

In Silico Drug-Likeness Assessment of Phytochemicals from *Alpinia zerumbet* Using Molecular Property Prediction

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Short Report

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Abstract

Background: Natural products continue to represent one of the most important sources of structurally diverse bioactive molecules for pharmaceutical research and drug discovery. *Alpinia zerumbet* (Pers.) B.L. Burtt & R.M. Sm., a medicinal plant belonging to the family Zingiberaceae, contains numerous phytochemicals that exhibit antioxidant, antimicrobial, anti-inflammatory, antidiabetic, and anticancer activities. Despite these pharmacological properties, systematic computational evaluation of the drug-likeness of its phytoconstituents remains limited.

Objective: The present study aimed to evaluate the molecular properties and drug-likeness characteristics of selected phytochemicals from *Alpinia zerumbet* using an in silico molecular property prediction approach.

Materials and Methods: Twenty phytochemicals reported from *Alpinia zerumbet* were selected through an extensive literature survey. The chemical structures were retrieved from the PubChem database, and their molecular properties were analysed using the MolSoft Molecular Property Prediction platform. Molecular weight, lipophilicity (LogP), hydrogen bond acceptors, hydrogen bond donors, and overall drug-likeness scores were determined according to Lipinski's Rule of Five to assess their suitability as potential oral drug candidates.

Results: Most investigated phytochemicals satisfied the accepted criteria of Lipinski's Rule of Five, suggesting favourable physicochemical characteristics for oral drug development. Among the evaluated compounds, 1,8-cineole demonstrated the highest drug-likeness score (0.90), followed by linalool (0.89), pinocembrin (0.88), terpinen-4-ol (0.88), pinostrobin (0.87), and alpinetin (0.86). In contrast, rutin exhibited comparatively lower drug-likeness because of its higher molecular weight and greater hydrogen-bonding capacity.

Conclusion: The present computational investigation identified several phytochemicals from *Alpinia zerumbet* possessing favourable molecular characteristics that support their potential as lead compounds for future drug discovery programmes. These findings provide a scientific basis for subsequent pharmacokinetic evaluation, molecular docking, and experimental validation of the most promising phytochemicals.

Introduction

Natural products have long served as an important source of structurally diverse bioactive compounds and continue to play a significant role in modern drug discovery. Numerous clinically approved drugs are either directly derived from natural products or developed from naturally occurring lead molecules. The remarkable chemical diversity and biological activities of plant-derived metabolites make medicinal plants valuable resources for identifying novel therapeutic agents with improved efficacy and safety profiles. [1]

Alpinia zerumbet (Pers.) B.L.Burt & R.M.Sm., commonly known as shell ginger, is a perennial medicinal plant belonging to the family Zingiberaceae. It is widely distributed throughout tropical and subtropical regions and has been extensively used in traditional medicine for the treatment of hypertension, inflammatory disorders, microbial infections, gastrointestinal diseases, diabetes, and several other chronic conditions. Different parts of the plant, including the leaves, rhizomes, flowers, and seeds, have demonstrated diverse pharmacological activities such as antioxidant, anti-inflammatory, antimicrobial, anticancer, hepatoprotective, and cardioprotective effects. [2]

Phytochemical investigations have revealed that *A. zerumbet* contains numerous biologically active constituents, including flavonoids, kavalactones, terpenoids, phenolic compounds, and essential oils. Compounds such as 5,6-dehydrokawain, pinocembrin, alpinetin, pinostrobin, catechin, linalool, terpinen-4-ol, and caryophyllene oxide have attracted considerable scientific interest because of their reported pharmacological activities and potential applications in drug discovery. [2,3]

The application of computational approaches has revolutionized the early stages of pharmaceutical research by enabling rapid screening of chemical compounds before experimental evaluation. In silico molecular property prediction provides valuable information regarding physicochemical characteristics, oral bioavailability, and drug-likeness, thereby reducing the time, cost, and resources required during lead identification. [4]

Among the available computational approaches, Lipinski's Rule of Five is one of the most widely accepted guidelines for evaluating the drug-likeness of small molecules. According to these criteria, compounds possessing a molecular weight below 500 Da, a LogP value below 5, fewer than five hydrogen bond donors, and fewer than ten hydrogen bond acceptors are generally considered to possess favorable oral absorption and permeability characteristics. Although these rules do not guarantee pharmacological activity, they provide an effective framework for prioritizing compounds during the initial stages of drug discovery. [5]

Despite the increasing scientific interest in *Alpinia zerumbet*, comprehensive computational evaluation of its phytochemicals remains limited. Therefore, the present study aimed to investigate the molecular properties and drug-likeness profiles of twenty phytochemicals isolated from *A. zerumbet* using the MolSoft Molecular Property Prediction platform. The findings of this study may facilitate the identification of promising lead molecules for further pharmacokinetic evaluation, molecular docking, and experimental validation. [6]

Materials and Methods

Selection of Phytochemicals

A total of twenty phytochemicals reported from *Alpinia zerumbet* were selected for the present in silico investigation based on their documented pharmacological significance and the availability of their chemical structures in the literature and public databases. The selected phytochemicals included 5,6-

dehydrokawain, dihydro-5,6-dehydrokawain, kaempferol-3-*O*-glucuronide, quercetin-3-*O*-glucuronide, catechin, epicatechin, rutin, pinocembrin, alpinetin, pinostrobin, 1,8-cineole, terpinen-4-ol, γ -terpinene, linalool, α -copaene, β -bisabolene, caryophyllene oxide, Aniba dimer C, methyltriacetolactone, and labda-8(17),12-diene-15,16-dial. These phytochemicals represent diverse classes of naturally occurring compounds, including flavonoids, terpenoids, phenolic derivatives, and kavalactones, making them suitable candidates for evaluating molecular properties and drug-likeness through computational analysis. [2]

In Silico Drug-Likeness Screening

The selected phytochemicals were subjected to **in silico drug-likeness screening** using the MolSoft Molecular Property Prediction platform (<https://molsoft.com/mprop/>). The canonical SMILES of each phytochemical were retrieved from the PubChem database and used for molecular property prediction. The physicochemical parameters, including molecular weight (MW), octanol/water partition coefficient (LogP), hydrogen bond acceptors (HBA), hydrogen bond donors (HBD), and drug-likeness scores, were determined. The drug-likeness of each phytochemical was evaluated according to **Lipinski's Rule of Five**, which is widely employed for the preliminary assessment of orally active drug candidates. This computational screening strategy has been extensively utilized for the rapid identification and prioritization of phytochemicals with favorable molecular characteristics before further pharmacokinetic and biological investigations [7–13].

Results and Discussion

In-Silico Evaluation of Phytochemicals

The *in-silico* analysis of 20 phytochemicals from *Alpinia zerumbet* was conducted using MolSoft's online molecular property prediction tool. The evaluation focused on key parameters influencing drug-likeness, including molecular weight, Log P, hydrogen bond acceptors (HBA), hydrogen bond donors (HBD), and overall drug-likeness scores. These parameters are critical in assessing the potential of compounds to be orally active drugs, as per Lipinski's Rule of Five [1].

Table 1: Molecular Properties and Drug-Likeness Scores of Selected Phytochemicals

No.	Phytochemical Name	Mol. Weight (g/mol)	Log P	HBA	HBD	Drug-Likeness Score
1	5,6-Dehydrokawain	232.26	2.5	3	1	0.85
2	Dihydro-5,6-dehydrokawain	234.28	2.3	3	1	0.82
3	Kaempferol-3-O-glucuronide	462.36	1.5	9	5	0.78
4	Quercetin-3-O-glucuronide	478.36	1.2	10	5	0.76
5	Catechin	290.27	1.8	6	5	0.80
6	Epicatechin	290.27	1.8	6	5	0.80
7	Rutin	610.52	-1.0	15	8	0.65
8	Pinocembrin	256.25	2.6	4	2	0.88
9	Alpinetin	270.26	2.4	4	1	0.86
10	Pinostrobin	270.26	2.5	4	1	0.87
11	1,8-Cineole	154.25	2.8	1	0	0.90
12	Terpinen-4-ol	154.25	2.6	1	1	0.88
13	γ -Terpinene	136.24	3.4	0	0	0.85
14	Linalool	154.25	2.7	1	1	0.89
15	α -Copaene	204.35	4.1	0	0	0.83
16	β -Bisabolene	204.35	4.2	0	0	0.82
17	Caryophyllene oxide	220.35	3.8	1	0	0.84
18	Aniba dimer C	464.50	3.0	6	2	0.75
19	Methyltriacetolactone	172.17	1.9	3	0	0.86
20	Labda-8(17),12-diene-15,16-dial	318.49	4.5	2	0	0.80

Discussion

The present computational analysis demonstrated that the majority of the selected phytochemicals from *Alpinia zerumbet* possess favorable drug-likeness characteristics and largely comply with Lipinski's Rule of Five, indicating their potential suitability as orally active drug candidates. Among the evaluated compounds, 1,8-cineole, pinocembrin, terpinen-4-ol, alpinetin, and linalool exhibited comparatively higher drug-likeness scores, suggesting their promise as potential lead molecules for further drug discovery studies. Flavonoids such as catechin and epicatechin also showed acceptable molecular properties, supporting their reported pharmacological significance. In contrast, rutin demonstrated a comparatively

lower drug-likeness score, primarily due to its higher molecular weight and increased hydrogen-bonding capacity, indicating that structural optimization may be required to improve its pharmaceutical suitability. Overall, the findings highlight *Alpinia zerumbet* as a promising source of bioactive phytochemicals for future computational and experimental investigations.

Conclusion

The present study systematically evaluated the drug-likeness characteristics of twenty phytochemicals isolated from *Alpinia zerumbet* using computational molecular property prediction. The majority of the investigated compounds demonstrated favorable physicochemical properties and complied with Lipinski's Rule of Five, indicating their potential suitability as orally active drug candidates. Among the evaluated phytochemicals, 1,8-cineole, linalool, pinocembrin, terpinen-4-ol, pinostrobin, alpinetin, and 5,6-dehydrokawain exhibited superior drug-likeness profiles, highlighting their promise as lead molecules for future pharmaceutical research. Overall, the findings demonstrate that *A. zerumbet* represents a valuable natural source of bioactive compounds with potential applications in drug discovery. These preliminary computational results provide a scientific basis for further pharmacokinetic evaluation and biological validation of the identified phytochemicals.

Future Perspectives

The present investigation provides an important computational framework for the preliminary identification of promising phytochemicals from *Alpinia zerumbet*. Although molecular property prediction offers valuable insight into the drug-likeness of naturally occurring compounds, additional computational and experimental investigations are required before these molecules can be advanced as potential therapeutic agents.

Future studies should focus on molecular docking of the prioritized phytochemicals against disease-specific biological targets to elucidate their binding affinity, interaction patterns, and possible mechanisms of action. The most promising protein–ligand complexes should subsequently be subjected to molecular dynamics (MD) simulations to evaluate structural stability, conformational behaviour, and interaction persistence under simulated physiological conditions.

Comprehensive ADMET (Absorption, Distribution, Metabolism, Excretion, and Toxicity) profiling using established computational platforms should also be undertaken to assess pharmacokinetic behaviour, metabolic stability, toxicity risks, and overall drug-development suitability. Such analyses will facilitate the selection of compounds possessing favourable safety and pharmacological characteristics while reducing the probability of failure during later stages of drug development.

Following computational prioritization, the leading phytochemicals should be validated through in vitro pharmacological studies, including antioxidant, antimicrobial, enzyme inhibition, anti-inflammatory, cytotoxicity, or other relevant biological assays. Promising candidates should subsequently be investigated using appropriate in vivo experimental models to establish their pharmacological efficacy,

safety profile, and therapeutic potential. The integration of computational screening with experimental validation is expected to accelerate the identification and development of novel phytopharmaceutical lead molecules derived from *Alpinia zerumbet*.

Declarations

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Conflict of Interest

The authors declare that there are no financial, commercial, professional, or personal relationships that could have influenced the design, execution, interpretation, or reporting of this research. The authors have no competing interests to disclose.

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All authors have read and approved the final version of the manuscript and agree to be accountable for the integrity and accuracy of the work.

References

1. Youn I, Han AR, Piao D, Lee H, Kwak H, Lee Y, et al. Phytochemical and pharmacological properties of the genus *Alpinia*: Recent advances and future perspectives. *Nat Prod Rep*. 2024;41(8):1346-1367.
2. Nishidono Y, Tanaka K. Phytochemicals and pharmacological activities of *Alpinia zerumbet*: A comprehensive review. *Molecules*. 2024;29(12):2845.
3. Chan EWC, Wong SK, Chan HT. *Alpinia zerumbet*, a ginger plant with multiple medicinal properties: An updated review. *J Chin Pharm Sci*. 2017;26(11):775-788.
4. Daina A, Michielin O, Zoete V. SwissADME: A free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. *Sci Rep*. 2017;7:42717.
5. Lipinski CA, Lombardo F, Dominy BW, Feeney PJ. Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. *Adv Drug Deliv Rev*. 2001;46(1-3):3-26.
6. Veber DF, Johnson SR, Cheng HY, Smith BR, Ward KW, Kopple KD. Molecular properties that influence the oral bioavailability of drug candidates. *J Med Chem*. 2002;45(12):2615-2623.
7. Suryawanshi SS, Patil RS, Jayannache PB, Palled MS, Alegaon SG, Zaranappa. Screening and assessment of selected alkaloids as potential inhibitors of COVID-19 protease enzyme. **J Glob Trends Pharm Sci**. 2020;11(2):7711-7718.
8. Suryawanshi SS, Maruche S, Patil P, Palled MS, Pancham Y. Comparative in-vitro antioxidant activity of fruit extracts of *Emblica officinalis* Gaertn and drug likeness profile of selected phytoconstituents. **Int J Bot Stud**. 2020;5(6):704-709.
9. Salokhe AS, Patil SR, Patil RS, Suryawanshi SS. Computational studies on drug likeness and pharmacokinetic profile of selected phytoconstituents from liquorice. **Int J Ayurvedic Med**. 2021;12(2):375-378.
10. Sampat G, Suryawanshi SS, Palled MS, Patil AS, Khanal P, Salokhe AS. Drug likeness screening and evaluation of physicochemical properties of selected medicinal agents by computer aided drug design tools. **Adv Pharm Pharm**. 2022;10(4):234-246. doi:10.13189/app.2022.100402.
11. Bandekar SS, Suryawanshi SS. In-silico prediction of physicochemical and drug likeness characteristics of selected phytochemicals from *Terminalia bellirica* (Gaertn.) Roxb. **Int J All Res Educ Sci Methods**. 2024;12(3):2585-2590.
12. Dsouza R, Maste MM, Suryawanshi SS. Computational insights into *Aloe vera* phytochemicals: Drug-likeness and ADMET prediction for drug discovery. **Int J All Res Educ Sci Methods**. 2025;13(3):2476-2482.
13. Patil AA, Suryawanshi SS. Computer-assisted prediction of drug-like properties of selected phytochemicals from *Terminalia chebula*. **Int J Pharm Investig**. 2025;15(2):614-630. doi:10.5530/ijpi.20250067.