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In Silico Study of Bioactive Compounds from Koro Benguk (*Mucuna pruriens* (L.) DC.) as Potential Modulators of CYP7A1 for Hypercholesterolemia Therapy

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Abstract: Hypercholesterolemia is a major risk factor for cardiovascular diseases and remains a significant global health concern. Cholesterol 7α-hydroxylase (CYP7A1), the rate-limiting enzyme in the classical bile acid synthesis pathway, plays a crucial role in hepatic cholesterol catabolism and represents a promising therapeutic target for cholesterol regulation. Natural product-derived compounds have attracted increasing attention as potential antihypercholesterolemic agents due to their structural diversity and biological activities. However, studies evaluating phytochemicals from Mucuna pruriens as CYP7A1 modulators remain limited, particularly those integrating molecular docking with pharmacokinetic prediction. Therefore, this study aimed to evaluate the potential of bioactive compounds from Mucuna pruriens as modulators of CYP7A1 using an in silico approach. Twenty-eight phytochemical compounds identified through GC-MS profiling were screened using Lipinski's Rule of Five. Selected compounds were further analyzed by molecular docking against the CYP7A1 protein (PDB ID: 3DAX), followed by ADMET prediction. Docking protocol validation through redocking of the native ligand showed good conformational agreement at the active site (RMSD < 2 Å), confirming the reliability of the docking parameters. Binding affinity and RMSD were used to evaluate ligand–protein interaction stability. Sterculic acid exhibited the strongest binding affinity with a docking score of −6.6.1 kcal/mol and RMSD of 1.51 Å, slightly stronger than the reference ligand 7-ketocholesterol (−7.335 kcal/mol). Interaction analysis revealed hydrogen bonding with key residues, including Asn126 and Lys98, as well as hydrophobic interactions within the active pocket. Other fatty acid derivatives, including octadecanoic acid and heptadecanoic acid, also showed competitive binding energies. ADMET prediction indicated high intestinal absorption (HIA > 90%), no CYP3A4 inhibition, and low predicted toxicity. These results highlight sterculic acid as a promising CYP7A1 modulator and support the potential of Mucuna pruriens phytochemicals for further molecular dynamics studies and experimental validation in the development of hypercholesterolemia therapy.

Keywords: CYP7A1; Hypercholesterolemia; Molecular Docking; *Mucuna pruriens*.

Introduction

Hypercholesterolemia is one of the most prevalent health disorders worldwide. This condition is characterized by elevated blood cholesterol levels exceeding the normal threshold (≥ 240 mg/dL) [1]. Increased cholesterol levels are strongly associated with a higher risk of coronary heart disease and may accelerate mortality risk by up to threefold.

Hypercholesterolemia is a major risk factor for cardiovascular disease and contributes significantly to global morbidity and mortality [2]. Numerous global studies have further confirmed that among modifiable risk factors, abnormal serum cholesterol levels represent one of the most significant contributors to the incidence of cardiovascular diseases, especially ischemic heart disease [3]. The management of this condition generally involves a combination of lifestyle modifications and pharmacological therapy to reduce low-density lipoprotein cholesterol (LDL-C) levels and achieve clinical targets. Non-pharmacological interventions include adherence to a diet low in saturated fat and cholesterol, increased physical activity, smoking cessation, and body weight control [4]. These approaches are recommended as first-line strategies, as they have been shown to effectively improve lipid profiles and reduce overall cardiovascular risk [5].

When lifestyle modifications fail to achieve the desired LDL-C targets, pharmacological therapy becomes the primary indication. Statins are recommended as first-line agents due to their ability to inhibit 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, thereby reducing hepatic cholesterol biosynthesis and significantly lowering the risk of major cardiovascular events [6]. Although effective, long-term use of these agents has been reported to be associated with adverse effects, including elevated liver enzymes, myopathy, gastrointestinal disturbances, and, in certain populations, an increased risk of type 2 diabetes mellitus [7]. These limitations have encouraged the exploration of alternative therapeutic strategies that offer comparable efficacy with improved safety profiles.

In recent years, natural product–based approaches have gained considerable attention as promising sources of novel antihyperlipidemic agents. Various phytochemical compounds have been reported to exhibit antioxidant and anti-inflammatory activities, as well as lipid metabolism–modulating effects that may contribute to cholesterol regulation [8]. One plant that has demonstrated such potential is *Mucuna pruriens* (L.) DC., locally known as velvet bean or koro benguk. This plant is reported to contain a diverse range of secondary metabolites, including flavonoids, alkaloids, terpenoids, and phenolic compounds

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that function as bioactive agents [9]. In addition to its antioxidant activity, several studies have reported that extracts and bioactive compounds derived from Mucuna pruriens exhibit potential lipid-lowering effects. These include reductions in total cholesterol, triglycerides, and low-density lipoprotein (LDL) levels in hyperlipidemia models [10]. These findings suggest that the bioactive constituents of this plant may play an important role in modulating lipid metabolism.

At the molecular level, cholesterol 7α-hydroxylase (CYP7A1) plays a central role in the hepatic conversion of cholesterol into bile acids [11]. This enzyme catalyzes the rate-limiting step in the classical bile acid biosynthesis pathway, thereby directly contributing to systemic cholesterol homeostasis [12]. Modulation of CYP7A1 activity may enhance hepatic cholesterol catabolism and reduce circulating cholesterol levels, making it a promising therapeutic target for the management of hypercholesterolemia [13].

However, information regarding the molecular interactions between bioactive compounds from Mucuna pruriens and the CYP7A1 target remains limited, particularly studies employing modern computational approaches such as molecular docking and ADMET prediction, which are widely utilized in natural product-based drug discovery. These computational approaches enable a more comprehensive evaluation of ligand protein interactions, including the assessment of binding affinity, stability of the ligand–protein complex, and the prediction of pharmacokinetic and toxicity profiles of candidate compounds. Therefore, integrating molecular docking and ADMET prediction is an important strategy for early-stage identification of potential drug candidates prior to experimental validation.

Based on this background, the present study aims to evaluate the potential of bioactive compounds derived from *Mucuna pruriens* as candidate modulators of CYP7A1 using an in silico approach. Computational analyses were conducted to assess binding affinity, ligand–protein complex stability, and interaction patterns with key active-site residues. The findings of this study are expected to provide preliminary scientific insights into the development of natural product-based therapeutic candidates for the safer and more effective management of hypercholesterolemia.

Research Methods

Tools

The computational analysis was performed using a computer equipped with an Intel® Core™ i5-1035G1 processor @ 1.00 GHz (1.20 GHz) and 12 GB of RAM. The software utilized included Molecular Operating Environment (MOE), the Protein Data Bank (PDB), and PubChem.

Ligand and Protein Preparation

Twenty-eight major bioactive constituents of Koro Benguk (*Mucuna pruriens* (L.) DC.) were compiled from published studies reporting phytochemical profiling using gas chromatography–mass spectrometry (GC-MS) [14]. The selected compounds represent the major phytochemical constituents identified in the GC-MS chromatograms, based on their relative abundance and the reliability of their identification reported in the literature. These compounds were chosen as representative bioactive molecules potentially responsible for the biological activities of Mucuna pruriens and were subsequently used as ligands for further computational analysis. All compounds were subsequently evaluated through computational analysis and compared with 7-ketocholesterol as the control ligand to assess their relative potential as CYP7A1 modulators in cholesterol metabolism regulation [15]. The chemical structures were retrieved as SMILES codes from the PubChem database (https://pubchem.ncbi.nlm.nih.gov/), along with a clinically validated reference compound for comparison. Each ligand was protonated under physiological pH conditions and subjected to energy minimization using the AMBER10 force field to ensure parameter consistency with the prepared protein structure [16]. The optimized ligands were subsequently saved in Molecular Operating Environment (MOE) database format (.mdb) for the docking process.

The macromolecular structure of human cholesterol 7α-hydroxylase (CYP7A1) in its crystallographic form was obtained from the Protein Data Bank (PDB) (https://www.rcsb.org/). The protein structure used in this study corresponds to PDB ID: 3DAX [17]. Protein preparation was performed using the QuickPrep module within the Molecular Operating Environment (MOE) software. The preparation protocol involved the removal of crystallographic water molecules and co-crystallized ligands not directly involved in ligand–receptor interactions. The structure was further processed by deleting water molecules, correcting structural issues, removing the native ligand, and identifying the protein's active site.

Lipinski's Rule of Five Screening

The bioactive constituents detected in the leaves of Mucuna pruriens (L.) DC. were systematically screened for their drug-likeness profile using Lipinski's Rule of Five as a preliminary criterion to estimate their feasibility as orally administered therapeutic agents. The evaluated descriptors comprised molecular weight (< 500 g/mol), hydrogen bond donor count (< 5), hydrogen bond acceptor count (< 10), and partition coefficient (LogP < 5), in accordance with established drug-likeness thresholds [18]. All physicochemical and pharmacokinetic parameters were calculated by submitting the SMILES structures to the SwissADME web server (https://www.swissadme.ch/).

Molecular Docking Studies

Molecular docking simulations were performed using the Dock module implemented in the Molecular Operating Environment (MOE). Ligand binding was performed at the predefined active site, defined using dummy atoms. The placement method applied was the Triangle Matcher algorithm with the London dG scoring function, generating 30 initial poses for each ligand. Subsequently, a refinement step was carried out using the Rigid Receptor protocol with the GBVI/WSA dG scoring function, and the top five poses for each ligand were selected for further analysis.

The docking results were saved in .mdb format and analyzed using the MOE Database Viewer. The evaluated parameters included the Docking Score (S) and Root Mean Square Deviation (RMSD) values. The ligand–CYP7A1 interaction profiles were visualized to identify the types of molecular interactions formed, such as hydrogen bonds and hydrophobic interactions.

The Docking Score values were used as an indicator to predict the potential of bioactive compounds from *Mucuna pruriens* leaves as candidate modulators of the CYP7A1 enzyme in cholesterol metabolism regulation. Compounds with more negative docking scores were interpreted as having stronger binding affinity for the CYP7A1 active site. In addition, RMSD values ≤ 2 Å were considered to indicate acceptable conformational stability of the ligand within the binding pocket. Interaction analysis was further performed to identify key amino acid residues involved in hydrogen bonding and hydrophobic interactions that contribute to the stability of the ligand protein complex.

Pharmacokinetic Studies

Pharmacokinetic and toxicity properties were predicted using the PreADMET program, accessed via the pkCSM online platform (https://biosig.lab.uq.edu.au/pkcsm/) [19]. The predicted ADMET parameters were interpreted to evaluate the pharmacokinetic suitability of the tested compounds. High human intestinal absorption (HIA) values indicate favorable oral absorption potential, while compounds predicted as non-inhibitors of CYP3A4 suggest a lower possibility of metabolic drug-drug interactions. Toxicity parameters such as the Ames test and hepatotoxicity prediction were also considered to identify compounds with safer pharmacological profiles.

Results and Discussion

Lipinski's Rule of Five prediction

Lipinski's Rule of Five serves as an initial parameter to evaluate the suitability of a compound as an oral drug candidate based on its physicochemical properties. This rule states that compounds with favorable oral bioavailability generally meet the following criteria: molecular weight < 500 g/mol, hydrogen bond donors < 5, hydrogen bond acceptors < 10, logP value < 5, and molar refractivity within the range of 40–130 [18]. These parameters are widely applied to predict a compound's ability to permeate biological membranes and achieve systemic distribution [20].

Table 1. Results of the Linpinski Rule of Five screening

Compounds	Lipinski's parameter			
	Molecular weight (<500 g/mol)	Proton donor (<5)	Proton acceptor (<10)	Log P (<5)
Hexadecanoic acid	256.42	1	2	5.20
Geraniol	154.25	1	1	2.74
3-Aminobenzamide	136.15	1	1	0.32
Octadecanoic acid	282.46	1	2	5.77
4-Hydroxycinnamic acid	164.16	2	3	1.26
Benzyl Acetate	150.17	0	2	1.94
Carvacrol	150.22	1	1	2.82
Pentalene	102.13	0	0	2.02
Bicyloheptane	194.36	0	0	4.98
2-Acetyl-3-methylpyrazine	136.15	0	3	0.71
Cyclopropanecarboxylic acid	86.09	1	2	0.51
3-tert-Butyl-4-hydroxyanisole	260.31	1	5	2.09
Benzofuranone	118.13	0	1	2.22
4-tert-Octylphenol	206.32	1	1	3.88
Isobornyl acrylate	208.30	0	3	3.35
(2Z)-3,7-Dimethylocta-2,6-dien-1-yl 3-oxobutanoate	238.32	0	3	3.23
Morpholine	87.12	1	2	0.09
Zedoarondiol	252.35	2	3	2.09
Artemin	266.33	2	4	1.64
(E)-2-Methyl-2-buten-1-ol O-beta-D-Glucopyranoside	248.27	4	6	-0.46
Prenyl glucoside	248.27	4	6	-0.53
Beta-pinene	136.23	0	0	3.42
Alpha-pinene	136.23	0	0	3.44
1-Phenyl-1-nonyne	200.32	0	0	4.90
Sterculic Acid	294.47	1	2	5.42
2(1H)-Naphthalenone	144.17	0	1	1.99
Heptadecanoic acid	270.45	1	2	5.57
7-Ketocholesterol (control)	400.64	1	2	5.99

An excessive number of hydrogen bond donors and acceptors may reduce membrane permeability due to increased energetic requirements during the absorption process [21]. The logP value reflects the balance between lipophilicity and hydrophilicity; excessively high values indicate pronounced hydrophobic character, which may enhance retention within the lipid bilayer and increase the risk of toxicity [22]. Furthermore, compounds with molecular weights exceeding 500 g/mol generally exhibit lower permeability, rendering them less favorable as oral drug candidates [23].

The predicted results of Lipinski's Rule of Five for the 28 bioactive compounds of *Mucuna pruriens* (L.) DC., along with 7-ketocholesterol as the control ligand, are presented in Table 1. Based on the analyzed parameters, the majority of compounds satisfied the criteria for molecular weight (< 500 g/mol), hydrogen bond donors and acceptors (< 5 and < 10, respectively), as well as logP value (< 5), indicating their theoretical potential for favorable oral bioavailability.

However, several compounds, including hexadecanoic acid, octadecanoic acid, sterculic acid, heptadecanoic acid, and 7-ketocholesterol, exhibited logP values exceeding the recommended threshold, suggesting high lipophilicity and potential limitations in membrane permeability or systemic distribution. Compounds that fulfilled Lipinski's criteria were subsequently considered for further evaluation through pharmacokinetic and toxicity prediction, as well as molecular docking studies against CYP7A1.

Docking Validation

The validation process was performed by redocking the reference ligand into the active site of the CYP7A1 protein (PDB ID: 3DAX) using MOE 2019.01, with the same parameters used for docking the test compounds. This step was intended to evaluate the ability of the docking protocol to consistently reproduce the ligand orientation and interaction pattern within the enzyme's catalytic site [24]. The redocking results demonstrated that the ligand formed a hydrogen bond as an acceptor with the key residue HIS101 at a distance of 2.97 Å, with an interaction energy of −6.9 kcal/mol, indicating a significant stabilizing contribution. Additional hydrogen-bonding interactions were observed with ASN362 (3.90 Å) and the water molecule HOH663 (3.01 Å; −3.9 kcal/mol), which reinforced the interaction network within the active pocket. Furthermore, π–H interactions with residues ALA285, ASN289, and PRO445 at distances ranging from 3.62 to 3.92 Å suggested the involvement of hydrophobic forces in maintaining the stability of the ligand–protein complex.

As illustrated in Figure 1, the superimposition (overlay) of the native ligand and the redocked ligand demonstrated excellent conformational agreement, as evidenced by the nearly identical structural overlap within the protein active site. This alignment indicates that the docking protocol was able to accurately reproduce the ligand binding orientation [25]. Therefore, the applied docking method was considered validated and suitable for subsequent evaluation of the bioactive compounds of *Mucuna pruriens* (L.) DC against the CYP7A1 target.

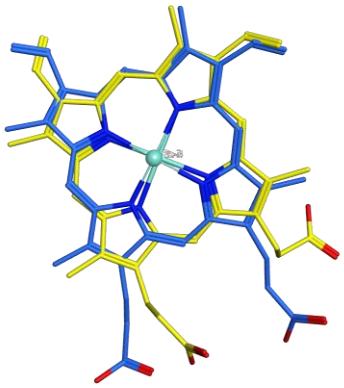

Figure 1. Overlap between native ligand (blue) and re-docking ligand (yellow)

Analysis of Molecular Docking Result

Molecular docking simulations were performed against the CYP7A1 enzyme (PDB ID: 3DAX) to evaluate the binding potential of 28 bioactive compounds from Mucuna pruriens leaves, compared with 7-ketocholesterol as the positive control. The evaluation was based on binding affinity (S score) and Root Mean Square Deviation (RMSD) parameters. More negative S values indicate stronger binding affinity, whereas RMSD ≤ 2 Å suggests conformational stability and validity of the ligand within the enzyme's active pocket [26].

Based on the docking results in Table 2, sterculic acid exhibited the highest binding affinity with an S value of −7.789 kcal/mol and an RMSD of 1.19 Å, lower than that of the positive control 7-ketocholesterol (−7.335 kcal/mol; RMSD 1.26 Å). This energy difference indicates the formation of a more stable ligand–receptor complex. Interaction analysis revealed hydrogen bond formation with residue Asn126 (3.44 Å; −0.7 kcal/mol) and interaction with Lys98 (3.26 Å; −1.5 kcal/mol). The involvement of these polar residues highlights the contribution of electrostatic interactions in enhancing complex stability within the enzyme active site [27].

Octadecanoic acid also demonstrated competitive affinity with a score of −7.29 kcal/mol (RMSD 1.65 Å), forming a π–H interaction with the aromatic residue Phe129 (3.76 Å; −0.7 kcal/mol), indicating a dominant role of hydrophobic forces in ligand stabilization. Hexadecanoic acid (−6.962 kcal/mol; RMSD 1.60 Å) formed a hydrogen bond with Cys444 at a distance of 3.24 Å, whereas isopropyl myristate (−6.652 kcal/mol; RMSD 0.84 Å) and 1-phenyl-1-nonyne (−6.613 kcal/mol; RMSD 1.51 Å) interacted through π interactions with Phe437, suggesting the involvement of aromatic domains in binding nonpolar ligands.

(2Z)-3,7-Dimethylocta-2,6-dien-1-yl 3-oxobutanoate exhibited an S value of −6.355 kcal/mol (RMSD 1.02 Å) with hydrogen bond formation at Asn289 (3.00 Å; −3.2 kcal/mol). Notably, Asn289 was repeatedly identified in the interaction patterns of several ligands, including cyclopropanecarboxylic acid and heptadecanoic acid, indicating its critical role in substrate recognition and stabilization within CYP7A1. Overall, the dominant interacting residues included Asn289, Glu453, Phe129, Phe437, Cys444, Ser360, Lys98, and Asn126. The interaction patterns comprised hydrogen bonds, π–H

interactions, and hydrophobic contacts that synergistically maintained the stability of the ligand–protein complex.

Compared with the positive control, sterculic acid demonstrated superior binding affinity while maintaining conformational stability (RMSD < 2 Å), suggesting its potential as a candidate CYP7A1 inhibitor for modulation of cholesterol metabolism. Structurally, compounds bearing long carbon chains combined with polar functional groups exhibited the capacity to simultaneously establish hydrophobic and electrostatic interactions within the enzyme active pocket [28]. These findings provide a rational basis for further investigation through molecular dynamics simulations and experimental validation to confirm their inhibitory potential against CYP7A1.

Table 2. Molecular Docking Results of Bioactive Compounds from *Mucuna pruriens* (L.) DC. Against CYP7A1

Compounds	S score (kcal/mol)	RMSD (Å)	Amino acid residue	Distance (Å)	Type of bond
Hexadecanoic acid	-6.96	1.59	CYS444	3.24	H-acceptor
Geraniol	-5.83	1.12	GLU453	3.04	H-donor
3-Aminobenzamide	-5.06	0.84	PRO436	3.36	H-donor
Octadecanoic acid	-7.29	1.65	PHE129	3.76	H-pi
4-Hydroxycinnamic acid	-4.94	1.19	GLU453	2.85	H-donor
			SER286	3.53	pi-H
			GLY446	4.06	pi-H
Benzyl Acetate	-5.22	1.74	SER286	3.60	pi-H
			GLY446	4.19	pi-H
Carvacrol	-5.19	1.02	GLY446	4.14	pi-H
Pentalene	-4.18	0.88	PHE129	3.68	cation-pi
Bicyloheptane	-5.41	0.85	PHE129	4.46	H-pi
2-Acetyl-3-methylpyrazine	-4.91	0.64	PHE437	4.71	pi-H
Cyclopropanecarboxylic acid	-3.77	0.89	ASN289	2.98	H-acceptor
			CYS444	3.25	H-acceptor
3-tert-Butyl-4-hydroxyanisole	-5.71	0.80	ASN289	3.30	H-acceptor
			CYS444	3.03	H-acceptor
			PHE129	4.30	H-pi
Benzofuranone	-4.58	1.21	SER286	3.61	pi-H
			GLY446	4.11	pi-H
4-tert-Octylphenol	-5.08	1.38	SER105	2.83	H-donor
Isobornyl acrylate	-5.67	1.89	HIS101	4.36	H-pi
(2Z)-3,7-Dimethylocta-2,6-dien-1-yl 3-oxobutanoate	-6.35	1.02	ASN289	3.00	H-acceptor
Morpholine	-3.77	0.42	ASN289	2.92	H-acceptor
Zedoarondiol	-5.92	0.94	LEU361	2.99	H-donor
			HOH663	2.87	H-acceptor
Artemin	-5.40	0.53	ASN289	2.90	H-acceptor
(E)-2-Methyl-2-buten-1-ol O-beta-D-Glucopyranoside	-6.37	0.84	HOH629	2.82	H-donor
Prenyl glucoside	-5.24	0.96	SER360	3.18	H-donor
			SER360	2.99	H-donor
			HOH663	2.92	H-donor
Beta-pinene	-4.59	1.17	HIS101	3.88	H-pi
Alpha-pinene	-4.59	1.83	HIS101	4.09	H-pi
1-Phenyl-1-nonyne	-6.65	0.84	PHE437	4.67	pi-H
Sterculic Acid	-6.61	1.51	ASN126	3.44	H-acceptor
			LYS98	3.26	H-acceptor
2(1H)-Naphthalenone	-4.84	1.19	PHE129	3.82	H-pi
Heptadecanoic acid	-7.33	1.26	ASN289	3.35	H-acceptor
7-Ketocholesterol (control)	-7.69	2.96	PRO436	2.80	H-donor

ADMET Validation

ADMET predictions were conducted to evaluate the pharmacokinetic feasibility and toxicity profiles of 28 bioactive compounds from Mucuna pruriens, compared with 7-ketocholesterol as the control. The analyzed parameters included absorption (Caco-2 permeability and human intestinal absorption, HIA), metabolism (CYP3A4 interaction), excretion (clearance), and toxicity (Ames test, hepatotoxicity, and LD50), as presented in Table 3.

Regarding the absorption parameters, the majority of compounds exhibited positive Caco-2 values (> 0), indicating adequate intestinal membrane permeability. Most compounds demonstrated Human Intestinal Absorption (HIA) values above 90%, including hexadecanoic acid (92.004%), octadecanoic acid (91.823%), benzyl acetate (96.603%), and sterculic acid (92.158%), suggesting favorable oral absorption potential. However, two glycosidic compounds, namely (E)-2-methyl-2-buten-1-ol O-β-D-glucopyranoside and prenyl glucoside, showed HIA values

of approximately 50%, indicating limited absorption likely due to their higher hydrophilicity.

From a metabolic perspective, all compounds were predicted to be non-inhibitors of CYP3A4, indicating a relatively low risk of drug–drug interactions in phase I metabolic pathways. The clearance parameter ranged from 0.03 to 1.927, within an acceptable range for elimination. Long-chain fatty acids, such as octadecanoic acid (1.927) and heptadecanoic acid (1.797), demonstrated relatively higher predicted excretion rates.

Table 3. In Silico ADMET Profiles of Bioactive Compounds from *Mucuna pruriens* (L.) DC.

Compound	Pharmacokinetic prediction		Metabolism	Excretion			Toxicity
	Caco-2 (nm/sec)	HIA (%)	CYP3A4	Clearance	Ames	Hepatotoxicity	LD50 (mol/kg)
Hexadecanoic acid	1.558	92.004	No	1.763	No	No	1.44
Geraniol	1.49	92.788	No	0.437	No	No	1.636
3-Aminobenzamide	0.637	80.238	No	0.293	Yes	No	2.078
Octadecanoic acid	1.563	91.823	No	1.927	No	No	1.419
4-Hydroxycinnamic acid	1.21	93.494	No	0.662	No	No	2.534
Benzyl Acetate	1.728	96.603	No	0.385	No	No	2.137
Carvacrol	1.606	90.843	No	0.207	No	Yes	2.074
Pentalene	1.381	97.808	No	0.18	No	No	1.919
Bicyloheptane	1.388	94.199	No	1.27	No	No	1.929
2-Acetyl-3-methylpyrazine	1.926	98.504	No	0.728	No	No	2.209
Cyclopropanecarboxylic acid	1.562	90.556	No	0.466	No	No	1.756
3-tert-Butyl-4-hydroxyanisole	1.055	95.246	No	0.246	No	No	2.182
Benzofuranone	1.581	95.557	No	0.353	No	No	2.323
4-tert-Octylphenol	1.596	91.803	No	0.81	No	No	2.157
Isobornyl acrylate	1.43	95.934	No	1.191	No	No	1.691
(2Z)-3,7-Dimethylocta-2,6-dien-1-yl 3-oxobutanoate	1.459	95.24	No	1.699	No	No	1.686
Morpholine	1.47	100	No	1.111	No	No	2.124
Zedoarondiol	1.273	94.791	No	1.068	No	No	1.816
Artemin	0.511	96.186	No	1.088	Yes	No	1.923
(E)-2-Methyl-2-buten-1-ol O-beta-D-Glucopyranoside	-0.067	50.592	No	1.578	No	No	1.513
Prenyl glucoside	-0.067	50.592	No	1.523	No	No	1.513
Beta-pinene	1.385	95.525	No	0.03	No	No	1.673
Alpha-pinene	1.38	96.041	No	0.043	No	No	1.77
1-Phenyl-1-nonyne	1.558	95.095	No	1.634	Yes	No	1.649
Sterculic Acid	1.557	92.158	No	1.615	No	No	1.456
2(1H)-Naphthalenone	1.519	97.328	No	0.182	No	No	1.911
Heptadecanoic acid	1.557	91.66	No	1.797	No	No	1.422
7-Ketocholesterol (control)	1.273	95.253	No	0.538	No	No	2.389

Toxicity evaluation indicated that the majority of compounds were predicted to be non-mutagenic based on the Ames test, including hexadecanoic acid, geraniol, octadecanoic acid, benzyl acetate, sterculic acid, and heptadecanoic acid. However, several compounds, such as 3-aminobenzamide, artemin, and 1-phenyl-1-nonyne, showed potential mutagenic activity and warrant further investigation. Hepatotoxicity prediction was predominantly negative for most compounds, except for carvacrol, which was indicated to possess hepatotoxic potential. The predicted LD_{50} values ranged from 1.419 to 2.534 mol/kg, suggesting acute toxicity at relatively low to moderate levels.

Compared with 7-ketocholesterol as the control, most bioactive compounds demonstrated ADMET profiles comparable to or better than those of 7-ketocholesterol, particularly in mutagenicity and hepatotoxicity parameters. Overall, compounds such as sterculic acid, hexadecanoic acid, octadecanoic acid, and heptadecanoic acid exhibited a favorable combination of absorption profiles, non-inhibitory effects on CYP3A4, and low toxicity, thereby supporting their suitability for further evaluation through molecular dynamics simulations and experimental validation.

These findings are consistent with previous pharmacokinetic studies suggesting that compounds with moderate molecular weight and balanced lipophilicity tend to exhibit favorable membrane permeability and oral bioavailability. The predicted high human intestinal absorption (HIA) values, therefore, indicate that these compounds may possess suitable pharmacokinetic characteristics for further drug development studies [29].

Conclusion

This study demonstrates that several bioactive compounds from *Mucuna pruriens* (L.) DC. possess promising potential as CYP7A1 modulators based on molecular docking and pharmacokinetic predictions. Among the evaluated compounds, sterculic acid exhibited the most

favorable binding affinity and interaction stability, supported by acceptable ADMET characteristics. The predominance of hydrogen bonding and hydrophobic interactions within the enzyme active site suggests that structural features combining long hydrocarbon chains with polar functional groups are advantageous for CYP7A1 binding. These findings provide a preliminary computational basis for the development of natural product derived compounds targeting cholesterol metabolism and highlight the potential of Mucuna pruriens as a promising source of candidate molecules for antihypercholesterolemic therapy. However, this study is limited to computational predictions and lacks experimental validation. Therefore, further investigations such as molecular dynamics simulations and enzyme inhibition assays through in vitro studies are necessary to confirm the stability of ligand protein interactions and the biological activity of the identified compounds.

Author's Contribution

C.A. Paradhise: developed and structured the research design, compiled the bioactive compound dataset, and carried out the molecular docking simulations. She established the methodological approach, performed a comprehensive literature review in pharmacoinformatics, supervised the in silico analyses and data processing, and contributed to the interpretation of the results. T.K. Sari: initiated the research concept, organized and prepared the manuscript framework, and conducted the final review and revisions prior to submission.

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