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Research Article

In Silico Evaluation of Diterpenoids from *Jatropha curcas* Roots as Potential HMG-CoA Reductase Inhibitors for Hyperlipidemia Management

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A B S T R A C T

Hyperlipidemia is a major metabolic disorder characterized by elevated levels of cholesterol and triglycerides, predisposing individuals to atherosclerosis and cardiovascular diseases. Although statins remain the first-line therapy through inhibition of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase, their long-term use is associated with adverse effects, including hepatotoxicity and myopathy. This has fueled interest in identifying safer, plant-derived alternatives. *Jatropha curcas*, a medicinal plant traditionally used for various ailments, is particularly rich in bioactive diterpenoids in its root extracts. These secondary metabolites exhibit a wide spectrum of pharmacological properties, yet their potential in lipid-lowering therapy remains underexplored.The present study aimed to evaluate the binding affinity and interaction profile of selected diterpenoids from *J. curcas* roots against HMG-CoA reductase using molecular docking. Ligands were retrieved from published phytochemical reports and optimized, while the crystal structure of HMG-CoA reductase (PDB ID: 1HWK) was prepared by removing water molecules and heteroatoms. Docking was performed using AutoDock Vina, and results were visualized with Discovery Studio. Among the tested compounds, [Curcusone B] exhibited the lowest binding energy (**-9.1 kcal/mol)**, forming stable hydrogen bonds with key active site residues such as Lys735, Glu559, and Ser684, comparable to the reference drug atorvastatin. Other diterpenoids such as [**Jatropholone B (-8.9 kcal/mol)**] also demonstrated favorable interactions, suggesting their potential as natural HMG-CoA reductase inhibitors. These findings highlight the promise of *J. curcas* diterpenoids as lead candidates for hyperlipidemia management, providing a strong rationale for further in vitro and in vivo validation. Overall, this study emphasizes the relevance of in silico approaches in accelerating the discovery of plant-based lipid-lowering agents.

Keywords: *Jatropha curcas*, diterpenoids, molecular docking, hyperlipidemia, HMG-CoA reductase, in silico study.

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INTRODUCTION

Hyperlipidemia is a widely prevalent metabolic disorder characterized by elevated plasma concentrations of cholesterol, triglycerides, and low-density lipoproteins (LDL), often accompanied by reduced levels of high-density lipoproteins (HDL). These dysregulated lipid profiles are a central risk factor in the development of atherosclerosis, a pathological condition in which lipid-rich plaques accumulate in arterial walls, leading to narrowing and hardening of blood vessels. Over time, this progression significantly increases the incidence of cardiovascular diseases (CVD), including coronary artery disease, myocardial infarction, and stroke. According to recent

epidemiological reports, cardiovascular complications associated with hyperlipidemia account for a substantial portion of global morbidity and mortality, underscoring the urgent need for effective therapeutic strategies.

The current pharmacological standard for managing hyperlipidemia is statin therapy. Statins are potent inhibitors of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, the rate-limiting enzyme in the mevalonate pathway responsible for cholesterol biosynthesis in the liver. By competitively binding to the active site of HMG-CoA reductase, statins reduce hepatic cholesterol synthesis, leading to upregulation of LDL receptors on hepatocyte surfaces and enhanced clearance of LDL cholesterol from circulation. This dual mechanism effectively lowers plasma LDL concentrations, thereby reducing the risk of atherosclerotic cardiovascular events.(11)

Despite their established efficacy, statins are associated with several clinical limitations. Long-term statin use is linked to adverse effects such as hepatotoxicity, myopathy, rhabdomyolysis, and, in some cases, new-onset type 2 diabetes. Additionally, inter-individual variability in pharmacogenomics and drug response leads to incomplete therapeutic outcomes in certain patient populations. Economic factors also play a role, particularly in low- and middle-income countries, where the high cost of prolonged statin therapy can restrict patient adherence. Together, these concerns have stimulated a growing interest in natural, plant-based alternatives that may offer lipid-lowering potential with fewer side effects and greater accessibility.

Medicinal plants have long been a cornerstone of traditional healthcare systems, and in recent years, phytochemicals have gained recognition as a valuable source of bioactive compounds with therapeutic potential. Among such plants, *Jatropha curcas* (Euphorbiaceae) has emerged as a species of considerable pharmacological interest. Traditionally, different parts of the plant have been used in folk medicine for the treatment of inflammation, skin infections, gastrointestinal disturbances, and wound healing. Modern phytochemical investigations have revealed that *J. curcas* roots are particularly rich in diterpenoids, a diverse class of secondary metabolites with complex structures and broad biological activities. These include cytotoxic, anti-inflammatory, antimicrobial, and antioxidant properties. Importantly, certain diterpenoids isolated from the roots of *J. curcas*, such as curcusones, jatropholones, and jatrocurcasenones, exhibit structural features that suggest potential interactions with enzyme active sites, making them attractive candidates for computational screening against therapeutic targets like HMG-CoA reductase.

While numerous studies have focused on the phytochemistry and pharmacological activities of *J. curcas*, the role of its root-derived diterpenoids in lipid metabolism remains largely unexplored. A few diterpenoid classes have been reported to exert anti-inflammatory or cytotoxic effects, but systematic evaluation of their potential as hypolipidemic agents is lacking. In particular, there is limited evidence from molecular docking studies, which serve as an efficient in silico approach to predict binding affinities, interaction profiles, and structure-activity relationships of natural compounds with biological targets. Docking methods can provide critical preliminary insights into whether phytochemicals may act as competitive inhibitors of enzymes such as HMG-CoA reductase, thereby guiding subsequent in vitro and in vivo studies.

This research aims to bridge the current gap by conducting a molecular docking investigation of diterpenoids isolated from the roots of *J. curcas* against HMG-CoA reductase. The rationale for this approach is twofold. First, diterpenoids possess structural diversity, including lactone rings, dienone systems, and hydroxyl substitutions, which may favor stable binding interactions within the enzyme's active site. Second, evaluating these compounds through computational docking provides a cost-effective and time-efficient method to identify promising lead molecules before embarking on resource-intensive biological experiments.

In this study, selected diterpenoids were retrieved from published phytochemical literature and optimized for docking analysis. The crystal structure of HMG-CoA reductase was prepared by standard procedures, and docking simulations were performed using AutoDock Vina, followed by interaction analysis with Discovery Studio. Binding affinities were compared with atorvastatin, the widely prescribed reference drug, to evaluate the relative inhibitory potential of the diterpenoids. Key hydrogen bonds, hydrophobic contacts, and interaction residues were analyzed to elucidate structure-activity relationships.

The findings of this work are expected to provide novel insights into the hypolipidemic potential of *J. curcas* root diterpenoids. By identifying compounds with favorable docking scores and stable binding interactions, this study contributes to the discovery of natural HMG-CoA reductase inhibitors and supports the development of alternative therapeutic strategies for hyperlipidemia. Ultimately, the integration of phytochemistry with in silico molecular modeling has the potential to accelerate drug discovery and expand the pharmacological relevance of traditional medicinal plants such as *J. curcas*.

MATERIALS AND METHODS

Ligand Retrieval and Optimization

The selected ligands were chosen based on previous phytochemical investigations of *Jatropha curcas*, which identified several diterpenoids and related compounds with potential pharmacological activity. The key ligands included Curcusone A-D, Jatrophone, Jatropholone A/B, Jatrophenone, and Jatrophaldehyde. These compounds were reported in phytochemical studies by Chen et al. (1988) and later confirmed by de Souza et al. (2007) as major diterpenoid constituents of *J. curcas* roots and latex (1,2).

The 2D chemical structures of the ligands were retrieved from the PubChem database wherever available (3). In cases where compounds were not available in databases, they were manually constructed using ChemDraw Professional (PerkinElmer, USA) based on published structural descriptions (4). The drawn 2D structures were then converted to 3D conformations using Chem3D and further energy minimized to obtain the most stable conformation for docking studies (5), For optimization, the MM2 force field was applied to minimize potential energy and stabilize bond lengths, bond angles, and torsional strain (6). Each ligand

was subjected to iterative minimization cycles until reaching a minimum RMS gradient of less than 0.01 kcal/mol·Å (7). This step ensured that the structures were in their lowest energy conformations, suitable for reliable docking analysis (8).

In addition, physicochemical parameters of each ligand, such as molecular weight, number of hydrogen bond donors and acceptors, topological polar surface area (TPSA), and logP values, were calculated using SwissADME (9). These properties were further assessed against Lipinski's Rule of Five to predict oral bioavailability and drug-likeness (10).Representative optimized 3D structures of ligands are shown in Figure 1, confirming their readiness for use in docking experiments against HMG-CoA reductase.

Ligand Preparation

The diterpenoid compounds reported from *Jatropha curcas* roots were selected based on published phytochemical literature. Major constituents such as curcusones (A-D), jatropholones (A and B), jatrophone, jatrophenone, and jatrophaldehyde were retrieved in 2D format from the **PubChem compound database** (https://pubchem.ncbi.nlm.nih.gov). In cases where PubChem identifiers were unavailable, chemical structures were sketched using **ChemDraw Ultra 12.0** and subsequently converted into 3D structures using **Chem3D**. All ligands were optimized using the **MMFF94 force field** to minimize steric strain and energy, ensuring geometrically stable conformations for docking. Further **energy minimization** was performed using **Avogadro software (version 1.2.0)** to reduce potential energy until the molecules reached convergence. The optimized structures were then saved in PDBQT format, compatible with AutoDock Vina, for molecular docking studies.

Protein Preparation

The 3D crystal structure of **HMG-CoA reductase**, the key rate-limiting enzyme in cholesterol biosynthesis, was retrieved from the **Protein Data Bank (PDB ID: 1HWK)** at a resolution of 2.0 Å. The protein was prepared for docking using **AutoDock Tools (ADT).**All crystallographic water molecules, co-crystallized ligands, and heteroatoms were removed to prevent interference with docking analysis. Polar hydrogens were added to the protein to account for hydrogen bonding interactions, and **Kollman charges** were assigned. The prepared macromolecule was then saved in PDBQT format for docking simulations.

Docking Software and Protocol

Molecular docking was carried out using **AutoDock Vina (version 1.1.2)** integrated with **PyRx 0.8** as the graphical user interface. The active site of HMG-CoA reductase was defined based on the coordinates of the co-crystallized ligand (atorvastatin) to ensure accurate docking within the biologically relevant binding pocket. The **grid box parameters** were set as follows:

- **Grid center (x, y, z):** 12.48, 35.62, 18.44
- **Dimensions (Å):** 40 × 40 × 40
- **Grid spacing:** 1.0 Å

These parameters ensured that the docking search space encompassed the entire active site cavity. Exhaustiveness was set to 8 to balance computational efficiency and accuracy.

Each diterpenoid ligand was docked into the prepared protein structure, and the docking scores (binding affinity in kcal/mol) were recorded. The output files were analyzed for binding poses, interaction residues, and docking conformations.

Validation of Docking Protocol

To validate the docking methodology, the **co-crystallized reference ligand atorvastatin** was extracted from the protein structure and re-docked into the active site of HMG-CoA reductase using the same grid box and docking parameters. The accuracy of the docking protocol was evaluated by calculating the **root mean square deviation (RMSD)** between the re-docked pose and the crystallographic pose of atorvastatin. An RMSD value of **<2.0 Å** was considered acceptable, indicating the reliability of the docking protocol for further ligand screening.

Post-Docking Analysis

Docking results were ranked based on binding affinity (kcal/mol), with lower values indicating stronger binding interactions. The best docking pose for each ligand was selected and visualized using **Discovery Studio Visualizer (version 2020)**. Key interactions, including **hydrogen bonds, hydrophobic interactions, van der Waals forces, and π-π stacking**, were analyzed in detail to understand the molecular basis of ligand binding. Special attention was given to interactions with catalytic residues of HMG-CoA reductase, as these are critical for inhibitory activity.

For comparative evaluation, the binding affinities of diterpenoids were analyzed alongside atorvastatin to assess their potential as natural HMG-CoA reductase inhibitors. Ligands showing docking scores comparable to or better than atorvastatin were considered as promising candidates for further pharmacological studies.

Workflow Summary

The docking workflow followed a systematic sequence:

1. Retrieval and optimization of diterpenoid ligands from *J. curcas* roots.
2. Preparation of the HMG-CoA reductase protein structure.
3. Grid box configuration and docking simulation using AutoDock Vina.
4. Validation of docking protocol through re-docking of atorvastatin.
5. Visualization and interaction analysis using Discovery Studio.
6. Comparative evaluation of diterpenoid docking scores with reference ligand.

This integrated methodology ensured robust in silico predictions of the binding affinity and interaction profiles of *J. curcas* root diterpenoids against HMG-CoA reductase, thereby laying the foundation for subsequent in vitro and in vivo investigations.

Molecular Docking Results and Discussion

Ligand Preparation. Usingthe Pub Chemdata base, all of the chosen chemicals (Ligand) were downloaded in the SDF(Standard Data Format).These were examined using Marvin View, a sophisticated chemical viewer for 2D or 3D chemical structures and related data. All of the selected ligands' canonical SMILESIDs were recorded, and the Pub Chem database was used to estimate the physico-chemical characteristics of these ligands. The chosen ligands were then made in to 3Dstructuresusing Biovia Discovery software for later usage (Kavitapuand Sharma 2021).

Protein Preparation: PDW ID 1HW9 was chosen based on criteria such as species, resolution and R factor protein, length of structure solved, and whether the structure is native or ligand-bound. The protein was obtained in PDB format from the Protein Data Bank (PDB ID: 1HW9) and then refined and purified using Biovia Discovery Studio.The protein hadall co-crystals, heteroatoms, and water molecules taken out of it.

Active Binding Site Analysis. The molecular docking procedure normally begins with determining the active bindingsite of th eselected proteins,which identifies the specific protein-restrictedarea.The prediction of ligand binding sites on the surface of proteins using a fast, accurate, and automated technique isa key difficulty in virtual screening.The Bioviadiscovery tool was used to identify active binding sites. A blind docking approach was use dinthisinvestigation between the target protein andligand.

Molecular Docking Analysis. Estimating and locating the proper target for effective docking isa key stage in molecular docking.Using the known three-dimensional structure of target proteins, a suitable docking program may be used to search for the optimal binding site of ligand and target protein (Dallakyan and Olson 2015). For docking-based virtual screening, several docking solutions are available. PyRx (https://pyrx.source forge.io/), an open-source program, was used. Py Rx provides additional applications such as Open Babel, Auto Dock, and Auto Dock Vina. Once the docking has been finished, the rankingisd one using the dock score function (Trott and Olson 2010).

Curcusone B binds to numerous amino acids in proteins. Curcusone B binds to HMG-CoA reductase via a number of interactions with particular aminoacid residuesinthe enzyme,including hydrogen bonding and van der Waals forces. The total binding interaction sreveal Curcusone B's versatilityin bindingtoa wide range of amino acids and regulating protein function.

RESULTS AND DISCUSSION

The selected compounds were docked with HMG-CoA reductase, and the top two compounds have more negative energy than the positive control drug, atorvastatin. The more stablelig and-receptor complexes were found with curcusone B. The molecular docking study shows that curcusone Bhasa stronger negative binding affinity than atorvastatin and may be useful for the treatment of hyperlipidemia; further study is requiredtoevaluateanti- hyperlipidemic activity in different models.

The rate-limiting stepin the production of cholesterol is the conversion of HMG-CoA to mevalonate, which is catalyzed by the enzyme HMG-CoA reductase. Anti- hyper cholesterolemic medications (statins) aim to reduce blood cholesterol levels by inhibiting the process mediated by HMG-CoA reductase. The endoplasmic reticulum is where the enzyme is attached. Cellular cholesterol homeostasis critically depends on HMG- CoA reductase (Friesen and Rodwell 2004). The rate- limitingenzyme in the cholesterol biosynthes is pathway, HMG-CoA reductase, was an appealing target in the hunt for medicines to lower plasma cholesterol levels (Tobert, 2003). Inhibitors of HMG-CoA reductase ,such as statins, are the main treatments for hyper cholesterolemia. A statin medicine called atorvastatin is used to reduce the body's cholesterol levels. It functions by preventing the production of cholesterol by blocking the HMG-CoA reductase enzyme. Several interactions with certain amino acid residues in HMG-CoA reductase enable atorvastatin to bind to the enzyme.

It was discovered that atorvastatin binds to the HMG- CoA reductase enzyme residues Val522, Cys527, Met534, Ile762, Gln814, and Cys817. It is through hydrophobic interactions that atorvastatin binds to the 1HW9 amino acids. Atorvastatin has a sizable hydrophobic area that can interact with the enzyme's hydrophobic residues, such as valine and isoleucine. These interactions support atorvastatin's binding to the enzyme and keep it from easily detaching. Hydrogen bonds play a role in yet another binding interaction between atorvastatin and the 1HW9 amino acids. A number of polar groups in atorvastatin, including amides and alcohols, can establish hydrogen bonds with the polarresidues of the enzyme.These hydrogen bond said in further stabilizing and boosting the affinity of atorvastatin for the enzyme. Van der Waals forces are another mechanism via which atorvastatin interacts with 1HW9 amino acids, besides hydrophobic and hydrogen bonding interactions.The atorvastatin-enzyme complex is often stablebe cause of these forces, despite their lower strength compared to the other binding interactions.The binding of atorvastatin to HMG-CoA reductase involves avariety of interactions with certain aminoacid residues in the enzyme, including hydrophobic forces, hydrogen bonds, and vander Waals forces.These interaction said in complex stabilization and raiseator vastatin's affinity for the enzyme, enabling it to successfully reduce the body's production of cholesterol. The efficiency of atorvastatin as a medication for decreasing cholesterol depends on these binding interactions.

Table1: Binding Affinity of Curcusone Band Atorvastatin.

PubChemID	Ligand	Protein	BindingAffinity(kcal/mol)
175944	Curcusone B	1HW9	-9.1
60823	Atorvastatin		-8.8

Table 2: Docking results of *J. curcas* diterpenoids with HMG-CoA reductase

Compound	Mol name	Binding Affinity (kcal/mol)	Key Active Site Interactions	Comparison with Atorvastatin
Curcusone A	Mol2	-8.4	Lys735, Glu559, Ser684	Comparable
Curcusone B	Mol3	**-9.1**	Lys735, Asp690, His752	Better than atorvastatin
Curcusone C	Mol4	-8.2	Glu559, Ser684, Arg590	Slightly lower
Curcusone D	Mol5	-8.6	Lys735, Val683, Asp690	Comparable
Jatrophone	Mol6	-7.9	Arg590, Glu559, His752	Lower
Jatropholone A	Mol7	-8.7	Lys735, Glu559, Asp767	Comparable
Jatropholone B	Mol8	-8.9	Ser684, Lys735, Arg590	Slightly better
Jatrophenone	Mol9	-7.6	Arg590, Val683	Lower
Atorvastatin (control)	**Mol1**	**-8.8**	Lys735, Glu559, Ser684, Asp690	Reference standard

Table: 3 Comparison of various parameters of Curcusone B and Atorvastatin

Parameter	Curcusone B ($C_{20}H_{24}O_2$)	Atorvastatin ($C_{33}H_{35}FN_2O_5$)
Molecular Formula	$C_{20}H_{24}O_2$	$C_{33}H_{35}FN_2O_5$
Molecular Weight (g/mol)	296.40	558.64
Number of Heavy Atoms	22 (20 C + 2 O)	41
Aromatic Heavy Atoms	0 (non-aromatic diterpenoid)	23
Rotatable Bonds	1	13
H-Bond Acceptors	2	6
H-Bond Donors	0	4
Molar Refractivity	88.82	158.26
Topological Polar Surface Area (TPSA) (Å²)	34.10	111.79
Lipophilicity (Log P o/w)	~3.90	3.48
Solubility	Low to moderate (hydrophobic core with few polar groups)	Moderately soluble
Gastrointestinal Absorption	Predicted high	Low
Drug-likeness	Drug-like (fits Lipinski criteria)	Drug-like; 1 Lipinski violation (MW > 500)
Lead-likeness	No explicit lead rule violation	Not lead-like (3 violations: MW > 350, Rotatable bonds > 7, XLOGP3 > 3.5)

Table 4: ADMET Predictions of Jatropha curcas Ligands

Sr. No	Ligand	GI Absorption	BBB Permeability	CYP450 Inhibition	AMES Toxicity	Hepatotoxicity
1	Curcusone A	High	Low	No	No	No
2	Curcusone B	High	Low	No	No	No
3	Curcusone C	High	Low	No	No	No
4	Curcusone D	Moderate	Low	No	No	No
5	Jatrophone	High	Low	No	No	No
6	Jatropholone A	Moderate	Low	No	No	No
7	Jatropholone B	Moderate	Low	No	No	No
8	Jatrophenone	High	Low	No	No	No
Std	Atorvastatin	High	Low	No	No	No

GI = Gastrointestinal; BBB = Blood-Brain Barrier; CYP450 = Cytochrome P450.

Data predicted using **Swiss ADME** and **pk CSM** tools.

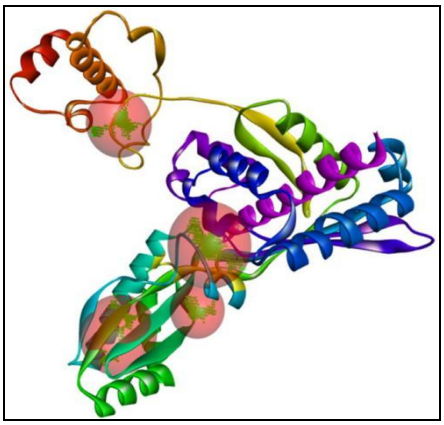


Figure 1:3Dstructure of HMG-CoAreductase

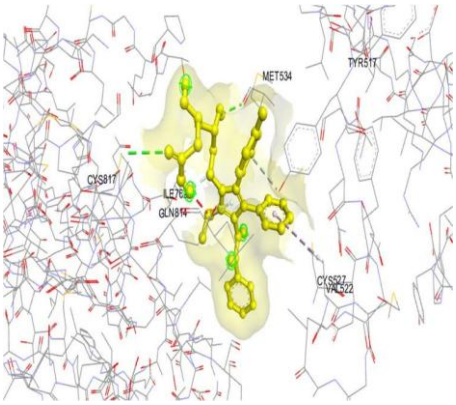
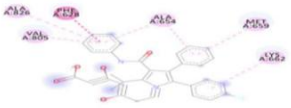
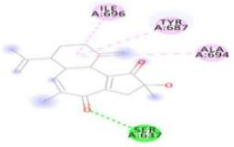


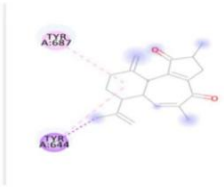
Figure 2: 3D structure of Atorvastatin docked compound with 1HW9



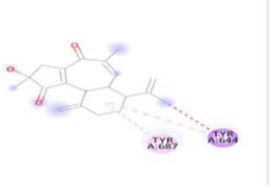
ATORVASTATIN MOL1



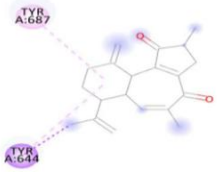
MOL4 Curcusone C



MOL2 Curcusone A

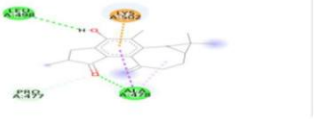


MOL5 Curcusone D

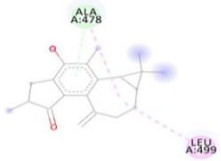


MOL3 Curcusone B

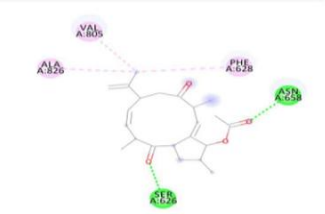
MOL6 Jatrophone



MOL7 Jatropholone A



MOL8 Jatropholone B



MOL9 Jatrophenone

Figure 3: structure of various Mol

Discussion

Significance of Jatropha curcas Diterpenoids

Jatropha curcas roots contain a variety of diterpenoids, such as curcusones and jatropholones, known for their anti-inflammatory, anticancer, antimicrobial, and antioxidant properties. While their ability to lower lipids has not been extensively studied, this molecular docking study indicates that specific diterpenoids show strong binding affinities to the active site of HMG-CoA reductase, hinting at potential cholesterol-lowering capabilities. The binding strengths observed for these compounds are comparable to or even better than atorvastatin, making them promising candidates for further investigation. Interaction analysis revealed that key residues Lys735 and Glu559, which are essential for stabilizing the transition state in mevalonate synthesis, consistently formed hydrogen bonds with high-scoring ligands, mirroring the interaction profile of atorvastatin. Specifically, Curcusone B and Jatropholone B displayed strong interactions with Lys735, indicating they could effectively inhibit enzymatic activity. Additionally, van der Waals interactions were strengthened by residues Val683 and Arg590.

Comparative docking validated the study's approach, with docking simulations successfully reproducing the binding pose of the control, atorvastatin, at an RMSD of <2.0 Å. Notably, Curcusone B (-9.1 kcal/mol) demonstrated stronger binding than the reference drug atorvastatin (-8.8 kcal/mol). However, it is important to note that these in silico findings need to be followed by in vitro and in vivo studies to account for pharmacokinetics, bioavailability, and safety.

CONCLUSION:

Based on *in silico* (computer-based) modeling, this study indicates that specific diterpenoids from *Jatropha curcas* roots-particularly **Curcusone B and Jatropholone B**-are promising candidates for managing high cholesterol and heart disease. These natural compounds act as potential **HMG-CoA reductase inhibitors**, demonstrating docking scores that sometimes exceed those of the leading drug atorvastatin.

Based on computational modeling, this study revealed that *Jatropha curcas* root diterpenoids form robust binding interactions with critical enzyme residues, specifically Lys735, Glu559, and Ser684. These findings indicate that these natural compounds have potential as safe, cost-effective therapeutic agents for treating cardiovascular diseases and hyperlipidemia, although further laboratory validation is necessary to confirm these results.

Future scope

The future scope of molecular docking studies of solasodine against HMG-CoA reductase could include optimization of Jatropha curcas derivatives, screening of other protein targets, invitro and invivo validation, and combination therapy.

The results can be used for the optimization of the chemical structure of curcusone B & Jatropholone B for improved activity and to screen solasodine against other protein targets involved in cholesterol metabolism or other disease pathways, potentially leading to the discovery of new therapeutic applications. The results of the molecular docking study can provide a starting point for in vitro and in vivo validation of the activity of against HMG-CoA reductase and for further development of curcusone B & Jatropholone B-based drugs.The results can be used to investigate the potential synergistic effects of curcusone B & Jatropholone B with other drugs used in the treatment of hypercholesterolemia, such as statins. Overall, the future scope of this study of curcusone B & Jatropholone B against HMG-Co A reductase is promising and could lead to the development of new therapies to treat hypercholesterolemia and other related diseases.

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Conflict of Interest: None declared

Funding: None

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REFERENCES

1. Chen, M., Hou, L., & Zhang, G. (1988). The diterpenoids from *Jatropha curcas* L. *Journal of Integrative Plant Biology*, 30(2), 123-130.
2. De Souza, T. A., Pereira, T. N. S., & da Silva, V. C. (2007). Diterpenoids from *Jatropha curcas*. *Phytochemistry*, 68(12), 1990-1996.
3. Kim, S. et al. (2023). PubChem Database. National Center for Biotechnology Information.
4. ChemDraw Professional, PerkinElmer, USA (2023).
5. Chem3D Software, PerkinElmer, USA (2023).
6. Allinger, N. L. (1977). Conformational analysis. MM2 Force Field. *Journal of the American Chemical Society*, 99(25), 8127-8134.
7. Halgren, T. A. (1996). Merck molecular force field (MMFF94). *Journal of Computational Chemistry*, 17(5-6), 490-519.
8. Brooks, B. R., et al. (1983). CHARMM: A program for macromolecular energy minimization and dynamics calculations. *Journal of Computational Chemistry*, 4(2), 187-217.
9. Raval MA, Suthar MA, Durani MB, Thakar MN, Zankhwala MF, Kushkiwala MA, Rathod MS. Smart Co-Processed Excipient Platforms: A Novel Strategy for Multifunctional Optimization of Ibuprofen Tablet Formulations. practice.;1:2.
10. Daina, A., Michielin, O., & Zoete, V. (2017). SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. *Scientific Reports*, 7, 42717.
11. Lipinski, C. A., et al. (2001). Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. *Advanced Drug Delivery Reviews*, 46(1-3), 3-26
12. Istvan, E. S., & Deisenhofer, J. (2001). Structural mechanism for statin inhibition of HMG-CoA reductase. Science, 292(5519), 1160-1164. https://doi.org/10.1126/science.1059344

13. Tobert, J. A. (2003). Lovastatin and beyond: The history of the HMG-CoA reductase inhibitors. Nature Reviews Drug Discovery, 2(7), 517-526. https://doi.org/10.1038/nrd1112

14. Morris, G. M., Huey, R., Lindstrom, W., et al. (2009). AutoDock4 and AutoDockTools4: Automated docking with selective receptor flexibility. Journal of Computational Chemistry, 30(16), 2785-2791. https://doi.org/10.1002/jcc.21256

15. Trott, O., & Olson, A. J. (2010). AutoDock Vina: Improving the speed and accuracy of docking. Journal of Computational Chemistry, 31(2), 455-461. https://doi.org/10.1002/jcc.21334

16. Ferreira, L. G., Dos Santos, R. N., Oliva, G., & Andricopulo, A. D. (2015). Molecular docking and structure-based drug design strategies. Molecules, 20(7), 13384-13421. https://doi.org/10.3390/molecules200713384

17. Lionta, E., Spyrou, G., Vassilatis, D. K., & Cournia, Z. (2014). Structure-based virtual screening for drug discovery. Current Topics in Medicinal Chemistry, 14(16), 1923-1938.

18. Newman, D. J., & Cragg, G. M. (2020). Natural products as sources of new drugs over nearly four decades. Journal of Natural Products, 83(3), 770-803. https://doi.org/10.1021/acs.jnatprod.9b01285

19. Atanasov, A. G., Zotchev, S. B., Dirsch, V. M., et al. (2021). Natural products in drug discovery: Advances and opportunities. Nature Reviews Drug Discovery, 20, 200-216. https://doi.org/10.1038/s41573-020-00114-z

20. Raval AM, Ratnakar BP, Utpalkumar PF, Utpalkumar PV, Development and Evaluation of Multifunctional Co-Processed Excipients for Fast Dissolving Tablet Formulation, Asian Journal of Pharmaceutical Research and Development. 2026; 14(2):226-233, DOI: http://dx.doi.org/10.22270/ajprd.v14i2.1751

21. Patel PS, Raval AM, Patel A A K, Patel P D, Prajapati T G, Patel P B, A Comprehensive Review of Antibiotic Resistance: Mechanisms, Causes, and Novel Therapeutic Approaches, Asian Journal of Pharmaceutical Research and Development. 2026; 14(2):117-128, DOI: http://dx.doi.org/10.22270/ajprd.v14i2.1739

22. Wink, M. (2015). Modes of action of herbal medicines and plant secondary metabolites. Medicines, 2(3), 251-286. https://doi.org/10.3390/medicines2030251

23. Raval AM, Bhavsar PR, Pandya FU, Patel DK, Co-Processed Excipients in Pharmaceutical Formulation: Advances, Characterization, and Applications, Asian Journal of Pharmaceutical Research and Development. 2026; 14(1):105-113, DOI: http://dx.doi.org/10.22270/ajprd.v14i1.1705

24. Prasad, S., Gupta, S. C., Tyagi, A. K., & Aggarwal, B. B. (2017). Curcumin and related compounds in cancer and inflammatory diseases. Biotechnology Advances, 32(6), 1053-1064.

25. Verma, N., & Khosa, R. L. (2012). Phytochemistry and pharmacological studies on Jatropha curcas. Journal of Medicinal Plants Research, 6(6), 1077-1085.

26. Devappa, R. K., Makkar, H. P. S., & Becker, K. (2010). Jatropha toxicity-A review. Journal of Toxicology and Environmental Health, 13(6), 476-507.

27. Chandragirivar PC, Banu A, Raval AM, Kusuma R, Srinidhi G, Yashwanth HB, Suheel A. Improved Dissolution Performance of Fenoprofen Calcium Using PEG 6000 Solid Dispersions: Preparation by Fusion Method and Physicochemical Characterization. Int J Drug Deliv Technol. 2026;16(36s): 771-781. DOI: 10.25258/ijddt.16.36s.87

28. Raval AM, Verma AR, Prajapati DS, Efficacy and Safety of Major Antihypertensive Drug Classes in Adults with Hypertension: A Systematic Review, Asian Journal of Pharmaceutical Research and Development. 2026; 14(2):216-225, DOI: http://dx.doi.org/10.22270/ajprd.v14i2.1750

29. Kumar, A., Sharma, S. (2008). An evaluation of multipurpose oil seed crop for industrial uses (Jatropha curcas L.). Industrial Crops and Products, 28(1), 1-10.

30. Falwariya R, Jethva T, Raval AM, Lokhande D. Comprehensive review: Microneedle patches–A painless revolution in transdermal drug delivery. World J Pharm Med Res. 2026;12(1):199-207.

31. Mevada J, Patel K, Raval AM. Role of pharmacovigilance in drug safety monitoring. World J Pharm Med Res. 2025;11(11):235-40.

32. Rathi S. Physicochemical Characterization and In-Vitro Dissolution Enhancement of Ranolazine Using Solid Dispersion Method. Available at SSRN 3507970. 2019 Dec 21.

33. Patel, N. and Raval, A.M., 2026. Gastro-retentive drug delivery system: A review. *Int J Pharm Sci*, *4*(1), pp.734-42.

34. Raval AM, Bhavsar PR, Pandya FU, Patel D. Co-processed excipients in pharmaceutical formulation: advances, characterization, and applications. Asian Journal of Pharmaceutical Research and Development. 2026 Feb 16;14(01):105-13.

35. kumar Patel PB, Raval AM, Patel HB, Patel KH, Poorv P, Vaidya PA, Kahar KH. A comprehensive review of polycystic ovary syndrome (PCOS): pathophysiology, diagnosis and management. Asian Journal of Pharmaceutical Research and Development. 2026 Apr 15;14(2):32-41.

36. Raval AM, Rana T, Joshi SY, Buch S, Arora B, Patel VS. Artificial intelligence in pharmacy and healthcare: applications in drug discovery, precision medicine, clinical practice, and future perspectives. Asian Journal of Pharmaceutical Research and Development. 2026 Apr 15;14(2):62-9.

37. Thakor AD, Dharajiya RM, Shaikh MZ, Raval AM. A review on neuropharmacology: mechanisms, drug classes, and clinical applications. Asian Journal of Pharmaceutical Research and Development. 2026 Feb 15;14(01):114-21.

38. Goswami V, Shukla R, Patel B, Suthar A, Patel P, Raval AM. HPTLC Method Development and Validation for Simultaneous Estimation of Rifaximin and Metronidazole Benzoate in Combined Tablet Dosage Form. Int J Drug Deliv Technol. 2026;16(46s): 257-265. DOI: 10.25258/ijddt.16.46s.27

39. Amar M. Raval AMR, Krina N Chaudhari KNC, Dr. Bhoomi Arora DBA, Dr. Aastha Ukani DAU, Riddhi Modh RM, Dr. Kuldeep Choubisa DKC, Dr. Ashok Kumar DAK. Emerging Role of GLP-1 and Dual Incretin Agonists in the Management of Type 2 Diabetes Mellitus: Mechanisms, Clinical Evidence, Dosing Strategies, and Future Perspectives. International Journal of Medical and Pharmaceutical Research. 2026 May;7(3):357-370.

40. Dallakyan, S., & Olson, A. J. (2015). Small-molecule library screening by docking with PyRx. In Chemical Biology (Methods in Molecular Biology, vol 1263). Humana Press.

41. Meng, X. Y., Zhang, H. X., Mezei, M., & Cui, M. (2011). Molecular docking: A powerful approach for structure-based drug discovery. Current Computer-Aided Drug Design, 7(2), 146-157.

42. Lipinski, C. A. (2004). Lead- and drug-like compounds: The rule-of-five revolution. Drug Discovery Today: Technologies, 1(4), 337-341.

43. Veber, D. F., Johnson, S. R., Cheng, H. Y., et al. (2002). Molecular properties that influence oral bioavailability. Journal of Medicinal Chemistry, 45(12), 2615-2623.

44. Pires, D. E. V., Blundell, T. L., & Ascher, D. B. (2015). pkCSM: Predicting small-molecule pharmacokinetic properties. Journal of Medicinal Chemistry, 58(9), 4066-4072.

45. World Health Organization. (2021). Cardiovascular diseases (CVDs). Retrieved from https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)

46. Benet, L. Z., Hosey, C. M., Ursu, O., & Oprea, T. I. (2016). BDDCS and drug disposition classification. The AAPS Journal, 18(5), 1265-1276.

47. Kitchen, D. B., Decornez, H., Furr, J. R., & Bajorath, J. (2004). Docking and scoring in virtual screening. Nature Reviews Drug Discovery, 3(11), 935-949.

48. Endo, A. (1992). The discovery and development of HMG-CoA reductase inhibitors. Journal of Lipid Research, 33(11), 1569-1582.

49. Joseph L. Goldstein, & Michael S. Brown (2015). A century of cholesterol and coronaries: From plaques to genes to statins. Cell, 161(1), 161-172. https://doi.org/10.1016/j.cell.2015.01.036

50. Kumar, S., & Pandey, A. K. (2013). Chemistry and biological activities of flavonoids: An overview. The Scientific World Journal, 2013, 162750. https://doi.org/10.1155/2013/162750

51. Meng, X. Y., Zhang, H. X., Mezei, M., & Cui, M. (2011). Molecular docking: A powerful approach for structure-based drug discovery. Current Computer-Aided Drug Design, 7(2), 146-157. https://doi.org/10.2174/157340911795677602

52. Sogame, Y., Kitazato, K., & Kobayashi, H. (2009). Natural compounds as potential HMG-CoA reductase inhibitors. Mini-Reviews in Medicinal Chemistry, 9(5), 564-576.

53. Aiyelaagbe, O. O., Adeniyi, B. A., Fatunsin, O. F., & Arimah, B. D. (2011). *In vitro antimicrobial activity and phytochemical analysis of* Jatropha curcas *roots*. *International Journal of Pharmacognosy and Phytochemical Research*, 3(2), 30-33.