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Comparision of Kinetic Energies of Caffeine Analogs in Two Different Systems (Solvent and Protein Copmplex)

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Abstract: Caffeine is a bitter, White crystalline Purine a methylxanthine alkaloid, and is chemically related to the adenine and guanine bases of Deoxyribonucleic acid(DNA) and Ribonucleic acid(RNA). Caffeine is a central nervous system stimulant and is a potential Antagonist for Adenosine A1 Receptor. Adenosine A1 Receptor is responsible for Orthostatic Hypo tension. The best Caffeine Analog will be find out by perfoming molecular dynamics in solvent system and protein complex system at constant temperature, Considering Kinetic Energy as the parameter.

Keywords: Caffeine, Solvent, Protein Complex, Adenosine A1 Receptor, Orthostatic Hypo Tension.

I. INTRODUCTION

1.1 Caffeine: It is the world's most widely consumed phycoactive drug unlike many other substances,it is legal and unregulated in all parts of the world. We have several main effects of Caffeine the most prominent one is reversibly blocks the action of Adenosine on its Receptor there by consequently prevents the Drowsiness induced by the Adenosine.

It is found in the seeds, nuts, or leaves of a number of plants native to South America and East Asia and helps to protect them against predator insects and to prevent germination of nearby seeds. The most well known source of caffeine is the coffee bean, a misnomer for the seed of Coffea plants. . Beverages containing caffeine are ingested to relieve or prevent drowsiness and to improve performance.

1.2 USE:

Caffeine is used in:

- Bronchopulmonary dysplasia in premature infants for both prevention and treatment. It may improve weight gain during therapy and reduce the incidence of cerebral palsy as well as reduce language and cognitive delay. On the other hand, subtle long-term side effects are possible.
- Apnea of prematurity as a primary treatment but not prevention.
- Orthostatic hypotension treatment.

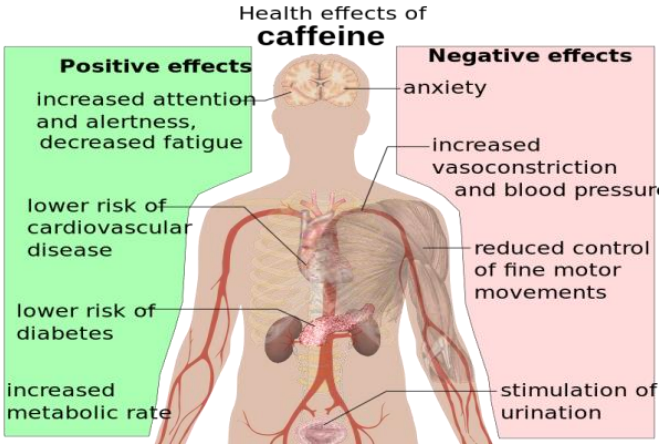
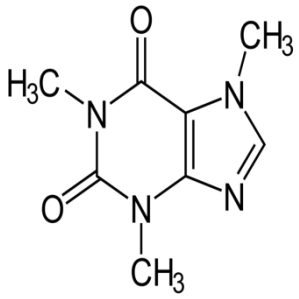


Fig: 1(Health Effects of Caffeine)



Formula: C8H10N4O2 *Fig2: Caffeine Original Structure*

1.3 Caffeine Analogs:

R-Group : - CH3
- CH2CH2CH3
- H
- CF2OH
- Br
- F
- Cl

II. LITERATURE SURVEY

2.1 Kinetic Energy: Any object which is in motion has kinetic energy.
It is defined as the work needed to accelerate a body of a given mass from rest to its stated velocity. Having gained this energy during its acceleration, the body maintains this kinetic energy unless its speed changes. The same amount of work is done by the body in decelerating from its current speed to a state of rest.
Energy due to motion depends on

-mass of the object
-speed of the object

$$K.E=1/2mv^2$$

m = mass(kg) v = velocity(metre/sec) K.E = joules.

2.2 Adenosine A1 Receptor:
The Adenosine A_1 receptor is one member of the adenosine receptor group of G protein-coupled receptors with adenosine as endogenous ligand. And is responsible for Orthostatic Hypo tension.

A_1 receptors are implicated in sleep promotion by inhibiting wake-promoting cholinergic neurons in the basal forebrain. A_1 receptors are also present in smooth muscle throughout the vascular system. The adenosine A_1 receptor has been found to be ubiquitous throughout the entire body.

2.3 Orthostatic Hypo Tension:

Orthostatic hypotension, also known as postural hypo tension or shortened to ortho stasis and colloquially called head rush, occurs when a person's blood pressure falls when suddenly standing up from a lying or sitting position. It is defined as a fall in systolic blood pressure of at least 20 mm Hg or diastolic blood pressure of at least 10 mm Hg when a person assumes a standing position. It occurs predominantly by delayed constriction of the lower body blood vessels, which is normally required to maintain an adequate blood pressure when changing position to standing. As a result, blood pools in the blood vessels of the legs for a longer period and less is returned to the heart, thereby leading to a reduced cardiac output. Mild orthostatic hypotension is common and can occur briefly in anyone, although it is prevalent in particular among the elderly and those with known low blood pressure. Severe drops in blood pressure can lead to fainting, with a possibility of injury.

There are numerous possible causes for orthostatic hypotension, such as certain medications, autonomic neuropathy, decreased blood volume, and age-related blood vessel stiffness.

2.4 Hyperchem Software:

is the powerful computational chemistry tool than any other tools. Structure Input and Manipulation are done by this tool. Building molecules with Hyper Chem is simple just choose an element from the periodic table, and click to sketch a structure. Mouse can control rotations bonds, stereochemistry Display bond showing bond length and bond angles. Displays protein backbones using ribbons, with optional display of side chains

III. METHODOLOGY

3.1 Solvent: A solvent is a substance that dissolves a solute , resulting in a solution. A solvent is usually a liquid but can also be a solid or a gas. The quantity of solute that can dissolve in a specific volume of solvent varies with temperature. Common uses for organic solvents are in dry cleaning, as paint thinners , as nail polish removers and glue solvents , in spot removers , in detergents and in perfumes (ethanol). Water is a solvent for polar molecules and the most common solvent used by living things; all the ions and proteins in a cell are dissolved in water within a cell. Solvents find various applications in chemical, pharmaceutical, oil, and gas industries, including in chemical syntheses and purification processes.

3.2 Protein Complex: A protein complex is a complex containing multiple proteins that interact with each other. A multi protein complex is a group of two or more associated polypeptide chains. The different polypeptide chains may have different functions. This is distinct from a multi enzyme polypeptide, in which multiple catalytic domains are found in a single polypeptide chain. Protein complexes are a form of quaternary structure. Proteins in a protein complex are linked by non-covalent protein–protein interactions, and different protein complexes have different degrees of stability over time. These complexes are a cornerstone of many (if not most) biological processes and together they form various types of molecular machinery that perform a vast array of biological functions. Increasingly, scientists view the cell as composed of modular supra molecular complexes, each of which performs an independent, discrete biological function.

3.3 Procedure:

1.Draw the Caffeine structure in Hyperchem
(Build – default element – choose element)

2.Add H& model build
3.compute – Geometry Optimization.
4.Repeat the same procedure for different Caffeine Analogs by changing the R-group
5. Save the structures.

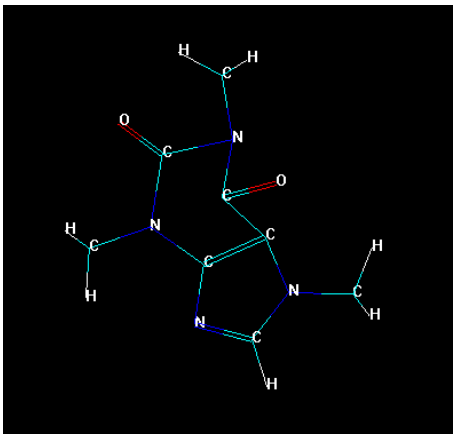


Fig: 3 Caffeine Structure

GEOMETRY OPTIMIZATION:
Energy: 489.78
Gradient: 4.27
Converged: NO

QSAR PROPERTIES:
LogP: -1.06
Refractivity:50.01A^3
Polarizability: 18.87A^3
Hydration Energy:-194.19kcal/mol
Mass:550.35amu
Surface Area(grid):359.51A^2
Surface Area(approx):317.04A^2

MOLECULAR DYNAMICS:
Time:1ps
Total Energy:66.2879kcal/mol
Temprature:281.115k

IV. RESULTS

4.1.Solvent Proces: (Interaction of Caffeine with Water)

1. click on setup-periodic box
2. perform Geometry optimization
3. Remove water molecule
4. perform Molecular Dynmics.
5. note down the Results.

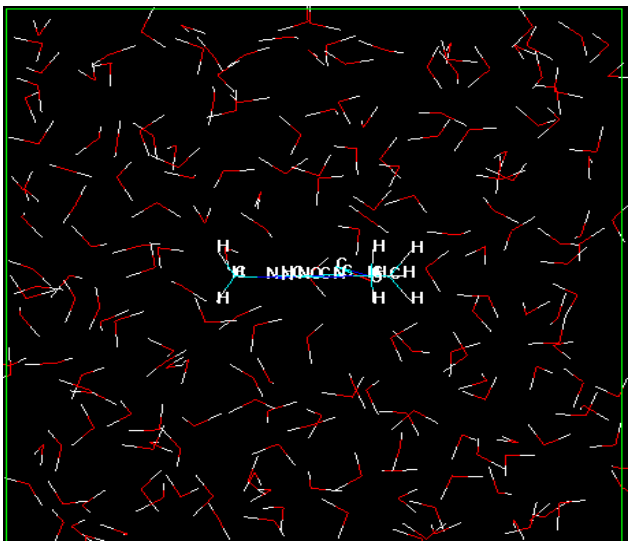


Fig: 4

Geometry Optimization:

R-Group	Energy	Gradient
CH3	489.78484	4.27
CH2CH2CH3	483.312012	19.301
H	481.638641	4.27
Br	484.050232	8.874192
F	476.52143	2.1051
Cl	482.142	8.87424

Table :1

4.2: Protein Process: (Interaction of Caffeine with Adenosine A1 receptor)

1. Download the PDB structure of Adenisine A1 receptor
2. Make Caffeine to interact with Adenosine A1 receptor
3. Perform Geometry Optimization
4. Remove the Protein
5. Perform Molecular Dynamics.

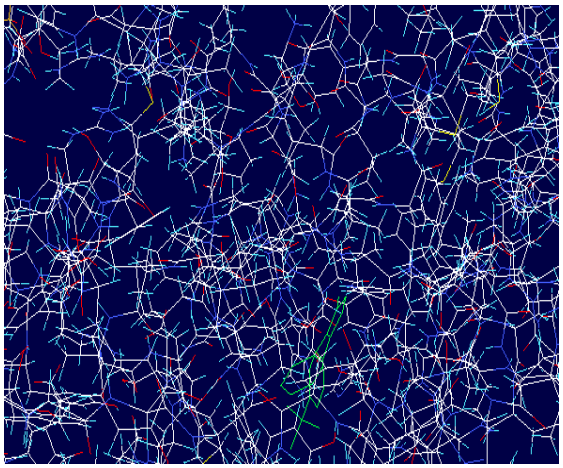


Fig: 5

Geometry Optimization:

R-Group	Energy	Gradient
CH3	116.254	0.4578
CH2CH2CH3	117.69	0.3726
H	119.25	0.09908
Br	42.954	0.949736
F	40.850	0.090266
Cl	46.28	0.098262

Table :2

4.3 Kinetic energy in solvent and protein

Time 1 ps

Molecule	Kinetic energy (solvent)	Kinetic energy (protein)
CH3	44.20	66.20
CH2CH2CH3	53.27	63.27
H	45.21	59.21
CF2OH	**68.29**	**69.20**
BR	49.18	57.18
F	54.17	64.17
CL	68.29	67.29

Table :3

Time 2ps

Molecule	Kinetic energy (solvent)	Kinetic energy (protein)
CH3	46.24	54.20
CH2CH2CH3	55.22	63.27
H	47.26	55.21
CF2OH	**67.29**	**66.29**
BR	43.16	59.18
F	57.12	64.17
CL	65.23	58.29

Table :4

Time 3ps

Molecule	Kinetic energy (solvent)	Kinetic energy (protein)
CH3	46.26	64.20
CH2CH2CH3	57.22	63.27
H	47.27	55.21
CF2OH	**67.41**	**68.24**
BR	48.11	59.18
F	59.12	58.17
CL	62.19	61.29

Table :5

Time 4ps

Molecule	Kinetic energy (solvent)	Kinetic energy (protein)
CH3	48.22	64.20
CH2CH2CH3	58.21	63.27
H	43.28	58.21
CF2OH	**67.21**	**68.19**
BR	43.18	59.18
F	58.17	64.17
CL	62.23	65.29

Table :6

Time 5ps

Molecule	Kinetic energy (solvent)	Kinetic energy (protein)
CH3	41.20	66.20
CH2CH2CH3	56.27	63.27
H	49.20	59.21
CF2OH	**68.29**	**69.20**
BR	42.13	57.18
F	58.10	64.17
CL	63.29	67.29

Table :7

V. CONCLUSION

According to the time dependent properties (Kinetic energy) of all the Caffiene analogs, CF2OH is a more stable and efficient molecule when kinetic energies compared with two different systems i.e., solvent and protein. This is considered to be the efficient drug with less side effects for the treatment of Orthostatic hypotension.

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