Journal of Rare Cardiovascular Diseases
ISSN: 2299-3711 (Print) | e-ISSN: 2300-5505 (Online)
www.jrcd.eu
RESEARCH ARTICLE

Angiotensin-Converting Enzyme (ACE)Inhibitory Activity of Adansonia digitata L: An In-Vitro and In-Silico Investigation

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Article History
Received: 11.07.2025
Revised: 12.08.2025
Accepted: 05.09.2025
Published: 31.10.2025

Abstract: The study explores *Adansonia digitata L*'s potential in hypertension management through phytochemical and protein analysis. Seven identified phytoconstituents, belonging to alkaloid, terpene, and steroid class, were predicted to modulate hypertension proteins. Network analysis revealed a significant role for Kaempferol-3-O-rutinoside in interacting with SIRT1, CHKA, NOS3, PTGS1, SIRT3, GSTP1, IDH1, CYP3A4 key molecules. The molecular docking study concluded that Kaempferol-3-O-rutinoside showed ACE inhibition with -7.9 Kcal/mol interactions with ASP140, ARG350, THR358, ALA334, ALA332, HIE331 and cation interaction with HIP361as compared to standard drug -7.2 kcal/ mol Sampatrilat with GLH362, HIP361, LYS489, GLN259, TYR498, TYR501, ARG500 and pi-pi stacking with PHE505 and HIP361 amino acidresidues. Furthermore, ADMET predictions indicated some deviations from ideal oral bioavailability for compounds, emphasizing considerations for its pharmaceutical application. The analysis also confirmed the non-toxic nature of compounds, elucidating its safety profile. It is evident from the results that hydroalcoholic extract and Flavonoid fraction of *Adansonia digitata L* shows the promising percentage inhibition of angiotensin-converting enzyme with 70.01% and 75.54% of inhibition at 1000 mg/ml, respectively. The present study concluded that *Adansonia digitata L* possesses potential ACE inhibition properties in the treatment of hypertension based on the computer aided drug design models and *in-vitro* activity.

Keywords: Molecular Docking, Network pharmacology, ACE enzyme inhibition, Kaempferol-3-O-rutinoside, Anti-hypertensive.

INTRODUCTION

Ancient texts such as the Charaka Samhita (1000 B.C.) shed light on the wealth of herbal wisdom in Ayurvedic and Unani medicine. This early Indian medical treatise extensively discusses the use of over 2000 plants for medicinal purposes, reflecting a profound heritage of knowledge and benefits derived from herbal remedies[1]. Among the versatile medicinal herbs highlighted in these ancient texts is the Baobab (*Adansonia digitata* L.), a majestic sub-tropical tree belonging to the Malvaceae family and native to Africa. Revered as the "arbre a palabre," this iconic tree serves as a communal space for elders to address important issues in various African cultures. Beyond its symbolic role, the Baobab has captured the attention of pharmaceutical companies and researchers in recent years due to its diverse traditional applications[2]. The Baobab's roots extend into the realms of medicine, nutrition, and cosmetics, making it a subject of interest for potential benefits. This botanical giant, widespread across numerous African countries, represents a convergence of heritage and modern exploration. The past decade has witnessed a renaissance in the exploration of the Baobab's multifaceted and valuable properties, signaling a renewed appreciation for its cultural significance and potential contributions to various fields[3]. Medicinal herbs, housing a natural abundance of therapeutic compounds within their reservoirs, present valuable solutions for addressing various health concerns like Hypertension or high blood pressure, it stands as one of the most prevalent diseases globally. In 2010, an estimated 31.1% of adults worldwide were reported to have hypertension, a figure projected to surge by approximately 60% by 2025. This condition not only elevates the risk factors for cardiovascular disease but is also linked to severe complications, including stroke, heart attack, and kidney failure[4]. A cornerstone medication in managing high blood pressure is Angiotensin-converting enzyme (ACE) inhibitors emerge as key therapeutic agents in the management of hypertension. As a vital component within the reninangiotensinaldosterone system, ACE assumes a critical Contribution to the maintenance of

blood pressure equilibrium[5]. It is a crucial enzyme that regulates the formation of angiotensin I (Ang I) to angiotensin II (Ang II) and, in turn, blood pressure (BP). This enzyme is a part of the reninangiotensinaldosterone system (RAAS). ACE inhibitors have a therapeutic role in regulating the level of blood pressure and, thus, preventing cardiovascular diseases (CVDs)[6].

After noticing the information mentioned above, researchers wanted to explore making new drugs from plants or their derivatives. The study describes a way to use computer simulations to predict if certain plant compounds could be effective against high blood pressure by targeting the ACEinhibitors. They also used techniques like molecular docking and pharmacokinetic studies to guess how these plant compounds might bind to the ACEinhibitors. By using computer methods like molecular modeling and simulations, scientists have made a big impact on how they discover new drugs. These methods help them predict and understand how molecules interact at a very tiny level, giving them important information about how potential drugs might work.

1.1 Chemical composition

Analysis of *Adansonia digitata L*. highlights crucial phytochemicals essential for ACE enzyme inhibition. Phytocompounds are detailed in **Figure 1**, illuminate the chemistry of significant chemical components in Baobab. This exploration unveils the plant's potential in harnessing specific compounds vital for modulating ACE inhibitory activity, contributing to its medicinal relevance.

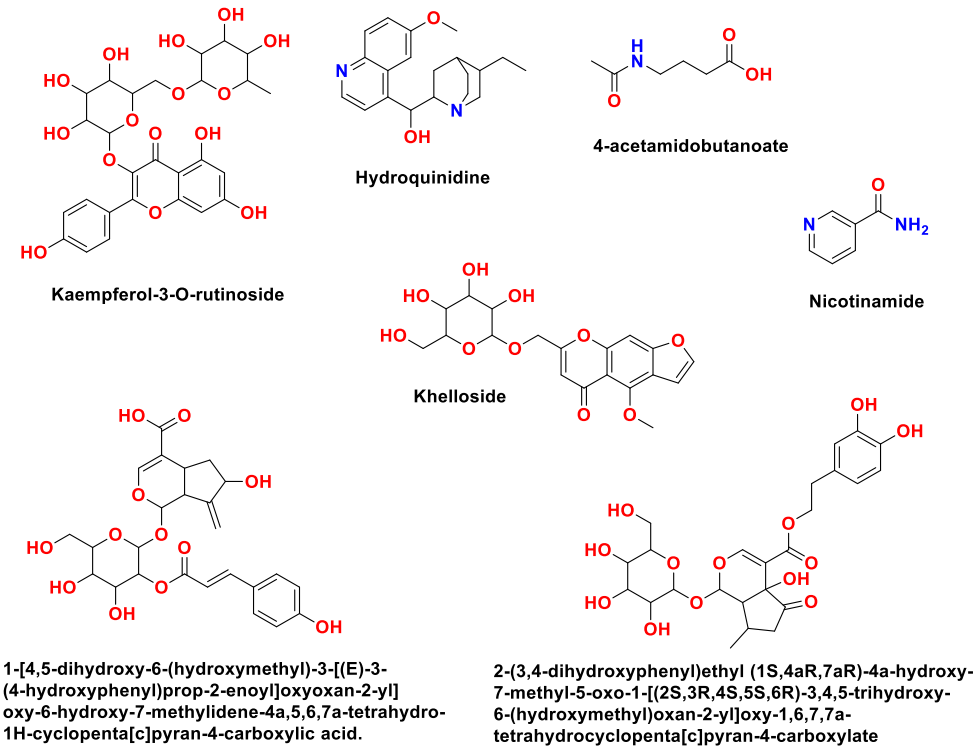

Figure 1: Phytochemistry of selected Phytocompounds of *Adansonia digitata L.*

MATERIALS AND METHODS

2.1 Preparation of Extract and Flavonoid Fractionation

The process began by collected plant leaves and fruits from Miraj, Maharashtra India and authenticated from Botanical Survey of India, Western Regional Centre, Koregaon Road, Pune (No.BS1/WRC/100-1/Tech/2020/126). The fruits were cleaned, cut, dried and ground. The fruit powder was extracted with ethanol and water (70:30 v/v) using Soxhlet apparatus. The hydroalcoholic extract was concentrated using a rotary vacuum evaporator [7]. The flavonoids were separated using ethyl acetate [8].

2.2 *In-vitro* ACE inhibition assay

ACE inhibition activity was carried out by Cheung *et al* [9] and Chaudhary *et al* [10] method with some modification 50 µL of ACE (25mU/mL) with 50 µL test extract and Fraction in the different concentration (100 to 1000 µg/ mL) was preincubated at 37°C for 10 min. Afterword 150 µL HLL substrate solution was added to above mixture and incubated at 37°C for 30 min. at the end the reaction was stop solution by 250 µL of 1M HCl the add 500 µL ethyl acetate and centrifuged by refrigerated centrifuge at 800g for 15 min. 200 µL evaporated at room temperature and then add 1000 µL distilled water and lastly measured at 280nm UV spectrophotometer. All experiments are performed in triplicate and captopril is used as standard at the concentration 3.6ng/mL.

The percentage inhibition of the ACEI (Angiotensin-Converting Enzyme Inhibitor) was derived through computational analysis using the formula:

$$\textbf{\textit{Percentage inhibition}} = \frac{(A-B)}{(A-C)} * 100 =$$

Where A = is OD at 228 nm with ACE but without inhibitor.
B= is the OD in the presence of both ACE and inhibitor.
C= is the OD without ACE and inhibitor

2.3 Identification of phytocompounds and their target identification

Phytochemicals present in *Adansonia digitata L* were selected by using an extensive literature survey and mining of public repositories such as Dr. Duke's DB and IMPATT. All the chosen compounds SMILES were obtained from the PubChem database (https://pubchem.ncbi.nlm.nih.gov) and searched for protein-based prediction in DIGEP-Pred at a probable activity (Pa)>0.5 and Probable inactivity (Pi) ratio.

2.4 Mining of phytoconstituents and proteins involved in hypertension:

Phytoconstituents derived from *Adansonia digitata L* were systematically gathered from a database was compiled to encompass information about these phytoconstituents, detailing their types, SMILES, and PubChem CID. To ensure data accuracy, duplicate entries of phytoconstituents were removed during the database construction process. The canonical SMILES and PubChem CID for each phytoconstituent were obtained from the PubChem Database [11]. Utilizing the Digip pred [12] tool, SMILES data were scrutinized to predict potential targets. Concurrently, proteins associated with hypertension were pinpointed by referencing established targets reported in the Therapeutic Target Database (TTD)[13]. The Gene ID for each protein identified as a hypertension target was subsequently extracted from Uniport [14].

2.5 Network construction

The STRING database was searched for a list of proteins that were up- and down-regulated. The KEGG (Kyoto Encyclopaedia of Gene and Genomes) pathway database was used to locate the regulated protein and its related pathways. The active ingredients and their interaction targets related to hypertension were constructed, and the data was subsequently submitted to the Cytoscape 3.7.2 software to "visualize and analyze the network from high to low modulating". To find the appropriate protein targets modified by the phytoconstituents of *Adansonia digitata L.*Target network was built, graphically examined, and screened using Cytoscape 3.7.2 to explore the relationship between phytocompounds and protein targets of hypertension compounds[12,15].

2.6 Molecular docking studies

Glide extra precision mode (XP) of Schrodinger's was considered for docking to identify the binding interaction and orientation of highly modulated genes like sodium-potassium pump and human Angiotensin-1 converting enzyme pocket [16]. The Ligprep panel of Schrodinger's suit was used for building ligands. Optimized potential for liquid simulation (OPLS4) was used for energy minimization. Torsional flexibility was given to obtain a better complimentary pose. Crystal structure coordinates of the sodium-potassium pump and human Angiotensin-1 converting enzyme complex with Sampatrilat (PDB ID: 3KDP and 6F9V) were retrieved from a protein data bank (https://www.rcsb.org) by comparing the initial binding conformation in crystal structure. The proteins were pre-processed by removing water molecules and ligands from the PDB file, assigning bond orders, and generating PKa values at PH7± 2. The protein was further optimized by energy minimization using an OPLS4 force field to obtain a stable structure for further studies[17]. The grid was generated using the co-crystal ligand withSampatrilatto specify the binding site within the target receptor. The binding affinity of ligands with receptors were described in terms of docking score, hydrogen bonds, and pi-pi interactions before docking using Glide software in extra precision (XP) mode. The binding affinity of ligands with receptors were described in terms of docking score, hydrogen bonds, and pi-pi interactions before docking using Glide software in extra precision (XP) mode[18,19] and Pharmacokinetic properties were assessed using Physicochemical and ADME properties, calculated using the Qikprop module of Schrödinger[20,21].

RESULTS

3.1 *In-vitro* ACE inhibition assay

Angiotensin-converting enzyme (ACE) inhibition activity of *Adansonia digitata L*extract and Flavonoid fraction was analyzed. The percentage inhibition of each concentration is shown in **Figure 2**. It is evident from the results that hydroalcoholic extract and Flavonoid fraction of *Adansonia digitata L* shows the promising percentage inhibition of angiotensin-converting enzyme with 70.01% and 75.54% of inhibition at 1000 mg/mL. Hence, the Flavonoid fraction has an activity against hypertension that is comparable to the ACE inhibition activity achieved with the standard drug captopril with 84.27% at 3.6ng/mL.

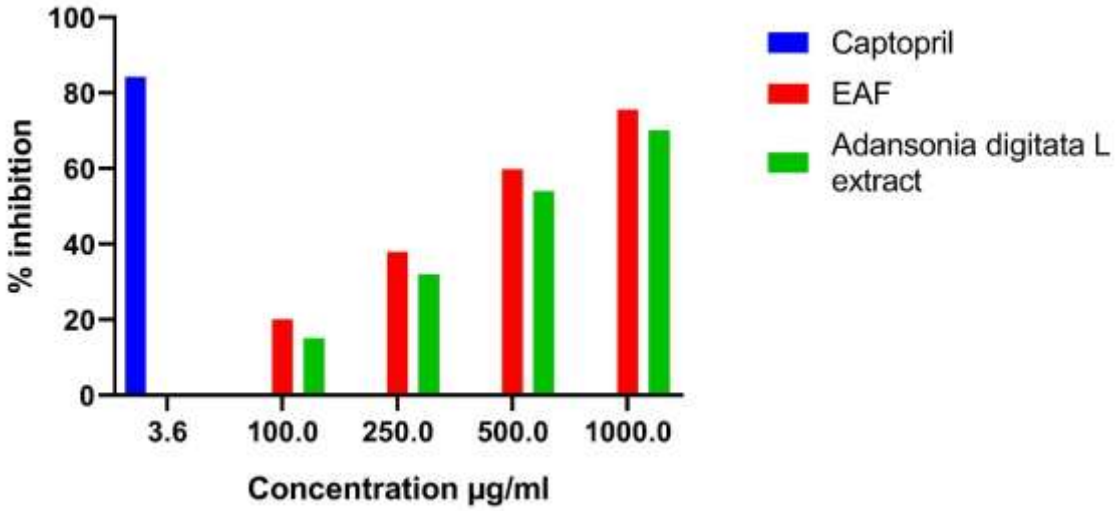

Figure 2: Determination of % inhibition of Angiotensin-converting enzyme (ACE) activity.

3.2 Exploration of phytochemical compounds and proteins implicated in hypertension:

Seven distinct phytoconstituents were discovered within Adansonia digitata L. based on data from publicly available sources. These phytoconstituents, classified as alkaloids, terpenes, and steroids, were predicted to have a regulatory effect on protein molecules associated with hypertension, as indicated in **Table 1**. Likewise, the predominant targeted hypertension protein molecules were identified as surface proteins and enzymes.

Table 1: Enrichment analysis of modulated proteins by the *Adansonia digitata L*.

Term ID	Term description	Observed gene count	False discovery rate	Matching proteins in network(labels)
hsa04066	HIF-1 signaling pathway	7 105	1.03E-11	MAPK1, EP300, NOS3,TLR4,SLC2A1, PIK3R1, HIF1A
hsa04624	FoxO signaling pathway	6 102	9.53E-09	SIRT1, MAPK1, EP300 CDK2, MAPK8, PIK3R1
hsa04657	Toll-like receptor signaling pathway	5 92	4.53E-06	MAPK1, TBK1, TLR4, MAPK8, PIK3R1
hsa04024	Sphingolipid signaling pathway	5 107	9.35E-06	MAPK1, NOS3, MAPK8 ABCC1, PIK3R1
hsa04210	NOD-like receptor signaling pathway	5 121	1.83E-05	MAPK1, TBK1, HSP90AA1, TLR4, MAPK8
hsa04217	ErbB signaling pathway	4 127	3.03E-05	MAPK1, ABL1, MAPK8 PIK3R1
hsa04621	IL-17 signaling pathway	4 123	3.89E-10	MAPK1, TBK1, HSP90AA1, MAPK8
hsa05418	PI3K-Akt signaling pathway	6 117	1.50E-09	MAPK1, CDK2, NOS3 HSP90AA1, TLR4, PIK3R1
hsa04922	Th17 cell differentiation	4 95	0.00012	MAPK1, HSP90AA1 MAPK8, HIF1A
hsa04910	Ras signaling pathway	5 102	0.00032	MAPK1, TBK1, ABL1, MAPK8, PIK3R1
hsa04932	cAMP signaling pathway	4 126	0.00046	MAPK1, EP300, MAPK8 PIK3R1
hsa04662	TNF signaling pathway	3 68	0.0012	MAPK1, MAPK8, PIK3R1
hsa04750	Metabolic pathways	8 82	0.0018	SIRT1, CHKA, NOS3 PTGS1, SIRT3, GSTP1 IDH1, CYP3A4
hsa04215	Rap1 signaling pathway	3 20	0.0041	MAPK1, CNR1, PIK3R1

3.3 Enrichment analysis of phytoconstituents protein targets

Fourteen distinct pathways, influenced by proteins implicated in hypertension, were identified through gene set enrichment analysis. Peer interpretation of protein interaction via KEGG pathway analysis revealed four pathways directly associated with the pathogenesis of hypertension. Notably, the highest count of gene sets and the lowest false discovery rate (refer to **Table 1**). Similarly, among the seven bioactive compounds, Kaempferol-3-O-rutinoside was anticipated to exert the greatest influence, demonstrating interactions with 8 genes: SIRT1, CHKA, NOS3, PTGS1, SIRT3, GSTP1, IDH1, CYP3A4 with metabolic pathway. Nevertheless, network analysis pointed seven molecules as depicted in **(Figure 3)**. The (**Figure 1**) phytocompounds-target network of *Adansonia digitata L* in modulating antihypertension responses. The down arrow shape nodes represent the molecular pathways, the triangle shape represents targets and the square shape represents phytocompounds.

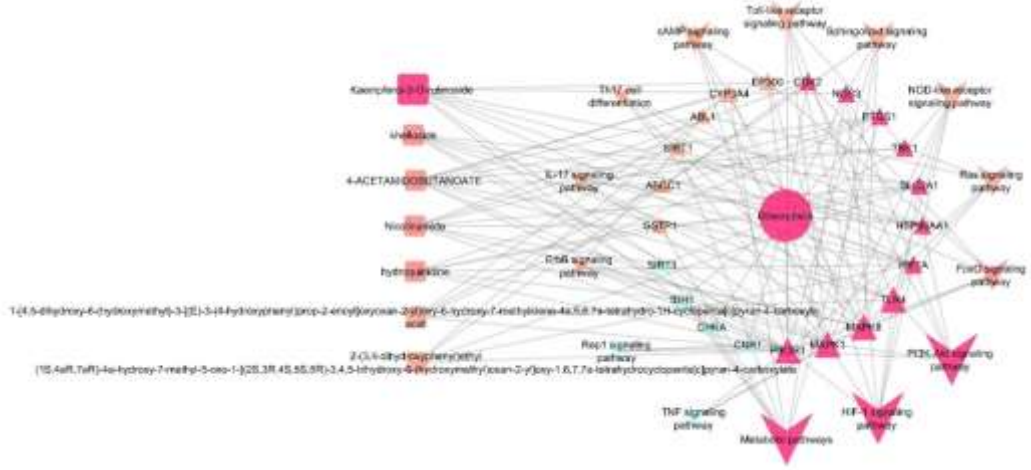

Figure 3: Component-disease-target-pathway network construction of *Adansonia digitata L*.

3.4 Computer-based molecular docking investigation

To anticipate the optimal conformational arrangement within the active site of the target protein, the chosen compounds underwent docking against the selected target protein. The outcomes of the molecular docking assessment are presented in **Table 2**. Each generated docked complex was scrutinized based on its minimum energy values (measured in Kcal/mol) and the pattern of bonding interactions, including hydrogen bonds, hydrophobic interactions, and electrostatic interactions.The Kaempferol-3-O-rutinoside possesses -8.6Kcal/mol, Glide energy of -41.38 kcal/mol (3D, 2D cartoon **Figure 4 and 5**) and hydrogen bond interactions with GLU1013, ILE35 residues as compared to standard drug Sampatrilat possesses -7.6 Kcal/mol, Glide energy of –43.41 kcal/mol (**Figure 6 and 7**) and hydrogen bond interactions withARG500, GLH362, HIP361, TYR498, GLN259, LYS489, ASP393 residues against the sodium-potassium pump **(PDB ID: 3KDP)** and in human Angiotensin-1 converting enzyme pocket **(PDB ID:6F9V)** the Kaempferol-3-O-rutinoside possesses -7.9Kcal/mol, Glide energy of -51.38 kcal/mol (**Figure 8 and 9**) and hydrogen bond interactions with ASP140, ARG350, THR358, ALA334, ALA332, HIE331 and cation interaction with HIP361 residues as compared to standard drug Sampatrilat possesses -7.2 Kcal/mol, Glide energy of –53.41 kcal/mol (**Figure 10 and 11**) and hydrogen bond interactions withGLH362, HIP361, LYS489, GLN259, TYR498, TYR501, ARG500 and pi-pi stacking with PHE505 and HIP361 residues, respectively.

Table 2: Binding affinity of Phytocompounds

Sr No.	Compounds	Docking scores in kacl/mol	
		PDB ID: 3KDP	PDB ID:6F9V
1	Hydroquinidine	-5.9	-6.1
2	4-acetamidobutanoate	-7.1	-7.0
3	Kaempferol-3-O-rutinoside	**-8.6**	**-7.9**
4	Khelloside	-7.6	-5.2
5	Nicotinamide	-6.2	-6.1
6	2-(3,4-dihydroxyphenyl) ethyl (1S,4aR,7aR)-4a-hydroxy-7-methyl-5-oxo-1-[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl) oxan-2-yl] oxy-1,6,7,7a-tetrahydrocyclopenta[c]pyran-4-carboxylate	-6.8	-5.5
7	1-[4,5-dihydroxy-6-(hydroxymethyl)-3-[(E)-3-(4-hydroxyphenyl) prop-2-enoyl] oxyoxan-2-yl] oxy-6-hydroxy-7-methylidene-4a,5,6,7a-tetrahydro-1H-cyclopenta[c]pyran-4-carboxylic acid	-5.2	-6.9
Std	Sampatrilat	-7.6	-7.2

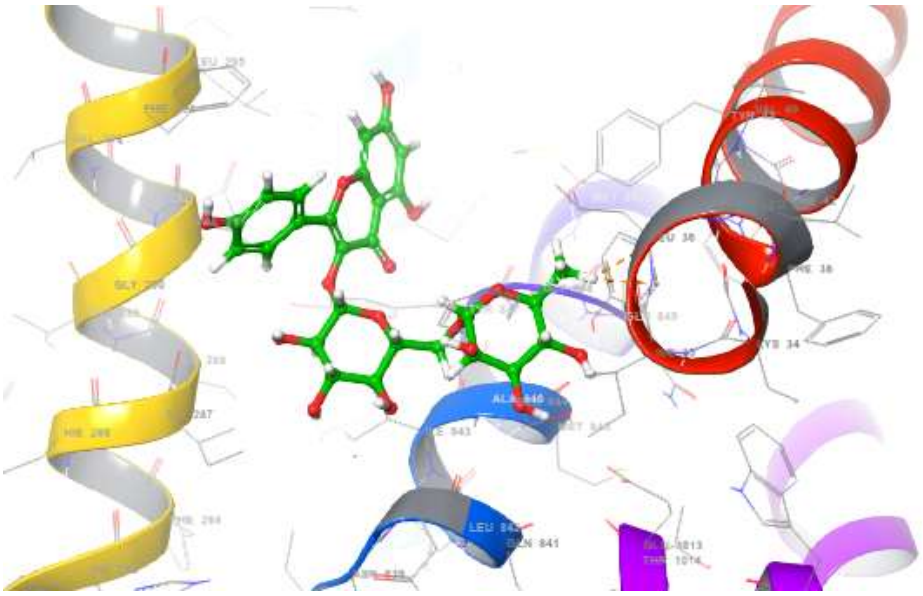

Figure 4: 3D Pose of Kaempferol-3-O-rutinoside in sodium-potassium pump (PDB ID: 3KDP):

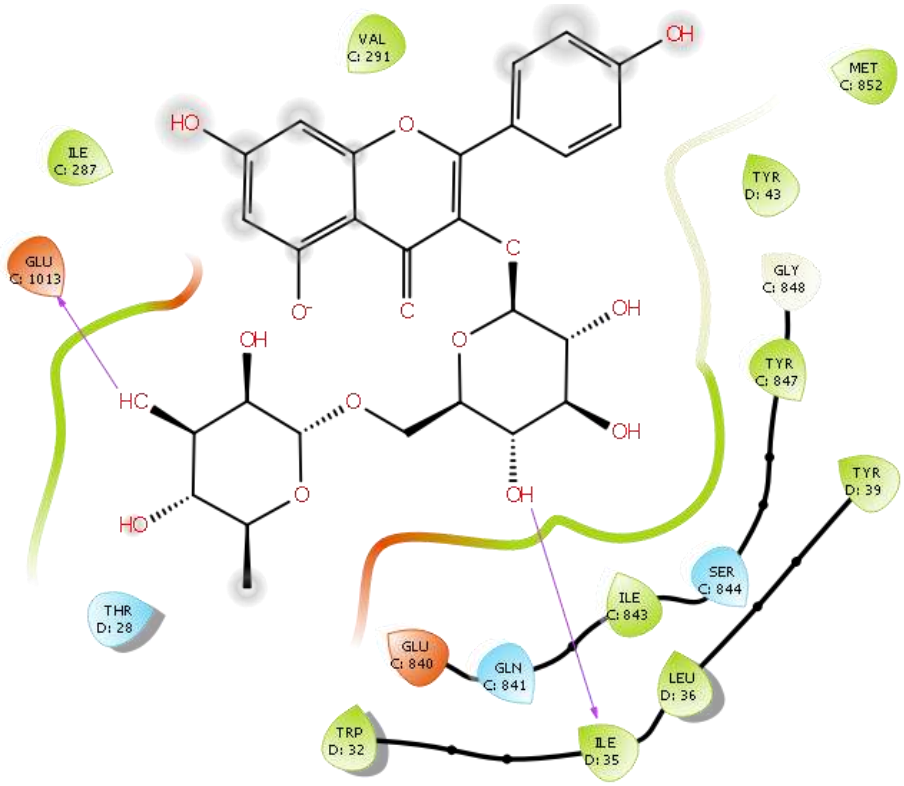

Figure 5: 2D Pose of Kaempferol-3-O-rutinoside in sodium-potassium pump (PDB ID: 3KDP):the oxygen atom of compound forms Hydrogen bonds with GLU1013, ILE35.

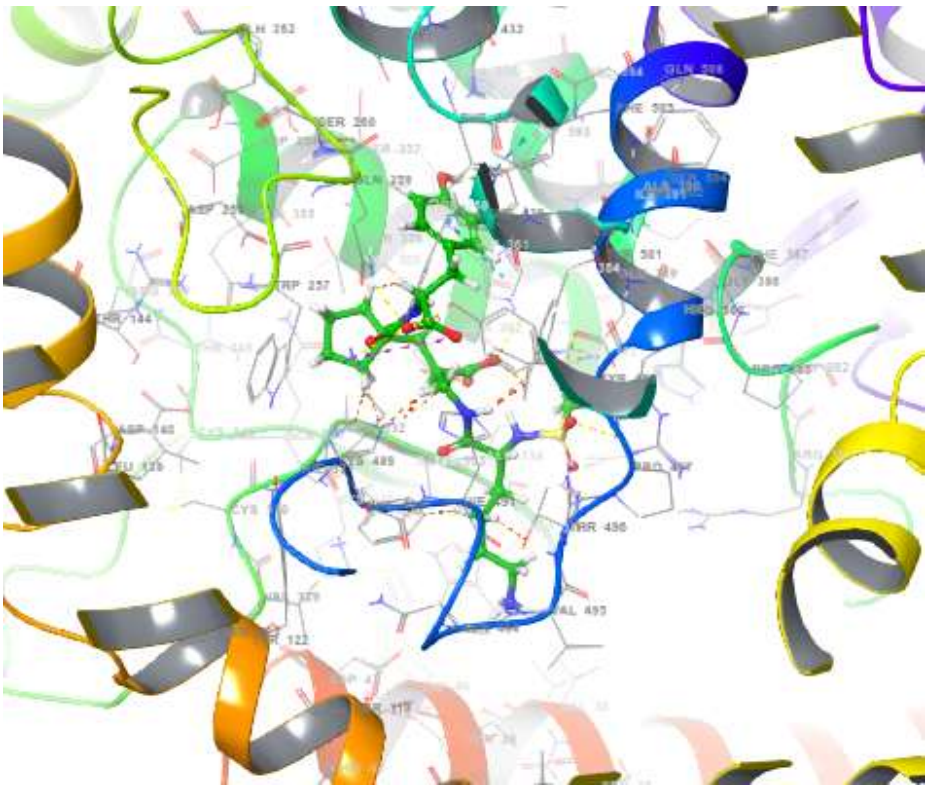

Figure 6: 3D Pose of standard drug Sampatrilatin sodium-potassium pump (PDB ID: 3KDP)

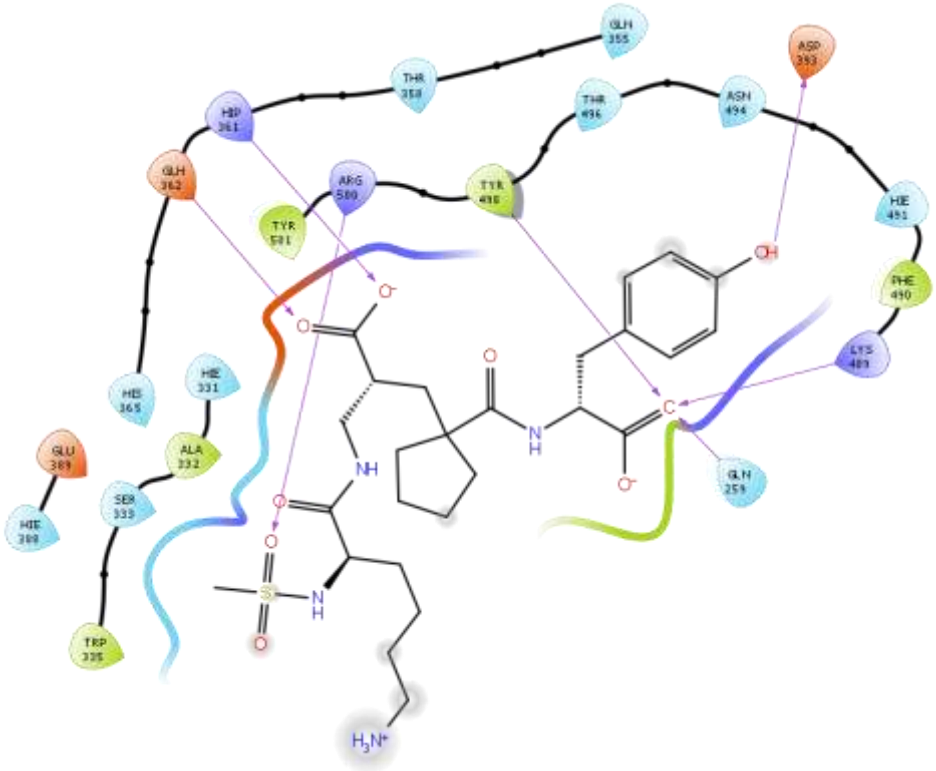

Figure 7: 2D Pose of standard drug Sampatrilatin sodium-potassium pump (PDB ID: 3KDP):the oxygen atom of compound forms Hydrogen bonds with ARG500, GLH362, HIP361, TYR498, GLN259, LYS489, ASP393.

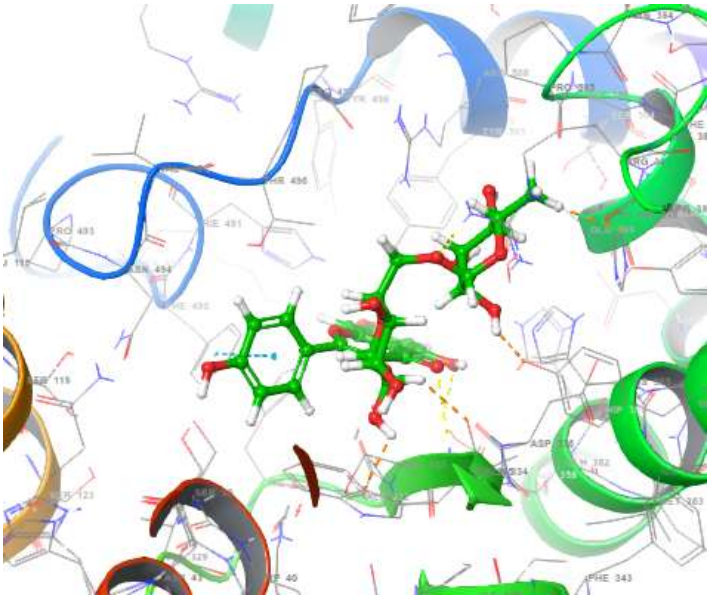

Figure 8: 3D Pose of Kaempferol-3-O-rutinoside in human Angiotensin-1 converting enzyme pocket (PDB ID:6F9V):

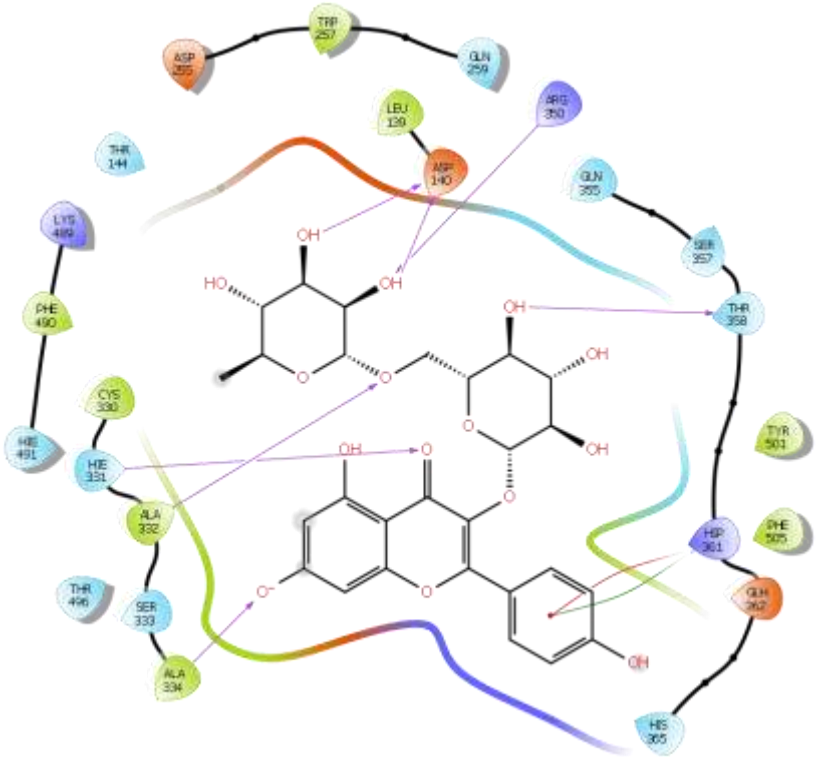

Figure 9: 2D Pose of Kaempferol-3-O-rutinoside in human Angiotensin-1 converting enzyme pocket (PDB ID:6F9V): the oxygen atom of compound forms Hydrogen bonds with ASP140, ARG350, THR358, ALA334, ALA332, HIE331 and cation interaction with HIP361.

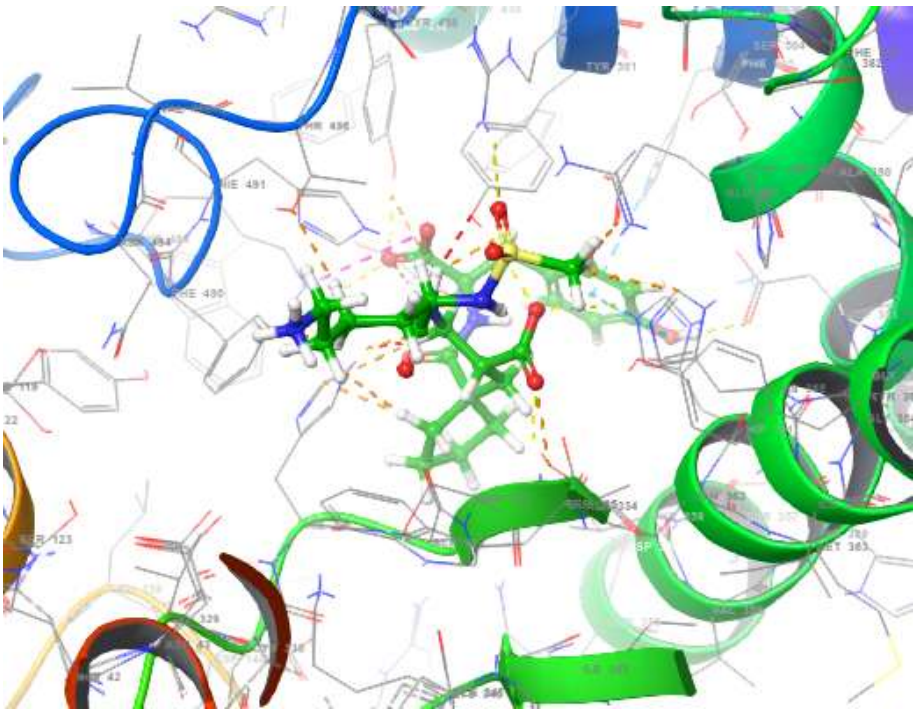

Figure 10: 3D Pose of standard drug Sampatrilatin human Angiotensin-1 converting enzyme pocket (PDB ID:6F9V):

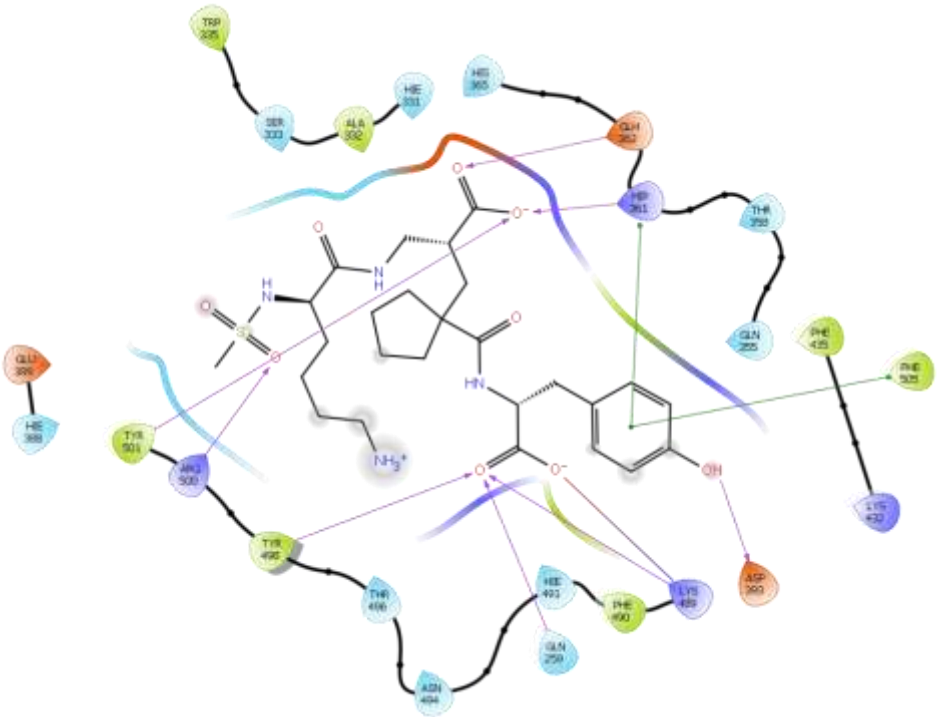

Figure 11: 2D Pose of standard drug Sampatrilatin human Angiotensin-1 converting enzyme pocket (PDB ID:6F9V): the oxygen atom of compound forms Hydrogen bonds with GLH362, HIP361, LYS489, GLN259, TYR498, TYR501, ARG500 and pi-pi stacking with PHE505 and HIP361.

3.5 Prediction of Physicochemical Properties

Hydrogen bond donors, hydrogen bond acceptors, hydrophilicity, molecular weight, permeability, binding to human serum albumin, and human oral absorption were predicted for ADMET using the Qikprop module of Schrodinger's software. Violations of Lipinski's rule of five and Jorgensen's rule of three were predicted and compared with recommended values **[Table 3]**.

Table 3: Pharmacokinetic parameters

QPP MDCK: apparent MDCK permeability (nm/sec) (<25 poor, >500 great). **QPlog Khsa:** prediction of binding to human serum albumin (-1.5 to 1.5). **QPlog BB:** predicted brain/blood partition coefficient (-3.0 to 1.2). **QPlogPo/w:** octanol/water partition coefficient (<5). **QPlogS:** Aqueous solubility (-6.5 to 0.5). **QPlogHERG:** IC_{50} value for blockage

of HERG K^+channels (<5). **QPPCaco:** apparent Caco-2 permeability (nm/sec) (<25 poor, >500 great). **PSA:** Polar surface area (7-200). **HOA:** Percent human oral absorption (>80% is high <25% is poor). **CNS:** Predicted central nervous system activity (-2.0 to + 2.0). **ROF:** Rule of fiveviolations (<1).

QikProp Parameters	QPlog Po/W	QP logS	QPlog HERG	CNS	QPlog BB
Hydroquinidine	2.374	-2.707	-4.115	1	-0.979
4-acetamidobutanoate	2.039	-3.768	-5.081	-2	-1.293
Kaempferol-3-O-rutinoside	-1.212	-3.349	-6.139	-2	-3.988
Khelloside	-2.227	-1.042	-2.739	-2	-1.56
Nicotinamide	3.268	-3.44	-2.455	2	0.848
2-(3,4-dihydroxyphenyl) ethyl (1S,4aR,7aR)-4a-hydroxy-7-methyl-5-oxo-1-[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl) oxan-2-yl] oxy-1,6,7,7a-tetrahydrocyclopenta[c]pyran-4-carboxylate	2.961	-2.688	-3.106	1	0.188
1-[4,5-dihydroxy-6-(hydroxymethyl)-3-[(E)-3-(4-hydroxyphenyl) prop-2-enoyl] oxyoxan-2-yl] oxy-6-hydroxy-7-methylidene-4a,5,6,7a-tetrahydro-1H-cyclopenta[c]pyran-4-carboxylic acid	2.108	-2.1	-3.509	1	0.214
QPP Caco	**QPP MDCK**	**PSA**	**QP log Khsa**	**RoF**	**HOA**
790.698	383.806	120.927	-0.51	0	3
178.594	76.861	96.383	0.095	0	3
8.129	2.725	235.989	-1.243	3	1
70.825	28.284	116.387	-0.878	0	2
9906.038	5899.293	0	0.302	0	3
4936.425	2778.733	19.143	0.122	0	3
5382.137	3050.883	20.831	-0.336	0	3

DISCUSSSION

In recent years, the utilization of herbal medicines for hypertension treatment has garnered increasing attention due to their rich phytochemical composition and diverse biological activities. Adansonia digitata L., commonly known as baobab, was selected for study, and its phytoconstituents were identified (refer to **Figure 1**). These secondary metabolites possess various biological and therapeutic properties. The extraction process involved successive liquid extraction of hydroalcoholic extracts using ethyl acetate. The resulting ethyl acetate fraction (EAF) was obtained by concentrating each fraction under reduced pressure until dryness. Subsequently, the EAF was evaluated for its ACE inhibitory activity, compared with the standard drug captopril, through biochemical assays.It is evident from the results that hydroalcoholic extract and Flavonoid fraction of *Adansonia digitata L* shows the promising percentage inhibition of angiotensin-converting enzyme with 70.01% and 75.54% of inhibition at 1000 mg/ml. Hence, the Flavonoid fraction has an activity against hypertension that is comparable to the ACE inhibition activity achieved with the standard drug captopril with 84.27% at 1 mg/ml.Further, among the seven bioactive compounds, Kaempferol-3-O-rutinoside was anticipated to exert the greatest influence, demonstrating interactions with 8 genes: SIRT1, CHKA, NOS3, PTGS1, SIRT3, GSTP1, IDH1, CYP3A4 with metabolic pathway. Notably, the process had the lowest false discovery rate and the greatest amount of gene sets (**refer to Table 1**). Moreover, in-silico molecular docking analyses, as depicted in **Table 2**, involved docking the selected compounds with the designated target protein to predict the most favorable conformational arrangement within the protein's active siteand The Kaempferol-3-O-rutinoside possesses -8.6Kcal/mol, Glide energy of -41.38 kcal/mol (**Figure 9**) and hydrogen bond interactions with GLU1013, ILE35 residues as compared to standard drug Sampatrilat possesses -7.6 Kcal/mol, Glide energy of –43.41 kcal/mol (**Figure 10**) and hydrogen bond interactions with ARG500, GLH362, HIP361, TYR498, GLN259, LYS489, ASP393 residues against the sodium-potassium pump **(PDB ID: 3KDP)** and in human Angiotensin-1 converting enzyme pocket **(PDB ID:6F9V)** the Kaempferol-3-O-rutinoside possesses -7.9Kcal/mol, Glide energy of -51.38 kcal/mol (**Figure 9**) and hydrogen bond interactions with ASP140, ARG350, THR358, ALA334, ALA332, HIE331 and cation interaction with HIP361 residues as compared to standard drug Sampatrilat possesses -7.2 Kcal/mol, Glide energy of –53.41 kcal/mol (**Figure 10**) and hydrogen bond interactions with GLH362, HIP361, LYS489, GLN259, TYR498, TYR501, ARG500 and pi-pi stacking with PHE505 and HIP361 residues, respectively.

CONCLUSION

In the present work, the role of plant *Adansonia digitata L* as adjuvants in the treatment of hypertension is analyzed through *in-vitro* Angiotensin-1 converting enzyme inhibition and *in-silico* gene expression, enrichment, and network analysis methods. The molecular docking studies projected the potential of Kaempferol-3-O-rutinoside as promising adjuvants in

the human Angiotensin-1 converting enzyme inhibition and further, the plasma protein binding model predicts strong receptor binding, good absorption, a low BBB, and low toxicity. The current results must be further verified using carefully constructed wet lab techniques, which is the future focus of the project, as they are entirely based on database searches and knowledge-based computer simulations. This offers compelling scientific evidence to explore further, focusing on identifying the lead compounds found in the plant. Additionally, it encourages the evaluation of its potential for antihypertensive effects using in vivo animal models. Subsequently, there's an opportunity to initiate human trials to assess its efficacy in treating hypertension.

List of abbreviations:
ACEN -Arjuna callus extract nanoparticles
LC-MS -Liquid chromatography-mass spectrometry
PVP K30 -Polyvinylpyrrolidone K30
RH -Relative humidity
PPL -Porcine pancreatic lipase
p-NPB -p-nitrophenyl butyrate
DPPH -1,1-Diphenyl-2, Picryl-Hydrazyl
TC -Total cholesterol
TG -Triglyceride
HDL -High-density lipoprotein
LDL- Low-density lipoprotein
VLDL -Very-low-density lipoprotein
FTIR -Fourier transform infrared

Declaration

Acknowledgements:
The authors gratefully thank to Dr. Babasaheb Ambedkar Central Nursery Kagal, India; Seema Biotech, Pvt Ltd, Warana nagar, India; Indian Institute of Technology, Bombay; Shivaji university, Kolhapur; Appasaheb Birnale College of Pharmacy, Sangli, Indian and Rajarambapu College of Pharmacy, Kasegaon, Sangli, Dr Shivajirao Kadam, College of Pharmacy, Digraj, India for materials and technical assistance.
Data statement: The data will be provided upon request.
Ethical Approval: Not Applicable
Conflict of Interests: The authors declare no conflict of interest.
Funding: No funds were received for said study.

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