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Theoretical DFT study on spectroscopic signature and molecular dynamics of neurotransmitter and effect of hydrogen removal

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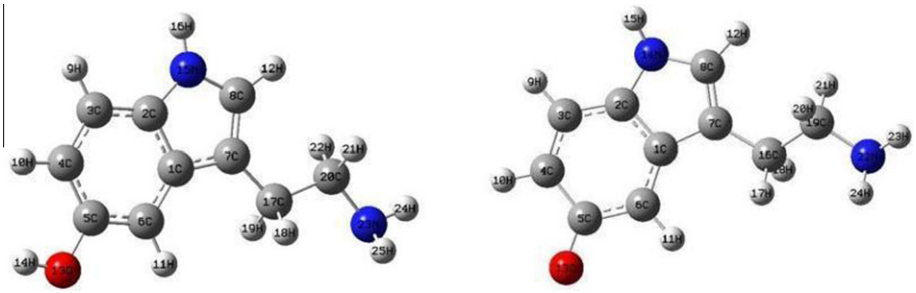
HIGHLIGHTS

- This paper presents vibrational molecular dynamics of a neurotransmitter (serotonin) and its deprotonated form.
- The effect of deprotonation upon geometry and normal modes are studied.
- Dependency of Raman intensity upon temperature and exciting laser frequency are studied.
- NBO analysis of serotonin and its deprotonated form are studied and a comparison is presented.

GRAPHICAL ABSTRACT



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ABSTRACT

Vibrational spectroscopic study has been made for the serotonin molecule and its deprotonated form. The Infrared and Raman spectra in optimum geometry of these two molecules are calculated using density functional theorem and the normal modes are assigned using potential energy distributions (PEDs) which are calculated using normal coordinate analysis method. The vibrational frequencies of these two molecules are reported and a comparison has been made. The effect of removal of the hydrogen atom from the serotonin molecule upon its geometry and vibrational frequencies are studied. Electronic structures of these two molecules are also studied using natural bond orbital (NBO) analysis. Theoretical Raman spectrum of serotonin at different exciting laser frequencies and at different temperatures are obtained and the results are discussed. Present study reveals that some wrong assignments had been made for serotonin molecule in earlier study.

Introduction

Serotonin or 5-hydroxytryptamine (5-HT) is a monoamine neurotransmitter, biochemically derived from tryptophan. Serotonin is primarily found in the gastrointestinal (GI) tract, platelets, and in the central nervous system (CNS) of animals including humans. It is popularly thought to be a contributor to feelings of well-being and happiness [1]. Approximately 90% of the human body's total serotonin is located in the enterochromaffin cells in the gut, where it is used to regulate intestinal movements [2]. The remainder is synthesized in serotonergic neurons of the CNS where it has various functions. These include the regulation of mood, appetite, and sleep. Serotonin also has some cognitive functions, including memory and learning. Modulation of serotonin at synapses is thought to be a major action of several classes of pharmacological antidepressants.

Serotonin also is a growth factor for some types of cells, which may give it a role in wound healing. One type of tumor, called carcinoid, sometimes secretes large amounts of serotonin into the blood, which causes various forms of the carcinoid syndrome of flushing, diarrhea, and heart problems. Because of serotonin's

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growth promoting effect on cardiac myocytes, persons with serotonin-secreting carcinoid may suffer a right heart (tricuspid) valve disease syndrome, caused by proliferation of myocytes onto the valve. Its widespread presence in many seeds and fruits may serve to stimulate the digestive tract into expelling the seeds. In our body, serotonin is synthesized from the amino acid tryptophan by various enzymes.

Being a biologically important molecule, it is of great importance to study vibrational molecular dynamics of serotonin. The conformational flexibility of the ethylamine side chains in serotonin plays an important role in its binding to receptor sites and knowledge of this interaction is important in drug design. Also because of their pharmacological significance in particular, serotonin have been studied extensively by X-ray crystallographic and theoretical methods, investigating the relationship between their pharmacological activities and conformational isomers [3–9]. Mouric and Emson [8] performed theoretical study of the conformational landscape of serotonin and assigned frequencies for conformers only in the region 3000–2800 cm^{-1}.

Both the experimental and theoretical vibrational spectra of serotonin have been reported earlier [10] and recently, a work has been reported containing the comparison of performance of different DFT methods for the molecular structure and vibrational spectrum of serotonin [11]. However, in both the study only IR spectrum of serotonin has been reported and also potential energy distributions (PEDs) have not been calculated to assign normal modes of vibration. The observed or calculated frequencies were assigned to their corresponding normal modes using animation picture available in Gauss View program which sometimes is not very reliable. In addition, the conformational landscape of protonated serotonin has been explored in the gas phase and aqueous solution (IEF-PCM) with full geometry optimization [12].

In present study, we have reported theoretical IR and Raman spectra of serotonin and its deprotonated form in minimum potential energy state. We have also calculated potential energy distributions (PEDs) to make conspicuous assignment of the normal modes. The change in the electron density (ED) in the antibonding orbitals (σ^*) and E(2) energies have been calculated by natural bond orbital (NBO) analysis to give clear evidence of stabilization of the title molecule. In addition, we have theoretically studied the effect of temperature as well as the exciting laser source in obtaining Raman spectrum of serotonin. The effect of removal of

Table 1
Local symmetry coordinates and scale factors.

Nos.	Symbols	Symmetry coordinates	Scale factors[a]
Stretching			
1–8	rCC (ring)	R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8	0.93518
9	rCC1 (exocyclic)	R_9	0.93518
10	rCC2 (exocyclic)	R_{10}	0.93518
11–12	rCN (ring)	R_{11}, R_{12}	0.94932
13	rCN1 (exocyclic)	R_{13}	0.94932
14	rCO	R_{14}	1.01940
15	rOH	R_{15}	0.92868
16	rNH	R_{16}	0.92868
17–20	rCH	R_{17}, R_{18}, R_{19}, R_{20}	0.94105
21–22	rCH2ss	$(R_{21}+R_{22})/\sqrt{2}$, $(R_{23}+R_{24})/\sqrt{2}$	0.94105
23–24	rCH2as	$(R_{21}-R_{22})/\sqrt{2}$, $(R_{23}-R_{24})/\sqrt{2}$	0.94105
25	rNH2ss	$(R_{25}+R_{26})/\sqrt{2}$	0.92868
26	rNH2as	$(R_{25}-R_{26})/\sqrt{2}$	0.92868
Bending			
27–30	bCCC	R_{27}, R_{28}, R_{29}, R_{30}, R_{31}, R_{32}, R_{33}, R_{34}	0.98696
31	bCCN	R_{35}, R_{36}	0.98696
32	bCNC	R_{37}	0.98696
33–36	bCCH	R_{38}, R_{39},R_{40}, R_{41}	0.97638
37	bCCO	R_{42}	1.08695
38	bCOH	R_{43}	0.92094
39	bCNH	R_{44}	0.93824
40	bCCC1	R_{45}	0.91671
41	bCCC2	$(5R_{46}+R_{47})/\sqrt{26}$	0.94720
42	bCCN1	$(5R_{48}+R_{49})/\sqrt{26}$	0.94720
43–44	CH2 (scissoring)	$(R_{46}+5R_{47})/\sqrt{26}$, $(R_{48}+5R_{49})/\sqrt{26}$	0.94182
45–46	CH2 (rocking)	$(R_{50}-R_{51}+R_{52}-R_{53})/2$, $(R_{54}-R_{55}+R_{56}-R_{57})/2$	0.94182
47	NH2 (scissoring)	$(2R_{58}-R_{59}-R_{60})/\sqrt{6}$	0.94705
48	NH2 (rocking)	$(R_{59}-R_{60})/\sqrt{2}$	0.94705
Wagging			
49–50	CH2	$(R_{50}+R_{51}-R_{52}-R_{53})/2$, $(R_{54}+R_{55}-R_{56}-R_{57})/2$	0.94182
51	NH2	R_{61}	0.94705
52–55	γCH	R_{62}, R_{63}, R_{64}, R_{65}	0.97638
56	γCO	R_{66}	1.08695
57	γOH	R_{67}	0.92094
58	γNH	R_{68}	0.93824
59	γCC1	R_{69}	0.91671
Twisting			
60–61	CH2	$(R_{50}-R_{51}-R_{52}+R_{53})/2$, $(R_{54}-R_{55}-R_{56}+R_{57})/2$	0.94182
62	NH2	R_{70}	0.94705
63–66	τCC	R_{71}, R_{72}, R_{73}, R_{74}, R_{75}, R_{76}, R_{77}, R_{78}	0.98696
67	τCN	R_{79}, R_{80}	0.98696
68	τCC1	R_{81}	1.02023
69	τCC2	R_{82}	1.02023

[a] Incorporated only 10 different scale factor values.