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Review Article

A Systematic Review on Phytochemistry and Pharmacological Activity of the Plant *Hymenocallis littoralis* (Jacq.) Salisb

Saurav Talukdar[1], Suman Kumar[2,*], Sarbanga Bezbaruah[1], Prerana Kashyap[1], Mohsin Ahmed[1], Rupjyoti Majumder[1], Rajsekhar Das[1], N. Anirudh Singh[3]

[1]Royal School of Pharmacy, The Assam Royal Global University, Betkuchi Guwahati, Assam, INDIA.
[2]Department of Pharmaceutical Science, Rabindranath Thakur Vishwavidyalaya, Hojai, Assam, INDIA.
[3]Faculty of Pharmaceutical Science, Assam Down Town University, Guwahati, Assam, INDIA.

ABSTRACT

Hymenocallis littoralis (Jacq.) Salisb., commonly known as the Beach spider lily is a perennial herbaceous plant that belongs to the family Amaryllidaceae; well known for its distinctive ethnomedicinal uses against different serious ailments. The review critically analysed the distribution, traditional uses, phytoconstituents, and pharmacological activity of the plant *H. littoralis*. All the information described in this study was collected by using the electronic databases comprising PubMed and Google Scholar using the general search terms "*Hymenocallis littoralis*", "traditional uses", "phytochemical", and "pharmacological activity". The outcome of the study reveals that different parts of the plant, such as the bulb, root, stem, leaves, and flower, contain a wide variety of phytoconstituents, including alkaloids, flavonoids, phenolics, and volatile oils. To date, more than 30 alkaloids have been isolated from different parts of the plant. Among them, pancratistatin and lycorine are most commonly present, exhibiting diverse pharmacological activities. Similarly, other secondary metabolites such as phenolics and volatile oils are also isolated and reported in various scientific literature. The plant has also been reported for its significant traditional use by various indigenous communities in China, Mexico, Central America, and the Philippines for the management of wound healing, rheumatic joint pain, inflammation and pain, hemorrhoids, freckles, and blemishes. The pharmacological activity reveals that the plant shows potential anti-microbial, anthelmintic, anti-fungal, anti-cancer, anti-viral, and wound healing activity in various *in vitro* as well as *in vivo*. The study provides comprehensive and updated information regarding the plant profile and advocates the need for a clinical trial to find out unexplored lead molecules for drug discovery.

Keywords: Ethnomedicine, *Hymenocallis littoralis*, Pharmacology, Phytoconstituents.

Correspondence:
Dr. Suman Kumar
Assistant Professor, Department of Pharmaceutical Science, Rabindranath Thakur Vishwavidyalaya, Hojai-782435, Assam, INDIA.
Email: smnkmr33@gmail.com
ORCID: 0000-0002-9109-9020

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INTRODUCTION

Medicinal plants are integral to primary healthcare, especially in rural communities, where they serve as key therapeutic agents. According to the World Health Organization (WHO), approximately 80% of global population trusts on herbal remedies to cure various ailments.[1] These plants have historically contributed to drug discovery, with active phytochemicals forming the basis of many modern pharmaceuticals.[2] The systematic review plays an important role in understanding ethnomedicinal use and pharmacological evaluation, attracting researchers to gather recent and updated information regarding highly used plant species.[3] *Hymenocallis littoralis* (Jacq.) Salisb. is a perennial herbaceous plant that classified under the family Amaryllidaceae; well known for its distinctive ethnomedicinal uses against different serious ailments. The plant is widely distributed in tropical and seaside regions of Asia, Africa, North America, and South America.[4] The plant, commonly referred to as the Beach spider lily and also Melong Kecil, is admired for its striking white blossoms that emit a pleasant fragrance and resemble fine spider legs. Its vibrant green leaves form a basal rosette, enhancing its decorative value even when it doesn't bloom.[5-9] The plant has been utilizing in folk medicine for its wound-healing properties.[10] Extracts from its leaves and bulbs have been commonly used in traditional Chinese medicine to treat conditions such as rheumatic joint pain, traumatic inflammation and pain, carbuncle-related swelling, and haemorrhoids.[10] Another closely related species of the Amaryllidaceae family i,e, *Crinum asiaticum* is well documented in Ayurveda for the management of snake bites, fever, joint pain, skin diseases, and

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leucorrhea.[11] The genus *Hymenocallis* comprises a diverse group of bulbous plants characterized by their unique, spider-like white flowers. Recent investigations have identified over 70 species within the genus *Hymenocallis*, primarily inhabiting riverbanks, coastal areas, and woodlands, with several species including *H. occidentalis, H. speciosa, H. coronaria, H. liriosme*, and *H. caribaea* noted for their ethnopharmacological relevance.[12,13] The genus is widely known for its diverse bioactive compounds for specially Amaryllidaceae-type alkaloids for their notable pharmacological activities such as antitumor, antiviral, anti-inflammatory, and cholinesterase inhibitory effects.[14,15] For example, Galantamine is an FDA approved anti Alzheimer's drug that belongs to Amaryllidaceae-type alkaloids isolated from *Galanthus woronowii* (snowdrop). The phytochemical analysis of the particular plant revealed the presence of numerous bioactive phytoconstituents such as o-methyllycorinine, macronine, homolycorine, trazettine, littoraline, narciclasine etc.[16] Pancratistatin, an alkaloid derived from the bulbs of *H. littoralis*, has been utilized in the development of anticancer agents.[17] In addition to its anticancer potential, *H. littoralis* displays a range of pharmacological activities, including wound healing, anti-inflammatory, antimicrobial, and neuroactive effects, as well as applications in managing arthralgia.[6,18-21] Additionally, this plant has shown efficacy against *Candida albicans*, a prevalent opportunistic fungal pathogen known for its resistance to conventional antifungal treatments.[22] On the other hand, the plant is commonly grown for its ornamental purposes and has a considerable horticultural value. The Amaryllidaceae family comprises several prominent ornamental species, such as snowflakes (*Leucojum*), daffodils (*Narcissus*), and snowdrops (*Galanthus*).[23] This specific plant is commonly grown for its fragrant white blossoms and evergreen leaves. Along with its attractive, sweet aroma, its membranous corona has added to its decorative appeal.[24]

The plant under investigation has been extensively used in traditional medicine by different tribal communities for centuries.[12] The plant used to cure a wide range of ailments that the tribal people commonly face in their daily lives, such as inflammatory diseases, digestive disease, infections, and other chronic and acute illnesses. The presence of several bioactive compounds distributed throughout the plant's leaves, roots, bark, and fruits is the main reason for these traditional uses. It is believed that these phytoconstituents have an important role in the plant's therapeutic properties.[10]

Over the past few decades, various scientific studies have verified the presence of numerous pharmacologically active compounds in this plant, such as alkaloids, flavonoids, and volatile oils. These constituents have demonstrated a broad range of biological effects, including anti-oxidant, anti-inflammatory, anti-microbial, and anti-cancer effects.[6,18,20,25,26] However, despite these findings, comprehensive efforts to integrate and update all available scientific knowledge regarding the plant's phytochemistry, pharmacological potential, and its correlation with traditional medicinal applications remain limited.

This review article aims to bridge this gap by systematically compiling and critically analyzing the most recent findings related to the plant's phytochemical profile and pharmacological activities, while simultaneously drawing connections with its ethnomedicinal uses. By presenting a consolidated and up-to-date resource, this article intends to provide a valuable reference for researchers working in the field of natural product chemistry, pharmacognosy, and drug discovery. Furthermore, the review also highlights unexplored research areas and suggests future directions, including advanced mechanistic studies, clinical validations, and sustainable utilization strategies. Such comprehensive insight will not only facilitate scientific exploration of this plant but also support its development into evidence-based therapeutic applications.[27]

METHODOLOGY

All relevant information about *Hymenocallis littoralis* was compiled from peer-reviewed literature published in the English language. Data were collected from several electronic databases, including PubMed, Google Scholar, Scopus, ScienceDirect, and SpringerLink. The search strategy incorporated combinations of keywords such as "*Hymenocallis littoralis*" AND "phytoconstituents," OR "bioactive compounds," "traditional application," "pharmacological activity," OR "toxicological studies." Studies were included if they were published in English and contained data on the phytochemistry, traditional uses, or pharmacological and toxicological properties of *Hymenocallis littoralis*. Exclusion criteria encompassed (a) publications in languages other than English and (b) studies presenting insufficient or unclear data. The primary aim of this review was to consolidate recent findings regarding the plant's phytochemical composition, ethnobotanical relevance, pharmacological potential, and safety profile. Relevant books and abstracts meeting the inclusion criteria were also considered. The selection process for eligible sources is illustrated in the PRISMA flow diagram (Figure 1).

Botanical Description

Synonyms

Pancratium littorale Jacq., *Nemepiodon littorale* (Jacq.) Raf., *Hymenocallis caribaea* var. *littoralis* (Jacq.) Herb., *Hymenocallis pedalis* Herb., *Hymenocallis expansa* (Small) Traub.

Morphological features

This perennial plant typically grows up to 2-3 feet tall and thrives in sandy soils, making it well-suited for beach and coastal gardens.[28] The large, trumpet-shaped blooms appear in clusters atop long, slender stems, creating a beautiful display that attracts pollinators like butterflies and hummingbirds.[29] Generally, *H. littoralis* is characterized by narrow sword-shaped leaves. Around

12 white flowers bloom in a group and carry a 2-foot-long stalk, which originates from the centre of the petals.[30] The leaves are dark green, crowded, and have a shiny appearance. It is 0.5-1 m tall and 6-7 centimeters wide.[31]

Habitat and geographical distribution

Beach spider lily thrives in full sun to partial shade and is well-adapted to coastal environments due to its tolerance to salt spray. While it requires moderate watering, it becomes drought-tolerant once established.[24] The species is widely distributed across tropical as well as sub-tropical regions, particularly along coastal areas. Reports indicate its presence in countries such as Mexico, the western coast of Florida, the West Indies, India, Bangladesh, Pakistan, and parts of China, including Fujian, Yunnan, Guangdong, and Guangxi provinces.[10,32-35] In India, it is notably found in the lower Himalayan belt, with significant distribution in the northeastern and southern regions. Tripura is recognized as a key habitat,[36] and the Botanical Survey of India has documented its presence in Tamil Nadu, Kerala, Maharashtra, and Gujarat (Figure 2).[21]

Ethnobotanical uses

Traditional applications

Traditionally *H. littoralis* has been used across various cultures for its potential medicinal properties. In the Philippines, it served as a recuperative remedy, while in Indonesia, it was applied for skin conditions such as freckles and blemishes.[5,9,37] The leaves and bulbs of the plant were used to treat rheumatic arthralgia, traumatic injuries, swellings, and haemorrhoids in traditional Chinese medicine for their detumescence and analgesic activity.[16,38] According to historical records, species from the Amaryllidaceae family, which includes *H. littoralis*, were used to treat cancers as early as the 4th century BC.[34] Furthermore, some indigenous groups have used the herb for wound healing and have linked its bioactive components to emetic and anti-inflammatory activities.[10] Since lycorine was first isolated in the 1920s, Amaryllidaceae species have demonstrated pharmacological potential with notable biological activities and phytochemical studies dating back to that time.[14,39,40] All the reported traditional applications of the plant have been listed in Table 1.

Cultural significance

Spider lily (*H. littoralis*) holds significant cultural and horticultural value, particularly in South Gujarat and various regions of South India, where it is cultivated extensively as a prominent loose flower crop.[29] Renowned for its distinctive, long, white, vanilla-scented floral buds that resemble spider claws, this plant has earned its common name, "spider lily." Flowers have been closely tied to human culture since the dawn of civilization, symbolizing beauty, devotion, and celebration. In India, the world's largest producer of loose flowers, the spider lily plays an important role in traditional rituals, decorative practices, and the floral industry.[44]

Phytochemical constituents

Phytochemical investigations of *H. littoralis* have led to the identification of numerous bioactive constituents. Some alkaloids have been obtained from the plant, including lycorine, hippeastrine, littoraline, diacetyllycorine, norpluvine, lycoranine, mhomolycorine, haemanthamine, vittatine, crinine, tazettamide, hymenolitatine G, pancratistatin, norciclasine, lycoridine, isocarbostyril, lycoramine, and trisphaeridine.[14,16,20,21,35,38,45] In addition to alkaloids, various phenolic compounds, particularly flavonoids, have been detected in different plant parts. Furthermore, more than 30 volatile oil components have been reported from multiple tissues of *H. littoralis*. Key alkaloids, phenolics, and volatile constituents, alongside their chemical structures, are summarised in Table 2.

Pharmacological activities

Anti-inflammatory activity

The plant *H. littoralis* has long been traditionally acknowledged for its anti-inflammatory properties. Researchers worldwide have investigated its anti-inflammatory potential using various *in vitro* and *in vivo* animal models. Karthikeyan *et al.*, have evaluated the *in vitro* anti-inflammatory activity of the flower part of the plant by using the HRBC membrane stabilization method. The findings reveal that the ethanolic extract of the plant shows 83.46% and 84.72% protection at a concentration of 100 and 500 µg/mL. Moreover, the activity of the ethanolic extract mentioned is dose-dependent. Additionally, the extract has also been screened using the phago-burst assay to understand the viable mechanism of the activity. The study specifies that the ethanolic extract of the plant causes 68% macrophage burst at a low dose of 500 µg/mL, which is comparable with that of the standard drug diclofenac sodium (87%) at the same dose.[25] Similarly, in another study, Zhang *et al.*, have reported the potential anti-inflammatory activity of *H. littoralis* against Lipopolysaccharide (LPS)- induced macrophages and *in vivo* HCl/EtOH-induced gastritis mucosal injury models. The Griess assay, RT-PCR, and real-time PCR were used to assess the production of pro-inflammatory cytokines and their mediators. According to this study, *H. littoralis* plays a key role in reducing the production of Nitric Oxide (NO) in RAW264.7 cells. Moreover, the study also highlighted the reduced phosphorylation of c-Fos and c-Jun, and also a decrease of JNK1, ERK2, and MKK7 in HEK 293T cells. Collectively, it can be concluded that ethanolic extract of the plant possess a remarkable *in vivo* anti-inflammatory activity in HCl/EtOH-induced gastritis mice model.[10]

Antimicrobial activity

The plant *H. littoralis* has been reported for its wide spectrum of anti-microbial activity against different gram-positive as well as gram-negative microorganisms. Following the updated research on the anti-microbial activity, it has been noted that most of

the studies have been conducted in an *in vitro* model. Noormi *et al*., has investigated the antimicrobial potential of extracts obtained from the different parts of juvenile and flowering plant stages against twelve microbial strains, including both gram-positive, gram-negative, as well as fungal pathogens. The tested gram-positive bacteria included *Micrococcus* spp., *Bacillus subtilis, Bacillus thuringiensis*, and *Staphylococcus aureus*; while the gram-negative group comprised *Escherichia coli, Pseudomonas aeruginosa, Salmonella* spp., *Proteus mirabilis*, and *Klebsiella pneumoniae*. The fungal strains evaluated were *Candida albicans* and *Aspergillus niger* using disc diffusion method. The findings of the study indicates that the root extracts from flowering-stage plants demonstrated the highest antibacterial activity, particularly against *Bacillus subtilis*, with a zone of inhibition measuring 29.0±0.04 mm. This was followed by notable activity from the old leaves of flowering-stage plants against *Micrococcus* spp. and *Bacillus thuringiensis*. Minimum inhibitory concentration analysis revealed that the most potent inhibition (MIC = 6.25 mg/mL) was observed with extracts from juvenile roots and flowering old leaves against *Micrococcus* spp.[6] In an independent study, Nadaf *et al*., demonstrated that the methanolic extract of *H. littoralis* leaves displayed notable antimicrobial activity against five microbial strains, specifically *Candida albicans, Staphylococcus aureus, Bacillus subtilis, Salmonella typhimurium*, and *Proteus vulgaris*. The extract showed particularly strong inhibitory effects against *S. aureus* and *C. albicans*, with minimum inhibitory concentrations of 45 µg/mL and 70 µg/mL, respectively, highlighting its potential as an effective antimicrobial agent.[21] In a comparative study, different parts, such as root, leaves, and stem of two different plants, *Tinospora cordifolia* and *Hymenocallis littoralis*, are extracted using different solvents, and antimicrobial activity has been assessed using the agar well diffusion method. The study highlighted that stems extract from the *H. littoralis* against *Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa, Salmonella typhimurium,* and *Candida albicans* produced the highest zone of inhibition at 24 mm, 21 mm, 18 mm, 17 mm, and 17 mm, respectively.[28,42]

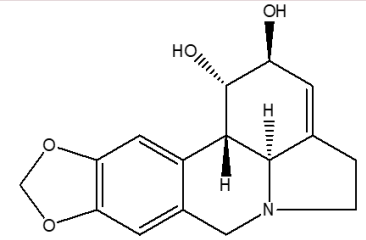
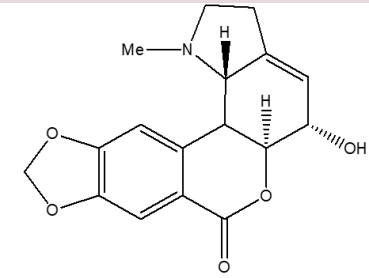
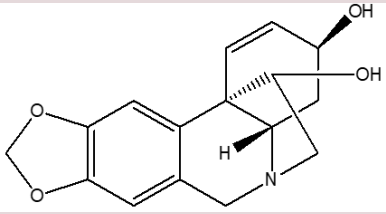
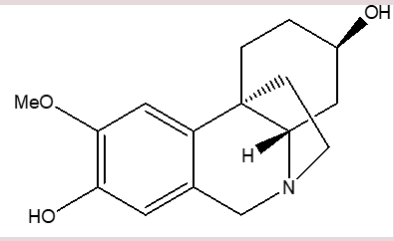
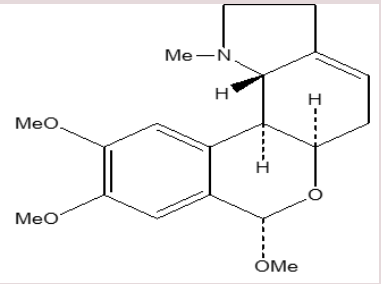
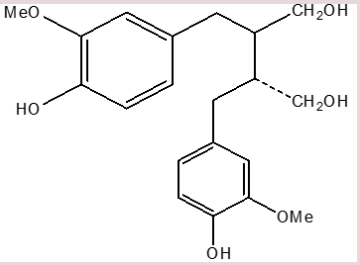
Wound healing activity

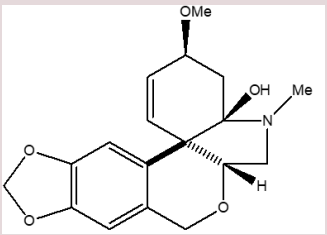
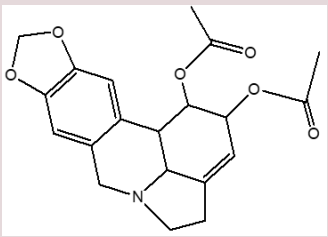
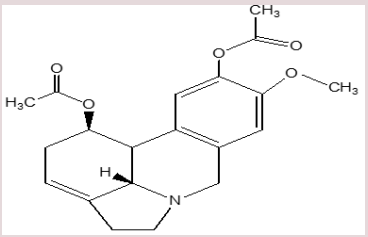
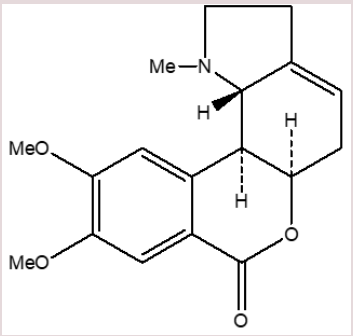
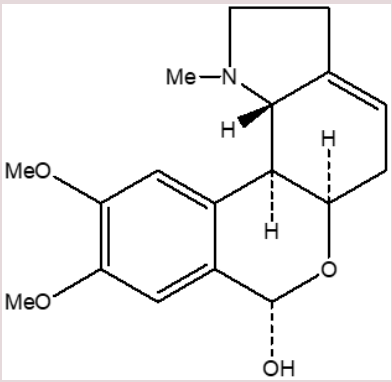
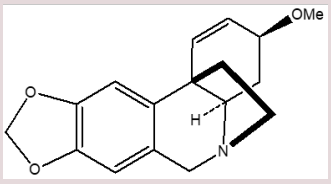
Sundarasekar *et al*., have studied the *in vitro* wound healing activity of all the major parts of the plant, from which the bulb and root show promising wound healing assessment using scratch assay with the human foreskin fibroblast (Hs27; ATCC CRL-1634) cell line. From this study, they have uncovered that methanolic extracts of bulb and root confirm wound healing activity after 36 hr at the concentration of 1 µg mL^{-1}. Additionally, it has been estimated that treatment with the methanolic extract of the plant significantly increases different growth factors and cytokines responsible for healing efficacy. The secondary metabolites found in the extract have a crucial role in the upregulation of different growth factors, such as PDGF, EGF, and KGF, and downregulation of different pro-inflammatory cytokines, such as TNF-α, IL-6,

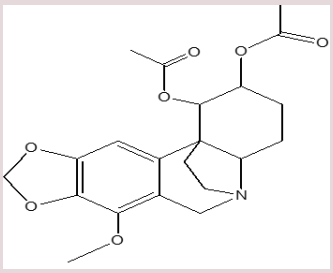
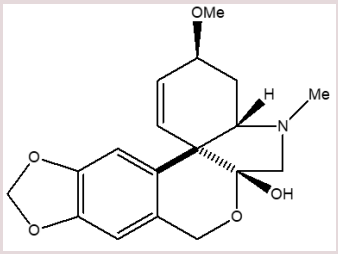
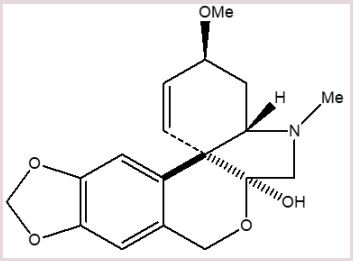
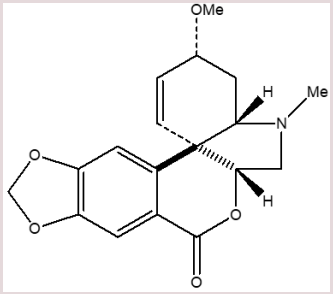
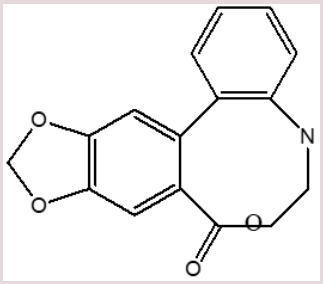
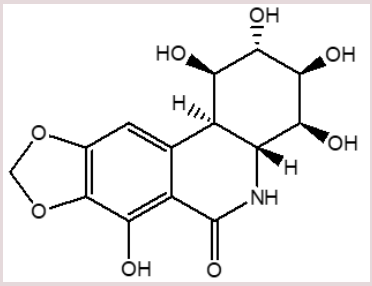
Table 1: Ethnomedicinal significance of *H. littoralis* in different parts of the world.

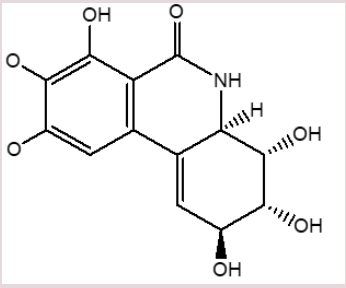
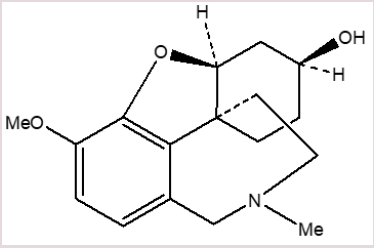
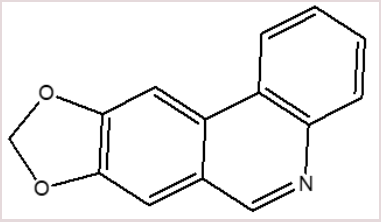
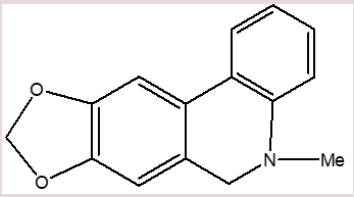
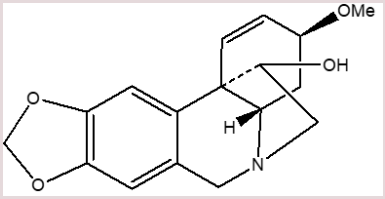
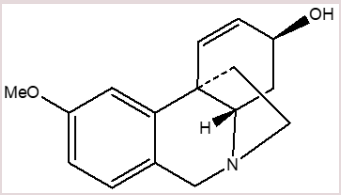
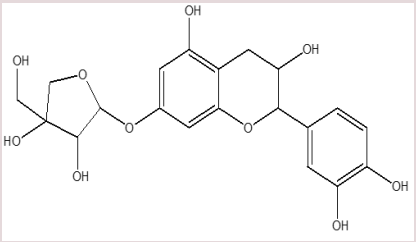
Region	Part use	Mode of traditional utilization	Reference
Southern Mexico, Central America, and Western Florida	Whole plant	Plant paste was used as an emetic and to treat swelling, sores, and varicose veins.	[10]
Malaysia	Bulbs	Bulb paste was used to treat skin issues like freckles and blemishes.	[5,41,42]
Central America, southern Mexico, Andhra Pradesh	Bulbs	A mixture of crushed bulbs and oil is applied to the face to help treat blemishes and freckles.	[19,32]
Central and South America	Bulbs of *Hymenocallis littoralis*	Decoctions of bulb of the plant is used to treat viral infections.	[24]
India especially in Gujarat, Andhra Pradesh, and Maharashtra	Flower	Flower paste is used for the wound healing purpose.	[21,32]
Andhra Pradesh, India	Bulb	Bulb paste was used as an emetic, anti-neoplastic, cytotoxic, and anti-viral.	[32]
Central America, Western Florida, and Southern Mexico	Leaf, bulb, stem, flower and root	Extraction of the plant used for wound healing and as a anti-microbial and anti-oxidant	[21]
Central America	Bulb	Bulb was used as an orally administered decoction to treat asthma and as a poultice on boils.	[43]
Indonesia	Roots	Roots boiled in water was used for testicles too low due to running.	[32]
China	Leaves	The plant leaves were used externally to treat bruishing and swelling.	[43]
Philippines	Bulbs	Paste of the bulb was used as a vulnerary.	[43]

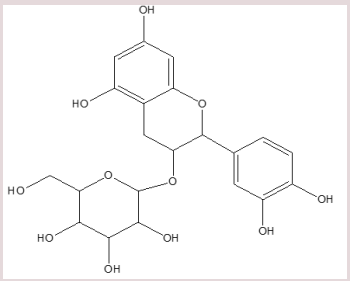
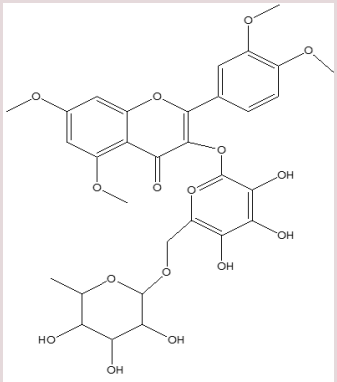
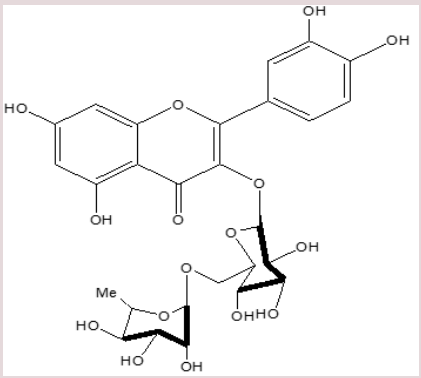
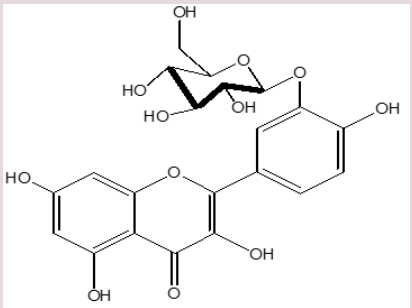
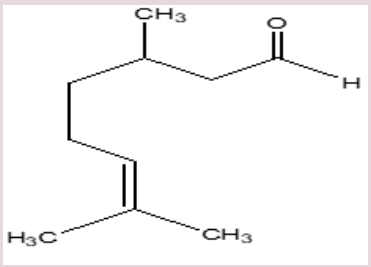
Table 2: Phytochemical constituents present in different parts of the plant *H. littoralis*.

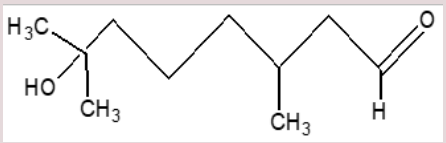
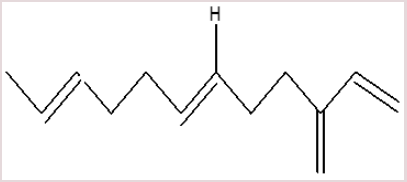
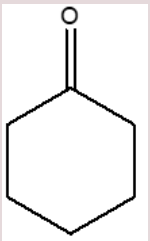
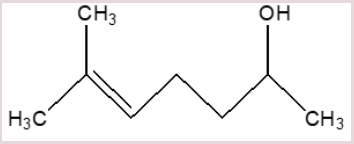
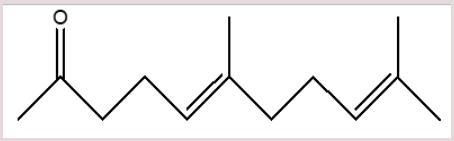
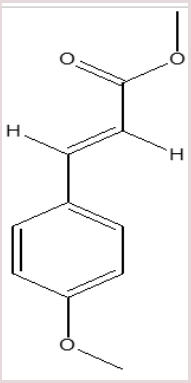
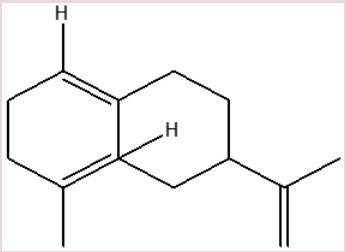
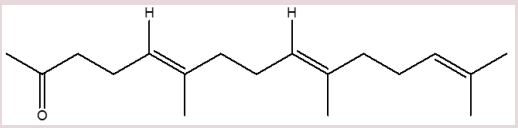
Sl. No.	Name of the phytoconstituents	Isolated from	Chemical structure	Reference
			Alkaloids	
1	Lycorine	Bulb		[16]
2	Hippeastrine	Bulb		[45]
3	11-hydroxyvittatine	Bulb		[45]
4	+8-O-d-methylmaritidine	Bulb		[45]
5	O-methylcorenine	Whole Plant		[16]
6	Secoisolariciresinol	Whole Plant		[16]

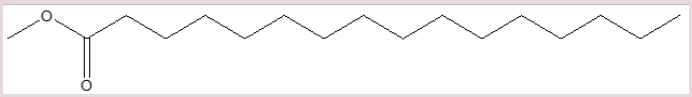
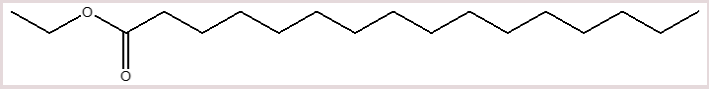
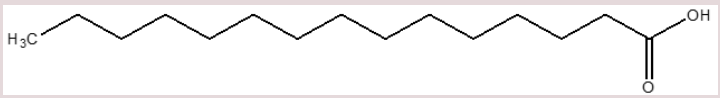
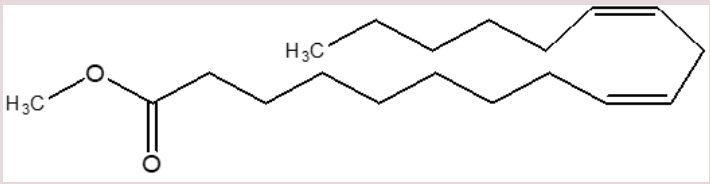
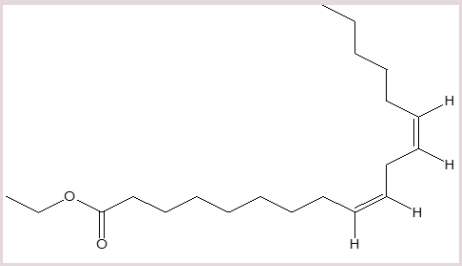
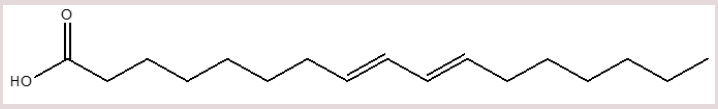
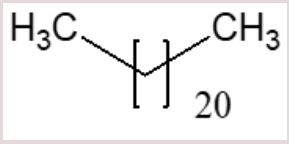
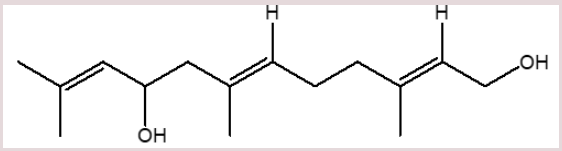
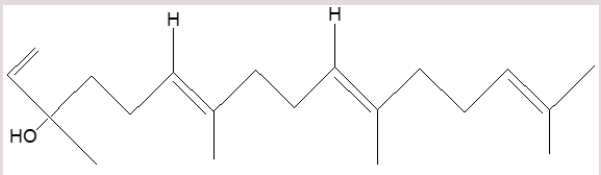
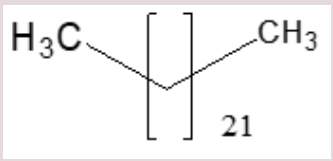
Sl. No.	Name of the phytoconstituents	Isolated from	Chemical structure	Reference
7	Littoraline	Whole plant		[16]
8	Diacetyllycorine	Whole plant		[16]
9	Norpluvine	Whole plant		[16]
10	Homolycorine	Whole plant		[20]
11	Lycoranine	Whole plant		[20]
12	Vittatine	Whole plant		[20]

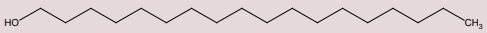
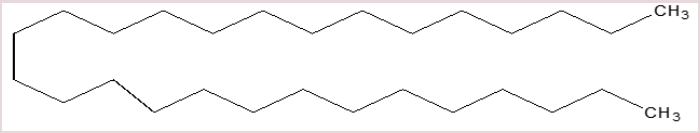
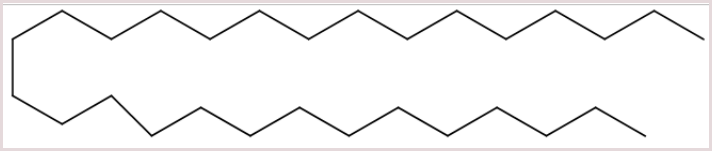
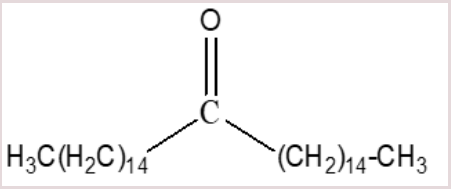
Sl. No.	Name of the phytoconstituents	Isolated from	Chemical structure	Reference
13	Bowdensine	Whole plant		[20]
14	Tazaettine	Whole plant		[20]
15	Pretazettine	Whole plant		[20]
16	Macronine	Whole plant		[20]
17	Hymenolitatine G	Whole plant		[20]
18	Pancratistatin	Whole plant		[38]

Sl. No.	Name of the phytoconstituents	Isolated from	Chemical structure	Reference
19	Norciclasine	Whole plant		[38]
20	Lycoramine	Whole plant		[20]
21	Trisphaeridine	Bulb		[20]
22	5,6-dihydrobicolorine	Whole plant		[20]
23	Haemanthamine	Whole Plant		[16]
24	Demethylmaritidine	Whole Plant		[16]
			Flavonoids	
25	Catechin 7-O- apiofuranoside	Flower		[21]

Sl. No.	Name of the phytoconstituents	Isolated from	Chemical structure	Reference
26	Epicatechin 3-O- β-D-glucopyranoside	Flower		[21]
27	Quercetin 5,7,3',4'-tetramethyl ether 3-rutinoside	Flower		[21]
28	Rutin	Flower		[45]
29	Quercetin-3'-O-glucoside	Flower		[45]
	Volatile oils			
30	Citronellal	Flower		[45]

Sl. No.	Name of the phytoconstituents	Isolated from	Chemical structure	Reference
31	Hydroxycitronellal	Flower		[45]
32	Fernesene	Flower		[45]
33	Cyclohexanone	Flower		[45]
34	6-Methylhept-5-en-2-one	Flower		[45]
35	Geranyl acetone	Flower		[45]
36	Methyl4-methoxycinnamate	Flower		[45]
37	Germacrene A	Flower		[45]
38	Farnesyl acetone C	Flower		[45]

Sl. No.	Name of the phytoconstituents	Isolated from	Chemical structure	Reference
39	Methyl palmitate	Flower		[45]
40	Ethyl palmitate	Flower		[45]
41	Palmitic acid	Flower		[45]
42	Methyl linoleate	Flower		[45]
43	Ethyl linoleate	Flower		[45]
44	Linoleic acid	Flower		[45]
45	Docosane	Flower		[45]
46	Farnesol 2	Flower		[45]
47	3-Methylbutyl hexadecanoate	Flower		[45]
48	Geranyl linalool	Flower		[45]
49	Tricosane	Flower		[45]

Sl. No.	Name of the phytoconstituents	Isolated from	Chemical structure	Reference
50	Tetracosane	Flower		[45]
51	Pentacosane	Flower		[45]
52	Hexacosane	Flower		[45]
53	Octacosane	Flower		[45]
54	Nonacosane	Flower		[45]
55	Palmitone	Flower		[45]

and IL-8. Although the plant is showing a significant wound healing activity against the human foreskin fibroblast, there is no support from *in vivo* studies to understand the viable mechanism of the different phytoconstituents in regulating the wound healing process.[46]

Anti-viral activity

In a recent investigation, it has been noticed that eleven Amaryllidaceae alkaloids isolated from*H. littoralis* show potential antiviral activity against the SARS-CoV-2 virus. A study was conducted by Le *et al*., that reveals several lycorine-type alkaloids, including *O*-demethyl-norlycoramine, 6α-hydroxyhippeastidine, 6β-hydroxyhippeastidine, 2-*epi*-lycorine, zephyranthine, and 9-O-demethyl-7-*O*-methyllycorenine, showed weak inhibition of SARS-CoV-2 (EC_{50}= 40-77 μM) with no cytotoxicity (CC_{50}>100 μM). Among all the tested compounds *O*-demethyl-norlycoramine, 6α-hydroxyhippeastidine, 6β-hydroxyhippeastidine and zephyranthine demonstrated the highest level of activity. However, the compounds lycorine and pancratistatin have a poor selective antiviral activity as they were toxic to Vero-E6 cells (CC_{50}=1.2 μM and 0.13 μM, respectively). This finding stands in contrast with previously reported results which showed high activity and no toxicity.[20] The antiviral activity of *H. littoralis* has been studied against two notable members of the Picornaviridae family: poliovirus and coxsackievirus, using HeLa cell cultures. Among the tested Amaryllidaceae species, *H. littoralis* exhibited relatively low susceptibility to poliovirus. The reduction in viral titers across various species of Amaryllidaceae, *H. littoralis*, demonstrates the significant antiviral efficacy.[23]

Anticancer activity

A study was conducted by Geetha Sahgal and team evaluating the brine shrimp cytotoxicity activity using methanolic extracts of different parts of *H. littoralis* including root, stem, leaves, bulb, anther, and flower. The finding reveals that methanolic extracts of leaves shows highest cytotoxic activity compared to other part of the plant on *Artemia salina* nauplii. While, on the other hand, the flower extract shows minimum cytotoxic activity at tested concentrations for the observed time point.[47] In another study, Anh *et al*.; have evaluated the *in vitro* cytotoxic activity of seven synthetic derivatives of alkaloids isolated from *H. littoralis*, including 11-*O*-acetyltazettine, 2-*O*-acetyllycorine, and 11-O-acetylhaemanthamine. All the alkaloids and their derivatives were tested for cytotoxic activity against nasopharyngeal carcinoma (KB) and hepatocellular carcinoma (Hep G2) cell lines. The finding of the study showed that the acetylation of the alkaloids decreases the cytotoxic activities to KB and Hep G2 cell lines.[48] Griffin *et al*., analysed the outcome of an alkaloid (pancratistatin) present in the different parts of *H. littoralis* against leukaemia by assessing peripheral blood mononuclear cells of 15 leukaemia patients before clinical intervention. The clinical data of the study reveals that pancratistatin shows remarkable and selective anti-cancer agent specially in leukaemia.[49]

Anti-fungal activity

Sundarasekar *et al*., studied the inhibitory effects of *H. littoralis* methanol extracts against *Candida albicans*. Various parts of the plant, such as the bulb, flower, anther, root, leaves, and stem, were tested against this opportunistic organism and found that the

flower and anther were effective at 6.25 mg/mL. the cytological and morphological expression of the extract-treated fungal strains was observed using a Transmission Electron Microscope (TEM) and Scanning Electron Microscope (SEM). The study reveals the destruction pattern of the nucleus and internal organelles. Moreover, it also highlighted the fissure on the membrane cells by the treatment of crude methanolic extract.[50]

Anthelmintic activity

Khan *et al.*, reported the anthelmintic activity of *H. littoralis* leaves extract, both aqueous and ethanolic, on the Indian earthworm. It is due to the presence of various alkaloids, flavonoids, and essential oils that this plant shows anthelmintic activity. They observed that the higher the concentration of the plant extracts, induced more rapid paralysis and the time of death was reduced in all tested worms. Both the extracts exhibit anthelmintic properties, but the ethanolic extracts displayed a dose-dependent response., at concentrations of 50 mg/mL and 100 mg/mL, the ethanolic extract significantly decreased the time to paralysis and death. Specifically, at 50mg/mL, the average paralysis time was 26.44±1.35 min, and the average death time was 157.27±1.19 min. In comparison, the standard reference drug Albendazole (10 mg/mL) induced paralysis at 11.30±1.1 min and caused death at 34.15±1.34 min.[51]

Toxicological studies

Scientific investigations have revealed the potential toxic effects of *H. littoralis* extracts, particularly following oral administration. The bulb is considered the most toxic part of the plant, primarily due to the alkaloids such as lycorine and tazettine, present in the bulb part, which are associated with symptoms including gastrointestinal discomfort, neurological disturbances, and, in severe cases, convulsions. In a recent study, Ds *et al.*, evaluated the haemato-biochemical toxicity of an aqueous extract of *H.*

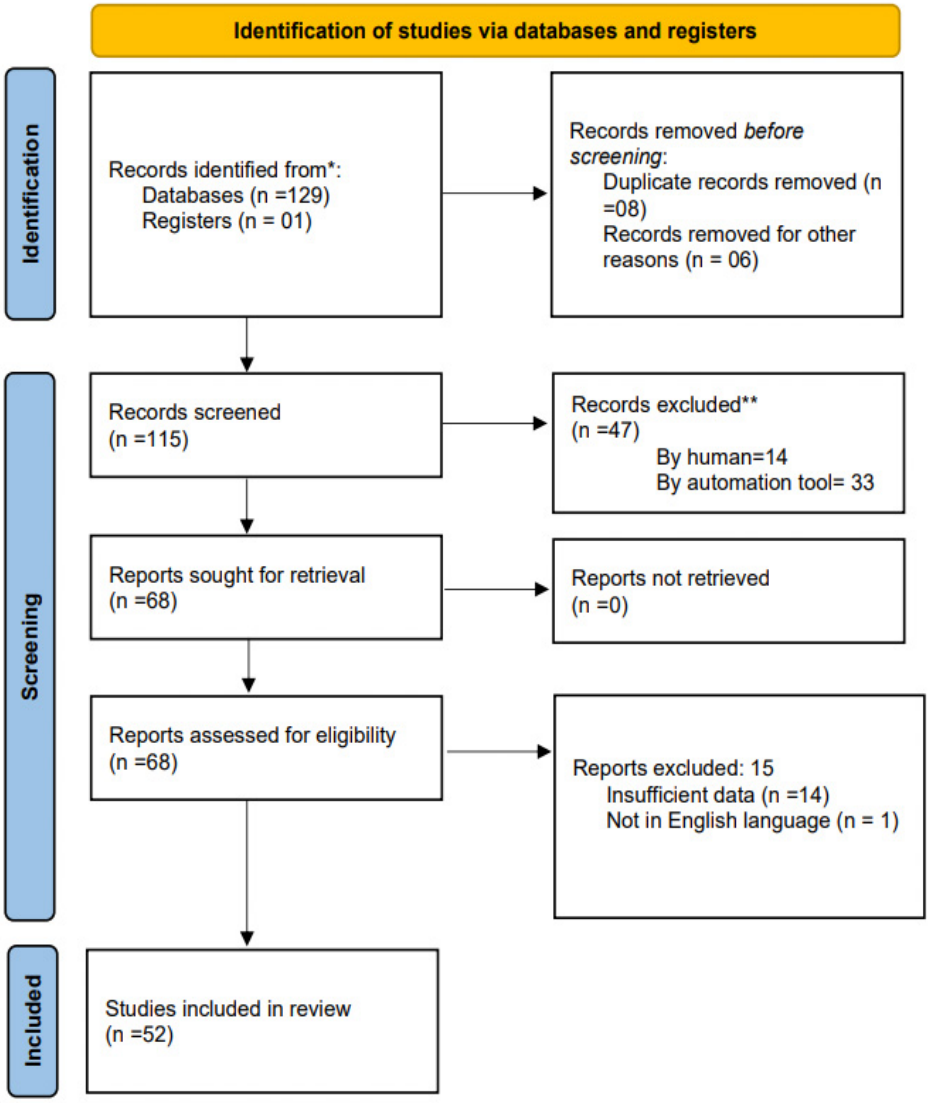


Figure 1: PRISMA flow diagram.

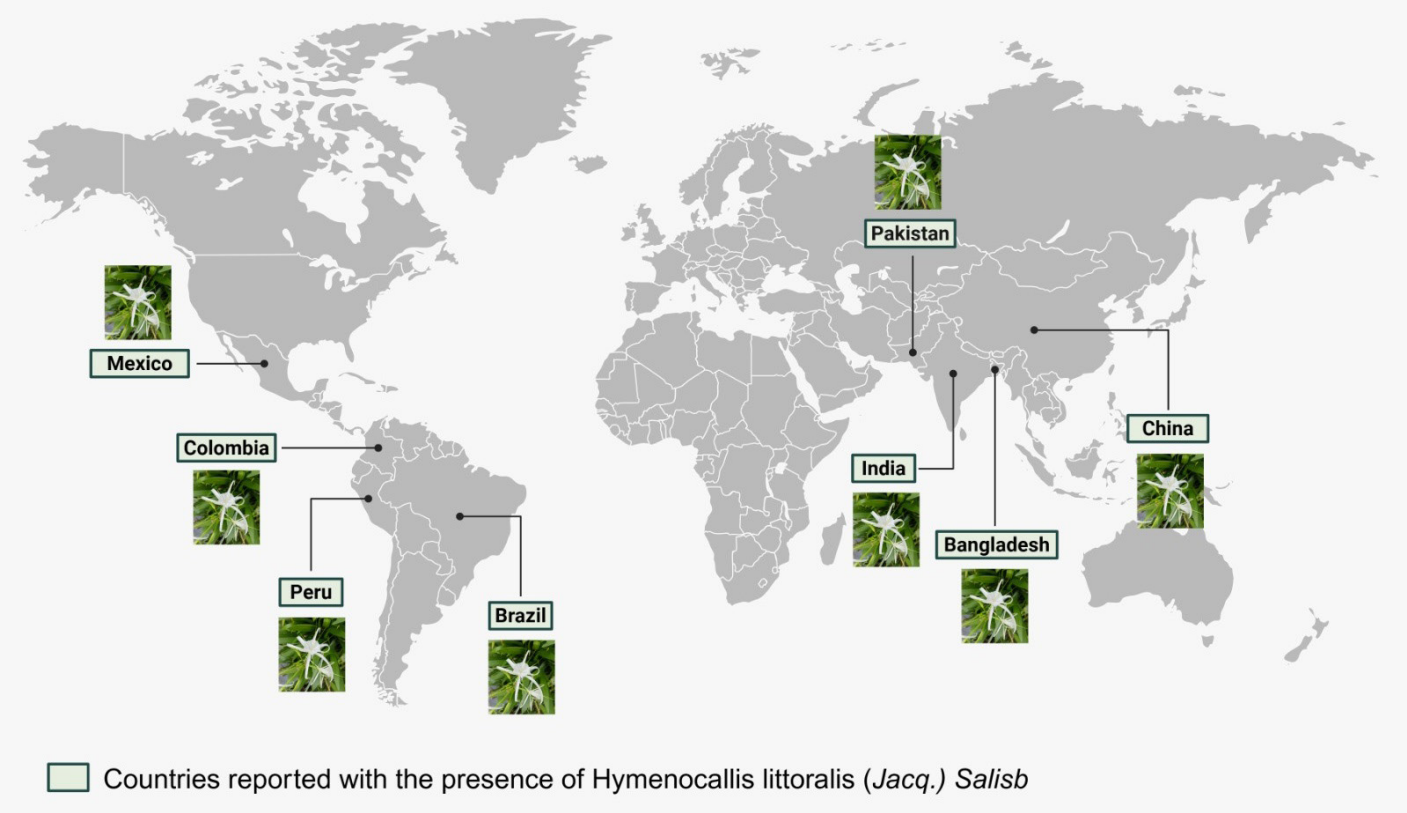


Figure 2: Geographical distribution of the plant *H. littoralis*

littoralis in Wistar rats administered orally at a dose of 1000 mg/kg body weight for 28 consecutive days. The results demonstrated a significant reduction in haematological parameters, including Haemoglobin (Hb), Total Erythrocyte Count (TEC), and serum total protein, compared to the control group. Furthermore, a notable elevation in biochemical markers related to liver (AST, ALT) and kidney function (creatinine, BUN) was observed, indicating potential toxicity to these vital organs.[52]

CONCLUSION

H. littoralis is a medicinal plant traditionally used by various indigenous communities across the world for the treatment of diverse ailments. Numerous scientific investigations have validated the pharmacological potential of this plant through both *in vitro* and *in vivo* experimental models. Results from these studies indicate that different parts of the plant exhibit significant antimicrobial, anti-inflammatory, anticancer, and wound-healing activities. Furthermore, phytochemical analyses have revealed that *H. littoralis* is rich in a variety of alkaloids and their derivatives, which may contribute to its therapeutic properties.

This review aims to compile and present updated information on the traditional uses, phytochemical constituents, and pharmacological activities of *H. littoralis*. Despite its promising biological activities, the plant remains underexplored in terms of clinical trials and product-oriented research, highlighting the need for further investigations to fully harness its medicinal potential.

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ABBREVIATIONS

WHO: World Health Organization; **LPS:** Lipopolysaccharide; **NO:** Nitric Oxide; **RT-PCR:** Reverse Transcription Polymerase Chain Reaction; **MIC:** Minimum Inhibitory Concentration; **PRISMA:** Preferred Reporting Items for Systematic Reviews and Meta-Analyses; **Hb:** Haemoglobin; **TEC:** Total Erythrocyte Count.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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AUTHORS CONTRIBUTION

Conceptualization, ST and SK; validation, ST and SK; formal analysis, SK; writing-original draft, ST and SK; writing-review and editing, ST, SB, PK, MA, RM, RD, NAS, and SK; graphical abstract, NAS; supervision and final approval of the manuscript, ST and SK. All authors have read and agreed to the published version of the manuscript.

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