In-silico anti–microbial, anti-inflammatory and hypoglycemic evaluation of active phytoconstituents of the plant: *Leucas aspera* (Willd.)

Mr. Sariful Islam
Rahman Institute of Pharmaceutical Sciences and Research (RIPSR), Tepesia, Kamrup Metro, Assam
Mr. Hrishikesh Bhagawati (hrishikeshbhagawati.12@gmail.com)
Rahman Institute of Pharmaceutical Sciences and Research (RIPSR), Tepesia, Kamrup Metro, Assam
Miss. Arifa Tanjim
Rahman Institute of Pharmaceutical Sciences and Research (RIPSR), Tepesia, Kamrup Metro, Assam
Mr. Masayek Mehboob
Rahman Institute of Pharmaceutical Sciences and Research (RIPSR), Tepesia, Kamrup Metro, Assam
Mr. Mrinal Kashyap Sarma
Rahman Institute of Pharmaceutical Sciences and Research (RIPSR), Tepesia, Kamrup Metro, Assam
Miss. Chinmoyee Borah
Dibrugarh University
Mr. Aminul Islam
Rahman Institute of Pharmaceutical Sciences and Research (RIPSR), Tepesia, Kamrup Metro, Assam
Mr. Pankaj Basumatary
Rahman Institute of Pharmaceutical Sciences and Research (RIPSR), Tepesia, Kamrup Metro, Assam

Research Article

Keywords: Leucas aspera, Lipinski rule of five, Leucasperol A, Amyl Propionate, Isololiolide, SwissADME, PyRx, Molsoft L.L.C.

Posted Date: August 16th, 2023

DOI: https://doi.org/10.21203/rs.3.rs-3243014/v1

Abstract

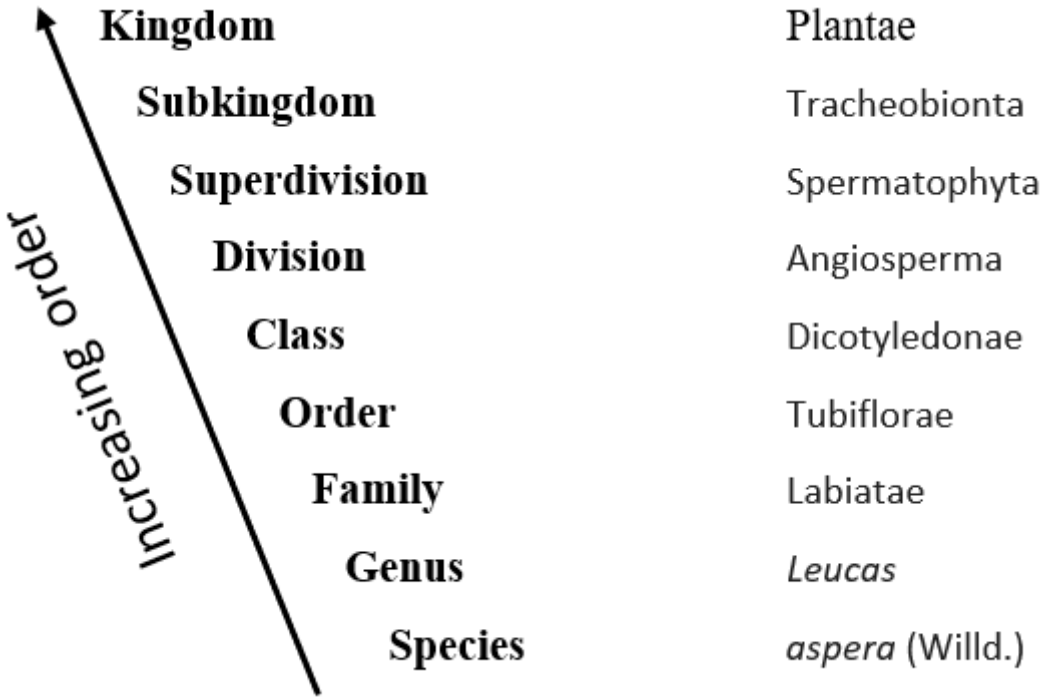
Leucas aspera (willd.) (Labiatae family) is a dietary herb with a wide variety of biological activities, including antimicrobial activity. In this study, we used *in-silico* docking to see how well bioactive phytoconstituents from *L. aspera* might operate against an inflammatory-triggering protein. Three phytoconstituents were selected from a list of thirty based on their ability to satisfy the Lipinski rule of five. Molsoft L.L.C. databases were used to forecast the drug-likeness score and adverse effects for the chosen compounds. SwissADME was used to make predictions about the pharmacokinetics and toxicological characteristics of the selected phytoconstituents. Docking studies were carried out using the PyRx to predict the binding affinity of the selected phytoconstituents with the protein from the protein data bank. Among the drugs tested, Leucasperol A had the highest drug-likeness score (-0.11) and Amyl propionate had the lowest (-1.24). In molecular docking investigations, the ligands were found to bind to the active site of the target protein with minimal binding energy values. In terms of binding affinities with the target proteins (4DX5 and 5V5Z), Leucasperol A had the highest (-8.8 kcal/mol & -8.6 kcal/mol) and Amyl propionate had the lowest (-4.5 kcal/mol & -4.5 kcal/mol). In terms of binding affinities with the target proteins (6LW5 and 1ILR), Leucasperol A had the highest (-8.7 kcal/mol & -7.5 kcal/mol) and Amyl propionate had the lowest (-5.2 kcal/mol & -4.1 kcal/mol). In terms of binding affinities with the target proteins (3BJM and 6LN2), Leucasperol A had the highest (-8.3 kcal/mol & -8.4 kcal/mol) and Amyl propionate had the lowest (-4.3 kcal/mol & -4.5 kcal/mol). Our results suggested that the phytochemicals we examined in *L. aspera* might have anti-microbial, anti-inflammatory & hypoglycaemic properties, suggesting that this plant might be useful as a treatment option.

Introduction

Some of the most often used edible plants include ferns, shrubs, and herbs, whether they are harvested from the wild or farmed. Leaves, berries, young shoots, and branches, as well as the rhizome and, in certain cases, the whole plant, are all edible. The 1st written record for the plant was dated 10000 years back in the *Neolithic revolution.* Which cites the domestication of the plants and animals. Also, among herbs, ferns & shrubs, ferns are the primitive and herbs/ shrubs are the plants which are evolved as per the habitat which indicates that they have more evolved form of xylem and phloem for absorbing water, nutrients, and photosynthesized food for proper growth. Also, this indicates that these plants are having the highest phytoconstituents leading to better medicinal properties. *Leucas aspera* (willd.) (Lamiaceae), a well-known family, mostly eaten, broadly distributed to most of the parts of India, and other countries. The taxonomic classification has been listed via the chart. Globally, Leucas is known by different names, but commonly it is known as *Goma madhupati in Hindi, Thumba* in English*, Durun Khak* in Assamese*, Thumbe gida* in Kannada*, Dronapushpi* in Sanskrit, etc. The ethnobotanically L. aspera was used as source of insecticides and fever reducer. Also, flowers as emmenagogue, insecticides, diaphoretic and stimulant. Leaves for psoriasis, eczema, and chronic rheumatism along with snakebites by the use of bruised leaves.[26] Various solvent extracts of the *L. aspera* has been showing the hypoglycaemic, anti-inflammatory, anti-microbial and many more characteristic activities which has been tabulated (Table 2),

which conclude that L. aspera is nutritious and healthy. To the best of our knowledge, no comprehensive *in-silico* study has been conducted on the different metabolites of *L. aspera* to determine their hypoglycaemic [12], anti-inflammatory [34], and anti-microbial [22] characteristics. Therefore, the purpose of the current research was to screen numerous important phytoconstituents of *L. aspera* and to dock them with the protein of diabetes mellitus, anti-inflammatory, and anti-microbial activities and compare the mechanism of the standard drug with the screened drug. Further investigation into the phytochemical properties of this plant may be facilitated by our results, which may serve as a foundation for the synthetic modification of bioactive phytoconstituents and the *de novo* synthesis of structural motifs.

Hierarchical classification: As per Integrated Taxonomic Information System (ITIS)



Common Names

Table 1- Common Names

Assamese	Durun khak
Hindi	Ghopa or Goma madhupati
English	Thumba or Leucas

Botanical Description and distribution

Leucas aspera [Figure 1] is a biennial herb with a sturdy and hispid sharply quadrangular stem and branches that can reach a height of 15-60 centimetres. White sessile flowers cluster at the end of the stem or in the axils. Subsessile or short petiolate, linear, or linearly lanceolate, obtuse, and hairy best describe the leaves of this plant. Small, very oblique, not villous, upper part produced forward; teeth small, triangular, bristled, ciliate, tissue upper tooth being the largest; calyx variable, tubular, 8-13 mm long; tube curved, contracted above the nutlets; lower half usually glabrous and membranous, upper half ribbed and hispid. The corolla is 1 centimetres in length, the tube is 5 millimetres long and pubescent above, annulate in the middle, the top lip is 3 millimetres long and densely white-woolly, and the lower lip is nearly twice as long, with a broad, rounded central lobe and small, subacute lateral lobes. Nutlets of fruit that are 2.5 mm in length, brown in colour, smooth on the inside and with sharp angles on the outside.

The aromatic *Leucas aspera* tree thrives in the warm climates of India, the Philippines, Java, the lowlands of Mauritius, tropical Asia, and Africa. This annual herb thrives in a variety of environments, including sandy soils, wastelands, roadside ditches, and highland crop fields. It has a quadrilateral stem and branch structure and can reach a height of 15-60 cm. [26, 27]

Pharmacological Properties

Table 2- Pharmacological properties of *Leucas aspera*

Ethnomedicinal Properties	References
Anti-fungal activity, Anti-hyperglycaemic activity, Anti-inflammatory activity, Anti-microbial activity, Anti-nociceptive activity, Anti-oxidant activity, Hepatoprotective activity, Larvicidal activity	2, 4, 6-9, 11-13, 15-20, 23-37

Phytoconstituents Reported

Table 3- Phytoconstituents reported.

No	Name	Molecular Weight	Molecular Formula
1	Oleanolic acid	456.7	$C_{30}H_{48}O_3$
2	Ursolic acid	456.7	$C_{30}H_{48}O_3$
3	α-sitosterol	426.72	$C_{30}H_{50}O$
4	β-sitosterol	414.7	$C_{29}H_{50}O$
5	Galactose	180.16	$C_6H_{12}O_6$
6	Leucasperone A	788.9	$C_{38}H_{60}O_{17}$
7	Leucasperone B	436.5	$C_{24}H_{36}O_7$
8	Leucasperol A	352.5	$C_{20}H_{32}O_5$
9	Leucasperol B	352.5	$C_{20}H_{32}O_5$
10	Leucasperoside A	788.9	$C_{38}H_{60}O_{17}$
11	Leucasperoside B	626.7	$C_{32}H_{50}O_{12}$
12	Leucasperoside C	772.9	$C_{38}H_{60}O_{16}$
13	Asperphenamate	506.6	$C_{32}H_{30}N_2O_4$
14	Maslinic acid	472.7	$C_{30}H_{48}O_4$
15	Isololiolide	196.24	$C_{11}H_{16}O_3$
16	Nectandrin B	344.4	$C_{20}H_{24}O_5$
17	Meso-dihydroguaiaretic acid	330.4	$C_{20}H_{26}O_4$
18	Macelignan	328.4	$C_{20}H_{24}O_4$
19	Acacetin	284.26	$C_{16}H_{12}O_5$
20	Chrysoeriol	300.26	$C_{16}H_{12}O_6$
21	Chicanine	342.4	$C_{20}H_{22}O_5$
22	Licarin A	326.4	$C_{20}H_{22}O_4$
23	α-thujene	136.234	$C_{10}H_{16}$
24	Menthol	156.27	$C_{10}H_{20}O$
25	Amyl propionate	144.21	$C_8H_{16}O_2$
26	Isoamyl propionate	144.21	$C_8H_{16}O_2$
27	Palmitic acid	256.42	$C_{16}H_{32}O_2$
28	Stearic acid	284.5	$C_{18}H_{36}O_2$
29	Oleic acid	282.5	$C_{18}H_{34}O_2$
30	Linoleic acid	280.4	$C_{18}H_{32}O_2$

Materials and Method

Literature Search

All of the relevant data and information about the *Leucas aspera* was obtained from a number of sources, such as PubMed, Science Direct, Sci-hub and Google Scholar evaluation and analysis papers from published works that have been subjected to peer review. We also looked at a few materials from the so-called 'grey literature,' which included ethnobotanical books and chapters.

Softwares

PyRx is a virtual screening tool for computational drug discovery that could potentially used to test compound libraries against pharmacological targets. PyRx (PyRx - Virtual Screening Tool download | SourceForge.net) is a tool for medicinal chemists that facilitates the entire virtual screening process, from data preparation through job submission and analysis of findings, regardless of the platform being used. Although there is no magic solution in the drug discovery process, PyRx's docking wizard and user-friendly interface make it a powerful tool for CAD. In addition to its chemical spreadsheet-like features, PyRx also boasts a robust visualisation engine, both of which are crucial in the realm of Rational Drug Design.

Biovia Discovery Studio 2021

Increased specificity and safety requirements, new types of therapeutics, and intricate disease mechanisms are only some of the examples of complexity in today's biopharmaceutical sector. Understanding therapeutic behaviour more thoroughly is necessary to keep up with this complexity. Modelling and simulation techniques offer a novel approach to investigating biochemical and physical processes at the molecular level. To speed up the discovery and development process, this can help direct physical experiments. Over 30 years of scholarly work and state-of-the-art In-silico methods, including molecular mechanics, free energy calculations, biotherapeutics developability, and more, are brought together in BIOVIA Discovery Studio 2021 (Free Download: BIOVIA Discovery Studio Visualizer - Dassault Systèmes (3ds.com). From Target ID through Lead Optimisation, it equips scientists with everything they need to probe the intricacies of protein chemistry and accelerate the discovery of small and big molecule therapies.

Open Babel GUI

Open Babel GUI (https://openbabel.org*)* is a chemical toolbox that aims to translate between different types of chemical data. Data from molecular modelling, chemistry, solid-state materials, biochemistry, and related fields can be searched, converted, analysed, and stored in this open, collaborative effort.

ChemDraw

The powerful prediction skills in ChemDraw Ultra (https://chemdrawdirect.perkinelmer.cloud/js/sample/index.html) make it a useful tool for creating chemical structures for use in database queries, creating figures for lab reports and scientific articles, and more.

Selection and preparation of the protein

Protein three-dimensional structures have been downloaded from the RCSB Protein Data Bank (https://www.rcsb.org/). Protein was chosen based on its ability to bind reactive compounds and the microorganisms from which it was generated. Protein 4DX5, 5V5Z, 6LW5, 1ILR, 3BJM, 6LN2 (PDB IDs) are displayed. (Figure 2)

Selection of bioactive phytoconstituent and structure

Amyl propionate, Isololiolide, Leucasperol A from *Leucas aspera* have been isolated and reported. [26] The phytoconstituents Amyl propionate, Isololiolide, Leucasperol A has been analysed using specific paper and PubChem (https://pubchem.ncbi.nlm.nih.gov). As the Amyl propionate, Isololiolide, Leucasperol A is not reported on PubChem, so it has been created as a MDL mol format with the help of ChemDraw Ultra and ACD/ ChemSketch and further minimization has been done. To predict ligand-protein docking, the ligands were converted to Protein Data Bank (.pdb) format using the Open Babel GUI. The molecular weight and structural formula of the phytochemicals found in *Leucas aspera* that passed screening for Lipinski's rule, absorption, distribution, metabolism, and toxicity (Table 4).

Table 4- Screened phytoconstituents with molecular weight and structural formula

Phyto chemicals	Molecular weight (gm/mol)	Structural Formula
Amyl propionate	144.21	$C_8H_{16}O_2$
Isololiolide	196.24	$C_{11}H_{16}O_3$
Leucasperol A	352.5	$C_{20}H_{32}O_5$

The remainder of the compounds have been screened for each specific activity, and some of them have violations and errors.

Drug likeness score prediction and side effect of ligand

Following the Lipinski rule of 5, Amyl propionate, Isololiolide, and Leucasperol A to check out the drug-likeness score on the online server Molsoft L.L.C. (http://molsoft.com/mprop/). The server determines the drug-likeness score, log P value, number of hydrogen bond acceptors and donors, and molecular weight (g/mol).

Pharmacokinetics prediction (ADME) and Toxicity identification

SwissADME (http://www.swissadme.ch/) was used to make predictions about the pharmacokinetic properties of the selected phytoconstituent. To predict ADME and toxicity data, this web-based tool employs in-silico algorithms. Which has been shown with the help of the table. (Table 5)

Ligand preparation

Open Babel GUI (https://openbabel.org) was used to convert the 3D.sdf files of phytoconstituents like Amyl Propionate, Isololiolide, and Leucasperol A (Table 4) downloaded from the PubChem database (https://pubchem.ncbi.nlm.nih.gov).

Protein preparation

RCSB's Protein Data Bank (PDB) (https://www.rcsb.org/) was mined to locate the protein of interest (4DX5, 5V5Z, 6LW5, 1ILR, 3BJM, 6LN2). The molecules have been assembled with the ligands. To further reduce docking interference, we used the BIOVIA Discovery Studio 2021 visualising tool to remove water molecules and add polar hydrogen before saving the file in.pdb format.

Ligand protein docking

Docking the phytoconstituents with the target protein was accomplished with the help of the PyRx (PyRx - Virtual Screening Tool download | SourceForge.net). After docking, the optimal Ligand was chosen based on the binding energy (Kcal/mol) in BIOVIA Discovery Studio 2021, which further generated and visualised 2D and 3D structural representations of the binding interaction between the ligand and protein.

Results

In-Silico Studies of The Reported Compound

Drug Likeness and pharmacokinetics property of Phytoconstituents: For the identification of new drug candidates, pharmacodynamic qualities and the pharmacokinetic procedure are used, as summarised in a table (Table 6), to determine their potential efficacy and side effects.

Table 6- Drug Likeness and Pharmacokinetic Property

Phytoconstituent/ API/ Parameters	Leucasperol A	Isololiolide	Amyl propionate	Amoxicillin	Clotrimazole
MF	$C_{20}H_{32}O_5$	$C_{11}H_{16}O_3$	$C_8H_{16}O_2$	$C_{16}H_{19}N_3O_5S$	$C_{22}H_{17}ClN_2$
MW (g/mol; <500)	352.5	196.24	144.21	365.4	344.8
HBD (<5)	2	1	1	4	0
HBA (<10)	5	3	1	6	1
Bioavailability Score	0.5	0.55	0.55	0.55	0.55
SOLUBILITY					
Water Solubility	Soluble	Highly Soluble	Soluble	Moderately Soluble	Soluble
PHARMACOKINETIC					
BBB permeation	Yes	Yes	Yes	No	Yes
GI absorption	High	High	High	Low	High

Molecular Docking Study

Early in the drug development process, protein-ligand docking may assist in the identification of promising compounds. Since the PyRx programme focuses on protein-ligand binding interactions, molecular docking was utilised to verify the suggested strategy. In the discovery studio 2021, the docking findings were analysed and visualised. The figures illustrate that Isololiolide, Amyl propionate and Leucasperol A has a robust binding contact with the proteins and exhibits a good binding interaction. The binding figures along with protein bonded has been reported below (Figure 5).

The binding energy of the **Leucasperol** A is depicting the best form of anti-microbial activity, anti-inflammatory and hypoglycaemic activity by showing the lowest and almost similar binding energy

compared to standard drugs against the same proteins. The binding energies (Kcal/mol) of every ligand with different proteins has been tabulated (Table 7).

Table 7- Binding Energies of the Phytoconstituents

Activity	Ligand (Std. & Phyto.)	Protein (PDB ID)	Binding energies (kcal/mol)
Anti-microbial Activity	Leucasperol A	4DX5 5V5Z	-8.8 -8.6
	Isololiolide	4DX5 5V5Z	-6.7 -6.4
	Amyl propionate	4DX5 5V5Z	-4.5 -4.5
	amoxicillin	4DX5	-7.7
	clotrimazole	5V5Z	-9.2
Anti-inflammatory Activity	Leucasperol A	6LW5 1ILR	-8.7 -7.5
	Isoliolide	6LW5 1ILR	-6.7 -6.2
	Amyl propionate	6LW5 1ILR	-5.2 -4.1
	Aspirin	6LW5	-6.4
	Diclofenac	1ILR	-6.1
Hypoglycaemic Activity	Leucasperol A	3BJM 6LN2	-8.3 -8.4
	Isololiolide	3BJM 6LN2	-6.2 -6.4
	Amyl propionate	3BJM 6LN2	-4.3 -4.5
	Metformin	3BJM	-5.2
	Vildagliptin	6LN2	-7.7

Conclusion

In conclusion, phytochemicals in *Leucas aspera* were screened i*n-silico* for their potential drug-likeness. Leucasperol A, Isololiolide, and Amyl propionate (Table 4), all derived from *Leucas aspera*, were discovered to have good binding affinity (Table 7) for their respective protein targets 4DX5, 5V5Z, 6LW5, 1ILR, 3BJM, 6LN2. Also, we can conclude that the ligands (phytoconstituents) are able to show the same mechanism the ligands (standards) are following with the particular protein to achieve the therapeutic action which can be made cleared by undergoing further *in-vitro* and *in-vivo* evaluation over ligands (phytoconstituents).

Declarations

- **Ethical Approval Statement**- This study did not involve any human or animal subjects, and therefore did not require ethical approval.

- **Competing Interests**- The authors declare no competing interest, financial or otherwise.

- **Author's Contribution**- Authors 1, 3, 4 are the students under me who has undergone the thorough study related to the plant.

Author 2 (corresponding author) is the guide and Assistant Professor for authors 1, 3, 4.

Author 5 is the Assistant Professor from the department of Pharmacology who has helped in understanding the Pharmacology. Author 6 has helped us to identify the plant for the commencement of the research.

Author 7, 8 has helped to prepare the content in the manuscript.

Finally, Author 2 (Corresponding author) has framed the manuscript with all the necessary details and communicated to the journal.

- **Funding-** The author declare that this research article is not funded.

- **Availability Of Data And Material-** All relevant data and information on topic entitled "In-silico anti–microbial, anti-inflammatory and hypoglycemic evaluation of active phytoconstituents of the plant: *Leucas aspera* (Willd.)" were compiled utilizing a variety of databases including PubMed, PDB,

SwissADME, Biovia Discovery Studio, PyRx, Science Direct, Springer- link, Google Scholar, review, and analysis papers from peer-reviewed publications. Some grey literature sources were also inspected.

-

- **Plagiarism-** Turnitin Plagiarism report stated 18% plagiarism over some specific terms which can be changed by any means.

References

1. Annapandian, V. M., & Rajagopal, S. S. (2017). Phytochemical evaluation and in vitro antioxidant activity of various solvent extracts of *Leucas aspera* (Willd.) Link leaves. Free Radicals and Antioxidants, *7*(2), 166–171.
2. Antony, J. J., Nivedheetha, M., Siva, D., Pradeepha, G., Kokilavani, P., Kalaiselvi, S., Sankarganesh, A., Balasundaram, A., Masilamani, V., & Achiraman, S. (2013). Antimicrobial activity of *Leucas aspera* engineered silver nanoparticles against Aeromonas hydrophila in infected Catla catla. Colloids and surfaces. B, Biointerfaces, *109*, 20–24. Https://doi.org/10.1016/j.colsurfb.2013.03.020
3. Arani, G. R., & Banu, N. (2017). Anti-fungal activity of metallochlorophyllins from *Leucas aspera* L. Research Journal of Pharmacy and Technology, *10*(2), 513–515.
4. Babu, A., Mohamed, M. S. N., Jaikumar, K., Anand, D., & Saravanan, P. (2016). In-vitro antifungal activity of leaf extracts of *Leucas aspera* and Leucas zeylanica. International Journal of Pharmaceutical Sciences and Research, *7*(2), 752.
5. Calhoun C, Wermuth HR, Hall GA. Antibiotics. [Updated 2022 Jul 31]. In: statpearls [Internet]. Treasure Island (FL): statpearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK535443/
6. Chew, A. L., Jessica, J. J. A., & Sasidharan, S. (2012). Antioxidant and antibacterial activity of different parts of *Leucas aspera*. Asian Pacific Journal of Tropical Biomedicine, *2*(3), 176–180.
7. Chouhan, H. S., & Singh, S. K. (2011). A review of plants of genus Leucas. Journal of Pharmacognosy and Phytotherapy, *3*(3), 13–26.
8. Das, B. K., Das, B., Arpita, F. K., Morshed, M. A., Uddin, A., Bhattacherjee, R., & Hannan, J. M. A. (2011). Phytochemical screening and antioxidant activity of *Leucas aspera*. International Journal of Pharmaceutical Sciences and Research, *2*(7), 1746.
9. Elumalai, D., Hemavathi, M., Hemalatha, P., Deepaa, C. V., & Kaleena, P. K. (2016). Larvicidal activity of catechin isolated from *Leucas aspera* against Aedes aegypti, Anopheles stephensi, and Culex quinquefasciatus (Diptera: Culicidae). Parasitology research, *115*, 1203–1212.
10. Enjamoori, V. K., Nampalli, A., Vasudha, B., Gangarapu, K., & Boggula, N. (2019). A review on *Leucas aspera* for phytopharmacological studies. INNOSC Theranostics and Pharmacological Sciences, *2*(1).

11. Gangadharan, a., & benny, p. J. (2018). Phytochemical analysis and in vitro anti-inflammatory activity of three indigenous plants by rbc membrane stabilization method
12. Gupta, N., Subhramanyam, E. V. S., & Sharma, R. K. (2011). Antidiabetic and hypoglycaemic activity of the crude extracts of the plant *Leucas aspera*. Int. J of Pharma. Innovations, *1*(1), 1–8.
13. Hossan, A. N. M. F., Zaman, F., Barman, M. R., Khatoon, S., Zaman, M., Khatun, F.,… Rahmatullah, M. (2011). Antinociceptive activity of Xanthium indicum J. Koenig ex Roxb.(Asteraceae) leaves and *Leucas aspera* (Willd.) Link (Lamiaceae) whole plants. *Advances in Natural and Applied Sciences*, *5*(2), 214–217.
14. Informedhealth.org [Internet]. Cologne, Germany: Institute for Quality and Efficiency in Health Care (iqwig); 2006-. What are microbes? 2010 Oct 6 [Updated 2019 Aug 29]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK279387/
15. Karthikeyan, S., Sivakumar, A., Anbalagan, M., Nalini, E., & Gothandam, K. M. (2013). Finger printing of alkaloids, steroids and flavonoids using HPTLC of *Leucas aspera* L. Whole plant methanolic extract. Journal of pharmaceutical sciences and research, *5*(3), 67.
16. Kovendan, K., Murugan, K., Vincent, S., & Barnard, D. R. (2012). Studies on larvicidal and pupicidal activity of *Leucas aspera* Willd.(Lamiaceae) and bacterial insecticide, Bacillus sphaericus, against malarial vector, Anopheles stephensi Liston.(Diptera: Culicidae). Parasitology Research, *110*, 195–203.
17. Latha, M. S., Latha, B., Oommen, S. K., & Rajalekshmi, R. (2012). Hepatoprotective and antioxidant effects methanolic extract of *Leucas aspera* against carbon tetra chloride induced oxidative damage in rats. Int. J. Adv. Pharm. Res, *4*, 1331–1337.
18. Maheswaran, R., Sathish, S., & Ignacimuthu, S. (2008). Larvicidal activity of *Leucas aspera* (Willd.) Against the larvae of Culex quinquefasciatus Say. And Aedes aegypti L. *Int J Integr Biol*, *2*(3), 214–217.
19. Mangathayaru, K., Lakshmikant, J., Sundar, N. S., Swapna, R. G. X. F., Grace, X. F., & Vasantha, J. (2005). Antimicrobial activity of *Leucas aspera* flowers. Fitoterapia, *76*(7–8), 752–754.
20. Manivannan, R. (2016). Isolation of apigenin-7-O-(6″-OE-caffeoyl)-β-D-glucopyranoside from *Leucas aspera* L. With anti-inflammatory and wound healing activities. Journal of Pharmacy & Pharmacognosy Research, *4*(2), 54–61.
21. Meghashri, S., Kumar, H. V., & Gopal, S. (2010). Antioxidant properties of a novel flavonoid from leaves of *Leucas aspera*. Food chemistry, *122*(1), 105–110.
22. Microbes, W. (2019). What are microbes?. Institute For Quality and Efficiency in Health Care (Iqwig). Retrieved from https://www.ncbi.nlm.nih.gov/books/NBK279387/) Accesses on 07/01/2023
23. Nagarajan, S. K., Rani, V., Narayanasamy, A., & Masthan, M. K. (2019). *Leucas aspera* to Treat Pan Oral Disorders-An Experimental Study. *Dental Journal*.
24. Nirmala, K. A., & Kanchana, M. (2018). *Leucas aspera*–A Review of its Biological activity. Systematic Reviews in Pharmacy, *9*(1), 41–44.

25. Phaneendra, P., Kumar, M. R., Bodhanapu, S., Rahaman, F. O. M., & Tamizmani, T. (2011). Hepatoprotective herbs: an overview. Int J Pharm Res Dev, *3*, 105–111.
26. Prajapati, M. S., Patel, J. B., Modi, K., & Shah, M. B. (2010). *Leucas aspera*: A review. Pharmacognosy reviews, *4*(7), 85.
27. Priya, R., Nirmala, M., Shankar, T., & Malarvizhi, A. (2018). Phytochemical compounds of *Leucas aspera* L. Pharmacological Benefits of Natural Products, *1*, 19–35.
28. Rahman, M. A., & Islam, M. S. (2013). Antioxidant, antibacterial and cytotoxic effects of the phytochemicals of whole *Leucas aspera* extract. Asian Pacific journal of tropical biomedicine, *3*(4), 273–279. Https://doi.org/10.1016/S2221-1691(13)60062-3
29. Rajalkshmi, G., Ramarendran, R., & Gomathi, N. (2013). Phytochemical screening and antifungal activity of medicinal plant. Indian. J. Pharm. Sci, *2*, 8–9.
30. Rani, G. R., & Banu, N. (2017). Anti fungal activity of metallochlorophyllins from *Leucas aspera* L. Research Journal of Pharmacy and Technology, 10(2), 513–515.
31. Reddy, M. K., Viswanathan, S., Sambantham, P. T., Ramachandran, S., & Kameswaran, L. (1986). Effect of *Leucas aspera* on experimental inflammation and mast cell degranulation. Ancient Science of Life, *5*(3), 168.
32. Riazunnisa, K., Chandra Obulu, Y., Sai Sudha, G., & Habeeb Khadri, C. (2013). In vitro antibacterial activity and phytochemical studies of some medicinal plants. Int. J. Pharm. Sci. Rev. Res, *23*, 77–80.
33. Sadhu, S. K., Okuyama, E., Fujimoto, H., & Ishibashi, M. (2003). Separation of *Leucas aspera*, a medicinal plant of Bangladesh, guided by prostaglandin inhibitory and antioxidant activities. Chemical and pharmaceutical bulletin, *51*(5), 595–598.
34. Singh, M. P., & Gindha, G. S. (2017). *Leucas aspera* a perfect poor man remedy. Journal of Pharmacognosy and Phytochemistry, *6*(1), 275–277.
35. Suganya, G., Karthi, S., & Shivakumar, M. S. (2014). Larvicidal potential of silver nanoparticles synthesized from *Leucas aspera* leaf extracts against dengue vector Aedes aegypti. Parasitology research, *113*, 875–880.
36. Thenmozhi, M., Dhanalakshmi, M., Devi, K. M., Sushila, K., & Thenmozhi, S. (2013). Evaluation of hepatoprotective activity of *Leucas aspera* hydroalcoholic leaf extract during exposure to lead acetate in male albino Wistar rats. Asian J Pharm Clin Res, *6*(1), 78–81.
37. Vasudha, K., Archana, D., Mutyalamma, B., & Kishori, B. (2019). Phytochemical screening, antimicrobial, and antioxidant activities of root and leaf extracts of *Leucas aspera*. Asian J Pharm Clin Res, (3), 141–147.

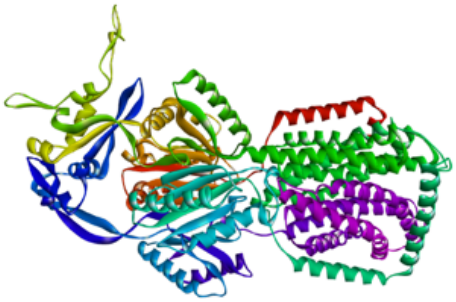
Tables

Table 5 is available in the supplementary files section.

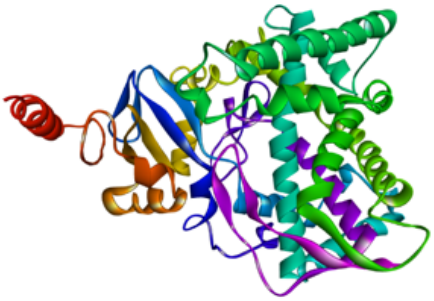
Figures

Figure 1

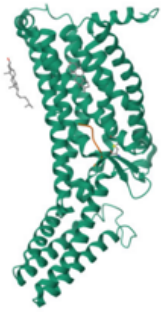
Leucas aspera (Willd.) [10]



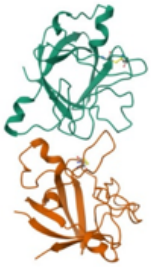
Protein 1- 4DX5



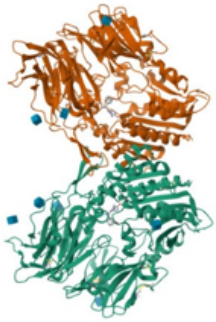
Protein 2- 5V5Z



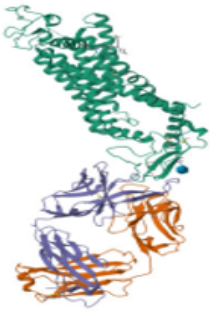
Protein 3- 6LW5



Protein 4- 1ILR



Protein 5- 3BJM



Protein 6- 6LN2

Figure 2

Proteins

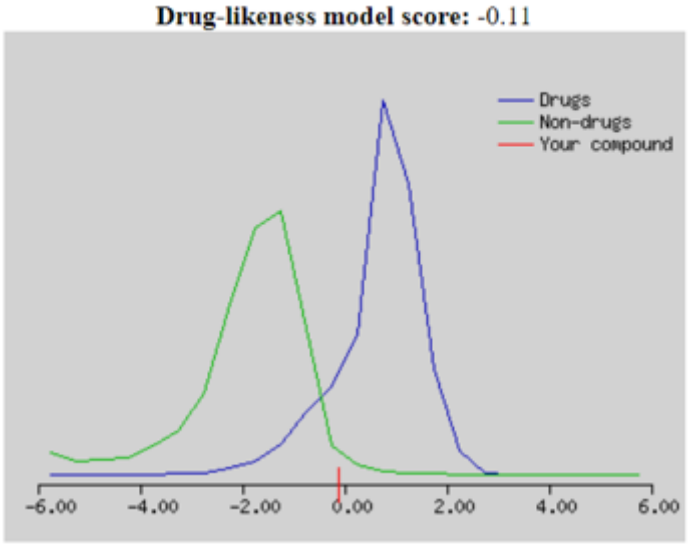


Figure 3

Drug-likeness Leucasperol A

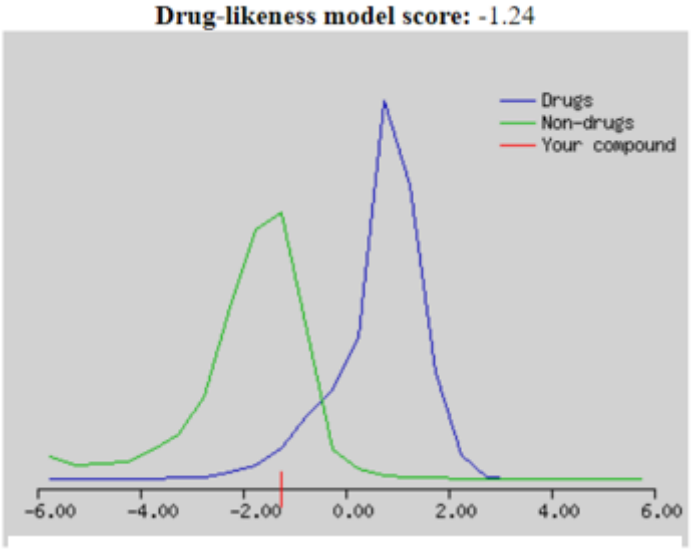


Figure 4

Drug-likeness Amyl propionate

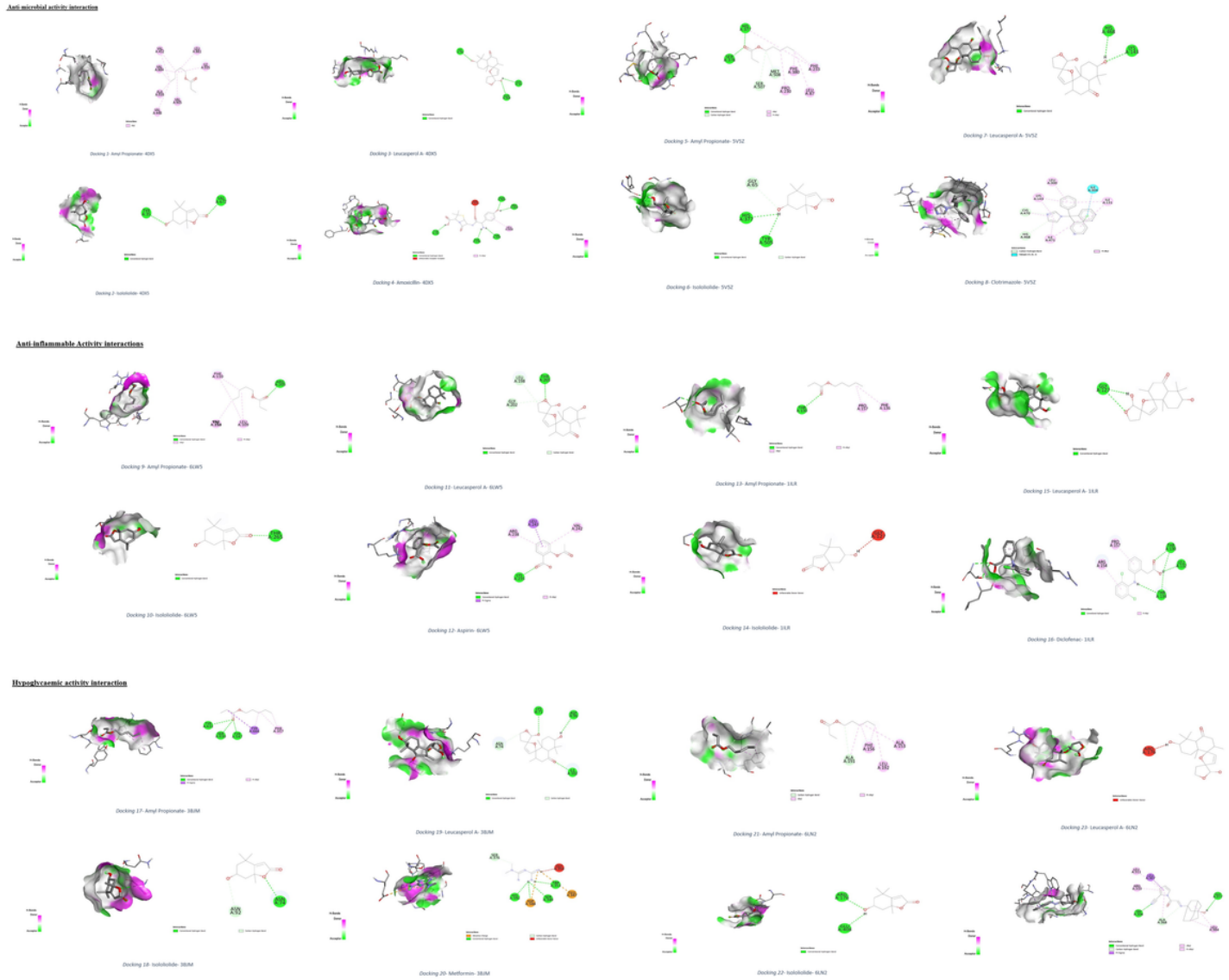


Figure 5

Docked (2D & 3D) interactions between Protein and Ligand (Phytoconstituents & Standard)

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Table5.docx