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A comprehensive exploration of phytochemistry and pharmacological activities of *Ipomoea hederifolia*

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Abstract
Ipomoea hederifolia L., commonly known as scarlet morning glory, is an annual, herbaceous climbing vine that belongs to the Convolvulaceae family. This plant is widely distributed across tropical and subtropical regions and serves a dual role as both an invasive agricultural weed and a valuable ornamental and medicinal plant. This review consolidates current knowledge concerning its botanical characteristics, phytochemical constituents, and pharmacological activities. Data for this review were obtained through systematic searches in various scientific databases, including Google Scholar, Web of Science, Scopus, PubMed, and authoritative botanical books on herbal medicines. The plant is known to contain a wide range of bioactive secondary metabolites, including flavonoids, alkaloids (notably ipangulines), pyrrolizidine alkaloids, calystegines, cyanogenic glycosides, and resin glycosides, such as hederifolic acids A-D. These compounds are recognized for their diverse therapeutic properties. Pharmacological studies have shown that extracts of *I. hederifolia* exhibit potential antimicrobial, antioxidant, anti-inflammatory, anthelmintic, thrombolytic, genotoxic, and anticancer activities. The traditional uses of the plant align with these scientific evaluations, indicating its effectiveness in treating skin infections, inflammation, oxidative stress, and parasitic infestations, while also demonstrating cytotoxicity against various cancer cell lines. The presence of structurally unique and pharmacologically active compounds highlights the importance of further research into their potential for novel drug development.

Keywords: *Ipomoea hederifolia,* phytochemistry, ipangulines, pharmacology

Introduction
Climber plants have long been valued in ethnomedicine and are recognized as a rich source of novel bioactive compounds with potential for treating various diseases. However, harnessing their pharmaceutical potential presents several significant challenges, particularly in the areas of material procurement, high-throughput screening, and the scale-up of bioactive compounds. These plants play a vital role in traditional medicine worldwide. They are appreciated not only for their therapeutic properties but also for their ecological and socio-economic significance. Many tribal and rural communities depend on climber plants to treat a wide range of ailments, including digestive disorders, respiratory issues, skin diseases, fever, pain, and inflammation. Their diverse applications, cultural importance, and contribution to community health highlight the necessity for further research, documentation, and conservation efforts [1]. *Ipomoea hederifolia* L. is a climbing plant or vine that belongs to the Convolvulaceae family, which includes around 2,000 species and 58 genera, primarily found in tropical and subtropical regions worldwide. This family is characterized by herbaceous or woody plants that either twine or climb, often featuring heart-shaped leaves and funnel-shaped flowers. The genus *Ipomoea* is the largest within this family, containing approximately 600 species globally [2]. Commonly known as scarlet morning glory, jitirana, scarlet creeper, star ipomoea, and trompillo, the name "*Ipomoea*" is derived from the Ancient Greek words “ips,” meaning “worm,” and “homoios,” meaning “resembling.” The species epithet “*hederifolia*” is a Latin term meaning “ivy-leaved.” Thus, *I. hederifolia* can be interpreted as a “worm-like twining plant with ivy-shaped leaves.”
In India, *I. hederifolia* is referred to in various regional languages: Halu balli in Kannada, Theepori mulla in Malayalam, Kanavalli kodi in Tamil, and Kasiratnam in Telugu [3]. The term "Morning Glory" is used for species like *I. hederifolia* because of their unique flowering behavior, where the flowers open early in the morning and gradually close or fade by late afternoon or evening [4]. This vine is an annual, herbaceous, twining plant native to the tropical and subtropical regions of the Americas, including Brazil. It is widely distributed across areas ranging from the southern United States through Central America to northern Argentina.

Additionally, it has become naturalized in Australia, Africa, Asia, and various Pacific islands. Over time, it has spread throughout the world's tropical regions, leading to its classification as a pantropic species [5].

The plant primarily reproduces by reseeding itself and thrives in fertile soils with good humidity. Its growth and development are closely linked to the climate and seasonality of its environment, showing optimal development during the austral summer, autumn, and early winter [6]. However, it is also a significant agricultural weed, commonly found along roadsides and in fields disturbed by human activities. This weed causes considerable economic losses by reducing crop yields, complicating harvests, and affecting the quality of crops, particularly in sugarcane, maize, and soybeans [7]. *Ipomoea hederifolia* holds significant economic value as an ornamental plant. Its attractive foliage and vibrant, funnel-shaped red flowers make it a popular choice for gardens, landscapes, and as a decorative vine in hedges. This plant is appreciated for its ability to add vivid colour to various settings and is also valued for its role in attracting pollinators such as butterflies, hummingbirds, and different bird species, thereby enhancing its appeal in wildlife and ornamental gardens [8]. Additionally, *I. hederifolia* is well-regarded in traditional and folk medicine across many cultures. Various parts of the plant like leaves, stems, seeds, roots, and fruits are commonly utilized, typically prepared as infusions or decoctions. These preparations are used to treat a range of conditions, including dermatitis and skin diseases, rheumatism and joint pain, nervous system disorders, tumors, stomachaches, intestinal parasites, and as a purgative drug [9]. This review discusses the phytochemistry and pharmacological activities of *I. hederifolia*.

Botanical description

The growth habit of *I. hederifolia* is an annual, herbaceous, twining or climbing vine that grows over other vegetation (Fig. 1). It is often found at forest edges, along roadsides, and in gardens and agricultural fields as a weed. The leaves are simple, alternate, and can be entire or deeply lobed with 3-5 lobes. They have various shapes, including cordate (heart-shaped), ovate, or suborbicular, measuring between 2.8 to 8.6 cm in length and 2.5 to 10.8 cm in width [10]. The leaves feature well-defined palisade and spongy mesophyll layers, with paracytic stomata and palmate venation. Additionally, they possess a mix of unicellular, multicellular, glandular, and eglandular trichomes. The vascular system of the leaf consists of bicollateral bundles located in the midrib [11]. The stem of *I. hederifolia* is climbing, slender, and herbaceous. It can be glabrous or sparsely pubescent and has a bicollateral conjoint open type of vascular system. The pith is made up of small, thin-walled, isodiametric parenchyma cells. The plant has a taproot system and may exhibit anomalous secondary growth, which leads to the formation of a periderm [12]. The inflorescence of *I. hederifolia* is a terminal, lax, umbellate cyme. The flowers are bright red to reddish-yellow, often with yellow in the throat, and are trumpet-shaped. Each flower has a calyx with five oblong sepals and a corolla with five fused funnel-shaped petals. There are five stamens, and the ovary is superior. The fruit is a subglobose capsule that contains four black, pear-shaped seeds. Flowering and fruiting typically occur from September to January [13].

Fig 1: Habit of *Ipomoea hederifolia*: **a** Plant morphology **b** Flowers (Picture: photography by K. Ravikumara: Place of collection: University of Mysore, Manasagangotri Campus, Mysuru, Karnataka, India)

Phytochemicals

The pharmaceutical significance of medicinal plants is largely attributed to the presence of various bioactive phytochemical compounds. The stem of *I. hederifolia* contains several secondary metabolites, including flavonoids, phenols, saponins, carbohydrates, tannins, alkaloids, steroids, anthraquinones, and cardiac glycosides [14]. These secondary metabolites primarily serve to protect the plants from biotic and abiotic stressors, such as pathogens, herbivores, predators, and harsh environmental conditions like drought, salinity, osmoregulation, extreme temperatures, and UV radiation. They function as a defense mechanism, deterring potential attackers and promoting the plant's survival [15]. Phytochemical screening of *I. hederifolia* vine extract was conducted using various standard tests to identify the presence of different phytochemicals. These tests include Mayer's test and Wagner's test for detecting alkaloids, the Lead acetate test and H_2SO_4 test for flavonoids, the ferric chloride test and Lead acetate test for phenols, Benedict's test for carbohydrates, the gelatin test for tannins, the foam test for saponins, Salkowski's test for steroids, Borntrager's test for anthraquinones, and Keller-Killani test for cardiac glycosides [16]. The plant is known to possess significant chemical compounds, such as ipagulines, isoipagulins, pyrrolizidine alkaloids, calystegines B1 and B2, cyanogenic glycosides, ergoline derivatives, and various isoenzymes [17].

Ipagulines and Isoipagulins

Ipanguline and isoipanguline are a pair of pyrrolizidine alkaloids that mark the first such compounds isolated from *I. hederifolia*, specifically from seeds collected in Sri Lanka. Both ipanguline and isoipanguline are diesters of the necine base platynecine and have phenylacetic acid as an acyl group attached at the C-7 hydroxyl position as shown in figure 2. These compounds serve as chemotaxonomic markers for the genus *Ipomoea*. For structural elucidation, techniques such as infrared (IR) spectroscopy, mass spectrometry, and proton nuclear magnetic resonance (^{1}H NMR) are utilized to identify the molecular formula $C_{21}H_{29}NO_6$, characterized by an $[M]^+$ at m/z 391 for both alkaloids [18]. Three key ipangulines isolated from the aerial parts of *I. hederifolia* include: a) 9-O-[2-hydroxy-3-(2-acetoxy)-2-methylbutyryl]-7-O-salicyloylplatynecine (ipanguline B_2), b) 9-O- [2-hydroxy-3-(2-methylbutyryloxy)-2-methylbutyryl]-platynecine (ipanguline D_{10}) and c) 9-O-salicyloylplatynecine (ipanguline

D_{11}). These compounds are identified as pyrrolizidine alkaloids with platynecine backbones and esterified moieties, including hydroxy, acetoxy, methylbutyryl, and salicyloyl groups. They are structurally characterized by the presence of platynecine, with variations in ester substitutions at specific oxygen positions (9-O and 7-O) [19].

Pyrrolizidine alkaloids

Pyrrolizidine alkaloids are a notable class of secondary metabolites found in certain plants. The primary pyrrolizidine alkaloids unique to this plant are known as ipangulines, and their necine base is platynecine, which is a structural epimer of turneforcidine. These alkaloids can be classified into different types based on their chemical structure, including senecionine-type (cyclic diesters), lycopsamine-type (open-chain esters), monocrotaline-type, and others (Fig. 2). The toxicity of these compounds is closely related to the structure of the necine base and the type of esterification present. Pyrrolizidine alkaloids serve as potent chemical defenses against herbivores and some pathogens. Their significance arises from their strong toxicity, particularly their hepatotoxic (liver-damaging), genotoxic (DNA-damaging), and carcinogenic effects on humans and animals [20].

Calystegines B1 and B2

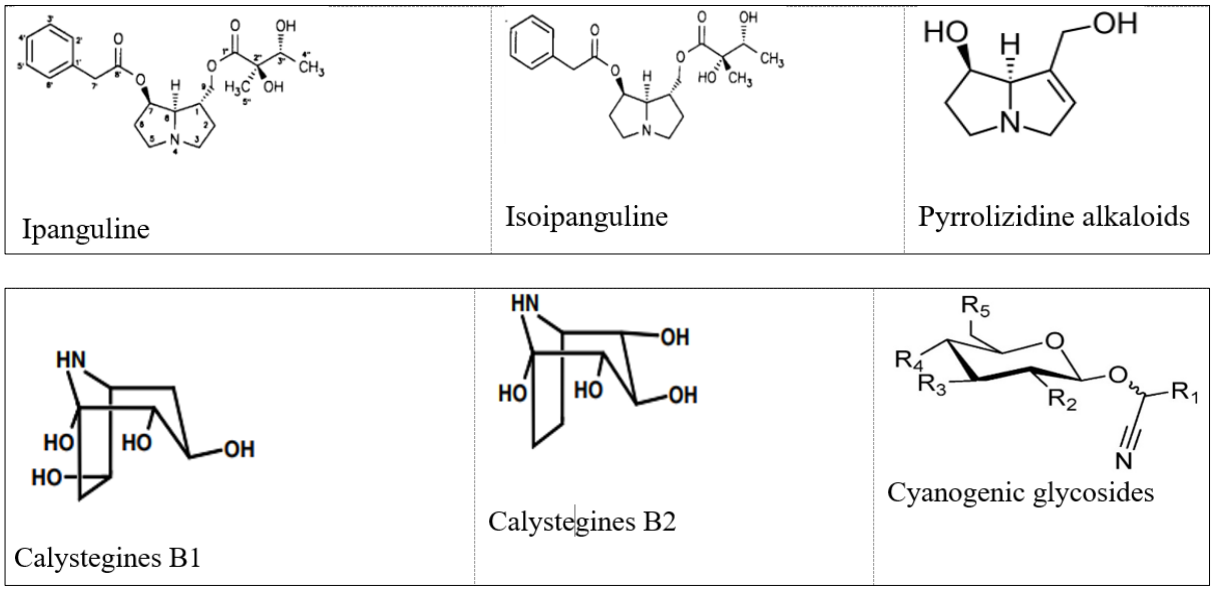
Calystegines B1 and B2 are chemical compounds found in *I. hederifolia*. They belong to a group of polyhydroxylated nortropane alkaloids known for their ability to inhibit glycosidase enzymes (Fig. 2). Biologically, these compounds may reduce carbohydrate absorption in the intestine by inhibiting these enzymes, which could potentially affect blood glucose levels. Although they are present in common edible plants, there are concerns regarding potential toxicity from high intake due to this enzyme inhibition. However, no cases of intoxication in humans have been reported so far [21].

Cyanogenic glycosides

Cyanogenic glycosides are chemical compounds found in various plants, including *I. hederifolia*. These compounds are known for their ability to release hydrogen cyanide when they undergo hydrolysis. Chemically, cyanogenic glycosides are glucosides derived from α-hydroxynitriles, which are in turn formed from amino acids such as phenylalanine, tyrosine, valine, and isoleucine, among others (Fig. 2). Typically, these compounds consist of an aglycone portion-often sourced from the aforementioned amino acids and featuring a nitrile group-attached to a sugar moiety, most commonly glucose, though other sugars may also be present. When they are enzymatically degraded, cyanogenic glycosides can release hydrogen cyanide, a potent toxin that plays a significant role as a defense mechanism against herbivores and pathogens [22].

Hederifolic acids A-D

Ipomoea hederifolic acids A-D are four peracetylated glycosidic acid derivatives derived from the scarlet morning glory, a plant recognized for its medicinal properties. These compounds are categorized as heptaglycosides, which consist of seven sugar units, and hexaglycosides, which consist of six sugar units, both linked to hydroxy fatty acid aglycones. Specifically, these acids are connected to 3S,12S-dihydroxyheptadecanoic acid, 12S-hydroxyheptadecanoic acid, and 11S-hydroxyhexadecanoic acid, showcasing the diversity of hydroxy fatty acids attached to the oligosaccharide chains (Fig. 2). The sugar moieties form hepta- and hexasaccharide chains that are glycosidically linked to these hydroxy fatty acids. Hederifolic acids B and D are dehydroxylated at the C-3 position compared to A and C, highlighting subtle structural variations among them. These compounds belong to a class of molecules known as resin glycosides, which are typical in the Convolvulaceae family and consist of a macrolide or oligosaccharide linked to long-chain fatty acids. Resin glycosides like the hederifolic acids A-D are being investigated for their pharmacological potential, including modulation of antimicrobial resistance and cytotoxic activity against cancer cells. Their study enriches understanding of natural product chemistry in *Ipomoea* species, aiding possible drug lead discoveries [23].



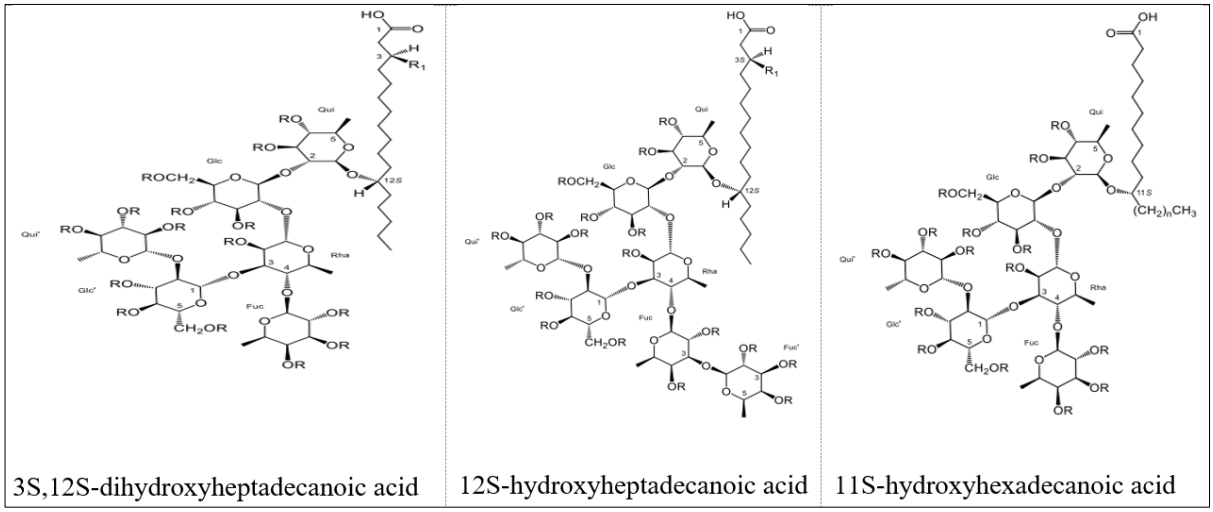


Fig 2: Structures of Chemical compounds isolated from *Ipomoea hederifolia* L.

Pharmacological activities

Research on the pharmacological properties of the *I. hederifolia* plant indicates that its extracts and pure compounds may possess specific medicinal effects. Previous studies have examined the chemistry and pharmacology of this plant, revealing that its crude extracts and compounds exhibit significant bioactivity. As a result, detailed pharmacological studies are outlined below.

Antimicrobial activity

Antimicrobial compounds derived from plants have historically and currently played a crucial role in the development of modern antibiotics, demonstrating excellent safety and potency against various microbes. Plants produce a diverse range of secondary metabolites that can inhibit microbial pathogens, including bacteria, fungi, viruses, and protozoa. In the present study, the total ethanolic extract of the leaves of *I. hederifolia* was evaluated for its antibacterial activity against gram-positive bacteria (*Bacillus subtilis*, ATCC-6633) and gram-negative bacteria (*Escherichia coli*, NCIM-1056). Using the cylindrical method or tube assay, the extract showed the highest antibacterial effectiveness against *B. subtilis* and *E. coli*, achieving a zone of inhibition of 18 mm at a concentration of 200 mg/ml. In comparison, the standard antibiotic Gentamicin exhibited zones of inhibition of 19 mm and 20 mm for *B. subtilis* and *E. coli*, respectively. Additionally, an herbal ointment derived from *I. hederifolia* demonstrated antibacterial effectiveness with zones of inhibition of 16 mm against *B. subtilis* and 15 mm against *E. coli*, whereas the standard Gentamicin showed zones of inhibition of 20 mm and 19 mm, respectively [24]. Hossain *et al.* studied the antimicrobial activity of *I. hederifolia* stem extract (IHSE), which demonstrated both antibacterial and antifungal activity. The extract was tested against gram-positive *Staphylococcus aureus* and *Enterococcus faecalis*, as well as gram-negative bacteria such as *E. coli* and *Klebsiella pneumoniae*, along with two fungi, *Aspergillus niger* and *Aspergillus flavus*. Using the Kirby-Bauer disk diffusion method, methanolic IHSE showed moderate antibacterial effectiveness, with a zone of inhibition measuring 0.5 cm against *S. aureus* and *E. faecalis,* and 0.25 cm against *E. coli* and *K. pneumoniae*, at a concentration of 80 µg/disc. In comparison, the positive control ciprofloxacin exhibited a significantly higher zone of inhibition, ranging from 3.5 to 7 cm at a concentration of 30 µg/disc against all tested bacterial pathogens. However, no zone of inhibition was recorded for *A. niger* and *A. flavus* with IHSE, whereas the standard antifungal ketoconazole showed a zone of inhibition ranging from 2 to 2.5 cm at a concentration of 30 µg/disc, indicating no significant antimicrobial activity from IHSE for these fungi [14]. Nataraj *et al*. investigated *I. hederifolia* zinc oxide nanoparticles (Ih-ZnO-NPs) for their antibacterial activity against gram-positive *S. aureus* (MTCC 7443) and *B. subtilis* (MTCC 121), as well as gram-negative bacteria *E. coli* (MTCC 7410) and *Salmonella typhi* (MTCC 733). Utilizing the disc diffusion assay, Ih-ZnO-NPs exhibited high antibacterial effectiveness, with zones of inhibition of 17.90 ± 0.17 mm against *S. aureus*, 12.46 ± 0.29 mm against *B. subtilis*, 15.36 ± 0.26 mm against *E. coli*, and 10.56 ± 0.20 mm against *S. typhi* at a concentration of 2 mg/disc. In comparison, the standard antibiotic Streptomycin demonstrated maximum antibacterial activity at a concentration of 0.025 mg/disc, showing a zone of inhibition of 23.26 ± 0.24 mm. The minimum inhibitory concentration studies indicated that a concentration ranging from 0.312 to 1.25 mg/ml was required to inhibit the tested bacteria [25].

Antioxidant activity

Living cells naturally produce free radicals and reactive oxygen species as by-products of normal physiological and biochemical processes. These free radicals can damage important cellular components such as lipids, proteins, and DNA, contributing to the development of chronic diseases like cancer and diabetes. Plants are particularly rich in natural antioxidant compounds, including vitamins, terpenoids, phenolic acids, flavonoids, tannins, alkaloids, and others. These molecules help to scavenge free radicals, protecting plant cells, and when consumed in the human diet, they also support human health by reducing oxidative stress and the risk of disease [26]. The DPPH radical scavenging technique was employed to assess the antioxidant activity of the methanolic extract of *I. hederifolia* stem (IHS). The extract demonstrated a high inhibition rate of 88.82% in DPPH radical scavenging activity compared to standard references such as ascorbic acid (AA), which showed 91.77%, and butylated hydroxytoluene (BHT), which displayed 88.30%, at a concentration of 500 µg/mL. The IC_{50} values for AA, BHT, and IHS were 102.28, 88.52, and 174.08 µg/mL, respectively. These findings indicate that IHS possesses potent antioxidant activity. In contrast, the Reducing Power Activity (RPA) assay revealed the maximum absorbance for AA, BHT, and IHS at 500 µg/mL to be 4.12, 2.523, and 0.775, respectively.

The EC_{50} values for AA, BHT, and IHS were 23.12, 50.84, and 279.58 µg/mL, respectively, indicating that IHS has moderate antioxidant activity compared to the standards [14]. Suchiang *et al*. investigated the antioxidant potential of the methanolic extract of *I. hederifolia* leaves, demonstrating strong DPPH, hydroxyl radical scavenging, reducing power, and phosphomolybdenum scavenging activities in comparison to standard ascorbic acid [27]. Nataraj *et al.* studied the antioxidant activity of Ih-ZnO-NPs, which showed the highest inhibition of DPPH radical scavenging activity at 70.6% at 2 mg/mL, with an IC_{50} of 0.94 mg/mL. Overall, these studies conclude that the aerial parts of *I. hederifolia* extracts possess significant antioxidant activity [25].

Anti-inflammatory activity

Anti-inflammatory activity involves a multi-level suppression of the inflammatory response. This is achieved through the modulation of signaling pathways, reduction of pro-inflammatory mediators, enhancement of anti-inflammatory molecules, and strengthening of antioxidant defenses. Plant extracts offer a diverse range of bioactive compounds that target these processes through complementary mechanisms. Their efficacy is often evaluated in experimental edema models that focus on both pro- and anti-inflammatory mediators [28]. In this study, the methanolic extract of *I. hederifolia* (MEIH) at a dosage of 300 mg/kg demonstrated a potent inhibition of 54.63% in carrageenan-induced rat paw edema. In comparison, the standard treatment, indomethacin, inhibited the swelling by 57.55% three hours after the carrageenan injection. In a chronic inflammatory model, MEIH at 300 mg/kg led to a 22.24% reduction in granuloma weight, while indomethacin resulted in a 29.63% reduction. These findings suggest that MEIH exhibits significant anti-inflammatory activity in both acute and chronic inflammation [4].

Anthelmintic activity

Anthelmintic activity refers to the ability of a substance, particularly plant-derived compounds, to expel or destroy parasitic worms (helminths) from the body. Gastrointestinal parasites, especially helminths such as nematodes, cestodes, and trematodes, significantly constrain human and livestock productivity in developing nations. The use of anthelmintic plants, backed by ethnoveterinary knowledge and scientific research, offers a sustainable alternative to chemical dewormers. These strategies can help maintain livestock productivity, combat drug resistance, and enhance animal welfare [29]. Hossain *et al*. investigated the anthelmintic properties of IHSE and found that its activity was dose-dependent. At concentrations ranging from 10 to 60 mg/ml, the time for paralysis varied from 84.71 ± 0.79 minutes to 12.50 ± 0.23 minutes, while the time until death ranged from 107.36 ± 1.08 minutes to 25.23 ± 0.23 minutes, respectively. In comparison, the standard drug Albendazole demonstrated a paralysis time of 63.34 ± 0.5 minutes and a death time of 55.67 ± 0.58 minutes at a concentration of 15 mg/ml. These findings indicate that the anthelmintic activity of the IHSE extract at various concentrations was significantly higher than that of the standard reference [30].

Thrombolytic activity

Plants play a significant role in thrombolytic activity due to their bioactive compounds, which can dissolve or prevent blood clots. Plant extracts may promote fibrinolysis, inhibit platelet aggregation, or enhance the body's natural clot-dissolving mechanisms [31]. A study by Hossain *et al*. examined the thrombolytic properties of IHSE extract and found it to have potential effects that depend on the dosage. Specifically, at a concentration of 20 mg/ml, the extract exhibited a moderate clot lysis effect of 37.168 ± 2.4%, compared to the standard streptokinase, which showed a lysis effect of 40.130 ± 2.401% at 100 µl [30].

Genotoxicity

Genotoxicity refers to the capacity of certain substances to damage genetic material within cells, resulting in mutations that can disrupt normal cellular processes, including mitotic division. During mitosis, genotoxic agents can lead to various chromosomal abnormalities and cytological irregularities, which interfere with proper cell division and may result in mutations, impaired growth, or even cell death. In the present study, it was observed that bio-synthesized ZnO nanoparticles (Ih-ZnO-NPs) exhibit potentially genotoxic effects during mitotic division. Specifically, the rate of cell division decreased from 87.38% to 43.55% as the concentration of ZnO-NPs increased from 0.25 to 2 mg/ml. This indicates that the genotoxic effects of these nanoparticles effectively inhibit mitotic division. In comparison, the positive control, methotrexate, showed a significantly lower cell division rate of 19.47% at a concentration of 0.5 mg/ml. These findings suggest that ZnO-NPs therapy increases chromosomal aberrations, thereby reducing the number of successful mitotic divisions [25].

Anticancer activity

Hossain *et al*. investigated the anticancer properties of methanolic extract of *I. hederifolia* stems (IHSE) on brine shrimp nauplii. They observed 100% mortality at a concentration of 100 µg/ml, using Vincristine sulfate as a positive control anticancer drug, which had an IC_{50} value of 0.865 µg/mL. In comparison, the IC_{50} value of IHSE for achieving 50% mortality in brine shrimp nauplii was 4.544 µg/mL [30]. Other studies have also shown significant anticancer activity of *I. hederifolia*. Additionally, a compound called Convolvulin was isolated from the roots of *I. hederifolia*. This compound demonstrated effects on rat aorta and ileum rings and exhibited activity against Caco-2 and KB cancer cell lines. Along with Convolvulin, several new tetrasaccharides, glycosides, and statins (1-5) were isolated from the roots of *I. hederifolia*, which showed notable cytotoxicity against the nasopharyngeal carcinoma KB cell line, as well as the OVCAR and UISO-SQC-1 cancer cell lines [4].

Conclusion

In conclusion, this review has gathered current knowledge about *I. hederifolia*, covering its botanical description, traditional uses, ecological importance, phytochemistry and pharmacological activities. *Ipomoea hederifolia* is a promising medicinal plant enriched with a diverse range of phytochemicals, including alkaloids (Ipanguline), flavonoids, phenols, saponins, carbohydrates, tannins, steroids, anthraquinones, and cardiac glycosides. These bioactive constituents contribute to its broad spectrum of pharmacological activities such as antimicrobial, antioxidant, anti-inflammatory, anthelmintic, thrombolytic, genotoxicity, and anticancer effects. The existing literature provides compelling evidence supporting its traditional uses and highlights its therapeutic potential. However, despite these encouraging findings, comprehensive toxicological

assessments, clinical trials, and studies on the mechanisms of action are still limited. Future research should focus on isolating and characterizing specific bioactive compounds, understanding their pharmacokinetics, and validating their efficacy and safety in clinical settings. *Ipomoea hederifolia* will pave the way for the development of standardized, evidence-based herbal drug formulations.

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