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THEORETICAL APPROACH ON STRUCTURAL ASPECTS OF APIGENIN BY HYPERCHEM 7.5 SOFTWARE

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Abstract: Apigenin a flavone compound is abundant in parsley, celery, celeriac, and chamomile flowers. It possesses strong antioxidant, anti-inflammatory, antimicrobial and anticancer properties and is used in lowering blood pressure. In order to overcome diseases such as rheumatoid arthritis, autoimmune disorders, Parkinson's disease, Alzheimer's disease, and various type of cancers Apigenin is used as potent therapeutic agent. In the present paper, detailed accounts of the properties of apigenin by Hyperchem study have been discussed.

Keywords: Apigenin, Hyperchem 7.5 Software, QSAR

Introduction

Apigenin is a yellow crystalline solid known as 4′,5,7-trihydroxyflavone. It is a natural flavonoid present in many foods[1], including Vegetables(Parsley, celery, onions, and celeriac), Fruits(Oranges and kumquats),Herbs(Chamomile, thyme, oregano, and basil) and Plant-based beverages(Tea, beer, and wine)

Apigenin possess strong antioxidant, anti-inflammatory, and antimicrobial properties[2,3]. This compound is also used as anticancer agent and has been shown to inhibit cell growth and promote cell death in cancer cells[4-9]. Apart from these Apigenin has other potential health benefits like Lowering blood pressure, Improving impaired glucose tolerance, Protecting against neuro degeneration and Improving learning, memory, and neurovascular activity. Experimental studies demonstrated that apigenin has numerous molecular targets involved in inflammation. Systemic bioavailability of Apigenin is increased by delayed plasma clearance and slow decomposition in liver.

Apigenin is also used for reducing pain and for supporting Heart Health. Other uses of Apigenin include boost of Brain function and also for ease from Anxiety and Depression. Several experiments were carried out to show that Apigenin has tumor suppression efficiency on cancer cells in both conditions of in vivo and in vitro.

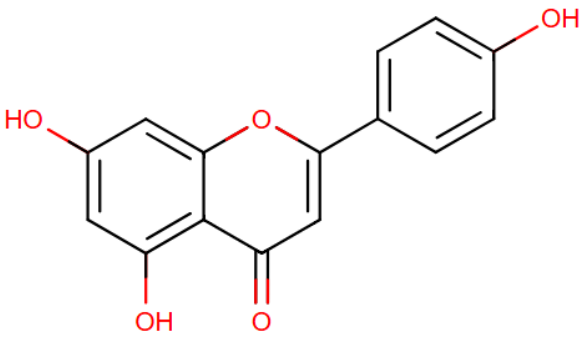
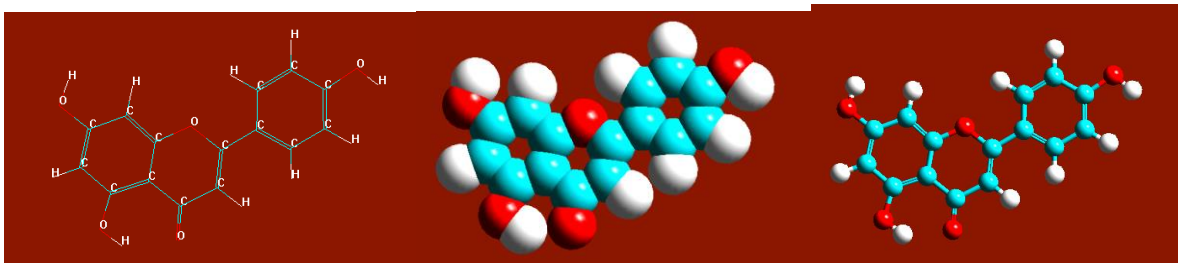


Fig 1. Structure of Apigenin

Results and Discussion

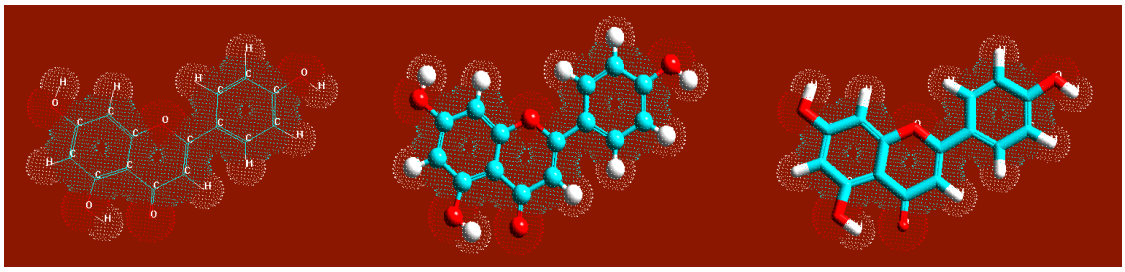
Active conformations of Apigenin

Quantum mechanical calculations used to obtain spectral data were performed by applying HyperChem 7.5 software. Molecule is built by Hyperchem tools and by using Ab Initio method the geometry optimization was done (Figs.2 & 3). By applying single point AM1 method approximation spectral data is generated for Apgenin. Input parameter values such as molecular geometry, bond lengths and values of coulombic, resonance and overlap integrals were influencing the calculations.



Sticks model **Balls model** **Ball ad cylinder model**

Fig 2. Sticks model and balls model and ball and cylinders model of Apigenin



Sticks model with dots **Ball ad cylinder model with dots** **Tubes model with dots**

Fig 2. Sticks model and ball and cylinders model and tubes model with dots of Apigenin

From Potentiometric titrations it has been observed that pKa value of apigenin representing its strongest acidic dissociation, is approximately 6.57. This indicates that apigenin is a relatively weak acid

Theoretical studies of Apigenin using Hyperchem software

Quantitative structure activity relationship studies (QSAR studies) of Apigenin

By applying single point AM1 method QSAR properties like surface area, volume, hydration energy, log P, refractivity, polarisability, mass, total energy etc. of Apigenin were determined[10,11] (Table.1). A variety of molecular descriptors commonly used in quantitative structure activity relationship (QSAR) studies were calculated . Structural descriptors of compounds were related with their physicochemical properties and biological activities by applying this analysis.

From the results of AM1 calculation it is evident that Binding energy of apigenin is -3511.590088 kcal/mol and its heat of formation is -129.4251709 kcal/mol. Its electronic energy is -494599.6563 kcal/mol and nuclear energy is 410220.0625 kcal/mol(Table.2). Dipole moment of of Apigenin is 4.67379D and its RMS gradient is 0.00804 kcal/^{o}Amol. These calculations indicated that the trends of the molecular properties of apigenin so obtained are in good agreement with the experimental results.

Table.1 QSAR properties of Apigenin

QSAR properties	
Surface area appro	**363.20 $^{o}A^{2}$**
Surface area grid	**443.60 $^{o}A^{2}$**
Volume	**724.88 $^{o}A^{3}$**
Hydration energy	**23.94 kcal/mol**
Log P	**-2.09**
Refractivity	**79.88 $^{o}A^{3}$**
Polarisability	**27.27 $^{o}A^{3}$**
Mass	270.24 amu

Table.2 Molecular properties of Apigenin

Total energy	**-84379.60156 kcal/mol**
Binding energy	**-3511.590088 kcal/mol**
Heat of formation	**-129.4251709 kcal/mol**
Electronic energy kcal/mol	**-494599.6563 kcal/mol**
Nuclear energy	**410220.0625 kcal/mol**
Dipole moment	**4.67379 D**
Dipole X	**2.93968 D**
Dipole Y	**-3.63349 D**
Dipole Z	**-0.01676 D**
RMS gradient	**0.00804 kcal/^{o}Amol**

Quantum Chemical Studies of Apigenin

In order to study of reaction mechanisms of chemical compounds Quantum chemical calculations were done. Quantum chemical parameters like energy of the highest occupied molecular orbital (E_{HOMO}), energy of the lowest unoccupied molecular orbital (E_{LUMO}), the energy gap ($E_{LUMO-HOMO}$) were determined from these calculations. These values of E_{HOMO} , E_{LUMO} & $E_{LUMO-HOMO}$ of Apigenin[12,13] were found to be -9.15887 eV, -9.15887 eV & 0 eV respectively(Fig 3,4).The reactivity of a chemical species were predicted by the significant parameters of frontier molecular orbital energies i.e., EHOMO and ELUMO.

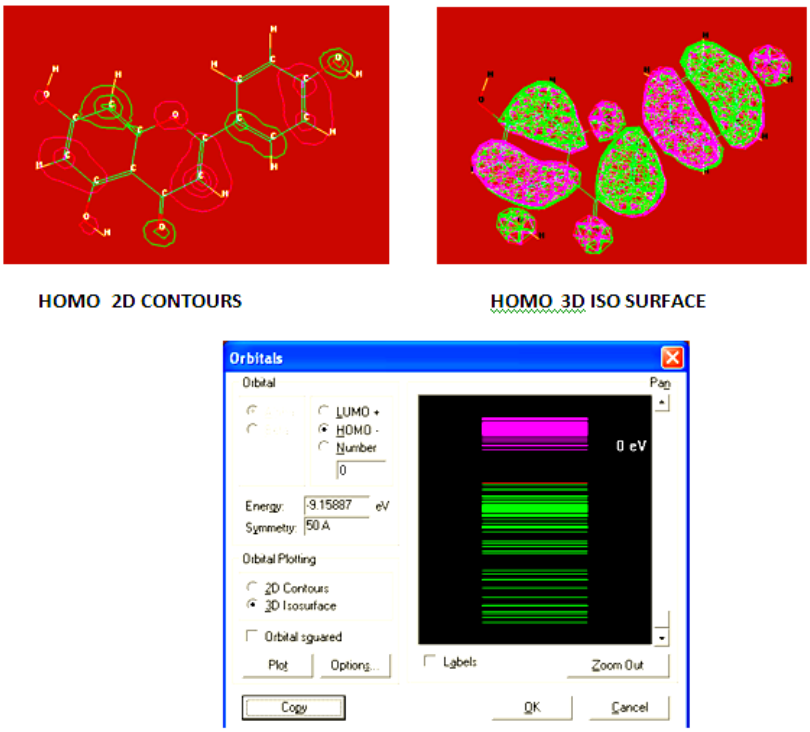


Fig 3.Highest occupied molecular orbital (HOMO) of Apigenin

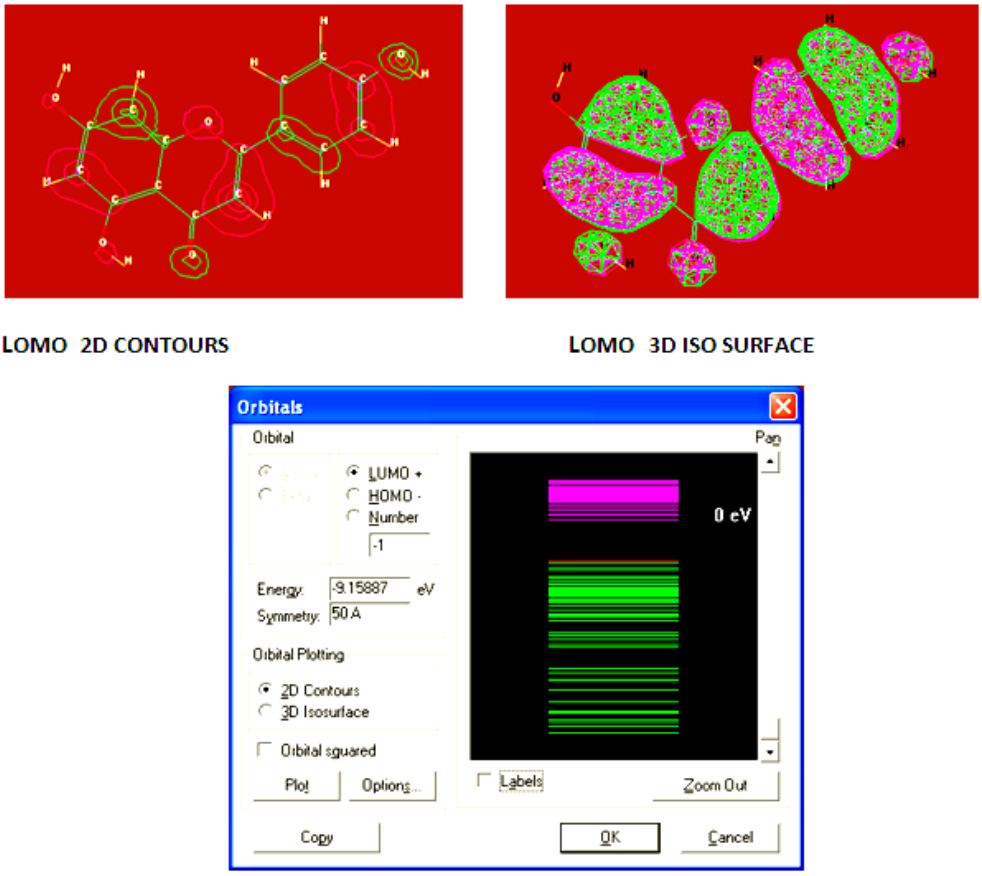


Fig 4.Lowest unoccupied molecular orbital (LUMO) of Apigenin

Molecular Graphs

Electrostatic Potential Graphs of Apigenin

Hyperchem calculates the electrostatic potential at points on a grid surrounding the molecule. The distribution of electrical charge on the molecule's surface is represented by Electrostatic potential (ESP) maps generated using Hyperchem (Fig 5). This is aided in understanding its reactivity and interactions of Apigenin with other molecules. These maps are color-coded, with regions of positive potential (electron-poor) in green and regions of negative potential (electron-rich) in orange.

Green color indicate regions of low electron density, associated with electropositive atoms like hydrogen, or areas where electrophilic attack might occur. Orange color indicate regions of high electron density, often associated with electronegative atoms like oxygen or nitrogen, or areas where nucleophilic attack might occur.

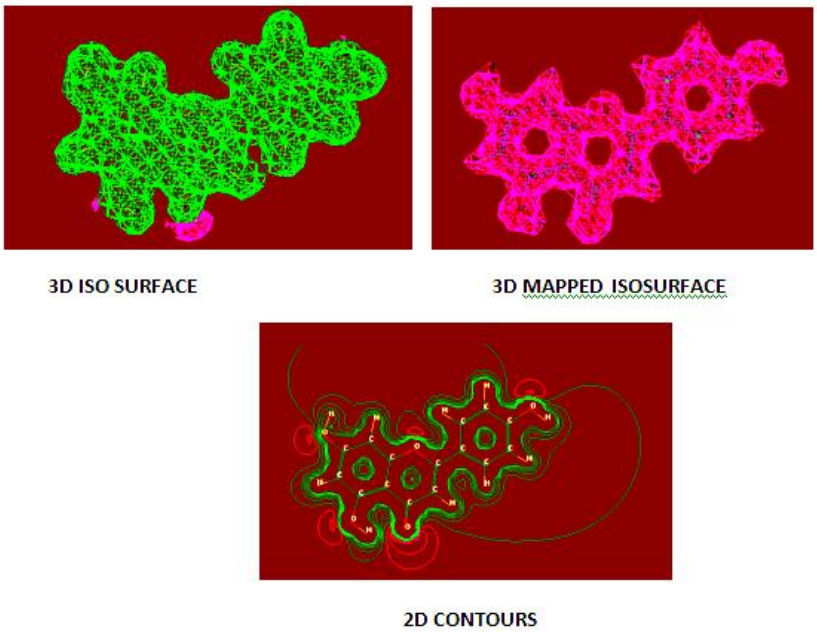


Fig 5. Electrostatic Potential Graphs of Apigenin

Total Charge Density of Apigenin

In Hyperchem total charge density of apigenin is determined and this reveals how the molecule's electrons are distributed. The areas of high and low electron density are highlighted and it also influences its overall chemical behavior. Properties like chemical reactivity, electrostatic interactions are influenced by the charge density distribution. In apigenin the hydroxyl groups have a higher charge density and be involved in hydrogen bonding.

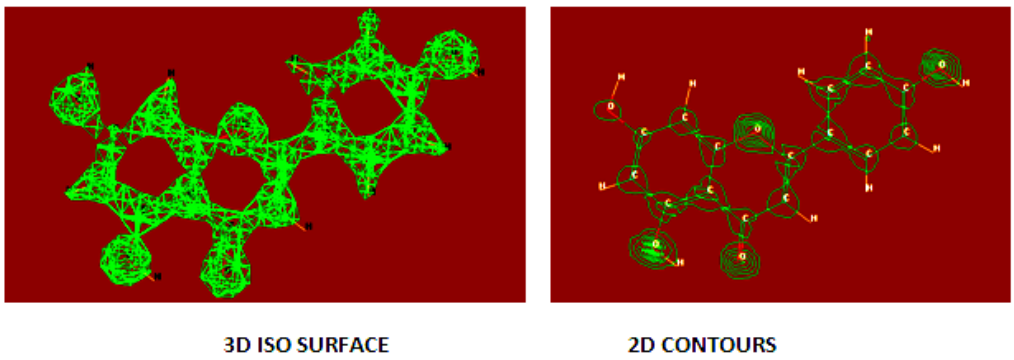


Fig 6. Total Charge Density of Apigenin

Conclusions:

The theoretical study of Apigenin by Hyperchem software is informative in understanding various physicochemical aspects of compounds. The HOMO and LUMO frontier orbital energies computed for the optimized molecule of Apigenin indicated that this compound possess potential electron donor atoms. QSAR parameters generated with semi empirical single point AM1 method are nearly in good agreement with experimental data.

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