

Chemical Constituents & Therapeutic Uses of *Eclipta prostrata* Linn

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ABSTRACT

Eclipta prostrata Linn, commonly referred to as "False Daisy" or "Bhringraj," is a medicinal plant extensively utilized in traditional medical systems, particularly in Ayurveda and traditional Chinese medicine. This review paper aims to consolidate and assess existing literature concerning the chemical constituents and therapeutic benefits of *Eclipta prostrata*. The plant's recognition for harboring a diverse array of bioactive compounds and its potential in addressing various health conditions adds significance to this review. By shedding light on the pharmacological properties and therapeutic applications of *Eclipta prostrata*, this review paper paves the way for further research and the development of its therapeutic potential.

Keywords: *Eclipta prostrata*, Ayurveda, antimicrobial, anti-inflammatory, Hepatoprotective.

Introduction

Since ancient times, people have relied on numerous plants in traditional medicine, and even in modern times, this practice continues due to the concerns over the side effects and drawbacks associated with synthetic medicines. The medicinal properties of these plants are primarily attributed to the presence of chemical molecules, which have led to the exploration of new drug possibilities [1].

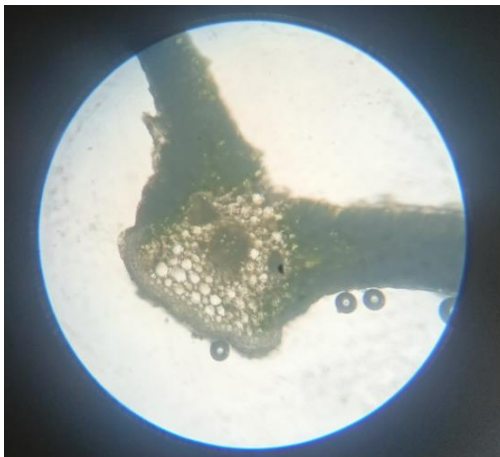
For millennia, plants have held a vital role in preserving human health and enhancing the overall quality of life. In contemporary times, there has been a growing global emphasis on plant research, accumulating a substantial body of evidence showcasing the tremendous potential of medicinal plants utilized in diverse traditional systems. Presently, there is a significant surge in public interest regarding the utilization of herbal remedies [2]. *Eclipta prostrata* enjoys widespread traditional acclaim as a medicinal herb, particularly in tropical and subtropical regions across the globe [3]. *Eclipta prostrata* (L.) L. (Syn.: *Eclipta alba* (L.) Hassak, Family: Asteraceae) is a well-known herbal plant, recognized by various names worldwide. In English, it is commonly referred to as False daisy or Ink plant, while in the Nepali language, it is locally known as Bhringraj, Bhumiraj, Aali jhar, and Nash jhar[4] [5].



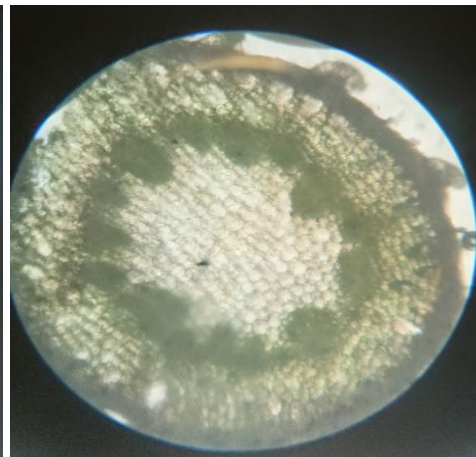
The herb contains wedelolactone and demethylwedelolactone, both of which possess potent antihepatotoxic properties[6]. In addition to wedelolactone and demethylwedelolactone, the herb contains other prominent chemical constituents such as Ecliptal, Ecliptine, Ecliptalbine, α Terthienylmethanol, β -amyrin, Sigmasterol, Polypeptides, among others. Moreover, the plant exhibits various pharmacological activities, including antiviral, antibacterial, spasmogenic, hypotensive, analgesic, and antioxidant effects[7]. *E. prostrata* juice can be consumed orally or applied topically to stimulate hair growth[8].

Botanical Characters-

It exhibits a straightforward leaf arrangement, with leaves that are opposite, ovate, or oblong-lanceolate, measuring 2 to 10 cm in length and 1 to 3 cm in width. The leaf tips can be either sharp or rounded. Clusters of small white flowers emerge from the leaf axils, with each flower head reaching approximately 1 cm in diameter. The marginal ray flowers are 2-3 mm long, pistillate and fertile, with a white corolla and ligulate shape. Central disk flowers are numerous, 1.5-2 mm long, perfect and fertile, with a whitish tubular corolla. Each flower features five stamens with separate filaments, and their anthers merge to create a tube around the style. In a single growing season, an *Eclipta* plant can yield as many as 17,000 seeds.[9]



T. S. of leaf of *Eclipta alba*



T. S. of stem of *Eclipta alba*

Therapeutic Uses-

- **Treatment of neurodegenerative Diseases-**

Various neurodegenerative disorders, such as Parkinson's disease, present distinct challenges in individuals' lives. The development of Parkinson's disease is significantly influenced by oxidative stress. This oxidative stress is primarily triggered by the neurotoxin 6-hydroxydopamine, which is implicated in the progression of neurodegenerative conditions associated with Parkinson's. *E. prostrata* is known for its abundant phenolic compounds, offering antioxidant properties to mitigate oxidative stress. The ethyl acetate extract of *E. prostrata* demonstrates protective effects against 6-hydroxydopamine-induced neurotoxicity in SHSY5Y cells. Pre-treatment of cells with this extract prior to exposure to 6-hydroxydopamine significantly enhances cell survival and reduces intracellular reactive oxygen species (ROS) levels in a concentration-dependent manner. Additionally, the ethyl acetate extract of *E. prostrata* diminishes the Bax/Bcl-2 ratio and reduces the activity of caspase-3, a critical regulator of cellular

apoptosis. With its antioxidant capacity, this extract from *E. prostrata* effectively mitigates apoptotic signaling induced by 6-hydroxydopamine and prevents SH-SY5Y cell death[10].

Hair Growth Promoting Activity-

Both external and psychological stresses have the potential to cause hair loss, which can negatively impact one's quality of life and influence interpersonal relationships and daily social interactions. *E. prostrata* has a longstanding history of use in traditional Asian medicine for addressing skin conditions. Furthermore, research has explored the effects of *E. prostrata* on enhancing hair growth, with in vivo and in vitro studies conducted on mice[11]. Mondal et al. conducted an evaluation of hair growth promotion activity by shaving the dorsal region and observing its impact on hair growth in Wister rats[12]. Traditionally, *E. prostrata* has found widespread application as an ingredient in shampoo production, as it is believed to contain compounds that offer nourishment to hair. With a growing population experiencing hair loss, the market has seen the commercialization of various chemically formulated products for hair loss prevention and treatment. Utilizing *E. prostrata* in shampoo for scalp treatment resulted in increased hair density and thickness after 10 weeks of use, along with the added benefit of cleaner skin[13]. Albino rats were used to evaluate the hair growth-promoting activity of *E. prostrata* extracts in petroleum ether and ethanol. These extracts were integrated into an oleaginous cream with a water-in-oil cream base and topically applied to the shaved and denuded skin of male albino rats. In comparison to the control group that received no treatment, the extracts significantly reduced the time required for hair growth by half. A quantitative analysis of hair growth following the application of petroleum ether extract (5%) revealed a greater number of hair follicles in the anagenic phase (69 ± 4), which was notably higher than the control group (47 ± 13)[14].

Treatment of Diabetes-

Diabetes mellitus is a metabolic disorder characterized by elevated blood glucose levels. Plants with potential anti-diabetic properties are those that contain compounds capable of inhibiting the conversion of carbohydrates into glucose. The administration of Ecclalbasaponin II, a compound found in the methanol extract of *E. prostrata*, to alloxan-induced diabetic rats resulted in a substantial reduction in blood glucose levels. Both *E. prostrata* extract (at a dose of 300 mg/kg) and Ecclalbasaponin II (at a dose of 10 mg/kg) led to a significant decrease in blood glucose levels when compared to diabetic rats that did not receive treatment[15]. In a 28-day study on male CF strain rats with streptozotocin-induced diabetes, an Ayurvedic formulation comprising *Withania somnifera*, *Tinospora cordifolia*, *Eclipta alba*, *Ocimum sanctum*, *Picrorhiza kurroa*, and shilajit was administered orally at doses of 100 and 200 mg/kg once daily. This treatment demonstrated a dose-dependent reduction in STZ-induced hyperglycemia and mitigated the STZ-induced decrease in pancreatic islet superoxide dismutase (SOD) activity. It has been proposed that the development of STZ-induced hyperglycemia was associated with the reduced SOD activity within the islets.[16].

Used as an anti-inflammatory agent-

Inflammation is the body's response triggered in the presence of an infection or injury. Chemical factors such as histamine, bradykinin, serotonin, leukotrienes, and prostaglandins, released by immune system cells, serve as inflammatory mediators. They work to safeguard surrounding tissues from the further spread of infection.[17] The anti-inflammatory effect of the plant was evaluated using carrageenan,

mediators such as histamine and serotonin induced paw oedema, and cotton pellet induced granuloma tests for their effect on acute and chronic phase inflammation models in rats. The results indicated potent anti-inflammatory activity of the plant in all the models tested[18].

Antimicrobial activity-

Microorganisms are responsible for a range of infectious diseases, including respiratory, digestive, and others. The reliance on antibiotics can contribute to the emergence of resistant microbes, prompting ongoing efforts to discover novel antimicrobial agents. In the context of microbial control, natural products or ingredients, such as *E. prostrata*, are often considered a safer option when compared to synthetic materials[19]. The ethanol and ethyl acetate extracts obtained from the plant's leaves exhibit activity against a range of bacteria, including *E. coli*, *K. pneumoniae*, *Shigella dysenteriae*, *Salmonella typhi*, *P. aeruginosa*, *Bacillus subtilis*, and *S. aureus*. Their Minimum Inhibitory Concentrations (MIC) fall within the range of 4.5 to 90 $\mu\text{L}/\text{mL}$ [20].

The n-butanol extract exhibited inhibitory effects against all nine species, including *B. cereus*, *B. subtilis*, *C. albicansi*, *Erwinia carotovora*, *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *S. typhi*, and *S. aureus*. In contrast, the petroleum ether, dichloromethane, methanol, and aqueous extracts displayed different degrees of inhibition against select microorganisms among these species[21].

The concentration of *E. prostrata* extract ranging from 1000 to 1,200 mg/l exhibited inhibitory effects on bacterial growth, while a concentration of 1,400 mg/l hindered fungal growth. In terms of sensitivity to the saponin fraction of *E. prostrata*, the order among pathogenic bacteria was *Pseudomonas aeruginosa*, *Escherichia coli*, *Salmonella typhi*, *Klebsiella pneumoniae*, *Pseudomonas mirabilis*, and *Staphylococcus aureus*. Among fungal pathogens, *A. fumigatus* was the most sensitive, followed by *Aspergillus niger* and *A. flavus*[22].

The inhibitory potential of the aqueous extract derived from the leaves, stems, and flowers of *E. alba* was evaluated against various test organisms. The leaf extract displayed effectiveness against *Enterobacter cloacae* and *K. pneumoniae*, while the stem extract exhibited inhibitory effects on *E. cloacae*, *Enterococcus faecalis*, *K. pneumoniae*, and *Staphylococcus saprophyticus*. The flower extract demonstrated effectiveness against *P. vulgaris*, *S. aureus*, and *S. saprophyticus*[23].

Hepatoprotective activity-

It has been documented that the plant offers protection against acute liver damage induced by carbon tetrachloride[24]. A hepatoprotective compound is one that safeguards the liver. In rats with acute hepatitis induced by CCl_4 (31.25 pL/kg, i.p.) or acetaminophen (600 mg/kg, i.p.), *E. prostrata* extract exhibited hepatoprotective activity. This extract effectively mitigated the acute rise in serum transaminases caused by CCl_4 and P-D-G-LN in mice. Additionally, the crude *E. prostrata* extract notably alleviated the histopathological alterations in the liver induced by either CCl_4 or GaLN in experimental animals[25].

Coumestans, specifically wedelolactone and demethylwedelolactone, have been proposed as potential constituents responsible for the protective effects on the liver and its disorders. Both of these compounds

demonstrated antihepatotoxic activity in tests involving CCl₄ (carbon tetrachloride), GalN (galactosamine), and phalloidin-induced cytotoxicity in rat hepatocytes. Furthermore, they exhibited a noteworthy stimulating effect on the regeneration of liver cells[26].

The hepatoprotective potential of an ethanol extract derived from the entire plant was evaluated in mice with paracetamol-induced hepatotoxicity. Treatment with 100 and 250 mg of the extract per 100 kg body weight resulted in significant decreases in paracetamol-induced serum alanine aminotransferase (ALT, also known as GOT) levels. Concurrently, histopathological examinations indicated notable reductions in paracetamol-induced fatty degeneration and centrilobular necrosis in the livers of mice treated with the extract[27].

The administration of fresh leaf powder at a dose of 500 mg/kg to rats was found to result in a notable hepatoprotective effect in rats with paracetamol-induced liver toxicity. Histopathological examinations revealed that the livers of rats administered paracetamol exhibited severe congestions, hydropic degeneration, and occasional necrosis, while those administered the leaf powder showed reduced hepatocyte damage[28].

Anticancer activity-

The crude methanol extract derived from *E. prostrata* has demonstrated the ability to impede the proliferation of colon cancer cells[29]. The methanolic extract of the aerial parts of the plant showed inhibitory activity on the proliferation of hepatic stellate cells or HSCs. Activity-guided fractionation led to the isolation of five oleanane-type triterpenoids, echinocystic acid, eclalbasaponin II, eclalbasaponin V, eclalbasaponin I, and eclalbasaponin III, which are all echinocystic acid derivatives. Among the five echinocystic acid derivatives isolated, echinocystic acid and eclalbasaponin II significantly inhibited the proliferation of HSCs in dose- and time-dependent manners[30]. The juice extracted from *E. alba* has demonstrated its capacity to impede the migration of HCC-S102 cells, a type of hepatocellular carcinoma. When tested on diverse human cancer cell lines derived from various tissues, including the liver, lung, and breast, this juice effectively hindered the migration of all these cell lines, with IC₅₀ values falling within the range of 31–70 µg/mL. This suggests that the plant holds promise in the prevention of cancer metastasis[31].

Anti-Oxidant-

The potential cerebroprotective and antioxidant effects of the hydroalcoholic extract from *E. alba* were assessed in a rat model of global cerebral ischemia. To induce global cerebral ischemia-reperfusion injury, the bilateral common carotid arteries (BCCA) were temporarily occluded for 30 minutes, followed by a 4-hour reperfusion period. BCCA occlusion resulted in a notable decrease in brain levels of superoxide dismutase (SOD), glutathione peroxidase (GPx), reduced glutathione (GSH), catalase (CAT), glutathione-S-transferase (GST), and glutathione reductase (GR), along with a significant increase in malondialdehyde (MDA) levels. Pre-treatment with the hydroalcoholic extract effectively restored the levels of these biochemical parameters and significantly reduced edema and the size of cerebral infarction when compared to the ischemic control group[32].

The assessment of in vitro antioxidant activity was conducted through the utilization of the 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical scavenging assay. The IC₅₀ value for the entire plant extract was established at 45.68 µg/mL, in contrast to the IC₅₀ value of 3.26 µg/mL for the standard, ascorbic acid. Similarly, when subjected to the hydrogen peroxide scavenging assay, the extract displayed robust activity, with IC₅₀ values of 1.34 µg/mL, compared to the IC₅₀ value of 1.03 µg/mL observed for ascorbic acid[33].

Antimalarial Activity-

The effectiveness of *Eclipta alba* leaf extract against *Plasmodium berghei* ANKA strain in mice was assessed for its anti-malarial properties. A standardized inoculum containing 1 x 10⁶ infected erythrocytes was employed. The methanolic leaf extract, administered at doses ranging from 250 to 750 mg/kg, displayed a dose-dependent chemosuppressive and schizontocidal effect in both early and established infection stages. Furthermore, it significantly extended the mean survival time (m.s.t.), particularly in the group receiving a daily dose of 750 mg/kg of the extract. Additionally, the plant extract exhibited a reservoir effect. These promising findings from the preliminary investigations with *E. alba* could have potential implications for malaria therapy[34].

The leaf extracts of *E. alba*, including crude hexane, ethyl acetate, benzene, chloroform, and methanol extracts, were assessed for their impact on the toxicity and repellency of two significant mosquito vectors, specifically *Culex quinquefasciatus* and *Aedes aegypti* (Diptera: Culicidae). *C. quinquefasciatus* is a carrier of *Wuchereria bancrofti*, avian malaria, and various arboviruses, such as St. Louis encephalitis virus, Western equine encephalitis virus, and West Nile virus. All the extracts demonstrated moderate adulticidal effects, and their mosquito repellent activities exhibited concentration-dependent behavior[35].

Effect of heart-

The cardiac inhibitory potential of ethanolic extracts obtained from both the leaves and leaf calluses of *E. alba* was investigated using isolated frog hearts. These extracts exhibited adverse effects on both the force of heart contraction (negative inotropic) and heart rate (negative chronotropic), ultimately leading to a reduction in cardiac output. Notably, the callus extract demonstrated a more pronounced cardiac inhibitory effect when compared to the leaf extract, especially at a 20 mg dose. Furthermore, the callus extract was observed to counteract the effects of adrenaline[36].

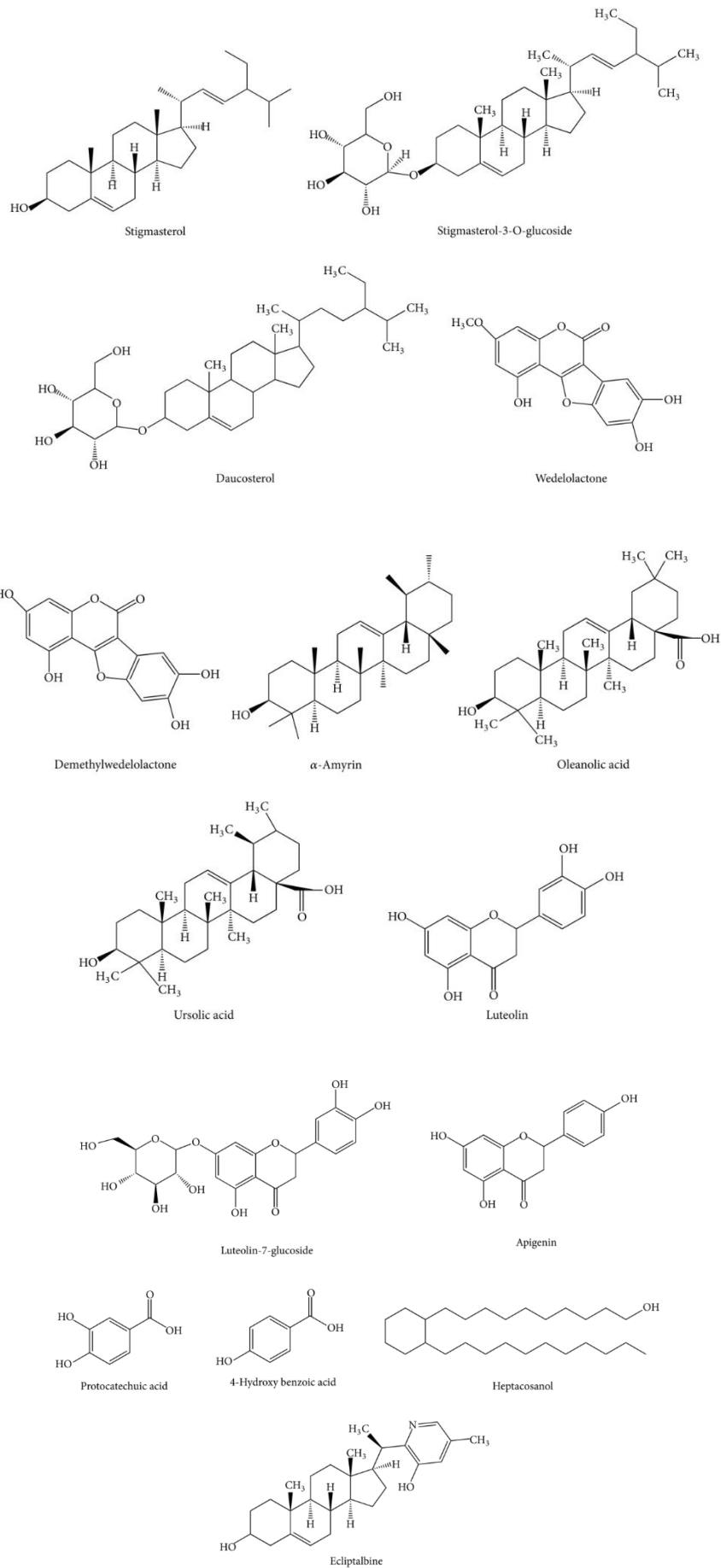
Antiepileptic effect-

The antiepileptic potential of the methanol extract obtained from powdered leaves of *E. alba* was assessed using the Maximal Electroshock Test (MES) in rats. The extract was orally administered to the rats for a period of 7 days, with doses of 50, 100, and 200 mg per kg of body weight. An hour following the final treatment, seizures were induced in the rats by delivering an electroshock of 150 mA for 0.2 s, using an electroconvulsimeter with a pair of ear clip electrodes. The reduction in the duration of hind leg extension served as the parameter to measure the anticonvulsant effect. Rats receiving the extract at various doses exhibited a significant reduction in the duration of time spent in the extensor phase, showing a dose-dependent response when compared to the control group. This antiepileptic activity was associated with the presence of wedelolactone, luteolin, and β-amyrin in the extract[37].

The ethanolic leaf extract of *E. alba* was found to induce a shorter onset of thiopental sodium-induced sleep in rats and to extend the overall duration of sleep when administered at doses of 200 and 400 mg/kg. Furthermore, the 400 mg/kg dose of the extract resulted in a reduction in the locomotor activity of rats, indicating a sedative effect. This observed central nervous system (CNS) depressant effect could be attributed to the presence of ursolic and oleanolic acids in the extract, which can act as GABA-A agonists[38].

Chemical Constituents- [39] [40]

Nature of phytoconstituent(s)	Phytoconstituent(s)
Coumestan	Wedelolactone, demethylwedelolactone, demethylwedelolactone-7-glucoside
Terpenoids and their glycosides	Eclalbasaponins VII–X (taraxastane triterpene glycosides), eclalbasaponins I–VI (oleanane triterpene glycosides), eclalbasaponins I–VI (triterpene glycosides), ecliptasaponins C and D (triterpenoid glycosides), α -amyrin, oleanolic acid, ursolic acid (triterpenoids)
Sterol	Stigmasterol, daucosterol, stigmasterol-3- <i>O</i> -glucoside
Alkaloids	[(20 <i>S</i>)(25 <i>S</i>)-22,26-imino-cholesta-5,22(<i>N</i>)-dien-3 β -ol] (verazine), [20- <i>epi</i> -3-dehydroxy-3-oxo-5,6-dihydro-4,5-dehydroverazine], [(20 <i>R</i>)-20-pyridyl-cholesta-5-ene-3 β ,23-diol] (ecliptalbine), [(20 <i>R</i>)-4 β -hydroxyverazine], [4 β -hydroxyverazine], [(20 <i>R</i>)-25 β -hydroxyverazine], [25 β -hydroxyverazine]
Flavonoids	Luteolin-7-glucoside, luteolin, apigenin, orobol (isoluteolin)
Sesquiterpene lactones	5-hydroxymethyl-(2,2'':5'',2)-terthienyl tiglate, 5-hydroxymethyl-(2,2:5,2)-terthienyl agelate, 5-hydroxymethyl-(2,2:5,2)-terthienyl acetate
Volatile oils	Heptadecane, 6,10,14-trimethyl-2-pentadecanone, <i>n</i> -hexadecanoic acid, pentadecane, eudesma-4(14),11-diene, phytol, octadec-9-enoic acid, 1,2-benzenediacarboxylic acid di isooctyl ester, (<i>Z,Z</i>)-9,12-octadecadienoic acid, (<i>Z</i>)-7,11-dimethyl-3-methylene-1,6,10-dodecatriene, (<i>Z,Z,Z</i>)-1,5,9,9-tetramethyl-1,4,7-cycloundecatriene
Saponins	Eclalbatin (triterpene saponin), dasyscyphin C
Polyacetylinic compounds	α -Terthienylmethanol, polyacetylenes, polyacetylene substituted thiophenes
Phenolic acids	Protocatechuic acid, 4-hydroxy benzoic acid
Substituted thiophenes	5-Hydroxymethyl-(2,2':5',2'')-terthienyl tiglate 5-Hydroxymethyl-(2,2':5',2'')-terthienyl agelate 5-Hydroxymethyl-(2,2':5',2'')-terthienyl acetate



Conclusion-

The plant known as *E. alba* is highly esteemed by traditional medicinal practitioners for its significant medicinal properties, particularly in the treatment of liver disorders, gastrointestinal issues, respiratory tract ailments, hair loss, skin problems, and fevers. Scientific research has provided substantial validation for many of the plant's ethnomedicinal applications, including its effectiveness in treating snake bites. Several crucial phytochemicals have been successfully isolated and identified in *E. alba*, such as wedelolactone, eclalbasaponins, α -amyrin, ursolic acid, oleanolic acid, luteolin, and apigenin. The available scientific literature strongly suggests that these compounds hold promise as the foundation for a new generation of medications to address conditions like cancer, arthritis, liver diseases, hair loss, and snake bites.

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