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## Pharmacological activities of *Eclipta alba* (L.) Hassk. (*Bhringaraja*): A Review

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### Abstract

*Eclipta alba* (L.) Hassk, family: Asteraceae (*Bhringaraja*) is traditionally used in medicaments in Asian countries including Sri Lanka. Pharmaceutical products containing *Eclipta alba* (*E.alba*) have been used for different kinds of diseases and it had been mentioned in different types of prescriptions in *Authentic texts in Ayurveda (Samhitha Grantha)*. Objective of this review is to discuss about the pharmacological activities and provides an integrated, synthesized overview of the current state of knowledge on *E. alba* with Ayurvedic and traditional knowledge. Data collected from Ayurveda texts, research papers, peer-reviewed indexed scientific journals, and authentic websites. *E. alba* is a small branched perennial herb, found in sandy and clay soils as waterlogged areas. *E. alba* has hepatoprotective, hair growth promoting, antidiabetic, analgesic, anti-inflammatory, neuropharmacological, antioxidant, antimicrobial, cardiovascular, immunomodulatory, anti-epilepsy, anti-venom, anticancer, antiulcer, anthelmintic, and anti-hyperlipidemic properties. The reason for these properties is stated to be its major chemical compounds such as wedelolactone, dimethyl wedelolactone, ecliptic, etc. Therapeutic actions such as relieving swelling (*Sothahara*), relieving pains (*Vedana Sthapana*), purifying wounds (*Vrana shodhana*), wound healing (*Vrana ropana*), giving normal colour to body parts (*Sa-varṇakarāṇa*), improving vision (*Chakshushya*), promoting hair growth (*Keshavardhana*), giving normal black to hair (*Kesha ranjana*) etc. have been mentioned in *Samhitha Grantha* and Ayurveda pharmacopeia.

**Keywords:** *Eclipta alba* (L.) Hassk. *Bhringaraja*; Ayurveda; Pharmacological activities

### 1. Introduction

*Eclipta alba* (L.) Hassk. Family: Asteraceae, known as False daisy and *Bhringaraja*, is a small annual herb commonly used for various medicinal purposes. It is vertical or horizontal, with many branches. Most of the second branches grow from large roots, up to 7 mm cylindrical and grey. The stem is round or flat, and rough due to oppressed white hair, distinct nodes and red in colour. Leaves 2.0–6.2 cm long, 1.5–1.9 cm wide, opposite, sessile to sub-sessile, oblong, lanceolate, sub-entire, acute to subacute, and strigose with hair oppressed on both faces. Flowers appear throughout the year. January to May and November is the time of fruiting. Flowers are numerous, white, ray-florets ligulate in two rows, female (often barren), disc-florets bisexual, regular both kinds together in heads about 7 mm in diameter, which are solitary or two together on stiff unequal peduncles (Fig.1), involucre bracts about 8, ovate-lanceolate or oblong, 5 mm long, 2mm broad, acute or subacute. Ray-florets are spreading, scarcely as long as bracts, linear, not toothed. Disc florets about 3mm long, calyx reduced to scantily hairy teeth. Pistil is bicarpellary. The ovary is inferior and unilocular with one basal ovule<sup>[1]</sup>. The fruit is achenial cypsela, one seed, cuneate, with small wings and brown. Many black seeds are present in the fruit (Fig.2). The seeds are 0.2–0.25 cm long, 0.1 cm wide, and dark brown.

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**Figure 1** Flower of *Eclipta alba* (L.)

**Figure 2** Fruit of *Eclipta alba* (L.)

This 30-40 cm tall plant is found growing wild in sandy and clay soils and is common on damp wetlands, roadsides, paddy, and other crop fields, preferably in warmer climates<sup>[2]</sup>. In sub continental Asia, two species of *E. alba* have been identified that can be classified according to their white and yellow flowers. *Nighantu* is mentioned in the blue flower variety, but it is not common in Sri Lanka. Plants with white flowers are generally used in Ayurvedic medicine and plants with yellow flowers equated with *Wedelia chinensis* Merrill and are known as *Kesharaja*<sup>[3]</sup>. *E. alba* is widespread throughout India, China, Thailand, and Brazil. It is also found in other countries including Indonesia, Sri Lanka, Philippines, Nepal, Malaysia, Myanmar, Japan, Korea, Hong Kong, and Pakistan. Today herbal products symbolize safety more than artificial science which is considered unsafe for humans and the environment. The plant of *E. alba* has an important role in Ayurveda, traditional medicine, Unani, Siddha, Homeopathy, and Chinese medical systems.

## 2. Methodology

Data were collected from authentic classical textbooks and websites, peer-reviewed scientific journals, research papers, and from Ola leaves.

Literature search was carried out using the terms “*E. alba*”, “False daisy”, “Pharmacological activities” and “uses”.

## 3. Results and Discussion

### 3.1. Different Dosages

In Ayurveda Pharmacopoeia, the dosage of the *Swarasa* (juice) of *E. alba* is mentioned as 1-2 *Karsha* (15-30g) and *Churna* (powder) is 6 -24 *Rakthika* (750 mg - 3g)<sup>[4]</sup>. *E. alba* is used as *Pralepa* (an external paste) on wounds also<sup>[5]</sup>.

### 3.2. *Eclipta alba* L.. according to Ayurvedic Medicinal System

Properties of *E. alba*, *Dosha-karma*, and pharmacological actions were fully mentioned in *Bhavaprakasha nighantu*.

### 3.3. Properties of *Eclipta alba* L.

- *Rasa* (Taste) - *Katu* (Pungent), *Tikta* (Bitter)
- *Guna* (Properties) - *Ruksha* (Rough), *Laghu* (Light)
- *Virya* (Potency) - *Ushna* (Hot)
- *Vipaka* (Final Effect) - *Katu* (Pungent)<sup>[3,6]</sup>

### 3.4. Effects on Dosha (Dosha-karma)

*Katu*, *Tikta Rasa*, *Rooksha* and *Laghu Guna* of *E. alba* has an ability to alleviate *Kapha dosha*. *Ushna Virya* alleviates *Vata dosha* and these special properties possesses *Kapha Vata Shamaka* action<sup>[6]</sup>.

### 3.5. Pharmacological actions (*Karma*) and Therapeutic indications (*Prayoga*) of *E.alba* L.

*E. alba* has several medicinal values to control the diseases and has properties such as; *Keshya* (hair growth), *Akalapalita* (premature graying of hair), *Keshyaroga* (diseases of hair), *Tvachya* (skin luster), *Kushta* (skin diseases), *Krimighna* (wormicide), *Kasa Svasha hara* (managing of cough and Asthma), *Shopha* (inflammation), *Shotha* (swellings), *Pandu*

(Anemia), *Dantya* (for healthy teeth), *Rasayana* (rejuvenation), *Balya* (strength promoting) and *Chakshuṣya* (good for eyes)<sup>[5]</sup>. Further, *Netraroga* (eye diseases), *Slipada* (elephantiasis), *Kamala* (Jaundice), *Granthi* (cysts), *Vrana* (wounds), *Bhrama* (giddiness), *Naktandhya*, (night blindness), *Arshas* (hemorrhoids), *Ajirna* (indigestion), *Jvara*, (fever), *Yakritroga* (liver disorders), *Hridroga* (heart diseases), *Sirah shula* (headache), *Mutra daha* (burning in urine) and *Pandu* (anemia)<sup>[3,5]</sup>. *E. alba* is better to use in fresh form and the different therapeutic indications were mentioned as in Table 01.

**Table 1** Therapeutic Indications of *Eclipta alba* L. Hassk

Therapeutic Indication	Formula
<i>Rakta athisara</i> (bloody diarrhea)	Paste of ground fresh leaves of <i>E. alba</i> with cold water.
<i>Kapaja kasa</i> (productive cough)	Juice of <i>E. alba</i> and the juice of tender leaves of <i>Solanum melongena</i> L. ( <i>Thai egg plant</i> ) with honey.
<i>Kasa</i> / <i>Shvasa</i> (cough/respiratory disorders)	Oil prepared from one portion of oil and ten portions of <i>E. alba</i> leave juice.
<i>Svithra</i> (leukoderma)	Cow's milk boiling with seeds of <i>E. alba</i> to drink.
<i>Amlapitta janitha Chardi</i> (emesis due to gastritis)	Powder of <i>Terminalia chebula</i> ( <i>Harithaki</i> ) and powder of <i>E. alba</i> with jaggery ( <i>Guda</i> ) for eating.
<i>Visarpa</i> (erysipelas)	Apply the paste prepared from an equal amount of <i>E. alba</i> and Turmeric grinding with cow's milk.
Maintaining natural black color of hair	Take an equal amount of the <i>E. alba</i> flower and <i>Hibiscus rosa sinensis</i> flower. Then it grinds with cow's milk and put into the metal vessel. Then bury the vessel for 01 week. Then takes it out and mix it with <i>E. alba</i> juice and apply the whole head and hair in the evening. Wash it off after night.
<i>Akalapilita</i> (premature graying of hair)	Prepare an oil using one part of <i>E. alba</i> juice, one part of goat's milk, and one <i>Palam</i> (60 g) of <i>Glycerrhiza glabra</i> (paste of <i>Yashti</i> ). Prepared oil is used for <i>Nasna karma</i> .
<i>Naktandhyata</i> (night blindness)	Prepare a mixture by cooking fish eggs with the juice of <i>E. alba</i> . Eat the preparation after one week.
<i>Upadansha</i> (syphilis)	Grind the whole plant of <i>E. alba</i> to make a paste, and apply the prepared paste to the penis.
Prevent miscarriages	Equal amount of <i>E. alba</i> juice and goat's milk to drink.
<i>Ardhavabheda</i> (migraine)	Prepared a liquid from the juice of <i>E. alba</i> and goat's milk keeping in a sunlight. Can use for <i>Nasna karma</i> .

Therapeutic Indications of *Eclipta alba* L. according to Ayurveda Pharmacopeia

### 3.6. Formulations and Preparations

Bhringaraja Taila, Bhringarajadī choorna, Bhringaraja ghrita, Bhringarajadyadi ghrita, Maha vatavidhvansana rasa, Shadbindu taila, Neelikadya taila, Neelibringadi taila, Ashvakunchaki rasa, Anandabhairava rasa, Sutashekhara rasa, Bhringarajaasava, Bhrngamalakadi taila are the common preparations mentioned in Ayurveda<sup>[3,7]</sup>. Some common preparations with the other ingredients are mentioned in table 02.

**Table 2** Different Formulae and preparations of *Eclipta alba* L.

Grahani Taila <sup>[8]</sup>	Mihira	-	Contains 12gm of <i>E. alba</i> /4 litres of Sesame oil, Recommended in case of fever, acidity problems, and respiratory problems
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Kayyanyadi Taila <sup>[8]</sup>	-	Juice (Svarasa) of <i>E. alba</i> , Paste of <i>Tenospora cordifolia</i> (Amutha) and <i>Glycerrhiza glabra</i> (Yashti) 2.26%, <i>Phyllanthus emblica</i> (Dhatri) 8%, <i>Anjana</i> (Pathrapakam) 0.58%, Sesame oil 84%, Milk 5%
Nilakadya Taila <sup>[8]</sup>	-	Contains 12 gm. of <i>E. alba</i> /3 litres of Sesame oil, Used for Abhyanga (application)
Neelibrngadi Taila <sup>[8]</sup>	-	Contains Leave juice of <i>E. alba</i> ( <i>Bhringaraja svarasa</i> ) 768 ml/6.5 litres of Sesame oil, Used externally for <i>Shirsha shula</i> (Headache).
Bhringaraja Churna	-	One portion of <i>E. alba</i> powder and one portion of Harithaki ( <i>Terminalia chebula</i> ) powder, with old Guda (jaggery) use for Amlapitta (gastritis)] after meals.
Bhringarajadi Churna	-	One portion of <i>E. alba</i> powder, half portion of <i>Sesamum indicum</i> (Sesame) powder, half a portion of <i>Phyllanthus emblica</i> (Dhatri) powder with two portions of jaggery or sugar. Churna (fine powder) 0.5 – 1 g dose is used as Rasayana therapy (rejuvenating and age-sustaining treatment)

### 3.7. *Eclipta alba* L. Uses in Unani Medical System

In Unani system, the juice of *E. alba* is used in 'Hab Miskeen Nawaz' along with aconite (*Croton tiglium*), "Trikatu" (*Piper nigrum*, *Piper longum*, *Zingiber officinale*) and minerals like mercury, sulphur, arsenic, borax etc. for various types of pains in the body. It is also a constituent of 'Roghan Amla Khas' for applying on hair<sup>[9]</sup>.

### 3.8. *Eclipta alba* L. Uses in Siddha Medical System

*E. alba* powder is an ingredient of *Seenthil Choornam* (*Agaththiya Vaidya Kaviyam*), prescribed with a specific butter for bronchitis, cough, rheumatism, and skin disease. According to Neeraja et al. 2015<sup>[9]</sup>, the leaves are ground into a paste and mixed with the leaf juice of this plant. It is then added to gingelly oil and boiled to a proper paste and the oil is extracted. This oil is applied daily on the scalp and helps treat hair loss, body aches, and loss of vision.

The root grinding juice of *E. alba* is given in doses of 20-30 ml twice a day for hepatomegaly, splenomegaly, indigestion, jaundice,

The root powder is given internally at a dose of 5 g daily for liver disease, spleen, and skin diseases. The leaves are finely ground and then the paste (*Karkam*) prepared is well rubbed and tied like a bandage over the scorpion bite site.

Smoke from the leaves with boiling water is toward the pile mass. The leaves are ground with gingili oil and applied over the burning limb due to filariasis.

For hematuria, 5-15 ml leaf juice is given daily twice a day. Two or three drops of leaf juice mixed with an equal amount of honey and given internally to the infant for the common cold. The powder of the roots of this plant is given as an adjuvant with Ayachendooram is an effective remedy for anemia, dropsy, and jaundice. Half (1/2) ounces of *Karisalai* juice is mixed with one ounce of castor oil and given internally very early or alternate for intestinal worms. The roots of the plant are made into powder and 2-5 g of this is given internally for one month with tender coconut water and the second month with honey. This medicine is *kayakarpam* (an ancient system for total body rejuvenation) therapy.

### 3.9. *Eclipta alba* L. Uses in Traditional Medicine of Various Countries

The stimulating property and an anti-ageing property of *E. alba* is common in Ayurvedic medicine<sup>[10]</sup>. Other than that, this plant is used in traditional medicine in different countries as mentioned in table 03.

**Table 3** Traditional Uses of *Eclipta alba* (L.) Hassk

Used parts	Uses	Country
Root	Purgative (root has emetic property) <sup>[1]</sup>	India
Whole plant	Stopping hemorrhages in women after childbirth, asthma, and bronchitis. Externally: as a counter-irritant in toothache and for strengthening of gums <sup>[1]</sup>	Malaya China Indo-China

Leaves	Apply on sores <sup>[1]</sup>	Assam (India)
Plant juice	Jaundice, Fever, Uterine hemorrhages <sup>[1]</sup>	
leaves and flower (Decoction)	Hepatitis. <sup>[1]</sup>	Philippine Island
Leaves	Leaves: as a food Externally - for ringworm and for tattooing to impart a blue color.	Java
Plant juice mixed with an aromatic oil	Catarrhal problem and jaundice <sup>[9]</sup>	Nepal
Leaves	Scorpion stings	
Leaf extract	Remove dandruff and make hair silky and shiny. <sup>[11]</sup>	Utter Pradesh of India
Paste (using whole plant) mix with black pepper and make small pills.	Anti-fever and Anti- jaundice <sup>[11]</sup>	Odisha (India)
Administer 5-10ml leaf juice daily	Against hepatic disorders <sup>[11]</sup>	Tripura state of India
Use leaves and flowers	Asthma, Cough, Jaundice, Urinary problem <sup>[11]</sup>	Rajasthan (India)
Oil extract	Hair tonic <sup>[11]</sup>	Rajasthan (India)
Leaf juice with honey	Anti-jaundice <sup>[11]</sup>	
Leaf extract with water	Control diarrhea <sup>[11]</sup>	
Apply 2-5g of the paste	Wounds and cuts <sup>[11]</sup>	Uttara Pradesh (India)
Plant paste	Blacken hair <sup>[11]</sup>	Maharashtra (India)
Dry powder	Energy tonic for elder People <sup>[11]</sup>	
Whole plant	Used as an antidote for snake bite <sup>[13]</sup>	Korea
Dried plant (Decoction)	Hemoptysis and hematemesis <sup>[13]</sup>	Philippines
Decoction of dried herb or tincture	Dysentery and haematuria urine <sup>[13]</sup>	
Medicated tea or tinctures	Household remedies for sprain and dermatitis <sup>[13]</sup>	
Plant juice	fever, liver problems, urinary and spleen trouble <sup>[14]</sup>	Nepal
Plant paste	wound, skin diseases <sup>[14]</sup>	
Plant extraction is prescribed with cow milk 3 times daily for 15 days before each meal	Acidity <sup>[15]</sup>	India
Leaf extract with the extract of other plants is given orally twice a day for three months	Alopecia <sup>[15]</sup>	India
Leaf paste is used to the affected parts	Allergy, athlete's foot and ringworm <sup>[15]</sup>	Pakistan
Ash of whole plant with honey : orally thrice a day for 03 months	Asthma <sup>[15]</sup>	India, Thailand
Juice of fresh leaves: orally twice a day for 5 days or till the patient recover	Body pain <sup>[15]</sup>	India

Decoction of the whole plant : orally with honey twice a day for 7 days	Bronchitis and Pneumonia <sup>[15]</sup>	India
Paste of the leaves : external use and extract of the plant is given orally twice a day	Burns <sup>[15]</sup>	India
Root powder: orally once a day for 3 days	Constipation <sup>[15]</sup>	India
Leaves and stem are crushed and mixed with mustard oil and applied on the skin	Skin infection Chickenpox <sup>[17]</sup>	Bangladesh
Whole plant extract: externally apply on the affected part	Cuts and wounds <sup>[18]</sup>	Nepal
Whole plant decoction : orally thrice a day for 7 days or till complete cure	Diarrhea and dysentery <sup>[15]</sup>	India
Extract of the whole plant : orally twice or thrice a day for 7 days or until the patient fully recovers	Fever <sup>[15]</sup>	India
Whole plant extract mixed with 3gm. of <i>Phyllanthus emblica</i> powder : orally twice a day for 6 weeks or till the patient fully recovers	General weakness <sup>[15]</sup>	India
The extract of leaves is given orally twice a day for 3 weeks or till the complete cure is achieved.	Gingivitis <sup>[15]</sup>	India
Root extract 3 times a day	Hemorrhoids <sup>[15]</sup>	India
Leaves extract 2 times daily with cow milk for 3 months	Hair fall <sup>[15]</sup>	India
The fruit of <i>Phyllanthus emblica</i> is mixed leaves of <i>E. alba</i> soaked in oil. The oil is heated. Following cooling, a small amount of camphor is mixed with oil and applied to the scalp.	Dandruff, Hair loss, to blacken hair <sup>[19]</sup>	Bangladesh
Whole plant decoction: twice or thrice a day for 3 months	High blood pressure <sup>[16]</sup>	India
Whole plant extract with honey: twice or thrice daily for 15 days	Jaundice <sup>[16]</sup>	India
Whole plant extract: 02 or 03 times daily	Liver enlargement <sup>[15]</sup>	India
Leaves extract before each meal for 15 days	Loss of appetite <sup>[15]</sup>	India
Whole herb extract 02 times a day	Oedema <sup>[15]</sup>	India
Leaves extract with honey thrice a day	Palpitation <sup>[15]</sup>	India
Whole plant paste used externally	Paronychia <sup>[15]</sup>	India
Fresh leaf juice extract with honey is given orally	Pimples <sup>[15]</sup>	India
Leaf extract used on hair	Premature graying of hair <sup>[15]</sup>	India
Whole plant paste used externally for 15 days	Skin disease <sup>[15]</sup>	India
Leaves extract mixed with honey, 02 or 03 times daily	Spleen enlargement <sup>[15]</sup>	India
Oral administration of the whole plant extract	Snake bite <sup>[20]</sup>	India

Oral administration of the whole plant 02 or 03 times in a day. Also used to wash genitalia externally	Urinary tract infection <sup>[16]</sup>	India
Leaves extract with cow milk : orally twice a day	Weakness of vision <sup>[15]</sup>	India
Leaves extract is used to wash wounds	Wounds <sup>[15]</sup>	India
Leaves extract combined with herb root powder :with cow milk 2 or 3 times a day for 3 months	Wrinkles <sup>[15]</sup>	India

Traditional uses of *E. alba* (*Bhringaraja*) with used part, formulae and the country.

#### 4. Pharmacological Actions of *Eclipta alba* L.

##### 4.1. Hepatoprotective Activity

*In vivo*, Hepatoprotective activity of *E. alba* leaves (ethanolic extract) have been studied in rats and mice against carbon tetrachloride-induced hepatotoxicity by <sup>[21]</sup>. Results showed that *E. alba* leaves contain coumestan wedelolactone and dimethyl wedelolactone as major constituents with apigenin, luteolin, 4-hydroxybenzoic acid, and protocateuic acid as minor constituents exhibited maximum hepatoprotective activity.

The combined hepatoprotective effect of Bi-herbal ethanolic extract was measured with CCl<sub>4</sub> induced rats <sup>[22]</sup>. Ethanolic extract from the Piper longum seeds and *E. alba* leaves at a dose of body weight of 50 mg/kg-1 were used orally daily for 14 days. Serum marker enzymes such as Serum Glutamic Pyruvic Transaminase (SGPT), glutamic-oxaloacetic transaminase (SGOT), Acid phosphatase (ACP), Alkaline phosphatase (ALP), Lactate dehydrogenase (LDH), and 5'Nucleotidase, which were significantly enhanced by the CCl<sub>4</sub> treatment, were restored. The biochemical parameters like total protein, total bilirubin, total cholesterol, triglycerides, and urea were also restored toward normal ranges. In addition, Bi-herbal ethanolic extract significantly reduced the liver weight of CCl<sub>4</sub> -intoxicated rats.

Hepatoprotective activity of methanolic extract with subfractions of leaves and chloroform extract with subfractions of roots of *E. alba* has been studied using carbon tetrachloride-induced Wistar albino rats <sup>[23]</sup>. Root chloroform extract and methanolic extraction of *E. alba* leaves showed significant activity and respectively resulted in a decrease in lysosomal enzymes respectively by 47.9% and 72.8%. The triterpenoid Eclabasaponin fraction from the methanolic leaf extraction significantly (78.78%) and the alkaloidal fraction (60.65%) increased the lysosomal enzyme in blood by reducing the carbon tetrachloride-induced. The Coumestan fraction and Triterpenoidal saponin fraction from the chloroform root extraction were increased the lysosomal enzyme in the blood very significantly (75.6%) and respectively (52.4) by reducing the CCl<sub>4</sub> induced.

##### 4.2. Anti-hyperlipidemic Activity

Antihyperlipidemic and hepatoprotective properties of *E. alba* were done using Albino mice caused by fatty foods <sup>[24]</sup>. Treatment of hypercholesterolemic mice with *E. alba* displayed a significant reduction in serum LDL (low-density lipoprotein) and very LDL cholesterol compared to hypercholesterolemic mice. High-fat diets have elevated levels of SGOT, SGPT, and ALP, while the same markers were significantly enhanced by the *E. alba* compared to the standard group.

##### 4.3. Neuropharmacological Activity

*E. alba* is traditionally use for memory enhancing and this quality was studied <sup>[25]</sup>. Dry shade leaves of *E. alba* was extracted with distilled water and administered. Suspension of *E. alba* containing 100 and 200 mg/kg was given to mice to test Transfer Latency in the high concentration line. Mice were placed in the middle of an open fieldwork area to test a habitual learning environment, observing 20 minutes of rearing and time spent during rearing using various doses for 30 minutes, 24 hours, 96 hours, and 144 hours. The results showed a significant improvement in retrieval memory

##### 4.4. Immunomodulatory Activity

Immunomodulatory activity of methanol extract of *E. alba* and *Centella asiatica* was studied in 2004 <sup>[26]</sup>. Experiments were performed that the immune function of methanol extract of whole plant *E. alba* (1.6% delolactone) and *Centella*

*asiatica* (0.18% asiaticoside) at five dose levels ranging from 100 to 500 mg/kg body weight. They used carbon clearance, antibody titer, and cyclophosphamide immunosuppression parameters. In the case of *E. alba*, the phagocytic index, antibody titer, Phagocytic index and White Blood Cell count was significantly increased.

Immunosuppressive effects of oral administration of the herbaceous plant, *E. alba* leaf extracts were studied [27] using *Oreochromis mossambicus* (*Tilapia*). Results showed that aqueous extract of *E. alba* administered as a dietary supplement significantly increased most of the non-specific immune parameters. After feeding with *E. alba* aqueous extract for 1, 2, or 3 weeks significantly increased Humoral responses, lysozyme activity significantly. A very high dose of 1% provided better protection than other values.

#### 4.5. Analgesic Activity

Analgesic effect on albino mice using ethanol and alkaloid extracts of *E. alba* was done using tail clip method, tail-flick method and acetic acid-induced wriggling response [28]. It has a good analgesic activity in the widely-used models. The total alkaloid fraction was the most effective of all tested models.

Further, alcohol extracts of *E. alba* were used to study the analgesic activity in albino rats and mice with a variety of experimental models [29]. *E. alba* alcoholic extract demonstrated a significant antinociceptive effect in a dose of 200 mg/kg.

#### 4.6. Anti-hyperglycemic activity

Anti-hyperglycemic activity of *E. alba* leaf was evaluated on alloxan-induced diabetic rats [30]. The activity of liver hexokinase and gluconeogenic enzymes such as fructose-1,6-bisphosphatase and glucose-6-phosphatase was studied. As a result of oral administration of *E. alba* (2 and 4 g/kg body weight) for 60 days caused a significant decrease in blood glucose, glycated hemoglobin, HbA1c, and decreased glucose-6-phosphatase, and fructose-1,6-bisphosphatase activity, and increased hexokinase activity in the liver. *E. alba*, at a dose of 2 g/kg body weight showed a reduction in sugar better than 4 g/kg of body weight. This study demonstrates that oral administration of *E. alba* has a strong antihyperglycemic activity.

Antidiabetic and diuretic activity of polyherbal formulation was evaluated [31]. As an ingredient in the polyherbal formulation *Pan-Five* (prepared from the powder of plants *Toddalia asiatica*, *Terminalia chebula*, *Terminalia bellirica*, *Eclipta alba*, *Enicostemma littorale*), *E. alba* has been scientifically and clinically proven to have antidiabetic and diuretic activity by restoration and regeneration  $\beta$  cell activity in pancreas.

Antidiabetic activity of the ethanol extract of *E. alba* associated with the inhibition of alpha-glucosidase and aldose reduction was considered in streptozotocin-induced diabetic rats was evaluated [32]. A single-dose treatment of *E. alba* in a streptozotocin-induced diabetic rat reduced blood glucose levels by 17.6% at a dose of 250 mg/kg<sup>-1</sup> within 5 hours of oral administration. The treatment of the animals after 10 weeks of *E. alba* (250 mg/kg<sup>-1</sup>) for 21 days significantly reduced the elevated blood glucose, % HbA1c, urea, uric acid, and creatinine and a significant increase in the low serum insulin level.

#### 4.7. Hair growth Activity

Petroleum ether and ethanol extract from *E. alba* were introduced to promote hair growth in albino rats. *E. alba* extract was induced into oil-based cream and applied to the shaved skin of albino mice. The length of time (in days) required for the onset of hair growth, as well as the completion of the hair growth cycle was recorded [33]. The 2% Minoxidil solution was topically applied and served as a positive control for comparison. Hair growth initiation time was significantly decreased to half in comparison with the control animals. Results showed that the effect of petroleum ether treatment was better than that of effective minoxidil treatment. The efficacy of methanol extract in *E. alba* as a hair growth promoter was also considered [34]. Hair growth potential was found to be a dose-dependent activator of the whole plant's methanol extract in C57 / BL6 mice. Activities were evaluated by studying melanogenesis in resected skin, the number of vesicles in the skin tissue, the thickness of the skin layer, and the surrogate markers in-vehicle control for the extracted animals. Findings suggest, methanol extract of *E. alba* has the potential to act as a hair growth stimulant.

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### 5. Prevention of skin disease

Role of *Rasayana* (Aphrodisiac therapy) and the prevention of recurrent Vichachrika (eczema) were studied and *E. alba* powder has been shown a complete remission to 22.65% and checked the recurrence of the disease in 89.5% of patients



with eczema [35]. These patients were first subjected to clearance of intestines (koshta shuddhi) done with *Cassia fistula* (Aragvadha) decoction administered orally at bedtime for an initial eight-day. Thereafter, 30ml of Shirishadi decoction and 6 g of Guduchi (*Tinospora cardifolia*) and *E. alba* powder were given with *Ghee*. Both drugs were taken twice daily after meals orally.

### 5.1. Antivenom Activity

Inhibition of snake venoms and phospholipase A2 by extracts from native and genetically modified *E. alba* was studied and the essence of *E. alba* has been shown to inhibit the snake venom phospholipase A2 activity, the venom of South American rattlesnake (*Crotalus duricus terrificus*) [36]. Coumestans is an important group of naturally occurring oxygenated and aromatic products, including Wedelolactone and its demethylated form, both of which are responsible for the major therapeutic effect of *E. alba* such as its anti-hypertensive, antiulcer, anti-hepatotoxic, anti-phospholipase A2, and antidote activities against snake venoms.

### 5.2. Antimicrobial Activity

*E. alba* extracts were prepared using solvent such as acetone, ethanol, methanol, aqueous, and hexane and which were used against selected gram-positive and gram-negative bacterial species to study the antibacterial activity [37]. The minimum inhibitory concentration assay (MIC) and Minimum bactericidal concentration (MBC) methods were also used. Hexane extract of *E. alba* showed high antibacterial activity against *Staphylococcus aureus*, *Bacillus cereus*, *Escherichia coli*, *Salmonella typhi*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Streptococcus pyogenes*. The inhibitory functions of all reported substances were compared with standard antibiotics (Ciprofloxacin 25µg/ml). Acetone, ethanol, methanol, and aqueous extract showed intermediate activity against *Staphylococcus aureus*, *Bacillus cereus*, *Escherichia coli*, *Salmonella typhi*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, *Proteus mirabilis*, and *Streptococcus pyogenes*.

Microbial activity in the aqueous extract of leaves, stems, and flowers of *E. alba* was tested [38] and leaf extract of *E. alba* has been shown effective against *Klebsiella pneumonia* and *Escherichia coli*. Aqueous extract of *E. alba* stem has been shown antimicrobial effect against *Staphylococcus saprophyticus*, *Enterococcus faecalis*, *Klebsiella pneumonia* and *Escherichia coli*. The aqueous extract of *E. alba* flowers has been shown an antimicrobial effect against *Staphylococcus saprophyticus*, *Proteus Vulgaris*, and *Staphylococcus aureus*.

### 5.3. Antiulcer Activity

Antiulcer activity of the methanolic extract of *E. alba* was assessed using Aspirin or ethanol induced or pylorus ligation plus Aspirin treatment caused injuries in Sprague Pawley rats who had been fasting for 36 hours [39]. Group receiving oral administration of *E. alba* extract showed a significant reduction in gastric inflammation as well as gastric ulcers after 4 hours of treatment when compared with the control groups. Moreover, the Antiulcer potential of *E. alba* is comparable to the activity of rabeprazole.

Further, *E. alba* extract at 50, 100, and 200 mg/kg<sup>-1</sup> was given twice daily (orally), for five days to prevent cold restraint stress ulcers and pylorus ligation-induced ulcers. Parameters such as acid secretion, gastric juice volume, P<sup>H</sup> and gastric wall mucus was estimated in the pylorus ligation-induced ulcer model [40]. Mucus production was significantly increased in mice treated with *E. alba*. A Significant decrease of the P<sup>H</sup> in the stomach relative to the control values were confirmed by the anti-secretory activity of *E. alba*. These findings were further supported by histopathological examination of the stomach in treated and controlled mice.

### 5.4. Anthelmintic activity

Anthelmintic activity was evaluated against *E. alba* whole plant methanolic extract for *Pheretima posthuma* (species of earthworm) in different concentrations (25-100 mg/ml) and recording the time taken for paralysis and the worm death [41]. Results showed paralysis of earthworm (*Pheretima posthuma*) at lower doses of 50, 75, and 100 mg/ml, and the worm died at 75 and 100 mg/ml concentrations when compared to the Albendazole standard.

### 5.5. Antimalarial activity

Adulticidal and repellent activity of *E. alba* leaves against two important vector mosquitoes namely *Culex quinquefasciatus* and *Aedes aegypti* were tested [42] and Benzene, hexane, ethyl acetate, chloroform, and methanol extracted from the leaf of *E. alba* and *Andrographis paniculata* were used. The adult mortality rate was observed 24 hours after exposure. All exceptions have been shown the effect of moderate adulticide effect. The repellent activity of benzene, hexane, ethyl acetate, chloroform, and methanol extraction of *E. alba* and *Andrographis paniculata* plant was

observed in three doses of 1.0, 2.5, and 5.0 mg/cm<sup>2</sup>. There, it was applied to the skin of the human forearm and exposed to female mosquitoes. In this view, these two plant crude extracts protected the test person from mosquito bites without any allergic reaction. Furthermore, the repellent activity depended on the strength of the plant extract.

Mosquito larvicidal and ovicidal activity of crude hexane, ethyl acetate, chloroform, benzene, and methanol extracts of three plant leaves, *E. alba*, *Andrographis paniculata*, and *Cardeospermum halicacabum*, tested with the early third instar larvae of *Anopheles stephensi*. Caterpillar death was detected after 24 hours of exposure. All plant extracts showed a moderate larvicidal effect. High rate of larval mortality was found in the methanol extract of *E. alba* and *Cardeospermum halicacabum* against the larvae of *Anopheles stephensi*. The 100% mortality rate was presented by the methanol extract of *E. alba* and the methanol and ethyl acetate extract of *Andrographis paniculata* at 200 ppm [43].

### 5.6. Anti-Inflammatory Activity

Anti-inflammatory effect was done using carrageenan mediators such as serotonin and histamine-induced granuloma paw edema and cotton pellet-induced granuloma in rats. Higher inhibition (55.85%) was recorded at a dose of 500 mg/kg after 3 hours of the drug treatment in carrageenan-induced paw edema, while indomethacin (standard drug) 61.30% inhibition was produced. The result showed a strong anti-inflammatory effect as well as the therapeutic efficacy of *E. alba* based on animal models, compared with Indomethacin [44].

### 5.7. Anti-epileptic Activity

*E. alba* L. has been reported to be a nerve tonic and has been used to treat epilepsy in folk medicine.

Anti-epileptic activity was done in chemically induced chronic and acute models in rats using isolated luteolin from methanolic extract of *E. alba* leaves [45]. In acute, luteolin (5, 10, 20 mg/kg) was administered 30 minutes before Pentylene-tetrazole injection (100 mg/kg) in albino rats. In chronic, pentylenetetrazole (35 mg/kg) was administered every alternative 48 days. Pretreatment with a single dose of luteolin before giving pentylenetetrazole injection to mice resulted in 100% protection from mortality and it did not show any effect on motor coordination. Result showed that luteolin had an anti-convulsant effect in the acute pentylenetetrazole-induced models.

### 5.8. Anticancer Activity

Anticancer effect of the hydro-alcoholic extract of *E. alba* was obtained various cancer cell lines like breast cancer, human colorectal carcinoma, human prostate cancer, and renal cell carcinoma [46]. They also studied the effect of normal human embryonic lung fibroblast cells using colony formation, methyl thiazol diphenyltetrazolium bromide assay, and migration assay. The methanolic extract of *E. alba* carried a significant amount of specificity against human colorectal carcinoma cells compared to other cancer cells and this extraction showed nontoxicity for normal human embryonic lung fibroblast cells. Accordingly, *E. alba* has anticancer activity and is less toxic to normal cells.

The role of *E. alba* as an anticancer agent, using human liver cell lines, rat glioma, and rat kidney cell lines as model systems [47]. MTT assay [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2H-tetrazolium bromide] was used to determine the cytotoxic effect and antiproliferation effect of *E. alba*. Results showed that the *E. alba* inhibited the cell proliferation of human liver, rat glioma, and rat kidney cell lines depending on the dose. The data has confirmed the existence of DNA damaging, anti-proliferative, and anti-metastatic properties of *E. alba*.

### 5.9. Antioxidant Activity

The antioxidant activity of the hydro-alcoholic extract of *E. alba* was studied and standard parameters like Fe+2 chelating ability, 1,1-diphenyl-2-picrylhydrazyl radical scavenging activity, reducing ability, hydroxyl radical scavenging activity, superoxide radical scavenging activity, and nitrous oxide radical scavenging activity were measured. Result showed that *E. alba* extract contains high content of wedelolactone, flavonoids, phenolics, ascorbic acid, and tannins. The hydrochloride alcohol extract of *E. alba* effectively removed free radicals from various concentrations, exhibited potent antioxidant power, and had a dose-dependent effect [48].

Antioxidant potential of the aerial parts of *E. alba* [ethylacetate fraction] has revealed the significant dose dependent activity in rat liver [49]. Doses (50 mg/kg, 100 mg/kg, and 200 mg/kg) were given orally for 7 days. *E. alba* significantly reduced the biochemical parameters: lipid peroxides and increased the activity of antioxidant enzymes like glutathione peroxidase, superoxide dismutase, glutathione reductase, and catalase as well as  $\alpha$ -tocopherol.

## 6. Chemical Compounds of *Eclipta alba* L.

Principal constituents of *E. alba* was evaluated and found them as coumestan derivatives like wedelolactone, (1.6%), dimethyl wedelolactone, desmethyl-wedelolactone-7 glucoside, and other constituents are ecliptic,  $\beta$ -amyrin, luteolin-7-O-glucoside, hentriacontanol, heptacosanol, and stigmasterol<sup>[50]</sup>. Phytochemical analysis showed the presence of steroids, flavonoids, carbohydrates, proteins, saponin, glycosides, alkaloids, and tannins. Chloroform extraction has shown the presence of saponin, tannin, protein, steroids, and terpenoids. The extraction of petroleum ether from plant leaves has shown the presence of steroids, proteins, carbohydrates, terpenoids, and saponin. According to the available results of laboratory tests and clinical trials.

**Table 4** Chemical Compounds of *Eclipta alba* L. and Pharmacological Activities

Compound	Compound	Major source	Pharmacological Activity
Wedelolactone	Coumestan	Leaves, Stem	Antihepatotoxi, Antibacterial, Trypsin inhibitor, Antivenom
Demethyl wedelolactone	Coumestan	Leaves	Antivenom
Ecliptalbine	Alkaloid	Seed	Analgesic, Lipid Lowering
Eclalbatin	Saponin	All plant parts	Antioxidant
Dasyscyphin C	Saponin	Whole plant	Anticancer, Antiviral
Ecliptine	Aldehyde	All plant part	Antioxidant

## 7. Conclusion

Present study showed that *E. alba* has Hepatoprotective, Immunomodulatory, Hair growth-promoting, Antiepileptic, Antidiabetic, Anti-venom, Analgesic, Anticancer, Anti-Inflammatory, Antiulcer, Neuropharmacological, Anthelmintic, Antioxidant, Antimalarial, Antimicrobial, Antihyperlipidemic activities. Most of the therapeutic actions mentioned in *Samhitha grantha* and Ayurveda pharmacopeia have been confirmed by modern laboratory tests, clinical trials, or animal trials. This study also analyses the recent advancements in relation to the pharmacological activities of *E. alba* in the field of modern medical sciences. Also, this study can be evidence for traditional medical claims of *E. alba* mentioned in Ayurveda classical texts and modern evidence-based medicine.

## Compliance with ethical standards

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### Disclosure of conflict of interest

No conflict of interest.

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