Spring 2021 Meeting of the APS Ohio-Region Section

Study on the Dynamics of Gene Mutation Due to DNA Adducts

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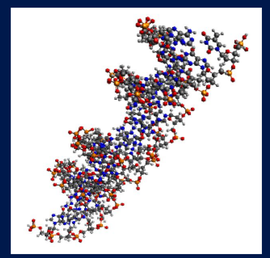
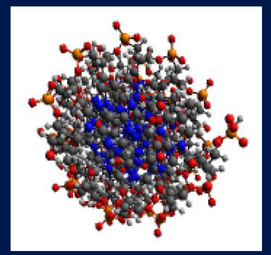
Abstract

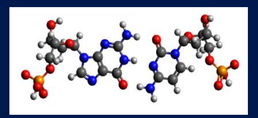
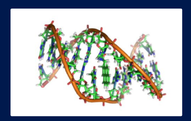
Density-functional theory and quantum mechanical modelling technique were used to study electronic structure of gene molecules. Using the DFT, the electron system was explained using computational simulations the progression of oxidation of DNA in nerve cells, which occurs during the enzymatic metabolism from benzo[a]pyrene to BPDE.

In the process, intercalation resulted in the formation of guanine benzopyrene through binding with guanine bases in the DNA. In the DNA intercalation, thermodynamic changes were observed while the guanine benzopyrene intercalates to form an adduct which the binding causes the alteration of the structure and the abnormal replication proceeds to gene mutation. Physical properties such as optimized energy, dipole moment and electrostatic potential maps were calculated to figure out how different the values of the different atoms in a molecule affect the stability of the system. Results showed that the optimization energy of the studied molecule increased as the weight and size of molecules increased. Optimization energy of the complex G-BPDE : C and C : G(3093.631kJ/mol) showed highest among the tested samples.

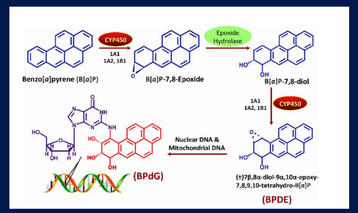
DNA Adduct

For the biochemical analysis of the DNA adduct which is a segment of DNA bound to a molecule causing cancer, molecular gene editing programs are used. Computational chemistry and Density Functional Theory (DFT) are further used to find the compounds' biophysical properties such as active energy and optimized molecular shape in assessing the thermodynamic stability of the molecular genes.

BP to BPdG

1. First oxidized to form a variety of products, including (+)benzo[a]pyrene-7,8-epoxide.
2. Metabolized by epoxide hydrolase, opening up the epoxide ring to yield (−)benzo[a]pyrene-7,8-dihydrodiol.
3. The ultimate carcinogen is formed after another reaction to yield the (+)benzo[a]pyrene-7,8-dihydrodiol-9,10-epoxide. It is this diol epoxide that covalently binds to DNA(adduct).



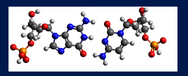
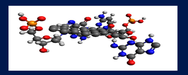
Opt. E / EPM

Opt. E / EPM

Molecule	Ball and Stick Model	Electrostatic Potential Map
Benzo[a]pyrene		
Benzo[a]pyrene-7,8 Epoxide		
Benzo[a]pyrene-7,8 Diol		
BPDE		
BPdG		

Stability of BPDE

The Optimized Energy of molecules with BPDE is much higher than that of the others, meaning that they are more unstable. This also expands the DNA in a section by breaking the hydrogen bonds that are interfered with by the BPDE. This would lead to improper DNA replication, which, if it affects a tumor suppressor gene, could lead to the development of cancer.

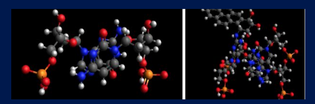



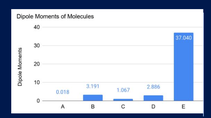
BPdG / G:C vs. G-BPDE:C

	Molecules	Opt. Energy(kJ/mol)	Dipole Moments	Chemical Formula	Molecular Weight(g/mol)
A	Benzo[a]pyrene	244.872	0.018	$C_{20}H_{12}$	252.309
B	BP-7-8 Epoxide	3954.547	3.191	$C_{20}H_{12}O$	266.293
C	Benzo[a]pyrene-7,8 Diol	274.266	1.067	$C_{20}H_{12}O_2$	284.308
D	BPDE	3969.755	2.886	$C_{20}H_{12}O_3$	298.292
E	BPdG	1086.037	37.040	$C_{20}H_{21}N_5O_6$	583.548

*Benzo[a]pyrene-7,8 Epoxide:BP-7-8 Epoxide, Benzo[a]pyrene-7,8 Diol: BP-7-8 Diol

Molecules	Opt. Energy(kJ/mol)	Dipole Moments	Molecular Weight(g/mol)
DNA	28735.347	9904.955	12965.020
BPdG-DNA	29067.773	9889.809	13263.311





3 Factors to check:

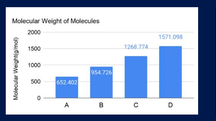
1. Optimized Energy
2. Dipole Moment(DM)
3. EPM(Electrostatic Potential Map)

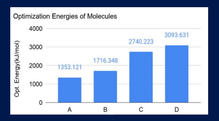
Molecule	Ball and Stick Model	Electrostatic Potential Map
G : C		
G-BPDE : C		
G : C C : G		
G-BPDE : C C : G		

Molecules		Opt. Energy(kJ/mol)	Dipole Moments	Chemical Formula	Molecular Weight(g/mol)
A	G : C	1353.121	26.350	$C_{38}H_{26}N_{10}O_{14}P_2$	652.402
B	G-BPDE : C	1716.348	27.892	$C_{39}H_{26}N_{10}O_{17}P_2$	954.726
C	G : C C : G	2740.223	85.975	$C_{58}H_{48}N_{16}O_{28}P_4$	1268.774
D	G-BPDE : C C : G	3093.631	215.129	$C_{58}H_{52}N_{16}O_{29}P_4$	1571.098

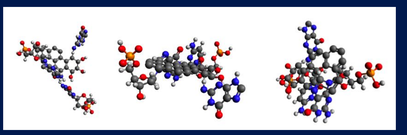
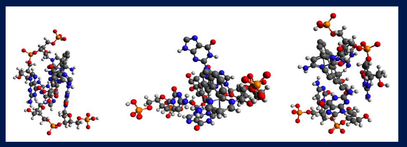
As the weight and size of molecules increase, the optimization energy of the molecule increases as well. The difference between the Opt E of G:C and G-BPDE:C (363.227 kJ/mol) is similar to that of the difference of Opt E between G:C,C:G and G-BPDE:C,C:G. (353.408 kJ/mol). BPDE adds about 358.318 kJ/mol to the final optimization energy.

Opt. E / DM





DNA Adduct / Adduct with G:C

Conclusion

In this research, biochemical and computational simulations were used to examine how vaping affects the metabolic and stereochemical conversions and to see how intercalation resulted in the formation of guanine benzopyrene through binding with guanine bases in the DNA.

Benzo[a]pyrene to enzo[a]pyrene 7,8-dihydrodiol-9,10-epoxide was analyzed and the progression of carcinogenesis that occurs during the enzymatic metabolism from benzo[a]pyrene to benzo[a]pyrene-7,8-dihydrodiol-9,10-epoxide(BPDE) was modeled using a molecular editing program.