



(REVIEW ARTICLE)



Eclipta prostrata (L.) L. (uses and bioactivities)

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Abstract

Eclipta prostrata has been long used by humans as traditional medicine and hair fertilizer. This study aims to explain the relationship between utilization and bioactivity of *E. prostrata*. The method used is a literature review of articles published online on Google Scholar using the keywords *E. prostrata*, uses *E. prostrata*, and bioactivity of *E. prostrata*. Ethnobotanically, *E. prostrata* is used to treat liver disorders, liver tonic, respiratory disorders (asthma, cough), hepatitis, snake venom poisoning, and gastritis. In the field of beauty *E. prostrata* is used to nourish hair and treat baldness. The *E. prostrata* has bioactivity to treat neurodegeneration, asthma, anti-cancer, overcoming baldness, anti-diabetes mellitus, anti-oxidant, anti-inflammatory, anti-microbial, hepatoprotective, anti-osteoporosis, and anti-hypercholesterolemia. The bioactivity of *E. prostrata* is related to the content of its secondary metabolite compounds. Echinocystic acid and ecclalbasaponin II from *E. prostrata* are associated with anti-cancer activity.

Keywords: *Eclipta prostrate*; Anti-cancer; Anti-oxidant; Bioactivities

1. Introduction

Eclipta prostrata is a species belonging Euphorbiaceae has been long used by various local communities in the world and Indonesia as traditional medicine and to beauty treatments [1,2]. This plant is easy and can be found in various landscapes such as yards, roadsides, rice fields, gardens and neglected lands and its considered a weed. By local people Indonesian, *E. prostrata* is used as a hair fertilizer and ingredient for making shampoo because its believed has compounds that are able to nourish hair.

Eclipta prostrata has been written in the Indian traditional system medicine such as ayurvedic to treat liver disease and as a liver tonic [2], while in Brazil it is used to treat asthma, respiratory system disorders [3]. The *E. prostrata* is one of the Chinese tonic drugs commonly used to treat loose teeth, dizziness, tinnitus, hemoptysis, hematuria, and uterine bleeding [4]. Chung et al [5] also reported, *E. prostrata* is efficacious in treating hepatitis, snake venom poisoning, gastritis, and respiratory diseases such as cough and asthma. Besides being used as a traditional medicine, *E. prostrata* is also widely used in the field of beauty, especially for hair. Lee et al [6] stated that *E. prostrata* has been commercialized for the prevention or treatment of hair loss has been commercialized.

The use of plants as traditional medicine related to their bioactivity and its secondary metabolite. Gani and Devi [2] reported that *E. prostrata* has activity as antioxidant, antiviral, antifungal, antibacterial, and antihepatotoxic. *E. prostrata* can be used as a potential herb to prevent stress-induced oxidative neurodegeneration in Parkinson's disease [7]. The *E. prostrata* has pharmacological anti-myotoxic, antihemorrhagic, antiproliferative, antioxidant, antitumor, antihyperglycemic, antidementia, antimicrobial, antihyperlipidemic, antivenom, anti-HIV, and larvicidal activities [5].

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Sharma et al [8] reported, *E. prostrata* contains various secondary metabolites such as alkaloids, flavonoids, polyacetals, triterpenes and glycosides.

Natural ingredients or natural products are considered fewer side effects than synthetic materials. This study aims to explain the botany and bioactivity of *E. prostrata* in a comprehensive. Comprehensive information the use of *E. prostrata* is one of the first steps for its development as a traditional medicine and in the field of beauty.

2. Methods

This study is based on a literature study on research results and articles published online at Google Scholar. The keywords used in the article search were *E. prostrata*, bioactivities of *E. prostrata* and secondary metabolites of *E. prostrata*. The results obtained were synthesized to explain the benefits and bioactivity of *E. prostrate*.

3. Results and discussion

3.1. Botany of *Eclipta prostrata* (L.) L.

Asteraceae is one of the large families in the Magnoliophyta group which is estimated to have about 20,000 species and 950 genera [9]. This family is very widely distributed and occupies various habitats because it has a high adaptability. The *E. prostrata* is one of the species in the Asteraceae family that has long been used by humans as an ingredient in traditional medicine.

Description *E. prostrata*: an annual plant, many branches, strigose, erect or prostrate plant, 20–90 cm tall. Leaves opposite, sharp at base, 4–13 × 0.8–2 cm, pilose, oblong to lanceolate, remotely serrated, sharply pointed, bottom sessile or petiolate. Terminal capitula and axilla, some too many, hemispherical, up to 1 cm wide, heterogamous. Stem length up to 7 cm. Herb bracts involucrum, ovate, acute, and pubescent in appearance, 6 mm long. The receptive scales are rigid, ciliated at the apex; perfect florets; ray-florets pistillate, with 4-5-fid corolla; ligule c. 6 mm, white, whole or bifid. The anthers in an apical direction are blunt, basically slightly slack (Fig. 1). Achenes of triangular ray-floret, from four-cornered florets, all tubular, black, downy, except for some apical feathers, depression-truncate at apex, with marginal 1-3 min teeth, about 3 mm long, slightly striped [10].

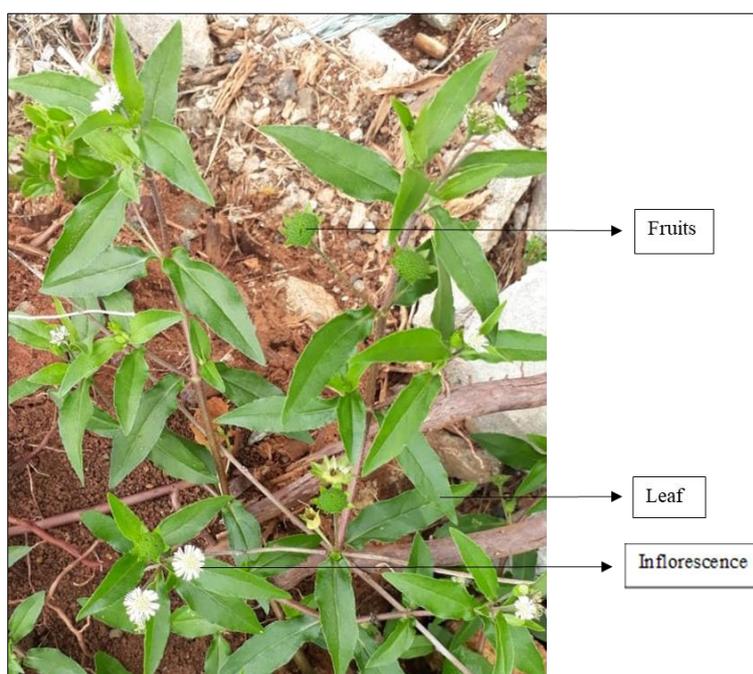


Figure 1 Habitus of *Eclipta prostrata* with leaves, flowers and fruits

3.2. Uses and Bioactivities

Drug development in the pharmaceutical industry is mostly adapted to local knowledge which is then scientifically tested according to the stages of drug development on a commercial scale. The *E. prostrata* in traditional medicine in Brazil is used to treat asthma and other respiratory diseases [3]. The herb *E. prostrata* is used as analgesic, antibacterial, antihepatotoxic, anti-hemorrhagic, antihyperglycemic, antioxidant, immunomodulatory properties [8]. The following describes the bioactivity of *E. prostrata* in more detail

3.2.1. Treat to Neurodegeneration

Various neurodegenerative diseases cause various problems in life such as Parkinson's. The oxidative stress plays an important role in the pathogenesis of Parkinson's disease. The neurotoxin 6-hydroxydopamine initiates cellular oxidative stress that has been implicated in the neurodegenerative conditions associated with Parkinson's disease. *E. prostrata* is a rich source of phenolic compounds that provide antioxidant activity so as to reduce oxidative stress. Ethyl acetate extract of *E. prostrata* had protective activity against 6-hydroxydopamine-induced neurotoxicity in SHSY5Y cells. Treatment of the ethyl acetate extract of *E. prostrata* before exposing cells to 6-hydroxydopamine significantly increased cell survival and reduced concentration-dependent intracellular reactive oxygen species (ROS). Ethyl acetate extract of *E. prostrata* suppressed the Bax/Bcl-2 ratio and reduced the activity of caspase-3, a key modulator of cell apoptosis. Ethyl acetate extract of *E. prostrata* has antioxidant capacity and attenuates SH-SY5Y cell death by blocking 6-hydroxydopamine-induced apoptotic signaling [7].

3.2.2. Treat to Asthma

The traditional medicine in Brazil, *Eclipta prostrata* is used to treat asthma and the other respiratory diseases [3]. Asthma is a chronic respiratory disorder characterized by inflammation and narrowing of the airways that causes shortness of breath or difficulty breathing. Extracts of *E. prostrata* had different effects on allergen-induced rats with asthma. Treatment with extracts of *E. prostrata* at a concentration of 250 mg/kg extract containing 0.745, 4.22 and 4.30 mg/kg/day of oroboside, demethylwedelolactone and wedelolactone respectively significantly reduced respiratory resistance and elastance. Such effects are comparable to those produced by dexamethasone. The total number of inflammatory cells and eosinophils in the bronchoalveolar lavage and the concentrations of interleukin (IL)-4, IL-5 and IL-13 in the lung homogenate were significantly reduced by the methanol extract of *E. prostrata* [3].

3.2.3. Anti-Cancer

The number of cancer patients is estimated to continue to increase, therefore the search for cancer drugs is continuously carried out, including *E. prostrata*. The anti-cancer compounds are compounds that inhibit the growth of cancer cells (cytotoxic) but not to normal cells. Research on the bioactivity of *E. prostrata* extracts as anti-cancer has been reported by Khanna and Kannabiran [11], Lirdpramongkol et al [12], Cherdtrakulkiat et al [13] and Lee et al [14]. The anticancer-cytotoxic compounds have been isolated from the leaves of *E. prostrata*, namely dasyscyphin C (C28 H40 O8). Dayscyphin C at 50 g/ml showed good cytotoxic activity (52%) on HeLa cells at 48 hours with an IC50 value of 50 g/ml [11]. Lirdpramongkol et al [12] reported that *E. prostrata* juice inhibited cancer invasion and migration, without affecting cell adhesion. Cell migration was inhibited in various types of cancer cells and in endothelial cells, with an IC50 value of 31–70 g/ml, much lower than the IC50 value for cytotoxicity of 203–1,217 g/ml for cancer cells and >4,000 g/ml for endothelial cells [12]. The ethyl acetate extract and the aerial fraction of *E. prostrata* showed cytotoxic activity (ED50 > 100 g/mL) on HuCCA-1 and KB cells [13]. Methanol extract of aerial parts of *E. prostrata* showed significant inhibitory activity on HSC proliferation [14]. The bioactivity of *E. prostrata* as anti-cancer is related to the content of its secondary metabolite compounds. Aerial methanol extract of *E. prostrata* containing echinocystic acid and eclalbasaponin II significantly inhibited HSC proliferation in dependent to dose and time manner [14].

3.2.4. Prevent Baldness

External and mental stress can result in hair loss lowering the quality of life and affecting interpersonal relationships and daily social life. *E. prostrata* has been widely used for the treatment of skin diseases in traditional Asian medicine [15]. The *E. prostrata* to increase hair growth in vivo and in vitro which has been tested in mice [15]. Empirically, that *E. prostrata* is widely used as an additive in the manufacture of shampoo because it is believed to have compounds that can nourish hair. The increasing population having hair loss, various products made chemically for the prevention or treatment of hair loss have been commercialized in the market. Scalp treatment using *E. prostrata* through shampoo showed an increase in hair density and thickness 10 weeks after use and the skin was clean [6].

3.2.5. Anti-Diabetes Mellitus

Diabetes mellitus is a metabolic system disorder that causes levels glucose blood to be above normal. The plants that have the potential as anti-diabetes mellitus are plants that produce compounds that can inhibit the breakdown of carbohydrates to glucose. Ecclalbasaponin II compound (compound in methanol extract of *E. prostrata*) administered to alloxan-induced diabetic rats showed a significant decrease in blood glucose levels. Blood glucose was significantly reduced with *E. prostrata* extract (300 mg/kg) and ecclalbasaponin II (10 mg/kg) compared to untreated diabetic rats [16].

3.2.6. Anti-Oxidant

The oxidative stress due to ultraviolet irradiation is directly or indirectly involved in various diseases. The bioactivity of *E. prostrata* as an antioxidant has been reported by Chen et al [17], Gani and Devi [2], and Lee et al [18]. The aqueous extract of *E. prostrata* had a potent effect in scavenging 1,1-diphenyl-2-picrylhydrazyl (DPPH), superoxide radicals, and iron chelating ions with IC50 values of 0.23 mg/mL, 0.48 mg/mL, and 1.25 mg/mL consecutively. Anti-oxidant bioactivity is related to the content of phenolic compounds [17].

Manganese (Mn) is one of the heavy metals used in various industrial chemical processes, but at certain levels Mn is toxic in the respiratory system and skin protection. Toxic Mn causes loss of mental health and quality of life by cerebrovascular and skin diseases [18]. The extract of *E. prostrata* effectively prevented the cytotoxicity caused by MnO₂ through its antioxidant effects such as xanthine oxidase (XO) inhibitory ability and radical scavenging ability of DPPH [18]. EP has high antioxidant activity which is closely correlated with increased anti-inflammatory activity of the skin by effectively suppressing tumor production of necrosis factor-alpha and interleukin-6 from macrophages. The production of prostaglandin E2 in human skin cells is also greatly reduced, compared to *E. prostrata* [19].

3.2.7. Anti-Inflammation

Inflammation or inflammation is a reaction caused by the body when an infection or injury occurs. Inflammation is stimulated by chemical factors (histamine, bradykinin, serotonin, leukotrienes, and prostaglandins) released by cells that act as inflammatory mediators in the immune system to protect surrounding tissues from the spread of infection. Various researchers reported the bioactivity of *E. prostrata* as an anti-inflammatory such as: Arunachalam et al [20], Lee [19] and Cuong et al [21].

Orally administered *E. prostrata* leaf methanol extract (100 and 200 mg/kg-1) had anti-inflammatory activity in Wistar albino rats comparable to the standard drugs indomethacin (10 mg/kg) and cyproheptadine (8 mg/kg) [20]. Wedelolactone is a compound that plays an important role in the regulation of zymosan-induced inflammation in murine bone marrow macrophages (BMDM). Zymosan-induced superoxide generation, NADPH oxidase, phosphorylation of p47phox in BMDM was significantly reduced by wedelolactone pretreatment (30 g/mL). Wedelolactone results in reduced zymosan macrophage BMDM induced inflammatory response [21].

3.2.8. Anti-Microbial

Microbes are the cause of various infectious diseases such as respiratory, digestive and other infections. The use of antibiotics can lead to the development of increasingly resistant microbes, because the search for new anti-microbial compounds is carried out. Natural products or natural ingredients are considered safer in microbial control compared to synthetic materials, including *E. prostrata*. The activity of *E. prostrata* extract as an antimicrobial has been widely reported including inhibiting the growth of bacteria [13, 22, 23] and fungi [23].

The *E. prostrata* has antimicrobial activity against Gram positive and Gram negative bacteria such as: *Moraxella catarrhalis*, *Corynebacterium diphtheriae*, *Streptococcus pyogenes*, and *Saccharomyces cerevisiae* (MIC 256 g/mL) [13]. The bioactivity of *E. prostrata* as an antimicrobial is related to the content of its secondary metabolites. Cherdtrakulkiat et al [13] reported that the aerial ethyl acetate extract of *E. prostrata* contained triterpenoid compounds, namely 3-acetylaleuritic acid, stigmaterol, a mixture of triterpenoids, and fat esters. Sixty-eight volatile compounds contained in *E. prostrata* are 35 hydrocarbons dominated by sesquiterpenes such as -Humulene, 6, 9-heptadecadiene, (E)- β -farnesene, and -phellandrene. [24].

The *E. prostrata* extract with a concentration of 1000 -1,200 mg/l inhibited bacterial growth and 1,400 mg/l inhibited fungal growth. The sensitivity of pathogenic bacteria varied to the saponin fraction of *E. prostrata* in the order *Pseudomonas aeruginosa*, *Escherichia coli*, *Salmonella typhi*, *Klebsiella pneumoniae*, *Pseudomonas mirabilis*, *Staphylococcus aureus*, while for the fungal pathogen *A. fumigatus* followed by *Aspergillus niger* and *A. flavus* [23]. Extracts of hexane, ethyl acetate, ethanol and water from the aerial part of *E. prostrata* have antibacterial activity against *E. coli*,

K. pneumoniae, *Shigella dysenteriae*, *Salmonella typhi*, *P. aeruginosa*, *Bacillus subtilis*, and *S. aureus*. The highest activity of both antibacterial and antioxidant was only observed in the ethanol and ethyl acetate extracts, while the hexane and aqueous extracts did not show significant results [22].

3.2.9. Hepatoprotective

Hepatoprotective is a compound that serves to protect the liver. *E. prostrata* extract had hepatoprotective activity in rats with acute hepatitis induced by CCl₄ (31.25 pL/kg, i.p.) or acetaminophen (600 mg/kg, i.p.). The *E. prostrata* extract significantly inhibited the acute increase in serum transaminases induced by CCl₄ in mice and by P-D-G~LN in mice. The crude extract of *E. prostrata* significantly ameliorated either CCl₄, or GaLN-induced histopathological changes in the liver of experimental animals [14]. The antifibrotic activity of *E. prostrata* and its triterpenoids may indicate a therapeutic potential against liver fibrosis [14].

3.2.10. Anti-Osteoporosis

Humans in old age often suffer from a lack of osteoblasts which can lead to bone fragility or osteoporosis. Osteoporosis is a condition of reduced bone density that causes bones to become porous and break easily. *E. prostrata* plays an important role in osteoblast bone formation [25]. Osteoblasts are bone-forming cells that work to form and secrete organic collagen and non-collagenous (components of bone matrix).

In a laboratory experiment, osteoporosis in rats was induced by ovariectomy. The *E. prostrata* restores levels of bone metabolic biomarkers in ovariectomized rats, including osteocalcin, alkaline phosphate, deoxyypyridinoline, and urinary calcium and phosphorus. *E. prostrata* (5 and 15 mg/kg/day) prevented changes in total bone mineral density in the femur caused by ovariectomy. Administration of *E. prostrata* decreased serum levels of IL-1 β and TNF- α in ovariectomized rats. *E. prostrata* can prevent the reduction of bone mass and strengthen and improve the cancellous bone structure and biochemical properties in ovariectomized rats. *E. prostrata* can serve as a new candidate or the main antiosteoporosis compound [26]. One flavonoid, diosmetin, and two isoflavonoids, 3'-hydroxybiochanin A and 3'-O-methylrobohol, were isolated from the methanol extract of *E. prostrata*, all three compounds significantly increasing osteoblast differentiation [27]. The volatile components and ethanol extract (1 g/mL to 100 g/mL) of *E. prostrata* significantly stimulated proliferation and increased alkaline phosphatase (ALP) activity of primary osteoblasts [25]. The aerial part of *E. prostrata* contains essential oils which are dominated by sesquiterpene hydrocarbons, followed by monoterpene hydrocarbons. *E. prostrata* oil is rich in -pinene followed by caryophyllene, - humulene, -pinene, camphene, allo-aromadendrene, amorphous, cis-muurole-4 (14), 5-diene eugenol [28].

3.2.11. Anti- Hypercholesterolemia

Hypercholesterolemia is a disease that occurs when cholesterol levels in the blood exceed normal limits. *E. prostrata* is used as a traditional medicinal plant to prevent lipidemia and atherosclerosis in Asia [29]. Lipidemia is a condition that arises because there is a disturbance in the metabolism of lipids (fats) in the body. Male rats fed a diet of 50 mg, or 100 mg of the freeze-dried fraction of *E. prostrata* per kilogram of feed for 6 weeks showed significantly reduced serum triacylglycerol, total cholesterol, and cholesterol-low density lipoprotein levels. The E50 and E100 groups also showed a significant increase in high-density cholesterol-lipoprotein levels (13.0% -19.1%) compared to the control group. The health-promoting effects of *E. prostrata* have implications for atherosclerosis and hypercholesterolemia in humans [29].

4. Conclusion

Ethnobotanically, *E. prostrata* is used to treat liver disorders, liver tonic, respiratory disorders (asthma, cough), hepatitis, snake venom poisoning, and gastritis. In the field of beauty *E. prostrata* is used to nourish hair and treat baldness. *E. prostrata* has bioactivity to treat neurodegeneration, asthma, anti-cancer, overcoming baldness, anti-diabetes mellitus, anti-oxidant, anti-inflammatory, anti-microbial, hepatoprotective, anti-osteoporosis, and anti-hypercholesterolemia. The bioactivity of *E. prostrata* is related to the content of its secondary metabolite compounds. Echinocystic acid and ecclalbasaponin II from *E. prostrata* are associated with anti-cancer activity.

Compliance with ethical standards

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