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ECLPITA ALBA Linn. - ANCIENT REMEDY WITH THERAPEUTIC POTENTIAL

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ABSTRACT
Eclipta alba (L.) Hassk. (Asteraceae) is classified as hair tonic and hepatoprotective in Ayurveda. The plant is characterized by presence of array of phytochemicals including alkaloids, glycosides, coumarins, flavanoids and sterols. The medicinal plant has and wedelolactone, isolated from it has demonstrated significant effects in animal studies. The review summarizes pharmacognositic and pharmacological investigations carried out on the plant.

KEYWORDS: *Eclipta alba*, Wedelolactone, Coumarins, Pharmacology.

INTRODUCTION

Eclipta alba (L.) Hassk. (Asteraceae) It grows commonly in moist places as a weed all over the world. In many parts of India it is grown commercially as a medicinal crop (Anonymous, 1952). It is an annual, erect or prostate entirely pubescent herb, often rooting at nodes with opposite, sessile, usually oblong, 2.5-7.5 cm long leaves with appressed hairs. Floral heads 6-8 mm in diameter, solitary, white; achene compressed and narrowly winged. Aerial parts of the plant are used in medicine (Chopra *et al.,* 1956).

TRADITIONAL MEDICINAL USES

India: According to Ayurvedic philosophy *E.alba* is bitter; alterative and anthelmintic. It is useful in inflammations, hernia, eye diseases, bronchitis, asthma, leucoderma, anemia, heart and skin diseases, right blindness, syphilis etc. It is reported as beneficial for complexion, hair, eyes, and teeth. Expressed juice of *E. alba* mixed with goat's milk is used in frontal sinusitis and nasal cattarh in children. Bhringraj taila and Bhringrajadi churana are official preparations (Anonymous, 1952; Chopra *et al.,* 1956).

In Unani system, the juice of *E. alba* is used in 'Hab Miskeen Nawaz' alongwith aconite, *Croton tiglium*, "triphala", *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, and of Ma'jun Murrawah-ul-arwah (Anonymous, 1952).

Korea: The plant is used as an antidote for snake bites in Korea (Anonymous, 1987).

Philippines: A decoction of the dried plant is used for heamoptysis and heamtemesis. For dysentery and heamturia urine, a decoction of the dried herb or tincture is used. Medicated tea or tinctures are used as household remedies for sprains, furuncle and dermatitis; the tea or tincture is excellent (Dan and Nhu, 1989).

Nepal: The plant juice, mixed with an aromatic (essential oil), is used in the treatment of catarrhal problems and

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jaundice. The leaves are used in the treatment of scorpion stings (Anonymous, 1993).

PHYTOCHEMISTRY:

Alkaloids: Alkaloids including ecliptine and nicotine (Pal and Narasimham, 1943; Khargava and Seshadri, 1974; Sikroria *et al.,* 1982). Bio-active steroidal alkaloids, verazine, 20-epi-3-dehydroxy-3-oxo-5, 6-dihydro-4, 5-dehydroverazine ecliptalbine, (20R)-4ß-hydroxyverazine, 4ß-hydroxyverazine, (20R)-25ß-hydroxyverazine and 25ß-hydroxyverazine have been identified from the methanolic extract (Abdel Kader *et al.,* 1998).

Coumarins*:* The dried leaves of *E.alba* have been reported to contain wedelolactone (Figure 1), a complex coumarin and its derivatives dimethylewedelolactone-7-glucoside and nor-wedelolactone (Bhargava *et al*., 1970; Wagner *et al.,* 1986). Demethylwedelolactone, isodemethylwedelolactone, and strychnolactone have been reported from by percolation and hot extraction of *E.alba* whole plant (Zhang & Guo, 2001).

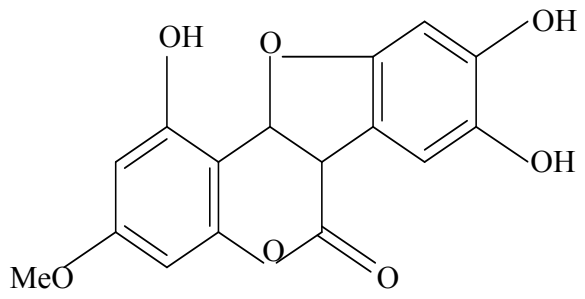

Fig 1: Structure of Wedelolactone

Hydrocarbons*:* Ddithienylacetylene ester (Jain & Singh, 1988), ecliptal or α-terthienyl aldehyde (Das & Chakravarty, 1991), α-terthienyl-methanol (Han *et al*., 1998) and α-formylterthienyl (Zhang *et al*., 1997).

Triterpenes*:* Ecliptasaponin C and D (Zhang *et al*., 1997), new triterpenoid glucosides, have been isolated from the whole plant of *E. alba.* A new triterpene saponin, eclalbatin, together with α-amyrin (Figure 2), β-amyrin (Figure 3), ursolic acid (Figure 4), oleanolic acid (Figure 5), and wedelic acid has been isolated (Upadhyay *et al.,* 2001). From the whole parts of six new oleanane triterpene glycosides, eclalbasaponins I-VI have been isolated (Yahara *et al.,* 2006).

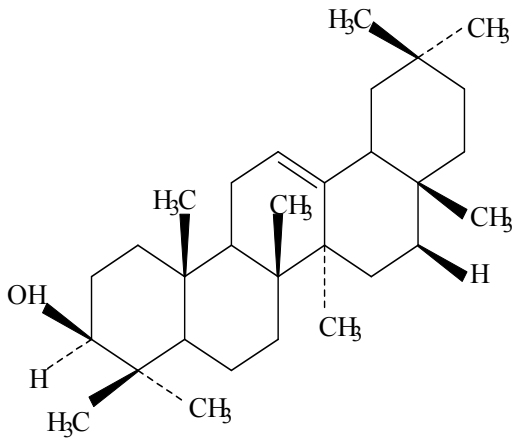

Fig 2. Structure of α-amyrin

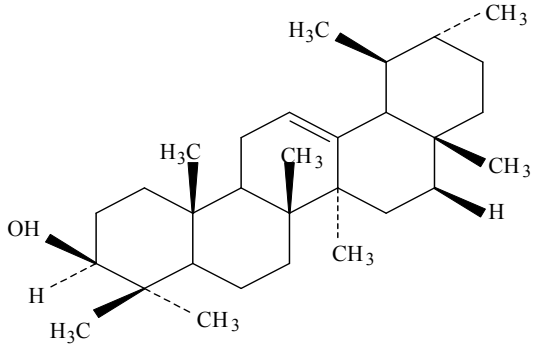

Fig 3. Structure of β-amyrin

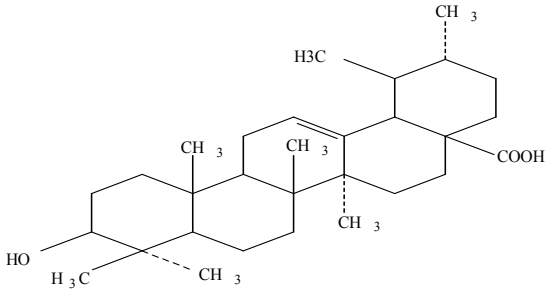

Fig 4. Structure of Ursolic acid

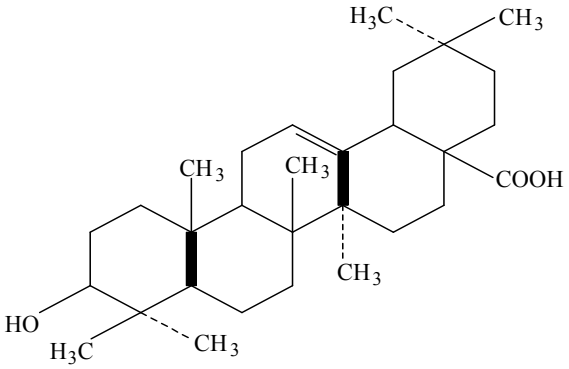

Fig 5. Structure of Oleanolic acid

Thiopenes: Polyacetylenic thiopenes 5'-senecioyloxymethylene-2-(4-isovaleroxybut-3-ynyl) dithiophene, 5'-tigloyloxymethylene -2-(4-isovaleroxybut-3-ynyl) dithiophene have been reported form the plant. The roots contain polyacetylene substituted thiophenes (Singh, 1988).

Sterols: The aerial parts of the plant have been reported to contain phytosterol; β glucoside of phytosterol, daucosterol and stigmasterol-3-O-glucoside (Zhang *et al*., 1997). The whole plant contains stigmasterol (Figure 6) (Han *et al*., 1998) and β-sitosterol (Figure 7) (Zhang & Guo, 2001).

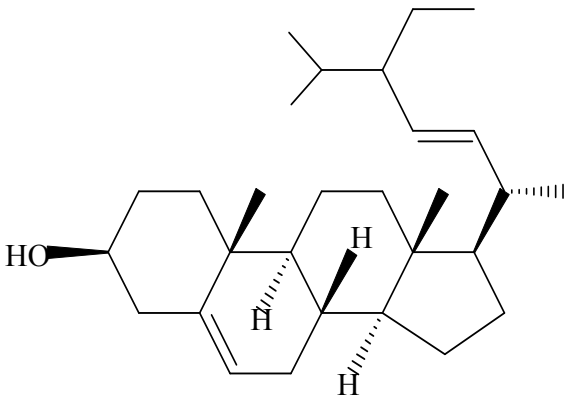

Fig 6. Structure of Stigmasterol

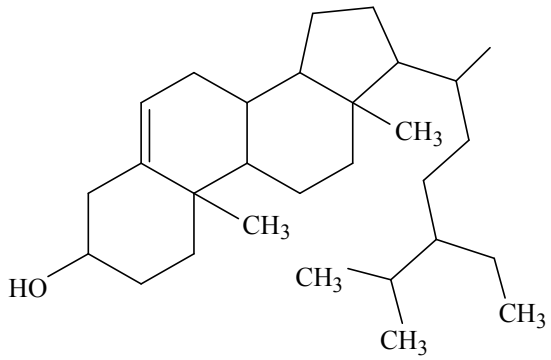

Fig 7. Structure of β-sitosterol

Flavonoids*:* Apigenin (Figure 8), luteolin (Figure 9) and luteolin-7-glucoside (Figure 10) (Zhang & Guo, 2001).

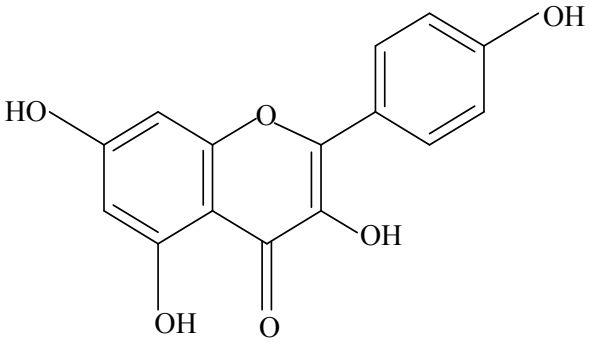

Fig 8. Structure of Apigenin

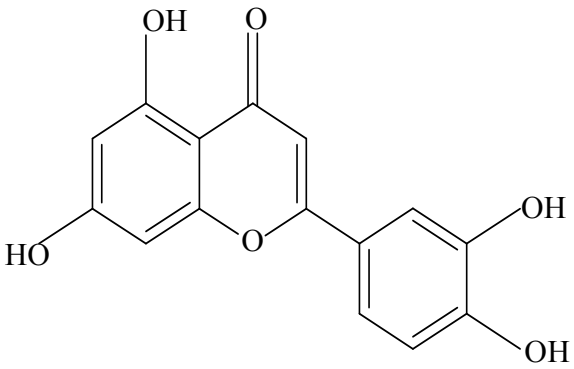

Fig 9. Structure of Luteolin

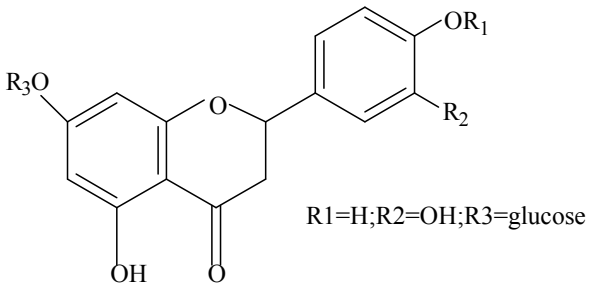

Fig 10. Structure of Luteolin-7-glucoside

Miscellaneous*:* Nonacosanol, stearic acid, lacceroic acid and 3, 4-dihydoxy benzoic acid (Zhang & Guo, 2001).

PHARMACOLOGY

Anti aggressive effect: The present study investigated the ability of 100 and 200mg/kg of aqueous extract of *E. alba* to circumvent aggression. Foot shock induced aggression and water competition test were utilized as models for screening of antiaggressive activity. *E. alba* significantly minimized dominance ($p<0.05$) which is correlated to the level of aggression particularly with 200mg/kg in the water competition test. A tangible behavioral submission was observed with 100 and 200mg/kg and of *E. alba* in the foot shock induced test (Lobo *et al.,* 2008).

Analgesic effect: The present experimental research investigated the analgesic activity of the total ethanol extract of *E. alba*, and isolated alkaloids in albino mice using the tail clip method, the tail flick method and the acetic acid induced writhing response. The ethanol extract and the total alkaloids produce significant analgesic activity in all the different models of analgesia used. However, the total alkaloidal fraction was the most efficacious in all models tested (Sawant *et al.,* 2004).

Anti-inflammatory effect: The methanolic extract administered by the oral route at a concentration of 100 and 200 mgkg-1 showed the significant dose dependent anti-inflammatory activity in carrageenan and egg white induced hind paw oedema in rats. Anti-inflammatory activity of the tested extract was comparable with that of the standard drug indomethacin (10 mg/kg) and cyproheptadine (8 mg/kg) (22).

Antimicrobial effect:

***Antibacterial*:** The antimicrobial activity of wedelolactone was evaluated using minimum inhibitory concentration and agar well diffusion method. The compound exhibited good activity against *Staphylococcus epidermidis* and *Salmonella typhimurium*. The MIC test showed the growth inhibition of *S. epidermidis* at a concentration of 15.0 µg/ml, ZOI 10.24 mm and of *S. typhimurium* at a concentration of 25.0 µg/ml (Arunachalam *et al.,* 2009; Dalal *et al*., 2009).

Antifungal: 25beta-hydroxyverazine showed good activity against *Candida albicans* (Abdel Kader *et al.,* 1998). The *in vitro* antifungal activity of whole plant of *E.alba* extract was investigated against Candida tropicalis, Rhodotorula glutinis and Candida albicans. The extract showed high degree of activity against all test fungi. The inhibitory effects of extracts are very similar to those of standard antibiotics used (Venkatesan & Ravi, 2004).

***Antimalarial*:** The anti-malarial activity of *Eclipta alba* leaves extract was evaluated against Plasmodium berghei ANKA strain in mice. A standard inoculum of 1 x 10(6) infected erythrocytes was used. The methanolic leaf extract (250-750 mg/kg) produced a dose-dependent chemosupression or schizontocidal effect during early and established infection and high mean survival time values particularly in the group administered 750 mg/kg/day of extract (Bapna *et al*., 2007).

Antihyperglycemic effect: Oral administration of leaf suspension of *E. alba* (2 and 4 g/kg body weight) for 60 days resulted in significant reduction in blood glucose (from 372.0 ± 33.2 to 117.0 ± 22.8), glycosylated hemoglobin HbA1c, a decrease in the activities of glucose-6 phosphatase and fructose1,6-bisphosphatase, and an increase in the activity of liver hexokinase. *E. alba* at dose of 2 g/kg body weight exhibited better sugar reduction than 4 g/kg body weight (Ananthi *et al.,* 2003).

Hepatoprotective effect: Ethanol/water extract significantly counteracted CCl_4-induced inhibition of the hepatic microsomal drug metabolizing enzymes. The loss of hepatic lysosomal acid phosphatase and alkaline phosphatase by CCl_4 was significantly restored by ethanol/water extract (Saxena, Singh & Anand, 1993). The EtOAc part of alcoholic extraction exhibited significant hepatoprotective activity against CCl_4-induced liver injury in rats (Zhang & Guo, 2001).

Treatment with 50% ethanol extract of *E.alba* (100&250mg/100g body weight) was found to protect the mice from hepato-toxic action of paracetamol as evidenced by significant reduction in the elevated serum transaminase levels. Histopathological studies showed marked reduction in fatty degeneration and centrizonal necrosis in animals receiving different doses of *E.alba* along with paracetamol as compared to the control group (Tabassum & Agrawal, 2004).

Hypolipdimeic effect: The total alcoholic extract of *E. prostrata* exhibited a dose-dependent activity in albino rats when compared to standard drugs. The activity was assessed by studying the lipid profiles of serum, liver and

heart of the control and drug-treated animals (Kumari *et al.,* 2006).

Charles River Sprague-Dawley CD rats were fed experimental diets supplemented with 0 mg (control), 25 mg (E25), 50 mg (E50), or 100 mg (E100) of a freeze-dried butanol fraction of *E prostrata* per kilogram of diet for 6 weeks. Serum triacylglyceride and total cholesterol levels were significantly lower in the E50 and E100 groups by 9.8% to 19.0% and by 10.7% to 13.4%, respectively, and low-density lipoprotein–cholesterol levels were significantly reduced in the same groups by 10.3% to 13.0% compared with the untreated control group (Kim *et al.,* 2008).

Neuropharmacological effects: The aqueous, hydroalcoholic extracts and hydrolyzed fraction of the aqueous extract of *E. alba* was subjected to neuropharmacological activities in rats. The findings indicated nootropic activity of the aqueous extract (300 mg/kg, p.o.) and its hydrolyzed fraction (30 mg/kg, p.o.). The aqueous extract and the hydrolyzed fraction exhibited gastro protective effect and normalized the white blood cell count in the milk induced leukocytosis challenge model (Thakur & Mengi, 2005).

The suspension of *E. alba* containing 100 and 200 mg/kg was administered to rats to evaluate Transfer Latency on an elevated plus maze. Mice were placed at the center of open field apparatus to assess spatial habitual learning, observed for 20 minutes for rearing and time spent during rearing using varied doses for 30 minutes, 24 hours and 96 hours and 144 hrs. The results revealed significant improvement of retrieval memory (Banji *et al*., 2008).

Hair growth promoting effects: The study was aimed to investigate the efficacy of methanol extract of *E. alba* as hair growth promoter. Pigmented C57/BL6 mice, preselected for their telogen phase of hair growth were used. The extract was applied topically to assess telogen to anagen transition. The methanol extract of whole plant when tested for hair growth promoting potential, exhibited dose dependent activity in C57BL6 mice (Datta *et al.,* 2009).

Effect on proteolytic and hemorrhagic activities: Wedelolactone and demethylwedelolactone, isolated from *E.alba* demonstrated significant trypsin inhibitory effects (Samiulla *et al.,* 2008).

The partially purified ethyl acetate extract of *E. prostrata* (containing 47% of wedelolactone) and wedelolactone demonstrated strong antiproteolytic and antihemorrhagic activity against Malayan Pit Viper venom in a dose-dependent manner. The extract, at 5 mg/ml, inhibited proteolytic activity of 100 µg of the venom and hemorrhagic activity of 3 minimum hemorrhagic doses to 95% and 65% respectively. At the same concentration, wedelolactone neutralized the proteolytic activity at around 76% and, at doses of 0.25-1.0 mg/ml, offered protection against hemorrhagic activity of the venom in the range 3-3.5% (Pithayanukul *et al.,* 2007).

Effect on osteoblast differentiation: Flavonoid, diosmetin (Figure 11), and isoflavonoids, 3'hydroxybiochanin A (Figure 12), and 3'*O*-methylorobol (Figure 13), isolated from the methanol extract of *E. prostrata* significantly increased osteoblast differentiation as assessed by the alkaline phosphatase activity (Lee *et al.,* 2008).

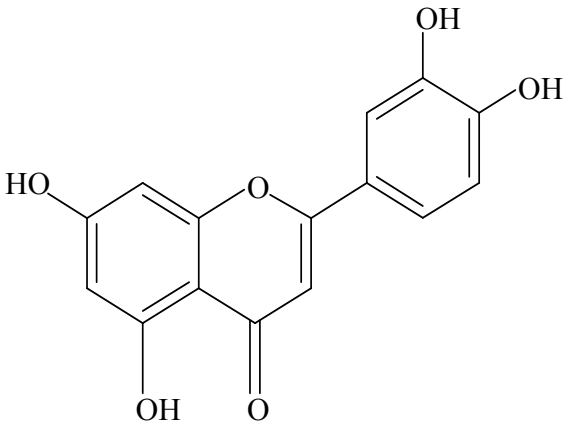

Fig 11. Structure of Diosmetin

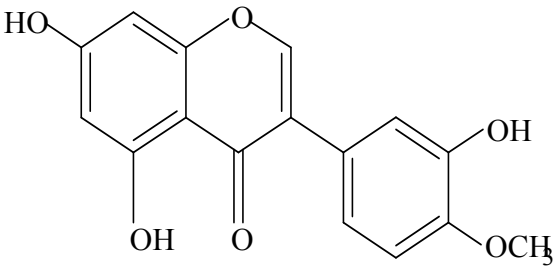

Fig 12. Structure of 3-hydroxybioachanin A

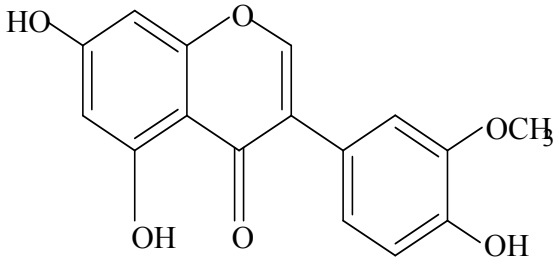

Fig 13. Structure of 3'-*O*-methyllorobol

CLINICAL STUDIES: Two studies reported efficacy of *E.alba* in the treatment of infective hepatitis in adults and jaundice in children, respectively (Dixit and Achar, 1979; Dixit and Achar, 1981). A clinical study reported diuretic, hypotensive, and hypocholesterolemic properties of *E. alba,* which helps in the alleviating oxidative stress-induced complications in hypertensive patients (Rangineni *et al.,* 2009).

CONCLUSION: *E.alba* is important plant of Ayurvedic materia medica. Animal investigations have justified traditional usage of the plant as hair-tonic and hepatoprotective. Keeping in mind the data accumulated from various animal studies, more studies are warranted to unearth the therapeutic potential of the plant.

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