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Research Paper

Performance comparison prediction of energy states of atoms in doxorubin and docetaxel using various computational simulations for cancer treatment

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Abstract

Every atoms or compounds must have ground state as well as excited state when they are participating in chemical reactions. Drug is also a chemical compound which also has the two states. Computing the physical properties of a drug compound and calculate its energy states and Comparing the ground state and excited state performance of aromatic cyclic cancer drugs like doxorubicin and docetaxel using various types of cheminformatics methods.in our work we are using so many physical properties like surface area of an atom etc. to check the efficiency of drug.

Keywords: *Molecular Energy; Free Energy; Virtual Screening.*

1. Introduction

Nowadays Because of the unpredictable structure of biomolecules display in uncommon hereditary diseases, for example, AIDS, malignancy, a mental imbalance, and Alzheimer's, medicinal scientists have discovered that medications are as yet a challenging task for therapeutic analysts. Without any plan the development of new effective disease-resistant medicines side effects is becoming more as well as accuracy will be less. Cheminformatics is a powerful information technology that addresses a range of issues in science. These computations have numerous applications in the field of drug discovery process, which will be usefull for various pharmaceutical companies. These methods can also be used in a variety of other forms of physical and chemical properties of drugs. Cheminformatics is otherwise called interface science because it consolidates physics, chemistry, biology, mathematics, biochemistry, Statistics and computation. The main focus of cheminformatics is to analyses, simulation, modeling, manipulation of chemical information that can be expressed in two-dimensional or three-dimensional structure. It manages drug in molecular as well as atom level, while bioinformatics deals with genes, proteins and other large biochemical compounds in various organisms. The chemical properties of the drug collected and design a chemical database and perform various operation and calculation in terms of various chemical parameters is a tedious process in manually way, we can resolve those things with the help of computation.
Cheminformatics is a significant application of information technology to help chemists for investigating new issues, organize, analyses, and understand scientific data needed improvement of new compounds, the main components of. cheminformatics is Computer-Aided Synthesis Design, Structure illustration and chemometric, Various forms of mechanical chemistry show the basic properties of chemical design. The database of chemical information is used for analysis and operation. Chemical structure Representation may be linear, 2D or 3D arrangement.

Every atoms or compounds must have ground state as well as excited state when they are participating in chemical reactions. Drug is also a chemical compound which also has the two states. Computing the physical and chemical properties of a drug compound and calculate its energy states and Comparing the ground state and excited state performance of aromatic cyclic cancer drugs like doxorubicin and docetaxel using various types of cheminformatics methods.in our work we are using so many physical properties like polar surface area bond angles of an atoms for checking the performance etc.

2. Literature survey

Houk [1] was proposed that Computational methods were used to predicting the organocatalytic reactions using the gaussion03 software utilized on either the transition state for a specific reaction or the arrangements of the compounds in their ground states. these techniques remain invaluable for optimizing existing drug designing. Jerry[2] was proposed that The GAMESS suite of programs is used to view the all molecular orbits and LLMP is constructed using MacMolPlt multiconfiguration self-consistent field (MCSCF) calculations and multiconfiguration quasidegenerate perturbation theory (MCQDPT) Ground state inversion Barriers are calculated using these two methods .by taking the bond angle, bond length ,geometries and symmetry are the parameters applying it in molecular dynamics then calculate the ground and excited state potential. Eugene [3] was proposed that applying Empirical Correlation to the experiment results we can predict the ground state reduction potential of Carbon-based molecules. the structures are implemented using WebMO interface and molecular dynamics calculations through gaussion03 then correlation is calculated using the experimental parameters.
George [4] was proposed that GAMESS quantum chemistry software package and with the help of density functional theory bond length and bond dissociation energy is calculated using configura-

tion interaction (CI) and whole active space self-consistent field (CASSCF) approaches. Hatcher [5] was proposed that CHARMM force field is a method which used in computer aided drug design with the help of computational chemistry and medicinal chemistry. Ariela [6] was proposed that improving the properties of drug and reducing the toxicity is the new trend rather than developing new trends .applying computational method for dendrimer drug interaction so that the calculation can predict in which place the drug to be bind inside the dendrimer with the help of MD simulations and docking simulations. yaminishi [7] was proposed that the interaction between unidentified drug and target by taking chemical structures and genomic sequence. Without the necessity of 3D structure using nearest profile, weighted profile and bipartite graph learning method. yaminishi [8] was proposed that including the pharmacological data from JAPIC the docking computation can be improved. Boiko [9] was proposed that In experimental and computational study of Singlet Excited-State Dynamics of 5-Fluorocytosine and Cytosine (5FC) is done by MOLCAS programs suite and gaussion03 software .Peter[10] suggested a method for calculating the polar surface area of polar atoms we need a 3D molecular geometry then calculate PSA and it is very time consuming. Vitali [11] suggested that PM324 and ab initio methods were used to calculate the geometry and energy of the Thioflavin T Torsional in excited state by the highest occupied molecular orbitals(HUMO) the lowest unoccupied molecular orbital (LUMO) using these geometrical method calculating the dipole moments and other molecular properties are calculated. Roberto [12] was proposed that polarizable continuum model are extended with the density functional theory electrostatic potential, the solute free energy, dipole moment are used as parameters invoked in the gaussion03 Software package. Christopher [13] was proposed that Appling DFT to a sequence of aryl substituted nitrenium ions and silylenes in order to compute S-T splitting these we can predict ground state. Hermann [14] was proposed that Drug Response in Breast Cancer Using Integrative Experimental technique VMSI tool is used to visualize the interactions. Manual Deomer [15] was proposed that the AMBER9 software with the addition of shake algorithm and the DFT calculations using the Gaussian G09. the structure of Cyclic Decapeptide examined in the method to predict the ground state structure .Varungopal [16] was proposed that Magnetic Nano particles is used to isolate the leukemia proteins from the infected human being using the Self-Optimized Prediction Method with Alignment tools by calculating the size of the Nano particles and the lowest binding energy then predicts the nanoparticles properties. Rudragayatri [17] was proposed that AD is effectively controlled by nanogene technique by applying gene silencing Nano molecular switch will help to control the desease.MD simulations, discovery studio and docking are the tools used in this method. Dipak Kumar [18] was proposed that influence of fluorescence and hydrogen bonding in anticancer drug in different solvents and their ground and excited state intramolecular double proton transfer mechanism is computed using the gaussion03 software and the dipole moments and density plots are calculated by DFT method the HUMO and LUMO are also calculated. Bipin [19] was proposed that suppressor drug for autism spectrum syndrome using a computational tool by the help of Cheminformatics it helps for designing new drugs and increasing the efficiency. The datas are taken from CheMBL and drug database. Honge-mei [20] was proposed that RIBLYP-D method and TD-HF method are used to figure ground state surface and excitations energy respectively density functional theory has provided an intermolecular potential energy of PBI dimers.

3. Problem formulation

From the present literature, studies compute bond dissociation energy which give only 58% accuracy, and even for laboratory calculation of bond dissociation energy and the bond lengths also comparitively less precise. the comparison is needed to be performed on the cancer patients and for studying more about the two drugs we have to construct a chemical lab environment.

4. Problrm definition

Here we are proposing the comparison of two aromatic drugs which are used in cancer as a part of chemotheraptic treatment, in our system we collect all the drugs which are used in the treatment of cancer from the drug bank, PubChem, and various such databases then we classify the drugs according to the usage of drugs and list out the common drugs which are used to cure most common cancers like Breast cancer, Brain cancer, Lung cancer, etc. from the list we got to know that docetaxel and Doxorubicin is mostly used to cure many types of cancers.

Every drug is built by the combination of atoms so we generate the chemical structure of the drug to know more detail about its structure and the type of bond between the atoms We obtain the parameters of the chemical compound like molecular mass, the number of atoms in the compound, Charge descriptors, generate the 3d structure of the drug and obtain the polar surface area is the aggregate of every single polar atom present in the compound, we also calculate the thermodynamic properties of the drug compound. we are overcoming all those things in our system by taking many numbers of parameters as well as we are using various cheminformatics methods to increase the efficiency of the drug, using simulation we are reducing the time for calculation the physical and chemical properties of various compounds present in the drug after calculating all parameters, we compare the properties and thermodynamics energies of docetaxel and doxorubicin the free energy calculated are plotted in a graph for analyzing

5. Architecture diagrom

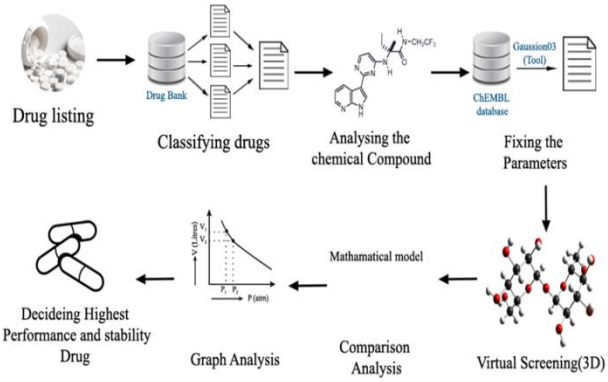

Fig. 1:

6. Algorithem

Algorithm I
Classification of drugs
Step 1: selecting the appropriate type of cancer.
Step 2: For every drug in the database search the type of cancer related to the drug.
Step 3: If the selected type of cancer equals to the drug's use
Insert the drug to the classified array
Algorithm II
Chemical structure depiction
Input: the SMILES string.
Output: The structure of the compound in image format.
Step 1: BEGIN
Step 2: input the SMILES string
Step 3 create the distance matrix
Step 4: compute the initial coordinates.
Step 5: omit the hydrogen and terminal atoms until the final stage, rings blocks are detected
Step 6: perform random sampling to improve the density

Step 7: check the 2D space by arbitrarily flipping the rotatable bonds in the arrangement or flip the bonds which have the shortest path between atoms
Step 8: bend (closing the openings) and shrink (make bond shorter)
Step 9: plot it in image
Step 10: End

Gibbs free energy $\Delta G = \Delta H - T\Delta S$

Enthalpy $\Delta H = \Delta U + P\Delta V$

7. Dataset

The datasets used in the system are drug name and its chemical formula obtained from the Drug bank, SMILES
Adjacency lists of the compound is used to compute the thermodynamic properties of the compound

```
1  C u0 p0 c0 {2,S} {45,S} {46,S} {47,S}
2  C u0 p0 c0 {1,S} {3,S} {4,S} {11,S}
3  H u0 p0 c0 {2,S}
4  C u0 p0 c0 {2,S} {5,S} {6,S} {44,S}
5  H u0 p0 c0 {4,S}
6  C u0 p0 c0 {4,S} {7,S} {8,S} {43,S}
7  H u0 p0 c0 {6,S}
8  C u0 p0 c0 {6,S} {9,S} {48,S} {49,S}
9  C u0 p0 c0 {8,S} {10,S} {11,S} {12,S}
10 H u0 p0 c0 {9,S}
11 O u0 p2 c0 {2,S} {9,S}
12 O u0 p2 c0 {9,S} {13,S}
13 C u0 p0 c0 {12,S} {14,S} {15,S} {19,S}
14 H u0 p0 c0 {13,S}
15 C u0 p0 c0 {13,S} {16,S} {50,S} {51,S}
16 C u0 p0 c0 {15,S} {17,S} {38,S} {42,S}
17 C u0 p0 c0 {16,S} {18,S} {52,S} {53,S}
18 C u0 p0 c0 {17,S} {19,D} {23,S}
19 C u0 p0 c0 {13,S} {18,D} {20,S}
```

Fig. 2: Adjacency List of Doxorubicin.

Adjacency list is obtained from the Smiles. Here(Fig-2) the u means the total of unpaired electrons, p0 is the count of paired electrons and c0 represent the charge of the atom. The last curly bracket says about the nature of bond.

8. Results

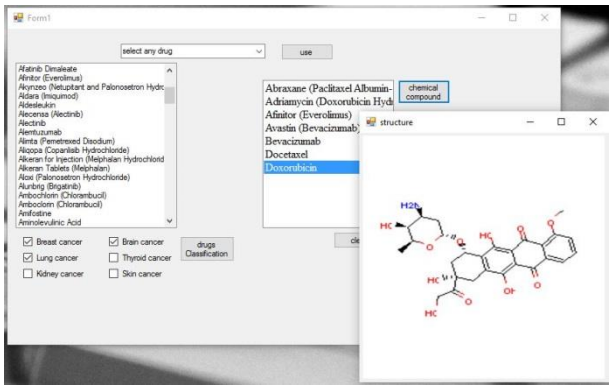

Fig. 3: Classification of Drugs and Structure Generation.

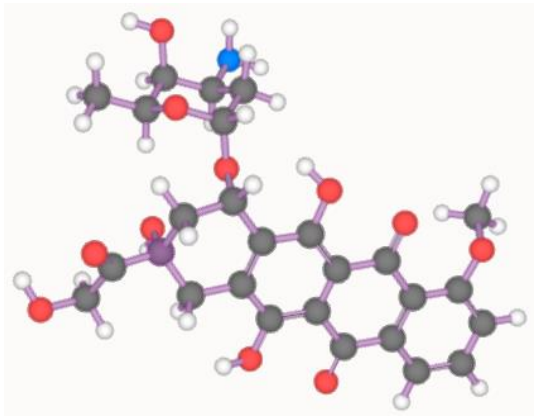

Fig. 4: 3D Structure of Doxorubicin.

Step	Potential Energy P	Kinetic Energy K	
0	124433.847243	0.000000	
50	124403.217908	30.576600	-
100	124295.288491	138.301500	-
150	124098.302265	335.871254	
200	123852.112957	585.344670	
250	123692.744979	753.564538	
300	123579.078287	875.365710	
350	123468.580724	1009.494898	
400	123599.481855	894.274022	
450	123627.682100	876.523159	
500	123593.475813	921.621312	

Elapsed wall clock time = 2472.96 seconds.

Fig. 5: Molecular Dynamics Simulation.

The molecular dynamics program (Fig-5) will check in the condition which have the spatial dimension 3, number of particles is 500 in the system we calculated 500 steps with the time step size of 0.1 seconds. It utilizes speed Verlet time joining strategy here the particles collaborate with central pair combine potential

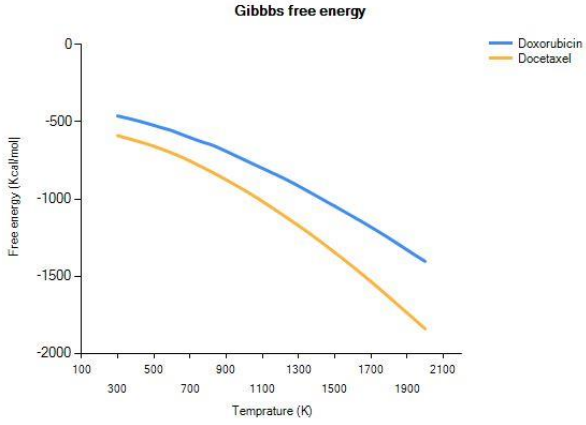

Fig. 6: Gibbs Free Energy of Doxorubicin and Docetaxel.

Gibbs free energy of doxorubicin and docetaxel is plotted in the graph (fig-6) here the temperature is in the Kelvin and plotted in the x-axis, in the y-axis the free energy is plotted, it is measured in kcal/mol.analyzing the graph, we can understand that the Gibbs free energy of docetaxel is less than doxorubicin throughout the graph

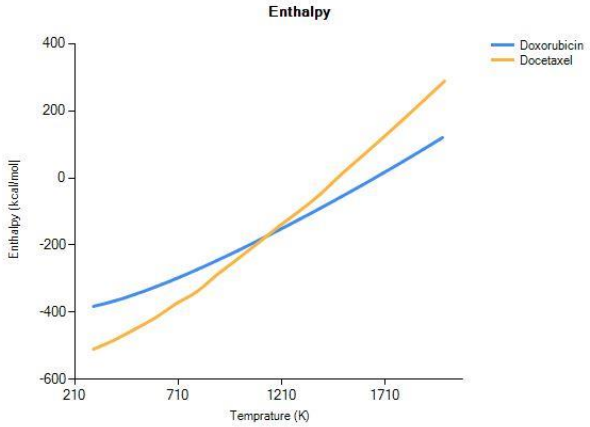

Fig. 7: Enthalpy of Doxorubicin and Docetaxel.

Enthalpy of doxorubicin and docetaxel is plotted in the graph (fig-7) here the temperature is in Kelvin and plotted in the x-axis, in the y-axis the Enthalpy is plotted, it is measured in kcal/mol. from the graph before the temperature 1000K doxorubicin has high enthalpy and after that, there is a sudden change, the enthalpy of docetaxel become high after the temperature 1000k

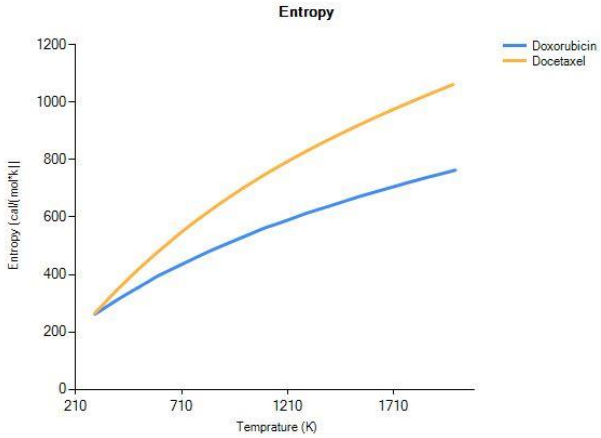

Fig. 8: Entropy of Doxorubicin and Docetaxel.

The entropy of doxorubicin and docetaxel is plotted in the graph (fig-8) here the temperature is in Kelvin unit and plotted in the x-axis, in the y-axis the Entropy is plotted, it is measured in (Cal/(mol*k)).in the graph, we analyzed that entropy of docetaxel is higher than the doxorubicin. Low entropy means ordered system.

9. Conclusion

The range of applications is very rich in the field of pharmaceutical industry as well as it will give new dimensions to the natural science areas like biology and chemistry. Our work will give a lot of implication towards drug discovery. We can study the effect and performance of drugs using these computational methods without using a wet lab. We can compute states of drug atoms which is more effective without testing the drug in the patients. One of the major application is computation will help in medical science for new possibilities in the area of drug discovery.

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