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Molecular structural investigation of adenosine using spectroscopic and quantum computational calculations

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ABSTRACT

In this study; spectroscopic investigation of adenosine having clinical importance was studied computationally and obtained results were compared with experimental ones. In this scope, geometric optimization and conformational analysis were studied and vibrational spectroscopic properties were studied on the most stable form. NMR and TD-DFT studies on the title compound were conducted with its experimental data. In addition atomic charge distribution, NBO, frontier molecular analysis, thermodynamic analysis and hyperpolarization features were studied.

1. Introduction

Adenosine is a nucleoside that is composed of adenine and D-ribose. Adenosine and its derivatives play many important biological roles in addition to DNA and RNA. Adenosine itself is a neurotransmitter; it functions as energy transfer – as adenosine triphosphate (ATP) and adenosine diphosphate (ADP) – as well as in signal transduction as cyclic adenosine monophosphate (cAMP). Adenosine is an endogenous occurring in all cells of the body. It is chemically 6-amino-9-β-D-ribofuranosyl-9-H-purine. It is a white crystalline powder. Adenosine also plays a role in regulation of blood flow to various organs through vasodilation [1–3].

Adenosine is used as medication, specifically as antiarrhythmic agent, to treat a number of supraventricular tachycardia that does not improve with vagal maneuvers [4]. In individual suspected of suffering from a supraventricular tachycardia, adenosine is used to help identify the rhythm. Adenosine is used an adjunct to thallous chloride TI201 myocardial perfusion scintigraphy in patients are unable to undergo adequate stress testing with exercise [5]. Adenosine is an endogenous purine nucleoside that modulates many physiological processes. Adenosine produces a wide range of biological effects by interacting with four cell surface receptor termed A_1, A_{2A}, A_{2B} and A_3. Adenosine is believed to be an anti-inflammatory agent at the A_{2A} receptor [6]. Adenosine A_{2A}receptor agonists may be important regulators of inflammation. Inflammation is a hall mark of asthma and chronic obstructive pulmonary disease. Of the four receptors adenosine A_{2A} receptor has been strongly linked to control inflammation. Adenosine is an endogenous agonist of the growth hormone secretagogue receptor [7,8]. Adenosine used as second messenger can be the result of de novo purine biosynthesis via adenine monophosphate, though it is possible other pathways exist [9]. Hair regression and balding are distressing concerns for an increasing number of people due to changes in life and serious nutritional imbalances. Adenosine promote thickening of hair on people with thinning hair [10,11]. Adenosine has a specific role in the investigation of primary pulmonary hypertension [12]. Adenosine is produced by myocardial metabolism under physiological or pathological conditions including myocardial is chemical. It regulates myocardial perfusion in both animals and humans [13–15].

Lot of works have been reported on adenosine [16–24] based on its applications. Bulluck et al. [16] found that the evidence of improved clinical outcome in terms of less heart failure in ST-segment elevation myocardial infarction (STEMI) patients administered intra coronary adenosine as an adjunct to reperfusion. This

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finding will need to be confirmed in large adequately powered prospective randomized controlled trials (RCT). Zhang et al. [17] found the possible anticancer mechanisms of chelerythrine and its interactions with adenosine were investigated by UV–Visible spectro photometric and spectro fluorimetric measurements and by thermodynamic calculations. Rozenberg et al. [18] discussed Low-temperature FT-IR spectra and hydrogen bonds in polycrystalline adenosine and uridine. Qiu et al. [19] presented a novel surface-enhanced Raman spectroscopy (SERS) substrate based on hybrid structure of graphene and Copper nanoparticles for adenosine detection. Pancur et al. [20] reported the excited electronic state lifetimes of the purine base adenine and its ribonucleoside adenosine in aqueous solution using femto second time-resolved fluorescence up-conversion spectroscopy. Mathlouth et al. [21] FT-IR and laser-Raman spectra of adenine in the solid state and the Raman spectrum of its aqueous sodium salt were recorded, and assignments of the frequencies observed are proposed. The FT-IR spectrum of adenosine in the solid state is compared to the spectra of D-ribose and adenine. Analysis of the observed frequencies of adenosine permitted identification of a region of frequencies characteristic of the sugar on the one hand, and of the base on the other. Hansia et al. [22] report the tri- and diphosphate fragments of ATP molecule indifferent charge states have been investigated by ab-initio quantum mechanical methods at the levels of HF, DFT and MP2.

To the best of our knowledge, neither quantum chemical calculations nor the vibrational spectra of adenosine have been reported till now. This inadequacy observed in the literature encouraged us to do this theoretical and experimental spectroscopic analysis on this molecule. A complete assignment and discussion of all the fundamental bands observed in experimental FT-IR and FT-Raman spectra are attempted. The electronic properties are thoroughly studied with the help of NBO, HOMO-LUMO and UV–Vis transition analysis. The study of Mulliken population analysis (MPA), APT charge analysis, NMR chemical shift analysis and NLO analysis are carried to understand the charge distribution and polarizability of the molecule.

2. Experimental details

No further purification is needed for recording the spectra as it has 99% of spectrographic grade, the compound under investigation namely adenosine was provided by Sigma Aldrich Chemicals, USA. FT-IR spectrum of the compound was recorded through Bruker IFS 66V spectrometer in the range of 4000–400 cm^{-1}, it resulted the spectral resolution of ±2 cm^{-1}. For another recording using the same instrument for FT-Raman spectrum of the compound with an FRA 106 Raman module equipped with a Nd:YAG laser source operating at 1064 nm line widths with 200 mW power, in the range of 4000–50 cm^{-1} with a scanning speed of 30 cm^{-1} $min^{-1}$and spectral width 2 cm^{-1} and the frequencies of all bands are accurate to ±1 cm^{-1}. The high resolution NMR spectra are recorded in CIF (Central Instrumentation facility), Pondicherry University using sophisticated multinuclear FTNMR model Avance II (Bruker). And the instrument is equipped with a cryomagnet of field strength 9.4 T with its frequency 400 MHz for ^1H and 100 MHz. The UV spectrum is recorded in ethanol solvent, between the wavelength range 200 nm–400 nm, with the scanning interval of 0.2 nm and slit width 1.0 nm using Shimadzu-UV-1700 series instrument in Pharma analytical lab, Pondicherry.

3. Computational details

Deriving the different computational analysis, the Gaussian 09 software programs [25,26] on a Pentium IV/3.02 GHz personal computer were used and so the wave numbers and geometrical parameters were computed using B3LYP and B3PW91 methods in combination with 6-311++G (d, p) basis set. The geometry of the title molecule adenosine was fully optimized using B3LYP functional with 6-311++G (d, p) basis set and the same geometry was used for the conformational analysis using semi-empirical method PM6. The same method and basis set were used to calculate NBO and HOMO-LUMO analysis. TD-SCF functional along with B3LYP method and 6-311++G (d, p) basis set has computed the electronic properties of the compound. With the help of gauge invariant atomic orbital (GIAO) method [27] in combination with B3LYP/6-311G + (2d, p), the NMR chemical shifts were carried out. In addition, the dipole moment, polarizability and the hyper polarizability of the title molecule were also computed using B3LYP method and 6-311++G (d, p) basis set. In order to improve the calculated frequency values in agreement with the experimental values, it is necessary to scale down the calculated harmonic frequencies. Hence, the vibrational frequencies were scaled by scaling factor for B3LYP & B3PW91 were 0.9200 & 0.8900with the range of wave numbers above 3000 $cm^{-1}$and by the factor 0.9800 & 0.9600for less than 3000 cm^{-1} respectively.

4. Result and discussion

4.1. Conformational analysis

The optimized geometry of the adenosine is obtained by using B3LYP with 6-311++G (d, p) basis set and used for conformational analysis of the molecule. Conformational analysis is performed by potential energy surface scan function using semi-empirical method PM6, varying the dihedral angle C3–N11–C15–C20 in the steps of 10° over one complete rotation 0–360°. The semi empirical method PM6 is recommended [28] for the conformational analysis, as it does the job faster than the DFT methods with reliable results. The graphical result, total energy verses scan coordinates, of this conformer analysis is presented in Fig. 1. While comparing the different structure of the conformer with respect to energies are analysed. The first conformer at 30° with energy −100.869 kcal mol^{-1}, in which the highly negative OH group found in trans conformer form, which are found much away from other OH groups in the molecule. This conformer has highest energy. The

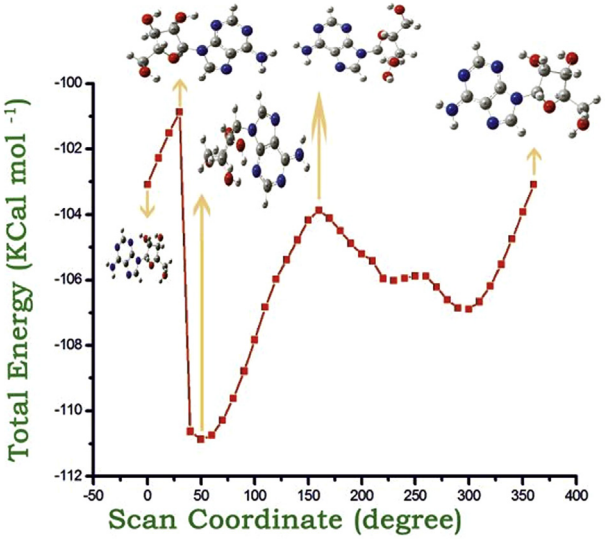

Fig. 1. Potential Energy Profile of Adenosine (minimum at 50^0 with lowest energy −110.863 kcal mol^{-1}) (Dihedral Angle of C3–N11–C15–C20 (degree)).