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In silico molecular docking and ADMET prediction of *Ginkgo biloba* biflavonoids as dual inhibitors of human HMG-CoA reductase and alpha-amylase

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Abstract: There is an increasing interest in investigating phytochemicals as inhibitors of HMG-CoA reductase (HMGR) and α-amylase enzymes. Inhibition of these enzymes helps manage hypercholesterolemia and diabetes by reducing cholesterol synthesis and blood sugar levels, respectively. In this study, computational techniques via molecular docking and ADMET prediction were used to determine the potential of five *Ginkgo biloba* biflavonoids (amentoflavone, bilobetin, ginkgetin, isoginkgetin, and sciadopitysin) as dual inhibitors of HMGR and α-amylase. Amentoflavone (-42.26 kJ/mol) and bilobetin (-41.00 kJ/mol) exhibited stronger binding affinities to HMGR compared to the reference drug atorvastatin (-38.91 kJ/mol). For α-amylase, amentoflavone (-48.12 kJ/mol), bilobetin (-47.28 kJ/mol), and ginkgetin (-46.44 kJ/mol) exhibited stronger binding affinities compared to the reference drug acarbose (-43.93 kJ/mol). These docking results indicate that amentoflavone and bilobetin have the potential to act as dual inhibitors of these two enzymes. ADMET analysis showed that bilobetin demonstrated favorable oral bioavailability and drug-likeness, adhering to Lipinski's rule of five. Despite exhibiting low gastrointestinal absorption, it was predicted to be neither mutagenic nor hepatotoxic. Therefore, bilobetin is a promising candidate for dual antidiabetic and antihypercholesterolemic applications. Further *in vitro* and *in vivo* studies are recommended to confirm these promising results.

Keywords: bilobetin; hypercholesterolemia; diabetes; binding affinity; pharmacokinetic properties; computer-aided drug discovery.

INTRODUCTION

HMG-CoA (3-hydroxy-3-methylglutaryl-coenzyme A) reductase (HMGR) and alpha-amylase (α-amylase) are two key human metabolic enzymes involved in chronic diseases such as hypercholesterolemia and diabetes. HMGR is the key regulatory enzyme in the mevalonate

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pathway, facilitating the conversion of HMG-CoA to mevalonate, which is an essential step in the synthesis of cholesterol.[1] Inhibition of this enzyme has proven to be an effective strategy for lowering cholesterol levels and helps prevent atherosclerosis, heart attack, and coronary heart diseases.[2,3] Statins (e.g., atorvastatin) are a class of cholesterol-lowering drugs that inhibit HMGR. However, prolonged use of statins is associated with various negative effects, commonly referred to as "statin-associated adverse effects". These effects include skeletal muscle disorders such as rhabdomyolysis and myopathy, liver dysfunction, and an increased risk of diabetes.[4,5] α-amylase, on the other hand, is a digestive enzyme primarily produced in the pancreas and salivary glands, responsible for the digestion of carbohydrates in humans.[6] Pancreatic α-amylase breaks down α-1,4 glycosidic bonds in complex carbohydrates like starch, converting them into oligosaccharides and disaccharides. These are then further degraded by glucosidases into glucose units that can be absorbed by the small intestine.[7,8] The rapid digestion of starch can lead to elevated postprandial blood glucose levels (hyperglycemia) in diabetic patients.[9] Postprandial hyperglycemia (PPHG) contributes to the development of type 2 diabetes mellitus and has been identified by epidemiological studies as an independent risk factor for cardiovascular disease.[10,11] Inhibiting the enzymatic action of α-amylase can help reduce PPHG and lower the risk of developing diabetes.[12] Acarbose, an inhibitor of α-amylase, is a medication used in the management of diabetes. While effective in controlling PPHG in many patients, its long-term administration is often associated with gastrointestinal adverse effects.[13] Given the adverse effects associated with current HMGR and α-amylase inhibitors, there is a need to explore alternative treatments that are both effective and have fewer side effects for managing hypercholesterolemia and diabetes.

Medicinal plants are increasingly being studied as potential sources of therapeutic and bioactive compounds for inhibiting HMGR and α-amylase.[14,15] They offer several benefits, like lesser side effects, safer profiles, effectiveness in treating diseases, widespread accessibility, and low cost.[16] One promising medicinal plant is *Ginkgo biloba*, commonly known as ginkgo or maidenhair tree. With a long history in traditional Chinese medicine, both its leaves and seeds have been utilized for centuries to treat a variety of diseases. Ginkgo has been used ethnomedicinally across different cultures worldwide, including in Asia, America, Europe, and Australia, for treating respiratory and cardiovascular diseases, nervous system disorders, urinary problems, and memory improvement.[17] Currently, ginkgo leaf extracts are primarily available as herbal supplements for improving memory.

The therapeutic and bioactive characteristics of *G. biloba* are thought to be associated with its flavonoids and terpene trilactones.[17] Biflavonoids, which are dimers of flavonoids, are important phytochemical constituents of *G. biloba*. The most predominant biflavonoids in *G. biloba* are sciadopitysin, ginkgetin, bilobetin, isoginkgetin, and amentoflavone. These compounds have been reported to possess various biological activities, including antibacterial, antifungal, antiviral, antioxidant, anticancer, and anti-inflammatory activities.[18] Although *G. biloba* biflavonoids are recognized as compounds with potent health-promoting properties, their specific potential role in the treatment of cardiovascular and metabolic diseases, such as hypercholesterolemia and diabetes, remains largely understudied.

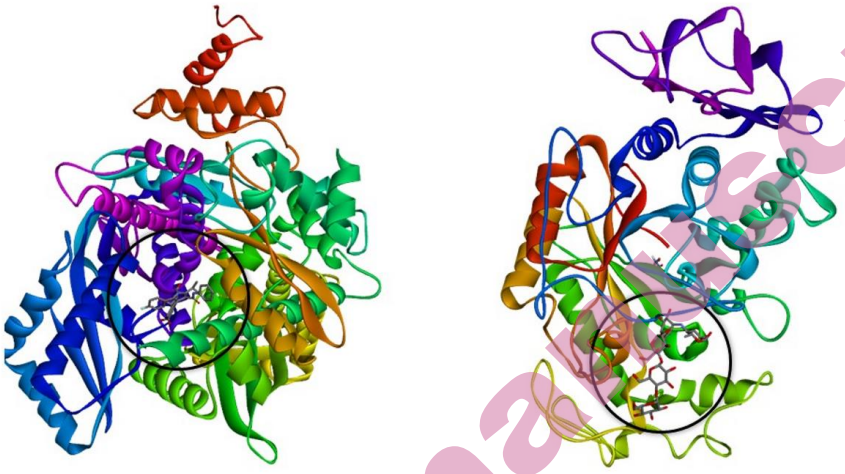
Traditional drug discovery is a complex, expensive, and lengthy process. On average, the traditional drug development pipeline requires around 12 years and 2.7 billion USD to bring a new drug from initial research to market.[19] In recent years, *in silico* or computer-aided drug discovery (CADD) approaches have been widely adopted to improve the efficiency of drug development.[20] These techniques enable researchers to virtually screen thousands of compounds, identify potential drug candidates at an early stage, and minimize the reliance on expensive and time-intensive laboratory experiments. Molecular docking, a key component of CADD, predicts the binding orientation and affinity of small molecules to target proteins or enzymes, which are crucial for determining drug efficacy.[21] Additionally, ADMET prediction, another component of CADD, estimates a drug's pharmacokinetic and toxicological properties, helping to prioritize compounds with favorable drug-like characteristics.

Currently, there is a lack of comprehensive *in silico* study investigating the potential of *Ginkgo biloba* biflavonoids as dual inhibitors of HMG-CoA reductase and α-amylase. To address this gap, molecular docking was used in this work to evaluate the binding affinities and interactions of five ginkgo biflavonoids (amentoflavone, bilobetin, ginkgetin, isoginkgetin, and sciadopitysin) with these two enzyme targets. Additionally, ADMET predictions were performed to evaluate the drug-likeness and potential pharmacokinetic properties of these compounds.

EXPERIMENTAL

Preparation of target proteins

The 3D crystal structures of the human HMG-CoA reductase (HMGR) enzyme (PDB ID: 1HWK)[22] in complex with atorvastatin, and the human pancreatic α-amylase enzyme (PDB ID: 2QV4)[23] in complex with acarbose (Fig. 1), were downloaded in PDB format from the Research Collaboratory for Structural Bioinformatics Protein Data Bank (PDB) (https://www.rcsb.org/). These structures have resolutions of 2.22 Å and 1.97 Å, respectively. Because HMGR is a symmetric tetramer, only chains A and B were used in the docking simulation.[24] In contrast, for α-amylase, which consists of a single protein chain, only chain A was used. The PDB files for both proteins were prepared using Discovery Studio Visualizer (DSV) software version 21.1.0.20298, with all bound substances, such as co-crystallized ligands, cofactors, and water molecules, removed from their structures. AutoDockTools[25] software version 1.5.6 was then used to further prepare the proteins by adding polar hydrogens and Kollman charges. Finally, the proteins were saved in PDBQT format, the required format for docking.



(a) (b)

Fig 1. 3D Crystal structures of human enzymes (a) HMGR (PDB ID: 1HWK) with co-crystallized atorvastatin (encircled in black) and (b) α-amylase (PDB ID: 2QV4) with co-crystallized acarbose (encircled in black) bound at the active site.

Preparation of ligands

The five most common ginkgo biflavonoids[18] were selected as ligands to target both HMGR and α-amylase, with their structural formulas shown in Fig. 2. The 3D structures of these ligands, in SDF format, were downloaded from the PubChem database (https://pubchem.ncbi.nlm.nih.gov/). Their structures were then optimized using Avogadro[26] software version 1.2.0, applying the universal force field and steepest descent algorithm. The ligands were further prepared using AutoDockTools, with the number of torsions set to default. Finally, the ligands were saved in PDBQT format, the required format for docking.

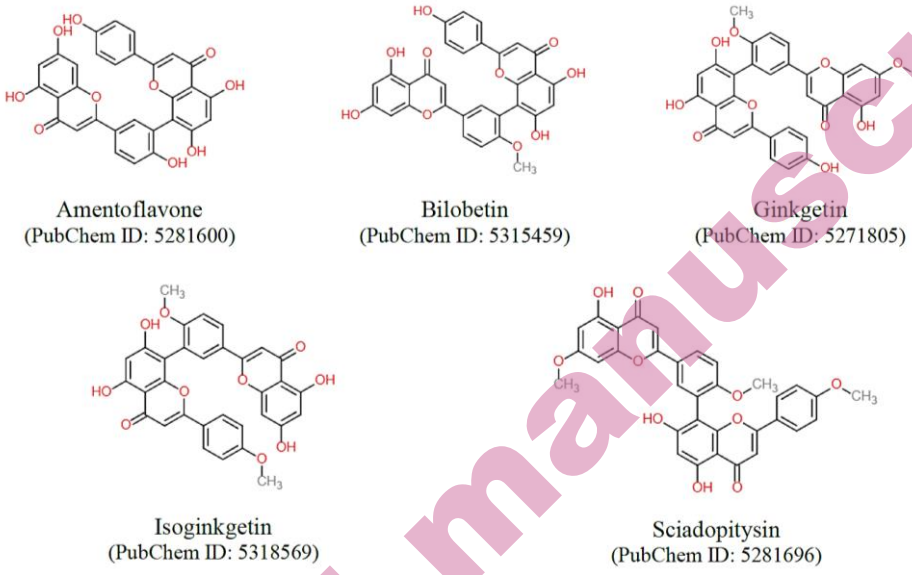


Fig 2. Structural formulas of the studied biflavonoids.

Molecular docking

AutoDock Vina[27] software version 1.1.2 was used for the rigid protein-flexible ligand molecular docking simulations. The search space for ligand binding was restricted to a grid box covering the binding sites of the co-crystallized ligands,[24] atorvastatin and acarbose. The spacing between grid points was set to 1 Å, with the grid coordinates provided in Table I. AutoDock Vina generated several docking conformations for each ligand, each with a specific binding affinity. The conformation with the most negative binding affinity for each ligand was recorded for further analysis. Protein-ligand interactions were then visualized and analyzed using DSV.[24]

TABLE I. Grid coordinates for the docking simulation targeting HMGR and α-amylase

Grid	HMGR			α-amylase		
	x	y	z	x	y	z
Center	2.894171	-9.553439	-12.241561	12.384745	48.136073	26.209218
Size	18	22	24	25	25	30

ADMET prediction

The drug-likeness and pharmacokinetic properties of the studied biflavonoids, including absorption, distribution, metabolism, excretion, and toxicity (ADMET), were predicted using the SwissADME[28] (http://www.swissadme.ch/) and pkCSM[29] (http://biosig.lab.uq.edu.au/pkcsm/prediction) online computational tools.

RESULTS AND DISCUSSION

Validation of docking protocol

AutoDock Vina's accuracy as a molecular docking tool was evaluated by redocking atorvastatin and acarbose into the active sites of HMGR and α-amylase, respectively, and comparing their orientations to the native crystal structures using root-mean-square deviation (RMSD). The obtained RMSD values of the superimposed structures (Fig. 3) were 0.8061 Å for atorvastatin and 1.2590 Å for acarbose, both below the 2.0 Å threshold,[24,30] confirming the reliability of AutoDock Vina for docking the five biflavonoids into the active site of these target proteins.

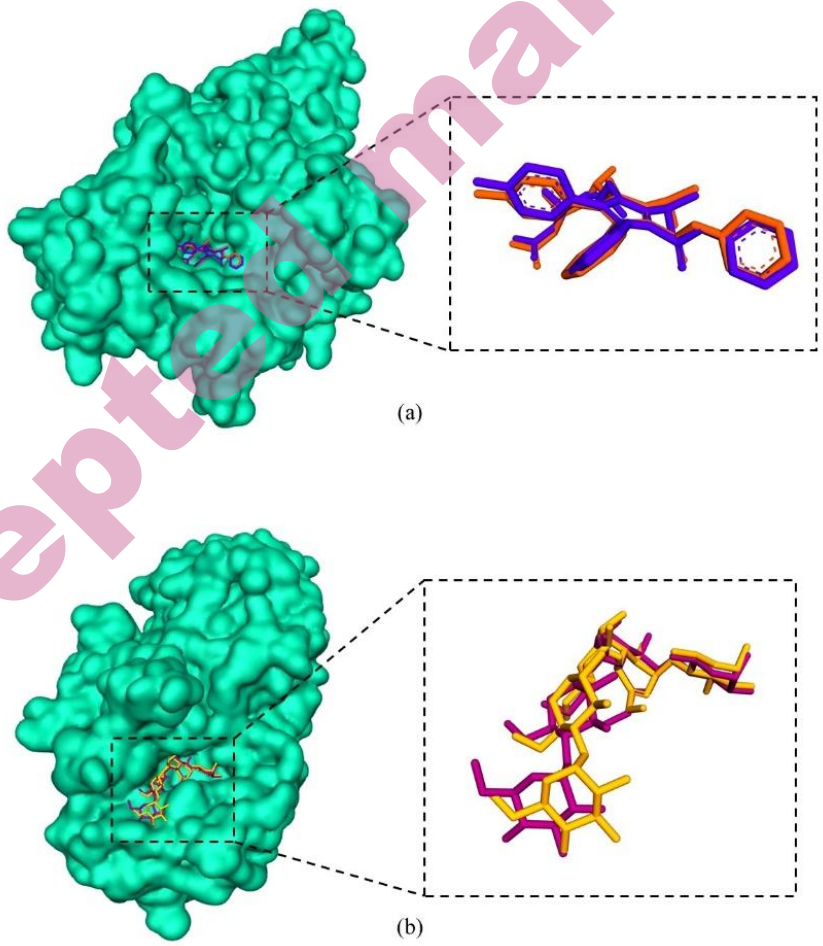


Fig 3. Superimposed 3D structures of (a) the co-crystallized (orange) and docked (blue) orientations of atorvastatin within the active site of HMGR, and (b) the co-crystallized (dark fuchsia) and docked (yellow) orientations of acarbose within the active site of α-amylase.

Molecular docking results

The efficacy of a drug depends on its binding affinity and interactions with the target protein.[21] Binding affinity measures how strongly a ligand interacts with a target protein[31] and is typically expressed in energy units, specifically kilojules per mole (kJ mol^{-1}). In this study, molecular docking was employed to determine the binding affinities of five ginkgo biflavonoids towards HMGR and α-amylase. As presented in Table II, the binding affinities of the studied biflavonoids ranged from -34.73 to -42.26 kJ mol^{-1} for HMGR and from -42.26 to -48.12 kJ mol^{-1} for α-amylase. The negative sign indicates that the binding interaction between the biflavonoid ligands and the target proteins is spontaneous and energetically favorable, allowing the ligands to naturally bind to the target proteins without external energy input. More negative values also suggest stronger affinities and more stable binding.[32,33]

TABLE II. Binding affinity values of the five *Ginkgo biloba* biflavonoids towards human enzymes HMGR and α-amylase

Ligand name	Binding affinity, kJ mol^{-1}	
	HMGR	α-amylase
Amentoflavone	-42.26	-48.12
Bilobetin	-41.00	-47.28
Ginkgetin	-37.24	-46.44
Isoginkgetin	-38.07	-42.68
Sciadopitysin	-34.73	-42.26
Atorvastatin [a]	-38.91	—
Acarbose [b]	—	-43.93

[a] Reference HMGR inhibitor; [b] Reference α-amylase inhibitor

Docking results showed that two biflavonoids, amentoflavone (-42.26 kJ/mol) and bilobetin (-41.00 kJ/mol), exhibited stronger binding affinities to HMGR compared to the reference drug, atorvastatin (-38.91 kJ/mol). For α-amylase, three biflavonoids—amentoflavone (-48.12 kJ/mol), bilobetin (-47.28 kJ/mol), and ginkgetin (-46.44 kJ/mol)—showed stronger binding affinities than the reference drug, acarbose (-43.93 kJ/mol). A ligand with a highly negative binding affinity is generally considered to have good inhibitory potential, as strong binding to the enzyme's active site usually correlates with effective inhibition of the enzyme's activity by preventing it from performing its normal function. These docking results indicate that amentoflavone and bilobetin have the potential to act as dual inhibitors of HMGR and α-amylase, potentially offering better inhibitory activity than the standard drugs. Since HMGR is responsible for cholesterol synthesis and α-amylase is involved in the metabolism of carbohydrates into simple sugars, the strong binding of these biflavonoids to both enzymes could potentially inhibit their activities, leading to reduced cholesterol and blood sugar levels. Therefore,

amentoflavone and bilobetin may possess both antihypercholesterolemic and antidiabetic properties.

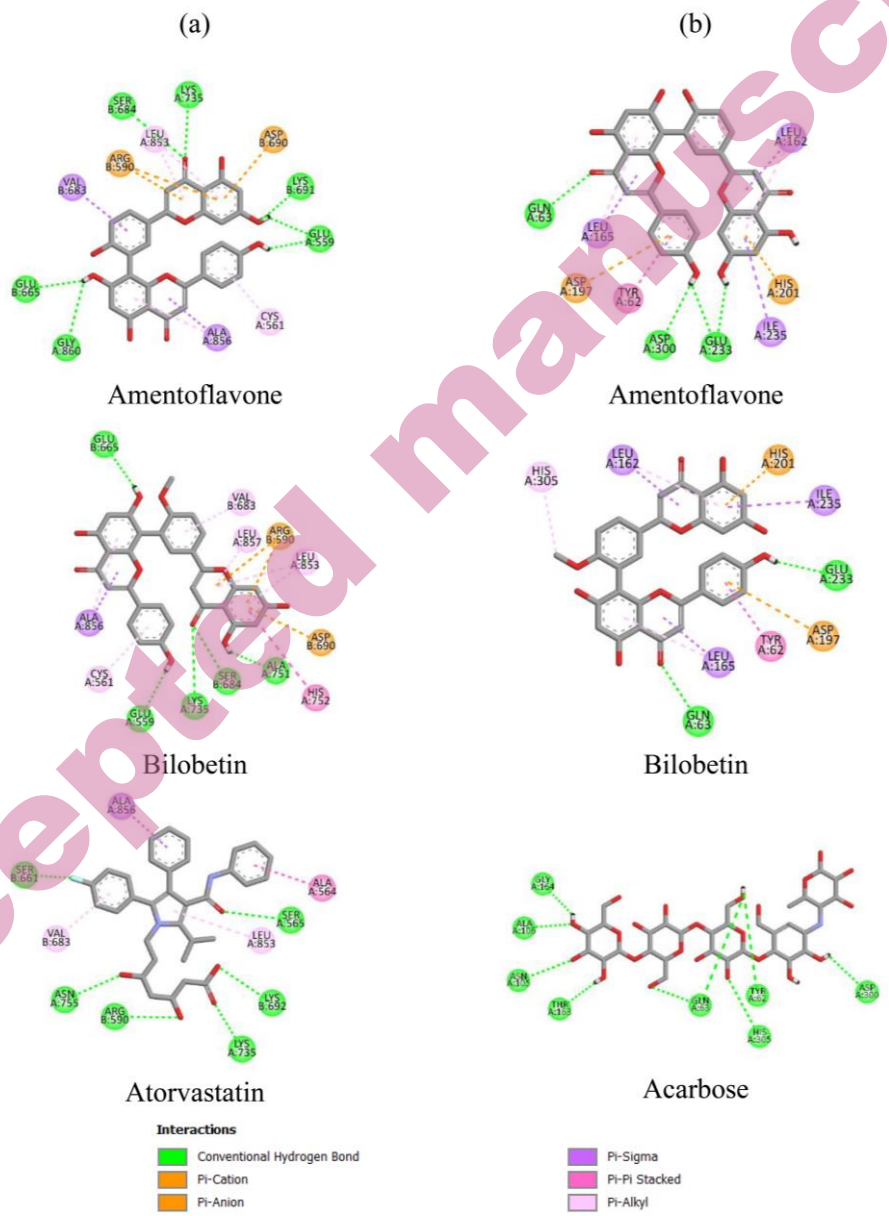


Fig 4. 2D interaction diagrams of (a) amentoflavone, bilobetin, and atorvastatin in complex with HMGR and (b) amentoflavone, bilobetin, and acarbose in complex with α-amylase. Pi-sigma, pi-pi stacked, and pi-alkyl interactions are classified as hydrophobic interactions, while pi-cation and pi-anion interactions are classified as electrostatic interactions.

The molecular interactions of the top two ligands with dual inhibitory potentials, amentoflavone and bilobetin, with HMGR and α-amylase, are presented in Fig. 4. The amino acids involved in the protein-ligand interactions are summarized in Table III and Table IV. The docking study predicted the existence of hydrogen bonds, hydrophobic, and electrostatic intermolecular noncovalent interactions between the biflavonoids and HMGR and α-amylase. These interactions are crucial for stabilizing the protein-ligand complexes.[34]

TABLE III. Molecular interactions of the top two biflavonoids with HMGR amino acids

Ligand Name	HMGR Amino Acids Involved in Interaction		
	Hydrogen Bonds	Hydrophobic Interactions	Electrostatic Interactions
Amentoflavone	Lys735A, Ser684B, Lys691B, Glu559A, Gly860A, Glu665B	Ala856A, Val683B, Cys561A, Leu853A	Arg590B, Asp690B
Bilobetin	Lys735A, Ser684B, Glu559A, Ala751A, Glu665B	Ala856A, His752A, Cys561A, Val683B, Leu853A, Leu857A	Arg590B, Asp690B
Atorvastatin [a]	Ser565A, Lys735A, Asn755A, Arg590B, Ser661B, Lys692B	Ala856A, Ala564A, Leu853A, Val683B	None

[a] Reference HMGR inhibitor

TABLE IV. Molecular interactions of the top two biflavonoids with α-amylase amino acids

Ligand Name	α-amylase Amino Acids Involved in Interaction		
	Hydrogen Bonds	Hydrophobic Interactions	Electrostatic Interactions
Amentoflavone	Gln63, Glu233, Asp300	Leu162, Leu165, Ile235, Tyr62	His201, Asp197
Bilobetin	Gln63, Glu233	Leu162, Leu165, Ile235, Tyr62, His305	His201, Asp197
Acarbose [a]	Gln63, Asn105, Ala106, His305, Thr163, Gly164, Tyr62, Asp300	None	None

[a] Reference α-amylase inhibitor

Analysis of the HMGR-amentoflavone complex (Fig. 4a) revealed that amentoflavone formed multiple hydrogen bonds with key residues Lys735A, Ser684B, Lys691B, Glu559A, Gly860A, and Glu665B. It also established hydrophobic interactions with Ala856A, Val683B, Cys561A, and Leu853A, and electrostatic interactions with Arg590B and Asp690B. Similarly, bilobetin demonstrated a stable binding profile, forming hydrogen bonds with Lys735A, Ser684B, Glu559A, Ala751A, and Glu665B amino acids of HMGR. Its binding was further stabilized by hydrophobic interactions involving Ala856A, His752A, Cys561A, Val683B, Leu853A, and Leu857A, as well as electrostatic interactions with Arg590B and Asp690B.

In comparison, atorvastatin, the standard drug, also interacted with HMGR through hydrogen bonds with Lys735A, Ser565A, Asn755A, Arg590B, Ser661B,

and Lys692B. Its binding was stabilized by hydrophobic interactions with Ala856A, Ala564A, Leu853A, and Val683B. However, unlike amentoflavone and bilobetin, atorvastatin lacked electrostatic interactions (Table III), which may account for its relatively weaker binding affinity compared to the two biflavonoids.

Interestingly, amentoflavone and bilobetin share key hydrogen bonds with Lys735A and hydrophobic interactions with Ala856A and Val683B, similar to atorvastatin. As a competitive inhibitor of HMGR, atorvastatin competes with the enzyme's natural substrate (HMG-CoA) for binding at the active site, thereby inhibiting the enzyme's ability to catalyze the conversion of HMG-CoA into mevalonate, a crucial step in cholesterol biosynthesis. These findings suggest that amentoflavone and bilobetin may inhibit HMGR through a similar mechanism.

On the other hand, analysis of the α-amylase-amentoflavone complex (Fig. 4b) revealed that amentoflavone formed hydrogen bonds with key residues Gln63, Glu233, and Asp300, while also establishing hydrophobic interactions with Leu162, Leu165, Ile235, and Tyr62. Additionally, it formed electrostatic interactions with His201 and Asp197. Bilobetin similarly demonstrated strong binding to α-amylase, forming hydrogen bonds with Gln63 and Glu233. It also formed hydrophobic interactions with Leu162, Leu165, Ile235, Tyr62, and His305, along with electrostatic interactions with His201 and Asp197.

Acarbose, the standard antidiabetic drug, primarily interacted with α-amylase through a network of hydrogen bonds involving residues Gln63, Asn105, Ala106, His305, Thr163, Gly164, Tyr62, and Asp300. Notably, acarbose lacked the hydrophobic and electrostatic interactions observed with both amentoflavone and bilobetin (Table IV). The stronger binding affinity of amentoflavone and bilobetin to α-amylase, compared to acarbose, may be attributed to their hydrophobic and electrostatic interactions. This suggests that these two biflavonoids might inhibit α-amylase better than acarbose.

When comparing these interactions, it is evident that both amentoflavone and bilobetin share key hydrogen bonding with the Gln63 and Tyr62 amino acids, similar to acarbose. Acarbose also functions through competitive inhibition by binding to the active site of α-amylase, thereby inhibiting the catalytic breakdown of carbohydrates into simpler sugars. The similarity in interactions suggests that these two biflavonoids may inhibit α-amylase through a mechanism of action similar to that of acarbose.

Drug-likeness and ADMET profiles

The Lipinski's rule of five (Ro5), also known as Pfizer's rule of five, is a widely recognized set of guidelines used in the pharmaceutical industry to evaluate the drug-likeness and oral bioavailability of compounds during the early stages of drug development. The rule[35] states that an orally active drug should generally not violate more than one of the following criteria: hydrogen bond donors < 5, hydrogen bond acceptors < 10, molecular weight < 500 g/mol, and octanol-water

partition coefficient (MlogP) < 5. Table V presents the drug-like properties of the top two ligands with dual inhibitory potentials, amentoflavone and bilobetin. Bilobetin violates only the molecular weight criterion, whereas amentoflavone violates both the molecular weight and hydrogen bond donor criteria. These results suggest that bilobetin is more likely to be an orally active drug in humans compared to amentoflavone. Furthermore, the calculated bioavailability scores indicate that bilobetin has a 55% probability of being bioavailable, while amentoflavone has only a 17% probability. Therefore, bilobetin is a more promising drug candidate with better drug-like properties than amentoflavone.

TABLE V. Drug-like properties of the top two biflavonoids predicted by SwissADME

Property	Amentoflavone	Bilobetin
Molecular Weight, g/mol	538.5	552.5
MlogP	0.25	0.44
Hydrogen Bond Acceptors	10	10
Hydrogen Bond Donors	6	5
Lipinski's Rule Violations	2	1
Bioavailability Score	0.17	0.55

TABLE VI. ADMET (Admission, Distribution, Metabolism, Excretion, Toxicity) profiles of the top two biflavonoids

Parameter	Pharmacokinetic Property	Amentoflavone	Bilobetin
Absorption [a]	Gastrointestinal Absorption	Low	Low
	P-glycoprotein Substrate	No	No
Distribution [a]	Blood-Brain Barrier Permeability	No	No
Metabolism [a]	CYP1A2 Inhibitor	No	No
	CYP2C19 Inhibitor	No	No
	CYP2C9 Inhibitor	No	Yes
	CYP2D6 Inhibitor	No	No
	CYP3A4 Inhibitor	No	No
Excretion [b]	Total Clearance, mL min^{-1} kg^{-1}	3.05	3.72
Toxicity [b]	AMES Toxicity (Mutagenicity)	No	No
	Hepatotoxicity	No	No

[a] Predicted by SwissADME; [b] Predicted by pkCSM

Table VI presents the pharmacokinetic properties and ADMET profiles of amentoflavone and bilobetin. Both compounds exhibit low gastrointestinal (GI) absorption which may limit their effectiveness as orally administered drugs. However, both are not substrates for P-glycoprotein (P-gp), suggesting they may not be actively transported out of cells by this transporter,[36] potentially enhancing their bioavailability. Moreover, both biflavonoids do not penetrate the blood-brain barrier (BBB), indicating that they are unlikely to cause central nervous system side effects. Since the targets of these compounds, HMGR and α-amylase, are not located in the central nervous system, BBB penetration is not necessary for their therapeutic effects.[37] Cytochrome P450 (CYP450) enzymes play crucial roles in

drug metabolism and detoxification. They oxidize drugs and other xenobiotics in the body for excretion. There are several CYP450 isoforms, including CYP1A2, CYP2C19, CYP2C9, CYP2D6, and CYP3A4 which are involved in biotransformation of drugs. Inhibition of these CYP450 isoforms can affect drug metabolism and can lead to toxicity due to bioaccumulation.[29,37] The results showed that amentoflavone is a non-inhibitor of all these CYP450 isoforms, while bilobetin is a non-inhibitor of most of them, except for CYP2D6. This suggests that both compounds are metabolized efficiently and are less likely to interfere with the body's normal drug-metabolizing processes, reducing the risk of adverse drug interactions. The excretion parameter reveals that bilobetin has a slightly higher total clearance (3.72 ml/min/kg) compared to amentoflavone (3.05 ml/min/kg). These values are important for determining dosing rates to achieve steady-state concentrations.[29] Importantly, bilobetin and amentoflavone exhibit no mutagenic or hepatotoxic properties, suggesting favorable safety profiles. This lack of toxicity is a significant advantage for their therapeutic use, as it indicates a lower risk of side effects during treatment. Given the adverse effects associated with current HMGR and α-amylase inhibitors, amentoflavone and bilobetin present promising alternatives for managing hypercholesterolemia and diabetes. Their combination of effectiveness and low toxicity positions them as potential candidates for further development as safer therapeutic agents.

CONCLUSION

This study reports for the first time that both amentoflavone and bilobetin possess dual inhibitory activity against HMG-CoA reductase (HMGR) and α-amylase, as revealed by molecular docking, with binding affinities superior to those of the reference antihypercholesterolemic and antidiabetic drugs, atorvastatin and acarbose, respectively. These findings suggest that both compounds have the ability to inhibit key enzymes involved in cholesterol biosynthesis and carbohydrate metabolism. Pharmacokinetic predictions indicate that bilobetin is a more promising drug candidate than amentoflavone due to its better compliance with Lipinski's rule of five and a higher probability of oral bioavailability. Although bilobetin shows low gastrointestinal absorption, it is predicted to be non-mutagenic and non-hepatotoxic, supporting its favorable safety profile. Therefore, bilobetin is a potential candidate for treating hypercholesterolemia and diabetes, which could be more effective and safer to use. Further *in vitro* and *in vivo* studies are recommended to confirm these promising results.

Conflict of interests: The author declares no conflict of interests.

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И З В О Д

IN SILICO МОЛЕКУЛСКИ ДОКИНГ И ADMET ПРЕДВИЂАЊЕ БИФЛАВАНОИДА ИЗ *GINKGO BILOBA* КАО ДУАЛНИХ ИНХИБИТОРА ХУМАНЕ HMG-COA РЕДУКТАЗЕ И АЛФА АМИЛАЗЕ

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Повећава се занимање за фитохемикалије као инхибиторе ензима HMG-CoA редуктазе (HMGR) и α-амилазе. Инхибиција ових ензима помаже у третирању хиперхолестеролемије и дијабетеса редукујући синтезу холестерола, односно ниво шећера у крви. У овој студији су коришћене рачунарске технике за ADMET предвиђање да би се одредио потенцијал пет *Ginkgo biloba* бифлаваноида (аментофлавона, билобетина, гинкгетина, изогингкетина, и сајадоптисина) као дуалних инхибитора HMGR и α-амилазе. Аментофлавон (-42.26 kJ/mol) и билобетин (-41.00 kJ/mol) испољили су јачи афинитет везивања за HMGR у поређењу са референтним леком аторвастатином (-38.91 kJ/mol). За α-амилазу, аментофлавон (-48.12 kJ/mol), билобетин (-47.28 kJ/mol), и гинкгетин (-46.44 kJ/mol) испољен је јачи афинитет везивања у поређењу са референтним леком акарбозом (-43.93 kJ/mol). Резултати доковања указују да аментофлавон и билобетин имају потенцијала да делују као дуални инхибитори за ова два езима. ADMET анализа је показала да је билобетин испољио повољну оралну биодоступност и сличност са лековима, због поштовања правила петице Липинског. Упркос испољавању ниске гастроинтестиналне апсорпције, претсказано је да није ни мутаген ни хепатотоксичан. Према томе, билобетин је обећавајући кандидат за дуалну антидијабетску и антихиперхолестеролемијску примену. Препоручене су даљње *in vitro* и *in vivo* студије за потврђивање ових обећавајућих резултата.

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