DRUG DISCOVERY

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Structural insight into antagonist action of multi-targeted phytochemicals on cardiovascular drug targets

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ABSTRACT

In Cardiovascular diseases while doing multi targeted drugs designing, we investigated that the targets and plants can be given for cardiovascular diseases. One drug one target is not favourable to treat the disease in better way, so many of the modern researchers focused on the one drug multiple target and poly herbal pharmacology. In this study ACE, COX, HMGR, and RENIN were taken as the drug targets, those proteins involved in the biochemical pathways of cardiovascular disease. Molecular docking studies with phytochemicals of certain plants, which are suggested by the ayurvedic physicians and the multiple target proteins helps to screen multi targeted drug and develop the poly herbal formulation. In this study the highly interacted and multi targeted phytochemicals has been screened as Shinpterocarpin, 6H-Quinindoline, Glabridin, Jusbetonin, Rheediaxanthone-A, and Friedelin. In docking study, all the screened phytochemicals showed very good binding affinities against the cardiovascular drug targets. Hence, these phytocompounds can be used lead molecules to develop drugs for the treatment of cardiovascular diseases after successful experimental investigations.

Keywords: Cardiovascular diseases, drugs designing, herbal pharmacology, multi targeted drug, docking.

1. INTRODUCTION

Cardiovascular disease which is the most common and tragedic disease found all over the world as major one. It is caused due to alcohol consumption, smoking and high levels of cholesterol which makes heart to function abnormally and risk factors occurs [1, 2]. All life style modifications are the main reasons for the main cause of cardiovascular disease. The conditions that involve narrowed or blocked blood vessels that can lead to a heart attack or stroke [3, 4]. The fact is revealed that cardio diseases are more probably due to cholesterol metabolism. Class of drugs used for cholesterol biosynthesis

inhibition. Symptoms depend on various specific conditions. Type-2 diabetes and Hypertension may initially cause no symptoms at all for these conditions. Pain or pressure in the chest, which may indicate angina. Pain or discomfort in the arms, left shoulder, elbows, jaw or back, Shortness of breath, Nausea and fatigue, Cold sweats, Dizziness and light headedness. All these symptoms are common ones for cardiovascular diseases. The lifetime risk of cardiovascular disease can cause in both men and women. Smoking, Physical (in)activity, blood pressure, eating habits, obesity and some physiological factors are the certain factors that can cause cardiovascular disease.

Treatment for cardiovascular disease will vary depending on type of heart disease, for example some heart infections may require medications, some need few simple lifestyle changes includes quitting smoking, exercising, eating a healthy diet, using amino acids. Medications consists of Statins, ACE inhibitors, Calcium channel blockers done for lowering blood pressure or cholesterol or decreasing heart rate [5-8]. There are also alternative treatments available for cardiovascular diseases which includes Ayurveda treatment, can cure the disease other than controlled by lifestyle modifications, drugs like statins, calcium channel blockers, β blockers. Ayurveda using herbal plants which are also available for cardiovascular diseases. Ayurveda is a traditional healthcare system of Indian medicine since ancient times. It is meant not only for curing the diseases but also for prevention of the occurrence of illness. Basic principle of this system includes to make the patient aware about the cause of disease and also prevention of disease [9-11]. The Phyto constituents of medicinal plants are available through properly executed harvesting techniques therefore it is mandatory to collect the herbs to get optimum qualities and good therapeutic effects. Hridaroga(cardio vascular disease) which is most common disease occurs as one fifth of deaths in India, it is most important not to control alone also to cure and to prevent this by ayurvedic systems. Recent drugs available for hridaroga are Rauwolfia serpentine used for hypertension, Madhumega chooranam used for diabetes mellitus, Sarpanganyha tablets, Venthamarai chooranam used to control cholesterol levels. Plants which my work based are *Glycyrrhiza glabra* (athimathuram), *Tinospora cordifolia* Willd, *Allium sativum*, *Commiphora wightii* Arn, *Garcinia cambogia* (Kodampuli), *Gloriosa superb* (sengathal poo), *Terminalia arjuna* (arjuna tree),*Adhatoda vasica* (justiciaa dhatoda), *Andrographis paiculata* nees, *Cyperus rotundus* L. Plants which we have been used for my work for the process of Insilico docking method of analysis using phytochemicals of certain herbal plants are Flame lily or sengathal poo, liquorice or athimathuram, Green chiretta or nila vembu, Marutha maram or arjuna tree, Malabar nut or adhatoda vasica, Malabar tamarind or kudampuli. My study is based on the antagonist action of cardiovascular drugs targets, which is done by molecular docking method by auto dock, visualize and consolidating the structures and giving binding energy for compounds.

Docking using Auto Dock was performed for 67 small molecules which depends upon certain phytochemicals related to cardiovascular diseases, with 4 selected target proteins (ACE2, RENIN, HMGR, COX) [12-16]. For each protein top 10 interacting ligands were selected based on maximum binding energy. Among the selected compounds the compounds Shinpterocarpin, Quinindoline, Glabridin, Jusbetonin, Rheediaxanthone, Friedelin had repeated interaction with 4 proteins and also it had we selected compounds having least binding energy.

2. MATERIALS AND METHODS

Target protein identification

The target protein for CVD were identified from KEGG pathway database and literature survey. The pathway maps in the database are identified by pathway identifiers. The code prefix has been used to search the pathways in *Homosapiens* and the keyword Cardio was used to find the pathway defects which leads to cardio pathways [17, 18].

Protein file preparation

The proteins were downloaded from the Protein Data Bank database in the pdb format. Each protein has a unique PDB identifier which is a four-character alphanumeric identifier. The protein structure predicted by the X-ray diffraction pattern was preferred over other methods. The downloaded protein file was modified using molecular visualization software PyMOL by removing water molecules, and adding hydrogen bonds to provide interaction with the ligands. The protein data bank will provide information about the ligand bound to the protein; the ligand molecule name specified by the Protein Data Bank was used to identify the binding site of the protein. The residues within 6A° alone was selected and saved in a separate PDB file.

Ligand file preparation

The photochemical from the traditionally used medicinal plants was chosen as the ligand molecule. From the study the majorly used turmeric, garlic and green tea play an important role in curing our ailments for ages. The traditional medicinal plants were chosen based on the literature survey, IMPPAT (Indian Medicinal Plants, Phytochemistry and Therapeutics). For every

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photochemical the 3D conformation was downloaded from PubChem as SDF format. PubChem is a database maintained by NCBI which contain the information about the molecules and their bio assays. The SDF file of the ligand molecule was converted to the PBD format using open babble in auto dock.

Molecular docking

The docking was carried out using Auto Dock PyRx Python prescription-0.8, which is a virtual screening tool used to screen libraries of compounds against potential targets. The Auto Dock wizard in the PyRx was selected and the add macromolecule was selected and the desired protein downloaded in the PDB format was loaded. Some pdb files had missing atoms, were corrected using the PyMol by removing all the water molecules obstructing the docking procedure. The small molecules were loaded using open babel option which can load files in SDF format into PyRx. Once the file is loaded it will be displayed in the open babel wizard and it was selected and converted to file supporting docking format (pdbqt). The auto grid box was set with dimensions X: 25.000, Y: 25.000, Z: 25.000 and the run vina was selected.

Post docking analysis

The amino acids interacting with the inhibitors were visualised using Maestro Version 11.9.011, MMshare Version 4.5.011, Release 2019-1. The docked output from the PyRx were stored in mgtools folder in pdbqt format. The protein structure used for docking was imported to maestro followed by the inhibitor molecule output pdbqt file. The docked results from PyRx were opened in PyMol as pdbqt format in the order of protein molecule followed by the inhibitor. The protein object was selected and show as surface was chosen and the colour was set to Gray. The inhibitor was selected and show as sticks was chosen and a different colour was used to differentiate from the protein. The image was saved in png format.

3. RESULTS AND DISCUSSION

Target protein identification

The degradation of cholesterol pathway was studied to find the proteins which can be targeted to prevent cardiovascular diseases (Table 1). Structural view of the target proteins were displayed in Fig 1.

Table 1: Active site amino acids of target proteins

	PDB ID	Active Site Amino Acid
a	**2V0Z** Crystal Structure of Renin with Inhibitor 10 (Aliskiren)	ASP 244, ASP 11, GLU 116, LYS 239
b	**1CX2** CYCLOOXYGENASE-2 (Prostaglandin synthase-2) complexed with a selective inhibitor, SC-558	GLU 380, GLU 524, GLU 465, ASP 125, ARG 467, ARG 469, LYS 468, LYS 83, ARG 120, LYS 532, LEU 472 (OH), PRO 86, PHE 470, TYR 466, LEU 152, ALA 151, LEU 525, PRO 528, PHE 529, ILE 124, LEU 123, TYR 122, SER 471, THR 521, SER 121, SER 119
c	**1O86** Crystal Structure of Human Angiotensin Converting Enzyme in complex with lisinopril.	ASP 465, ASP 507, LYS511, ARG 468, ARG 186, ARG 489(OH), TYR 520, ILE 514, PRO 508.TRP 467, VAL 464, LEU 463, PHE 460, PHE 457, ALA 272, LEU 275, LEU 495, TRP 486, TRP 485, TRP 182, MET 278, TRP 279, ALA 280, POLAR INTERACTION-GLN 493, SER 461, THR 282, GLN 281, ASN 277
d	**1HW8** Complex of the catalytic portion of human HMG-COA reductase with compacting (also known as mevastatin)	GLU 559, GLU 665, ASP 690, LYS 662, LYS 692, LYS 691, LYS 735, ARG 590(OH)

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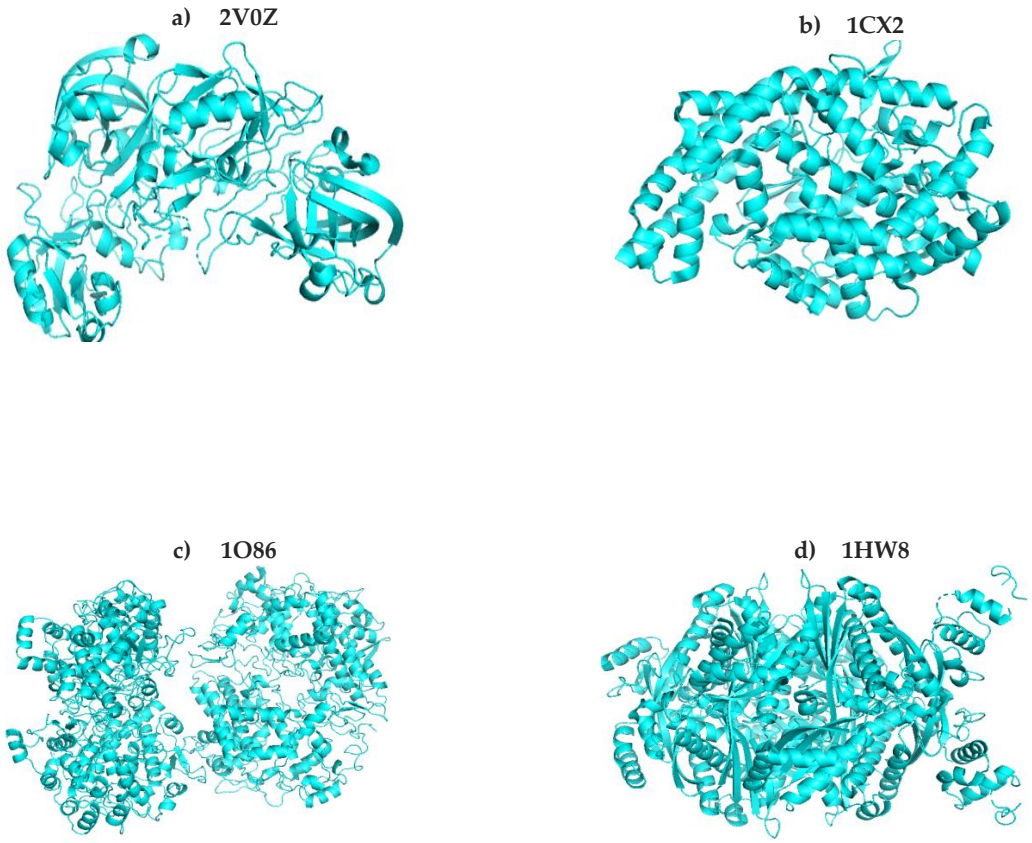

Figure 1: Target proteins a) Renin, b) Cyclooxygenase-2, c) ACE2, d) HMG- CoA

Selection of ligand

212 phytochemicals were selected, among that 67 alone selected as ligand based on the Lipinski rule. Ligands details given in supplementary data (Table 1).

Molecular docking

Docking using Auto Dock was performed for 67 small molecules with 4 selected target proteins (Docking results are attached in annexure). For each protein top 10 interacting ligands were selected based on maximum binding energy. Among the selected compounds the compounds Shinpterocarpin, Quinindoline, Glabridin, Jusbetonin, Rheediaxanthone, Friedelin had repeated interaction with 4 proteins (Table 2).

Table 2: Binding energy for ligand with proteins

Ligand PubChem ID	Protein Name	Binding Energy (kcal/mol)	No of favorable interactive proteins
Renin			
10336244	active_site_2VOZ	-8.8	3
67484	active_site_2VOZ	-8.7	3
124052	active_site_2VOZ	-8.6	3
21576272	active_site_2VOZ	-8.5	3
51666248	active_site_2VOZ	-8.4	2
42607541	active_site_2VOZ	-8.4	2
102060338	active_site_2VOZ	-8.3	3

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73145	active_site_2VOZ	-8.1	2
91472	active_site_2VOZ	-8	3
5280445	active_site_2VOZ	-8	2
Cyclooxygenase			
5318057	Active_site_1cx2	-8.9	2
91472	Active_site_1cx2	-8.8	3
102060338	Active_site_1cx2	-8.5	3
21576272	Active_site_1cx2	-8.1	3
442774	Active_site_1cx2	-8	1
42607541	Active_site_1cx2	-8	2
124052	Active_site_1cx2	-8	3
5320092	Active_site_1cx2	-7.6	1
67484	Active_site_1cx2	-7.5	3
10336244	Active_site_1cx2	-7.5	3
Angiotensin			
442935	Active_Site_1086	-8.3	1
72610	Active_Site_1086	-8	1
57473313	Active_Site_1086	-7.4	1
5281855	Active_Site_1086	-7.2	1
10336244	Active_Site_1086	-7.1	3
102060338	Active_Site_1086	-7.1	3
5318057	Active_Site_1086	-7	2
73145	Active_Site_1086	-6.9	1
4486241	Active_Site_1086	-6.8	1
HMGR			
5281605	Active_Site_1HW8	-10.7	1
5317652	Active_Site_1HW8	-10.6	1
21576272	Active_Site_1HW8	-10.3	3
5280443	Active_Site_1HW8	-10.2	1
5280445	Active_Site_1HW8	-10.1	2
51666248	Active_Site_1HW8	-10.1	2
155206	Active_Site_1HW8	-10.1	1
71629	Active_Site_1HW8	-10	1
124052	Active_Site_1HW8	-10	3
67484	Active_Site_1HW8	-9.9	3

Binding pocket analysis

Binding pocket analysis of rennin

In RENIN protein 6 different types of drug targets binds and gives a best result. Grey colour represents the protein and green color indicates the inhibitor binding site whereas each red color shows different type of drug targets binds. 10336244- Shinpterocarpin, 67484- 6H- Quinindoline, 124052- Glabridin, 21576272 - Jusbetonin, 102060338- Rheediaxanthone-A, 91472- Friedelin (Table 3). The important amino acid residues in RENIN involved in binding with the known inhibitor is shown in the figure. Six different targets were used (10336244- Shinpterocarpin, 67484- 6H- Quinindoline, 124052- Glabridin, 21576272 - Jusbetonin, 102060338- Rheediaxanthone-A, 91472- Friedelin).

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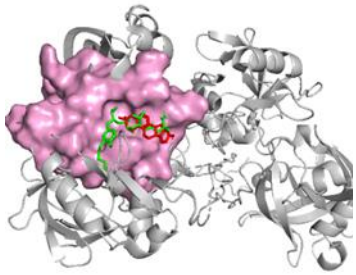
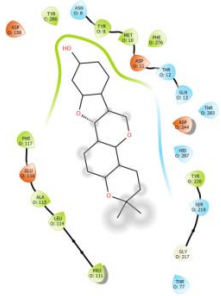
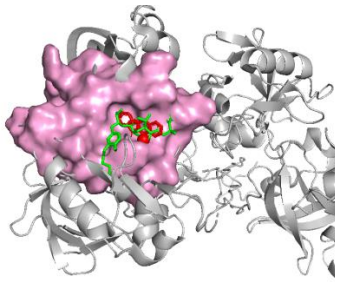
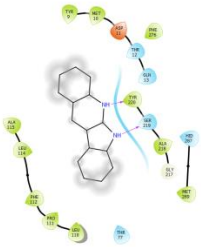
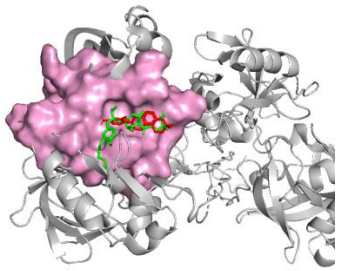
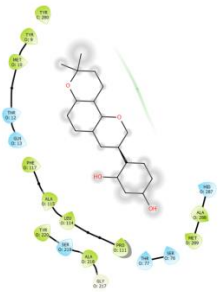
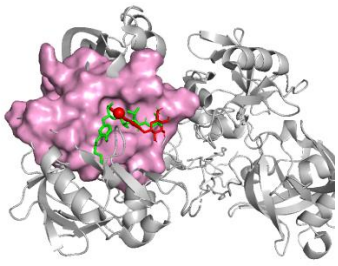
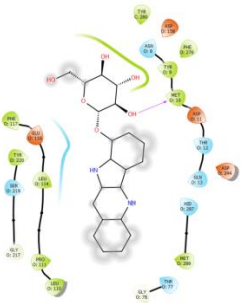
Table 3: Binding pocket analysis of rennin

Ligand-PubChem Id	Standard and ligands in Binding pocket	Active site aminoacid interaction	Interaction Type
10336244			NEGATIVE CHARGE INTERACTION-ASP 158, ASP 11, ASP 244, GLU 116
67484			NEGATIVE CHARGE INTERACTION: ASP 11 HYDROPHOBIC INTERACTION-TYR 9, MET 10, PHE 276, TYR 22O(NH), ALA 218, MET 289, LEU 110, PRO 111, PHE 112, LEU 114, ALA 115 POLAR INTERACTION-THR 12, GLN 13, SER 219(NH), HID 287, THR 77
124052			NEGATIVE CHARGE INTERACTION: ASP 11 HYDROPHOBIC INTERACTION-TYR 9, MET 10, PHE 276, TYR 22O(NH), ALA 218, MET 289, LEU 110, PRO 111, PHE 112, LEU 114, ALA 115 POLAR INTERACTION-THR 12, GLN 13, SER 219(NH), HID 287, THR 77
21576272			NEGATIVE CHARGE INTERACTION- ASP 158, ASP 244, ASP 11, GLU 116 HYDROPHOBIC INTERACTION-MET 10(OH)

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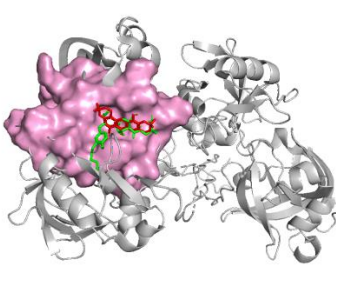
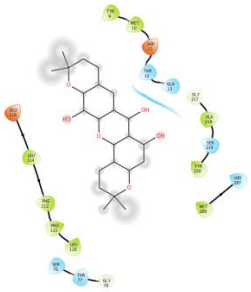
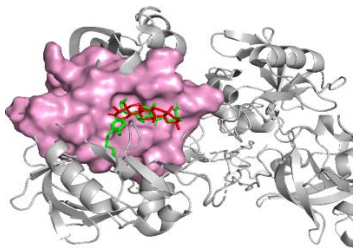
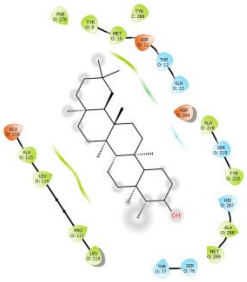
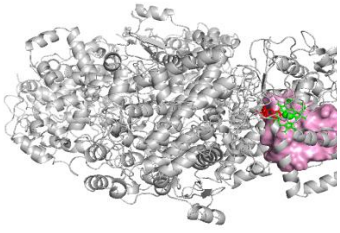
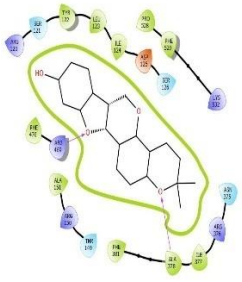
102060338			NEGATIVE CHARGE INTERACTION-ASP 11, GLU116 HYDROPHOBIC INTERACTION-TYR 9, MET 10, ALA 218, TYR 220, LEU 114, MET 289, PHE 112, PRO 111, LEU 110 POLAR INTERACTION-THR 12, GLN 13, SER 219, HID 287, SER 76, THR 77
91472			NEGATIVE CHARGE INTERACTION-ASP 11, ASP 244, GLU 116

Binding pocket analysis of COX

In COX protein 6 different types of drug targets binds and gives a best result. Grey color represents the protein and green color indicates the inhibitor binding site whereas each red color shows different type of drug targets binds. 10336244- Shinpterocarpin, 67484- 6H- Quinindoline, 124052- Glabridin, 21576272 - Jusbetonin, 102060338- Rheediaxanthone-A, 91472- Friedelin (Table 4). The important amino acid residues in COX involved in binding with the known inhibitor is shown in the figure. Six different targets were used (10336244- Shinpterocarpin, 67484- 6H- Quinindoline, 124052- Glabridin, 21576272 - Jusbetonin, 102060338- Rheediaxanthone-A, 91472- Friedelin).

Table 4: Binding pocket analysis of COX

Ligand-PubChem Id	Standard and ligands in Binding pocket	Active site aminoacid interaction	Interaction Type
10336244			NEGATIVE CHARGED INTERACTION - ASP 125 POSITIVE CHARGED INTERACTION-ARG 120, 469,150,376, LYS- 532 HYDROPHOBIC INTERACTION- PHE-529,470,381 PRO-528, ILE-124,377 ALA-378,151, LEU-123 TYR-122 POLAR INTERACTION- SER-121,126 THR-149, ASN-375

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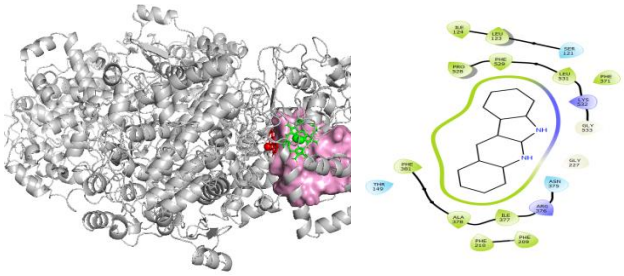
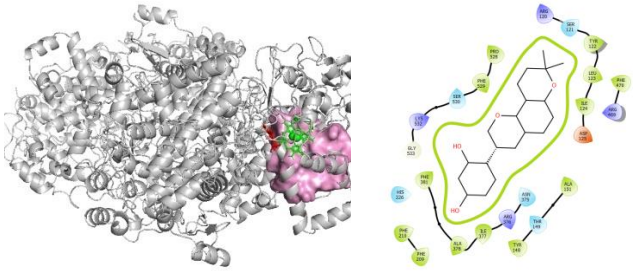
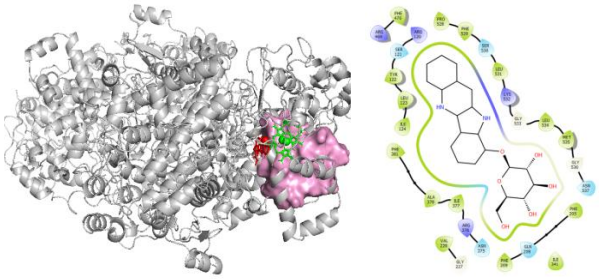
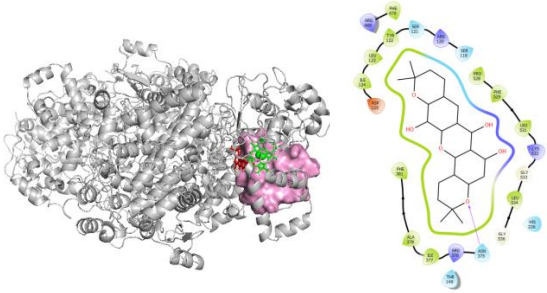
67484		NEGATIVE CHARGED INTERACTION- 0 POSITIVE CHARGED INTERACTION-ARG 376, LYS 532 HYDROPHOBIC INTERACTION-ILE 124, LEU-123, PHE-371, PHE-529, LEU-531, PRO-528, ILE 377, PHE-209, ALA 378, PHE 210. PHE-381 POLAR INTERACTION- THR 149, ASN 375, SER 121 GLYCINE INTERACTION –GLY 227,533
124052		NEGATIVE CHARGE INTERACTION- ASP 125 POSITIVE CHARGE INTERACTION-ARG 469, ARG 120, LYS 532, ARG376 HYDROPHOBIC INTERACTION-PHE 470, ILE 124, LEU 123, TYR 122, PRO 528, PHE 529, PHE 381, ALA 151, ILE 377, TYR 148, ALA 378, PHE 209, PHE 210 POLAR INTERACTION-THR 149, ASN 375, HIS 226, SER 530, SER 121
21576272		POSITIVE CHARGE INTERACTION-ARG 469, ARG 120, LYS 532, ARG 376 HYDROPHOBIC INTERACTION-PHE 470, MET 535, LEU 534, LEU 531, PHE 529, PRO 528, TYR 122, LEU 123, ILE 124, PHE 381, ALA 378, ILE 377, PHE 205, ILE 341, VAL 228, PHE 209 POLAR INTERACTION-SER 530, ASN 537, GLN 208, ASN 375, SER 121
102060338		NEGATIVE CHARGE INTERACTION- ASP 125 POSITIVE CHARGE INTERACTION-ARG 469, ARG 120, LYS 532, ARG 376 HYDROPHOBIC INTERACTION-PHE 470, ILE 124, LEU 123, TYR 122, PRO 528, PHE 529, LEU 531, LEU 534, ILE 377, ALA 378, PHE 381 POLAR INTERACTION-SER 121, SER 119, HIS 226, ASN 375, THR 149

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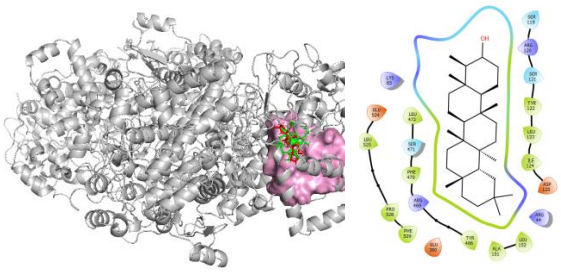
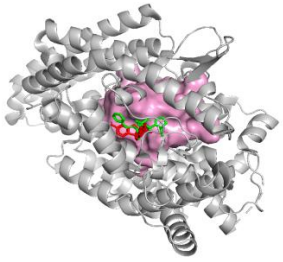
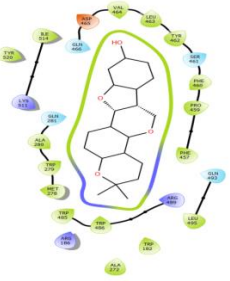
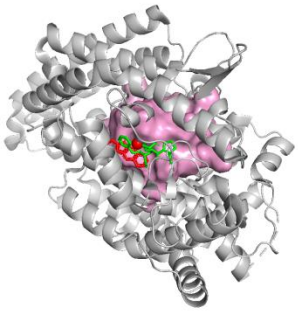
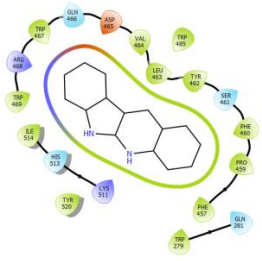
91472			NEGATIVE CHARGE INTERACTION-GLU-524, ASP125, GLU-360 POSITIVE CHARGE INTERACTION-ARG 120, LYS 83, ARG 469, ARG 44 HYDROPHOBIC INTERACTION-TYR 122, LEU 123, ILE 124, LEU 472, PHE 470, LEU 525, PRO 528, PHE 529, TYR 466, ALA 151, LEU 152 POLAR INTERACTION-SER 119, SER 121, SER 471

Binding pocket analysis of ACE 2

In ACE 2 protein 6 different types of drug targets binds and gives a best result. Grey color represents the protein and green color indicates the inhibitor binding site whereas each red color shows different type of drug targets binds. 10336244- Shinpterocarpin, 67484- 6H- Quinindoline, 124052- Glabridin, 21576272 - Jusbetonin, 102060338- Rheediaxanthone-A, 91472- Friedelin) (Table 5). The important amino acid residues in ACE 2 involved in binding with the known inhibitor is shown in the figure. Six different targets were used (10336244- Shinpterocarpin, 67484- 6H- Quinindoline, 124052- Glabridin, 21576272 - Jusbetonin, 102060338- Rheediaxanthone-A, 91472- Friedelin).

Table 5: Binding pocket analysis of ACE2

Ligand-PubChem Id	Standard and ligands in Binding pocket	Active site aminoacid interaction	Interaction Type
10336244			NEGATIVE CHARGE INTERACTION-ASP 465 POSITIVE CHARGE INTERACTION- LYS 511, ARG 489, ARG 186 HYDROPHOBIC INTERACTION-LEU 495, TRP 182, ALA 272, TRP 486, TRP 485, MET 278, TRP 279, ALA 280, TYR 520, ILE 514, VAL464, LEU463, TYR462, PHE460, PRO459, PHE457 POLAR INTERACTION-SER 461, GLN 493, GLN 281, GLN 466
67484			NEGATIVE CHARGE INTERACTION-ASP 465 POSITIVE CHARGE INTERACTION-LYS 511, ARG 468 HYDROPHOBIC INTERACTION-TRP 279, TYR 520, ILE 514, TRP 469, TRP 467, VAL 464, LEU 463, TYR 462, PHE 460, PRO459, PHE 457, TRP 279, TRP 485 POLAR INTERACTION-SER 461, GLN 466, HIS 513, GLN 281

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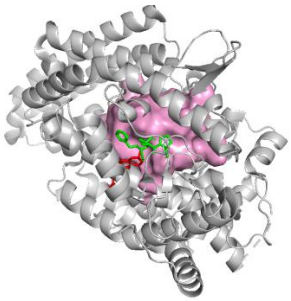
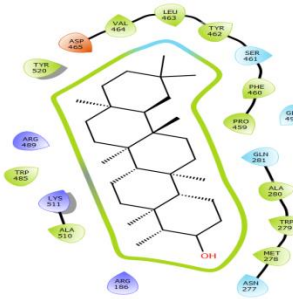
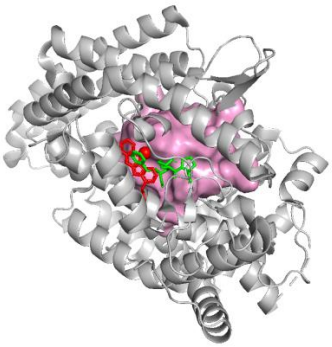
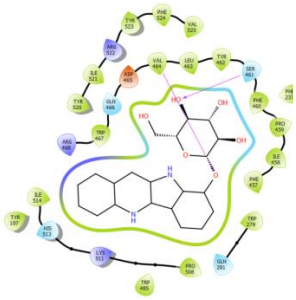
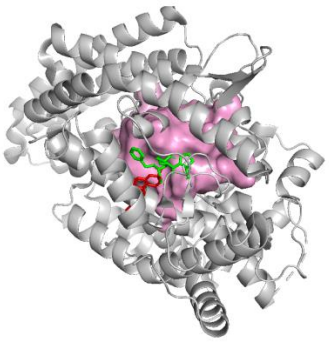
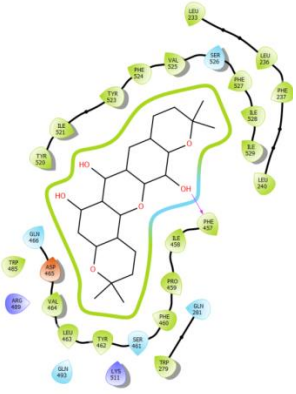
124052			NEGATIVE CHARGE INTERACTION-ASP 465 POSITIVE CHARGE INTERACTION-ARG 489, LYS 511, ARG 186 HYDROPHOBIC INTERACTION-TYR 520, VAL 464, LEU 463, TYR 462, PHE 460, PRO 459, ALA 280, TRP 279, MET 278, TRP 485, ALA 510 POLAR INTERACTION-SER 461, GLN 493, GLN 281, ASN 277
21576272			NEGATIVE CHARGE INTERACTION-ASP 465 POSITIVE CHARGE INTERACTION-LYS 511, ARG 468, ARG 522 HYDROPHOBIC INTERACTIONS-VAL525, PHE 524, TYR 523, ILE 521, TYR 520, ILE 514, TYR 197, TRP 485, PRO 508, TRP 279, PHE 57, ILE 458PRO 459, PHE 460, TYR 462, LEU 463, VAL 464, TRP 467, PHE 237 POLAR INTERACTION-SER 461(OH), GLN 281, HIS 513, GLN 466
102060338			NEGATIVE CHARGE INTERACTION-ASP 465 POSITIVE CHARGE INTERACTION-ARG 489, LYS 511 HYDROPHOBIC INTERACTION-LEU 233, LEU 236, PHE 237, LEU 240, ILE 529, ILE 528, PHE 527, VAL 525, PHE 524, TYR 523, ILE 521, TYR 520, TRP 485, VAL 464, LEU 463, TYR 462, PHE 460, PRO 459, ILE 458, PHE 457(OH), TRP 279 POLAR INTERACTION-SER 526, GLN 466, GLN 281, SER 461, GLN 493

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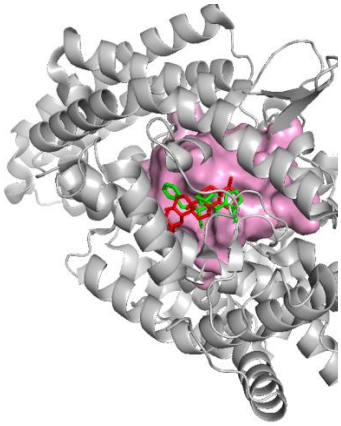
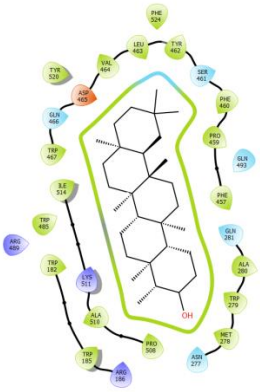
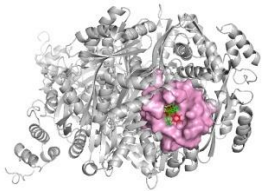
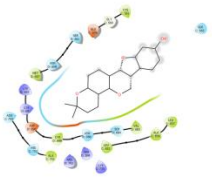
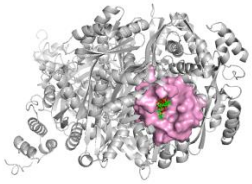
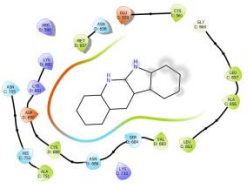
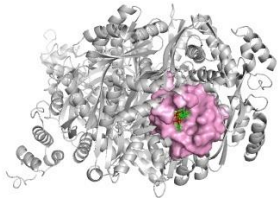
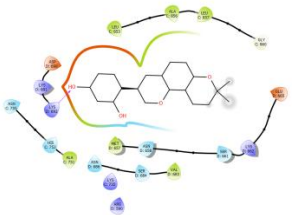
91472			NEGATIVE CHARGE INTERACTION-ASP 465 POSITIVE CHARGE INTERACTION-ARG 489, LYS 511, ARG 186 HYDROPHOBIC INTERACTION-PHE 524, TYR 462, PHE 460, PRO 459, PHE 457, ALA 280, TRP 279, MET 278, PRO 508, TRP 185, ALA 510, TRP 182, TRP 485, ILE 514, TRP 467, TYR 520, VAL 464, LEU 463 POLAR INTERACTION-SER 461, GLN 493, GLN 281, GLN 466, ASN 277

Binding pocket analysis of HMGR

In HMGR protein 6 different types of drug targets binds and gives a best result. Grey color represents the protein and green color indicates the inhibitor binding site whereas each red color shows different type of drug targets binds. 10336244- Shinpterocarpin, 67484- 6H- Quinindoline, 124052- Glabridin, 21576272 - Jusbetonin, 102060338- Rheediaxanthone-A, 91472- Friedelin) (Table 6). The important amino acid residues in HMG involved in binding with the known inhibitor is shown in the figure. Six different targets were used. (10336244- Shinpterocarpin, 67484- 6H- Quinindoline, 124052- Glabridin, 21576272 - Jusbetonin, 102060338- Rheediaxanthone-A, 91472- Friedelin)

Table 6: Binding pocket analysis of COX

Ligand-PubChem Id	Standard and ligands in Binding pocket	Active site aminoacid interaction	Interaction Type
10336244			NEGATIVE CHARGE INTERACTION-GLU539, ASP 690 POSITIVE CHARGE INTERACTION-LYS 692, LYS 691, ARG 702, ARG 590LYS 735
67484			NEGATIVE CHARGE INTERACTION-GLU 559, ASP 690 POSITIVE CHARGE INTERACTION-ARG590, LYS 692, LYS 691, LYS 735
124052			NEGATIVE CHARGE INTERACTION-ASP 690, GLU-665 POSITIVE CHARGE INTERACTION-LYS 691, LYS 692(OH), LYS 662, LYS 735, ARG 590

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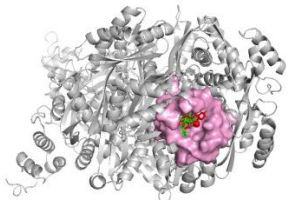
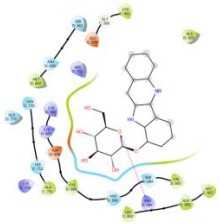
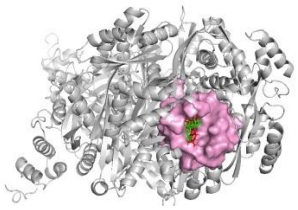
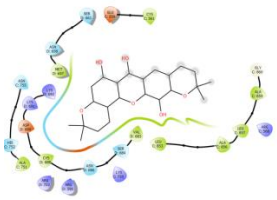
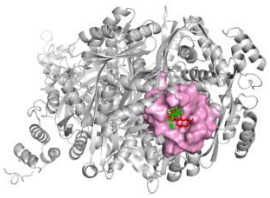
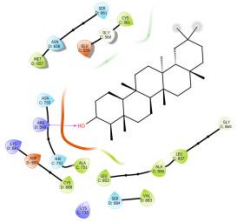
21576272			NEGATIVE CHARGE INTERACTION-GLU 559, ASP 690 POSITIVE CHARGE INTERACTION-ARG 590(O), LYS 835, LYS 691, LYS 692, ARG 702
102060338			NEGATIVE CHARGE INTERACTION-GLU559, ASP 690 POSITIVE CHARGE INTERACTION-LYS 692, ARG 568, LYS 735, ARG 590, ARG 702, LYS 691
91472			NEGATIVE CHARGE INTERACTION-GLU 559, ASP 690 POSITIVE CHARGE INTERACTION-LYS 691, ARG 590(OH)LYS 735

The selected molecules (10336244- Shinpterocarpin, 67484- 6H- Quinindoline, 124052- Glabridin, 21576272 - Jusbetonin, 102060338- Rheediaxanthone-A, 91472- Friedelin) was analysed for other possible targets. According to the report from Swiss target prediction the majority of the protein target in which the selected molecule bound was found to be the receptors responsible for causing cardiovascular diseases. The selected molecules act as the inhibitor in such receptors.

4. CONCLUSION

In docking study, all the screened phytochemicals showed very good binding affinities against the cardiovascular drug targets. Hence, these phytocompounds can be used lead molecules to develop drugs for the treatment of cardiovascular diseases after successful experimental investigations.

Funding:
This study has not received any external funding.

Conflict of Interest:
The authors declare that there are no conflicts of interests.

Ethical approval
Not applicable.

Data and materials availability:
All data associated with this study are present in the paper.

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