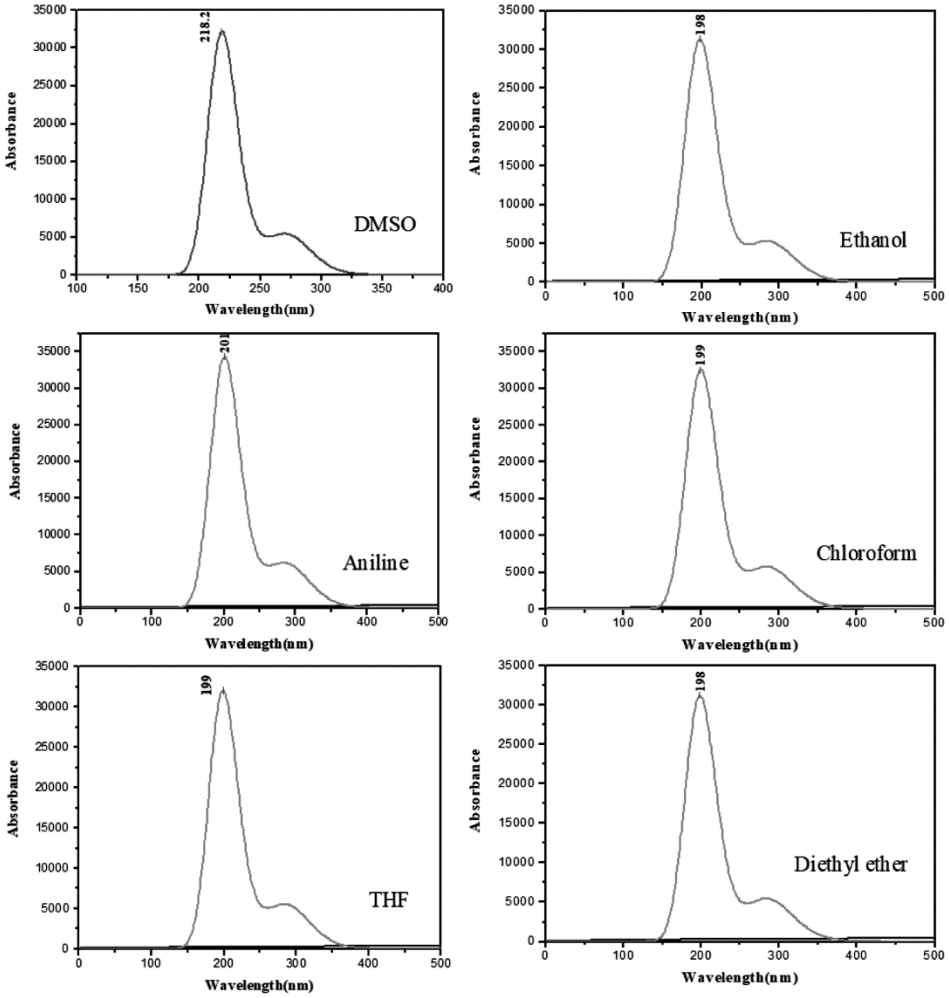

Figure 5 — Melatonin UV-Vis spectra using some solvents

UV-Visible spectrum and chemical reaction, as well as in the electrical and optical properties, border molecular orbitals play an important role[44]. HOMO and LUMO are denoted to donate an electron and obtain an electron correspondingly. The B3LYP/6-31G(d, p) method is used to measure the orbital energy of HOMO and LUMO and the energy difference between LUMO and HOMO. For the melatonin compounds, 3D plots of the HOMO and LUMO orbitals are shown in Figure 6. It can be seen in Figure 6 the orbitals were localized in indole part of methionine for both HOMO and LUMO. The energy of HOMO and LUMO are equal to −0.19751 and −0.01686eV mustered by B3LYP/6-31G(d,p), while the value of energy gap between them equal to 4.914eV. The energy difference between HOMO and LUMO has recently been used to assess the bioactivity of intramolecular charge transfer[45 46]. Also, the HOMO and LUMO energy levels have

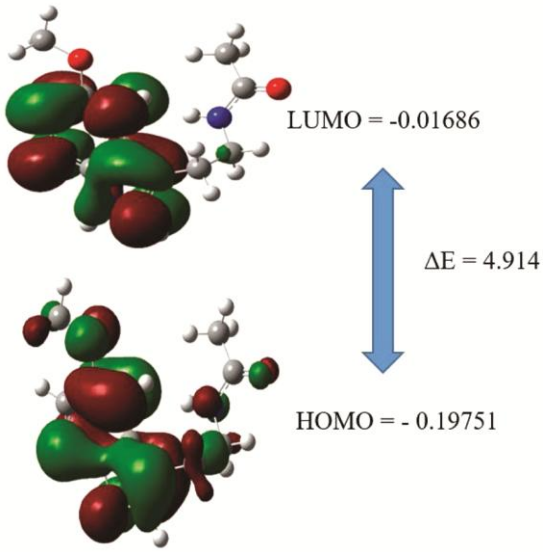

Figure 6 — HOMO and LUMO energy orbital for melatonin molecule

Table VII — Electronic parameters for melatonin compounds.

B3LYP/ 6-31g(d,p)	Equations	Results
E_{LUMO} (eV)	E_{LUMO} (eV)	-0.016
E_{HOMO} (eV)	E_{HOMO} (eV)	-0.197
ΔE	HOMO - LOMO	4.915
I (eV)	$I= - E_{HOMO}$	5.3606852
A (eV)	$A= - E_{LUMO}$	0.4353856
X (eV)	X= I+A/2	2.8980354
η (eV)	η = I-A/2	2.4626498
μ (eV)	μ = -(I+A/2)	-2.8980354
S (eV)	S = 1/2η	1.2313249
ω (eV)	ω = μ2/2η	10.34141661

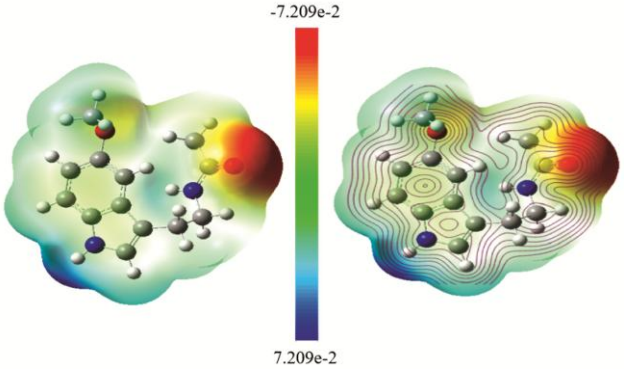

Figure 7 — Molecular electrostatic potential (MEP) surfaces of compound melatonin compound

described ionization potential ($I=-E_{HOMO}$), electronic affinity ($A=-E_{LUMO}$), Electronegativity $\chi= (I + A)/2$, chemical potential $\mu= -\chi$, chemical hardness = (I - A)/ 2. softness $s= 1/2\eta$, electrophilicity index = $\mu 2/2\eta$ all results were shown in Table VII.

Molecular electrostatic potential (MEP) surfaces

A visual tool for understanding the connection between molecular structures containing drugs and biomolecules and their physiochemical properties is given by molecular electrostatic potential (MEP)[47]. The molecular electrostatic potential (MEP) surface have been plotted for melatonin at the B3LYP/6-31G(d,p) basis set as shown in Figure 7. MEP surfaces were really useful parameters for studying reactivity to an approaching electrophile is attracted to negative areas. Different colours reflect the different electrostatic potential values of the surface. Potential rises in red < orange < yellow < green < blue. For the melatonin compound, the MEP map colour code was within the range of −0.07209 a.u (deepest red) to 0.07209 a.u. (deepest blue). Where the blue area shows the greatest attraction and the red area shows the greatest repulsion. In most MEPs, the maximum positive area favored the site as the blue colour for the nucleophilic attack, while the maximum negative area favoured the site as the red and yellow colour for electrophilic reactive[48]. The findings show that the negative potential areas normally associated with the lone pair of electronegative atoms are primarily over the electronegative oxygen atoms and the nucleophilic reactive hydrogen atoms are over the positive potential areas. The red colour displays the greatest repulsion and the highest attraction is displayed by the blue colour. We may tell from these findings that the greatest repulsion is displayed by the O (Oxygen) atoms. We may tell from these observations that the O21 atoms exhibit the most repulsion comparative with the oxygen (O13) single bond. The (N-H) groups are found in the highest positive regions in the melatonin compound. This result also provides details on the region of intermolecular interaction melatonin compound.

Table VIII — Thermodynamic properties of Melatonin used by B3LYP/6-31G(p.d).

Parameters	B3LYP/cc-pVDZ
Zero-point vibrational energy(kcal/mol^{-1})	173.421
Total energy (a.u.)	-1157.799
Rotational constants (GHz)	
	0.523
	0.433
	0.260
Rotational temperatures (K)	
	0.025
	0.020
	0.012
Entropy (Kcal mol^{-1} K^{-1})	
Rotational	0.889
Translational	0.889
Vibrational	181.277
Total	183.055

Thermodynamic Properties

Numerous thermodynamic parameters have been measured, such as specific heat power, thermal energy, rotational temperatures, rotational constants, zero-point vibration energy, and entropy used B3LYP/6-31G(d,p) at 1.00 atm pressure and 298K for melatonin molecule which were shown in Table VIII.

Conclusion

In this study, both methods (HF and DFT) for measuring band gap energies of the melatonin molecule were investigated. DFT/6-31G(d,p) was chosen for all calculations of melatonin structure. The HOMO-LUMO energies and the energy

differentiation between them and the physical properties of the molecules were determined. The IR indicates all-atom vibrations; the result was a strong agreement with previous literature. NMR was used to describe the structure of the molecules, and the atom peaks in NMR were related to the reference forms. In ^{13}C NMR the peak value for both references HF/6-31G(d)GIAO, andCH4 HF/6-31G(d)GIAO are very close or equal to each other but different from the TMS B3LYP/6-311+G(2d,P)GIAO references. However, for the ^{1}H NMR, all peaks were gradually increased for both references (HF/6-31G(d)GIAO, andCH4 HF/6-31G(d)GIAO). The nitrogen and oxygen peak values were different for each reference. In the solvation models, the wavelength for melatonin has appeared from 198 to 218.2 nm. DMSO was a good solvent for dissolving the Melatonin compound, due to higher wavelength and high-intensity peaks. The HOMO and LUMO energy levels provided the properties of the structure of melatonin. The positive potential locations are around the atoms of hydrogen and electronegative atoms are the negative potential sites shown by the MEP map.

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