Perspectives On Bioactive Compounds And Pharmacological Applications Of *Lawsonia Inermis* L.

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Abstract
Lawsoniainermis, commonly known as henna and belonging to the Lythraceae family, is a versatile plant with significant therapeutic potential. Beyond its cosmetic applications, various parts of the plant are widely used in traditional medicine. This present study reviews the pharmacology and phytochemistry of L. inermis to provide reliable scientific evidence for its biological activities. Research has revealed its antibacterial and antifungal properties against several strains, including those responsible for skin infections. Compounds from henna may inhibit key enzymes of the SARS-CoV-2 virus, offering promise for COVID-19 treatment. It also exhibits antioxidant properties and has shown potential in memory enhancement and Alzheimer's disease management. Henna's anticonvulsant effects suggest its usefulness in managing seizures, and it has displayed potential in wound healing and hair growth. It shows notable antioxidant activity and selective cytotoxicity against certain cancer cells, sparing healthy ones. In diabetes management, henna exhibits hypoglycemic effects and alpha-glucosidase inhibition. Additionally, it accelerates wound closure, aids in pressure ulcer healing, and may have effects on the estrous cycle. Henna's larvicidal properties make it a natural insecticide against malaria vectors and mosquitoes, showcasing its diverse therapeutic applications. Phytochemical analyses of Lawsoniainermis (henna) extracts indicate the presence of various compounds, including tannins, phenolic compounds, flavonoids, glycosides, terpenoids, alkaloids, resins, and steroids. Notably, specific compounds like pseudoephedrine, phytol, oleanolic acid, 3-O-(Z)-coumaroyloleanolic acid, betulinic acid, β-sitosterol, lawsone, fraxetin, and luteolin-3-O-glucoside have been identified in henna extracts. These phytochemicals contribute to the diverse therapeutic properties and potential applications of henna in various fields. The medicinal properties of L. inermis are diverse and continue to be a subject of investigation, highlighting its potential for various therapeutic applications. This review underscores the diverse therapeutic possibilities of L. inermisand collectively offer valuable insights into the multifaceted therapeutic applications of L. inermis.

Keywords: Lawsoniainermis, henna, review, phytochemistry, pharmacology

INTRODUCTION

Plants have been a valuable resource for humanity throughout history, providing essential elements in the form of food, medicine, and cosmetics. Numerous plant species have been extensively documented in traditional systems like Siddha, Ayurveda, Unani, and Allopathy, where they are utilized to address a wide range of health issues. (Leela K and Dr. Anita R J Singh, 2020).Indeed, traditional healers have a deep history of using plants to prevent or treat infectious diseases, and modern science has validated this knowledge. Approximately half of today's pharmaceuticals have their origins in plant compounds. (Habbal et al., 2011).

Conventional therapies, particularly the use of medicinal plants, maintain their vital role in meeting fundamental public health requirements. Natural products represent a significant source of both traditional and synthetic herbal remedies, serving as a cornerstone of primary healthcare. The demand for herbal medicines in primary healthcare remains substantial, spanning across developed and developing nations. This is owing to their extensive biological and therapeutic attributes, improved safety profiles, and cost-effectiveness. (Khairul et al., 2022).Traditional herbal medicine practitioners have documented the therapeutic effectiveness of numerous indigenous plants in the treatment of various diseases (D. K. Singh & Luqman, 2014).

Plants of ethnopharmacological significance are currently a subject of great interest, as they hold the potential for the isolation of bioactive compounds that can offer benefits across various aspects of medication. Many of the fundamental sources of medicine in use today are still derived from traditional medicinal herbs. The search for novel drug treatments has involved ethnobotany and ethnopharmacology, providing a new avenue as a crucial source of knowledge that has led to remarkable findings and the discovery of new compounds (Naidu et al., 2022) .

Plants offer abundant sources of diverse secondary metabolites, including alkaloids, terpenoids, tannins, and flavonoids, which have demonstrated a broad spectrum of therapeutic potential. These natural compounds remain highly valuable in the contemporary field of drug discovery and development in modern medicine (Habbal et al., 2011).As a result, the development of new drugs opens up additional avenues for safeguarding human health. Consequently, there is a

significant demand for natural alternatives aimed at addressing a variety of diseases and disorders with both high efficacy and safety(Elebeedy et al., 2022).

Lawsoniainermis Linn, commonly known as henna and belonging to the Lythraceae family, is a highly branched, hairless shrub or small tree that reaches a height of 2-6 meters. It is primarily cultivated for its leaves, although various parts of the plant, including the stem bark, roots, flowers, and seeds, have found applications in traditional medicine. This plant is globally recognized for its cosmetic purposes, as it is used to dye hair, skin, and nails(Agarwal et al., 2014).The entire plant, encompassing the roots, leaves, fruits, stem, bark, bulbs, seeds, flowers, and oil, has been extensively employed in the treatment of various ailments (Fatahi Bafghi et al., 2022).However, despite its medical significance, there remains a paucity of information regarding its therapeutic uses, and its phytochemical properties have not been thoroughly investigated. Hence, there is a compelling need to explore this plant further in order to gain a better understanding of its properties and efficacy. Consequently, this review has been compiled to provide a comprehensive overview of the diverse beneficial aspects of the medicinal plant, L. inermis.

METHODOLOGY

This review gathered scientific information on L. inermis' therapeutic properties, phytoconstituents, and toxicity from various databases such as PubMed, Elsevier's Science Direct, Springer, ResearchGate, and Google Scholar. The articles' relevance to the research topic was assessed by reviewing their titles and abstracts, and only fully accessible scientific papers were included. Additionally, the references cited in the chosen articles were meticulously reviewed through manual screening to verify content accuracy and reliability.

Antibacterial Activity

In a prior investigation, researchers tested the antibacterial properties of henna leaf and seed extracts using the well-diffusion technique. They assessed its effects on various microorganisms, including a standard Pseudomonas aeruginosa strain and 11 clinical P. aeruginosa isolates from patients. The findings indicated antibacterial activity against all tested isolates (Habbal et al., 2011).In another study, the antibacterial activity of chloroform, ethanol, and water extracts from L. inermiswere tested against Bacillus subtilis, Staphylococcus aureus, Proteus vulgaris and Escherichia coli using the cup-plate method. The results indicated that the ethanol extract did not display antibacterial activity against S. aureus and B. subtilis, while the others exhibited such activity. Notably, the aqueous extract demonstrated significant antibacterial activity among all the tested extracts (Wadekar et al., 2016).A study investigated the antibacterial effects of L. inermis leaf extracts (aqueous, ethanolic, and petroleum ether) on S. aureus and P. aeruginosa clinical isolates using agar well diffusion method. All isolates were susceptible to the extracts at 1000µg/ml, with the aqueous extract showing the highest activity against S. aureus. The study implies that L. inermis has potential as an antibacterial agent(Usman & Rabiu, 2019).
In a recent study, the antibacterial impact of L. inermis fractions on S. aureus was examined through the well diffusion method. The methanol extract underwent fractionation with ethyl acetate and n-hexane. The findings revealed that the most substantial antibacterial activity against S. aureus was observed in the ethyl acetate fraction(Mulyaningsih S, 2022).A recent study examined the antibacterial properties of hydroalcoholic extracts from three L. inermis landraces namelyRudbar-e-Jonub, Shahdad and QhalehGan, against P. aeruginosa and Streptococcus agalactiae. The study used agar well diffusion and minimal inhibitory concentration (MIC) tests. QalehGanj proved more effective against S. agalactiae, while Shahdad was more potent against P. aeruginosa. The MIC method confirmed these results at a lower concentration(Fatahi Bafghi et al., 2022).

Antifungal Activity

A study explored the antifungal properties of ethanol and petroleum ether extracts from L. inermis leaves using the cup-plate agar diffusion method against various clinical isolates. The extracts exhibited antifungal activity against several strains, except Pichia fabianii, which was resistant. Minimum inhibition concentrations of 5, 7.5, and 10mg/mL effectively inhibited the growth of tested dermatophytes.(Suleiman & Mohamed, 2014)**.**

The study examined the antifungal properties of petroleum ether, ethanolic and aqueous extracts from L. inermis leaves against clinical isolates of Epidermophytonfloccosum and Candida albicans using agar well diffusion method. All isolates were susceptible to extracts at 1000µg/ml, with the highest activity observed in the aqueous extract against E. floccosum. These results indicated that L. inermis has potential as an antifungal agent. (Usman & Rabiu, 2019).

A recent study examined the antifungal properties of water and ethanol extracts from both fresh and dried L. inermis leaves against clinical Candida isolates from female patients. The study assessed zones of inhibition, MIC and minimum fungicidal concentration (MFC) of the extracts. The results indicated that both fresh and dried leaf ethanol extracts effectively inhibited fungal isolates, with MFC values ranging from 22.7mg/ml to 47.0mg/ml. The variations in MFC among the extracts were likely due to the varying resistance levels of isolates from different species with distinct genetic profiles. (Hassan et al., 2022)**.**

A randomized controlled trial investigated the impact of a vaginal cream containing an ethanol extract of L. inermia on women with vaginal candidiasis. The study cultured vaginal discharge and assessed vaginal pH, lactobacillus growth, colony formation, and subjective symptoms of vaginitis. The results showed that women in the treatment group did not experience discharge, itching, burning sensation, irritation or dyspareunia. Furthermore, there was a significant increase in lactobacillus formation and a notable decrease in vaginal pH in the henna group. Additionally, the cream reduced colony formation and vaginal pH while increasing lactobacillus formation (Yaralizadeh et al., 2022)**.**

Anti-Trichomonas effect

In a recent study, the anti-Trichomonas vaginalis activity of hydroalcoholic extracts from three L. inermis landraces (Rudbar-e-Jonub, Shahdad, and QhalehGan) was investigated using the Hemocytometry method. The extracts were tested against Trichomonas vaginalis isolated from female vaginal discharge. Results indicated that all the landraces had MIC against S. agalactiae. All tested extracts effectively prevented the growth of T. vaginalistrophozoites in a dose-dependent manner. Notably, Rudbar-e-Jonub extract demonstrated superior effectiveness, evident from its lower IC50 values for T. vaginalistrophozoites. The growth inhibitory effect of Rudbar-e-Jonub extract was significantly different compared to the other two landraces(Fatahi Bafghi et al., 2022).

Antidermatophyte Activity

A study explored the antidermatophyte properties of sequential extracts from Egyptian privet L. inermis against 30 clinical dermatophyte isolates, such as Trichophytonmentagrophytes, T. rubrum and Microsporumcanis,. Ethanol and qcetone extracts exhibited the highest activity. SEM analysis revealed structural changes in dermatophytes treated with both extracts, including hyphal collapse, distortion, inflating, crushing, corrugation of walls, and surface depressions. Both extracts, containing the major compound fraxetin, effectively inhibited dermatophyte species (Taha et al., 2022)**.**

Antiviral activity

A recent study explored the potential of compounds isolated from L. inermis roots and leaves to inhibit M^{pro}, a key enzyme in SARS-CoV-2, using molecular docking and dynamics simulations. The results indicated that these compounds spontaneously bonded within Mpro's catalytic pockets. Some compounds, notably the triterpenoid glycoside suavissimoside, exhibited stronger binding and lower IC50 values than the commercial COVID-19 inhibitor remdesivir. Moreover, suavissimoside demonstrated low toxicity, making it a promising candidate for further in vitro and in vivo studies against SARS-CoV-2. These findings offer valuable insights for developing novel drug formulations for COVID-19 prevention and treatment (Tuan et al., 2022)**.**

Antipyretic activity

In a previous research work, the antipyretic effects of aqueous and alcoholic extracts from L. inermis L. were assessed in Wistar rats. Fever was induced by injecting boiled cow milk, and rectal temperature measurements were taken. The alcoholic extract notably reduced the elevated body temperature (Humaish, 2017).

Analgesic and anti-inflammatory activities

In a previous study, both aqueous and alcoholic extracts of L. inermis L. were tested on Wistar rats to evaluate their analgesic and anti-inflammatory effects. The study employed hot plate and tail immersion tests to measure pain response and assessed the extracts' ability to reduce the acetic acid induced writhings. Moreover, the anti-inflammatory activity was evaluated using the formalin-induced paw edema method and measuring tumor necrosis factor alpha (TNF-α) levels. The results indicated that the alcoholic extract exhibited effects similar to the standard drug ketoprofen. It significantly increased reaction time on the hot plate, prolonged tail withdrawal from hot water, and reduced abdominal constriction. Moreover, the alcoholic extract demonstrated anti-inflammatory activity by significantly reducing edema size induced by formalin injection and decreasing TNF-α levels (Humaish, 2017).

In a recent study, the analgesic and anti-inflammatory properties of lawsone isolated from L. inermis leaves were evaluated in mice. The hot plate method was used to assess analgesic effects, and carrageenan-induced paw edema method was employed to measure anti-inflammatory effects. The study determined the LD50 of oral lawsone as 96 mg/kg, with a maximum safe dosage of 80 mg/kg, which did not cause any fatalities among the experimental animals. The results demonstrated that the isolated lawsone exhibited both analgesic and anti-inflammatory effects (Talab et al., 2022). A study demonstrated the anti-inflammatory potential of the ethyl acetate fraction (EAF) of ethanolic leaf extract from L. inermis L. The research employed heat-induced hemolysis and hypotonic solution-induced hemolysis methods, revealing that EAF exhibited robust anti-inflammatory properties (Khatun et al., 2022).

Nootropic activity

A study explored the memory-enhancing potential of L. inermis ethanol extract (Li.Et) and chloroform extract (Li.Chf) in Swiss albino mice, employing both amnesia-induced and non-induced methods via diazepam. The study also analyzed oxidative stress markers (glutathione (GSH), catalase (CAT), superoxide dismutase (SOD)) in mouse brain tissue. Results showed that Li.Et and Li.Chf extracts inhibited DPPH free radicals, indicating antioxidant activity. Both extracts improved learning and memory, as seen in reduced transfer latency and increased step-down latency in passive shock avoidance elevated plus maze paradigm models. Additionally, Li.Et and Li.Chf at 25 mg/kg (oral) significantly increased GSH, SOD, and CAT levels compared to control groups. This study suggests L. inermis as a potential source of memory-enhancing and antioxidant compounds (Mir et al., 2019).

Anti-Alzheimer activity

The study assessed methanolic extracts from various plants, including L. inermis (Henna), O. basilicum (Basil), C. limon (Lemon), C. reticulata (Mandarin orange), B. ceiba (Red silk-cotton), M. spicata (Spearmint), and E. globulus (Eucalyptus), for their antioxidant properties, acetylcholinesterase (AChE) and butyryl-cholinesterase (BuChE)

inhibition, and neurotoxicity. Eucalyptus and henna extracts were the most potent cholinesterase inhibitors (ChEIs), and all extracts displayed concentration-dependent free radical scavenging abilities, with Eucalyptus being the most effective antioxidant. L. inermis leaf extract was the strongest inhibitor of both AChE and BuChE. Notably, Galantamine and the methanolic extract of L. inermis were potent inhibitors. E. globulus exhibited the highest antioxidant capacity, followed by M. spicata, L. inermis, O. basilicum, and B. ceiba. However, Eucalyptus also showed the highest toxicity to neuronal cells(Amat-Ur-rasool et al., 2020)**.**

A study investigated various fractions of L. inermis seeds in Alzheimer's disease (AD) related biological assays, focusing on AChE and BChE inhibitory activities, metal chelating ability, and DPPH antioxidant activity. The ethyl acetate and dichloromethane fractions selectively inhibited BChE. However, none of the fractions showed activity against AChE. Among the isolated compounds, 3-O-β-acetyloleanolic acid and oleanolic acid displayed potent inhibitory activity against BChE. Molecular docking studies confirmed favorable interactions between these compounds and the BChE active site. Additionally, the ethyl acetate and methanol fractions demonstrated excellent antioxidant activity in DPPH assays. These findings highlight the potential of L. inermis seeds in AD treatment due to their antioxidant and metal chelating properties(Balaei-Kahnamoei et al., 2021).

In another study, the in vivo anti-Alzheimer's properties of Methanolic Extract of L. inermis Seeds (MELIS) were investigated in male albino rats with D-galactose-induced Alzheimer's disease (AD). The study assessed acetylcholine (ACh) content and AChE activity in the cerebral cortex. Additionally, in silico molecular docking analysis was performed to evaluate the interaction of MELIS compounds with AChE. The results demonstrated that MELIS exhibited anti-Alzheimer's effects in experimental rats by modulating ACh and AChE levels. The in silico analysis identified ten MELIS compounds, including 3-Deoxyguanosine, N-(3-indolylacetyl)-lisoleucine, Leupeptin, Zearalenone, Sulfamerazine, Trimethoprim, Moricizinesulfone, Quercitrin, Dihydromyricetin and Lecanoric acid which displayed anti-AChE properties by forming hydrogen bond interactions with active site amino acids. These findings suggest that MELIS compounds possess anti-Alzheimer properties.(Jyothi & Yellamma, 2021).

Anticonvulsant activity

In a study, the anticonvulsant effects of chloroform, ethanol, and water extracts from L. inermis leaves were investigated in male albino mice using the electroshock method. The study measured the abolition of hind limb tonic extensor spasm as an indicator of anticonvulsant activity. The findings revealed that both chloroform and ethanol extracts of henna demonstrated anticonvulsant activity. However, the chloroform extract exhibited significant activity against maximal electroshock-induced convulsions in mice(Wadekar et al., 2016).

Wound healing activity

A study investigated the wound healing effects of a mixture of L. inermis L. powder and honey in male rabbits. Animals treated with this combination exhibited superior results, including a significantly shorter necrosis duration, early detachment of the first crust, and reduced overall healing time compared to other groups. The study concluded that the topical application of L. inermis powder and honey accelerates the burn wound healing process in rabbit models. (Djerrou et al., 2016).

A study investigated the wound healing and antimicrobial properties of pomegranate, henna, and myrrh extract ointments either individually or in a combination of all three, using dead space and excision wound models in Wistar rats. The blended formulation demonstrated the most significant increase in wound contraction percentage and a reduction in epithelization time compared to the other formulations. It produced results comparable to the standard ointment from days 16 to 20. Histological analysis revealed that all formulation and gentamycin-treated groups exhibited healed skin structures with normal epithelization, adnexa restoration, and dermal fibrosis. In contrast, the control group exhibited slower progress in granulation tissue formation(Elzayat et al., 2018).

Promoting Hair growth

In a study examining hair growth, male rabbits treated with a mixture of L. inermis powder and honey exhibited the most significant hair growth promotion, as evidenced by increased surface coverage and longer hair length compared to other groups. (Djerrou et al., 2016).

Antioxidant activity

In a study, the in vitro antioxidant potential of the butanolic fraction of L. inermis L. leaves (But-LI) was investigated using ferric reducing antioxidant power (FRAP) assay, lipid peroxidation inhibition and deoxyribose degradation. The findings revealed that But-LI effectively scavenged hydroxyl radicals with an IC50 value of 149.12 µg/ml in the deoxyribose degradation assay. The fraction also inhibited lipid peroxidation and exhibited significant reducing potential in the FRAP assay(Kumar et al., 2017).

In a study examining Egyptian privet L. inermis, different extracts were evaluated for their total phenolic content (TPC), total flavonoids (TF), and antioxidant activity. Ethanol and acetone extracts displayed the highest antioxidant potential, as determined through methods such as DPPH free-radical scavenging, β-Carotene/linoleic acid bleaching inhibition, and ferric reducing antioxidant capacity. Notably, strong and significant positive correlations were found between TPC, TF, and antioxidative potential in these extracts. (Taha et al., 2022).

Anthelmintic activity

In a study, the anthelmintic (anti-parasitic) activity of chloroform, ethanol, and water extracts from L. inermis leaves was evaluated using adult earthworms (Eiseniafetida). The findings revealed that higher concentrations of L. inermis extracts induced a paralytic effect much faster, and the time to death was shorter. All the extracts demonstrated significant anthelmintic activity at all tested concentrations. Notably, among all the extracts, the aqueous extract displayed substantial anthelmintic activity. (Wadekar et al., 2016).

The study investigated the efficacy of an aqueous extract from plant leaves against protoscolices (PSCs), the infective stage of the tapeworm Echinococcusgranulosus, obtained from camel lungs. Normal PSCs, when exposed to the L. inermis extract, effectively prevented plant pigment uptake after 10 minutes, maintaining their original color. In contrast, heat-killed PSCs absorbed the plant pigment, changing color. The treatment outcomes, scored as 0 for viable PSCs and 5 for dead ones, showed a statistically significant distinction between viable and dead PSCs in response to the treatment (Elowni et al., 2020).

In a recent investigation, the ethanol extract derived from the bark of L. inermiswas examined for its antioxidant activity through the KMnO4 scavenging method. The findings indicated that the L. inermis bark extract exhibited a notable capacity for scavenging free radicals, with an observed antioxidant ability showing a 41.4% KMnO4 radical scavenging activity. This suggests that L. inermis bark has substantial potential as an antioxidant and is effective in removing free radicals from the body. (Abuh Omachoko Leonard et al., 2022).

Anticancer activity

In a study, the chloroform extract from L. inermis leaves was tested for anticarcinogenic properties using the MTT assay on various human cell lines, including HepG2, Caco-2, MCF-7, MDA-MB-231, and normal human liver cells (Chang Liver). The initial findings showed significant cytotoxic effects on HepG2 and MCF-7 cells, with IC50 values of 0.3 and 24.85 µg/ml, respectively. No IC50 values were obtained for Caco-2 and MDA-MB-231 cells in the studied concentrations. Importantly, the extract didn't harm normal human liver cells, indicating selective cytotoxicity. This potent cytotoxicity may be linked to its high antioxidant activity, which was also explored(Endrini et al., 2002).

An another study examined the cytotoxicity and genotoxicity of the ethanolic extract of L. inermis. They assessed these effects by measuring the mitotic index (MI), sister chromatid exchanges (SCE), and cell proliferation kinetics (CPK). The findings revealed that the MI and frequency of SCEs in the ethanolic plant extracts closely resembled those of the control group. This suggests that Lawsoniainermis plant extracts had no significant cytotoxic or genotoxic effects on cultured blood lymphocytes. (Munawar T et al., 2022).

Antidiabetic activity

In a study, the hypoglycemic and antihyperglycemic effects of an ethanolic extract were examined in both normal and streptozotocin-induced diabetic albino rats over 28 days. The results demonstrated that oral administration of the ethanolic extract from L. inermis to diabetic rats significantly lowered their blood glucose levels. Notably, the effect was more pronounced with a 500 mg/kg dose of the extract (Choubey et al., 2010).

An investigation studied the effects of L. inermishydroalcoholic extract (LIHE) on diabetic dyslipidemia in alloxan-induced hyperglycemic male Wistar rats, while also assessing its safety profile. Results showed that LIHE at a dose of 400 mg/kg led to a 39.08% reduction in blood glucose levels on day 21, comparable to standard drugs glibenclamide (44.77%) and metformin (46.30%). This decrease in blood glucose levels significantly improved lipid profile, plasma albumin, total plasma protein, and serum creatinine. LIHE notably enhanced lipid and lipoprotein patterns in diabetic rats, possibly due to improved insulin secretion or action, suggesting its potential for treating diabetes mellitus-associated dyslipidemia(S. Singh et al., 2015).

In a study, the effects of distilled water (AE), ethanol (EE), ethyl acetate (EAE) andn-hexane (HE), extracts from L. inermis leaves were examined on glucose levels in normal and streptozotocin-induced diabetic rats. The study also assessed acute hypoglycemic, glucose tolerance, and antihyperglycemic effects. In normal rats, HE significantly decreased blood glucose levels, while AE inhibited the rise in glucose levels after intraperitoneal glucose challenge. Moreover, among the extracts, only EAE demonstrated significant antihyperglycemic activity when administered as a single dose(Widyawati et al., 2019).

In a study evaluating the anti-diabetic properties of extracts from various plants including L. inermis, Ziziphusmauritiana, Dryobalanopsaromatica, Punicagranatum, and Ocimumbasilicum, different parts of these plants were tested for Alpha-glucosidase inhibition. Among the extracts, D. aromatica displayed the most potent anti-diabetic activity in all forms (bark, leaves, and seeds), with IC50 values below 13.00 µg/mL, except for the hexane extract. Additionally, methanol extracts from the barks of L. inermis, Z. mauritiana, and D. aromatica as well as the seeds of P. granatum, exhibited the highest inhibitory activities compared to other extracts within their respective plants. (Rozenan et al., 2021).A recent study explored the antidiabetic properties of the pet-ether fraction (PEF) and ethyl acetate fraction (EAF) derived from the ethanolic leaf extract of L. inermis L. using an alpha-amylase inhibitory assay, comparing the results to Acarbose. PEF emerged as a potent antidiabetic candidate, showing more favorable IC50 (µg/ml) values compared to EAF (Khatun et al., 2022).

Hepatoprotective activity

In a study, the protective effect of methanolic extract from L. inermis leaves against CCl4-induced liver damage in rats was assessed. This involved evaluating serum levels of liver toxicity markers, including total proteins, bilirubin, alkaline phosphatase (ALP), aspartate aminotransferase (AST) and alanine aminotransferase (ALT) as well as examining liver histopathology. The findings indicated a dose-dependent liver protective effect of the plant extract. This was demonstrated by a significant reduction in serum levels of AST, ALT, ALP, and bilirubin, along with improved liver histopathology when compared to animals treated with CCl4 alone(Mohamed et al., 2016).

In another study, the in vivo hepatoprotective potential of the butanolic fraction from L. inermis leaves (But-LI) was evaluated in male Wistar rats with 2-acetylaminofluorene (2-AAF) induced hepatic damage. Exposure to 2-AAF resulted in elevated hepatic parameters such as AST, ALT, ALP, and lipid peroxidation. The administration of various concentrations of But-LI exhibited significant hepatoprotective effects by reducing the levels of AST, ALT, ALP, and lipid peroxidation induced by 2-AAF. Furthermore, But-LI administration restored normal liver structure, as confirmed by histopathological examinations. (Kumar et al., 2017).

Antiulcer activity

In a clinical trial, the impact of applying a decocted extract from L. inermis on grade one pressure ulcers in patients was assessed using the Pressure Ulcer Scale for Healing (PUSH) tools, which measure ulcer surface area and exudate amount. The findings revealed a decrease in the mean PUSH score in the intervention group. Although there was no significant difference observed within the first three days and between the fourth and seventh days, a significant decrease was observed on the seventh day. These results suggest that henna is effective in promoting the recovery of pressure ulcers in hospitalized patients(Davoudi-Kiakalayeh et al., 2017).

In a study, the antiulcer effects of aqueous, chloroform, and ethanol extracts from L. inermis leaves were investigated in Swiss albino rats using pylorus ligation and aspirin-induced models. The antiulcer activity was assessed by determining the ulcer index, volume of gastric juice, free acidity, and total acidity. The results demonstrated that the chloroform extract significantly reduced ulcers in a dose-dependent manner in aspirin-induced ulcers. Additionally, the aqueous, ethanol, and chloroform extracts significantly decreased the volume of gastric acid secretions, free acidity, total acidity, and ulcer index(Kulshreshtha et al., 2011).

Abortifacient activity

A study investigated the abortifacient and antiovulatory effects of an ethanol extract from L. inermis roots in female adult Wistar rats. The results showed that the ethanolic extract significantly reduced the duration of the estrous and metestrous phases, with no impact on the diestrous phase. It also significantly increased the duration of the proestrous phase. The extract led to a significant decrease in ovarian weight and an increase in both preovulatory and atretic follicles. Furthermore, there was a highly significant rise in ovarian cholesterol levels. Importantly, the ethanolic extract did not demonstrate abortifacient activity at a dose of 200mg/kg, but it displayed a highly significant abortifacient effect at 400mg/kg. (S Rani, R Manavalan, 2009).

In a study, the abortifacient activity of L. inermis root was evaluated through in silico docking analysis with the progesterone receptor using the GOLD software. The study also conducted Absorption, Distribution, Metabolism, and Excretion (ADME) analysis and assessed pharmacokinetic parameters. Results revealed that among the 41 compounds derived from L. inermis, D-allose exhibited the highest binding affinity with the progesterone receptor, with a GOLD score of 32.08. D-allose, found in henna, inhibits progesterone activity, induces abortion, and satisfies ADME parameters(Rajeswari & Rani, 2015).

Skin Irritation Studies

In a skin irritation test, a formulated hair dye gel was examined containing henna extract, tea and hibiscus leaves powder and amla fruit extract on albino rats. The physical and chemical properties of the formulated and commercially available formulations were similar in terms of color, appearance, and consistency. Skin irritation studies demonstrated the absence of erythema or edema, indicating that the formulation didn't cause any skin sensitivity or reaction. These findings suggest that the prepared formulation is safe and suitable for hair dyeing, as it caused no irritation or erythema. (Himangshu Kalita et al., 2022).

Larvicidal effect

A study explored the larvicidal potential of L. inermis against the malaria vector Anopheles stephensi, targeting both early and late larval stages. The larvae were cultivated in an insectarium, and their LC50 and LC90 values were determined using probit analysis and regression lines. The study revealed that L. inermis exhibited its highest toxicity at 4000 PPM and the lowest at 4 PPM for early larval stages (I and II), with similar effects observed for late larval stages (III and IV). This research suggests that L. inermis extract could serve as an alternative larvicidal agent for controlling A. stephensi(Bakhshi et al., 2014).

In a recent study, essential oils extracted from henna (L. inermis), Basil (Ocimumbasilicum), Clove (Syzygiumaromaticum), cumin (Cuminumcyminum) and ginger (Zingiberofficinale) were investigated for their insecticidal activity against fourth-stage larvae of Culexpipens. The essential oils from O. basilicum and C. cyminum exhibited moderate larvicidal effects, which were further enhanced when formulated into nanoemulsions, as indicated by a decrease in the LC50 value. However, the essential oils from S. aromaticum, L. inermis, and Z. officinale displayed

weaker insecticidal activity, and the nanoemulsions of these oils did not improve their insecticidal properties (Mahran, 2022).

Insecticidal effect

In an insecticidal study, the effectiveness of L. inermis Linn. against the Egyptian cotton leafworm, Spodopteralittoralis (Boisduval), was assessed using dipping and spraying techniques. Various concentrations of water extract were tested on both early (1st and 2nd instars) and late (3rd instar and above, including 4th, 5th, and 6th instars) stages of S. littoralis. Results at 24 and 48 hours demonstrated a significant increase in S. littoralis mortality with higher concentrations of the water extract. Furthermore, the study revealed that treatment with the water extract affected the biochemical activities of S. littoralis, leading to changes in enzymes like chitinase, protease, phenoloxidase, alkaline, and acid phosphatases, as well as disruptions in protein levels (Abd-El Razzik et al., 2018).

PHYTOCHEMISTRY

In a qualitative phytochemical screening of the alcoholic extract of L. inermis L., the results indicated positive tests for tannins, phenolic compounds, flavonoids, and glycosides, while saponins were not detected (Humaish, 2017). Similarly, in a study conducted on sequential extracts of L. inermis leaves, the results revealed the presence of triterpenoid and steroid compounds in hexane extract, alkaloids, tannins, flavonoids, saponins, and glycosides in ethanol and ethyl acetate extracts. In the case of water extract, tannins, flavonoids, saponins, and glycosides were identified(Widyawati et al., 2019).A recent study reported the presence of glycosides, tannins, flavonoids, terpenoidsalkaloids, resins, and steroids and absence of anthocyanin, phlobatannins, proteins and saponin in the pet-ether fraction and ethyl acetate fraction of ethanolic leaf extract of L. inermis. (Khatun et al., 2022).

In a GC-MS study of ethanol extract (Li.Et) and chloroform extract (Li.Chf) of L. inermis, 12 compounds were found, with pseudoephedrine, phytol, aspidofractinine-3-methanol, and 2,6-bis(1,1-dimethylethyl)-4-methylphenol being the most concentrated In Li.Chf. Phytol was the most concentrated compound in both extracts. 16 compounds were identified with 3-hexadecyloxy-carbonyl-5-(2-hydroxyethyl)-4-methyl imidazolium ion, E-2-tetradecen-1-ol, 2-tridecen-1-ol, phytol, 1-eicosanol, Z,Z-2,5-pentadecadien-1-ol, 3,7,11,15-tetramethyl-2-hexadecen-1 and squalene being the most abundant compounds in Li.Et. (Mir et al., 2019).

In a study, oleanolic acid, 3-O-(Z)-coumaroyloleanolic acid, 3-O-β-acetyloleanolic acid, betulinic acid, and β-sitosterol were isolated from the dichloromethane fraction of L. inermis seeds (Balaei-Kahnamoei et al., 2021). In a recent preliminary phytochemical study on a formulated hair dye gel containing henna and some other plant part extracts found that all the selected plants in the formulation contain carbohydrates,glycosides, proteins, fats, sterols, saponins, phenolic compounds, tannins, flavonoids, alkaloids, volatile oils, gums and mucilage(Himangshu Kalita et al., 2022).

In a study, the ethyl acetate fraction of L. inermis methanol extract was examined using TLC-bioautography. The results showed Rf values of 0.25 and 0.53, indicating the presence of naphthoquinones and phenolic compounds groups, respectively. These compounds were identified as responsible for the inhibition areas observed due to the antibacterial effect. (Mulyaningsih S, 2022).According to a high-performance liquid chromatography analysis, lawsone, fraxetin, and luteolin-3-O-glucoside were identified as the major phenolic compounds present in henna leaves(Taha et al., 2022)**.**

DISCUSSION

The studies discussed here collectively demonstrate the diverse pharmacological effects and potential therapeutic applications of different extracts from the Lawsoniainermis plant. These findings offer valuable insights into the plant's medicinal properties and its potential as a source of novel therapeutic agents.

The review indicated that L. inermis extracts possess significant therapeutic potential across various domains. The reviewed studies collectively indicate that L. inermis extracts possess promising antibacterial properties, particularly against clinically relevant bacteria, such as P. aeruginosa and S. aureus(Habbal et al., 2011).Additionally, Wadekar et al. (2016) documented significant antibacterial properties in the aqueous extract of L. inermis against S. aureus (Wadekar et al., 2016), which corresponds with the findings of Usman &Rabiu (2019) who also observed its efficacy against S. aureus clinical isolates (Usman & Rabiu, 2019). Notably, FatahiBafghi et al. (2022) emphasized differences in antibacterial effectiveness among various L. inermis landraces (Fatahi Bafghi et al., 2022).

Multiple studies have highlighted the effectiveness of various extracts in combatting fungal infections. Suleiman & Mohamed (2014) found that ethanol and petroleum ether extracts were effective against a range of fungal strains(Suleiman & Mohamed, 2014). Usman &Rabiu (2019) expanded on this by confirming the susceptibility of clinical isolates to aqueous, ethanolic, and petroleum ether extracts(Usman & Rabiu, 2019). Furthermore, Hassan et al. (2022) showed that both fresh and dried leaf ethanol extracts were effective in inhibiting fungal isolates(Hassan et al., 2022). For the treatment of candidiasis, Yaralizadeh et al. (2022) successfully conducted a trial using a henna-based vaginal cream(Yaralizadeh et al., 2022). Notably, FatahiBafghi et al. (2022) discovered potent anti-Trichomonas effects, particularly with the Rudbar-e-Jonub extract(Fatahi Bafghi et al., 2022). Lastly, Taha et al. (2022) demonstrated that acetone and ethanol extracts effectively combat dermatophyte infections(Taha et al., 2022). These studies collectively contribute to our understanding of diverse strategies for managing fungal infections.

A recent study revealed that compounds isolated from L. inermis roots and leaves, particularly suavissimoside, exhibit strong binding to the key SARS-CoV-2 enzyme Mpro, with lower IC50 values than remdesivir, suggesting their potential as low-toxicity candidates for COVID-19 treatment(Tuan et al., 2022).Chloroform extract of L. inermis leaves showed

significant cytotoxic effects against liver carcinoma (HepG2) and breast cancer (MCF-7) cells while not affecting normal liver cells (Chang Liver), potentially due to its high antioxidant activity(Endrini et al., 2002). However, a recent investigation found that the ethanolic extract of L. inermis did not have substantial cytotoxic or genotoxic effects on cultured blood lymphocytes(Munawar T et al., 2022).

Prior research found that L. inermis L. extracts had analgesic, antipyretic, and anti-inflammatory effects in rats.lawsone from L. inermis leaves had analgesic and anti-inflammatory effects in mice without fatalities, and the ethyl acetate fraction of the leaf extract showed strong anti-inflammatory properties ((Humaish, 2017); (Talab et al., 2022); (Khatun et al., 2022)and alcoholic extract from L. inermis L. significantly reduced fever induced by boiled cow milk in Wistar rats(Humaish, 2017). A study on Swiss albino mice found that ethanol and chloroform extracts from L. inermis exhibited antioxidant activity, improved learning and memory, and increased levels of antioxidant markers, suggesting L. inermis as a potential source of memory-enhancing and antioxidant compounds(Mir et al., 2019).A hair dye gel formulated with various ingredients in albino rats, finding that the formulated product did not cause any skin sensitivity, erythema, or irritation, indicating its safety for hair dyeing purposes (Himangshu Kalita et al., 2022).

The butanolic fraction of L. inermis leaves exhibited potent antioxidant activity by scavenging hydroxyl radicals, inhibiting lipid peroxidation, and showing significant reducing potential(Kumar et al., 2017). Another study on Egyptian privet L. inermis revealed that ethanol and acetone extracts demonstrated high antioxidant potential, with strong positive correlations between phenolic content, flavonoids, and antioxidative abilities (Taha et al., 2022). Multiple studies highlighted L. inermis's potential for addressing Alzheimer's disease, showcasing its significant cholinesterase inhibition and antioxidant activity, selective butyrylcholinesterase inhibition, and in vivo modulation of acetylcholine and acetylcholinesterase levels, with specific compounds in Methanolic Extract of L. inermis Seeds (MELIS) demonstrating anti-acetylcholinesterase properties(Amat-Ur-rasool et al., 2020); (Balaei-Kahnamoei et al., 2021); (Jyothi & Yellamma, 2021).

A blend of L. inermis powder and honey led to faster burn wound healing on rabbits, with significantly shorter necrosis duration and reduced overall healing time. A combination of henna, pomegranate, and myrrh extract ointments demonstrated substantial wound contraction and faster epithelization, comparable to the standard ointment, promoting healed skin structures on rats(Djerrou et al., 2016);(Elzayat et al., 2018) and showed the most substantial hair growth, with increased surface coverage and longer hair length, as observed in the study(Djerrou et al., 2016).

Chloroform, ethanol, and water extracts from L. inermis leaves demonstrated significant anthelmintic activity on adult earthworms, with the aqueous extract showing substantial efficacy (Wadekar et al., 2016). Another investigation focused on the aqueous extract's effectiveness against tapeworm Echinococcusgranulosusprotoscolices, demonstrating a clear distinction between viable and dead protoscolices based on their response to the extract, highlighting its potential as a treatment method (Elowni et al., 2020).

First and foremost, the antihyperglycemic and antidiabetic properties of Lawsoniainermis, as evidenced by (S. Singh et al., 2015); (Widyawati et al., 2019); (Rozenan et al., 2021); (Khatun et al., 2022) are particularly noteworthy. The ethyl acetate extract (EAE) showed significant antihyperglycemic activity, potentially making it a candidate for the development of antidiabetic drugs. Moreover, the inhibitory activity of L. inermis on alpha-glucosidase and the potent anti-diabetic properties of D. aromatica, both discussed in Rozenan et al. (2021), add to the plant's potential in managing diabetes(Rozenan et al., 2021).Additionally, the comparative analysis of L. inermis's leaf extract suggests that specific components within the plant may have varying antidiabetic effects.

Moving beyond diabetes, L. inermis also shows promise in hepatoprotection. Mohamed et al. (2016) demonstrated that the methanolic extract from L. inermis leaves exerts a dose-dependent hepatoprotective effect against CCl4-induced hepatotoxicity in rats. This suggests that the plant may have applications in protecting the liver from toxic damage, which is a significant finding in the context of liver health(Mohamed et al., 2016).Furthermore, Kumar et al. (2017) found that the butanolic fraction of L. inermis leaves exhibits significant hepatoprotective effects, reducing hepatic damage induced by 2-acetylaminofluorene and restoring normal liver architecture(Kumar et al., 2017). These findings corroborate the plant's potential as a source of hepatoprotective agents.

Intriguingly, the ethanolic extract from L. inermis roots was found to affect the estrous cycle in female rats and exhibited an abortifacient effect at a higher dose(S Rani, R Manavalan, 2009). The in silico analysis conducted by Rajeswari& Rani (2015) further identified D-allose from L. inermis as a compound with high binding affinity to the progesterone receptor, potentially explaining its abortifacient properties(Rajeswari & Rani, 2015). These findings raise questions about the plant's traditional use as an abortifacient and warrant further investigation into its safety and potential applications.

L. inermis exhibited significant larvicidal activity against malaria vector Anopheles stephensi and Culexpipens, suggesting its potential as an alternative larvicidal compound. Additionally, L. inermis water extract effectively controlled Egyptian cotton leafworm, altering the insect's enzymes and proteins(Bakhshi et al., 2014); (Mahran, 2022); (Abd-El Razzik et al., 2018).

L. inermis extracts were found to be abundant in flavonoids, phenolic compounds, tannins, and glycosides, with the absence of saponins, as reported in previous studies(Humaish, 2017); (Widyawati et al., 2019); (Khatun et al., 2022). Upon GC-MS analysis, specific compounds such as 2,6-bis(1,1-dimethylethyl)-4-methylphenol, phytol and pseudoephedrinewere identified in the chloroform extract, while the ethanol extract contained 3,7,11,15-tetramethyl-2-hexadecen-1 and phytol(Mir et al., 2019). Additionally, researchers isolated oleanolic acid, 3-O-(Z)-coumaroyloleanolic acid, betulinic acid, and β-sitosterol from L. inermis seeds (Balaei-Kahnamoei et al., 2021). The hair dye formulation comprised carbohydrates, glycosides, proteins, fats, sterols, saponins, phenolic compounds, tannins, flavonoids, alkaloids, volatile oils, gums and mucilage(Himangshu Kalita et al., 2022). Notably, the ethyl acetate fraction exhibited antibacterial

properties attributed to naphthoquinones and phenolic compounds(Mulyaningsih S, 2022). Furthermore, high-performance liquid chromatography analysis of henna leaves identified phenolic compounds such as fraxetin, lawsone, and luteolin-3-O-glucoside(Taha et al., 2022). These phytoconsitituents might be the responsible for the therapeutic activities of L. inermis. These findings collectively highlight the potential of Lawsoniainermis as a natural bioactive agent with diverse applications.This revealed the complexity of the plant's bioactive compounds and the need for further research to identify the most effective components.

In conclusion, the studies on Lawsoniainermis presented here underscore its diverse biological properties. , ranging from antidiabetic and hepatoprotective effects to potential effects on the reproductive system. These findings open up exciting avenues for future research, drug development, and a deeper understanding of the therapeutic potential of this plant. However, it's crucial to conduct further studies to isolate and identify the active compounds responsible for these effects and to ensure their safety and efficacy for human use.

CONCLUSION

The review of Lawsoniainermis (henna) reveals its diverse therapeutic potential. The extracts of this plant and its bioactive compounds exhibit antibacterial and antifungal properties against various strains and demonstrate antiviral potential against COVID-19. L. inermis offers analgesic and anti-inflammatory effects, displays antioxidant activity, and shows promise in Alzheimer's disease management. Additionally, it aids in wound healing, promotes hair growth, and has cytotoxic effects on cancer cells. Henna extracts possess antidiabetic and hepatoprotective properties, influence the estrous cycle, and are safe for hair dyeing. Furthermore, henna acts as a larvicidal and insecticidal agent, making it versatile in pest control. These findings suggest that L. inermis holds promise as a source of therapeutic agents, opening up exciting avenues for further research, drug development, and a deeper understanding of the therapeutic potential of this plant. However, it's crucial to conduct further studies to isolate and identify the active compounds responsible for these effects and understand their mechanisms of action at the molecular level to ensure their safety and efficacy for human use.

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