Review
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Lawsonia inermis Linn: A Breakthrough in Cosmeceuticals

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Abstract: Herbal cosmetics are formulated using different cosmetic ingredients to form the base in which one or more herbal ingredients are used to cure various skin ailments. The name suggests that herbal cosmetics are natural and free from all the harmful synthetic chemicals that otherwise may be toxic to the skin. Compared to other beauty products, natural cosmetics are safe to use. Cosmeceuticals are cosmetic-pharmaceutical hybrid products intended to improve the health and beauty of the skin by providing a specific result. There are numerous herbs available naturally that have different uses in cosmetic preparations for skincare, hair care, and as antioxidants. The current study included a review and authentication of the various aspects of the plant *Lawsonia inermis*. *L. inermis*, commonly known as henna, has been cultivated for thousands of years for its leaves, which contain a natural dye molecule called lawsone that is commonly used to dye hair, skin, and fabrics. Henna has a long history of use in traditional medicine, where it has been used to treat a variety of ailments. In addition to its medicinal and cosmetic uses, henna has cultural and religious significance in many parts of the world and is commonly used to decorate the skin for weddings, festivals, and other special occasions. Because of these properties, the *L. inermis* plant can be used as a medicine against a wide range of pathogenic organisms and diseases. This review covers the phytochemistry, pharmacological properties, and traditional uses of the plant.

Introduction

The most recent fashion and beauty trend are herbal cosmetics. Since natural products provide the body with nutrients, improve health, and provide satisfaction because they are free from synthetic chemicals and have comparatively fewer side effects than synthetic cosmetics, most women today choose natural products over chemicals for their care to enhance their beauty (1).

The word "cosmetic" originates from the Greek word "kosmos" which means power, arrangement, and skill in decoration. As cosmetics evolved throughout human history, a consistent narrative about their beginnings emerged. These topical corrective pharmaceutical combinations are intended to enhance beauty by using their constituents' appropriate characteristics needed for skin and hair care (2, 3).

The area of cosmetics market is expanding the fastest. Cosmeceuticals are cosmetic-pharmaceutical products that target a specific issue, such as acne control, anti-aging properties, or sun protection, to enhance the health and beauty of the skin. According to the theory put forth by Dr. Albert Klingman, "Cosmeceuticals are topical agents that are distributed across a broad spectrum of materials, lying somewhere between pure cosmetics (lipstick and rouge) and pure drugs" (antibiotics, corticosteroids) (4).

Methods

The search engines PubMed, Scopus, and Google Scholar were used to conduct a thorough literature review using the keywords *Lawsonia inermis* with cosmeceuticals, henna, pharmacological, antioxidant, and antifungal up until April 2023. Additionally, the predicted objective data was assembled.

The regulatory status of cosmeceuticals

Cosmeceuticals - cosmetics or drugs?

A product's intended use determines whether it is considered a cosmetic or a drug for legal purposes. The line between a cosmetic product and a drug is not clearly defined under the current concept, and different rules and laws are applied to various product categories. According to The Drugs and Cosmetics Act, of 1940, drugs are defined as "All medicines for internal or external use of human beings or animals and all substances intended to be used for; or in the diagnosis, treatment, mitigation or prevention of any disease or disorder in humans or animals" (5). And cosmetics are defined as -"Any article intended to be rubbed, poured, sprinkled or sprayed on or introduced into or applied to any part of the human body for cleansing, beautifying, promoting attractiveness or altering the appearance and includes any article intended for use as a component of cosmetic" (6).

Cosmetics and drugs

Some products fall under both the cosmetics and drug definitions. When a product has multiple intended uses, this might emerge. Shampoo, for instance, is a cosmetic because its main purpose is to clean hair. As a treatment for dandruff, an anti-dandruff shampoo considers a drug. Among the cosmetic/drug combinations are moisturizers with sun protection claims, deodorants that are antiperspirants, and toothpaste that contains fluoride (7). The Food and Drug Administration (FDA) review and approval process is required for claims made about drugs but not for claims made about cosmetics. Even though there isn't a specific legal category for cosmeceuticals, the term has come to be used to describe products that fall somewhere between cosmetics and pharmaceuticals (8, 9).

The term itself is not recognized by the Federal Food, Drug, and Cosmetics Act. Consumers frequently find it challenging to verify "claims" made about the actions or efficacy of cosmeceuticals in the absence of the FDA or another reputable regulatory body's approval. Some nations have product categories that fall between the two classifications of drugs and cosmetics, such as 'controlled cosmetics' in Thailand, 'Quasi-drugs' in Japan, and 'cosmetic-type drugs' in Hong Kong. The laws governing cosmeceuticals are not uniform across the USA, Europe, Asia, and other nations (10).

Herbs Used in Cosmetics/Cosmeceuticals

Numerous herbs are found in nature and have a variety of uses, including antioxidants, fragrances, and preparations for skin and hair care. Table 1 contains some crucial examples.

Table 1. Various herbs are used in different herbal formulations.

Action	Ingredients	References
Skincare	Coconut Oil, Sunflower Oil, Jojoba Oil, Olive Oil, Aloe	(11-14)
Anti-aging	*Rhodiola rosea*, Carrot, Ginkgo, Neem	(15-19)
Skin Protection	Green Tea, Calendula, Turmeric, Aloe, Jojoba Oil, Carrot Seed Oil, Wheat Germ Oil, Witch Hazel, Arnica	(20)
Dandruff Treatment	Henna, Shikakai	(21, 22)
Haircare	Amla, Eucalyptus Oil, Snake Grass, Coconut Oil, Shikakai, Reetha, Neem, Sandalwood Oil, Brahmi, Castor Oil, Babchi, Carrot Seed Oil, Witch Hazel Extract, Almond Oil, Lemmon Grass Oil	(23-26)
Antioxidant	Tamarind, Vitamin C, Vitamin E, Beta-Carotene, Retinol, Gingko, Green Tea, Flavonoids, Turmeric Oil, Glutathione, Coenzyme Q 10,	(27-31)
Oral Hygiene Product	Nutmeg, Clove oil, Neem oil, Miswak Extract, Eucalyptus Oil, Myrrh Extract, Tea Tree Oil, Piper Betel Extract, Tulsi Oil, Peppermint Oil, Babhul, Vajradanti, Majuphal, Wintergreen oil	(32-36)
Natural Colorants	Red poppy petals, Annatto, Red beetroot, Blue Tansy, Butterfly Pea, Flavoxanthin, Beta carotene pigment, Chamomile, saffron, curcumin, carthamin, red sandalwood, henna	(37-40)
Fixed oils	Coconut oil, almond oil, olive oil, sesame oil, castor oil,	(41-44)
Waxes	Beewax, carnauba wax,	(45-47)
Gums	Agar, tragacanth	(48, 49)
Perfumes	Rose oil, lavender oil, immortelle oil, German chamomile oil, neroli oil, rosemary essential oil, tea tree oil,	(50-53)
Bleaching agent	Licorice extract, kojic acid, *Phyllanthus emblica*, Giga white, willow bark extract	(54-60)

Figure 1. A picture of *L. inermis* (henna plant).

Lawsonia inermis Linn.

Until the 19th century, natural plant dyes served as the foundation for the cosmetic and food industries (Figure 1). In addition to their traditional medicinal uses, many plants in Iraq were used as natural dyes (61). Henna, also known as *L. inermis* Linn (Family: Lythraceae), is primarily found in subtropical and tropical regions and is used all over the world. It has been used as a dye for cosmetic purposes for more than 9,000 years. *L. inermis* contain phenolic, flavonoids, saponins, proteins, alkaloids, terpenoids, quinones, coumarins, xanthones, fat, resin, and tannins, according to phytochemical analysis. Additionally, 2-hydroxy-1,4 naphthoquinone is present (lawsone). Numerous alkaloids, naphthoquinone derivatives, phenolics, and flavonoids were discovered in *L. inermis*' various parts.

The results of the pharmacological studies indicated that *L. inermis* exhibited a wide range of pharmacological effects, like an antibacterial, antifungal, antiparasitic, molluscicidal, antioxidant, hepatoprotective, central nervous, analgesic, anti-inflammatory, antipyretic, wound and burn healing, immunomodulatory, antidiabetic hypolipidemic, antiulcer, antidiarrhoeal. The pharmacological properties and chemical properties of *L. inermis* will be highlighted in the current review (62).

Plant Profile

Synonyms

Alcanna spinosa, *Casearia multiflora*, *Lawsonia alba*, *Lawsonia speciosa*, *Lawsonia spinosa*, and *Lawsonia Rotantha combretoides* (63). Table 2 contains common/popular names of henna plants in different languages.

Historic Perspective

Issac Lawsone, a Scottish army doctor in the 18th century and a close friend of Carl Linnaeus, inspired the Latin name "Lawsonia" for the plant. The plant is commonly used in a wide range of religious and ritualistic ceremonies of the Hindu and Muslim communities and is a symbol of auspiciousness, prosperity, and happiness in South Asian nations like India, Pakistan, Iran, and the United Arab Emirates. Muslim men dyed their hair and beard with henna because they believed it to be a sunnah or an honorable practice of the Prophet Muhammad. Muslim women in the Middle East were urged to use henna to color their nails to show off their femininity and distinguish their hands from men (64).

Table 2. Common names of henna plants in different language(s).

Languages	Name
English	Henna, Samphire, Cypress shrub
Hindi & Urdu	Mehendi, Mehndi, Hinna
Sanskrit	Ragangi, Mendika, Madayanti, Timir
Tamil	Marithondi, Marithonali, Alvanam, Aivani
Gujarati	Medi, mendi
Bengali	Mendi, Mehadi
Turkish	Kenaag
German	Agyptische
French	Alcana d' orient, Henne
Malayalam	Mailanchi
Italian	Enne, Cipro
Kannada	Mayilanchi
Telugu	Gorintaku, Kormmi
Greek	Kypros
Marathi	Mendhi

Source: http://www.health-fundas/henna...synonyms/42060. The Ayurvedic Pharmacopoeia of India. Part-I, vol. IV, pp. 64.

Historical treasures and traditional use of henna show that women have long painted their hands, feet, nails, and hair with henna. The earliest piece of art depicting actual living women with henna stains on their hands, feet, and nails can be found in "The House of the Ladies," Room 1, East Section, North Wall in Akrotiri. Both women in this wall painting have henna stains on their fingernails and soles (65, 66). Bronze Age texts attest to women's ceremonial henna use. These confirm the usage of henna in the eastern Mediterranean before the Santorini eruption, which occurred around 1627 BCE (67).

Habitat

L. inermis is primarily grown for cosmetics and traditional medicine throughout the world, but it is native to Africa and Asia. It was distributed in Africa: Egypt, Ethiopia, Somalia, Sudan, Zaire, Niger, Benin, Burkina Faso, Cote D'Ivoire, Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Mali, Nigeria, Senegal, Sierra Leone, Togo, South Africa, Comoros, Seychelles; Asia: India, Pakistan, Sri Lanka. It is widely cultivated in tropical regions of the world, North and East Africa, the Arabian Peninsula, the Southern areas of the Middle East, and South Asia (68, 69).

Taxonomic Classification

Kingdom: Plantae, Subkingdom: Viridiplantae, Infrakingdom: Streptophyta, Superdivision: Embryophyta, Division: Tracheophyta, Subdivision: Spermatophytina, Class: Magnoliopsida, Superorder: Rosanae, Order: Myrtales, Family: Lythraceae, Genus: Lawsonia, Species: *Lawsonia inermis* (70)

Botanical Description

It grows to a height of 2.4-5 m and is a densely branched, globous, deciduous, occasionally spinescent shrub or small tree with greyish-brown bark. It is grown as a commercial crop for its dye in some Indian states and as a hedge plant throughout the country (71). The leaves are 1.3 -3.2 by 0.6-1.6 cm, elliptic or broadly lanceolate, acute, or obtuse, frequently micronucleate, and have a tapering base. Petioles are very short. Flowers are numerous,1.3 cm across, fragrant, white, or rose-colored, and borne in long, slender pedicels in large terminal pyramidal cymes. The lobes of the calyx, which is 3-5 mm long and broadly campanulate, are suborbicular or sub reniform and undulate. Eight stamens are inserted into the calyx tube in pairs. 6 mm-diameter capsules that are slightly veined on the outside, supported by the persistent calyx, and have the style (72). The red, globose, pea-sized seed capsules contain numerous tiny, pyramid-shaped, brown-pitted seeds (71).

Traditional Uses

The leaves of *L. inermis* are a major source of cosmetic dye. For centuries, the Middle East, the Far East, and Northern Africa have used henna leaves extensively as a dye for textiles, nails, hands, and hair. Additionally, henna was used to treat skin conditions, headaches, jaundice, amebiasis, and spleen enlargement (73, 74).

In the Charaka Samhita, this plant is mentioned as a remedy for jaundice, and epilepsy, and for coloring grey hair. It has been suggested as a treatment for malignant ulcers in Sushruta Samhita (71). The Ayurvedic Pharmacopoeia of India recommended using leaves for pruritus, dysuria, bleeding disorders, and other stubborn skin conditions (77). The leaf has a bitter taste and is used to treat spleen, vulnerary, headache, lumbago, bronchitis, boils, ophthalmia, syphilis, sores, and other conditions as well as to promote hair growth. An infusion of the flowers relieves headaches5. Flowers are used to treat insomnia and as a refrigerant (76). The bark is prescribed for jaundice and spleen enlargement, as well as for calculous affections, leprosy, and stubborn skin conditions (72). Due to its antibacterial, antifungal, anti-amoebiasis, astringent, antihemorrhagic, hypotensive, and sedative effects, it is used as a medicinal plant (75).

It was used as a folk remedy in parts of south India to treat skin conditions and ringworm infections (78-80). Traditional Yemeni healers used the henna plant to treat burn wounds and bacterial infections (81, 82). Additionally, it was mentioned in the Ebers Papyrus medical texts during the Roman Empire in Rome (83). Medicine of the Prophet listed specific applications for henna as a treatment for tumors, migraines, leprosy, ulcers, smallpox, and other conditions. (84) Initial research using purified henna plant constituents and extracts identified antibacterial (85), antifungal (86), antioxidant, immunomodulatory (86, 90), protein glycation inhibition (87), anti-sickling (88, 91), macrophage-stimulating (92), hepatoprotective (93), analgesic, anti-inflammatory, antipyretic (94), anticomplementary (95), and cytotoxic activities (96) in various fractions. There were no allergic or cancerous side effects associated with the bactericidal and fungicidal actions, which were attributed to the tanning effect of the plant (97, 98).

Medically Useful Plant Parts

Different diseases are treated with the entire plant, including the stem, leaves, roots, fruits, inflorescence, rhizomes, bulbs, latex, seeds, and flowers (99).

Leaf

Henna leaf has an orange-red dye, and leaf paste or powder is frequently used to add designs to hands, feet, and nails. It can also be used to dye hair. Jaundice, skin conditions, sexually transmitted diseases, smallpox, and spermatorrhoea are treated with it (100-102).

Table 3. Ethnopharmacological uses of *L. inermis*.

Plant parts	Ethnopharmacological uses	References
Bark	Antifungal, Antibacterial, Anti-parasitic, Virucidal	(188)
Leaves	Bitter, Astringent, Acrid, Diuretic, Oedema, Expectorant, Anti-inflammatory, Depurative, Liver Tonic, Jaundice haematinic, Styptic, Febrifuge, Trichogenous, Wound healing, Strangury, Cough, Bronchitis, Soothing agent, Cephalalgia, Hemicranias, Lumbago, Rheumatalgia, Diarrhoea, Dysentery, Leprosy, Leucoderma, Scabies, Hepatopathy, Splenopathy, Anti-haemorrhagic, Hemoptysis, Fever, Ophthalmia, Amenorrhoea, to stop hair fall, Hair dye,	(189, 190)
Flowers	Cardiotonic, Refrigerant, Sedatives, Febrifuge, Liver tonic, Cephalalgia, Soothing agent, Amentia, Insomnia, Fever	(191, 192)
Roots	Bitter, Depurative, Diuretic, Emmenagogue, Abortifacient, Soothing agent, Leprosy, Amenorrhoea, Hair dye	(192)
Seeds	Antipyretic, Memory enhancer, Recurrent fevers, Insanity, Diarrhoea, Dysentery and to improve the gastric flow	(193)

Table 4. Traditional medicinal uses of henna plant parts in various countries.

Country/ region	Medicinal use	Form applied	Administration	References
Africa	Induce abortion	Decoction of the whole plant	Oral	(197)
Cambodia	Diuretic, gonorrhoea, bronchitis	Roots	Oral	(198)
Egypt	Pain, skin infections, intestinal amoebiasis	Leaf paste, Decoction of leaf	Topical, Oral	(199)
Europe and America	Aromatherapy	Essential oils from aerial parts	Topical	(200)
India	Jaundice and other liver disorders, Itching, and other skin disorders	Decoction of stem bark, Leaf powder alone or mixed with other herbs, Leaves, Whole plant, seeds, leaf paste	Topical, Oral	(201, 110)
Iran	Recurrent unilateral headache	Leaf paste	Topical	(110)
Jordan	Hair loss, hair dyeing, and skin diseases	Leaf paste	Topical	(202)
Lebanon	Antirheumatic and antineuralgic	Leaves	Topical	(203)
Nigeria	Trypanosomiasis	Leaves, Whole plant	Oral	(204, 205)
Pakistan	Jaundice, as diuretic and blood purifier, skin diseases such as irritation of hands and feet, demulcent and resolvent, Hair, and skin problems	Decoction of Leaves, and leaf paste	Oral, Topical	(196)
Sudan	skin diseases	Whole plant	Topical	(194)
Saudi Arabia	Diabetic foot disorders	Whole plant	Topical	(195)

In the past, henna leaf paste was used to treat kidney lithiasis (104), diarrheal infusion, and skin inflammation (103) while leaf decoction was effective for cleaning and healing wounds (105). The tribes of the Andhra Pradesh region in India frequently used *L. inermis* leaves, Hibiscus rosa-sinensis, Eclipta prostrata, and Abrus precatorius seeds in equal quantities ground into a paste and soaked in sesame oil for 5 days as hair oil to prevent dandruff and hair fall (106). Tribes in Nigeria used leaves as a blood tonic 108), poliomyelitis treatment (107), and measles treatment (108). In Nigeria and Ivory Coast, *L. inermis* leaves were also recommended as a treatment for African trypanosomiasis (109).

Flowers

Flowers have a strong fragrance, and they are used to make perfume. Flower infusion is a useful treatment for bruises. The flower decoction is referred to as an emmenagogue. Seeds have a deodorizing effect.

Seeds

For liver disorders and related issues, seeds in powdered form are an effective treatment. Dysentery

can be treated with powered seeds infused with real ghee (clarified butter) (100-102).

Bark

Burns and scalds are treated with a decoction of the bark. It is administered internally for a variety of ailments, including spleen enlargement, jaundice, and leprosy as an alternative to external treatments for persistent skin conditions (100-102).

Root

The root is regarded as a powerful treatment for herpes and gonorrhea. The root is astringent and can be pulped and applied topically to sore eyes. The pulped root can also be used to treat boils on children's heads. A decoction is consumed as a diuretic in Cambodia. The root is typically decocted as an effective abortifacient along with prepared indigo. The root is thought to be effective in the treatment of nervous disorders and hysteria (100-102). Ancient tribes of the Bhoxa community of India frequently used a half-teaspoonful decoction made from *L. inermis* root taken orally twice daily for 10-15 days to treat jaundice (110). Table 3 contains Ethnopharmacological uses of *L. inermis.*

Modern-Day Use of Henna for Medicinal Purposes

L. inermis is used as traditional or folk medicine around the world to treat a variety of ailments that may seem unrelated to one another (Table 4). But in many instances, a pattern emerges that suggests similar uses by various cultural groups.

Cultivation and Production

Although henna trees can reach heights of six meters and can live for fifty years, they are frequently cut back to just one meter or less and their valuable leaves are harvested (111). Henna is grown in hedgerows because of its durability and tenacious roots, which protect the home garden from desert winds and soil erosion (112). Henna is primarily grown by family women because it doesn't require specialized tools or labor and can be found close to smallholder household compounds. When droughts kill off other crops, henna is a dependable source of income. A smallholder's henna tree is a valuable source of natural cures for minor illnesses. Henna can speed up the healing of wounds and treat ringworm and other fungal infections in children, adults, and livestock (113, 97). Henna's fungicidal, anti-inflammatory, and analgesic properties help nursing mothers with thrush-infected nipples (Candida albicans) (114, 115). The analgesic and antimicrobial properties are beneficial in household burn (116). For efficient dental self-care, cleaning the teeth, and preventing oral microbes, henna twigs are applied to the teeth (117). The belief that henna is "women's work" and that it is "old-fashioned" may have hindered efforts to develop, improve, and research the medicinal and economic potential of henna. Currently, men predominate in the commercial henna export and processing industries. Even though henna is a product of North Africa and the Middle East, it is grown commercially in Pakistan, India, Egypt, Somalia, Sudan, Morocco, Iran, Yemen, and Somalia (67). Present commercial cultivation of henna employs annual or semi-annual pruning to harvest twigs and leaves (118). The cuttings are dried, and the leaves are stripped off and sorted, pulverized, and sieved for use as hair dye and skin stain.

Globalization of Henna as Body Art and Product

In the last fifteen years, henna body art has popularized, spreading globally from its areas of origin, and changing from being a traditional bridal and festival adornment to an exotic fashion accessory (Figure. 2A). Although henna's traditional uses for beauty and wellness have not gained as much popularity as body art and hair dye, researchers are increasingly looking into these practices. They are not doing this because henna is "blessed" or has the power to prevent diseases brought on by the "evil eye," but rather because it is a proven therapeutic for skin care. To prevent the oxidation of lawsone, the substance that gives henna its color, a mildly acidic liquid is combined with the powder before use (114). Henna is applied with a variety of implements that all bring the wet paste into contact with skin, hair, or nails. Without using heat or a mordant, the colorant penetrates, stains, and binds to the keratin in the skin, nails, and hair. After that, the skin is scraped or rinsed off the paste. About 1% of the lawsone migrates into the blood-bearing, living layers of the skin, where it eventually gets carried away by the urine. The majority of the lawsone stays in the skin's outermost, dead layers (119).

Lawsone undergoes oxidation after attaching to keratin (120). The stains are lighter in color and only last for a week or two in regions where the skin is thin and has a high lipid content. Although torso stains are light, they provide a complete sun-blocking effect that lasts beyond the duration of the stain and can provide protection for up to a year at the location of the stain; potentially an effective proactive treatment for melanoma (121). Henna is ideal for body inscriptions that need to be durable, but not permanent (122). Topical applications of henna are usually harmless (123). Henna body art is most seen on palms and soles, where the stains last three to four weeks. For brides and social gatherings, ornamental henna body art is typically limited to the hands, forearms, feet, and legs. Henna body art is currently associated with Hindus, Christians, Jews, Zoroastrians, Sikhs, Animists, and Muslims. Islamic culture plays the largest role in the widespread adoption of henna bridal traditions and

women's health. From the Atlantic coast of Africa to Malaysia and the Philippines, from South Africa to the farthest extent that trade routes carried henna into the Ottoman Empire, Persia, and Central Asia, Muslim women have used henna as part of their celebrations, fitness, and weddings (Figure. 2B). Although henna is now exported to Europe and North America for use as hair dye and body art, it was never native to the Western Hemisphere.

Processing and Preparation of Henna

One of the main sources of natural dye is *L. inermis*, a plant whose leaves give off an orange color. Before the development of synthetic dyes, henna was frequently used to dye clothing in addition to hair and skin. *L. inermis*, which is non-grazable and is a successful cash crop for farmers in arid and semi-arid tropical regions, is grown as a hedge to protect crops and orchards from castles (124). Since ancient times, henna, also known as mehndi, has been used to dye hair, skin, and nails. It has also come to have special significance in both Islamic and Hindu cultures (125).

Henna is traditionally made in India, Pakistan, Bangladesh, and the United Arab Emirates by chopping freshly collected leaves into a paste, which is then ground in a kitchen mixer or with an old stone pistol. Because naphthoquinone, glycosides are present in henna and effectively split off when applied to the skin with water, henna gives hair and skin color. No color is produced by isolated lawsone for the skin or hair (126).

Factors such as the method of cultivation, harvesting, processing, and storage affect the dying properties of henna. Therefore, for better quality and to stop color loss and deterioration, the right method of collection and processing is required. Although shade drying can keep the leaf's green color, it is impractical for large-scale collection in December due to the low temperatures and rain. Maximum lawsone content (2.49%) is produced by using a herbal dryer for 3 hours at 50◦C, whereas sun dry takes longer (72 hours) and produces minimum content (1.69%) (126). Therefore, simple, and inexpensive processing must be used to maintain post-harvest high quality and get excellent returns. It also becomes crucial to adhere to good agricultural and manufacturing practices for henna production with the utmost attention to preserve its dying properties. For best results, it is advised to collect henna leaf during the hot summer as lawsone content has been reported to be maximum during this season. Henna leaves must be ground with water to create a paste. Henna leaves cannot be used for cosmetic purposes (hair and skin dye) in their intact form. In Yazd, Iran, and many other places, henna leaves were ground into powder using henna millstones that were driven by powerful men, camels, and other animals. These henna millstones are made of limestone and have grooves cut into their surfaces to make grinding easier (127). Henna is produced commercially on a large scale for industrial uses in many nations, including India, Pakistan, Bangladesh, and Sudan. India is a significant producer of the highest quality henna among them and has contributed significantly to the development of all major henna-exporting and cultivating nations. The market has expanded significantly because of its domestic utility and symbolic significance in culture. Henna produced in India is used for a variety of other purposes, including domestic products, and is exported to the USA, UAE, Turkey, and the Middle East in about 31% of cases (128). According to a report by the Directorate General of Commercial Intelligence and Statistics (DGCIS), Government of India, henna also contributes to about 8% of the total amount of medicinal plants and herbs exported from India.

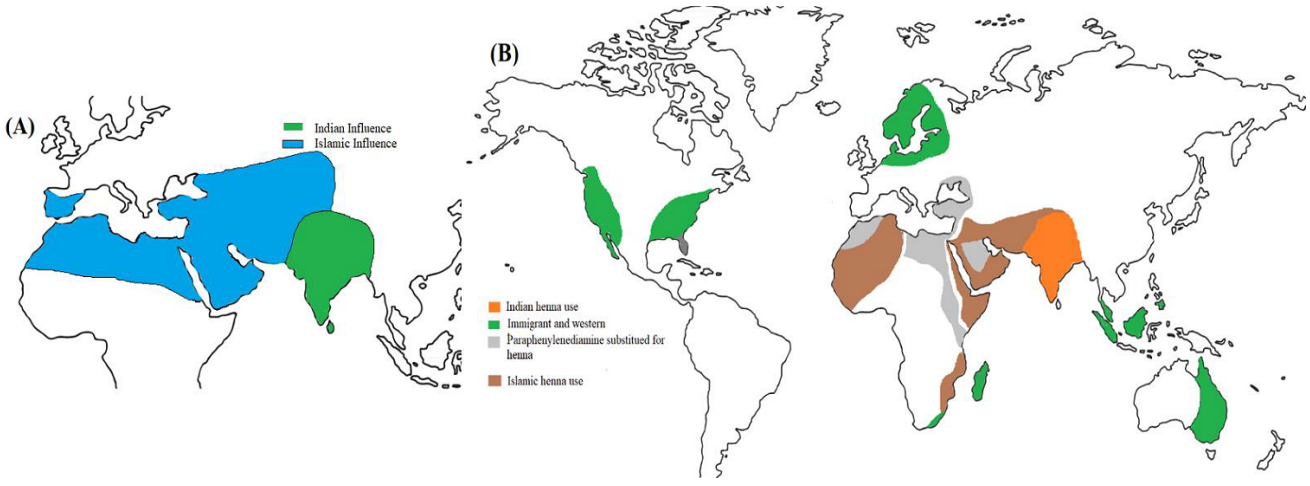

Figure 2. (A) Locations of artifacts with body markings consistent with henna or text mentioning henna between 700 and 1250 CE; (B) Regions where henna body art was practiced between 2000 and 2006.

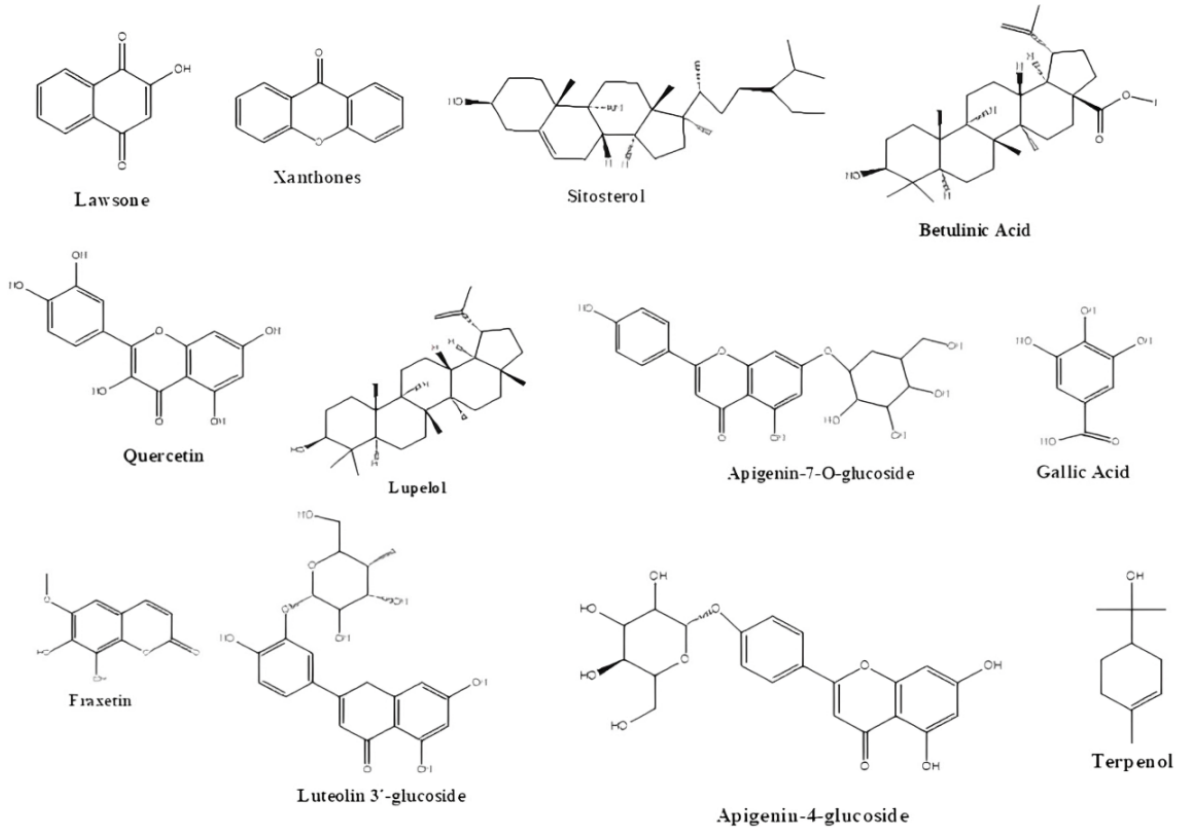

Figure 3. Chemical structures of a variety of compounds isolated from *L. inermis*.

Table 5. Some reported bioactive constituents of *L. inermis*.

Class of Compounds	Bioactive Constituents	Major Site of Occurrence	References
Napthoquinone	Lawsone (2-hydroxy 1,4-naphthoquinone) also called Hennotannic acid, 1, 3-dihydroxy naphthalene, 1, 4-naphthoquinone, 1, 2-dihydroxy-4-glucosyl naphthalene, Lawsoniaside (1,3,4-trihydroxynaphthalene 1,4-di- β -d-gluco-pyronoside), 5-hydroxy-2-methyl-1,4-naphthoquinone	Leaves, Stem, Bark	(109)
Polyphenolic components	Lalioside (2,3,4,6-tetrahydroxyacetoxy-2- β -d-glucopyranoside) Lawsoniaside B (3-(4-O-a-d-glucopyranosyl-3,5-dimethoxy) phenyl-2E-propanol), syringinoside, daphneside, daphnorin, agrimonolide 6-O- β -d-glucopyranoside, (+)-syringaresinol O- β -d-glucopyranoside, syringaresinol di-O- β -d-glucopyranoside, isoscutellarin, gallic acid	Stem, Bark, and Leaves	(206)
Terpenes and terpenoids	3β, 30-dihydroxylup-20(29)-ene (hennadiol), (the 20S)-3β, 30-dihydroxylupane, Lupeol, 30-nor-lupin-3-β -ol-20-one, Betulinic acid, Lawnermis acid (3 β -28 β -hydroxy-urs-12,20-diene-28-oic acid) and its methyl ester, -(Z)-2-hexenol, linalool, α- ionone, β- ionone, α -terpineol, terpinolene, δ-3-carene and γ -terpineol	Stem Bark, Seeds, and Essential Oil from Leaf and Flower	(206, 207)
Phytosterols and aliphatic compounds	Lawsaritol, Stigmasterol and β-sitosterol, 3-methyl-nonacosan-1-ol, n-tricontyl n-tridecanoate	Seeds, Stem, Root	(208)
Xanthones	Laxanthone I (1,3 dihydroxy-6,7 dimethoxy xanthone), Laxanthone II (1-hydroxy-3,6 diacetoxy-7-methoxyxanthone), Laxanthone III (1-hydroxy-6-acetoxy xanthone)	Whole Plant	(209)
Flavonoids	Quercetin, Apigenin, apigenin-7-glucoside, apigenin-4-glycoside, luteoline, luteolin-7-glucoside, luteolin-3-glucoside	Whole Plant, Leaves	(210, 211)
Miscellaneous chemical constituents	(+)-pinoresinol di-O-β-d-glucopyranoside Carbohydrate, proteins, fibres, and Trace metal–(Cu, Ni, Mo, V, Mn, Sr, Ba, Fe and Al) Minerals–Na2O, CaO and K2O	Whole Plant	(212)

Chemical Constituents

Aqueous extract *L. inermis* was subjected to a preliminary phytochemical analysis, which identified the following substances: 6% fat, 2-3% resin, 7-8% tannins, phenolic compounds, flavonoids, saponins, proteins, alkaloids, terpenoids, quinones, coumarins, and saponins (129-135). There was 2-hydroxy-1,4-naphthoquinone in *L. inermis* (lawsone). Lawsone concentrations in *L. inermis* flower, leaf, and branch extracts were determined by HPLC to be 116.7, 486.2, and 5.4 µg/g, respectively (136). Table 5 and Figure 3 contain some reported bioactive constituents of *L. inermis*.

Physicochemical Characteristics

Various physiochemical analyses of the leaf revealed that its total ash content was 14.60%, along with acid-insoluble ash of 4.50%, water-soluble ash of 3.0%, loss on drying of 4.5%, the alcohol-soluble extractive value of 3.8% w/w, and aqueous extractive value of 5.0% w/w (137).

Pharmacological Effects

Hypoglycaemic Activity

A study was done in 2008 by Syamsudin *et al*., (2008) to see how ethanolic extracts of *L. inermis* leaves affected the glucose levels of rats with artificially induced diabetes (138). Extract from ethanol plant leaves significantly reduced glucose levels, demonstrating hypoglycemic activity. Additionally, they noted that this extract has hypolipidemic properties. Arayne *et al*., (2007) showed a significant *in vitro* hypoglycaemic activity of *L. inermis* methanolic leaf extract (139).

Antimicrobial Activity

To assess the antimicrobial potential, *L. inermis* leaf samples were procured from the Dammar region, north of Sudan. Six human pathogenic fungi and four different types of bacteria were grown more slowly when crude extracts of water, methanol, and chloroform were obtained and bio-assayed *in vitro*. The three types of extracts' variations in bioactivity were examined. The water extract was superior despite the extreme activity variations. Anthraquinones, which are a major component of plant leaves and are frequently known to have antimicrobial activity, were discovered through phytochemical analyses (140, 141).

Antibacterial Activity

Twenty different plant species were used by Yemeni traditional healers to treat pathogenic illnesses. The antibacterial screening of various plant species uses both gram-positive and gram-negative bacteria. The ethyl acetate extract of *L. inermis* demonstrated the highest antibacterial activity of all the tested plant species (116). Quinone compounds from *L. inermis* were examined for their antimicrobial properties *in vitro* by Dama *et al*., (1999) (142). Lawsone was the subject of genotoxic studies by Kirkland and Marzin in 2003, who postulated that strain TA2637 of Salmonella typhimurium was more clearly mutagenic than strain TA98 and that the latter was a weaker bacterial mutagen (143). Overall, it appears that there is no genotoxic risk associated with *L. inermis* for consumers. The aqueous extract of leaves from *L. inermis* was also reported to have an antibacterial effect (144).

L. inermis leaf crude extracts in aqueous, methanol, and chloroform demonstrated *in vitro* antimicrobial activity by preventing the development of various strains of pathogenic bacteria (145-147). Studies on the tuberculostatic activity of *L. inermis* were reported by Sharma *et al*. (1990) in both *in vitro* and *in vivo* settings. He reported that 6 g/ml of the herb inhibits the growth of *Mycobacterium tuberculosis* H37Rv and Tubercle bacilli from sputum on the Lowenstein Jensen medium in studies on the *in vitro* tuberculostatic activity of henna. He also stated that in his in-vivo studies, guinea pigs and mice treated with Mycobacterium tuberculosis H37Rv infection experienced a significant resolution of experimental tuberculosis at a dose of 5 mg/kg body weight (148). *L. inermis* leaf ethanol extract demonstrated antibacterial activity in 1973, according to Abd-el-Malek *et al*. (1973) (149).

Antifungal Activity

Khan and Nasreen (2010) tested 10 phytopathogenic fungi and Candida albicans B017 for antifungal activity in methanolic extracts of five different plants. The target fungi's mycelial growth was most significantly inhibited by *L. inermis* among all the extracts tested (76.47–87.77%). In comparison to the nonprotein fractions, the protein fractions of *L. inermis* showed a four to five times greater percentage inhibition of the mycelial growth of Bipolaris oryzae and Colletotrichum lindemuthianum (150). According to Khan and Nasreen (2010), the active compounds responsible for the effectiveness against plant pathogens were proteinaceous in nature or proteins. Aqueous, methanol, and chloroform crude extracts of *L. inermis* leaves showed *in vitro* antimicrobial activity by inhibiting the growth of different strains of pathogenic fungi (145, 147).

Trypsin Inhibitory Activity

Lawsone (naphthoquinone), sugars, and tannins were detected in the preliminary phytochemical screening of the ethanolic extract. Trypsin inhibition was observed by *L. inermis* alcoholic extract of Lawsone (151).

Wound Healing Activity

L. inermis ethanolic extract was used to test the ability

to heal wounds in rats. The animals were given three sets of six in the excision designs and two sets of six in the dead space and incision designs. The excision wound group received topical treatment, whereas the dead space and incision wound group received oral treatment. When compared to the control group, animals treated with extracts had a 71% lower in the wound site. The use of *L. inermis* in wound healing management is supported by increased wound contraction, hydroxyproline, skin-breaking strength, and histological findings (98). According to the findings of the current study, henna leaf extracts can prevent the development of microorganisms that induce burn wound infections. As a result, this finding lends support to the use of henna in the treatment of burn wound infections. The primary intruders of burnt injuries were tested with water and chloroform extracts of leaves (152).

Anti-Cancer Activity

The anticancer activity of *L. inermis* chloroform extract using an MTT-based cytotoxic assay carried out by Endrini *et al*. (2002) (153). The mitochondrial dehydrogenase enzyme in these viable tumor cells converts the soluble tetrazolium salt into the insoluble colored formazone. A spectrophotometer is used to measure formazone after it has been dissolved. This extract was tested on normal liver cell lines as well as liver cancer cell lines. The IC50 value explains cell inhibition or cell killing. Cytotoxicity against liver and human breast cancer cell lines was determined using IC50 values of 0.3 and 24.85g/ml, respectively. Mice given *L. inermis* extract were compared to control mice given only water on the 12th day. Control mice had larger diameters of the gluteal solid tumor mass than *L. inermis* treated mice. It was also discovered that extract-treated mice had higher pH levels and lower levels of glutathione lipid peroxidation than control mice. It suggested that the extract could inhibit cancer cell metabolism (154). A similar study found that *L. inermis* extracts inhibited the multiplication of DLA-induced tumor cells in mice. It also increased mice's average survival time and life span. These findings suggest that *L. inermis* could be used as a novel drug in cancer treatment (155).

Antioxidant Activity

L. inermis, also known as henna, has been found to possess significant antioxidant activity. Antioxidants are molecules that help to protect the body's cells from damage caused by free radicals, which are unstable molecules that can cause oxidative stress and lead to various diseases. Studies have shown that henna contains high levels of phenolic compounds, which are potent antioxidants. These compounds are believed to scavenge free radicals and prevent cellular damage caused by oxidative stress. In addition, henna has been found to exhibit strong radical scavenging activity, which suggests that it may be effective in protecting the body against oxidative damage (156).

Philip *et al*. (2011) investigated the antioxidant as well as free radical scavenging properties of *L. inermis* seeds. The flavonoid and total phenolic content and antioxidant activity of four different extracts of *L. inermis* seeds are compared with an aqueous extract, ethanol extract, dichloromethane extract, and petroleum ether extract. They discovered that the *L. inermis* ethanolic extract is a more potent antioxidant than the aqueous, petroleum ether, and dichloromethane extracts because it contains a higher concentration of flavonoid and phenolic compounds (157).

Anticorrosion Activity

In a 1 molar HCL solution, henna extracts were used to investigate the inhibitory effect on mild steel corrosion using electrochemical techniques and surface analysis (SEM/EDS). All the tested compounds behave as mixed inhibitors, according to polarisation measurements, with inhibition efficiency rising with inhibitor concentration. The highest level of inhibition efficiency (92.06%) is attained at 1.2 g/l of henna extract. Inhibition becomes more effective in the following order: -D lawsone Tannic acid > glucose. Thermodynamic parameters and inhibition mechanisms are also covered (158).

Analgesic, Anti-Inflammatory, and Antipyretic Activity

In rats, a crude extract in ethanol had significant analgesic, anti-inflammatory, and antipyretic effects. The liquid-liquid extraction method separated the extract into butanol, chloroform, and water fractions, which were then tested for the mentioned activities. The analgesic, anti-inflammatory, and antipyretic effects of the butanol and chloroform fractions were stronger than those of the crude extracts, while the aqueous extract had a significantly lower effect. When compared to the other extracts, butanol extract was the most effective in the analgesic test. A pure compound was isolated from the chloroform extract and identified as 2-hydroxy-1,4- naphthoquinone using chromatographic and spectroscopic techniques (lawsone). The isolated compound was discovered to have an analgesic, anti-inflammatory, and antipyretic effect (159).

L. inermis leaves, which are used in indigenous medicine, were discovered to have anti-inflammatory activity (160).

Gupta *et al*. (1986) isolated and identified seven crystalline compounds from the chromatographic fraction of an alcoholic extract of *L. inermis* leaves. The fraction yielded luteolin (m.p. 237°C), with a yield of

0.95%. After concentration, the mother liquor yielded traces of lawsone. After removing laxanthone I and lawsone, the ethyl acetate extract was extracted with a saturated sodium carbonate solution (100ml). The alkaline layer was neutralized with concentrated sulphuric acid and extracted with 130ml. of ethyl acetate, yielding laxanthone II (m.p. 180°C), yield 0.47%. The concentration fraction yielded crystals of 3-Oglucoside of-sitosterol (m.p.285°C), yielding 1.87% (161).

Antiparasitic Activity

During an ethnopharmacological study of antiparasitic medicinal herbs used in the Ivory Coast, 17 medicinal plants were recognized and collected. Alkaloid, polar, non-polar, and extracts from different parts of these plants were tested *in vitro* for antiparasitic activity. The activities of antimalarial, leishmanicidal, trypanocidal, anti-helminthics, and anti-scabies drugs were determined. Among the plants studied, *L. inermis* demonstrated promising trypanocide properties (162).

Protein Glycation Inhibition

Protein glycation is a non-enzymatic reaction between proteins and reducing sugars, such as glucose or fructose, resulting in the formation of advanced glycation end products (AGEs). AGEs can accumulate in various tissues and have been implicated in several chronic diseases, including diabetes, neurodegenerative diseases, and cardiovascular diseases. Therefore, inhibiting protein glycation and reducing the formation of AGEs is a potential therapeutic approach to prevent or mitigate these diseases.

Research on *L. inermis* has suggested that it possesses protein glycation inhibitory activity. Studies have shown that the extracts of *L. inermis*, particularly its leaves, contain compounds that can inhibit protein glycation by blocking the formation of AGEs or scavenging reactive carbonyl species, which are involved in the glycation process. These compounds may include phenolic compounds, flavonoids, and other bioactive compounds present in *L. inermis* (163).

Hepatoprotective Activity

Hepatoprotective activity was found in a 90% ethanol extract of *L. inermis* and its ethyl acetate fraction by Chaudhary *et al*., (2012). Carbon tetrachloride caused hepatotoxicity in rats (CCl4). Ethanol extract and its ethyl acetate fractions of 200 and 400 mgkg1b.wt. reduced alkaline phosphatase (ALP), serum transaminases (AST and ALT), and total bilirubin significantly (TB). As a result, it has been suggested that *L. inermis* seeds be used to treat liver disorders. Against CCl4 (0.5 mL kg-1, i.p.) induced mice, this extract significantly increases albumin and total protein levels ($p<0.01$) in a dose-dependent manner. The seeds extract and its fraction also reduced hepatic malondialdehyde levels by inhibiting free radical production and prevented CCl4-induced oxidative stress by significantly increasing reducing glutathione levels.90% ethanol extract of *L. inermis* and its ethyl acetate fraction showed these biochemical parameters were supplemented by histopathological examination of liver sections, which revealed that the ethyl acetate fraction has a more significant ($p<0.05$) hepatoprotective effect against CCl4induced hepatotoxicity in rats (164).

Tapas *et al*. (2008) discovered that the presence of flavonoids causes hepatoprotective and lipid peroxidation inhibitory properties (165).

Immunomodulatory Effect

According to Mikhail *et al*. (2004), a 1 mg/ml methanolic extract of henna leaves exhibits immunomodulatory activity as evidenced by the stimulation of T-lymphocyte proliferative responses (166).

As per Dikshit *et al*. (2000), the Naphthoquinone fraction shows a significant immunomodulatory effect, obtained from leaves *L. Inermis* (167).

Ant Sickling Activity

Aqueous extract of *L. inermis* leaves was discovered to inhibit sickling and increase the oxygen affinity of HbSS blood (168).

Enzyme Inhibiting Activities

The IC50 values for trypsin inhibitory activity of ethanol extracts of *L. inermis* leaves and lawsone were 64.87 and 48.6g/ml, respectively (169).

Memory and Behavior Effectiveness

L. inermis influences memory and behavior that is mediated by monoamine neurotransmitters. Using elevated plus maze and passive shock avoidance paradigms, the impact of *L. inermis* extract in acetone-soluble pet. ether on memory was evaluated by Iyer *et al*., (1998). How clonidine affects hypothermia it causes to investigate the impact on noradrenaline, serotonin, and dopamine-mediated behavior, respectively, the effects of lithium on head twitches and the effects of haloperidol on catalepsy were observed. The pet. ether extract's acetone fraction showed pronounced nootropic activity. The portion that altered the behavior was mediated by 5-HT and NA. The leaves of *L. inermis* have the potential to explore a nootropic principle, it has been determined (140).

Nematicidal Effect

L. inermis has a suppressive effect on Meloidogyne incognita development. When tomato and henna were grown together, henna reduced the number of tomato

root galls, the number of egg-laying females, and the rate of nematode reproduction. Also, when tomato plants were grown in soil containing henna root exudates, a reduction in nematode biological processes was observed. When henna was grown alone, the root gall index and nematode production rate were reduced by 75% and 99%, respectively, when compared to tomatoes grown alone (170).

Anticoagulant Effect

Lawsone and its oxazine derivatives isolated from *L. inermis* leave shown to be potential anticoagulant agents (171).

Gingivitis Healing Activity

The efficacy of *L. inermis* leaves methanol extracts (62.500, 31.250, and 15.625 g/ml) in healing gingivitis was investigated in Sprague Dawley rats with mandibular labial gingiva inflammation induced by 10% H2O2. There was no difference in healing between the three concentrations of *L. inermis* leaves methanol extract and povidone-iodine, but there were differences between the three concentrations. A higher concentration (62.500 g/ml) can hasten inflammatory cell reduction and epithelial connective tissue repair (172).

Clinical trials were conducted to investigate the effect of *L. inermis* leaves infusion on gingivitis healing. Sixty-three gingivitis patients were instructed to rinse with *L. inermis* leaves infusion at three concentrations (50000, 10000, and 5000 g/ml), 0.1% hexetidine solution, and placebo as a control. *L. inermis* leaves infusion at 10000 g/ml concentration (80%) reduced bleeding index more than hexetidine 0.1% (76%) (173).

Anti-Urolithiasis Activity

L. inermis plants have traditionally been used to treat urolithiasis (kidney stones). Several studies have investigated the potential anti-urolithiasis action of *L. inermis*. One study evaluated the impact of *L. inermis* leaf extract in ethanol on calcium oxalate-induced urolithiasis in rats. The findings revealed that the extract significantly reduced the number and size of calcium oxalate crystals in the urine and kidneys of the rats, indicating a potential anti-urolithiasis activity (174).

Another study looked into the impact of *L. inermis* leaf extract in methanol on forming of calcium oxalate crystals *in vitro*. The extract significantly reduced the formation of calcium oxalate crystals, implying a potential anti-urolithiasis effect (175).

Antidiarrheal Effects

The castor oil-induced diarrhea model in mice was used to test the anti-diarrheal properties of an ethanol extract of the leaf of *L. inermis*. In comparison to the control group, the ethanol extract at a dose of 500 mg/kg had antidiarrheal activity and provided approximately 1.398 of the mean latent periods for the diarrhoeal episode ($p<0.002$) (176).

Diuretic Activity

Several studies have been conducted to evaluate the diuretic function of *L. inermis*. In one study, aqueous *L. inermis* extract was tested for diuretic activity in rats. The extract increased urine output and electrolyte excretion significantly more than the control group, indicating potential diuretic activity. In rats, *L. inermis* leaf extract in ethanol significantly increased urine output and electrolyte excretion, indicating a potential diuretic effect (177).

Anticataleptic Activity

An aqueous extract of henna was found to be effective in treating haloperidol-induced catalepsy in mice. At a dose of 400 mg/kg, there was a reduction in cataleptic scores and an increase in superoxide dismutase activity (178).

Synergistic Effect

According to Bhuvaneswari *et al*. (2002), *Staphylococcus aureus*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, and *Proteus mirabilis* are the primary causes of urinary tract infections. *S. aureus* causes boils, pimples, and other skin conditions that were previously treated with plant leaves (179).

Compared to medications (Gentamycin, Erythromycin, Tetracycline, Chloramphenicol, and Streptomycin) that inhibit protein synthesis, two classes of antibiotics— that inhibit cell walls and those that inhibit nucleic acids—are less effective. Since many organisms today are resistant to antibiotics, this study uses the synergistic effects of plant extracts to create drugs that treat various diseases (180).

Abortifacient Activity

The extract of *L. inermis* roots in methanol was studied for its abortifacient properties by Aguwa (1987), who found that it induces abortion in rats, mice, and guinea pigs in a dose-dependent manner. The results were confirmed by its ethnomedical use in some regions of Nigeria to induce human abortion (181).

Toxicity Studies in Henna

Most toxicological studies claim that hepatotoxicity is connected to toxic effects brought on using herbal medicine. Medical journals have also reported on mutagenicity, carcinogenicity, and other toxic effects on the kidney, nervous system, blood, and cardiovascular system. To conduct any cutting-edge biological experimental techniques have been employed to conduct standard safety tests before the efficacy study to the literature, *L. inermis* has been

shown to have significant analgesic, antioxidant, anti-inflammatory, antibacterial, hepatoprotective, and adaptogenic effects demonstrating that it is a substance that can be used as a drug regularly without causing harm (182).

Prospects of Henna Research

A few workers are looking into the many different uses of henna leaf, extracts, and powder. It's been proposed that the cold and hot aqueous leaf extracts of henna have good staining qualities and make a good substitute for the counter stains used in the Gram staining procedure (183). Henna extract in ethyl acetate demonstrated superior corrosion inhibition and may be used as a green inhibitor to prevent corrosion from aluminum alloy (184). Some of Lawsone's biological activities have been attributed in part to its capacity for redox cycling and the chelation of trace metal ions (114, 185). It has also been demonstrated that silver nanoparticles made from leaf aqueous extract have loculicidal activity (186, 187). Another study discovered that henna-derived molluscicides, either alone or in combination with acetogenins, reduced the fertility, and survival of young snails significantly (188).

Conclusions

Today, the cosmetics industry occupies a unique position. Cosmetic companies are free to develop and market products that are known to affect the structure and function of skin, with little oversight. Most consumers believe that cosmeceuticals are regulated and tested in the same way that drugs are. Consumers believe that ingredients have been tested for safety and that advertising claims are true. Consumers also believe that claims such as "natural," "cruelty-free," and "hypoallergenic" are true and substantiated. The truth is that active cosmeceutical and pharmaceutical ingredients have never been more closely related. When lawmakers mandated the regulatory structure for cosmetics decades ago, they could not have imagined this evolving field.

The data presented here indicated the use of *L. inermis* plant as herbal medicines and bioactive compounds for cosmetic purposes and treatment of various diseases, and it is based on the product's correcting redient requirements and superiority. Herbal cosmetics must be subjected to stringent quality control measures to ensure their safety. Exploration of various types of the literature reveals that the *L. inermis* plant has a broad spectrum of pharmacological activities, and these activities allow it to be used as a remedy in herbal medicines. Because this plant contains a wide range of phytoconstituents, it can treat a broad range of ailments. This plant has antibacterial, antiviral, antimycotic, antimicrobial, and antifungal properties, among others. Because this plant has a wide range of therapeutic properties, scientists and researchers should take it into account when developing a game-changing drug right now. However, more research is needed to uncover *L. inermis*' hidden potential and its therapeutic uses for the benefit of humans.

Declarations

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