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Research Article

Acorus calamus Exhibiting Antidiabetic Activity: An *in vitro* and *in silico* Approach

Saptarshi Samajdar*

Department of Pharmaceutical Technology, Brainware University, Ramkrishnapur Road, Kolkata, West Bengal, INDIA.

ABSTRACT

Background: Diabetes mellitus is a multifaceted metabolic disorder characterized by chronically elevated blood glucose levels. Existing therapeutic strategies often present limitations such as adverse toxicity and the emergence of drug resistance, necessitating the search for safer and more effective alternatives. **Aim and Objectives:** The present study aimed to evaluate the antidiabetic potential of natural compounds derived from *Acorus calamus* through *in vitro* α-amylase inhibition and *in silico* molecular docking approaches targeting key diabetic protein receptors. **Materials and Methods:** A total of 12 natural compounds extracted from *Acorus calamus* were subjected to α-amylase inhibition assays to assess their *in vitro* antidiabetic activity. Additionally, molecular docking studies were performed using AutoDock Vina against two key protein targets, PDB IDs: 1XU7 and 3C45. Toxicity prediction, drug-likeness, and pharmacokinetic properties were analyzed using SwissADME and ProTox-II platforms. Molecular dynamics simulations were conducted using the iMODS server. **Results:** The *Acorus calamus* extract demonstrated a superior α-amylase inhibitory activity with an IC_{50} value of 2.87±0.38 mg/mL, outperforming the standard drug metformin (3.25±0.47 mg/mL). Among the 12 tested compounds, Galgravin exhibited the highest binding affinities for both 1XU7 (-8.5 kcal/mol) and 3C45 (-7.7 kcal/mol), surpassing those of metformin (-7.3 kcal/mol and -6.7 kcal/mol, respectively). Galgravin also showed the lowest predicted toxicity, highest LD_{50} values, favorable drug-likeness, and excellent bioavailability. Molecular dynamics studies further confirmed its stable interaction and favorable dynamic behavior. **Conclusion:** The findings highlight Galgravin, a compound from *Acorus calamus*, as a promising natural inhibitor of key diabetic targets, potentially surpassing metformin in efficacy and safety. These results advocate further *in vivo* and clinical evaluations to validate its therapeutic potential in diabetes management.

Keywords: α-Amylase assay, Molecular Docking, ADME Studies, Toxicity Prediction, Molecular Dynamics.

Correspondence:
Dr. Saptarshi Samajdar
Department of Pharmaceutical Technology, Brainware University, 398, Ramkrishnapur Road, Kolkata-700125, West Bengal, INDIA.
Email: saptarshisamajdar20@gmail.com
ORCID: 0009-0007-6081-5809

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INTRODUCTION

Acorus calamus, also known as sweet flag and bach, has a long history of usage as traditional medicine in China and India, with numerous ethnomedicinal actions described. *A. calamus* is a monocot plant with enormous potential. The plant thrives in high-water environments, particularly on damp soil.[1] Throughout history, traditional medicinal systems such as Ayurveda, Unani, Siddha, and Chinese medicine have used it to treat a variety of disorders, including nervous system, digestive, respiratory infections, muscular distropy, rheumatism, anti-inflammatory, colic, flatulence, and more. The majority of this plant's therapeutic potential has been attributed to both its rhizomes and leaves. A few active constituents from leaves, rhizomes and essential oils of *A. calamus* have been isolated and characterized. Although there have been reports of the plant having multiple activities against various diseases, but the anti-diabetic property of the plant is not well delineated.[2]

Diabetes mellitus is a complex and diverse set of metabolic disorders that disrupt the metabolism of carbohydrates, fats, and proteins. Diabetes mellitus cases have increased significantly in recent years. India is one of the world's diabetes hotspots, with a large diabetes epidemic currently ranked second only to China. In 2019, an estimated 7.7 crore adults had type II diabetes, with the figure expected to climb to more than 13.4 crore by 2045.[3] The explanation for such a large increase in numbers could be increased urbanisation, sedentary lifestyles, and dietary trends towards processed foods and sugary beverages. Another concerning trend is that over 57% of patients with diabetes are unaware of their condition. The majority of these instances involve type 2 diabetes, which can lead to serious consequences such as heart disease, stroke, renal failure, and blindness. Diabetes is a serious public health issue and one of the leading causes

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of economic burden in India, accounting for total healthcare spending, productivity loss, and poor quality of life. This outbreak must be tackled comprehensively.[4] With a long course and major consequences that frequently result in a high death rate, diabetes treatment in all nations consumes a significant number of resources, including medicines, diets, physical training, and so on. Thus, hunting for a new class of chemicals is critical to overcoming diabetes difficulties. There is an ongoing hunt for alternative medications.[5] As mentioned earlier, *A. calamus* with immense ethnobotanical potential, having history of working against myriads of diseases like cancer, ulcer, hepatitis, spasm, schizophrenia, gout, arthritis, anorexia etc., can fill the gap in alternate therapy.[6] Thus, the current work aims to evaluate the phytochemical, *in silico*, and *in vitro* antidiabetic activity of a methanolic extract from *A. calamus* leaves and rhizhomes in order to establish anti-diabetic capabilities.

MATERIALS AND METHODS

Materials

The West Bengal Medicinal Plant Board in Kalyani, West Bengal, India, provided the verified fresh leaves and rhizhomes of *Acorus calamus*. The AR-grade solvents were purchased from Oxford Lab Fine Chem LLP. The SRL labs provided the additional chemicals and reagent. Every drop of water was deionised.

Details of the plant

A. calamus belongs to the Acoraceae family in the monocotyledonous class of the Arales order and Angiospermae phylum. *Acorus* plants are semi-evergreen, *Rhizomatous perennials* with tufts of linear or sword-shaped leaves and spike-like flowers on the leafy extremities of their core stems (Figure 1). They measure 5 to 6 cm long and have fleshy, fragrant, and fibrous roots. The leaves are basal, with membrane leaf sheaths on the basal sides that are 4-5 mm wide, tapering up to one-third of the leaf length and gradually breaking off.[7]

Extraction and chemical tests of plant material

The plant materials were dried and extracted in methanol and petroleum ether (40-60) using ultrasonic extraction 20 kHz (Labman LMU3CD). The presence of phytochemicals was detected by chemical tests of alkaloids (Wagner's Test), Anthraquinone glycosides, resins, tanins (Ferric Chloride test), gums (Precipitate test), proteins (Millon's test), volatile oil (Sudan III test) and fixed oil (Filter Paper test). Based on the results, it was observed that methanolic extracts had presence of higher primary and secondary metabolites as compared to the petroleum ether extract, so it was chosen for further experimentation.[8,9]

Inhibition of α-amylase enzyme

Incubate 0.5 mL of test samples and reference drug (0.5-5 mg/mL) in 0.20 mM phosphate buffer (pH 6.9) with 0.5 mL of α-amylase solution at 25°C for 10 min. After that, each tube was given 0.5 mL of a 1% starch solution in 0.02 M sodium phosphate buffer (pH 6.9). The reaction mixtures were then incubated at 25°C for 10 min. The test tubes were then placed in a boiling water bath for 5 min before returning to room temperature. The reaction mixture was then diluted with 10 mL of pure water, and the absorbance was read at 540 nm. Controls represent 100% enzyme activity and were conducted in a similar manner, substituting the extract with solvent.[10]

Calculation of 50% Inhibitory Concentration (IC_{50})

The concentration of plant extracts required to scavenge 50% of the radicals (IC_{50}) was determined using the percentage scavenging activities at five different extract concentrations.[11] Percentage inhibition (I %) was calculated by,

$$I\ \% = (Ac\text{-}As)/Ac\ x100$$

Where A_c is the absorbance of the control and A_s is the absorbance of the sample.

In silico studies

Ligands preparation and optimization

According to Jaiswal *et al.*, 12 ligands from *A. calamus* leaves and rhizhomes described in various literatures were drawn in Chem Draw Professional 8.0 (Figure 2). The three-dimensional structures of the ligands were created in Open Babel and saved in SDF format for further preparation and molecular docking study.[12]

Preparation of receptor protein

The protein data bank provided crystallographic structures of human 11beta-hydroxysteroid dehydrogenase type I (PDB: 1XU7), which has been associated to type II diabetes and obesity, as well as the human dipeptidyl peptidase IV/CD26 complex (PDB: 3C45). To prepare the protein for molecular docking, water molecules were eliminated. Then, using the BIOVIA Discovery Studio 2021 Client application, hydrogen atoms were added to correct the ionisation of the amino acid residues.[13]

Drug like properties of the ligands

The cutoff values for all ligands' physicochemical properties were derived using LogS, LogP, Lipinski's rule of five, and the bioavailability score. Drug likelihood was calculated using the Molecular Parameters MW (Molecular Weight), HBD (hydrogen bond donor), HBA (hydrogen bond acceptor), log P (lipophilicity log), and bioavailability. The parameters were constructed using the SWISSADME server (www.swissadme.ch/index.php).[14]

Molecular docking analyses and visualization

After saving and loading the proteins in pdb format, the PyRx application was used to execute molecular docking with the

Auto dock Vina tool. The PyPx programme was used to assess which conformer was the most dependable. The grid volume for 1XU7 was 56.90 Å x 47.88 Å x 54.54 Å, and for 3C45 it was 77.64 Å x 76.07 Å x 75.13 Å. The intermolecular interactions of the *A. calamus* leaf ligands and the diabetes-related protein were discovered and visualised using the Discovery Studio 2021 Client program.[15]

Toxicity prediction

The top-scoring ligands were screened for toxicity in human cells using the ProTox III software (https://tox-new.charite.de/protox_III/). The website accepts a two-dimensional chemical structure as input and offers the most likely toxicity profile of the molecule for five models with confidence scores.[16]

Molecular Dynamics

This study employed Molecular Dynamics (MD) simulations, a computer method for analysing atomic and molecule movement across time, to understand the dynamic features of biological systems. The iMod server (iMODS) improved simulations by offering increased Normal Mode Analysis (NMA) and a user-friendly interface for exploring various pathways and interacting with 3D objects. Docking simulations employed RMSD to assess structural stability, ligand-protein interactions, and binding energies.[17] MD simulations using iMod helped analyse dynamic behaviour and binding interactions in ligand-protein complexes, yielding vital insights into structural dynamics and functional implications.

Statistical analysis

All the data reported are an average of triplicate observations. The data were expressed as means±standard deviation.

RESULTS AND DISCUSSION

Extract yield

The extracts was allowed to dry at 50°C in hot air oven and the % yield was calculated. And the % yield was found to be 9.32±0.39% for methanolic extract as compared to 4.87±0.47% for petroleum ether extracts. The dried extracts were kept in airtight container for further use.[18]

Chemical Tests

Various chemical tests were performed, revealing the presence of various phytoconstituents in the methanolic and Petroleum ether extract of the plant has been depicted in Table 1. From the table it can be observed that, methanolic extract have presence of alkaloid, fixed oil, proteins, carbohydrates and glycosides which is categorically much higher as compared to the petroleum ether extract. Based on these results, all the further experiments were conducted in methanolic extracts.[19]

In vitro antidiabetic study

Evaluation of *in vitro* α-amylase inhibitory activities using *A. calamus* leaf and rhizome extract. There was a dose-dependent increase in % inhibitory activity against α-amylase. At 0.5 mg/mL of extract, the percentage inhibition was 24.62±0.19, while at 5 mg/mL it was 77.36±0.37. The extract had an IC_{50} of 2.87±0.38 mg/mL (Table 2). The IC_{50} value for the conventional medication metformin was 3.25±0.47 mg/mL.[20]

In silico antidiabetic study

Free energy binding of bioactive compounds

Table 3 revealed the potential of each bioactive ligand produced from *A. calamus* leaves and rhizhomes to bind with proteins linked with type II diabetes in people. The range of binding affinities for the 12 ligands that were generated from *A. calamus* in protein 1XU7 was -8.5 to -4.9 kcal/mol, whereas the range for protein 3C45 was -7.7 to -4.4 (Table 3). The type II diabetes

Figure 1: *A. calamus* plant.

receptor human 11beta-hydroxysteroid dehydrogenase and human dipeptidyl peptidase IV/CD26 complex, as well as the most active ligands, were visualised using the Discovery Studio 2021 Client programme (Figures 3-6).[21] These specimens exhibited the anticipated interactions with the amino acids in the proteins active region, suggesting potent antagonistic activity against the protein that binds to the receptor linked to diabetes and suppresses the specific diabetic receptors. Galgravin had the highest binding affinity of -8.5 kcal/mol for the protein 1XU7, whereas beta asarone had the lowest binding affinity (-4.9 kcal/mol) (Table 4). The binding affinities of two natural molecules, Galgravin and Episesamine, were discovered to be higher than those of the commonly used anti-diabetic medicine metformin (-7.3 kcal/mol), implying that they could be utilised in the future to control diabetes. Similarly, for protein 3C45, Galgravin had the highest binding affinity (-7.7 kcal/mol), followed by Eudesmin (-7.3 kcal/mol). Terpineol has the lowest value (-4.4 kcal/mol). Again, only two compounds, Galgravin and Eudesmin, demonstrated a similar value to standard metformin (-6.7 kcal/mol). This suggests that the leaf and rhizome extract from *A. calamus* especially the compound Galgravin may have promising anti-diabetic properties.[22]

ADME Studies

The lipophilicity of the ligands from SwissADME was shown by their LogP values, which ranged from 1.83 to 4.48. Thus, this indicates higher water solubility of the ligands. Their molecular weights ranged from 164.20 to 388.45g. Almost every ligand set predicted value came inside Lipinski's rule five cutoff marks. This shows that the ligands higher probability to be quickly be absorbed into the gastrointestinal tract, more or less, and that the ligands with high bioavailability values indicating easy administration of these ligands as drugs (Table 5). Hence combining ADME studies and molecular docking score values

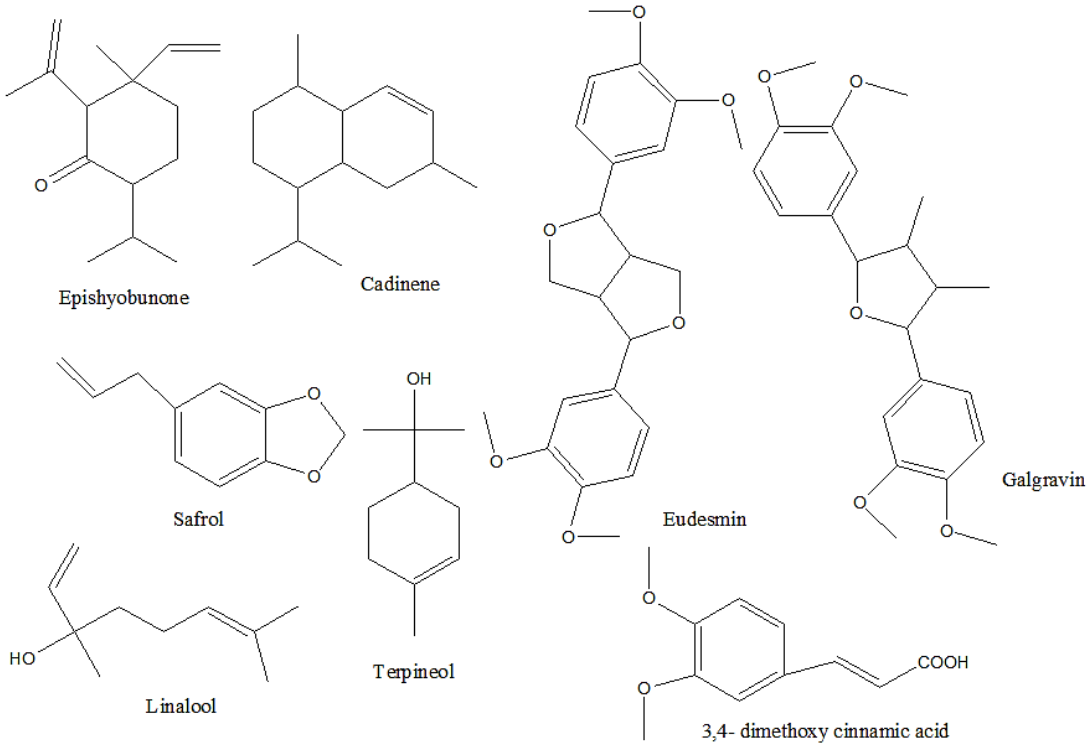

Figure 2: Ligands from *A. calamus* extract.

Table 1: Presence of phytoconstituents in the extracts.

Chemical tests	Phytoconstituents in Methanolic Extract	Phytoconstituents in Pet Ether Extract
Alkaloid	Present	Present
Saponin	Absent	Absent
Fixed Oil	Present	Absent
Protein	Present	Present
Polyphenols	Present	Absent
Anthraquinone Glycoside	Present	Present
Gums and Mucilage	Absent	Absent

Table 2: *In vitro* **antidiabetic study.**

Sample	Concentration (mg/mL)	% Inhibition	IC_{50} Value (mg/mL)
A. calamus extract	0.5	24.62±0.19	2.87±0.38
	1	31.92±0.12	
	2.5	43.88±1.21	
	5	77.36±0.37	
Metformin	0.5	18.17±0.45	3.25±0.47
	1	22.69±0.78	
	2.5	35.11±0.66	
	5	62.45±0.91	

Table 3: **Results of ligands docking in diabetic inhibitor target.**

Ligands	Binding Affinity (ΔG in kcal/mol)	
	1XU7	3C45
Epishyobunone	-5.7	-5.4
Beta Asarone	-4.9	-5.4
Surinamisinol A	-8.0	-6.6
Isoeugenol	-6.7	-6.3
3,4-dimethoxy cinnamic acid	-5.9	-4.4
Cedrenalol	-6.4	-7.6
Cadinene	-7.4	-6.6
Linalool	-6.9	-5.5
Eudesmin	-8.4	-7.3
Galgravin	-8.5	-7.7
Terpineol	-5.7	-4.4
Safrol	-7.0	-5.8
Metformin	-7.3	-6.7

for ligand detection, compound Galgravin may have very potent anti-diabetic qualities.[23]

Toxicity studies

All the ligands were studied for their oral toxicity using ProTox III software showed all 12 ligands had a predicted class 4-5 toxicity with high LD_{50} values indicating their safe usage in human (Table 6). From the table it can be observable that Galgravin have quite high LD_{50} value at 1500 µg/mL, with low level of toxicity (level 4) indicating the safety in oral and topical usage.[24]

Molecular dynamics

The iMod server employed molecular dynamics simulations and normal mode analysis to assess protein and ligand motions in docked complexes of Galgravin_1XU7 and Galgravin_3C45. Peaks on the main-chain deformability graph revealed exceptionally flexible places for both complexes, with atomic index 1000 exhibiting the largest peak with a deformability value of almost 1. iMod calculated the B-factor values, which represent protein structural flexibility and temperature changes. Higher B-factor values indicate higher atomic mobility and conformational changes in Galgravin in both proteins. Eigen values generated by iMod represent vibrational frequencies associated with collective atom motions, providing information about system dynamics, flexibility, and structural changes. Lower Eigen values in both cases indicate slower global motions of the compound in attachment to 1XU7 and 3C45 proteins. iMod's covariance map displays a value matrix, with each member indicating the covariance between atom pairs. The values are often represented by a covariance matrix, which indicates whether two residues are correlated (red), uncorrelated (white), or anticorrelated (blue). iMod simulations with Galgravin docking with both proteins reveal it to be flexibility, notably at the hinge. The covariance map in iMod represents atomic pair interactions in both proteins. It identifies locations with correlated or anti-correlated movements that are most likely associated with protein activity. This map broadens our understanding of protein dynamics and structure-function interactions.[25]

Table 4: Binding interactions of the most potent molecules.

Compound Name	Active Amino Acids	Bond Category
Galgravin_1XU7	Gly A:41	Carbon hydrogen
	Gly A:45	Van der Waal's
	Gly A:47	Van der Waal's
	Asn A:119	Van der Waal's
	Ile A:46	Van der Waal's
	Ile A: 218	Van der Waal's
	Leu A:215	Van der Waal's
	Leu A:126	Pi-Alkyl
	Val A:227	Van der Waal's
	Val A: 180	Pi-Alkyl
	Ser A:125	Van der Waal's
	Thr A:124	Van der Waal's
	Ala A:223	Pi-Alkyl
	Ala A:226	Pi-Alkyl
	Thr A: 222	Van der Waal's
	Thr A: 226	Van der Waal's
	Ile A: 121	Van der Waal's
	Lys A:44	Pi-Alkyl
Eudesmin_IXU7	Ile A: 121	Carbon hydrogen
	Val A: 180	Pi-Alkyl
	Tyr A: 183	Pi-Alkyl
	Ala A: 172	Pi-Alkyl
	Ala A:226	Pi-Alkyl
	Thr A:124	Conventional Hydrogen
	Leu A:126	Pi-Alkyl
	Asn A: 123	Carbon hydrogen
Galgravin_3C45	MMet A: 425	Van der Waal's
	Gln A:455	Carbon hydrogen
	Pro A:475	Pi-Alkyl
	Ser A:511	Van der Waal's
	Met A:509	Pi-Alkyl
	Leu A:561	Van der Waal's
	Thr A:565	Van der Waal's
	Pro A:510	Pi-Alkyl
	Arg A:560	Carbon hydrogen
	Phe A:559	Pi-pi T shaped
	Ile A:529	Pi-Alkyl
	Val A:558	Carbon hydrogen
	Lys A:512	Pi-Alkyl
	Asp A:556	Carbon hydrogen
	Thr A:557	Van der Waal's
	Leu A:514	Pi-Alkyl

Table 5: ADME prediction of ligands from *A. calamus*.

Ligands	Mol Wt. (g)	Log P	HBD	HBA	Violation	BB barrier Yes/No	GI Absorption	Bioavailability
Epishyobunone	203.26	3.9	0	1	0	Yes	High	0.55
Beta Asarone	205.26	2.69	0	3	0	Yes	High	0.55
Surinamisinol A	388.45	3.81	1	6	0	Yes	High	0.55
Isoeugenol	164.20	2.41	1	2	0	Yes	High	0.55
3,4- dimethoxy cinnamic acid	208.22	1.83	1	4	0	Yes	High	0.85
Cedrenalol	222.37	3.43	1	1	0	Yes	High	0.55
Cadinene	206.37	4.48	0	0	1	No	Low	0.55
Linalool	154.25	2.66	1	1	0	Yes	High	0.55
Eudesmin	386.44	3.06	0	6	0	Yes	High	0.65
Galgravin	372.45	3.84	0	5	0	Yes	High	0.75
Terpineol	154.25	2.58	1	1	0	Yes	High	0.55
Safrol	162.19	2.52	0	2	0	No	High	0.55

Table 6: Toxicity prediction of ligands from *A. calamus*.

Ligands	Level of Toxicity (1=highly toxic; 6= safe)	Predicted LD_{50} (µg/mL)
Epishyobunone	5	5000
Beta Asarone	4	418
Surinamisinol A	4	1000
Isoeugenol	4	1560
3,4- dimethoxy cinnamic acid	4	1772
Cedrenalol	5	2380
Cadinene	5	5000
Linalool	5	2200
Eudesmin	4	1500
Galgravin	4	1500
Terpineol	5	2400
Safrol	4	1940

DISCUSSION

From the above-mentioned results, it can be observed that % extractive value of the extracts were found to be 9.32±0.39% (for methanolic extract). The phytochemical tests yielded the presence of alkaloid, glycosides, volatile oil, flavonoids along with fixed oils, proteins and carbohydrates. The high yield may indicate presence of multiple compounds under the present phytochemical categories especially polyphenols which may be responsible for antidiabetic properties.[26] *In vitro* antidiabetic studies using α-amylase assay. The study was performed using 0.5-5 mg/mL of *A. calamus* extract against same concentration of proven antidiabetic Metformin. The result indicated that IC_{50} value of the extract (2.87±0.38 mg/mL) was less as compared to the standard, metformin (3.25±0.47 mg/mL). Based on literature reports of the GCMS studies on the extract yielded many potent phytochemical compounds which may be explored for their anti-diabetic properties *in silico* to pinpoint the specific compound associated to inhibit diabetes as observable from the *in vitro* studies. *In silico* studies on these compounds yielded a few ligands like Galgravin (-8.5 kcal/mol in 1XU7 and -7.7 kcal/mol in 3C45), Cedrenalol (-7.6 kcal/mol in 3C45) and Eudesmin (-8.4 kcal/mol in 1XU7) have the best binding energy as compared to the standard metformin indicating that the extract containing compound like Galgravin can find its usage as anti-diabetic drug.[27] Moreover, Galgravin was found to be drug-like and had high predicted bioavailability as well as low toxicity. The compound showed to be a dynamically stable molecule in both proteins with high

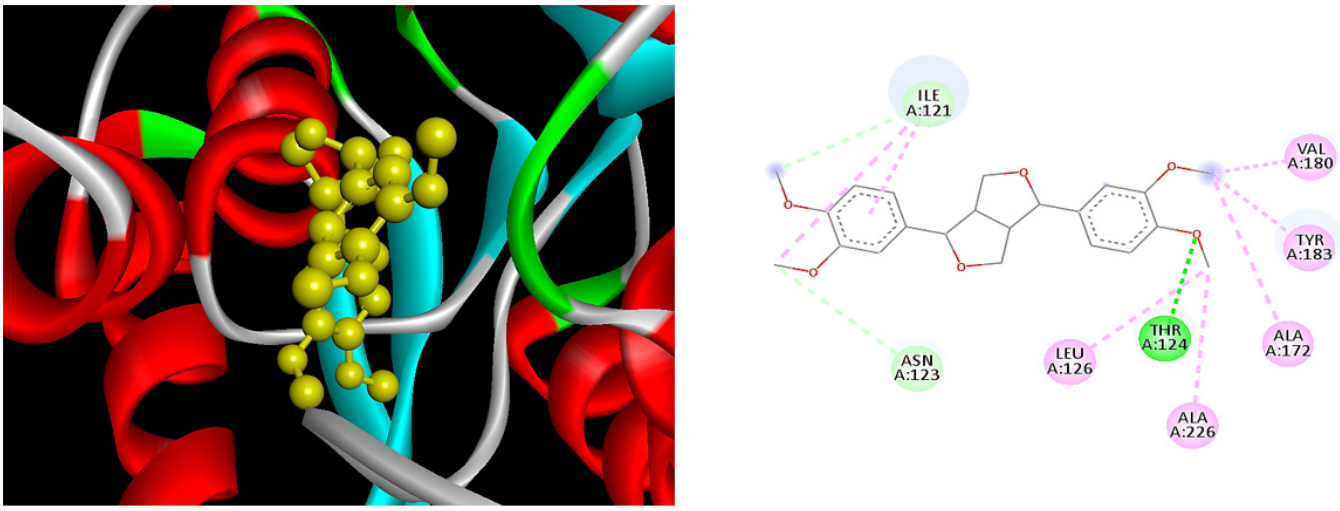

Figure 3: Interaction diagram of Eudesmin with the protein 1XU7.

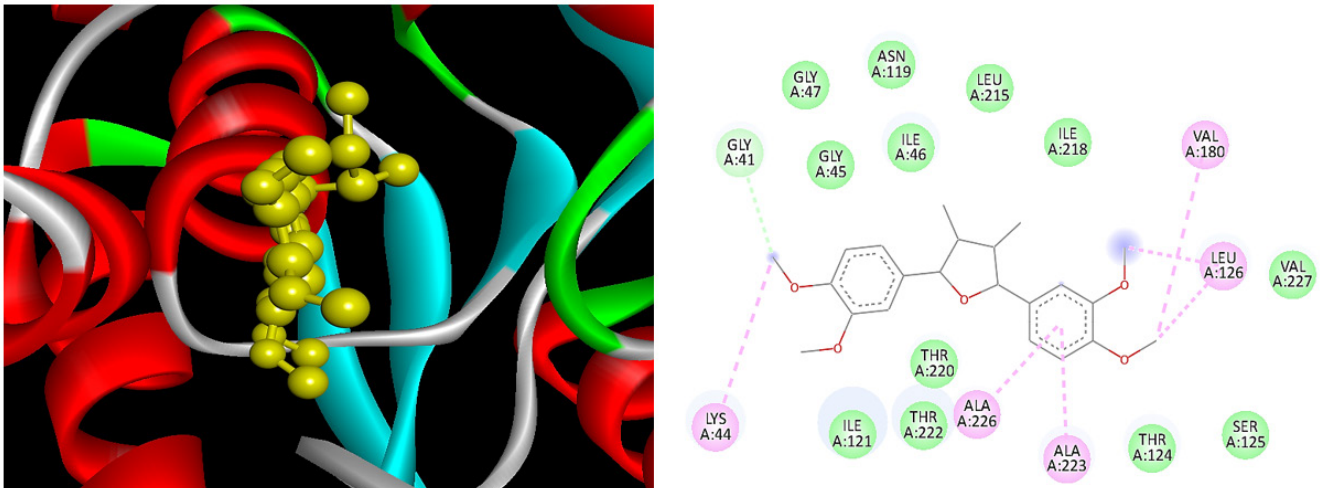

Figure 4: Interaction diagram of Galgravin with the protein 1XU7.

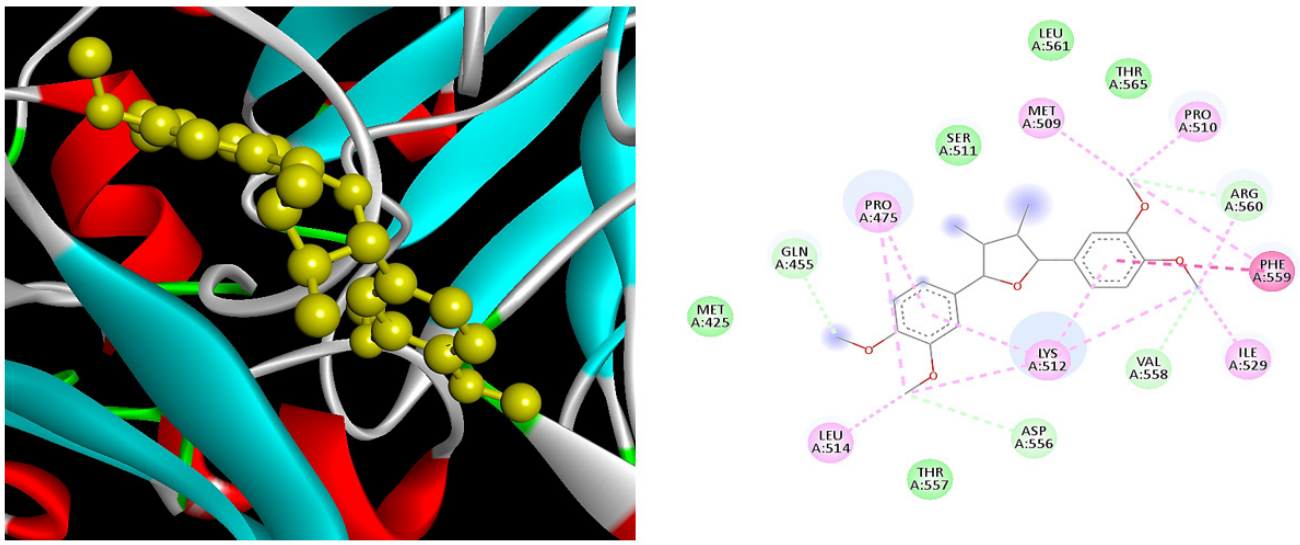

Figure 5: Interaction diagram of Galgravin with the protein 3C45.

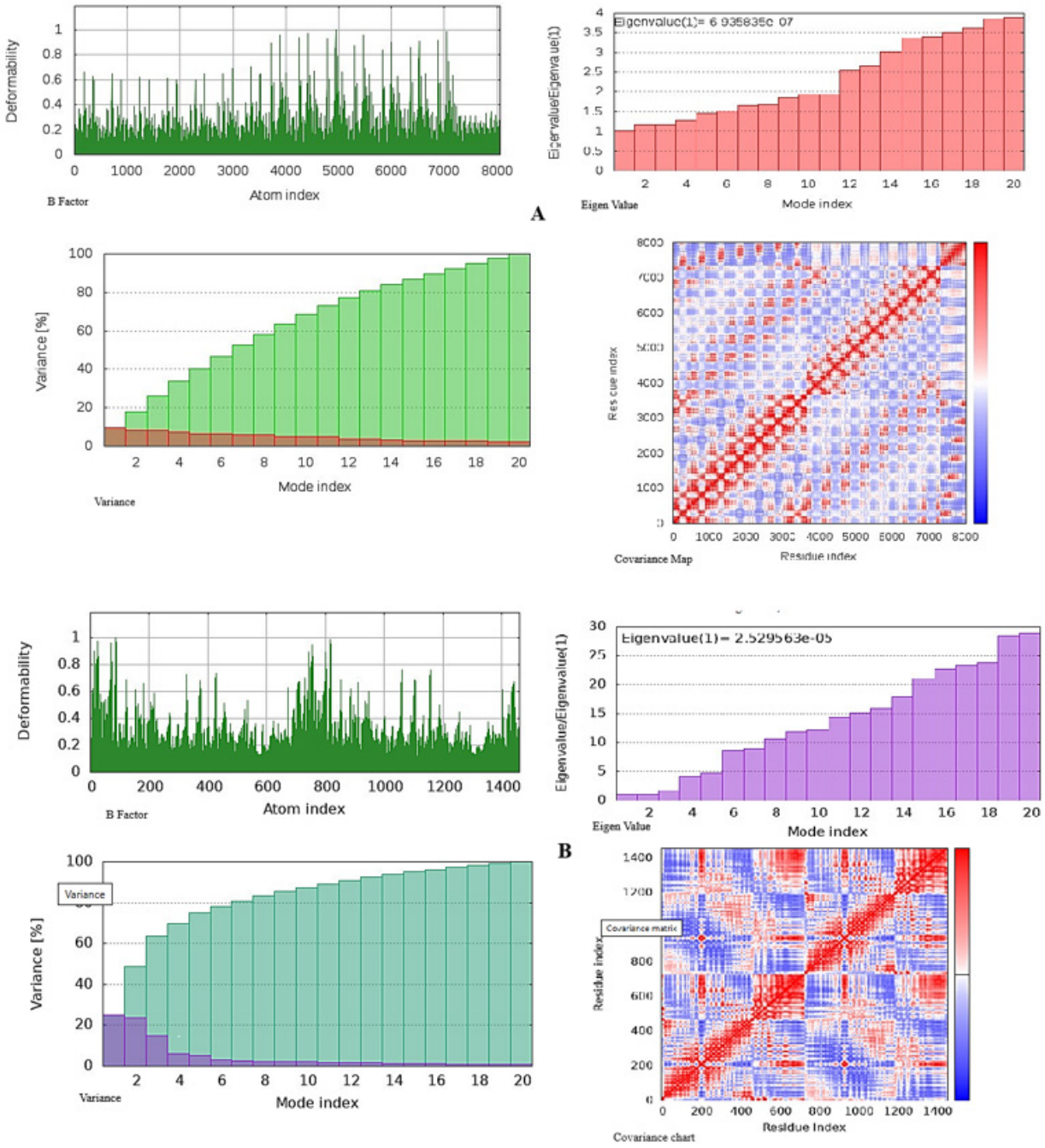

Figure 6: Outputs of Molecular dynamic simulation in iMODS for Galgravin with protein (A) 1XU7 and (B) 3C45 deformability factor plot, Eigen value, Variance plot and Covariance plot.

flexibility and low eigenvalue. Thus, all the evidence confirms that the presence of multiple compounds especially Galgravin prompts the extract to have anti-diabetic properties. With further research, a formulation could be developed for stable delivery of the extracts as anti-diabetic drugs.[28]

CONCLUSION

The current study provides compelling preliminary evidence supporting the potential of *Acorus calamus*-derived natural compounds, particularly Galgravin, as effective antidiabetic agents. The extract exhibited stronger α-amylase inhibitory activity than metformin, suggesting potent enzyme-blocking capabilities. Galgravin, among all tested ligands, demonstrated superior binding affinities to both diabetic target proteins (PDB: 1XU7 and 3C45), coupled with favorable pharmacokinetic properties, including high bioavailability, drug-likeness, and minimal predicted toxicity. Its elevated LD_{50} value and dynamic stability, as confirmed through molecular dynamics simulation, further strengthen its viability as a lead compound for drug development. Unlike conventional antidiabetic agents, which

often suffer from adverse effects and diminishing efficacy over time, natural bioactives like Galgravin offer a promising and potentially safer alternative. However, while *in vitro* and *in silico* findings are encouraging, comprehensive *in vivo* studies and clinical trials are essential to fully establish its pharmacological efficacy, mechanism of action, and safety profile in human subjects.

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ABBREVIATIONS

PDB: Protein Data Bank; **HBA:** Hydrogen Bond Acceptor; **HBD:** Hydrogen Bond Donor; **MW:** Molecular Weight; **MD:** Molecular Dynamics; **LD_{50}:** Lethal Dose 50%; **IC_{50}:** Half-Maximal Inhibitory Concentration.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS CONTRIBUTION

Conceptualization, Research, Writing, Proofreading: SS.

SUMMARY

This study explored natural compounds from *Acorus calamus* as potential antidiabetic agents, addressing limitations of existing therapies like toxicity and drug resistance. Researchers evaluated 12 compounds for *in vitro* α-amylase inhibition and conducted *in silico* molecular docking against key diabetic protein receptors (PDB IDs: 1XU7 and 3C45).

The *Acorus calamus* extract showed superior α-amylase inhibition (IC_{50} of 2.87±0.38 mg/mL) compared to metformin (3.25±0.47 mg/mL). Among the compounds, Galgravin demonstrated the highest binding affinities for both protein targets (-8.5 kcal/mol for 1XU7, -7.7 kcal/mol for 3C45), outperforming metformin. Galgravin also exhibited low toxicity, favorable drug-likeness, and excellent bioavailability, confirmed by molecular dynamics simulations. The findings suggest Galgravin as a promising natural inhibitor for diabetes, warranting further *in vivo* and clinical investigation.

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