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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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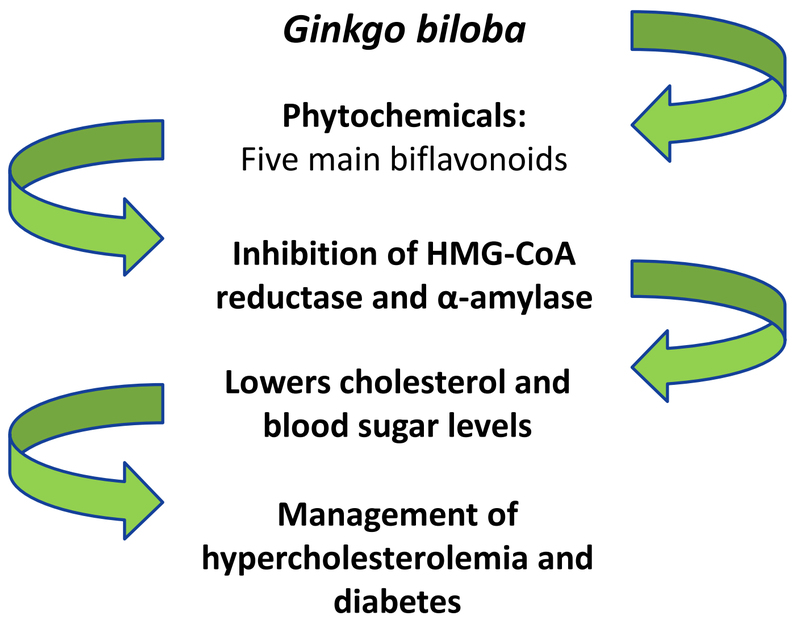
INTRODUCTION & AIM

HMG-CoA reductase (HMGR) and alpha-amylase are two key human metabolic enzymes linked to chronic diseases such as hypercholesterolemia and diabetes. While *Ginkgo biloba* biflavonoids exhibit various biological activities and health benefits, their antihypercholesterolemic and antidiabetic potential remains largely underexplored and understudied.

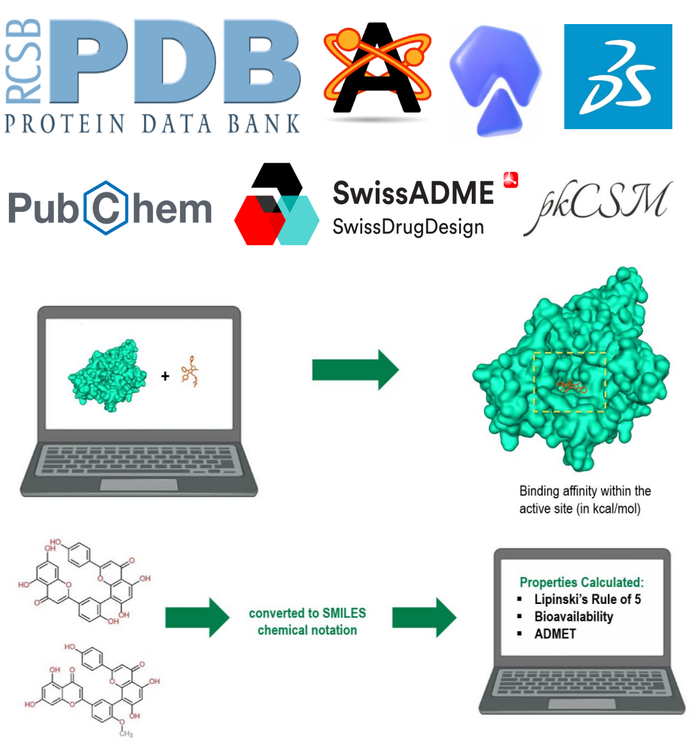


In this study, in silico or computational techniques via molecular docking and pharmacokinetic prediction were used to determine the potential of the five main *G. biloba* biflavonoids as dual inhibitors of human HMGR and α-amylase enzymes.

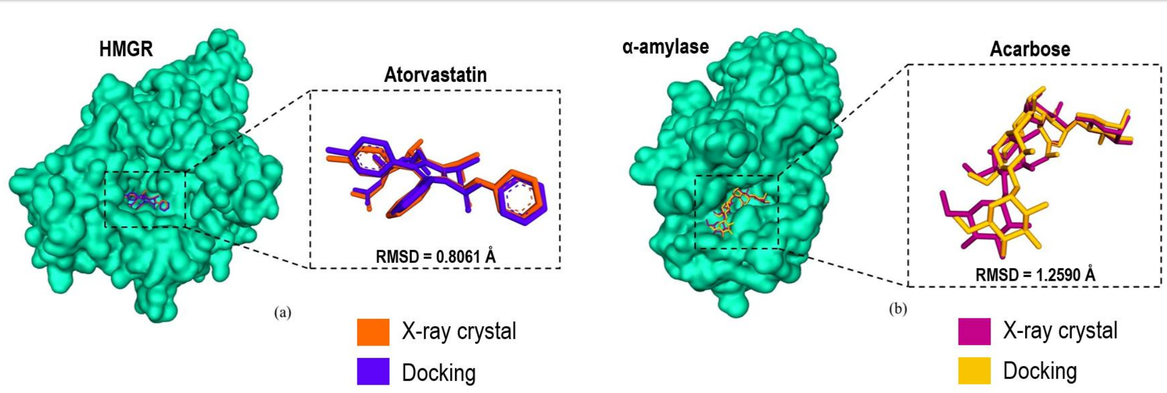
METHOD

Molecular docking using AutoDock Vina software was conducted to evaluate the binding affinities of five *G. biloba* biflavonoids (amentoflavone, bilobetin, ginkgetin, isoginkgetin, and sciadopitysin) with the two enzyme targets—HMGR and α-amylase. Their binding interactions were visualized using Discovery Studio Visualizer. Additionally, the drug-likeness and pharmacokinetic properties of the top biflavonoids, including absorption, distribution, metabolism, excretion, and toxicity (ADMET), were predicted using the SwissADME and pkCSM online computational tools.

G. biloba leaves



RESULTS & DISCUSSION



- The docked orientations successfully reproduced the experimentally determined X-ray crystal structures with RMSD < 2.0 Å, indicating valid and accurate predictions.

Table 1. Binding affinity values of the five *G. biloba* biflavonoids towards HMGR and α-amylase.

Ligand Name	HMGR Binding Affinity (kcal/mol)	α-amylase Binding Affinity (kcal/mol)
Amentoflavone	-10.1	-11.5
Bilobetin	-9.8	-11.3
Ginkgetin	-8.9	-11.1
Isoginkgetin	-9.1	-10.2
Sciadopitysin	-8.3	-10.1
Atorvastatin [a]	-9.3	—
Acarbose [b]	—	-10.5

[a] Standard HMGR inhibitor drug; [b] Standard α-amylase inhibitor drug

Table 2. Binding interactions of the top two biflavonoids with HMGR and α-amylase active site amino acids.

Ligand Name	Interactions with HMGR	Interactions with α-amylase
Amentoflavone	Hydrogen bonds, hydrophobic, and electrostatic	Hydrogen bonds, hydrophobic, and electrostatic
Bilobetin	Hydrogen bonds, hydrophobic, and electrostatic	Hydrogen bonds, hydrophobic, and electrostatic
Atorvastatin [a]	Hydrogen bonds and hydrophobic	—
Acarbose [b]	—	Hydrogen bonds

[a] Standard HMGR inhibitor drug; [b] Standard α-amylase inhibitor drug

Table 3. Pharmacokinetic properties of the top two biflavonoids.

Property	Amentoflavone	Bilobetin
Lipinski's Rule Compliance	No	Yes
Bioavailability Score	17%	55%
Absorption (Gastrointestinal)	Low	Low
Distribution, Metabolism, Excretion	Favorable	Favorable
Toxicity	Non-mutagenic, Non-hepatotoxic	Non-mutagenic, Non-hepatotoxic

CONCLUSION

- Amentoflavone and bilobetin, exhibited superior binding affinities compared to the standard drugs, atorvastatin and acarbose, highlighting their potential as dual inhibitors for both HMG-CoA reductase and α-amylase enzymes.
- Pharmacokinetic predictions indicate that bilobetin is a more promising drug candidate than amentoflavone due to its better compliance with Lipinski's rules and a higher oral bioavailability score.
- Bilobetin could be a potential candidate for treating hypercholesterolemia and diabetes, potentially offering better efficacy and safety than standard drugs.

FUTURE WORK

- It is recommended to conduct enzyme-based inhibition assays or experiments using animal models to further evaluate the therapeutic potential of these biflavonoids.