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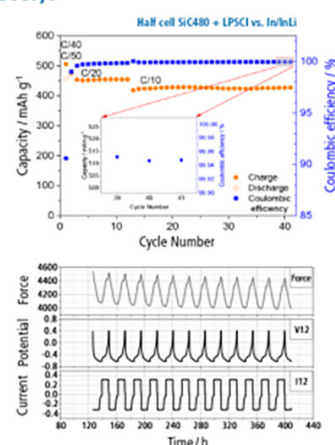
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In silico and phytochemical investigation of *Strychnos nux-vomica* leaf extract against LipL32 protein of *Leptospira* spp.

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Abstract. Leptospirosis remains a significant zoonotic disease caused by pathogenic *Leptospira* spp. The outer membrane lipoprotein LipL32 plays a critical role in virulence and host interaction, making it a promising molecular target. In this study, *Strychnos nux-vomica* leaf extract was subjected to qualitative phytochemical screening and UV-Visible spectroscopic analysis, followed by molecular docking and ADMET prediction of selected alkaloids against LipL32. Four major alkaloids—strychnine, brucine, colubrine, and vomicine—were evaluated. Vomicine exhibited the most favorable binding energy (−8.023 kcal/mol). ADMET analysis suggested acceptable gastrointestinal absorption while highlighting potential toxicity concerns for certain alkaloids. These findings provide preliminary computational insights into LipL32 inhibition and require further experimental validation.

Keywords: *Leptospira* spp., *Strychnos nux-vomica*, phytochemical analysis, molecular docking, ADMET, pharmacokinetics.

1. Introduction

A common zoonotic illness, leptospirosis, is brought on by pathogenic species of the genus *Leptospira* spp. Humans are usually affected by coming into direct or indirect contact with water or soil contaminated by the urine of animals carrying the infection, especially rats. The illness is common in tropical and subtropical areas and has a variety of clinical presentations, from minor flu-like symptoms to serious ones, including hepatic dysfunction, pulmonary haemorrhage, renal failure, and, in the worst situations, death. Despite its global health relevance, therapeutic options for leptospirosis remain limited, and treatment relies primarily on conventional antibiotics such as doxycycline and penicillin. The emergence of antimicrobial resistance and limited access to healthcare in endemic regions highlight the need for alternative and complementary therapeutic strategies [3–4].

Pathogenic *Leptospira* spp express several outer membrane proteins that play a crucial role in host–pathogen interactions and bacterial virulence. Among these, LipL32 is the most abundant outer membrane lipoprotein expressed during infection and is conserved across pathogenic



strains. LipL32 has been reported to participate in host tissue adhesion, immune modulation, and bacterial survival, making it a suitable molecular target for the exploration of potential anti-*leptospiral* agents. Targeting such conserved virulence-associated proteins through computational approaches provides a rational pathway for early-stage drug discovery.

Medicinal plants are rich sources of bioactive secondary metabolites, including alkaloids, flavonoids, phenolic compounds, tannins, and steroids [17–19]. *Strychnos nux-vomica* L., a member of the Loganiaceae family, is well known for its diverse phytochemical composition. Although the seeds are recognized for toxicity due to the presence of strychnine and brucine, the leaves are reported to contain comparatively lower levels of toxic alkaloids and may exhibit potential pharmacological properties when appropriately processed. Nevertheless, there are still few thorough studies on the possible anti-*leptospiral* significance of phytochemicals extracted from *S. nux-vomica* leaves [5–6]. In recent years, *in silico* approaches such as molecular docking, pharmacokinetic prediction, and ADMET analysis have emerged as effective tools for preliminary screening of bioactive compounds, enabling the identification of promising candidates prior to extensive experimental validation. These computational techniques reduce cost, time, and experimental complexity while providing insights into protein–ligand interactions and drug-likeness characteristics. In this context, the present study aims to investigate *Strychnos nux-vomica* leaf extract through preliminary phytochemical screening and spectroscopic analysis, followed by *in silico* evaluation of selected phytochemical constituents against the LipL32 protein of *Leptospira* [25–26]. Molecular docking was employed to assess binding interactions, while SwissADME and pkCSM tools were used to predict pharmacokinetic and toxicity profiles. The study is intended as a preliminary investigation to identify computationally promising phytochemicals that may warrant further *in vitro* and *in vivo* validation for anti-*leptospiral* applications.

2. Materials and Methods

2.1 Gathering and verifying plant material

In the Uttchapulli area of the Ramanathapuram district in Tamil Nadu, India, fresh *Strychnos nux-vomica* leaves were gathered. The gathered leaves were air-dried for three days at room temperature after being properly cleaned with distilled water to get rid of any dust or debris that might have stuck to them. The dried plant material was ground into a powder using a mechanical grinder and stored in sealed containers for further analysis.

2.2 Preparation of leaf extract

Using magnetic stirring, the powdered leaf material (1 g) was extracted at room temperature for 15 minutes using 10 mL of methanol. Whatman No. 1 filter paper was used to filter the extract.

2.3 Qualitative phytochemical screening

The methanolic leaf extract was subjected to a preliminary qualitative phytochemical screening using conventional protocols outlined by Harborne [7]. Based on distinctive color changes or precipitate formation, the extract was examined for the presence of significant secondary metabolites, such as alkaloids, flavonoids, phenols, tannins, steroids, triterpenes, and saponins.

2.4 UV-Visible spectroscopic analysis

A UV-Vis spectrophotometer operating in the 200–800 nm wavelength range was used to perform UV-visible spectroscopic analysis on the methanolic leaf extract. The blank was methanol. The existence of phenolic and alkaloid components in the extract was confirmed by recording the absorption peaks.

2.5 Selection of phytochemicals for *in silico* analysis

Four primary alkaloid constituents—strychnine, brucine, colubrine, and vomicine—were chosen for *in silico* investigations based on the qualitative phytochemical screening results and published literature on the phytochemical composition of *Strychnos nux-vomica* [5–6,13]. The PubChem database was used to obtain the chemical structures of the chosen compounds, which were then ready for docking and pharmacokinetic analysis.

2.6 Molecular docking studies

Using the DockThor-VS web server, molecular docking was used to assess how several phytochemicals interacted with *Leptospira*'s LipL32 protein. The crystal structure of LipL32 from pathogenic *Leptospira interrogans* (PDB ID: 2ZZ8; resolution 2.30 Å) was retrieved from the Protein Data Bank. [25]. Water molecules and heteroatoms were removed prior to docking, and the structure was energy-minimized using default parameters. In order to prepare proteins, atoms of hydrogen were added and partial charges were assigned utilizing the DockThor-VS platform. The MMFF94S force field was used to minimize the energy of ligands. Binding affinities were represented as binding energy values (kcal/mol), and docking calculations were performed with default parameters. Favorable protein–ligand interactions and the lowest binding energy were used to choose the optimal docking positions.

2.7 ADMET and pharmacokinetic prediction

Pharmacokinetic and ADMET properties of the chosen phytochemicals were predicted using SwissADME and pkCSM online servers. Each compound's canonical SMILES served as the input. Physicochemical characteristics, lipophilicity, water solubility, gastrointestinal absorption, bioavailability radar, and drug-likeness factors were all predicted using SwissADME. The toxicity of Ames, hepatotoxicity, maximum tolerated dosage, and acute toxicity to the mouth (LD50) were among the toxicity-related endpoints that were estimated using pkCSM. The anticipated parameters were utilized to assess the drug-likeness and safety profile of the phytochemicals.

2.8 Data analysis

To find phytochemicals with favorable binding affinity and appropriate pharmacokinetic profiles, docking scores, interaction energies, and projected ADMET parameters were tallied and compared. The findings were not regarded as conclusive biological validation, but rather as initial signs of possible anti-leptospirosis relevance.

3. Results and discussion

3.1 Phytochemical screening and UV-Visible spectroscopic analysis

Preliminary qualitative phytochemical screening of the methanolic leaf extract of *Strychnos nux-vomica* revealed the presence of alkaloids, flavonoids, phenolic compounds, tannins, and steroids, whereas saponins were not detected (Table 1). The selection of *S. nux-vomica* leaves for additional

in silico analysis is supported by the presence of alkaloids and phenolic compounds, which are compatible with previous observations on the phytochemical composition of the plant [7–8].

UV–Visible spectroscopic analysis of the methanolic extract exhibited characteristic absorption peaks in the range of 200–350 nm. These absorption bands are commonly associated with $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ electronic transitions of phenolic and alkaloid compounds. Although UV–Vis analysis does not provide compound-level identification, the observed spectral features qualitatively support the presence of conjugated phytochemical constituents detected during preliminary screening in Figure 1.

Table 1. Reported phytochemical groups of *Strychnos nux-vomica* (literature comparison)

Phytochemical groups	<i>Strychnos nux-vomica</i> (aerial parts) #	<i>Strychnos nux-vomica</i> (leaves)	<i>Strychnos nux-vomica</i> (root) #	<i>Strychnos nux-vomica</i> (flower parts) #
Flavonoid	+	+	+	+
Phenol	+	+	+	+
Tannins	+	+	+	+
Alkaloids	+	+	+	+
Saponins	–	–	–	–
Triterpenes	+	+	+	+
Steroids	+	+	+	+

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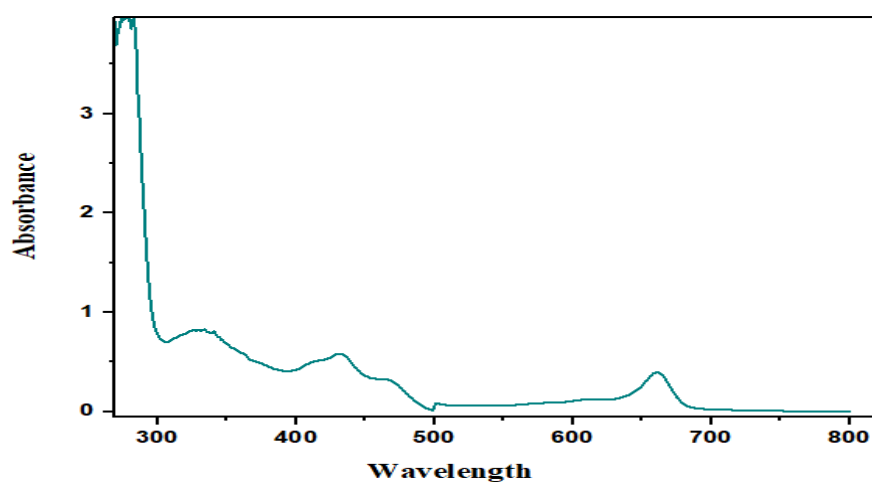


Figure 1. UV Vis Spectra of *S. Nux Vomica* Leaf Extract in methanol.

3.2 Analysis of molecular docking

All selected alkaloids demonstrated favourable predicted binding affinities toward LipL32 [25–26]. Among them, vomicine exhibited the lowest binding energy (-8.023 kcal/mol), suggesting comparatively stronger interaction within the active site as given in Table 2. The interactions were predominantly stabilized by van der Waals forces and electrostatic contributions. The rigid polycyclic scaffold of the indole alkaloids may enhance steric complementarity within the protein pocket. However, it is important to note that docking simulations represent static interaction models and do not account for protein flexibility or solvent dynamics. Molecular docking provides a structural model of ligand–protein interaction and does not account for dynamic conformational changes as shown in figure 2.

Table 2. Binding energy and factors affecting binding in protein pocket

Ligand	Binding Energy (kcal mol ⁻¹)	vdW Energy (kcal mol ⁻¹)	Elec Energy (kcal mol ⁻¹)
Brucine	-7.802	-15.508	-11.459
Colubrine	-7.597	-16.923	-11.270
Strychnine	-7.392	-12.945	-14.672
Vomicine	-8.023	-18.455	-12.065

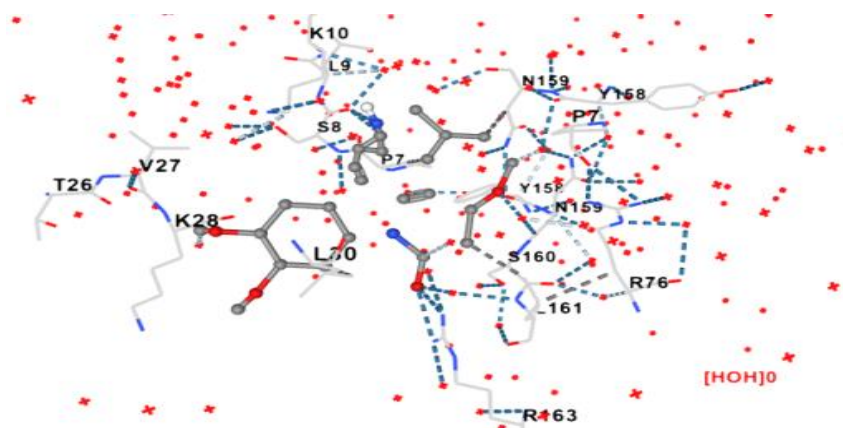


Figure 2. Molecular docking pose of brucine within the LipL32 protein binding pocket showing ligand orientation.

3.3 ADMET and pharmacokinetic prediction

SwissADME and pkCSM programs were used to assess the pharmacokinetic and toxicity profiles of the chosen phytochemicals [27–28]. The majority of the compounds showed acceptable physicochemical qualities, such as moderate lipophilicity and expected gastrointestinal absorption, according to SwissADME forecasts. Although certain aberrations were noted because of molecular stiffness and polarity, the bioavailability radar plots indicated that the compounds generally lie within the ideal range for oral bioavailability characteristics in Figure 3.

pkCSM toxicity predictions showed that the toxicity profiles of the chosen alkaloids varied as shown in Table 3. Strychnine in particular displayed anticipated toxicity signals, which is in line with its established toxicity. Though none of the chemicals can be deemed non-toxic based only on computational predictions, brucine, colubrine, and vomicine showed relatively lower anticipated toxicity values. These findings emphasize how crucial it is to analyze ADMET data carefully.

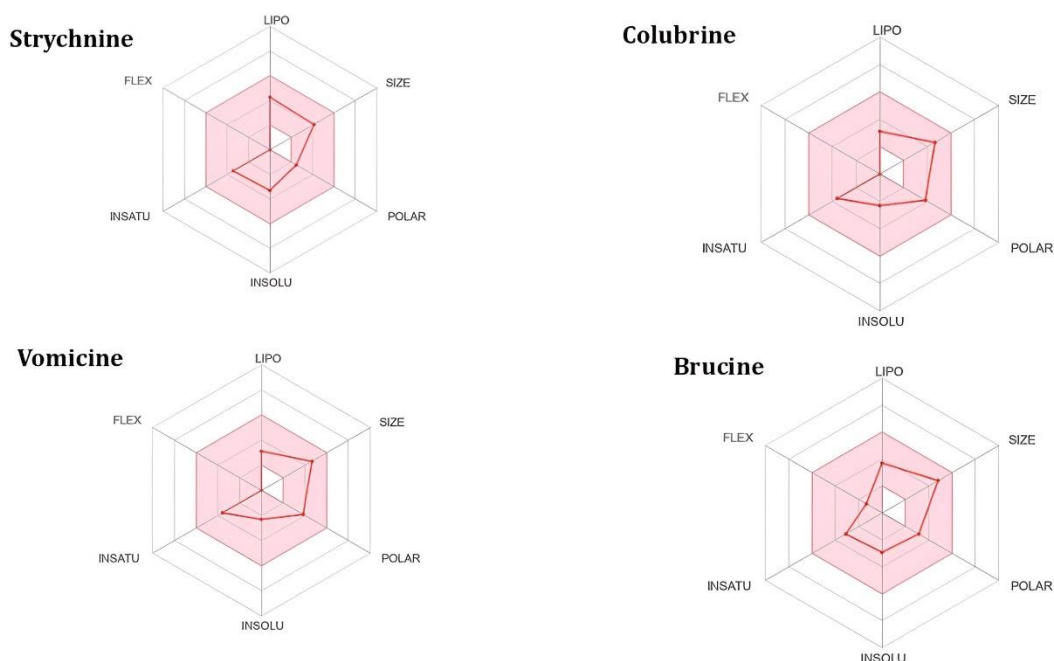


Figure 3. Bioavailability radar of phytochemicals (Lipophilicity (LIPO), Size, Polarity (POLAR), Solubility (INSOLU), Flexibility (FLEX), Saturation (INSATU)).

The comparative binding trend suggests that subtle structural variations among indole alkaloids significantly influence interaction energetics within the LipL32 binding domain. Further validation through molecular dynamics simulation and in vitro inhibition assays is required to confirm biological relevance. Although strychnine exhibited predicted toxicity signals in pkCSM analysis, it is important to distinguish between the highly toxic seed alkaloid fraction and comparatively lower alkaloid concentrations reported in leaf extracts. Selective fractionation techniques such as acid–base extraction and chromatographic purification can potentially reduce the proportion of neurotoxic constituents. Furthermore, structural derivatization strategies targeting the tertiary amine moiety may reduce blood–brain barrier penetration while preserving binding affinity toward LipL32.

Table 3. ADMET properties of phytochemicals

Parameters	Brucine	Strychnine	Colubrine	Vomicine
Water solubility	-3.50	-3.49	-3.43	-3.29
Caco2 permeability	1.08	1.66	1.19	0.02
Intestinal absorption (human)	100	99.03	100	97.68
Skin permeability	-3.73	-3.14	-3.48	-3.55
P-glycoprotein substrate	Yes	No	No	Yes
BBB permeability	-0.28	0.21	-0.09	0.14
CNS permeability	-2.95	-2.47	-2.66	-2.24
CYP3A4 substrate	Yes	Yes	Yes	No
Total clearance	1.02	0.93	0.95	0.92
Max. tolerated dose (human)	-0.33	-0.53	-0.46	-1.07
Oral rat acute toxicity (LD50)	2.14	2.89	2.97	3.09
Hepatotoxicity	Yes	No	No	Yes
Skin sensitisation	No	No	No	No
TPyriformistoxicity	0.33	0.39	0.36	0.30
Minnow toxicity	0.85	0.67	0.67	1.60

Nano formulation-based targeted delivery systems may also minimize systemic exposure. Nevertheless, these mitigation approaches require experimental validation through cytotoxicity assays and controlled dose–response studies.

4. Conclusion

This study provides preliminary computational evidence supporting the potential interaction of selected alkaloids from *Strychnos nux-vomica* leaf extract with the LipL32 protein of *Leptospira* spp [25–26]. Among the compounds analyzed, vomicine demonstrated the most favourable binding affinity. However, predicted toxicity profiles highlight the need for careful pharmacological evaluation. Alternatively, mitigation strategies such as selective fractionation, chromatographic purification, structural modification to reduce neurotoxicity, nano formulation-based targeted delivery, and dose optimization guided by cytotoxicity assays may improve therapeutic feasibility. However, further in vitro and in vivo experimental validation is necessary to confirm the therapeutic efficacy and safety profile of these phytocompounds.

5. Reference

- [1] Li Y M, Jiao P, Li Y, Gong X, Chen S and Sun S 2019 *Front. Microbiol.* **10** 2853
- [2] Liu W, Li L P, Zhang J D et al 2014 *PLoS One* **9** e103442
- [3] Morgan J, Meltzer M I, Plikaytis B D et al 2005 *Infect. Control Hosp. Epidemiol.* **26** 540–547
- [4] Pierce C G and Lopez-Ribot J L 2013 *Expert Opin. Drug Discov.* **8** 1117–1126
- [5] Joubouhi C, Tamokou J D D, Ngnokam D, Voutquenne-Nazabadioko L and Kuate J R 2017 *BMC Complement. Altern. Med.* **17** 17
- [6] Nzogong R T, Ndjateu F S T, Ekom S E et al 2018 *BMC Complement. Altern. Med.* **18** 159
- [7] Harborne J B 1973 *Phytochemical Methods: A Guide to Modern Techniques of Plant Analysis* (London: Chapman and Hall)
- [8] Ramde-Tiendrebeogo A, Tibiri A, Hilou A, Lompo M, Millogo-Kone H and Nacoulma O G 2012 *Int. J. Brain Cogn. Sci.* **6** 328–336
- [9] Chang C, Yang M, Wen H and Chern J 2002 *J. Food Drug Anal.* **10** 178–182
- [10] Padmaja M, Sravanthi M and Hemalatha K P J 2011 *J. Phytol.* **3** 86–91
- [11] Yu W, Zhao Y and Shu B 2004 *Food Chem.* **86** 525–529
- [12] Ebrahimzadeh M A, Nabavi S F, Eslami B and Nabavi S M 2009 *Pharmacologyonline* **3** 394–403
- [13] Nandjou Kenfack J, Tsafack Ngoudjou D, Kemvoufo Ponou B et al 2020 *Sci. J. Chem.* **8** 48–58
- [14] Turkmen N, Velioglu Y S, Sari F and Polat G 2007 *Molecules* **12** 484–496
- [15] Guha G, Rajkumar V, Kumar R A and Mathew L 2011 *Evid. Based Complement. Altern. Med.* **2011** 576456
- [16] Sourì E, Amin G, Farsam H and Barazandeh T M 2008 *J. Pharmacol. Sci.* **16** 83–87
- [17] Rios J L 2010 *J. Ethnopharmacol.* **128** 1–14
- [18] Agarwal S K, Singh S S, Verma S and Kumar S 2000 *J. Ethnopharmacol.* **72** 43–46
- [19] Rodrigues C G, Ferreira P R B, Ferreira C S O et al 2014 *J. Med. Plants Res.* **8** 1095–1100
- [20] Kountchou C L, Toukap E O M, Adamou V et al 2021 *Br. J. Med. Health Sci.* **3** 737–743
- [21] Boey K, Shiokawa K and Rajeev S 2019 *PLoS Negl. Trop. Dis.* **13** e0007499
- [22] Munoz-Zanzi C, Groene E, Morawski B M et al 2020 *Rev. Panam. Salud Publica* **44** e78
- [23] Bierque E, Thibeaux R, Girault D, Soupe-Gilbert M E and Goarant C 2020 *PLoS One* **15** e0227055
- [24] Pinto P S, Libonati H and Lilenbaum W 2017 *Trop. Anim. Health Prod.* **49** 231–238
- [25] Lo Y Y, Jiao P, Li Y, Gong X, Chen S and Sun S 2013 *J. Biol. Chem.* **288** 12335–12344
- [26] Pinne M and Haake D A 2013 *PLoS One* **8** e51025
- [27] Guedes I A et al 2024 *J. Mol. Biol.* **436** 168548
- [28] Guedes I A, Costa L S C, dos Santos K B et al 2021 *Sci. Rep.* **11** 5543
- [29] Muslikh F et al 2023 *Int. J. Contemp. Sci.* **1** 33–38
- [30] Khan M W et al 2024 *Int. J. Newgen Res. Pharm. Healthc.* **2** 176–186