Available online at
www.ijacskros.com

Indian
Journal of Advances in
Chemical Science

Indian Journal of Advances in Chemical Science 4(3) (2016) 314-320

Quantum Mechanical Study on the Proton Transfer Mechanism within Adenine-thymine and Guanine-cytosine Base Pairs of DNA Nucleobase

Bipul Bezbaruah[1]*, Chitrani Medhi[2]

[1]Department of Applied Sciences, Gauhati University, Guwahati - 781 014, Assam, India. [2]Department of Chemistry, Gauhati University, Guwahati - 781 014, Assam, India.

Received 27th June 2016; Revised 05th July 2016; Accepted 07th August 2016

ABSTRACT

Proton transfer mechanism between DNA nucleobases in biological system is a well-established natural phenomenon. Again it is experimentally established that the anticancer drugs directly bind with DNA nucleobases with different types of interactions. During these interactions, the proton transfer mechanism between nucleobases of DNA (adenine-thymine [AT] and guanine-cytosine [GC]) may be slightly changed. The proton transfer mechanism within DNA nucleobases, GC, and AT base pairs had been studied for normal base pairs and drug-base pair stacked models. Theoretically, it was observed that the stacking interactions of drugs with base pair of DNA results change in the proton transfer energies. The mechanism of proton transfer may also change the acid-base characteristics of nucleobase during proton transfer. Due to the stacking interaction between drug chromophore and nucleobase, the barrier of proton transfer energies might have changed, and it also indicates the shifting of equilibrium proton transfer between counter nucleobases.

Key words: *Ab initio method, DNA nucleobase, Proton transfer.*

1. INTRODUCTION

The continuous proton transfer mechanism within hydrogen bonds of Watson-Crick base pairs in DNA is a well-established phenomenon. The formations of tautomeric forms of nucleobase during proton transfer processes are also found [1-7]. The tautomers of nucleobase may be important species in mutagenesis [5]. It might be related to the generation of other mismatch base pairs in double helix DNA. The mechanism of proton transfer is a very critical chemical aspect that is related to the change of acid-base characteristics of the nucleobases in Watson-Crick base pair. Subsequent adjustment of acidic and basic characteristics of nucleobases with the surrounding water molecules or ions during proton transfer may be an essential process [6-14]. In such situation, the energetic and dynamical behavior of the proton may be depicted from the change of the acid-base characteristics of Watson-Crick base pairs [9-12]. On the contrary, the ions and water molecules present in solution should participate to neutralize the variation of acid-base behavior during proton transfer. The nucleobase may exist in different forms such as tautomers, radicals, and cations intermediate during proton transfer processes. However, all these species may not be easy to consider simultaneously during proton transfer. Initially, it is necessary to analyze the subsequent effect in base pair due to the change of acid-base characteristics within the base pair or the surrounding.

In the previous studies, we have preformed several calculations on the stacking interaction between aromatic chromophore with base pairs [11-14,16,17]. Such interactions may affect the proton transfer processes in normal double helix DNA. The topic is quite relevant to the understanding of other important biological processes. So, it is rather necessary to understand how the interactions of the drug within DNA sequences affect the proton transfer phenomena [15]. The energy barrier of proton transfer within base pair may be drastically affected due to the intercalation of drug molecules, and thereby disturb the equilibrium proton transfer reaction in normal double helix DNA. It may, in turn, play a central role in DNA replication, and in fact, the outcome of mismatched base pairs is possible [16-23].

2. METHODOLOGY

2.1. Models of Proton Transfer

Two different mechanisms of proton transfer (H-shifting) between counter nucleobases have been

*Corresponding Author:
E-mail: bipulbezbaruah@gmail.com
Phone: +91-9854634789

modeled, where the possibility of Ha transfer toward guanine, and Hb or Hc toward cytosine in GC is depicted in Figures 1, 2a and c. The two counter H-atoms, Ha and Hb, or Ha and Hc may be shifted between guanine and cytosine as shown in Figure 1. Likewise, the model for proton transfer between adenine and thymine in AT has been constructed (Figure 3). In these models, the pairwise proton transfer is examined independently. As we know that the basic concept of proton transfer in Watson-Crick base pair lies on the adjustment of acidic and basic sites within AT and GC during proton shifting [21-25,31]. Here, one of the hydrogen atoms is kept at a particular position say DÅ, which in fact represents the characteristic of acidic H atom, and the energetic of H transfer of the other H atom is monitored from the potential energy surface (Figures 2a-d, 4a and b). The changes in potential energy for various distances of H-shifting have been analyzed. The typical model study depicts the inter-nucleobase proton transfer under acidic or basic solvent environment[26]. At the moment, the generation of radicals and tautomerization of nucleobases are not considered, but the possible proton transfer pathways as a result of stacking interaction between aromatic drug and the base pair have been particularly examined.

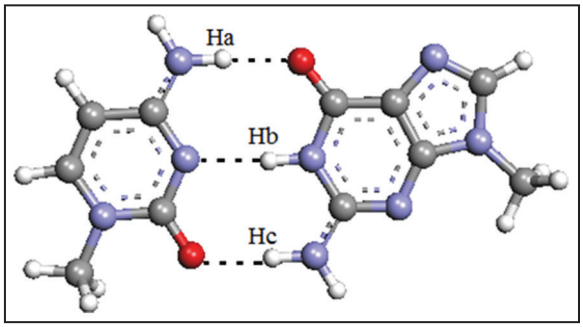

Figure 1: Optimized structure of guanine-cytosine base pair.

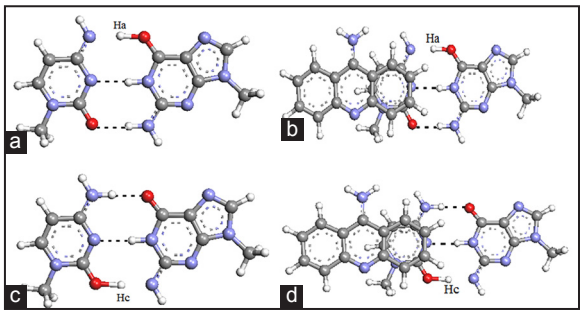

Figure 2: (a) Transition state structure of unstacked guanine-cytosine (GC) base pair for proton (Ha) transfer type PT1. (b) Transition state structure of stacked GC base pair for proton (Ha) transfer type PT1. (c) Transition state structure of unstacked GC base pair for proton (Hc) transfer type PT2. (d) Transition state structure of stacked GC base pair for proton (Hc) transfer type PT2.

2.2. Theory

All calculations are carried out with Gaussian 03 program code [32]. Complete geometry optimization of the base pairs and nucleobases (A, T, G, and C) has been performed with HF/6-31G** calculations. Single point calculations (MP2/6-31+G(d,p)) of the models used in depicting the proton transfer mechanism are performed. We have used JoinMolecules[8] program [21] for constructing the geometries of base pair and the stacked drug with the base pair. The position of each stacked drug has been kept fixed during proton shifting within counter nucleobases.

3. RESULTS AND DISCUSSIONS

The proton transfer mechanisms within GC and AT base pairs are analyzed separately. The potential energy surface for the proton transfer (PT1) of the first two hydrogen atoms and the second two hydrogen atoms (PT2) in GC are shown in Figure 5a-d. We have examined only one model of proton transfer (PT3) for AT base pair. As indicated in Figure 5a-d, the two energy minima in the potential energy surface of PT1 represent the existence of base pair, (GHa)C, and G(HaC). Similarly, the formation of

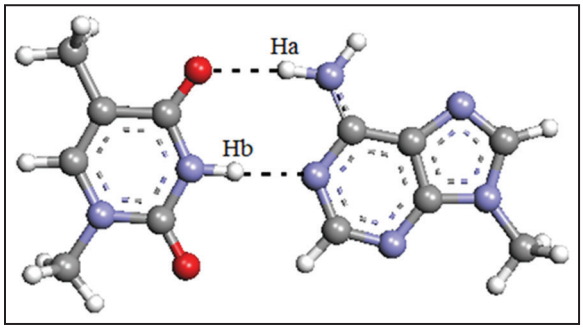

Figure 3: Optimized structure of adenine-thymine base pair.

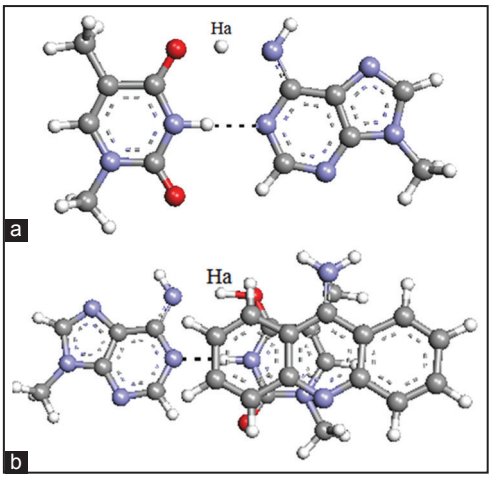

Figure 4: (a) Transition state structure of unstacked adenine-thymine (AT) base pair for proton (Ha) transfer type PT3. (b) Transition state structure of stacked AT base pair for proton (Ha) transfer type PT3.

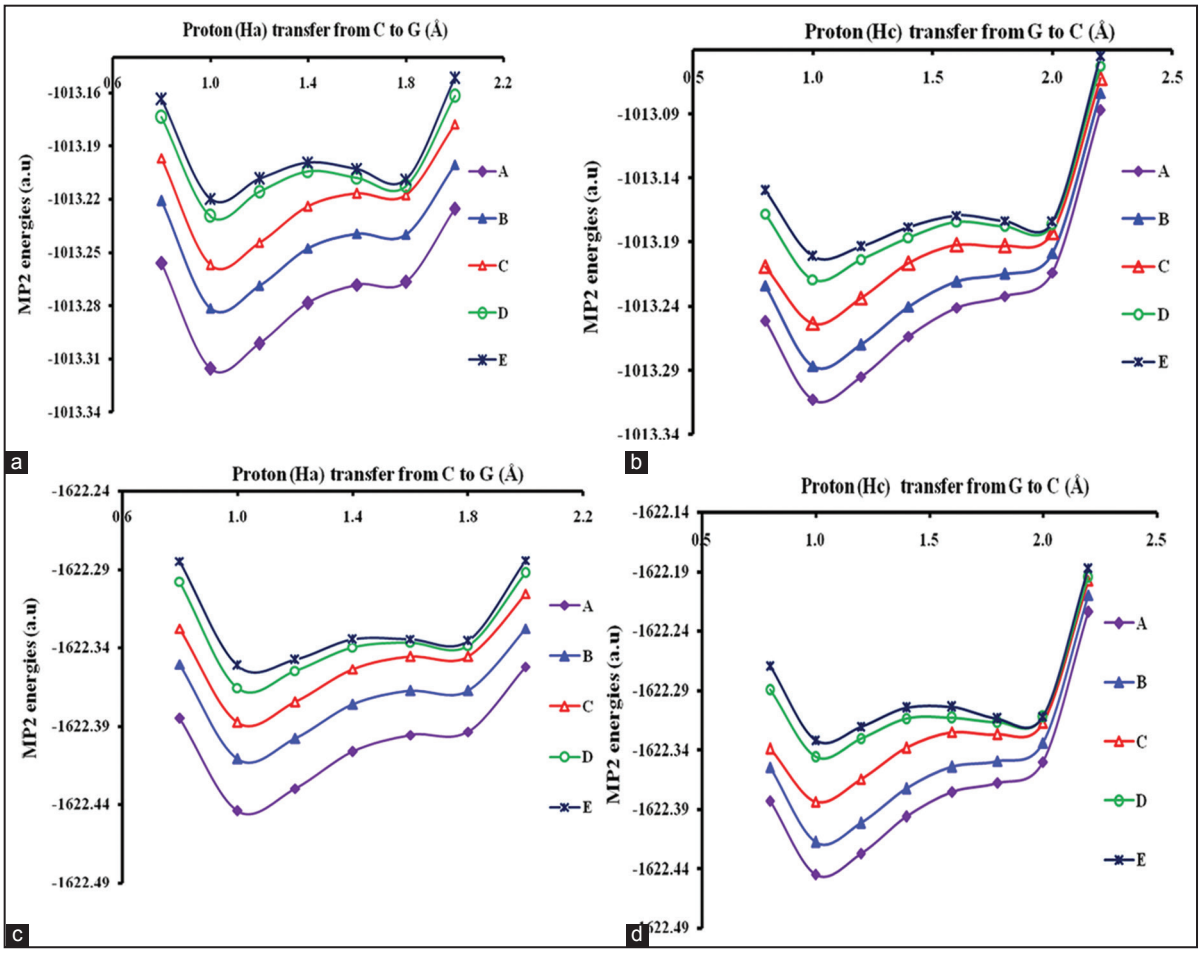

Figure 5: (a) Potential energy surface during proton transfer for unstacked guanine-cytosine (GC) base pair at different distances in angstrom, where A = 1.0Å, B = 1.3Å, C = 1.5Å, D = 1.9Å, and E = 2.1Å (Proton transfer type PT1). (b) Potential energy surface during proton transfer for unstacked GC base pair at different distances in angstrom, where A = 1.0Å, B = 1.3Å, C = 1.5Å, D = 1.9Å, and E = 2.1Å (Proton transfer type PT2). (c) Potential energy surface during proton transfer for unstacked GC base pair at different distances in angstrom, where A = 1.0Å, B = 1.3Å, C = 1.5Å, D = 1.9Å, and E = 2.1Å (Proton transfer type PT2). (d) Potential energy surface during proton transfer for stacked GC base pair at different distances in angstrom, where A = 1.0Å, B =1.3Å, C = 1.5Å, D = 1.9Å, and E = 2.1Å (Proton transfer type PT2).

(GHc)C and G(HcC) is found in the potential energy surface of PT2. The maxima in the potential energy surfaces indicate the transit point (TS) during the proton transfer. In these plots, the difference between the energy minima for the proton transfer in PT1 and PT2 becomes smaller as the proton shifts from G to C (Figure 5b and d). It is possible to locate the position of optimum energy level for the proton transfer reaction. In the sense, the existence of (GHa)C and G(HaC) at almost equal energy level can be identified at a particular distance, D (2.1Å). It indicates that under certain condition, the formation of both (GHa) C and G(HaC) is possible (Figure 2a and b). It may be the necessary condition for the feasibility of proton transfer (PT1) within GC base pair. Similarly, the formation of (GHc)C and G(HcC) is found from the energy minima in the plot of PT2 (Figure 2c and d). Based on these, energy minima (GHa)C and G(HaC) are considered as reactant and product for PT1 and (GHc)C and G(HcC) are found for PT2. We have estimated the energy barriers of proton transfer in PT1 and PT2, and the values are shown in Table 1. The corresponding energy barriers for AT base pair (PT3) are shown in Table 2. Moreover, the hydrogen bond distances for the transition state structure as well as for the reactant and products are shown in Table 3. In all these calculations, we have considered only the rigid monomer of the base pair and the relaxation of other geometrical parameters during proton transfer is not considered. However, there observed the significant variation of energy barriers for PT1 and PT2, and PT2 occurs at slightly higher energy level than PT1. The energies of formation of (GH)C and G(HC) obtained from the energy minima of PT1 are 10.541 kcal/mol and for PT2 are 17.234 kcal/mol, respectively.

Similarly, to investigate the proton transfer mechanism in AT base pair (PT3), we have followed the same model calculations used in GC base pair. The acidic nature of one of the counter bases has been adjusted by shifting the Hb atom at various distances (DÅ), the potential energy surfaces at each distance is explored (Figure 6a and b). Such model calculation could predict the equilibration between (AHa)T and A(HaT) for maintaining continuous proton transfer reaction within AT base pair.

Table 1: Computed energy barriers (kcal/mol) at minimum and equilibrium distance of different proton transfer for GC and stacked GC.

Proton transfer (Ha) From C to G	Energy barriers, ΔE (kcal/mol)	
	GC	Stacked GC
A (Hc=1.0Å)	29.707	30.495
B (Hc=1.3Å)	26.433	27.300
C (Hc=1.5Å)	25.228	26.413
D (Hc=1.9Å)	13.679	18.258
E (Hc=2.1Å)	10.542	10.541
Proton transfer (Hc) From G to C	**GC**	**Stacked GC**
A (Ha=1.0Å)	45.072	43.451
B (Ha=1.3Å)	41.249	39.742
C (Ha=1.5Å)	38.230	36.681
D (Ha=1.9Å)	28.193	20.370
E (Ha=2.1Å)	19.912	17.234

When Ha is transferred then Hc is kept constant and when Hc is transferred then Ha is placed at a constant distance. GC: Guanine-cytosine

Table 2: Computed energy barriers (kcal/mol) at minimum and equilibrium distance of different proton transfer for AT and stacked AT.

Proton transfer (Ha) From A to T	Energy barriers, ΔE (kcal/mol)	
	AT	Stacked AT
A (Hc=1.0Å)	47.154	45.531
B (Hc=1.3Å)	40.497	39.044
C (Hc=1.5Å)	39.810	38.854
D (Hc=1.9Å)	25.203	23.798
E (Hc=2.1Å)	14.717	16.401

When Ha is transferred then Hc is kept at a constant distance. AT: Adenine-thymine

The minima in the potential energy plot show the formation of (AHa)T and A(HaT) base pair, which are found significantly dependent on the acidic nature of one of the hydrogen bonds (Figure 4a and b). However, at highly acidic condition as designated by the closer approach of Hb from A to T, the difference of energy level of (AHa)T and A(HaT) becomes small. The situation is very essential for maintaining continuous proton transfer reaction within AT base pair. As we can see that the increase of acidic behavior of Hb (as depicted by the distance D = 2.1Å), the concomitant reduction of the difference of these two energy minima (Figure 6a and b). The model calculations are unique for maintaining proton transfer reaction within AT base pair.

Furthermore, we have analyzed the hydrogen bond distances of the base pair at the energy minima as well as at the transition state from the potential energy surface of equilibrium proton transfer (Table 3). The model study on proton transfer at this equilibrium potential energy surface may indirectly demonstrate the effect of solvent molecules, proton, and other cations that could participate in the proton transfer reaction. In this case study, we assume that the instantaneous effect of solvent molecules or ion could manifest the continuous proton transfer reaction. At a certain surrounding solvent environment, the estimation of equilibrium proton transfer potential within base pair is an essential measure to understand the H shifting ability within two equilibrium structures of AT, and also for GC, if the solvent environments truly contribute in this process. Figures 5a-d, 6a and b show the energetic of the two energy minima in the potential energy surface, which are significantly different except

Table 3: Hydrogen bond distances for proton during proton transfer within DNA base pair sequences (both for stacked and unstacked base pairs).

Types of proton transfer	Base pairs	Hydrogen bond distances of transferable proton (Å)		
		Reactant	Transition state	Product
PT1 (Ha)	GC	1.830	-	-
	Stacked GC	1.922	-	-
PT2 (Hc)	GC	1.922	-	-
	Stacked GC	1.830	-	-
PT3 (Ha)	AT	2.018	-	-
	Stacked AT	2.017	-	-

AT: Adenine-thymine, GC: Guanine-cytosine

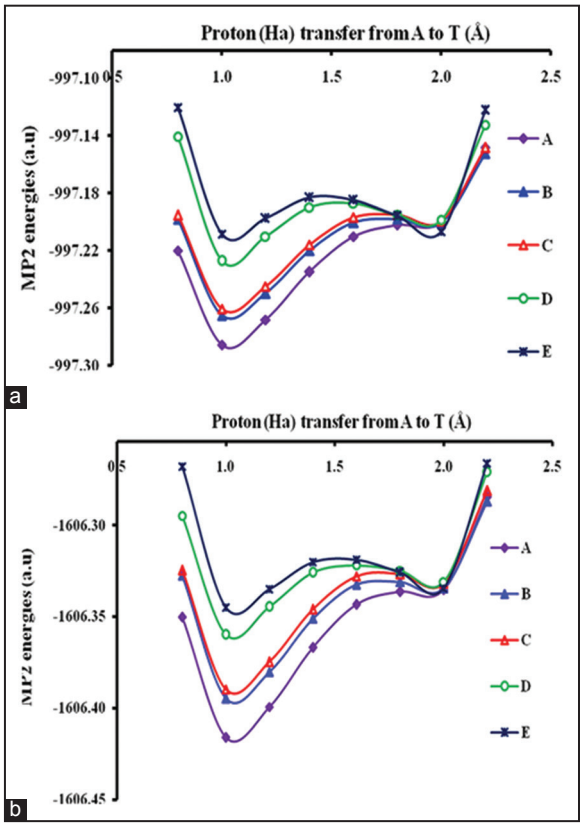

Figure 6: (a) Potential energy surface during proton transfer for unstacked adenine-thymine base pair at different distances in angstrom, where A = 1.0Å, B = 1.3Å, C = 1.5Å, D=1.9Å, and E = 2.1Å (Proton transfer type PT3). (b) Potential energy surface during proton transfer for stacked AT base pair at different distances in angstrom, where A = 1.0Å, B = 1.3Å, C = 1.5Å, D = 1.9Å, and E = 2.1Å (Proton transfer type PT3).

at the equilibrium situation of proton transfer (i.e., at D = 2.1Å for GC and D = 2.1 Å for AT). The energy differences as observed in other distances are not the feasible condition for undergoing equilibrium proton transfer reaction between two structures because the proton may be localized within certain region leading to the stabilization of a structure. In general, it is clear that lengthening of a hydrogen bond length results increase of acidic properties of the counter nucleobase, which can be used as model studies to rationalize the proton transfer in AT and GC. However, such changes in acidity can profoundly happen due to the influence of surrounding ions and molecules in the real solvent environment. The proton transfer reactions are usually assisted by surrounding ions or molecules to compromise the acidic or basic properties of counter nucleobases. However, the information obtained from gas phase calculation is also useful for explaining the equilibration of two structures for both AT and GC during proton transfer reaction.

The existence of proton transfer within base pair sequences of DNA has been explained in the many gas phase calculations, which is not a perfect model because such reactions are not completely independent of the surrounding water and ions present in solution [25,27-30]. In this regard, water assisted proton transfer is also highlighted in some studies [28]. Hence, the certain emphasis has been given on the metal or proton catalyzed proton transfer mechanism occurred due to the interaction with lone pair electrons present on the various atomic sites from the exterior region of the base pair [29-30]. It is worth mentioning that such effect cannot be neglected in the proton transfer reaction within AT or GC base pair. In real condition, the proton transfer reaction is catalyzed by various hydrogen bonding molecules of the surrounding solvent. So, in the present study, the important implication is to demonstrate the situations how the equilibrium proton transfer (EQ) could occur in base pair. It may be noted that the transient of a proton from G to C or A to T, and vice versa is possible at a particular distance (Figures 5a-d, 6a and b). As mentioned before, such model can indirectly reflect the adjustment of acidic and basic behavior of counter nucleobases (as taken by the position of H) of WC base pair as a result of the catalytic effect of ions or hydrogen bond effect from the surrounding solvent molecule.

Furthermore, we have analyzed that the deviation of equilibrium energy levels as well as the transition state energies of stacked base pair from those of non-stacked structures. The shift of potential energy surface due to the stacking interaction of drug and base pair is found quite significant. There observed differences of the transition state energies of PT1 and PT2. However, the similarity of proton transfer mechanism is well maintained in the stacked base pair with drug. We note that the proton transfer reactions for PT1 and PT2 in the stacked structures pass through higher energy barriers compared to the non-stacked structures (Table 1 and Figure 5a-d). The results naturally manifest that the presence of aromatic molecules stacked with base pair would inhibit the proton transfer phenomena within GC base pair. The details of the potential energy surfaces to predict preferable condition for proton transfer reaction for both the free and non-stacked base pair have been analyzed (Figure 5a-d). As we can see in Tables 1 and 2 and Figures 2a-d, 4a and b, a small shift of transition state is found. The increase of energy barrier for the shifting of proton within GC and AT due to stacking interaction between aromatic rings cannot be neglected. The results indicate that the proton transfer kinetics may be slowed down compared to that of non-stacked situation. During the dynamical proton transfer reaction, the relaxation of the geometrical parameters usually takes place to compensate the acid-base characteristics within WC hydrogen bonding region, and also as a result of various solvent polarities and other hydrogen bond formation capacity around DNA. However, the geometric

relaxation is not considered in the present study, and such relaxation might lead to other molecular species such as tautomers and radicals of nucleobases. Hence, the proton shifting within base pairs has been analyzed only for the rigid conformation.

4. CONCLUSION

It has been found that there is a significant variation of the energy barrier for proton shifting in GC base pair. PT2 occurs at slightly higher energy level than PT1. Such model calculation could predict the equilibration between (AHa)T and A(HaT) for maintaining continuous proton transfer reaction within AT base pair. Similarly, the model study for GC base pair shows the existence of (GH)C and G(HC) at almost equal energy level. The proton transfer reactions for PT1, PT2, and PT3 in the stacked structures are found at higher energy barriers compared to the non-stacked structures. Hence, the stacked aromatic molecules with base pair would inhibit the proton transfer phenomena within base pair.

5. ACKNOWLEDGMENTS

Authors are highly grateful to the UGC, for providing financial Assistance and also the Department of Applied Sciences Gauhati University.

6. REFERENCES

1. L. Gorb, Y. Podolyan, P. Dziekonski, W. A. Sokalski, J. Leszczynski, (2004) Double-proton transfer in adenine-thymine and guanine-cytosine base pairs. A post-Hartree-Fock Ab Initio study, ***Journal of American Chemical Society*****, 126:** 10119-10129.
2. L. Xifeng, C. Zhongli, S. D. Michael, (2001) DFT calculations of the electron affinities of nucleic acid bases: Dealing with negative electron affinities, ***Journal of Physical Chemistry A,*** **106:** 1596-1603.
3. I. R. Could, P. A. Kollman, (1994) Theoretical investigation of the hydrogen bond strengths in guanine-cytosine and adenine-thymine base pairs, ***Journal of American Chemical Society,*** **116:** 2493-2499.
4. I. R. Gould, N. A. Burton, R. J. Hall, I. H. Hillier, (1995) Tautomerism in uracil, cytosine and guanine - A comparison of electron correlation predicted by Ab Initio and density functional theory methods, ***Journal of Molecular Structure (THEOCHEM),*** **331:** 147-154.
5. N. J. Kim, (2006) DFT study of water-assisted intramolecular proton transfer in the tautomers of thymine radical cation, ***Bulletin of the Korean Chemical Society,*** **27:** 1009-1014.
6. V. I. Danilov, V. M. Anisimov, N. Kurita, D. Hovorun, (2005) MP2 and DFT studies of the DNA rare base pairs: The molecular mechanism of the spontaneous substitution mutations conditioned by tautomerism of bases, ***Chemical Physics Letters,*** **412:** 285-293.
7. J. Sponer, P. Hobza, (1994) Nonplanar geometries of DNA bases. Ab Initio second-order Moeller-Plesset study, ***Journal of Physical Chemistry A,*** **115:** 5903-5912.
8. H. Ushiyamaa, K. Takatsukab, (2001) Successive mechanism of double-proton transfer in formic acid dimer: A classical study, ***Journal of Chemical Physics,*** **98:** 3161-3164.
9. N. Zhanpeisov, J. Leszczynski, (1998) The specific solvation effects on the structures and properties of adenine−uracil complexes: A theoretical Ab Initio study, ***Journal of Physical Chemistry A,*** **102:** 6167-6172.
10. S. Kristyan, P. Pulay, (1994) Can (semi)local density functional theory account for the London dispersion forces? ***Chemical Physics Letters,*** **229:** 175-180.
11. J. M. Pérez-Jordá, A. D. Becke, (1995) A density-functional study of van der Waals forces: Rare gas diatomics, ***Chemical Physics Letters,*** **233:** 134-137.
12. E. Ruiz, D. R. Salahub, A. Vela, (1995) Defining the domain of density functionals: Charge-transfer complexes, ***Journal of American Chemical Society,*** **117:** 1141-1142.
13. T. A. Weselowski, O. Parisel, Y. Ellinger, J. Weber, (1997) A comparative study of weak van der Waals complexes using density functional theory: The importance of an accurate exchange-correlation energy density at high reduced density gradients, ***Journal of Physical Chemistry A,*** **101:** 7818-7825.
14. M. Hanus, M. Klabelac, J. Rejnek, F. Ryjacek, P. Hobza, (2004) Correlated Ab Initio study of nucleic acid bases and their tautomers in the gas phase, in a microhydrated environment, and in aqueous solution. Part 3. Adenine, ***Journal of Physical Chemistry B,*** **108:** 2087-2097.
15. C. F. Guerra, F. M. Bickelhaupt, S. Saha, F. Wang, (1998) Adenine tautomers: Relative stabilities, ionization energies, and mismatch with cytosine, ***Journal of Physical Chemistry A,*** **110:** 4012-4020.
16. M. Chachisvilis, T. Fiebig, A. Douhal, A. H. Zewail, (1998) Femtochemistry in nanocavities: Reactions in cyclodextrins, ***Journal of Physical Chemistry A,*** **102:** 1657-1660.
17. O. H. Kwon, A. H. Zewail, (2007) Double proton transfer dynamics of model DNA base pairs in the condensed phase, ***Proceedings of the National Academy of Sciences*****, 104:** 8703-8708.
18. V. Zoete, M. Meuwly, (2004) Double proton transfer in the isolated and DNA-embedded guanine-cytosine base pair, ***Journal of Chemical Physics,*** **121:** 4377-4388.
19. J. Bertran, A. Oliva, L. Rodriquiz–Santiago, M. Sodupe, (1998) Single versus double proton-transfer reactions in Watson-Crick base pair

radical cations. A theoretical study, ***Journal of American Chemical Society,*** **120:** 8159-8167.
20. S. Steenken, (1989), Purine bases, nucleosides, and nucleotides: Aqueous solution redox chemistry and transformation reactions of their radical cations and e-and OH adducts, ***Chemical Reviews,*** **89:** 503-520.
21. S. Steenken, (1997), Electron transfer in DNA? Competition by ultra fast proton transfer? ***Biological Chemistry*****, 378:** 1293-1297.
22. K. Kawai, T. Takada, S. Tojo, T. Majima, (2002) Regulation of one-electron oxidation rate of guanine and hole transfer rate in DNA through hydrogen bonding, ***Tetrahedron Letters,*** **43:** 8083-8085.
23. J. Taylor, I. Eliezer, M. D. Sevilla, (2001) Proton-assisted electron transfer in irradiated DNA − Acrylamide complexes: Modeled by theory, ***Journal of Physical Chemistry B,*** **105:** 1614-1617.
24. A. O. Colson, B. Besler, M. D. Sevilla, (1992) Ab Initio molecular orbital calculations on DNA base pair radical ions: Effect of base pairing on proton-transfer energies, electron affinities, and ionization potentials, ***Journal of Physical Chemistry,*** **96:** 9787-9794.
25. A. O. Colson, M. D. Sevilla, (1995) Structure and relative stability of deoxyribose radicals in a model DNA backbone: Ab Initio molecular orbital calculations, ***Journal of Physical Chemistry,*** **99:** 3867-3874.
26. A. O. Colson, M. D. Sevilla, (1995) Ab Initio molecular orbital calculations of radicals formed by H. bul. and bul. OH addition to the DNA bases: Electron affinities and ionization potentials, ***Journal of Physical Chemistry,*** **99:** 13033-13037.
27. M. D. Sevilla, B. Besler, A. O. Colson, (1995) Ab Initio molecular orbital calculations of DNA radical ions. 5. Scaling of calculated electron affinities and ionization potentials to experimental values, ***Journal of Physical Chemistry,*** **99:** 1060-1063.
28. A. Kohen, J. P. Klinman, (1998) Enzyme catalysis: Beyond classical paradigms, ***Accounts of Chemical Research,*** **31:** 397-404.
29. B. C. Gilbert, M. J. Davies, D. M. Murphy, M. D. Sevilla, D. Becker, (2004) ESR studies of radiation damage to DNA and related biomolecules, ***Electron Paramagnetic Resonance,*** **19:** 243-278.
30. D. M. Close, W. H. Nelson, E. Sangstuen, E.O. Hole, (1992) On the proton transfer behavior of the primary oxidation product in irradiated DNA, ***Radiation Research,*** **131:** 10-17.
31. R. Parajuli, R. Kalita, C. Medhi, (2006) Is Ab Initio DFT method useful in analysing sequence specificity of bases in nucleic acids? ***Indian Journal of Chemistry B,*** **45:** 782-791.
32. M. J. Frisch, G. W. Trucks, H. B. Schlegel, P. M. W. Gill, B. G. Johnson, M. A. Robb, J. R. Cheeseman, T. Keith, G. A. Petersson, J. A. Montgomery, K. Raghavachari, M. A. Al-Laham, V. G. Zakrzewaki, J. V. Ortiz, J. B. Foresmann, J. Ciolowski, B. B. Stefanov, A. Namayakkara, M. Challacombe, C. Y. Peng, P. Y. Ayala, W. Chen, M. W. Wong, J. L. Andres, E. S. Replogle, R. Gomperts, R. L. Martin, D. J. Fox, J. S. Binkley, D. J. Defrees, J. Baker, J. P. Stewart, M. Head-Gordon, C. Gonzalez, J. A. Pople, (2003), ***Gaussian 2003,*** Pittsburgh, PA: Gaussian Inc.

****Bibliographical Sketch***

Dr. Bipul Bezbaruah has been working as an Assistant Professor in the Department of Applied Sciences (Chemical Science Section) since 2010, in Gauhati University, Assam. His Research field is purely Theoretical Chemistry and currently, he has been working on Anticancer Drug Designing, Molecular Mechanics and Force field studies of DNA and Protein Binding Drugs, Quantum Mechanical Stacking of organic biomolecules.