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To Explore the Antihypertensive Activity of *Ficus Carica L.* Using *in Silico* Study

Renuka V. Kshirsagar *, Shrinivas R. Mane, Sarfaraz Kazi, Sanjay K. Bais
Fabtech College of Pharmacy, Sangola
Tal-Sangola, Dist.-Solapur
Maharashtra -413307

ABSTRACT

Worldwide, hypertension is a common ailment that plays a major role in cardiovascular illnesses. An abundance of bioactive chemicals with potential therapeutic applications can be found in traditional medicinal plants. Many cultures have long utilised common fig, Ficus carica, for its therapeutic benefits. The purpose of this work is to assess, via in silico techniques, the antihypertensive potential of bioactive chemicals derived from Ficus carica. Worldwide, hypertension is a common ailment that plays a major role in cardiovascular illnesses. An abundance of bioactive chemicals with potential therapeutic applications can be found in traditional medicinal plants. Many cultures have long utilised common fig, Ficus carica, for its therapeutic benefits. The purpose of this work is to assess, via in silico techniques, the antihypertensive potential of bioactive chemicals derived from Ficus carica. In this work, bioactive chemicals found in Ficus carica were identified and analysed using computational approaches. Angiotensin-converting enzyme (ACE), Endothelin-1, Renin, Carbonic anhydrase-2 are important enzymes involved in blood pressure regulation. Molecular docking simulations were utilized to assess how well these drugs bind to specific enzymes. The objective this research is to explore the antihypertensive Effect of Ficus carica. Various computational software tools were employed to predict and evaluate the bioactive components and their mechanisms of action in this plant.

Keywords: *High Blood pressure, Insillico analysis, Ficus Carica, Softwares.*

*Corresponding Author Email: - rvkshirsgar1252@gmail.com
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INTRODUCTION

Hypertension is a widespread condition that poses a significant threat to public health globally. It causes over 7.5 million deaths each year, accounting for 12.8% of all deaths worldwide[1]. By 2025, it's estimated that 1.56 billion adults will have hypertension. Hypertension, defined as a systolic blood pressure (SBP) over 140 mmHg or a diastolic blood pressure (DBP) over 90 mmHg, is a rapidly growing global health problem[2]. Researchers highlight that the increasing prevalence of hypertension is a significant global health issue. They emphasize that hypertension, affecting millions worldwide, is a major contributor to cardiovascular disease and mortality[3]. As hypertension becomes more common, it poses a growing threat to public health. Multiple observational studies have demonstrated a strong, consistent link between blood pressure and cardiovascular disease (CVD), with no safe lower limit within the typical blood pressure ranges observed in clinical practice[4]. Heart disease related to hypertension, stroke, and other cardiac conditions increases the risk associated with high blood pressure. Additionally, it affects heart health, as evidenced by various diagnostic tools like roentgenography, ECG, and echocardiography. Hypertension also impacts overall mortality rates and life anticipation[5].

The Hypertension is classified into two main types

Essential/primary hypertension: Essential hypertension (90-95%) is one of the most ordinary type develops eventually and typically has no recognizable cause and connected with lifestyle aspects like diet, physical inactivity, obesity, stress, and alcohol consumption, as well as genetic predisposition[6].

Secondary hypertension: Secondary hypertension occurs as a result of an underlying condition or medication. Unlike primary hypertension, secondary hypertension has a specific cause that can be identified and treated. Causes may include medication (such as NSAIDs, corticosteroids), hormonal disorders, chronic kidney diseases and illicit drugs (such as cocaine or amphetamines). Treatment of the underlying condition or discontinuation of the causative medication can often help control secondary hypertension[7].

The Renin-Angiotensin Pathway: Increased activity of the renin-angiotensinogen system can lead to higher levels of angiotensin II, causing vasoconstriction and increased blood pressure.. disruptions or dysregulation in the renin-angiotensinogen system can contribute to the development and progression of hypertension..

Peripheral resistance and Cardiac·optimal blood pressure is maintained by balancing heart output and systemic vascular resistance. High resistance in blood vessels increases the workload on the heart, raising blood pressure. High cardiac output means more blood is being pumped through the vessels, raising blood pressure. [7]

cardiovascular system: The cardiovascular network contributes to hypertension through mechanisms such as increased peripheral resistance caused by vasoconstriction and endothelial dysfunction, structural alterations such as arterial remodeling and stiffening, atherosclerosis development, and microvascular malfunction. These alterations in the blood arteries increase the stress on the heart and perpetuate the high blood pressure, leading to more vascular damage and a range of cardiovascular complications[8].

Nervous system: The neural network is crucial in controlling blood pressure and can contribute to hypertension through several mechanisms. When the sympathetic nervous system (SNS) becomes more active, it causes blood vessels to constrict, increases heart rate, and boosts cardiac output, all of which lead to higher blood pressure[9]. The CNS which includes the brainstem and hypothalamus, processes signal and adjusts autonomic functions that influence blood pressure.

Psychological stress and certain behaviors can also trigger the SNS, leading to persistently high blood pressure. Moreover, the nervous system interacts with hormones such as adrenaline and noradrenaline, which further impact blood pressure levels[10].

Ficus carica, normally acknowledged as the common fig and a fascinating species within extensive *Ficus* genus. Originating from Southwest Asia and the eastern Mediterranean region, this deciduous tree holds a prominent place in both horticulture and human history[12]. Its scientific name, *Ficus carica*, reflects its botanical classification within the Moraceae family. It is a deciduous tree that can grow up to 10-30 feet in height, although some cultivated varieties may be smaller or larger. The leaves of *F. carica* are palmate with three to seven lobes and are typically 4-10 inches long. The fruit, known as figs, are pear-shaped or spherical and vary in color from green to purple-black, depending on the variety and ripeness.

Figure No.1: Ficus carica

The taxonomical classification of ***Ficus carica***, is as follows[12]:

Kingdom **:** Plantae
Subkingdom **:** Tracheobionta
Division **:** Magnopliphyta
Class **:** Maghnolioside
Subclass **:** Hamamelididae
Order **:** Urticales
Family **:** Moraceae
Genus **:** Ficus
Species **:** F. carica

This tree has unveiled a treasure trove of Pharmacologically active compounds across its several parts, including peel, flesh, leaves, and fruits[13]. These compounds contribute to the fig's potential health-promoting properties, ranging from regulating cholesterol levels to enhancing cardiac strength and respiratory function[14].

Among the diverse array of phytochemicals found in figs are ceramides, steroids, pentacyclic triterpenes, flavonoids, and phenolic substances[15]. These compounds, along with soluble crude fiber, make figs a nutritional powerhouse with antioxidant potential, which is dynamic for complete health and well-being.Phenolic compounds, such as Chlorogenic, Gallic,Caffeic acid, Anthocyanins are particularly noteworthy for their antioxidant properties[16]. thereby promoting various health benefits.Furthermore, *Ficus carica* contains over 100 bioactive chemicals, including Phenolic Compounds, Triterpenoids , Steroids, **Ceramides**, Carotenoids. Triterpenoids is the most prevalent complexes identified in figs.These bioactive compounds collectively contribute to the medicinal potential of *Ficus carica*, making it a valuable resource in traditional and modern healthcare practices[17]. However, additional investigate is needed in the direction of fully clarify the mechanisms of action and therapeutic effects of these compounds for specific health conditions[18].

Ficus carica, known as the common fig, has been recognized for its medicinal properties, particularly in traditional medicine[17]. Its fruit is rich in various bioactive compounds, contributing to numerous health benefits, especially for cardiovascular health. *Ficus carica*, one of the five plants referenced in the Quran, is widely utilized in folk remedies for treating cardiac issues. While it has a long-standing history of medicinal use, there is limited scientific evidence supporting its antihypertensive properties. The flavonoids, phenols, and potassium present in *F. carica* fruit may account for its various heart-healthy effects, such as cardioinhibitory, antihypertensive, and diuretic properties, operating through distinct mechanisms[19].

The common fig fruit cover a diversity of chemical constituents that contribute to their nutritional and medicinal properties. Phenolic Compounds like. Anthocyanins, and ferulic acid[20].other compounds such as Tannin, Pectin, **Triterpenoids,** Fucosterol, Vanillin, Cyanogenic Glycosides like Amygdalin (in small amounts). These compounds play various roles in the overall health benefits of figs, including antimicrobial, antiviral, hepatoprotective, and anti-ulcer properties[21].

Sr No.	Plant extract	Chemical constituent	Pharmacological action
1	Fruit	Quercetin, Kaempferol, Gallic Acid	antioxidant properties, reduce inflammation, and may have anticancer effect
2	Bark	Lupeol, α-amyrin, β-amyrin	Anti-inflammatory, antimicrobial, and hepatoprotective
3	Leaves, root	Psoralen	Sunscreen, tanning activator
4	Latex	Ficin	Used in the treatment of digestive disorders
5	Fruits	Quinines	Antimalarial
6	Fruit	Stilbenes	Antioxidant, hemoptysis, antiseptic
7	seeds	Linoleic Acid, Oleic Acid	Support heart health, anti-inflammatory effects, and essential for healthy skin and hair.
8	Leaves	Rutin, luteolin	Antioxidant, anti-inflammatory, and antimicrobial properties.

Table No. 1: Pharmacological actions of several phytoconstituents found in various sections of *Ficus carica*[22]

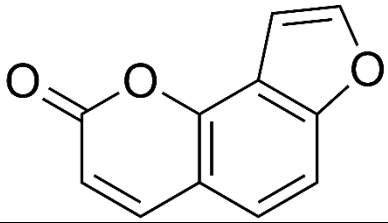
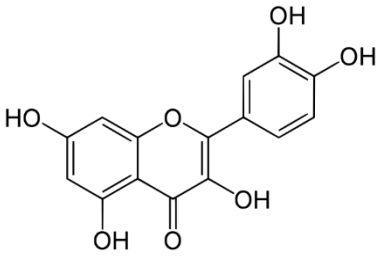
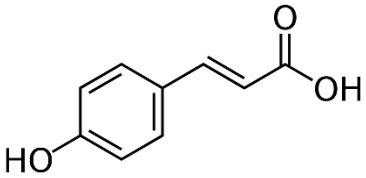
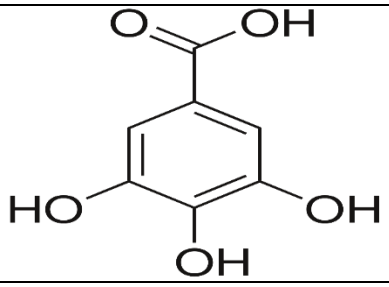
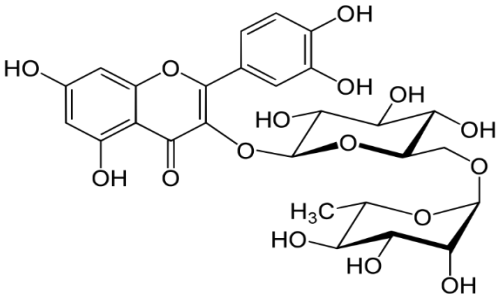
Sr No.	Phytochemical constituents	Structure
1	Angelicin	
2	Quercetin	
3	p-coumarin	
4	Gallic acid	
5	Rutin	

Table No.2: Chemical structure of phytochemical constituents

Over the past few decades, many chemical compounds have not been approved and made it to the market because of serious side effects and unexpected reactions seen in later clinical trials[23]. This has led to higher failure rates for new compounds[19]. To accomplish the desired impact in humans, drugs must modulate specific targets while preventing others to minimize adverse effects. Computational approaches can develop compounds with desired bioactivity profiles and predict secondary effects using current bioactivity data[24]. *In silico* techniques are widely used for preliminary pharmaceutical research and have a substantial impact on drug development. *"In silico*" is the use of computerized experimentation to investigate and analyze biological systems[25].

MD modelling use math to mimic how atoms and molecules move over time.

They start with the initial positions and speeds of these particles and then calculate the forces on them to see how they will move[22].This allows researchers to see how proteins, medicines, as well as other molecules interact with one another and their surroundings under different situationsThese simulations can help us understand protein structure and function, drug-target interactions, and molecular behaviore used[26]. In pharmaceutical R&D and molecular bioscience to predict the binding modes of minor molecules, such as drug candidates, inside the binding positions of target proteins, typically receptors or enzymes involves computational technique called as molecular docking[20]. It involves simulating the interaction between the ligand (small molecule) and the target protein to predict their binding affinity and orientation[27].

Docking has become an increasingly essential tool in pharmaceutical research due to the development of programs based on various algorithms. Several great reviews on docking have previously been published, and several comparative studies were undertaken to analyze the relative performance of the programs. Computational and bioinformatics technologies have become highly useful resources in identifying possible targets for various ligands[28].

Software Used in Molecular Docking

PyMOL

PyMOL allows users to visualize three-dimensional structures of molecules, including proteins, nucleic acids, small molecules, and complexes[26]. It provides various visualization options such as cartoon representation, surface rendering, and ball-and-stick models, helping users to explore and analyze molecular structures effectively. PyMOL enables users to analyze protein structures by measuring distances, angles, dihedral angles, and surface areas[27]. It also offers tools for calculating and visualizing electrostatic potentials, hydrogen bonds, and molecular interactions, facilitating the study of protein-ligand interactions, protein-protein interactions, and protein dynamics[28].It provides tools for homology modeling, allowing users to build three-dimensional models of protein structures based on homologous templates[29]. Users can align protein sequences, generate comparative models, and visualize structural alignments to assess the quality of predicted models. Additionally, PyMOL supports the visualization of virtual screening results and helps users identify potential drug candidates[30].

BIOVIA Discovery studio

Discovery Studio is a comprehensive molecular modeling environment for independent modelers[31]. The Pipeline Pilot open platform powers this standalone environment, which provides the necessary infrastructure for design and modeling. Experiment with Discovery Studio Scienc[32]. Easily see model, and study biological and chemical data using tools for drawing 3D molecules, watching changes over time, making 3D graphs, and more. Connecting the solo installation to a Pipeline Pilot Server allows for seamless data and workflow sharing. This configuration provides access to a wide range of Perl-based scripting commands[32].Predicts protein structures based on known homologous sequence, Simulates the folding process and dynamic behavior of protein, Identifies and optimizes lead compounds through structure-based and ligand-based methods, Predicts the binding affinities of drug candidates to their targets, helping in prioritizing compounds.it Studies the molecular mechanisms of diseases and biological processes[33].

The process of medication research and discovery is difficult, expensive, and time-consuming. It has accelerated due to the advancement of computing tools and procedures[34]. There are numerous molecular docking software options on the market today; however, a literature analysis revealed that Discovery Studio is a suite of tools for stimulating small and macromolecule systems. Accelarys is responsible for its development and distributio[35].

Auto Dock:

Auto Dock is a prominent software suite utilized for molecular modeling, specifically for predicting the binding interactions between small molecules, such as drug candidates, and macromolecular targets, like proteins[36]. One of the primary applications of Auto Dock is molecular docking, where it predicts how small molecules interact with a target protein. This capability is crucial for understanding the binding mechanisms of potential drugs and their biological targets. The software can also handle protein-protein docking, enabling the study of complex biological interactions[37].In virtual screening, Auto Dock is employed to screen vast libraries of compounds against a target protein to identify potential binders[38]. This high-throughput screening process significantly speeds up the drug discovery pipeline by highlighting the most promising candidates for further experimental validation. Through various marking purposes, Auto Dock approximations the binding affinities of these compounds, aiding researchers in prioritizing compounds based on their predicted effectiveness. Auto Dock plays a vital role in structure-based drug design[39]. By providing detailed insights into how ligands bind to their targets, the software aids in the optimization of lead compounds. This process involves modifying the chemical structure of lead compounds to enhance their binding affinity and specificity towards the target protein, thereby improving their potential as therapeutic agents. The user-friendly interface provided by Auto Dock Tools (ADT) simplifies the docking process, making it accessible to a broad range of users. ADT assists in preparing input files, running docking simulations, and analysing the results, enhancing the overall usability and effectiveness of the software. In this study we are using Auto Dock version 1.5.7 for converting ligand and protein in PDBQT format[40].

Material and Method:

1]Software Tools

Molecular Docking Software: AutoDock Tool

Molecular Modeling Software: BIOVIA Discovery Studio, PyMOL

Database Access: PubChem for obtaining 3D structures of phytochemicals.

2] Protein structure

The 3D structures of the target proteins Renin, ACE, Endothelin-1, and Carbonic Anhydrase were acquired through Protein Data Bank (PDB) database.Prepare the protein structures using tools like AutoDockTools, which include adding hydrogen atoms, removing water molecules, and defining the active site.

3]Ligand Selection

PubChem were used to endured the 3Dconformer compound of quercetin, angelicin, rutin, quercetin and gallic acid. In these research pyMOL used to visualized 3D conformer and edited using PyMOL. To prepare for molecular docking, the formats of these ligands were converted into PDBQT files using the Autodock tool, which generated the necessary atomic coordinates.

4]Targets and compound modification

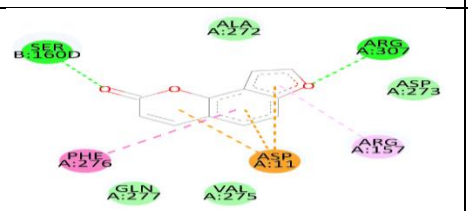
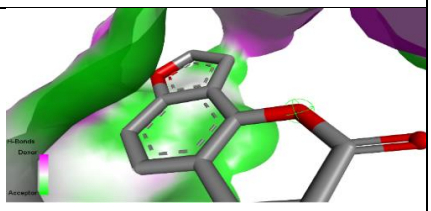
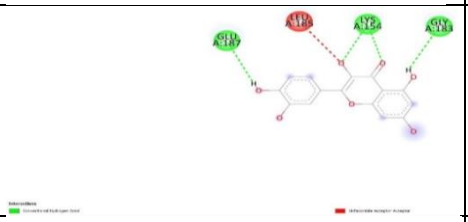
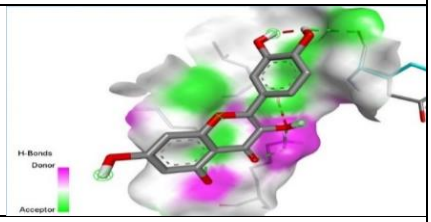
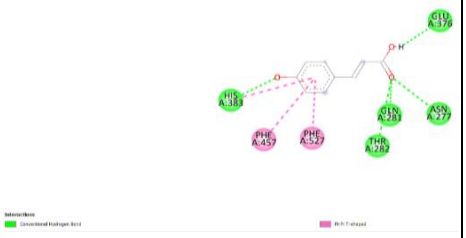
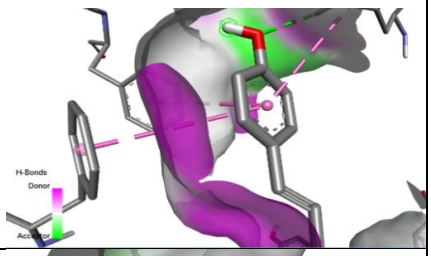
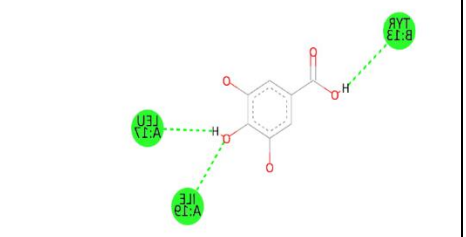
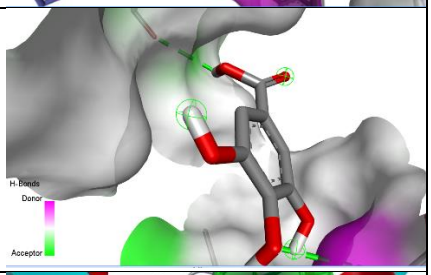
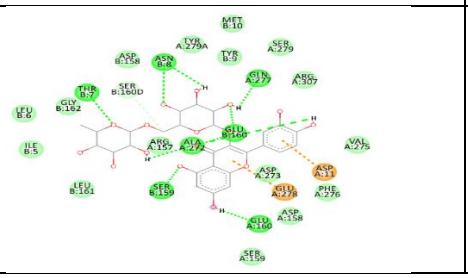
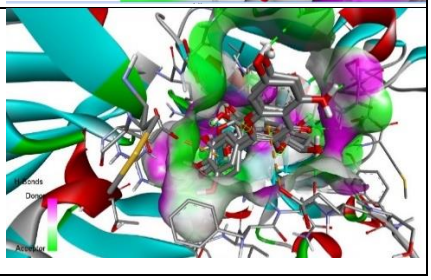
The PDB coordinates of specific protein like renin, ACE carbonic anhydrase 2, endothelin and ligand molecules were optimized for docking analysis using Drug Discovery Studio software.

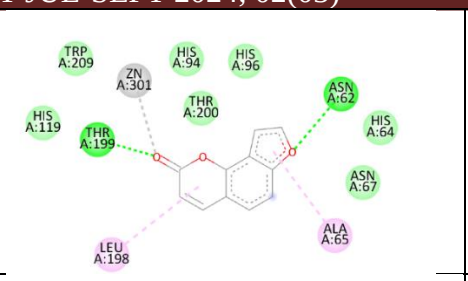
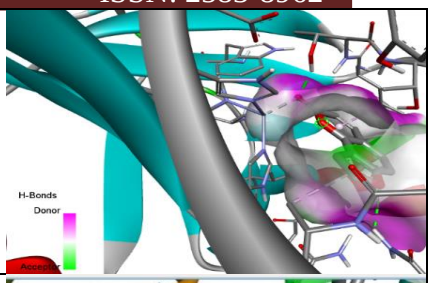
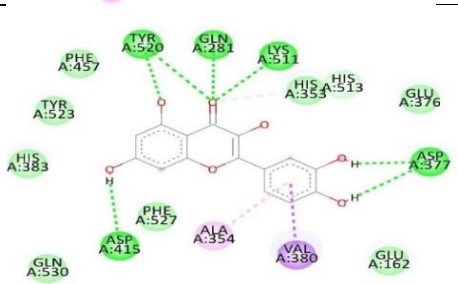
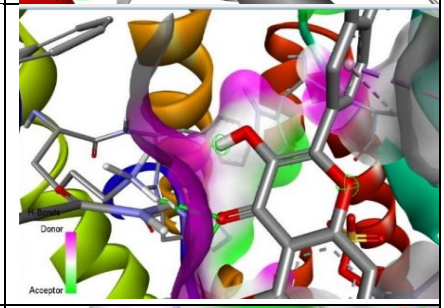
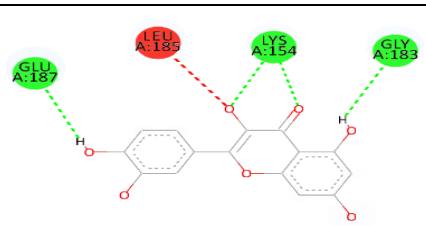
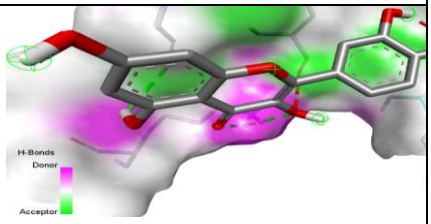
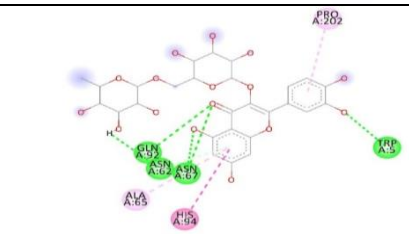
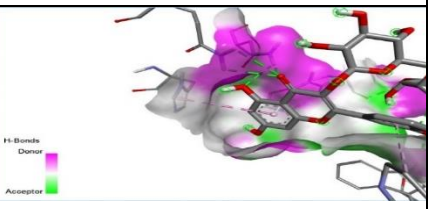
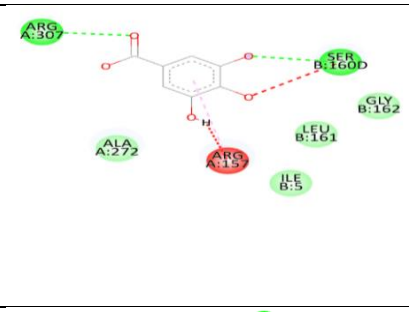
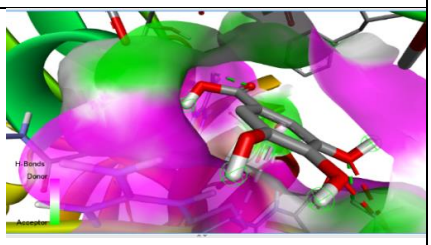
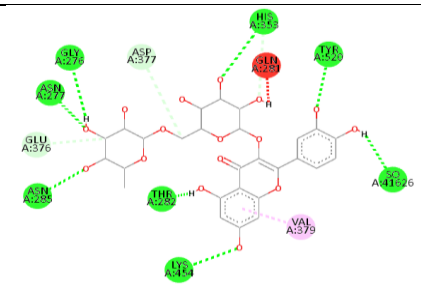
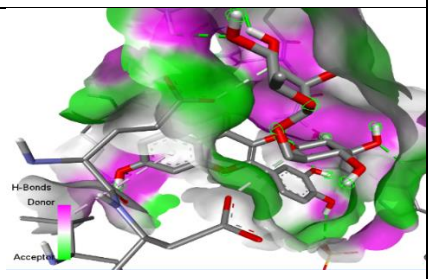
5]Investigation of the active obligatory sites

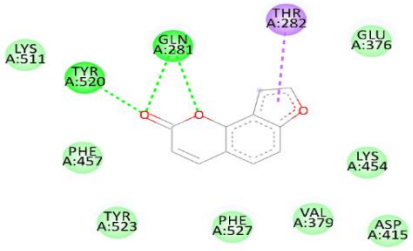
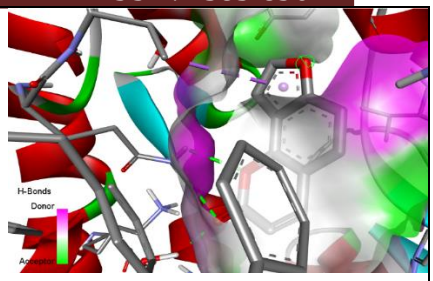
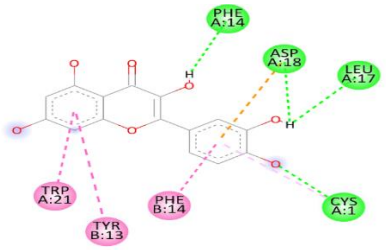
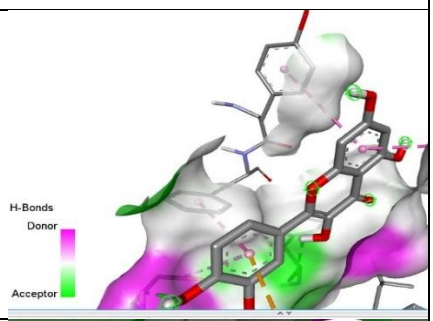
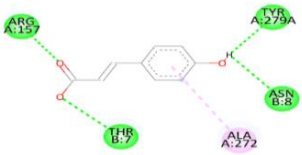
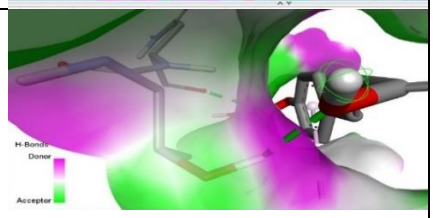
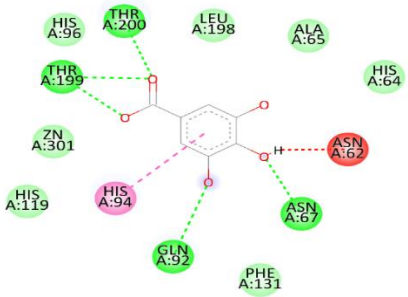
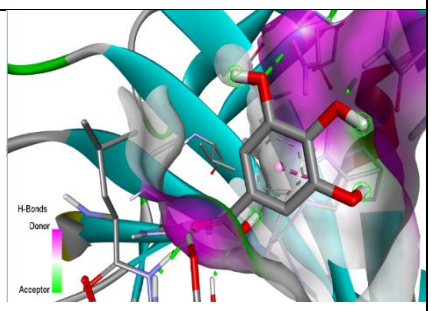
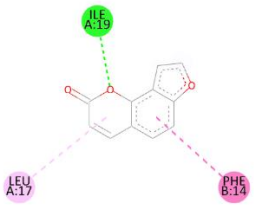
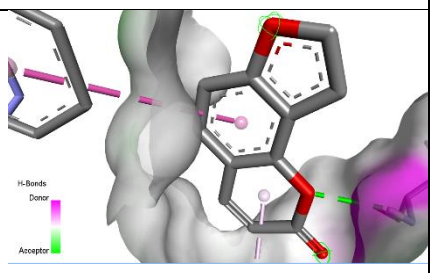
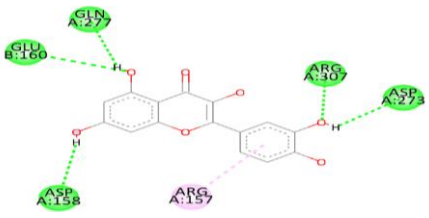
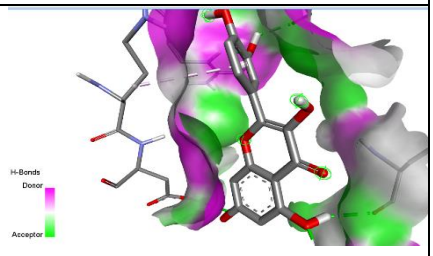
The active sites are the specific locations on the target proteins where the ligands bind. These sites were analyzed using BIOVIA.

6]Molecular Docking

Use the Auto Dock tool to create a grid box around the dynamic site of the protein target for docking. Adjust the settings, such as the number of runs, exhaustiveness, and binding modes. Then, run the docking simulations to see how the phytochemicals bind to the target proteins and measure their binding strengths (binding energies). Analyze these binding energies to understand how well the phytochemicals interact with the proteins.

Sr No.	Phytochemical constituents	Name of Protein	2D structure	3D structure
1	Angelicin	Renin		
2	Quercetin	Carbonic Anhydrase 2		
3	P-coumarin	Angiotensin converting enzyme		
4	Gallic Acid	Endothelin-1		
5	Rutin	Renin		

6	Angelicin	Carbonic Anhydrase 2		
7	Quercetin	Angiotensin converting enzyme		
8	p-coumarin	Endothelin-1		
9	Rutin	Carbonic Anhydrase 2		
10	Gallic Acid	Renin		
11	Rutin	Angiotensinconverting enzyme		

12	Angelicin	Angiotensine converting enzyme		
13	Quercetin	Endothelin-1		
14	p-coumarin	Renin		
15	Gallic Acid	Carbonic Anhydrase 2		
16	Angelicin	Endothelin-1		
17	Quercetin	Renin		

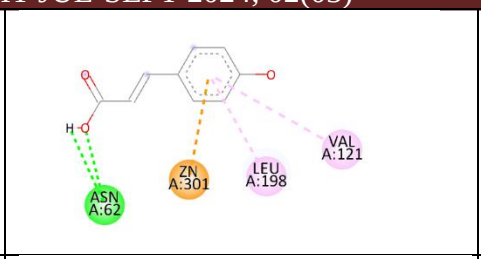
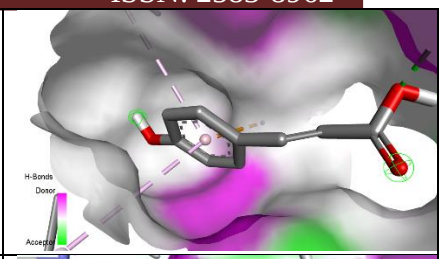
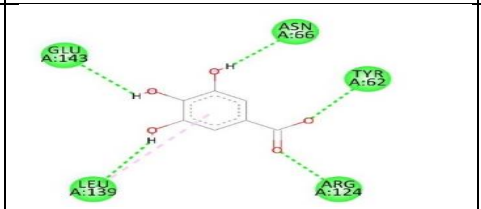
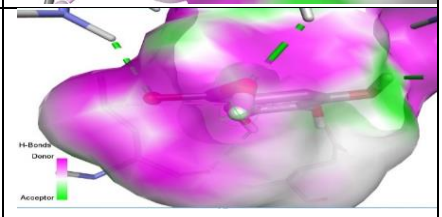
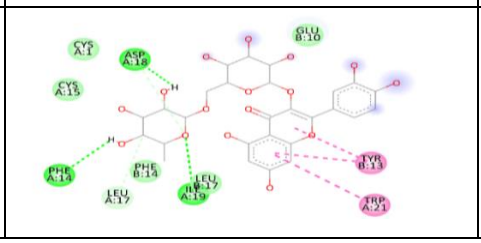
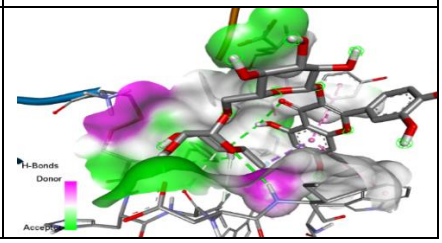
18	p-coumarin	Carbonic Anhydrase 2		
19	Gallic Acid	Angiotensin converting enzyme		
20	Rutin	Endothelin-1		

Table No.3: 2D and 3D structure of ligand- protein interaction

RESULT

In this *Insillico* study 5 Phytochemical constituents from *ficus carica* such as angelicin, Quercetin, p-coumarin, Gallic acid,Rutin are docked with target protein such as Renin, Carbonic Anhydrase 2, Angiotensin converting enzyme, Endothelin-1 and result are as follows:

Sr No.	Chemical constituent	Protein	Binding Energy Kcal/mol	Hydrogen Bonding
1	Angelicin	Renin	-6.8	3
2	Quercetin	Renin	-8.0	6
3	p-coumarin	Renin	-5.8	5
4	Gallic Acid	Renin	-6.1	7
5	Rutin	Renin	-9.2	12
6	Angelicin	Carbonic Anhydrase 2	-7.2	2
7	Quercetin	Carbonic Anhydrase 2	-5.8	5
8	p-coumarin	Carbonic Anhydrase 2	-5.3	2
9	Gallic Acid	Carbonic Anhydrase 2	-5.8	6
10	Rutin	Carbonic Anhydrase 2	-7.5	7
11	Angelicin	Angiotensin converting enzyme	-6.7	3
12	Quercetin	Angiotensin converting enzyme	-8.5	7
13	p-coumarin	Angiotensin converting enzyme	-5.8	5
14	Gallic Acid	Angiotensin converting enzyme	-6.1	5
15	Rutin	Angiotensin converting enzyme	-10.1	9
16	Angelicin	Endothelin-1	-6.1	1
17	Quercetin	Endothelin-1	-6.4	4
18	p-coumarin	Endothelin-1	-4.6	5
19	Gallic Acid	Endothelin-1	-4.8	3
20	Rutin	Endothelin-1	-6.1	5

Table No. 4: Chemical Constituents

DISCUSSION

The purpose of this work is to assess, via in silico techniques, the antihypertensive potential of bioactive chemicals derived from *Ficus carica.* In this work, bioactive chemicals found in *Ficus carica* were identified and analyzed using computational approaches. Angiotensin-converting enzyme (ACE), Endothelin-1, Renin, Carbonic anhydrase-2 are important enzymes involved in blood pressure regulation. Molecular docking simulations were utilized to assess how well these drugs bind to specific enzymes. The objective this research is to explore the antihypertensive Effect of *Ficus carica.* Various computational software tools were employed to predict and evaluate the bioactive components and their mechanisms of action in this plant.

CONCLUSION

From this In sillico study we conclude that antihypertensive potential of *Ficus carica* revealed that its bioactive compounds, such as quercetin, rutin, gallic acid, and angelicin, have significant interactions with key hypertension-related targets: ACE, endothelin-1, carbonic anhydrase 2, and renin. Molecular docking results showed strong binding affinities. These observations recommend that *Ficus carica* could be essential resource of antihypertensive agents. More laboratory and live animal studies were required for verifying in sillico outcomes and systematically comprehend the medical benefits for these compounds. This *in silico* study shows the effective approach for identifying promising candidates in the search for new antihypertensive treatments.

REFERENCES

1. Singh, S., Shankar, R. and Singh, G.P., Prevalence and associated risk factors of hypertension: a cross-sectional study in urban Varanasi, International journal of hypertension, 2017(1),5491838.
2. Delacroix, S., Chokka, R.G. and Worthley, S.G., Hypertension: Pathophysiology and treatment, J Neurol Neurophysiol,2014, *5*(6), 1-8.
3. Law, M.R., Morris, J.K. and Wald, N., Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies, *British medical journal*,2009, *338*.
4. Oparil, S., Acelajado, M.C., Bakris, G.L., Berlowitz, D.R., Cífková, R., Dominiczak, A.F., Grassi, G., Jordan, J., Poulter, N.R., Rodgers, A. and Whelton, P.K., Hypertension. *Nature reviews. Disease primers*, 2018,*4*,18014.
5. Stamler, J., Stamler, R. and Neaton, J.D., Blood pressure, systolic and diastolic, and cardiovascular risks: US population data. *Archives of internal medicine*,1993, *153*(5),598-615.
6. Cai, H. and Harrison, D.G.,Endothelial dysfunction in cardiovascular diseases: the role of oxidant stress. Circulation research, 2008,7(10), 840-844.
7. Sakshi R. Shahu, Gangasagar U. Shinde, Sakshi R. Manekar, Gauri G. Mankar, Swati Deshmukh, Current Scenario And Future Perspective Of Ayurvedic Medicine On Cardiovascular Disease, International Journal of Pharmacy and Herbal Technology,2024, 2 (2) ,1593-159.
8. Pagore, R. and Biyani, K., A review on types, treatment, awareness, prevention, pathophysiology and diagnosis of hypertension,2020,6(2) 2020
9. Beevers, G., Lip, G.Y. and O'Brien, E., The pathophysiology of hypertension. *British medical journal*, 2001,*322*(7291), 912-916.

10. Tomiyama, H., Vascular function: A key player in hypertension, *Hypertension Research*,2023, *46*(9), 2145-2158.
11. DeLalio, L.J., Sved, A.F. and Stocker, S.D., Sympathetic nervous system contributions to hypertension: updates and therapeutic relevance. *Canadian Journal of Cardiology*,2020, *36*(5), 712-720.
12. Hirooka, Yoshitaka,Role Of The Sympathetic Nervous System In Hypertension: Focused On The Central Nervous System. Journal Of Hypertension, 2023, 41(1)112.
13. S.Z., Naseer, B., Qadri, T., Fatima, T. and Bhat, T.A., Springer International Publishing. Fig (Ficus Carica)—Morphology, Taxonomy, Composition and Health Benefits. In *Fruits Grown in Highland Regions of the Himalayas: Nutritional and Health Benefits* ,2021,77-90.
14. Rahmani, A.H. and Aldebasi, Y.H., Ficus carica and its constituent's role in management of diseases, Asian J Pharm Clin Res,2017, 10(6), 49-53.
15. Gibernau, M., Buser, H.R., Frey, J.E. and Hossaert-McKey, M., Volatile compounds from extracts of figs of Ficus carica. *Phytochemistry*, 1997,*46*(2), 241-244.
16. Al-Snafi, A. E.,Nutritional and pharmacological importance of Ficus carica-A review, IOSR Journal of Pharmacy,2017, 7(3), 33–48..
17. Hajam, T.A. and Saleem, H., Phytochemistry, biological activities, industrial and traditional uses of fig (Ficus carica): A review. *Chemico-Biological Interactions*,2022, *368*, 110237.
18. Alamgeer, Iman, S., Asif, H. and Saleem, M., Evaluation of antihypertensive potential of Ficus carica fruit. Pharmaceutical biology, 2017,55(1), 1047-1053
19. dos Anjos Cruz, J.M., Corrêa, R.F., Lamarão, C.V., Kinupp, V.F., Sanches, E.A., Campelo, P.H. and de Araújo Bezerra, J., Ficus spp. fruits: Bioactive compounds and chemical, biological and pharmacological properties,*Food Research International*, 2022,*152*, 110928.
20. Shahrajabian, M.H., Sun, W. and Cheng, Q., A review of chemical constituents, traditional and modern pharmacology of fig (Ficus carica L.), a super fruit with medical astonishing characteristics, *Polish Journal of Agronomy*,2021, 44, 22-29.
21. Koutsoukas, A., Simms, B., Kirchmair, J., Bond, P.J., Whitmore, A.V., Zimmer, S., Young, M.P., Jenkins, J.L., Glick, M., Glen, R.C. and Bender, A., From in silico target prediction to multi-target drug design: current databases, methods and applications. *Journal of proteomics*,2011,*74*(12), 2554-2574.
22. Veberic, R., Colaric, M. and Stampar, F., Phenolic acids and flavonoids of fig fruit (Ficus carica L.) in the northern Mediterranean region, Food chemistry,2008, 106(1), 153-157.
23. Terstappen, G.C. and Reggiani, A.,In silico research in drug discovery, *Trends in pharmacological sciences*, 2001,*22*(1), 23-26.
24. Meng, X.Y., Zhang, H.X., Mezei, M. and Cui, M., Molecular docking: a powerful approach for structure-based drug discovery. *Current computer-aided drug design*,2011, *7*(2), 146-157.
25. Stanzione, F., Giangreco, I. and Cole, J.C., Use of molecular docking computational tools in drug discovery. *Progress in Medicinal Chemistry*,2021, *60*, 273-343.
26. Kitchen D, Decornez H, Furr J, Bajorath J , Docking and scoring in virtual screening for drug discovery: methods and applications, Nat Rev Drug Discov,2004, 3(11),935–949.
27. Bambang Wijianto, Ritmaleni ., Hari Purnomo, Arief Nurrochmad, In Silico and In Vitro Assay of hgv Analogue as Antibacterial, International Journal of Pharmacy and Herbal Technology , 2019,11(3), 78-85

28. Aditi sharma , salonikumar Vaishali Agrawal , Chhaya singh , manish dev,sharma,neha Chauhan molecular dockingan explanatory approach in structure – based drug designing and discovery , International Journal of Pharmacy and Herbal Technology,2021,13(6),6-12
29. Radhika T., Saisree K., Harinadha Babu V, Design, Docking and Synthesis of Novel Bromo Isatin Incorporated Isoxazole Derivatives as Vegfr-2 Inhibitors, International Journal of Pharmacy and Herbal Technology, 2019,11(4), 1-7
30. Seeliger, D. and de Groot, B.L., Ligand docking and binding site analysis with PyMOL and Autodock/Vina. *Journal of computer-aided molecular design*,2010 *24*(5), 417-422.
31. Yuan, S., Chan, H.S. and Hu, Z., Using PyMOL as a platform for computational drug design. *Wiley Interdisciplinary Reviews: Computational Molecular Science*, 2017,*7*(2), 1298.
32. DeLano, W.L., Pymol: An open-source molecular graphics tool. *CCP4 Newsl, Protein Crystallogr*, 2002,*40*(1), 82-92.
33. Jejurikar Bhagyashree L., Rohane Sachin H, Drug Designing in Discovery Studio, Drug Designing in Discovery Studio ,2021,14(2),135-138.
34. Morris, G. M., Huey, R., Lindstrom, W., Sanner, M. F., Belew, R. K., Goodsell, D. S. and Olson, A. J. Autodock4 and AutoDockTools4: automated docking with selective receptor flexibility,2009,14(2),2785-2787
35. Valentine, D., Zaslavsky, I., Richard, S., Meier, O., Hudman, G., Peucker-Ehrenbrink, B. and Stocks, K., EarthCube Data Discovery Studio: A gateway into geoscience data discovery and exploration with Jupyter notebooks. *Concurrency and Computation: Practice and Experience*,2021 *33*(19), 6086.
36. Kemmish, H., Fasnacht, M. and Yan, L., Fully automated antibody structure prediction using BIOVIA tools: Validation study, *PloS one*,2017, *12*(5), 0177923.
37. Sharma, S., Kumar, P. and Chandra, R., Applications of BIOVIA materials studio, LAMMPS, and GROMACS in various fields of science and engineering. *Molecular dynamics simulation of nanocomposites using BIOVIA materials studio, Lammps and Gromacs*,2019,329-341.
38. Gurung, A.B., Ali, M.A., Lee, J., Farah, M.A. and Al-Anazi, K.M., Molecular docking and dynamics simulation study of bioactive compounds from Ficus carica L. with important anticancer drug targets. Plos one, 2021,16(7), 0254035
39. Forli, S., Huey, R., Pique, M.E., Sanner, M.F., Goodsell, D.S. and Olson, A.J., Computational protein–ligand docking and virtual drug screening with the AutoDock suite. *Nature protocols*, 2016,*11*(5), 905-919.
40. El-Hachem, N., Haibe-Kains, B., Khalil, A., Kobeissy, F.H. and Nemer, G., AutoDock and AutoDockTools for protein-ligand docking: beta-site amyloid precursor protein cleaving enzyme 1 (BACE1) as a case study. *Neuroproteomics: Methods and Protocols*, 2017,391-403.