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IN SILICO AND PHARMACOKINETIC EVALUATION OF PLANT-DERIVED NATURAL COMPOUNDS FOR ANTI-HYPERTENSIVE POTENTIAL

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ABSTRACT

Natural products have long been recognized as a valuable source of therapeutic compounds for treating various human ailments. This study focuses on the anti-hypertensive potential of 13 plant-derived natural compounds. Using in-silico molecular docking via AutoDock software, we evaluated the interaction and binding affinity of these compounds with the Angiotensin-Converting Enzyme (ACE) protein. The compounds, including Allicin, Apigenin, Catechin, Charatin, Crocetin, Cyanidine, Luteolin, Prednisone, Quercetin, Resveratrol, Vitamin C, Withanolides, and Myricetin, demonstrated notable activity against ACE, suggesting their potential as lead molecules for ACE inhibition. The study identified ASP 415(A) and LYS 454(A) as key residues contributing to the protein-ligand interaction. Moreover, Osiris calculations indicated that compounds such as Catechin, Charatin, Crocetin, Cyanidine, Luteolin, Vitamin C, and Withanolides adhered to Lipinski's Rule of Five, indicating favorable drug-like properties and low toxicity. Comparative docking analysis revealed that these compounds are more promising than standard anti-hypertensive drugs like Enalapril and Lisinopril. These findings provide valuable insights for the design and development of new ACE inhibitors to combat hypertension.

KEYWORDS: Natural Products, Anti-Hypertensive, Molecular Docking, AutoDock, ACE Inhibition.

1. INTRODUCTION

Hypertension or high blood pressure is a very common and serious condition that can lead to or complicate many health problems. The risk of cardiovascular morbidity and mortality is directly correlated with blood pressure. Risks of stroke,

MI, angina, heart failure, kidney failure or early death from a cardiovascular cause are directly correlated with BP. Hypertension is often called "the silent killer" because it generally has no symptoms until serious complications develop.

Hypertension is one of the main health problems in the world, besides being considered a serious risk factor for cardiovascular diseases and one of the causes of the reduction of the quality and life expectancy of individuals. There are three general types of hypertension. Essential or primary hypertension occurs when the condition has no known cause. This form of hypertension cannot be cured, but it can be controlled. More than 90% of individuals with hypertension have essential hypertension. Genetic factor may play an important role in the development of essential hypertension. When hypertension is caused by another condition or disease process, it is called secondary hypertension. Fewer than 10% of patients have secondary hypertension; where either a co morbid disease or drug is responsible for elevating BP. In most of these cases renal dysfunction resulting from sever chronic kidney disease or renovascular disease is the most common secondary cause.

Hypertension has a variety of causes. Blood pressure generally tends to rise with age. Hypertension can also be caused by other medical conditions, such as thyroid disease or chronic kidney disease. Hypertension may also be a side effect of certain medications, such as over-the-counter cold medications and oral contraceptives and other hormone drugs. Obesity, heredity and life style also play a role in the development of hypertension. When symptoms do occur, they can differ between individuals depending on such factors as the level of blood pressure, age, underlying cause, medical history, the presence of complications and general health. For more information on symptoms and complications, refer to symptoms of hypertension.

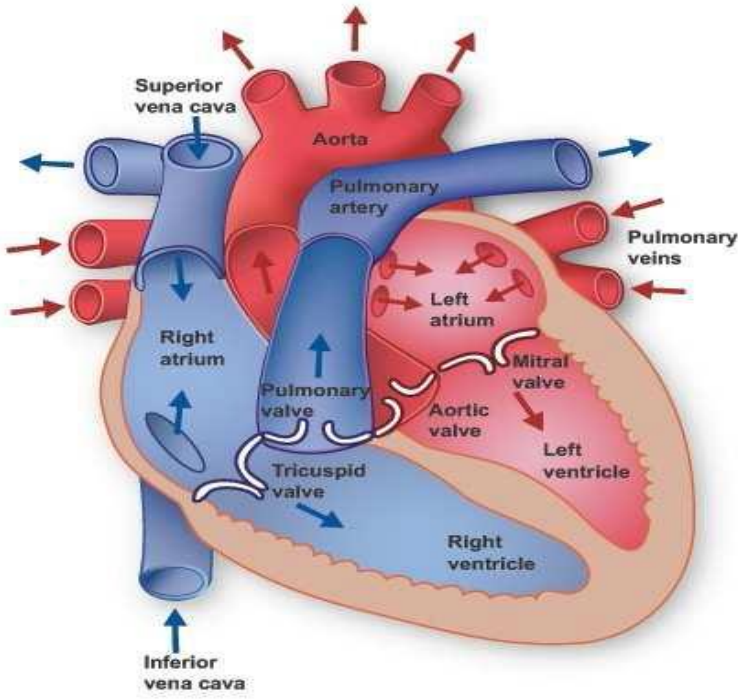


Fig. 1: Human Heart.

1.1 Molecular Docking Study

Molecular docking is a computational technique used to predict how two molecules, such as a drug and its target protein, interact to form a stable complex. It helps determine the binding orientation and affinity, which are essential for understanding the strength and type of biological signal produced. Docking is widely used in drug design to predict the activity of small molecules by optimizing their conformation and orientation with respect to their target, minimizing the system's free energy. The method relies on understanding molecular interactions such as van der Waals forces, hydrogen bonds, and electrostatics. Structural data from techniques like X-ray crystallography or NMR, as well as homology modeling, enable the discovery of high-affinity ligands. Computational docking methods rank potential ligands based on their ability to interact with a target, though reliable prediction of binding affinity remains challenging. Advances in consensus scoring, fast docking procedures, and virtual screening have accelerated the identification of lead compounds, making docking an indispensable tool in rational drug design.

Types of Docking

(a) Rigid body docking, where both the receptor and small molecule are treated as rigid.
(b) Flexible ligand docking, where the receptor is held rigid, but the ligand is treated as flexible; and
(c) Flexible docking, where both receptor and ligand flexibility is considered.

The most commonly docking algorithms use the rigid receptor/flexible ligand model. The principle docking methods that are used extensively employ search algorithms based on Monte Carlo, genetic algorithm, fragment-based and molecular dynamics. Some programs that are well-suited for high throughput docking of a large database of molecules include: DOCK, Flex X, GOLD, and ICM.

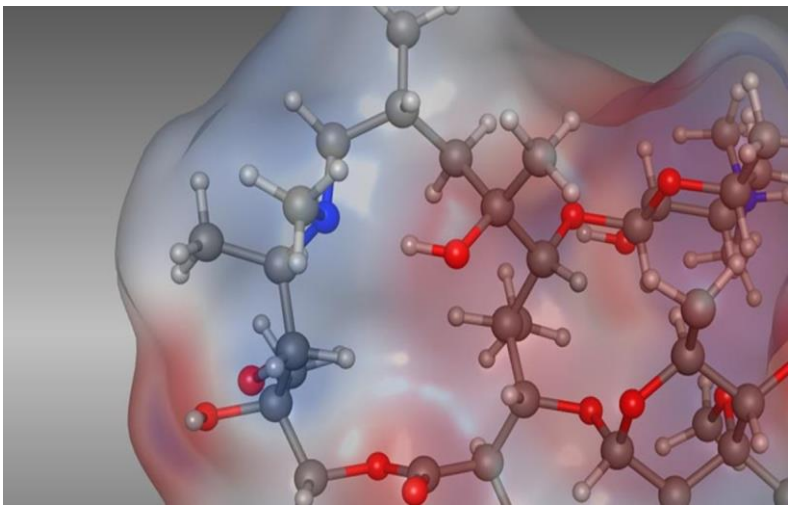


Fig. 2: Molecular Docking.

2. MATERIALS AND METHODS

2.1 Natural Compounds Selection

Thirteen natural compounds were selected as common reported antihypertensive natural compounds from various database and literature. All chemical structures of these compounds were sketched in Chem Draw Ultra 12.0 (Cambrigde Soft).

Table 1: Natural Compound.

S. No.	Compound	Mol. formula	Plant and food sources
1.	Allicin	$C_6H_{10}OS_2$	Allicin is a nonessential nutrient, an indole extracted from garlic high in allicin. Allicin rich foods include garlic, onions, shallots, Chinese chives and leeks
2.	Apigenin	$C_{15}H_{10}O_5$	Apigenin is abundantly present in common fruits such as grapefruit, plant-derived beverages and vegetables such as parsley, onions, oranges, tea, chamomile, wheat sprouts and in some seasonings. ... Other sources for apigenin include beverages such as wine and beer brewed from natural ingredients
3.	Catechin	$C_{15}H_{14}O_6$	Plants, fruits (such as apples, blueberries, gooseberries, grape seeds, kiwi, strawberries), green tea, red wine, beer, cacao liquor, chocolate, cocoa, etc.
4.	Charantin	$C_{32}H_{54}O_6$	Charantin is a chemical substance obtained from the Asian bitter melon (*Momordica charantia*), reputed to be responsible for the hypoglycemic properties of those plants. It was also found in the similar African species *M. foetida*,
5.	Crocetin	$C_{20}H_{24}O_4$	It is a natural apocarotenoid dicarboxylic acid that is found in the crocus flower and *Gardenia jasminoides* (fruits).
6.	Cyanidine	$C_{15}H_{11}O_6$	Cyanidin is present in most red coloured berries such as bilberry, blackberry, blueberry, cgerry, cranberry, elderberry, hawthorn, loganberry and raspeberry, but also in other fruits including apples, pears, peaches and plums. The highest concentrations of cyanidin are found in the skin of the fruit
7.	Luteolin	$C_{15}H_{10}O_6$	Capers, apples, and onions. Chrysin is from the fruit of blue passionflower, a tropical vine. Oranges, grapefruit, lemons, and other citrus fruits are good sources of eriodicytol, hesperetin, and naringenin
8.	Myricetin	$C_{15}H_{10}O_8$	Found in a lot of food sources such as grapes, onions, walnuts, herbs, berries, wine, and tea.
9.	Quercetin	$C_{15}H_{10}O_7$	Isoquercitrin include leafy vegetables, broccoli, red onions, peppers, apples, grapes, black tea, red wine, and some fruit juices.
10.	Resveratrol	$C_{14}H_{12}O_3$	It's found in foods such as peanuts, pistachios, grapes, red and white wine, blueberries, cranberries, and even cocoa and dark chocolate. The plants from which these foods come make resveratrol to fight fungal infection, ultraviolet radiation, stress, and injury
11.	Vitamin c	$C_6H_8O_6$	Indian gooseberry, citrus fruits, such as limes, oranges, and lemons; tomatoes and tomato juice; potatoes; green and red peppers; Kiwifruit, strawberries and cantaloupes; green leafy vegetables such as broccoli; fortified cereals
12.	Withanolides	$C_{28}H_{40}O_8$	Genera within the nightshade family that have been found to produce withanolides include: *Datura*, *Dunalia*, *Iochroma*, Lycium, Nicandra, *Physalis*, *Salpichroa*, *Solanum*, *Withania*, and *Jaborosa*.
13.	Prednisone	$C_{21}H_{26}O_5$	Hundreds of steroids are found in plants, animals and fungi.

2.2 Molecular Docking Study

Preparation Of Protein Structure: The crystal structure of the Angiotensin converting enzyme (ACE) (PDB ID: 1UZE) in complexed with anti-hypertensive drug enalaprilat analogue (Fig.No.3) solved by X-ray crystallography at 2.30Å was retrieved from the Protein Data Bank (http://www.pdb.org/pdb/home/home.do). Before initiating the docking simulations, all non-protein molecules were removed from 1UZE; for any alternative atom locations only the first location (A) was retained. All the docking calculations were performed by using Autodock 4.0. 1UZE was modified by adding polar hydrogens and then kept rigid in the docking process, whereas all the tensional bonds of ligands were set free by Ligand module in Autodock Tools-ADT.

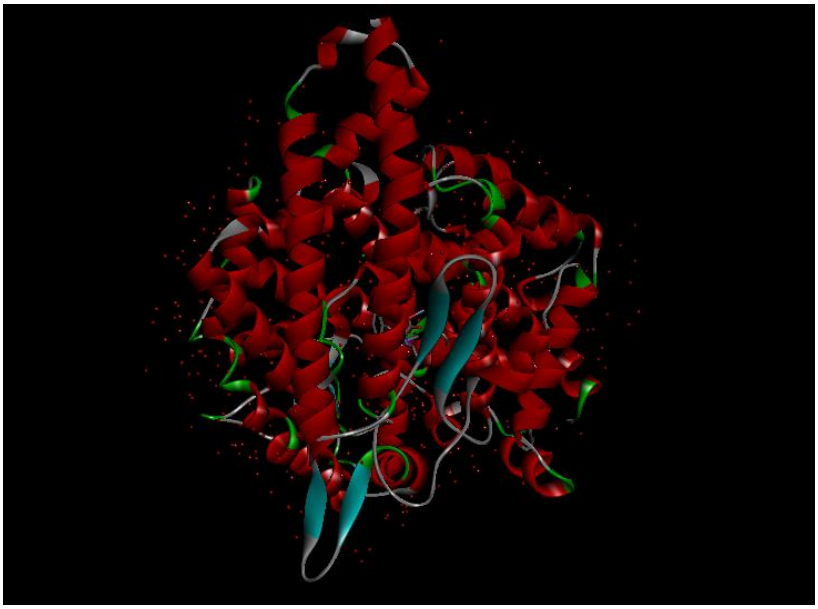
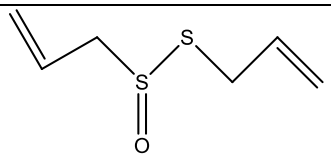
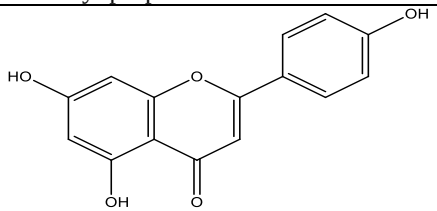


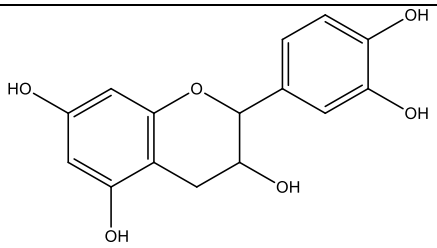
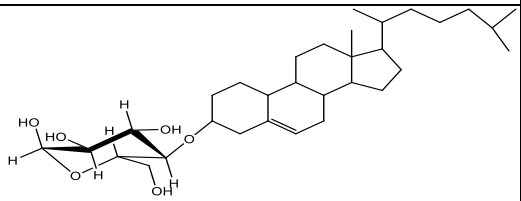
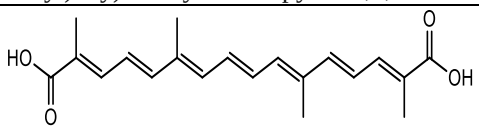
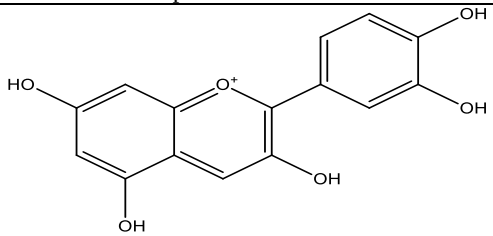
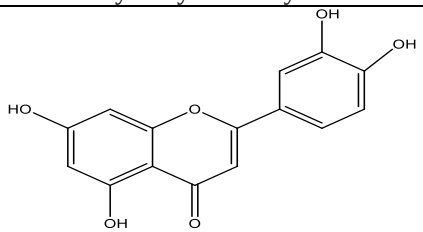
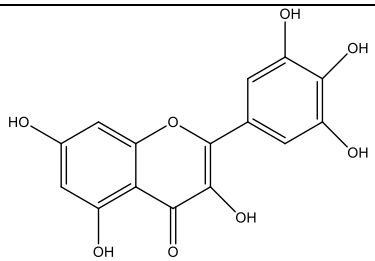
Fig. 3: The Crystal Structure Of The Angiotensin Converting Enzyme (ACE) (PDB ID: 1UZE).

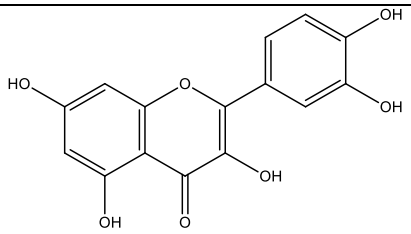
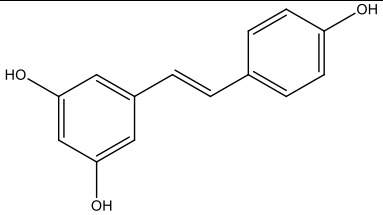
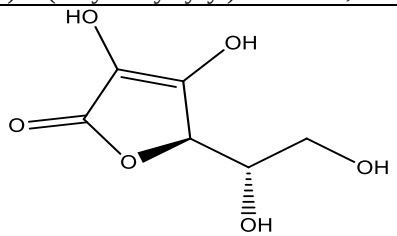
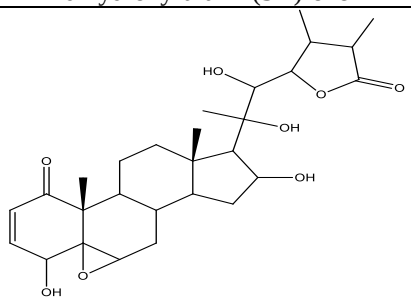
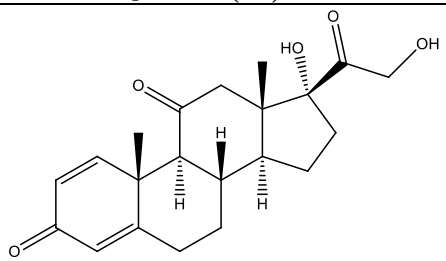
Preparation Of Ligand Structures: The chemical structure of all the 13 compounds were drawn in Marvin sketch is a tool, adding or deleting functional group or atoms, queries and reactions. Assigning stereochemistry, charge, valence, radicals and isotopes to each atom can be done and moreover single, double, triple bonds and aromatic forms can also be created (Table No.2)

- Marvin sketch window was opened.
- The ligand .pdb format was retrieved.
- Addition, deletion of functional group changes were made keeping in mind to increase solubility.
- The new molecules were saved in .pdb format for further docking studies.

Table: 2 Structure and Properties of Ligands used for docking Analysis.

S. No.	Name of the compound	Structure	Properties
1.	Allicin	 S-allyl prop-2-ene-1-sulfinothioate	Chemical Formula: $C_6H_{10}OS_2$ Molecular Weight: 162.27
2.	Apigenin	 5,7-dihydroxy-2-(4-hydroxyphenyl)-4H-chromen-4-one	Chemical Formula: $C_{15}H_{10}O_5$ Molecular Weight: 270.24

3.	Catechin	 2-(3,4-dihydroxyphenyl)chroman-3,5,7-triol	Chemical Formula: $C_{15}H_{14}O_6$ Molecular Weight: 290.27
4.	Charatin	 (2S,3R,4R,5S,6R)-6-(hydroxymethyl)-5-((13-methyl-17-(6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl)oxy)tetrahydro-2H-pyran-2,3,4-triol	Chemical Formula: $C_{32}H_{54}O_6$ Molecular Weight: 534.77
5.	Crocetin	 (2E,4E,6E,8E,10E,12E,14E)-2,6,11,15-tetramethylhexadeca-2,4,6,8,10,12,14-heptaenedioic acid	Chemical Formula: $C_{20}H_{24}O_4$ Molecular Weight: 328.40
6.	Cyanidine	 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxychromenylium	Chemical Formula: $C_{15}H_{11}O_6^+$ Molecular Weight: 287.24
7.	Luteolin	 2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-4H-chromen-4-one	Chemical Formula: $C_{15}H_{10}O_6$ Molecular Weight: 286.24
8.	Myricetin	 3,5,7-trihydroxy-2-(3,4,5-trihydroxyphenyl)-4H-chromen-4-one	Chemical Formula: $C_{15}H_{10}O_8$ Molecular Weight: 318.24

9.	Quercetin	 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy-4H-chromen-4-one	Chemical Formula: $C_{15}H_{10}O_7$ Molecular Weight: 302.24
10.	Resveratrol	 (E)-5-(4-hydroxystyryl)benzene-1,3-diol	Chemical Formula: $C_{14}H_{12}O_3$ Molecular Weight: 228.24
11.	Vitamin-C	 (R)-5-((S)-1,2-dihydroxyethyl)-3,4-dihydroxyfuran-2(5H)-one	Chemical Formula: $C_6H_8O_6$ Molecular Weight: 176.12
12.	Withanolides	 (9aS,11bR)-9-(1-(3,4-dimethyl-5-oxotetrahydrofuran-2-yl)-1,2-dihydroxypropan-2-yl)-4,8-dihydroxy-9a,11b-dimethyl-5a,6,6a,6b,7,8,9,9a,10,11,11a,11b-dodecahydrocyclopenta[1,2]phenanthro[8a,9-b]oxiren-1(4H)-one	Chemical Formula: $C_{28}H_{40}O_8$ Molecular Weight: 504.61
13.	Prednisone	 (8S,9S,10R,13S,14S,17R)-17-hydroxy-17-(2-hydroxyacetyl)-10,13-dimethyl-7,8,9,10,12,13,14,15,16,17-decahydro-3H-cyclopenta[a]phenanthrene-3,11(6H)-dione	Chemical Formula: $C_{21}H_{26}O_5$ Molecular Weight: 358.43

Basic Pharmacokinetics Parameters Calculation: A compound has to be passed through multiple filters to be considered a novel drug. Most of the compounds that fail in pre-clinical trials do so because they do not show the required pharmacological properties to be a drug molecule. Pharmacokinetics properties such as absorption,

distribution, metabolism, excretion, and toxicity (ADMET) have played a very crucial role in development of drug design to the final clinical success of a drug candidate. Therefore, prediction of ADMET properties was done earlier with the aim of decreasing the failure rate of the compound for further process in future. Pharmacokinetics properties of natural compounds such as MW (molecular weight), LogP, Hbd (number of hydrogen bond donors), Hba (number of hydrogen bond acceptors), TPSA (topological polar surface area), nrtB (number of rotatable bonds), nViolation (violations of Lipinski's rule of five) were calculated by OSIRIS Data Warrior (Drug LiknessTool) and Molinspiration Online tool (http://www.molinspiration.com/).

3. RESULTS AND DISCUSSION

3.1 Docking Analysis

Table 3: Value Of The Molecular Docking Energy Of The Compounds Against The ACE And The Standard Drug.

S. No.	Compound Name	1UZE				
		Binding Energy (kJ mol^{-1})	Vdw, Hydrogen Bond and Solubility Interaction Energy (kJ mol^{-1})	Eletrostatic Energy (kJ mol^{-1})	Torsional Energy (kJ mol^{-1})	Inhibition Constant (µM)
1.	Allicin	-4.2	-5.62	-0.07	1.49	839.37
2.	Apigenin	-4.93	-5.18	-0.05	0.3	244.01
3.	Catechin	-5.79	-6.14	-0.05	0.36	56.78
4.	Charatin	-6.48	-8.79	-0.07	2.39	17.9
5.	Crocetin	-5.78	-8.07	-0.1	2.39	57.56
6.	Cyanidine	-7.17	-7.4	-0.06	0.3	5.57
7.	Luteoin	-5.3	-5.45	-0.15	0.3	129.92
8.	Myricetin	-6.25	-6.49	-0.06	0.3	26.18
9.	Quercetin	-6.24	-6.2	-0.04	0.0	26.75
10.	Reveseratrol	-6.02	-6.63	0.01	0.6	38.55
11.	Vitamin c	-4.82	-5.09	0.27	0.0	293.27
12.	withanolides	-6.57	-7.53	-0.06	0.89	15.19
13.	prednisone	-5.55	-6.41	0.27	0.6	86.17
14.	Enalapril	-5.88	-9.5	0.63	2.98	48.76
15.	Lisinopril	-4.46	-8.11	0.07	3.58	533.78

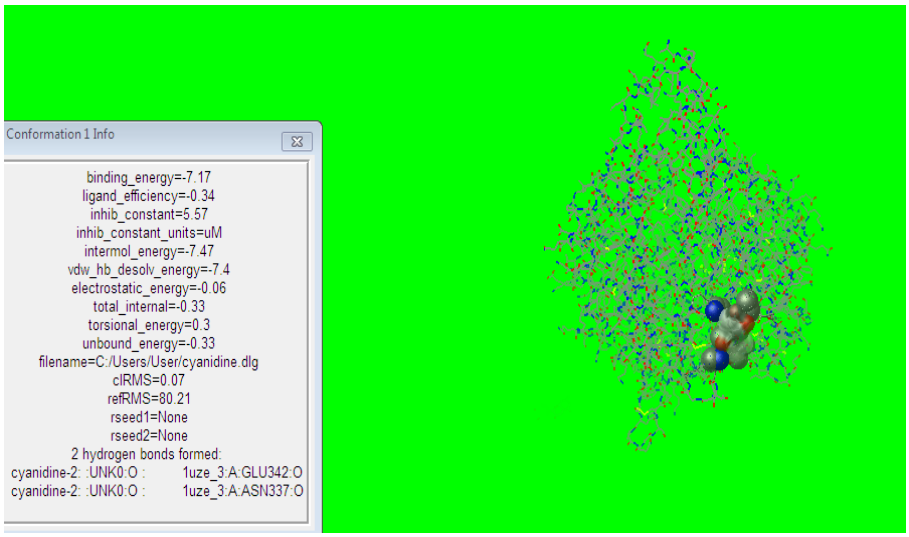


Fig. 4: Compound *Cyanidine* Docked At The Receptor Of Angiotensin Converting Enzyme.

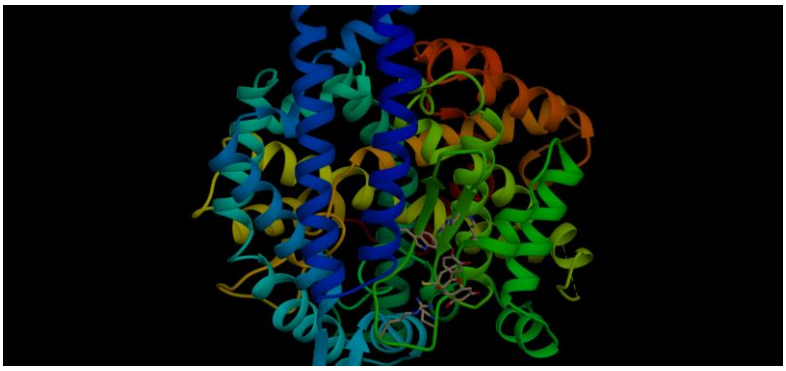


Fig. 5: Compound *Cyanidine* Docked At The Receptor Of Angiotensin Converting Enzyme In Chimera View.

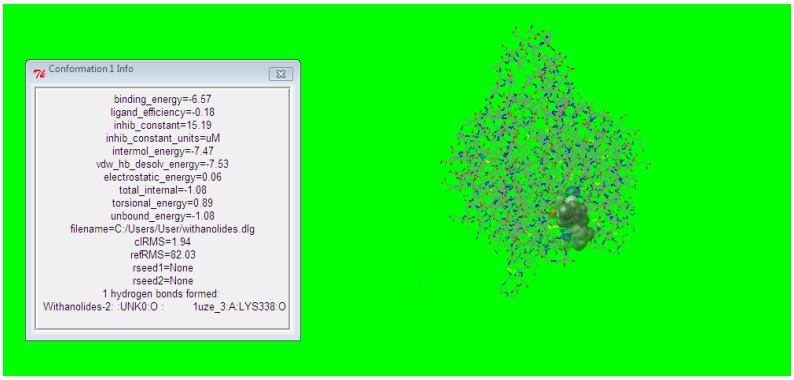


Fig. 6: Compound *Withanolides* Docked At The Receptor Of Angiotensin Converting Enzyme.

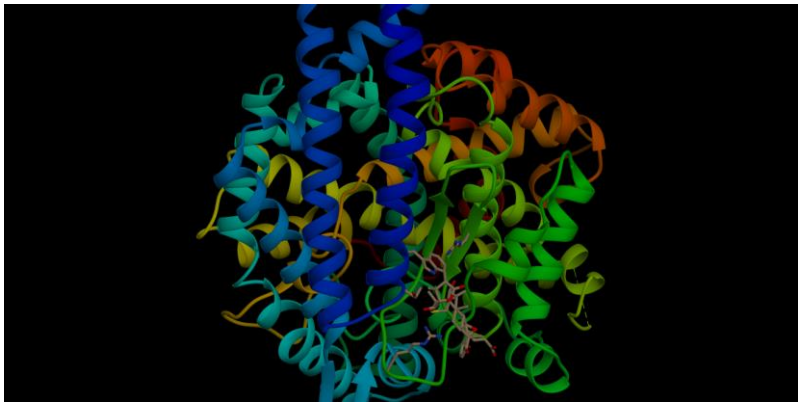


Fig. 7: Compound *Withanolides* Docked At The Receptor Of Angiotensin Converting Enzyme In Chimera View.

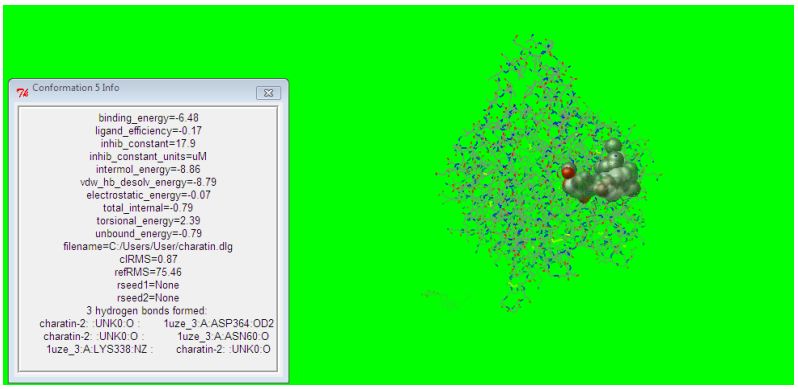


Fig. 8: Compound *Charatin* Docked At The Receptor of Angiotensin Converting Enzyme

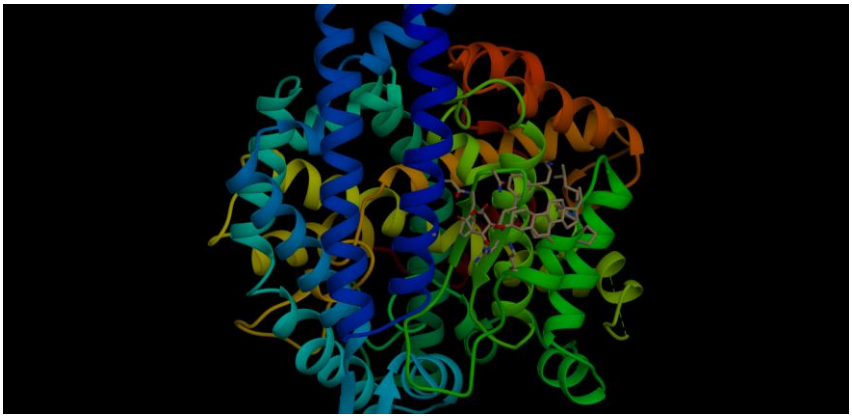


Fig. 9: Compound *Charatin* Docked At The Receptor Of Angiotensin Converting Enzyme In Chimera View.

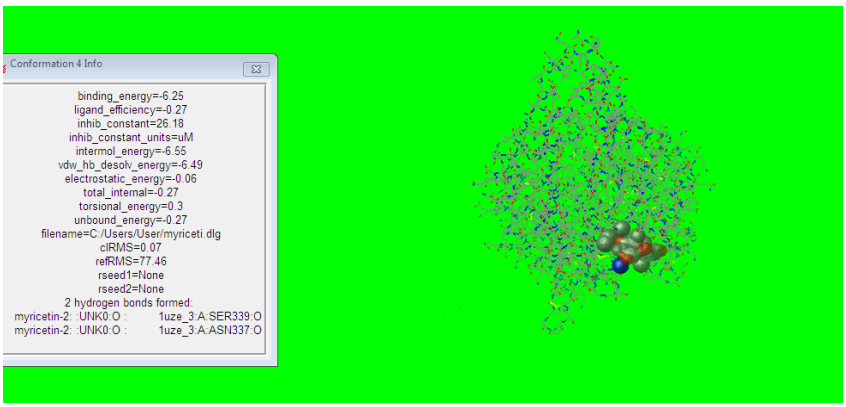


Fig. 10: Compound *Myricetin* Docked At The Receptor Of Angiotensin Converting Enzyme.

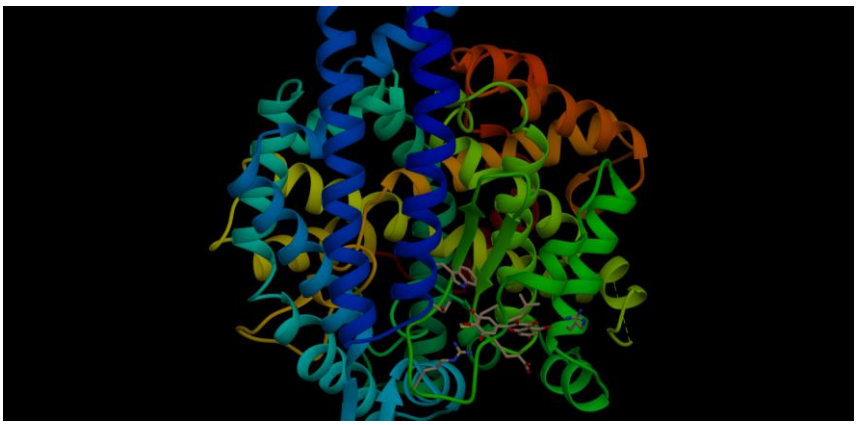


Fig. 11: Compound *Myricetin* Docked At The Receptor Of Angiotensin Converting Enzyme In Chimera View.

3.2 Validation of Ligands

QSAR and toxicity studies were performed to obtain the molecular properties of all ligands as shown in Table No.4. QSAR studies reveal that all ligands was passed and acted as a drug molecule by their adherence to the properties such as Absorption, Distribution, Metabolism and Excretion (ADME) as per the Lipinski Rule of 5. The result shows that all the values of analogues were relays within the optimal range. Also the compounds have molecular weight less than 500 Daltons and number of hydrogen bond donors and hydrogen bond acceptors of all the analogues is below 5 and 10 respectively.

All the values of partition coefficient and number of rotatable bonds were coming under the limit of 5. All these data indicates that the analogues show no more violations likely to be an orally active drug.

3.3 Assessment Of Toxicities, Drug Likeness, And Drug Score Profiles:

Osiris program used for prediction of the overall toxicity of the designed derivatives as the prediction process relies on a predetermined set of structural fragments that give rise to toxicity alerts in case they are encountered in the structure. All target compounds showed low in-Silico possible toxicity risks as shown in Table No.5. Osiris program was also used for calculating the fragment-based druglikeness of the designed compounds and a positive value indicates that the designed molecule contains fragments which are frequently present in commercial drugs.

Table 4: Analysis of Lipinski Rule Of 5 For The Natural Compounds.

S. No	Compound Name	Molecular weight	ClogP	ClogS	No. of Hba	No. of Hbd	No. of Rot.b
1.	Allicin	254.240	2.0904	-4.318	4	2	1
2.	Apigenin	270.239	2.3357	-2.856	5	3	1
3.	Catechin	290.270	1.5087	-1.764	6	5	1
4.	Charatin	534.775	5.0139	-5.762	6	4	8
5.	Crocetin	328.407	5.4464	-2.614	4	2	8
6.	Cyanidine	302.194	1.2774	-3.286	8	4	0
7.	Luteoin	286.238	1.99	-2.56	6	4	1
8.	Myricetin	318.236	1.1445	-2.195	8	6	1
9.	Quercetin	302.237	1.4902	-2.491	7	5	1
10.	Reveseratrol	228.246	2.8295	-2.864	3	3	2
11.	Vitamin c	176.124	-2.4646	-0.349	6	4	2
12.	withanolides	504.618	0.7331	-4.028	8	4	3
13.	prednisone	358.432	1.2851	-3.009	5	2	2
Drugs Commonly Prescribed In Hypertensive Disorders							
14.	Enalapril	376.451	-0.0245	-2.477	7	2	10
15.	Lisinopril	405.493	-2.5468	-2.428	8	4	12

Table 5: Analysis Of Drug Likeness For The Natural Compounds.

S. No	Compound Name	Molecular formula	Drug Likeness	Muta-genic	Tumo-rigenic	Irritant	Shape Index	TPSA
1.	Allicin	$C_{15}H_{10}O_4$	-1.1908	none	none	high	0.52632	74.6
2.	Apigenin	$C_{15}H_{10}O_5$	0.28194	high	none	none	0.55	86.99
3.	Catechin	$C_{15}H_{14}O_6$	0.31525	none	none	none	0.52381	110.38
4.	Charatin	$C_{32}H_{54}O_6$	-6.4373	none	none	none	0.55263	99.38
5.	Crocetin	$C_{20}H_{24}O_4$	1.2391	none	none	none	0.75	74.6
6.	Cyanidine	$C_{14}H_6O_8$	-1.5983	none	none	none	0.45455	133.52
7.	Luteoin	$C_{15}H_{10}O_6$	0.28194	none	none	none	0.52381	107.22
8.	Myricetin	$C_{15}H_{10}O_8$	-0.08283	high	none	none	0.47826	147.68
9.	Quercetin	$C_{15}H_{10}O_7$	-0.08283	high	high	none	0.5	127.45
10.	Reveseratrol	$C_{14}H_{12}O_3$	-1.6732	high	none	none	0.64706	60.69
11.	Vitamin c	$C_6H_8O_6$	0.023806	none	none	none	0.58333	107.22
12.	withanolides	$C_{28}H_{40}O_8$	1.7534	none	none	none	0.41667	136.82
13.	prednisone	$C_{21}H_{26}O_5$	3.8529	none	high	none	0.5	91.67
Drugs Commonly Prescribed In Hypertensive Disorders								
14.	Enalapril	$C_{20}H_{28}N_2O_5$	0.77856	none	none	none	0.51852	95.94
15.	Lisinopril	$C_{21}H_{31}N_3O_5$	0.99434	none	none	none	0.48276	132.96

Table 6: Description of The Hydrogen Bonds Formed Between Ligands And Active Site Of The Enzyme.

S. No	Compound Name	No. of H-bonds (n)	No. of Non-C/H Atoms	No. of Stereo centers	No. of Rotatable Bonds
1.	Allicin	1	4	0	1
2.	Apigenin	2	5	0	1
3.	Catechin	1	6	2	1
4.	Charatin	3	6	13	8
5.	Crocetin	2	4	0	8
6.	Cyanidine	2	8	0	0
7.	Luteoin	1	6	0	1
8.	Myricetin	2	8	0	1
9.	Quercetin	-	7	0	1
10.	Reveseratrol	2	3	0	2
11.	Vitamin c	2	6	2	2
12.	withanolides	1	8	15	3
13.	prednisone	1	5	6	2
Drugs Commonly Prescribed In Hypertensive Disorders					
14.	Enalapril	1	8	3	10
15.	Lisinopril	-	7	3	12

DISCUSSION

To ensure the interaction between the natural compounds and hypertensive disorder associated targets, we performed molecular docking analysis using Autodock4.2. Each of the compounds was docked with ACE targets individually. The output of all ligands was given by energy values in kcal/mol as shown in Table No.3.These compounds showed very good binding affinity with targeted Angiotensin converting enzyme receptor when compared to standard drugs. Docking score of the compounds targeted Angiotensin converting enzyme receptor was compared with the score of the drug Enalapril and Lisinopril which is used as a potent drug for the hypertensive disorder.

Table No.3 shows the results obtained through the docking study between the 13 compounds and standard drugs Enalapril and Lisinopril with the angiotensin-converting enzyme (ACE). Table No.3 shows that all compounds involved in this study interacted with the angiotensin converting enzyme (ACE) in an attractive manner when compared with standard drug, and the compound Cyanidine obtained lower interaction energy, being shown to be more stable in complex with the site of the macromolecule. It can also be observed that the ligand and Charatin compounds obtained van der waals interaction, hydrogen bonding and solvation energies as satisfactory as the Cyanidine, but with higher torsional energies, directly affecting the free energy of the docking .

Fig.No. 8,9,10,&11 shows the more stable conformation of the compounds Cyanidine, withanolides, Charatin, and Myricetin at the active site of the angiotensin converting enzyme (ACE). It can be observed that in addition to interacting with the amino acids of the active site, all compounds studied interact ion-dipole with the zinc ion (Zn ++). This fact is of great importance because the enzyme requires this component for the conversion of angiotensin I to angiotensin II, that is, with the occupation of the active site and interaction with Zn ++, the enzyme is unable to convert substrate into the final product. In Table No.6 the main characteristics of the hydrogen bonds formed between the binding compounds and the active site amino acids of the enzyme can be observed.

Ligands interacted through hydrogen bonds with similar active site amino acids, such as ASP 415, LYS 454 and others. This shows the importance of the polar groups of these compounds for the interaction with the active site of the enzyme, because in addition to the large number of hydrogen bonds, all interact with the zinc ion, as already mentioned

above In Auto dock the analogues were examined for their binding energies and hydrogen bonding. The conformations with highest binding energies and greater number of hydrogen bonds of all the ligands were taken in consideration for ranking the analogues. The interactions were stronger (energetically lesser) for all the ligands which are used for docking simulation.

4. CONCLUSION

Natural products have been used since ancient times and are well recognized as sources of drugs in several human ailments. The healing ability of these herbs and medicinal plants draw attention to study natural products as a potentially valuable resource of drug molecules, they are evolutionarily optimized as drug-like molecules and remain the best sources of drugs and drug leads . In our study, we chose 13 natural compounds that have remarkable anti hypertensive property.

In the present work we have used the Auto Dock software for finding the anti Hypertensive effect of the some natural analogues. From the in-silico based docking study it can be concluded that Allicin, Apigenin, Catechin, Charatin, Crocetin, Cyanidine, Luteoin, prednisone, Quercetin, Reveseratrol, Vitamin c, withanolides and Myricetin compounds show activity against the target protein. Computational method provides information on the interaction and binding affinity between the phytochemical and the ACE protein. The present study reveals that all the selected compounds could be potential lead molecule for the inhibition of ACE receptor. ASP 415(A) and LYS 454(A) are the important residues for potent drug target. These amino acid residues present on the active site of the target ACE protein are the main contributors to the protein-ligand interaction.

The protein-ligand interactions play a key role in the structure based drug discovery. Osiris calculation also shows that the tested compounds Catechin, Charatin, Crocetin, Cyanidine, Luteoin, Vitamin c and withanolides are nontoxic and have drug like properties as they obey lipnski's rule of five. Compound which doesn't obey this rule may have problem with bioavailability. By comparing the docking result and interactions in docking method it is found that Catechin, Charatin, Crocetin, Cyanidine, Luteoin, Vitamin c and withanolides analogues are more promising against hypertensive than standard drugs Enalapril and Lisinopril analogues. The result of the current study can be helpful for the designing and development of new ACE inhibitors that can consequently be used to treat hypertensive disorder.

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