Structural analysis of potent Tv drugs

Ashish sharma
Lovely Professional Unoversoty, Punjab

Throughout history, several references were found about pharmaceutical use of naturally occurring quinines. Streptonigrin is natural quinine with antitumor and antibiotic activity [7]. Kingston and co-workers [8] have isolated two new benzoquinones 2-methoxy-6-heptyl-1, 4-benzoquinone and 2-methoxy-6-pentyl-1, 4-benzoquinone from the leaves of Miconia lepidota present in Surinam forests.

Recently Sansom et al. [9] has isolated an antiproliferative bis-prenylated quinone,5-[1,1-dimethylprop-2-enyl-2-[3-methylbut-2-enyl]cyclohexa-2,5-diene-1,4-dione from the New Zealand brown alga Perithalia capillaries. This compound inhibited superoxide production by human neutrophils in vitro and was also reported to inhibit proliferation of HL60 cells.

Polyanoquinones A and B were used in Taiwan as tonic drugs from years. Heliotropiquinone A and B were used as antifungal, antibacterial [10]. 2-chloro-5-methoxy-3-methyl-cyclohexa-2, 5-diene-1, 4, dione and xylariaquinone were used as antimalarial [11]. Sesquiterepine [12] quinines were used as antiviral, antimicrobial and cyto-toxics

The budding applications of the quinones and their derivatives have inspired the scientists to calculate their oxidation and reduction potentials, and studying the molecular dynamics. Computational studies of these molecules can be supportive in understanding the physical parameters and properties that control the reactivity of the compounds in the human bodies. Due to rapid development of computer assisted calculations such as density functional theory and the semi-empirical calculations have simplified the complicated and tiresome quantum mechanical treatment of larger molecules. In theoretical research, one has to hypothesize complicated structures in quantum mechanics. Semi-empirical Methods are simplified versions of Hartree-Fock theory using empirical corrections in order to improve performance. The most frequently used methods (MNDO, AM1, PM3) are all based on the Neglect of Differential Diatomic Overlap (NDDO) integral approximation. Semi Empirical methods allow study of systems which were out of reach of more accurate method. These methods have made it possible to study molecules containing thousands of atoms

These methods were mainly used to:-

- Study QSAR to know about property trends for a group of similar compounds.
- Develop new algorithms
- Check the gross errors in experimental heat of formation data
- Preliminary optimization of geometries of highly complicated molecules and transition states
- Applications in which qualitative study of electronics structures is required

To overcome limitations of slow speed and compexicity, parameterization of contained integrates is used. So using different approximation, different semi empirical methods were devised. Semi empirical methods are useful in:

- electronic structure determinations
- geometry optimizations
- frequency calculations
- transition structures
- protein calculations, i.e. docking
- electron and charge distributions
- potential energy surfaces (PES)
- rate constants for chemical reactions (kinetics)
- thermodynamic calculations- heat of reactions, energy of activation

Literature survey

Quinones are electron and proton carriers that play a primary role in the aerobic metabolism of virtually every cell in nature. Most physiological quinones are benzoquinones. They undergo highly regulated redox reactions in the mitochondria, Golgi apparatus, plasma membrane and endoplasmic reticulum. Thus they are of key importance in producing energy during oxidative metabolism and photosynthesis [20] and have been area of great interest to scientists all over the world. Extensive research has been being carried out on quinones and its derivatives. Literature related to the proposed work is discussed as:

DFT studies of structure and vibrational spectra of bromanil formed on photoexcitation by Puranik et al. [21] showed that relative change in normal modes have brought the structural reorganization that occur in the molecule on electronic excitation, reduction and substitution.

In the study of Singlet state the geometries of p- benzoquinone and bromanil when optimized at same level of theory; bond length and angle values of p- benzoquinone and bromanil were compared with experimental data of p-benzoquinone,it was found that bromine atoms move away from each other towards oxygen atoms than the hydrogen atoms in quinone.

When Triplet states were investigated, electronic excitation in triplet state distorts the ring considerably in bromanil. The studies of the radical quinone and semiquinone radical of bromanil provide very significant information about effect of halogen substitution. The largest structural re organization is observed in the semi Quinone radical. The normal mode composition studies show that both electronic excitations and reduction affect normal mode composition.

Khan et al. [22] studied the absorption spectra of anthra quinone and found that intermolecular Hydrogen bonding greatly affects the character of excited states. In general, the intermolecular Hydrogen bonds are responsible for the stability of predominant confirm. IHBs greatly affect the electronic spectra hydroxy derivatives of quinones. To understand the characteristics of electronic states, absorption spectra were studied. These comparisons showed that result of ZINDO/S calculations were in better agreement with experimental data.

Ab initio molecular orbital study of pyrido quinones [23] shows that among all possible isomers of pyridoxine, the 215 isomers is most stable . In this study the structure of BQ & phylloquinone were optimized at HF/6-3/G and B3LYP/6 levels and single point energies were calculated.

Zafar et al. [24] implemented ZINDO/1, optimized Ground state nuclear geometries of C-60 & C-70.The planar structure of C-60 & C-70 were considered then converted into 3D structures. Using all valence electron ZINDO/S method, No. of configuration were chosen by using the energy cut off criterion. Then this energy cut off was varied systematically to get the best matching of calculated and observed electronics transitions energies. ZINDO/S method appeared to be a better computational method to calculate the experimental bands ofC-70. Each transition was well predicted by the ZINDO/S calculations and the calculated transitions matched with the observed spectral bands.

The calculated descriptor values will be analyzed with the help of various computational models i.e. algorithms and iterative sequences.

Then a proper criterion will be set for evaluation of credibility of each computational model used..Comparison of experimental and calculated data.Drawing conclusions

References:

[1] Baik W.; Kim, S.J.; Hurh, E. Y.; Koo, S.; Kim, B.H.; bull Korean chem. 1998.

[2] Tsutui, S.; Sakamato, K.; Yoshida, H; Kunai, J; organometallic chem.2005.

[3] Nayak, N.; Bajpai, M.; Razdan, B.; j. Afv. Pharm.Technol Res; vol 5, issue 1, 2014.

[4] Paengsri W.; Lee, V.S.; Chong, W. L.; Wahab, H.A.; Baramee, A.; Intl. J. Bio.chem.2012.

[5] Hazra, B.; Mukanganyama, S.; Chirisa, E.; Res. In pharm., 2012.

[6] Mital, A.; Negi, V.S.; Ramchandran, U.; Arkivoc, 2008.

[7] Sharma, M.C.; Sharma, S.; J. Pharm. Toxico., 2011.