Molecular Properties of Natural Bioactive Compounds Confined in *Zea Mays* and Its Application

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Abstract: Despite substantial progress in recent years, ample therapeutic challenges remain in the treatment of the various diseases. Addressing these challenges requires recognition of pristine classes of drugs and development of non invasive and lucrative methods to select the most appropriate therapeutic option for the disease. The present study discusses the drug property of a natural bioactive compounds contained in *Zea mays* and aims to establish the active principles of bioactivity The present study investigates the renoprotective properties of a natural non-protein compound pelargonidin-3-glucoside confined in *Zea mays* that inhibits Angiotensin-I Converting Enzyme. The compounds to be explored as better inhibitors with respect to binding of various drugs like Perindopril available in market and the interactions responsible for the bioactivity of the compound have been discussed using computational methods.

Keywords: ACE-II (Angiotensin-II converting enzyme), Bioactivity, LUMO pelargonidin-3-glucoside.

I. Introduction

Various plant products or metabolites were used to treat the various diseases in the ancient systems of medicine such as Ayurveda. The major advantages to be inexpensive and having either no or fewer side effects in human body were associated with the system. India is a country which has a large number of medicinal plants. 21st centaury may be the right time to use these plants as main natural resource with the help of modern science and technology for developing alternative medicines to control many epidemic diseases. The bioactivity of some natural compounds has already been reported. Angiotensin-I converting enzyme is a circulating enzyme involved in the body's renin-angiotensin system, which mediates extracellular volume, and arterial vasoconstriction. It is secreted by pulmonary and renal endothelial cells and catalyzes the conversion of decapeptide angiotensin I to octapeptide angiotensin II [1]. ACE also degrades bradykinin, a potent vasodilator, and other vasoactive peptide [2]. These two actions make ACE inhibition a brilliant stroke in the treatment of conditions such as high blood pressure, heart failure, diabetic nephropathy, and type 2 diabetes mellitus. Inhibition of ACE results in the decreased formation of angiotensin II and decreased metabolism of bradykinin, leading to systematic dilation of the arteries and veins and a decrease in arterial blood pressure. In addition, inhibiting angiotensin II formation diminishes angiotensin II-mediated aldosterone secretion from the adrenal cortex, leading to a decrease in water and sodium reabsorption and a reduction in extracellular volume [3]. Inhibition of this enzyme also decreases the risk of End Stage Kidney Disease in individuals suffering from diabetes mellitus [4]. Angiotensin II, the main effector of the Renin-Angiotensin-Aldosterone System (RAAS), is the product of a series of proteolytic reactions that starts with the cleavage of angiotensinogen by renin to form angiotensin I [5] [6]. This idea may explain why the inhibition of angiotensin II production or activity By Angiotensin-Converting-Enzyme (ACE) inhibitors or Angiotensin-II-Receptor Blockers (ARBs) might, in addition to acutely reducing blood pressure, lead to the amelioration of various cardiovascular diseases. The present study intends to find out the molecular interactions responsible for the bioactivity of the bio molecules contained in natural products using computational techniques as well as to establish a scientific basis of ethnic plants for development of a better and alternate medicine.

II. Materials and Methods

Structure of target was retrieved through Protein Data Bank and structures for the collected molecules were obtained through PubChem data base. Energy minimization of each ligand molecule was done by using Marvin Sketch [7] software. Docking of protein with natural compounds and drug was done in Autodock vina [8], Flex-X [9] and HEX 6.3 [10] at default parameters. The hydrogen bonding was analyzed using Hex6.3. The molecular dynamics was analyzed using MD Movie part of UCSF Chimera [11]. The ADME values of natural compounds were calculated using ADME beta tool of SIB and online ADME tool of SIMCYP [12]. Toxicity of the lead compound was calculated using Open-Tox online tool [13]. The molecular interactions of natural compounds and commercial drugs were examined using GAMESS and positive results were obtained [14]. Thereafter, investigated resultes were analysed using CHEMISSIAN [15], FACIO [16] and MoCalc [17]. The SDF file format was converted to GAMESS Input using suitable file converters and WINGAMESS calculation was done as child

process of FACIO. The resultant output files were saved and further viewed in CHEMISSIAN for molecular orbital and one dimentional electron density analysis and MoCalc for LUMO and dipole moment analysis. The comparative results were further collected as graphical representation shown in Fig. 1, 2 and 3.

III. Results and Discussions

The properties of lead compounds are given in Table I.

Table I: Molecular and ADME Properties of Compounds

Natural Compound [from Zea mays]	*Molecular Weight*	*H-bond Acceptor*	*H-bond Donor*	*LogP*	*Solubility*	*Molar Refractivity*	*TPSA*	*Autodock Scores*
Pelargonidin-3-glucoside	433.385	9	7	0.676	0.521 mg/ml	106.2712	173.21A^0	8.7
Perindopril [Commercial Drug]	368.46778	6	2	0.9	0.02928 mg/ml	96.175	95.9 A^0	5.2

These above scores establish pelargonidin-3-glucoside as better compound in comparison to commercial drugs like Perindopril [18].

Table II: Toxicity Calculation

Criteria	*Description*
pKa-SMARTS	4.79
Biodegradability	Class 2 (persistent chemical)
Acute toxicity to fish (lethality)	F96h-LogLC50mmol/L = 0.53
Carcinogenicity	Non carcinogen

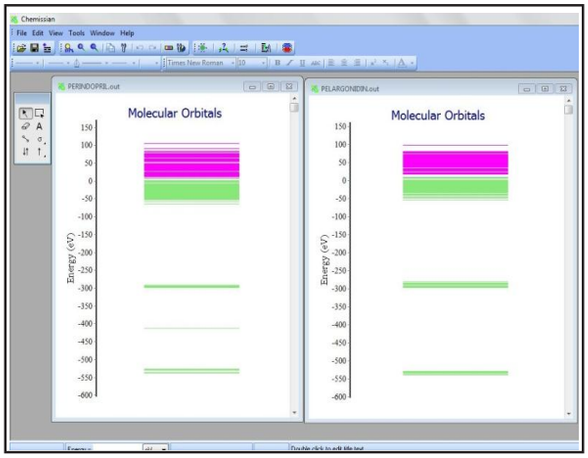

Fig. 1: Energy Band Diagram of Molecular Orbitals Obtained Using GAMESS Software and Viewed in Facio

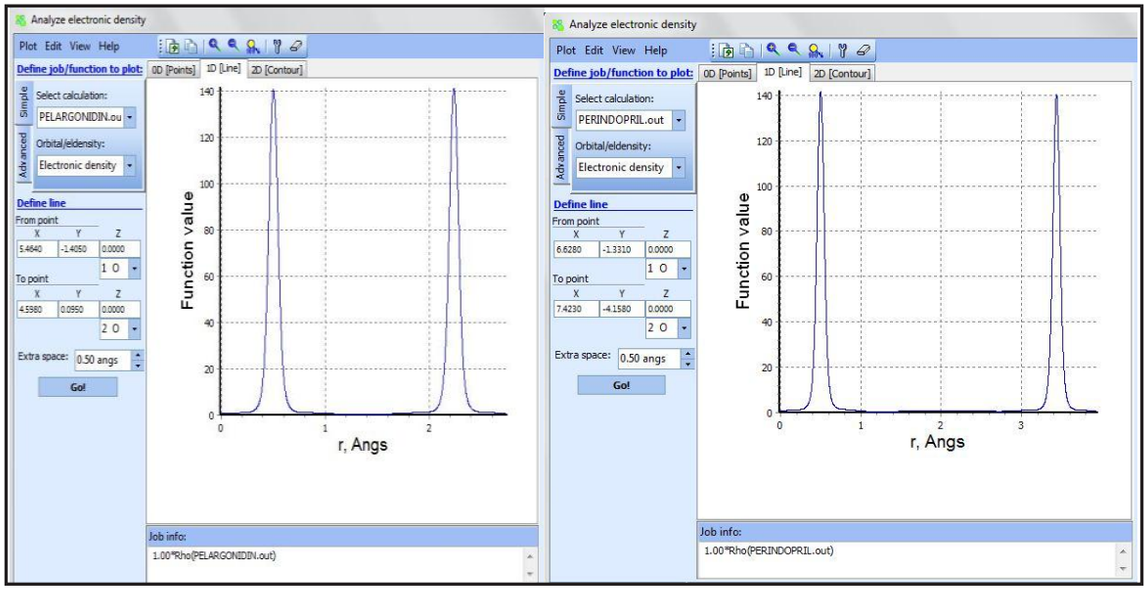

Fig. 2: Comparison of Electron Densities of Natural Compound Under Investigation with Available Drug Using DFT in GAMESS

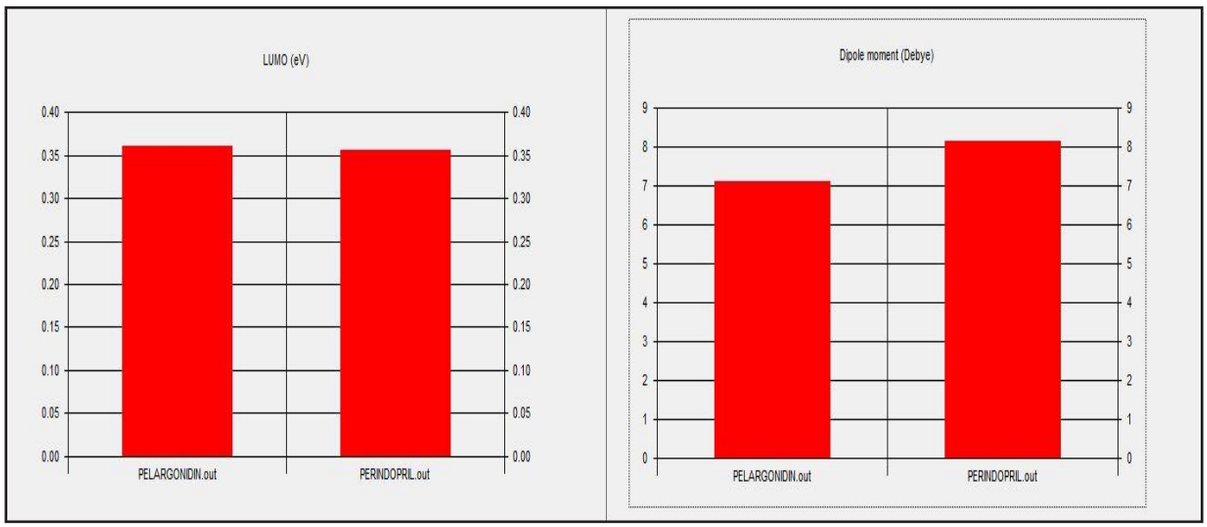

Fig. 3: The Quantum Mechanical Studies Reveal Quite Good Range of LUMO (Lowest Unoccupied Molecular Orbital) and Dipole Moment in Comparison to the Commercial Drug

Pelargonidin-3-glucoside is a zenith anthocyanin present in *Zea mays* [19] [20]. The above mentioned results for renoprotection are very first of its type in the current scientific arena. On the basis of results of docking score, molecular dynamics, hydrogen bonding pattern and ADME-T values we can conclude that natural compound pelargonodin-3-glucoside is better in comparison with synthetic drug like perindopril. The ADME properties showed satisfactory results for the Log P, Log (Sw), solubility, molar refractivity and topological PSA of pelargonidin-3-glucoside. The quantum chemistry calculations infer a significant probability of the said compound to exhibit drug like characteristics. The analysis of electron densities, energy band diagram of molecular orbitals, range of LUMO and dipole moment of the compound under investigation support its drug characteristics and hence it may be a beneficial natural medicinal compound against Hypertension and for decreasing the risk of End Stage Kidney Disease.

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