Exploration of Potentially Bioactive Compounds from Fingerroot (*Boesenbergia rotunda* L.) as Inhibitor of Atherosclerosis-Related Proteins (CETP, ACAT1, OSC, sPLA2): An *in silico* Study

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ABSTRACT

Boesenbergia rotunda L., commonly known as fingerroot, is recognized as one of Indonesia's medicinal plants with significant potential for treating various diseases, including atherosclerosis. This study aims to analyze the anti-atherosclerosis potential of bioactive compounds found in fingerroot by assessing their inhibitory effects on four proteins associated with atherosclerosis (CETP, ACAT1, OSC, and sPLA2). Bioactive compounds from B. rotunda were retrieved from the KnapSack database. The drug-likeness properties were predicted using the SwissADME web server, and the bioactivity of the compounds was assessed using the PASSOnline server. The identification of active sites on proteins and the validation of protein structures were performed using the SCFBio web server and Autodock Vina. Specific docking simulations between fingerroot compounds and the target proteins were carried out using AutoDock Vina. The analysis revealed that fingerroot contains 20 bioactive compounds with favorable drug-like properties. Among these, dihydrochrysin, sakuranetin, isopimaric acid, 2S-pinocembrin, 5,7-dihydroxy-8-C-geranylflavanone, 7,4'-dihydroxy-5-methoxyflavanone, and 5,7-dihydroxy-8,7-methoxy-5-hydroxy-8-geranylflavanone were predicted to exhibit anti-atherosclerosis activities. In the interactions with CETP, rubranine and (-)-4-hydroxypanduratin A showed the lowest binding affinity scores. Meanwhile, in interactions with ACAT1, OSC, and sPLA2, rubranine and 5,7-dihydroxy-8-C-geranylflavanone displayed the lowest binding affinities. In conclusion, fingerroot exhibits high potential as an anti-atherosclerosis agent through the inhibition of four proteins associated with atherosclerosis, as predicted through in silico analysis.
Keywords: ACAT1, atherosclerosis, CETP, molecular docking, OSC, sPLA2e.

INTRODUCTION

Atherosclerosis is an inflammatory disease initiated by the accumulation of lipids in the vessel wall, leading to vascular narrowing or blockage and disrupting blood flow[1]. According to WHO data from 2016, approximately 17.9 million people worldwide died from cardiovascular diseases, which were identified as the leading cause of death globally[2]. In Indonesia, one-third of all deaths are attributed to cardiovascular diseases, including

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atherosclerosis[3]. Several proteins play critical roles in the formation of atherosclerosis[4].

Proteins such as CETP, ACAT1, OSC, and sPLA2 have been implicated in atherosclerosis. Cholesteryl ester transfer protein (CETP) is responsible for transporting and converting cholesterol esters into LDL, IDL, and VLDL, which lowers HDL levels and raises LDL levels[5]. Acyl-CoA:cholesterol acyltransferase (ACAT1) is a protein involved in the re-esterification of cholesterol absorbed by macrophages, leading to the formation of foam cells[6]. Oxido-squalene-cyclase (lanosterol synthase, OSC) is the enzyme responsible for the cholesterol synthesis pathway[7]. Meanwhile, sPLA2 is involved in modifying lipoproteins, producing products that can induce inflammation and initiate the formation of atherosclerotic plaques[8]. Inhibiting these proteins could suppress the development of atherosclerosis[4]. Standard drugs used to treat cardiovascular diseases, such as statins, carry risks such as statin-associated muscle symptoms (SAMS), myopathy, and diabetes[9]. Herbal medicine is an alternative way to treat diseases.

Boesenbergia rotunda (fingerroot), a member of the Zingiberaceae family, is known as one of Indonesia's medicinal plants. Fingerroot has been used to treat gastrointestinal ailments, muscle pain, rheumatism, dyspepsia, inflammatory conditions like swelling and dermatitis, dysentery, diuretic, and diarrhea. Compounds found in fingerroot have reported antimicrobial, antiparasitic, anti-scabies, anti-cancer, antioxidant, and anti-inflammatory properties[10,13]. Through in silico analysis, one can assess the physicochemical and pharmacokinetic properties of drug candidates, thereby improving the quality of the drug development process[14]. This study aims to analyze the anti-atherosclerosis potential of bioactive compounds in fingerroot by examining their inhibitory effects on four proteins involved in atherosclerosis development (CETP, ACAT1, OSC, and sPLA2).

Experimental Section

Data Retrieval

The list of bioactive compounds from fingerroot (B. rotunda L.) was obtained from the KnapSack database (http://www.knapsackfamily.com/KNApSAcK/). The compound names, formulas, PubChem IDs, and SMILES representations are presented in Table 2.

Drug-likeness Prediction

In this study, drug-likeness prediction was conducted using the SwissADME web server (http://www.swissadme.ch/)[14,15]. The prediction results were selected based on Lipinski, Veber, and Egan rules. Various parameters were considered, including molecular weight, MlogP value, number of hydrogen bond acceptors (nON), number of hydrogen bond donors (nOHNH), total number of rotatable bonds, and total polar surface area (TPSA).

Bioactivity Prediction

Bioactivity prediction of the compounds was conducted using the PASSOnline web server (http://way2drug.com/PassOnline/). Several parameters related to atherosclerosis, such as cholesterol synthesis inhibition, anti-hypercholesterolemia, anti-inflammatory, and antioxidant properties, were taken into account[16–19]. Compounds with a probability of activity (Pa) greater than 0.7 are considered to have high pharmaceutical potential, while those with Pa values between 0.5 and 0.7 are considered to have low pharmaceutical potential[20].

Protein Active Site Prediction and Validation

Protein active site prediction aimed to predict the location of the active site of four proteins. Active site prediction performed using SCFBio web server (http://www.scfbio-iitd.res.in/dock/ActiveSite.jsp). The active site prediction is validated by blind docking between the protein and the reference inhibitor drug. Several inhibitors were used, such as anacetrapib

(11556427) for CETP, ART-101 (131679) for ACAT1, Ro 48-8071 (9853053) for OSC, and KH064 (164754) for sPLA2. The inhibitor which binds to the SCFBio predicted site was strongly predicted as the potential active site.

Molecular Docking Simulation

Proteins, including cholesteryl ester transfer protein (CETP), acyl-CoA:cholesterol acyltransferase (ACAT1), oxidosqualene cyclase (OSC), and acidic secretory phospholipase A2 (sPLA2), were prepared by removing contaminant molecules using Biovia Discovery Studio 2019 software (Dassault Systèmes Biovia, San Diego, California, USA). All compounds were subjected to energy minimization using the Open Babel tool integrated into the PyRx software. Specific docking was performed using the AutoDock Vina software, which is integrated into PyRx[21]. The grid positions were set at the active site of each protein (Table 1). The docking results were visualized using Biovia Discovery Studio 2019 software[22].

Tabel 1. Grid settings for specific docking

Proteins	PDB ID	Grid position					
		Center			Dimensions		
		X	Y	Z	X	Y	Z
CETP	4ews	12.7646	-3.2357	45.2502	25.000	25.4289	31.2910
ACAT1	6p2p	97.5383	154.6754	162.1431	30.9911	37.1683	35.1102
OSC	1w6k	42.2596	54.8271	27.1112	36.1945	43.1945	30.6761
sPLA2	1dcy	60.4890	29.4733	43.8285	16.3735	24.9770	22.1178

RESULTS AND DISCUSSION

Compounds Contained in Fingerroot

According to KnapSack, the majority of bioactive compounds in fingerroot belong to the flavonoid group, with some essential oils. Fingerroot contains a total of 14 flavonoid compounds. In our study, only one essential oil, E-geraniol, was identified in fingerroot. Additionally, fingerroot contains cylohexane derivatives such as (+)-Zeylenol and Crotepoxide. Another compound present in fingerroot is 2,4-dihydroxy-6-phenethyl-benzoic acid methyl ester (Table 2). The flavonoid group is the most abundant bioactive compound category found in fingerroot rhizomes, consisting of chalcones, flavones, and flavanones. Chalcones compounds include cardomonin and flavokawin A. Furthermore, perylanated chalcones such as boesenbergia A, rubranine, (-)-4-hydroxypanduratin A, and isopanduratin A are also present. The flavanones category includes compounds like sakuranetin, alpinetin, 5,7-dihydroxy-8-C-geranylflavanone, 7,4'-dihydroxy-5-methoxyflavanone, and 7-methoxy-5-hydroxy-8-geranylflavanone (Table 2).

Table 2. Compounds in Fingerroot obtained from KnapSack

Compounds	Formula	Pubchem ID	SMILES
(E)-geraniol[b]	$C_{10}H_{18}O$	637566	CC(=CCCC(=CCO)C)C
Dihydrochrysin[a]	$C_{15}H_{12}O_4$	238782	C1C(OC2=CC(=CC(=C2C1=O)O)O)C3=CC=CC=C3
Sakuranetin[a]	$C_{16}H_{14}O_5$	73571	COC1=CC(=C2C(=O)CC(OC2=C1)C3=CC=C(C=C3)O)O
Isopimaric acid[c]	$C_{20}H_{30}O_2$	442048	CC1(CCC2C(=CCC3C2(CCCC3(C)C(=O)O)C)C1)C=C
Cardamomin[a]	$C_{16}H_{14}O_4$	641785	COC1=CC(=CC(=C1C(=O)C=CC2=CC=CC=C2)O)O
Flavokawin A[a]	$C_{18}H_{18}O_5$	270057	COC1=CC=C(C=C1)CCC(=O)C2=C(C=C(C=C2OC)OC)O
Boesenbergin A[a]	$C_{26}H_{28}O_4$	6313827	CC(=CCCC1(C=CC2=C(C=C(C(=C2O1)C(=O)C=CC3=CC=CC=C3)O)OC)C)C
Rubranine[a]	$C_{25}H_{26}O_4$	42607681	CC1(C2CCC3(CC2C4=C(O3)C=C(C(=C4O1)C(=O)C=CC5=CC=CC=C5)O)C)C
Panduratin A[a]	$C_{26}H_{30}O_4$	6483648	CC1=CCC(C(C1CC=C(C)C)C(=O)C2=C(C=C(C=C2O)OC)O)C3=CC=CC=C3
Alpinetin[a]	$C_{16}H_{14}O_4$	154279	COC1=CC(=CC2=C1C(=O)CC(O2)C3=CC=CC=C3)O
5,7-Dihydroxy-8-C-geranylflavanone[a]	$C_{25}H_{28}O_4$	11143678	CC(=CCCC(=CCC1=C2C(=C(C=C1O)O)C(=O)CC(O2)C3=CC=CC=C3)C)C
7,4'-Dihydroxy-5-methoxyflavanonea	$C_{16}H_{14}O_5$	188424	COC1=CC(=CC2=C1C(=O)CC(O2)C3=CC=C(C=C3)O)O
(-)-4-Hydroxypanduratin A[a]	$C_{25}H_{28}O_4$	636530	CC1=CCC(C(C1CC=C(C)C)C(=O)C2=C(C=C(C=C2O)O)O)C3=CC=CC=C3
Isopanduratin A[a]	$C_{26}H_{30}O_4$	10069916	CC1=CCC(C(C1CC=C(C)C)C(=O)C2=C(C=C(C=C2OC)O)O)C3=CC=CC=C3
2,4-Dihydroxy-6-phenethyl-benzoic acid methyl ester[e]	$C_{16}H_{16}O_4$	14195786	CC1=CCC(C(C1CC=C(C)C)C(=O)C2=C(C=C(C=C2O)O)O)C3=CC=CC=C3
5,6-Dehydrokawain[a]	$C_{14}H_{12}O_3$	5273621	CC1=CCC(C(C1CC=C(C)C)C2=CC=CC=C2)C(=O)C3=C(C=C(C=C3OC)O)O
7-Methoxy-5-hydroxy-8-geranylflavanone[a]	$C_{26}H_{30}O_4$	129864052	COC(=O)C1=C(C=C(C=C1O)O)CCC2=CC=CC=C2
(+)-Zeylenol[d]	$C_{21}H_{20}O_7$	14283260	COC1=CC(=O)OC(=C1)C=CC2=CC=CC=C2
Crotepoxide[d]	$C_{18}H_{18}O_8$	161314	C1=CC=C(C=C1)C(=O)OCC2(C(C=CC(C2O)OC(=O)C3=CC=CC=C3)O)O

[a]Flavonoid group, [b]Essential oil, [c]rosin compounds, [d]cyclohexane derivatives, [e]other compounds

Drug-likeness Prediction

Drug-likeness prediction involves assessing the potential of compounds to become drug candidates based on factors such as chemical structure stability, solubility, and permeability. Most of the active compounds found in fingerroot exhibit favorable bioavailability as oral drugs, indicated by the satisfaction of the rule of Lipinski[23], Veber[24], and Egan[25] (Table 3). However, some compounds, including isopimaric acid, boesenbergin A, panduratin A, isopanduratin A, and 7-methoxy-5-hydroxy-8-geranylflavanone, violate specific criteria within these rules. For instance, isopimaric acid has an MlogP value exceeding 4.15, leading to a violation of one of Lipinski's rules. Compounds that violate two or more of the 'Lipinski Rule of Five' criteria are typically considered to have low druggability[26]. On the other hand, boesenbergin A, panduratin A, isopanduratin A, and 7-methoxy-5-hydroxy-8-geranylflavanone violate Egan's criteria for lipophilicity due to their WlogP values exceeding 5.88. When the WlogP value surpasses 5, it indicates high lipophilicity or low solubility, potentially affecting the compound's absorption within the body[27].

Table 3. Druglikeness prediction result

Compounds	Druglikeness parameters							Violation		
	MW (g/mol)	MlogP	nON	nOHNH	WlogP	RB	TPSA (Å²)	L[a]	V[b]	E[c]
(E)-geraniol	154.25	2.59	1	1	2.67	4	20.23	**0**	**0**	**0**
Dihydrochrysin	256.25	1.27	4	2	2.48	1	66.76	**0**	**0**	**0**
Sakuranetin	286.28	0.96	5	2	2.49	2	75.99	**0**	**0**	**0**
Isopimaric acid	302.45	4.54	2	1	5.21	2	37.30	**1**	**0**	**0**
Cardamomin	270.28	1.83	4	2	2.89	4	66.76	**0**	**0**	**0**
Flavokawin A	316.35	1.83	5	1	3.23	7	64.99	**0**	**0**	**0**
Boesenbergin A	404.50	3.51	4	1	5.99	7	55.76	**0**	**0**	**1**
Rubranine	390.47	3.46	4	1	5.39	3	55.76	**0**	**0**	**0**
Panduratin A	406.51	3.59	4	2	6.01	6	66.76	**0**	**0**	**1**
Alpinetin	270.28	1.52	4	1	2.78	2	55.76	**0**	**0**	**0**
5,7-Dihydroxy-8-C-geranylflavanone	392.49	3.38	4	2	5.72	6	66.76	**0**	**0**	**0**
7,4'-Dihydroxy-5-methoxyflavanone	286.28	0.96	5	2	2.49	2	75.99	**0**	**0**	**0**
(-)-4-Hydroxypanduratin A	392.49	3.38	4	3	5.71	5	77.76	**0**	**0**	**0**
Isopanduratin A	406.51	3.59	4	2	6.01	6	66.76	**0**	**0**	**1**
2,4-Dihydroxy-6-phenethyl-benzoic acid methyl ester	272.30	2.72	4	2	2.67	5	66.76	**0**	**0**	**0**
5,6-Dehydrokawain	228.24	2.06	3	0	2.6	3	39.44	**0**	**0**	**0**
7-Methoxy-5-hydroxy-8-geranylflavanone	406.51	3.59	4	1	6.02	7	55.76	**0**	**0**	**1**
(+)-Zeylenol	384.38	1.44	7	3	1.09	7	113.29	**0**	**0**	**0**
Crotepoxide	362.33	0.75	8	0	0.63	8	103.96	**0**	**0**	**0**

[a]L = Lipinsky: MW≤500, MlogP≤4.15, nON≤10, nOHNH≤5, [b]V = Veber: RB≤10, TPSA≤140, [c]E = Egan: WlogP≤5.88, TPSA≤131.6

Compounds Bioactivity Prediction

The PASS Online prediction results indicate that 5,7-dihydroxy-8-c-geranylflavanone and 7-methoxy-5-hydroxy-8-geranylflavanone are bioactive compounds with the highest cholesterol synthesis inhibitor activity among all the compounds found in fingerroot. These compounds also exhibit a high potential as anti-inflammatories (Fig. 1). In our study, isopimaric acid was identified as having a high potential for both anti-inflammatory and anti-hypercholesterolemia activities (Fig. 1). Additionally, PASS Online prediction identified six compounds with Pa > 0.7 values, signifying a high potential for anti-hypercholesterolemia activity. These compounds include dihydrochrysin, sakuranetin, 7,4'-dihydroxy-5-methoxyflavanone, isopimaric acid, and 7-methoxy-5-hydroxy-8-geranylflavanone. Furthermore, dihydrochrysin, 7,4'-dihydroxy-5-methoxyflavanone, 5,7-dihydroxy-8-c-geranylflavanone, and 7-methoxy-5-hydroxy-8-geranylflavanone exhibit the highest antioxidant activity with Pa > 0.7 values (Fig. 1). Previous research has suggested that sakuranetin can reduce inflammation in a rat asthma model[28]. Isopimaric acid was found in *C. Japonica* has antioxidant and anti-inflammatory activity[29].

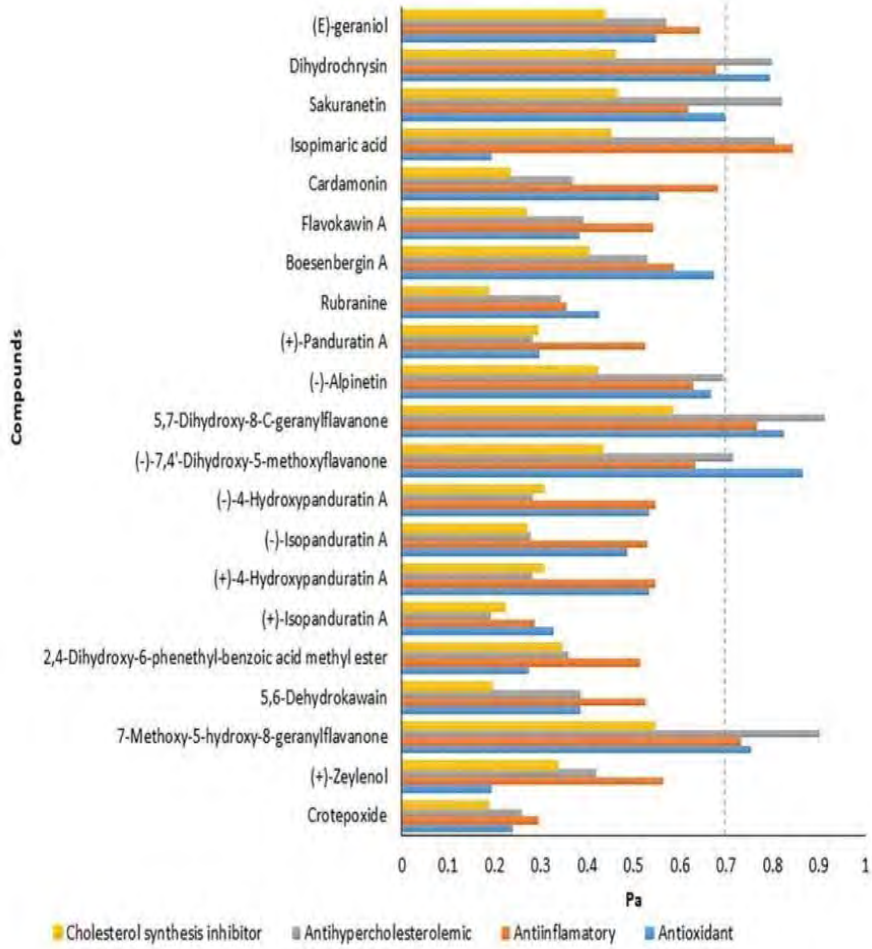

Figure 1. Bioactivity prediction of compounds contained in fingerroot.

Protein Active Site

The results of active site prediction indicated that nearly all the active sites of the four proteins were located within regions of high hydrophobicity (Fig. 2). The active site of CETP is situated around residues Ile15-Leu471 and exhibits high hydrophobicity. Similarly, the active site of ACAT1 is positioned around Glu170-Gln521 and displays a high level of hydrophobicity. In contrast, the active site of OSC is situated around the amino acid Phe74-Trp590 and has a lower degree of hydrophobicity. The active site of sPLA2 is located around the amino acid Asn1-Ser65 and demonstrates high hydrophobicity.

The results of blind docking simulations between the four proteins and their inhibitors confirmed that all inhibitors bound to the predicted active site of the respective protein, thereby reinforcing the accuracy of the active site predictions. The active site of a protein plays a crucial role in its overall activity, as it is involved in catalysis, substrate binding, and stabilizing the reactions occurring within the protein's cavity[30]. The protein's active site consists of residues that are important for carrying out binding and catalytic functions[31]. One effective strategy to inhibit protein activity is to block the protein's active site using competitive[32].

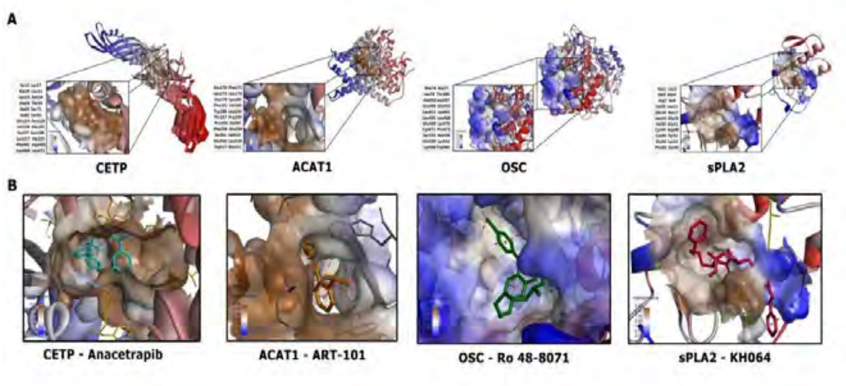

Figure 2. Active site prediction and validation. A) Active site position of four proteins analyzed using SCFBio webserver. B) Blind docking result, all inhibitor bound to proteins' active site

Molecular Docking Result

The docking results between CETP and the compounds revealed that two compounds exhibited the lowest binding affinity values and closely approached the inhibitors used as positive controls: rubranine and (-)-4-hydroxypanduratin A (Table 3). These two compounds formed bonds at the same residues as the inhibitor, namely Ile15, Val198, Phe441, and Phe461 (Fig. 2 and Table 4). The combination of their low binding affinity values and their binding positions identical to those of the inhibitor suggests that rubranine and (-)-4-hydroxypanduratin A have a high potential to act as CETP inhibitors. CETP plays a critical role in LDL formation by facilitating the transfer of cholesterol esters and triglycerides between HDL and LDL and VLDL, leading to the conversion of HDL into LDL or VLDL[5]. This CETP activity results in reduced HDL levels and elevated LDL levels, thereby increasing the risk of atherosclerosis[33]. Consequently, one approach to mitigating atherosclerosis is to inhibit the activity of the CETP protein[5].

Table 3. Binding affinity

Compound	CTEP	ACAT1	OSC	sPLA2
Inhibitor	-11.3	-9.3	-6.1	-8.2
(E)-geraniol	-5.8	-6.7	-4.8	-5.6
Dihydrochrysin	-7.8	-9.7	-7.5	-7.8
Sakuranetin	-7.6	-9.2	-7.1	-7.8
Isopimaric acid	-8.1	-9.6	-7	-7.3
Cardamomin	-7.2	-8.5	-6.7	-7.3
Flavokawin A	-6.8	-8	-6.1	-7.3
Boesenbergin A	-9	-10.1	-7.3	-8
Rubranine	-9.4*	-10.7*	-8.8*	-9.8*
Panduratin A	-9.3	-9.7	-8	-7.4
Alpinetin	-7.9	-9.6	-7.2	-7.9
5,7-Dihydroxy-8-C-geranylflavanone	-9.3	-10.7*	-8.5*	-8.7*
7,4'-Dihydroxy-5-methoxyflavanone	-7.2	-8.9	-7	-7.9
(-)-4-Hydroxypanduratin A	-9.4*	-9.6	-7.8	-7.7
Isopanduratin A	-9.1	-9.7	-7.5	-7.7
2,4-Dihydroxy-6-phenethyl-benzoic acid methyl ester	-7.1	-8.7	-6.6	-7.5
5,6-Dehydrokawain	-7.2	-8.4	-6.1	-7
7-Methoxy-5-hydroxy-8-geranylflavanone	-9.2	-9.6	-7.1	-8.6
(+)-Zeylenol	-8.6	-9.5	-7.6	-7.8
Crotepoxide	-7.3	-8.9	-6.8	-7.5

*: Indicate the lowest binding affinity values

The docking results for ACAT1-compound interactions revealed that Rubranine and 5,7-Dihydroxy-8-C-geranylflavanone exhibited the lowest binding affinity values. Rubranine formed three bonds at the same residues as the inhibitor, namely Phe381, Phe479, and Leu507 (Fig. 2E, F, and Table 4). On the other hand, 5,7-Dihydroxy-8-C-geranylflavanone formed the same four hydrogen bonds as the inhibitor at Leu377, Phe381, Trp420, and Phe479 (Fig. 2E, G, and Table 4). ACAT1 functions by transferring fatty acid groups from acyl-coenzyme A (Acyl-CoA) to the 3β-hydroxyl part of cholesterol, leading to the formation of cholesterol esters. These cholesterol esters then aggregate to create cytoplasmic lipid droplets within the[34]. Inhibiting ACAT1 activity has been shown to prevent the transformation of macrophages into foam cells[4]. Previous studies have suggested that inhibiting ACAT1 can be an effective strategy to prevent atherosclerosis by impeding foam cell formation[35].

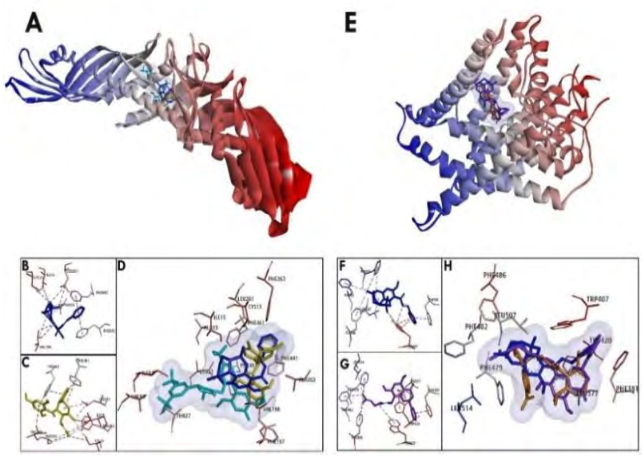

Figure 3. Protein-compounds interaction. The binding site of CTEP-compounds interaction (A). Details of interactions between CTEP-rubranine (blue) and CTEP-(-)-4-hydroxypanduratin A (yellow) (B and C). Comparison of interaction between compounds and inhibitors (anacetrapib) (Cyan) (D). Interaction between ACAT1 and compounds (E). Detail Interaction of ACAT1-rubranine (blue) and ACAT1- 5,7-dihydroxy-8-C-geranylflavanone (purple) (F and G). Comparison of the interaction between the compounds and the inhibitor (ART-101) (brown) in ACAT1 (H).

The results of the OSC-compound docking indicated that rubranine and 5,7-Dihydroxy-8-C-geranylflavanone had the lowest binding affinity values. Rubranine formed a bond at the same amino acid site as the inhibitor, namely Glu594 (Fig. 3A, B, and Table 4). On the other hand, 5,7-Dihydroxy-8-C-geranylflavanone bound to the same amino acids as the inhibitor, specifically at Glu398 and Lys46 (Figure 3A, C, and Table 4).

Based on these results, it can be concluded that rubranine and 5,7-dihydroxy-8-C-geranylflavanone have the potential to act as inhibitors of OSC. OSC plays a critical role in cholesterol synthesis, particularly in catalyzing the cyclization of 2,3-monoepoxysqualene to lanosterol and 2,3,22,23-diepoxysqualene to 24(S), 25-epoxylanosterol[7]. Inhibiting the activity of this protein has the potential to lower LDL levels in the plasma and prevent the accumulation of cholesterol in macrophages[36]. Previous studies have suggested that OSC inhibition could reduce cholesterol biosynthesis and potentially prevent atherosclerosis[37].

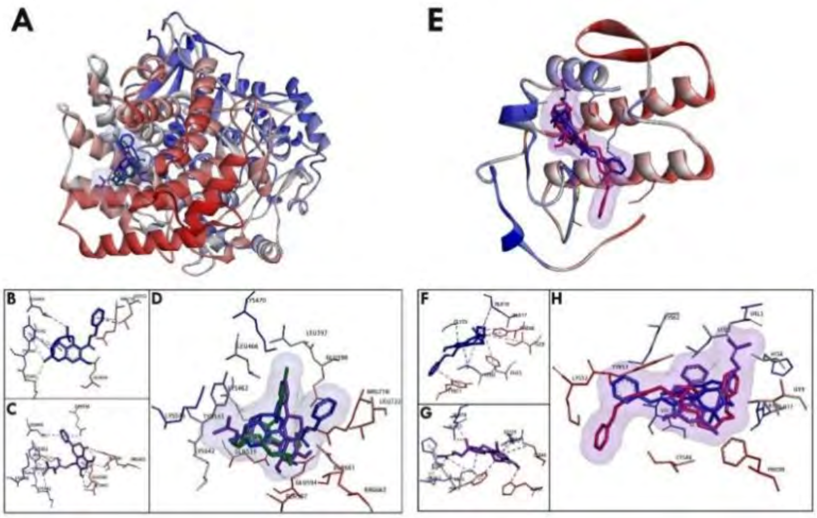

Figure 4. Protein-compounds interaction. The binding site of OSC-compounds interaction (A). Details of interactions between OSC-rubranine (blue) and OSC-(-)-4-hydroxypanduratin A (yellow) (B & C). Comparison of interaction between compounds and inhibitors (Ro 48-8071) (green) (D). Interaction between sPLA2 and compounds (E). Detailed interaction of sPLA2-rubranine (blue) and sPLA2- 5,7-dihydroxy-8-C-geranylflavanone (purple) (F & G). Comparison of interaction between the compound and the inhibitor (KH064) (red) in sPLA2 (H).

The interaction between sPLA2 and the compounds revealed that rubranine formed one hydrogen bond and six hydrophobic interactions with sPLA2 (Fig. 3E, F, and Table 4). On the other hand, 5,7-Dihydroxy-8-C-geranylflavanone formed one hydrogen bond and seven hydrophobic interactions. Rubranine bound to the same residues as the inhibitor, specifically at Gly29, Leu2, Ala17, and Ala18 (Fig. 3E, F, and Table 4). sPLA2 functions by hydrolyzing sn-2 ester bonds in glycerol phospholipids found in lipoproteins and cell membranes, resulting in the production of non-esterified fatty acids and lysophospholipids[38]. Both of these products can trigger inflammation leading to the development of atherosclerotic plaque[8]. Increased sPLA2 activity could induce the risk of atherosclerosis[39]. Previous studies suggested that inhibition of sPLA2 activity could prevent atherosclerosis[40]. In brief, medicinal plants compound had an essential role for therapeutic development[41]. Moreover, plants serve as rich sources of drug compounds in traditional medicine[42].

Table 4. Protein-ligand interaction in detail.

Protein	Ligand	Binding Affinity (kcal/mol)	Position of Chemical Interaction	
			Hydrogen bond	Hydrophobic interaction
CETP	Inhibitor (Anacetrapib)	-11.3	Thr27	Ile15, Ala19, Val74, Val84, Phe197, Val198, Phe441, Phe461, Phe463
	Rubranine	-9.4	-	Cys13, Ile15, Leu23, Val198, Leu261 Phe441, Phe461
	(-)-4-Hydroxypanduratin A	-9.4	-	Cys13, Ile15, Val198, Ala202, Leu261, Phe263, Phe441, Phe461
ACAT1	Inhibitor (ART-101)	-9.3	Trp420	Leu377, Phe381, Trp408, Phe479, Leu507
	Rubranine	-10.7	-	Phe381, Trp407, Phe479, Phe482, Phe486, Leu507
	5,7-Dihydroxy-8-C-geranylflavanone	-10.7	-	Leu377, Phe381, Trp407, Trp420, Phe479, Phe482, Phe486, Leu514
OSC	Inhibitor (Ro 48-8071)	-6.9	Ala661	Leu397, Glu398, Lys462, Lys470
	Rubranine	-8.8	Glu594	Lys462, Leu466, Lys542, Tyr543, Arg718, Leu722
	5,7-Dihydroxy-8-C-geranylflavanone	-8.5	Glu594, Arg663	Glu398, Lys462, Leu466, Lys542, Tyr543, Lys546, Ala597
sPLA2	Inhibitor (KH064)	-8.2	Gly29, Val30	Leu2, Ala17, Ala18, Gly31, Asp48, Lys52, Lys62
	Rubranine	-9.8	Gly29	Leu2, Phe5, Ile9, Ala17, Ala18, Tyr51, Phe98
	5,7-Dihydroxy-8-C-geranylflavanone	-8.7	Gly29	Leu2, Val3, Phe5, His6, Ala17, Ala18, Cys44

_: the same amino acids where inhibitors and compounds interact with protein

CONCLUSION

Flavonoids and essential oils were the predominant compounds found in fingerroot. All of the compounds present in fingerroot exhibit characteristics that make them suitable candidates for drug development. Seven compounds are predicted to possess anti-atherosclerosis activity, namely dihydrochrysin, sakuranetin, isopimaric acid, 2S-pinocembrin, 5,7-dihydroxy-8-C-geranylflavanone, 7,4'-dihydroxy-5-methoxyflavanone, 5,7-dihydroxy-8, and 7-methoxy-5-hydroxy-8-geranylflavanone. Several of these compounds bind to the active sites of atherosclerosis-related proteins (CETP, ACAT1, OSC, and sPLA2) with lower binding affinity values than the inhibitors. Based on this study, it can be concluded that fingerroot is predicted to have high potential as an anti-atherosclerosis agent by inhibiting the activity of the four atherosclerosis-related proteins. However, further research using in vitro and in vivo approaches is essential to confirm the exact anti-atherosclerosis potency of fingerroot.

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استكشاف المركبات النشطة بيولوجيًا المحتملة من Fingerroot (Boesenbergia rotunda L.) كمثبط للبروتينات المرتبطة بتصلب الشرايين (CETP، ACAT1، OSC، ، sPLA2:) دراسة في السيليكون

محمد هرماوان ويديانادا [1, 2]، كوني أنجي كورنياساري [1]، فجار موستيكا علم [1]، واهيو كورور رزكي [3]، تيم جوديفريدوس أنطونيوس دينجز [4]، عارف نور محمد أنصوري [5, 6]، يولاندا أنطونيوس [7]*

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ملخص

يُعرف Boesenbergia rotunda L. (fingerroot) بأنه أحد النباتات الطبية الإندونيسية ذات الفاعلية الكبيرة في علاج الأمراض المختلفة، بما في ذلك تصلب الشرايين. تهدف هذه الدراسة إلى تحليل الفعالية المضادة لتصلب الشرايين للمركبات النشطة بيولوجيًا في جذور الأصابع من خلال تثبيط أربعة بروتينات مرتبطة بتصلب الشرايين (CETP و ACAT1 و OSC و sPLA2). المركبات النشطة بيولوجيًا من B. rotunda المسترجعة من قاعدة بيانات KnapSack، تم التنبؤ بخاصية تشابه الدواء باستخدام خادم الويب SwissADME، وتوقع النشاط الحيوي للمركب باستخدام خادم PASSOnline. تم إجراء تنبؤ الموقع النشط والتحقق من صحة البروتينات باستخدام خادم الويب SCFBio و Autodock Vina. تم إجراء الالتحام المحدد بين مركبات الإصبع والبروتينات بواسطة AutoDock Vina. Fingerroot يحتوي على 20 مركبًا حيويًا مع خصائص دوائية قوية. علاوة على ذلك، dihydrochrysin، sakuranetin، isopimaric acid، S-pinocembrin2، 5،7-dihydroxy-8-C-geranylflavanone، 4،7'-dihydroxy-5-methoxyflavanone، 5 dan، 8-7-dihydroxy-، و 7-methoxy-5-hydroxy-8-geranylflavanone من المتوقع أن يمتلك أنشطة مضادة لتصلب الشرايين. كان للروبرانين و (-) - 4-هيدروكسي باندوراتين A أقل درجة تقارب ملزمة مع CETP. اثنان من المركبات ذات أقل تقارب ارتباط في التفاعل مع ACAT1 و OSC و sPLA2 هما الروبرانين و 5،7-ثنائي هيدروكسي-8-سي-جيرانيل فلافانون. يمكن الاستنتاج أن جذر الإصبع لديه إمكانات عالية كعامل مضاد لتصلب الشرايين من خلال تثبيط 4 بروتينات مرتبطة بتصلب الشرايين على أساس نهج السيليكو. **الكلمات الدالة:** ACAT1، تصلب الشرايين، CETP، الالتحام الجزيئي، OSC، sPLA2.

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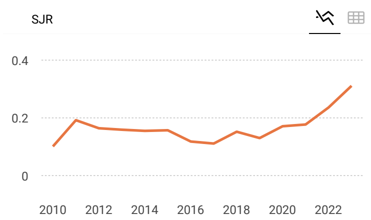

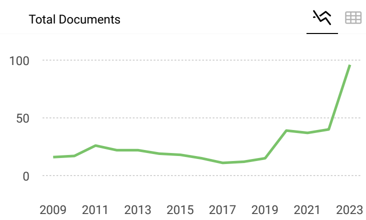

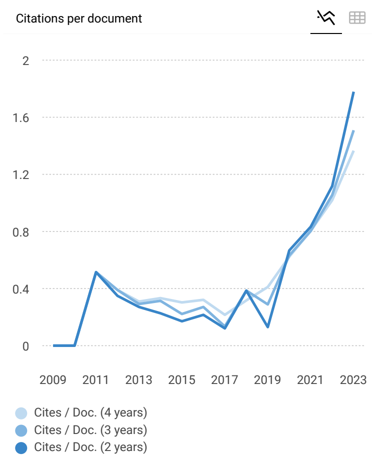

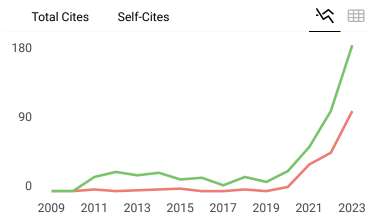

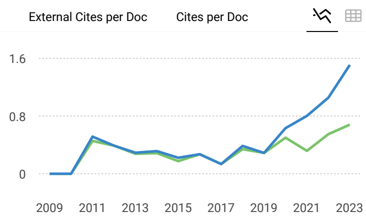

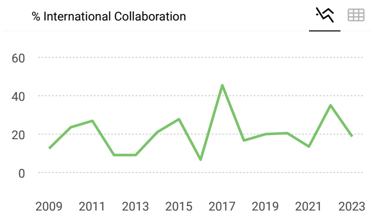

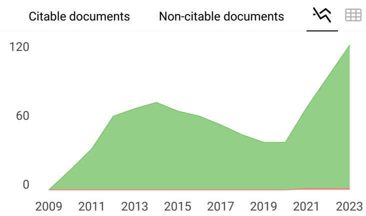

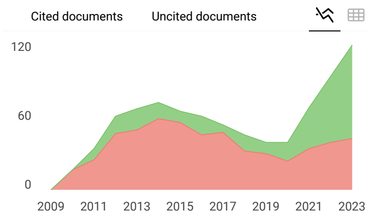

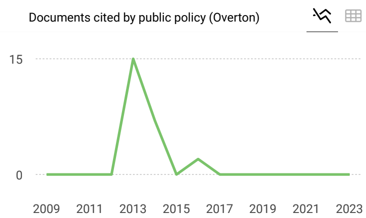

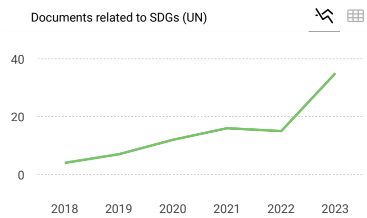

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A **Asri D.** 4 years ago

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What the meaning of coverage? Does It mean that the article that published in JJPS started in January 2021, not Scopus indexed anymore?
Thank you

reply

SCImago Team

Melanie Ortiz 4 years ago

Dear Asri,
Thank you for contacting us.
The Coverage data shown above indicates the period in which the journal has been indexed in Scopus database according to the latest update sent by Scopus (April 2020).
A paper will be considered as Scopus indexed as long as it has been published in the same period in which Scopus has indexed the journal.
Best Regards, SCImago Team

S **shatha ahmed** 4 years ago

تحية طيبة
لدي بحث ارغب بنشره في مجلتكم كم هي اجور النشر لطفا

reply

SCImago Team

Melanie Ortiz 4 years ago

Dear Shatha,
thank you for contacting us.
We are sorry to tell you that SCImago Journal & Country Rank is not a journal. SJR is a portal with scientometric indicators of journals indexed in Elsevier/Scopus.
Unfortunately, we cannot help you with your request, we suggest you visit the journal's homepage (See submission/author guidelines) or contact the journal's editorial staff , so they could inform you more deeply.
Best Regards, SCImago Team

B **bakli sabrina** 5 years ago

Hello,
I want to publish my article in Jordan Journal of Pharmaceutical Sciences.
cordially

reply

SCImago Team

Melanie Ortiz 5 years ago

Dear Bakli, thank you very much for your comment, unfortunately we cannot help you with your request. We suggest you look for author's instructions/submission guidelines in the journal's website. Best Regards, SCImago Team

Leave a comment

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Scopus Preview

Source details

Jordan Journal of Pharmaceutical Sciences

Years currently covered by Scopus: from 2009 to 2024

Publisher: The University of Jordan

ISSN: 1995-7157

Subject area: Pharmacology, Toxicology and Pharmaceutics: Pharmaceutical Science

Source type: Journal

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CiteScore 2023
1.7

SJR 2023
0.311

SNIP 2023
0.872

CiteScore | CiteScore rank & trend | Scopus content coverage

CiteScore 2023

$$1.7 = \frac{369 \text{ Citations 2020 - 2023}}{211 \text{ Documents 2020 - 2023}}$$

Calculated on 05 May, 2024

CiteScoreTracker 2024

$$1.8 = \frac{356 \text{ Citations to date}}{197 \text{ Documents to date}}$$

Last updated on 05 August, 2024 • Updated monthly

CiteScore rank 2023

Category	Rank	Percentile
Pharmacology, Toxicology and Pharmaceutics — Pharmaceutical Science	#108/183	41st

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