CHAPTER 11

PHARMACOLOGICAL PROPERTIES OF *ECLIPTA ALBA*

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1. Abstract

Eclipta alba can be found growing wild in Bangladesh's fallow plains, where farmers consider it a weed. Traditional Indian subcontinent medicinal systems, as well as tribal practitioners, regard the plant as having a wide range of medicinal properties, and use it to treat gastrointestinal disorders, respiratory tract disorders (including asthma), fever, hair loss and greying, liver disorders (including jaundice), skin disorders, spleen enlargement, and cuts and wounds. Wedelolactone, eclalbasaponins, ursolic acid, oleanolic acid, luteolin, and apigenin are among the phytoconstituents found in the plant. Plant extracts and specific phytoconstituents have been shown to have anticancer, hepatoprotective, snake venom neutralizing, anti-inflammatory, and antibacterial properties in pharmacological studies. Wedelolactone, ursolic and oleanolic acids, as well as luteolin and apigenin, are phytoconstituents that could be used to develop new medications to treat cancer, arthritis, gastrointestinal disorders, skin illnesses, and liver disorders.

2. Background

Eclipta alba (L.) Hassk. (Also known as *Eclipta prostrata* Roxb.) is a member of the Asteraceae family and is known in English as fake daisy and in Bangladesh and India as bhringoraj or bhringraj. It is recognised as a valuable ethnomedicinal plant. It is recognised as bhringoraaja, bhangraa, and karissalaankanni in the three primary forms of traditional medicinal systems in the Indian subcontinent, namely Ayurveda, Unani, and Siddha. The herb is classified as hepatoprotective by the Indian Ayurvedic Pharmacopoeia.

3. Ethnomedicinal Reports

The plant and plant parts are used for treatment of a variety of diseases by folk medicinal practitioners and tribal medicinal practitioners of the Indian subcontinent.

Ethnomedicinal uses of the plant have been reported from Bangladesh, India, Nepal, and Pakistan.

4. Pharmacological Activity Reports

4.1. Hepatoprotective Activity

The plant has been shown to protect against acute liver damage caused by carbon tetrachloride. Coumestans (wedelolactone and demethylwedelolactone) have been suggested as possible components of the protective effect on the liver and against liver disorders; both compounds showed antihepatotoxic activity in rat hepatocytes in assays using CCl4 (carbon tetrachloride), GalN (galactosamine), and phalloidin-cytotoxicity. They also had a substantial stimulatory effect on the regeneration of liver cells. The liver to body weight ratio, pentobarbitone sleep time, serum levels of glutamate pyruvate transaminase (GPT) and glutamic oxaloacetic transaminase (GOT), alkaline phosphatase (ALP), and bilirubin were all found to have good antihepatotoxic action in CCl4-induced liver damage in albino rats. There was an increase in liver weight, pentobarbitone sleep time, and GOT, GPT, SALP, and serum bilirubin levels in CCl4-treated rats. At a dose of 200 mg/kg, the alcoholic extract significantly reversed these effects.

In CCl4-induced hepatotoxicity in rats, the hepatoprotective efficacy of the plant's ethanol/water (1:1) extract (Ea) was investigated. The hepatic microsomal drug metabolising enzyme amidopyrine N-demethylase and membrane bound glucose 6-phosphatase were both strongly inhibited by CCl4, but Ea was unable to reverse the extremely high degree of inhibition of another drug metabolising enzyme aniline hydroxylase. Ea substantially reversed the loss of hepatic lysosomal acid phosphatase and alkaline phosphatase caused by CCl4. Ea's hepatoprotective action has been attributed to its ability to regulate the levels of hepatic microsomal drug metabolising enzymes.

Each fraction of the ethanolic extract of the plant's leaves was tested for hepatoprotective efficacy against CCl4-induced hepatotoxicity in rats and mice (hot water insoluble (EaI), ethyl acetate fraction of hot water soluble (EaII), and remaining hot water-soluble fraction (EaIII)). The effects of the drugs on hexobarbitone sleep duration, zoxazolamine paralysis time, bromsulfalein clearance, serum transaminases (GPT, GOT), and serum bilirubin were used to determine their hepatoprotective activity. CCl4 raised all of the experimental parameters, although fraction EaII (10–80 mg/kg, p.o.) dose-dependently and dramatically reversed these effects. The principal ingredients of Fraction EaII were coumestan wedelolactone and demethylwedelolactone, with minor compounds apigenin, luteolin, 4-hydroxybenzoic acid, and protocatechuic acid.

E. alba extract has been shown to suppress the hepatitis C virus (HCV). The extract contained three compounds: wedelolactone, luteolin, and apigenin, according to phytochemical research. *In vitro*, these chemicals inhibited HCV replicase in a dose-dependent manner and had anti-HCV replication activity in a cell culture system. The findings suggest that the plant or individual components could be used to combat HCV.

The hepatoprotective activity of an ethanol extract of the entire plant against paracetamol-induced hepatotoxicity in mice was investigated. Paracetamol-induced serum alanine aminotransferase (ALT, commonly known as GOT) levels were significantly reduced after treatment with 100 and 250 mg of the extract per 100 kg body weight. At the same time, histological examinations in the liver of extract-treated mice revealed significant decreases in paracetamol-induced fatty degeneration and centrizonal necrosis.

In rats and mice, an alcoholic extract of freshly collected *Eclipta alba* showed dose-dependent (62.5–500 mg/kg p.o.) significant hepatoprotective activity against carbon

tetrachloride-induced liver injury, as determined by various tests such as hexobarbitone-induced sleep, zoxazolamine-induced paralysis, bromsulfalein (BSP) clearance, serum transaminases, bilirubin.

In rats, a combination of ethanolic extracts of *E. alba* leaves and *P. longum* seeds showed stronger hepatoprotective effect than either extract alone against CCl4-induced hepatotoxicity. With carbon tetrachloride treatment, serum marker enzymes such as alanine aminotransferase (ALT/GOT), aspartate aminotransferase (AST, also known as GOT), acid phosphatase (AP), lactate dehydrogenase (LDH), -glutamyl transferase (GGT), and 5′-nucleotidase were elevated, which were restored to normal by the combined extract. At the same time, the combined extract corrected alterations in biochemical parameters such as total protein, total bilirubin, total cholesterol, triglycerides, and urea to near-normal levels.

Fresh leaf powder (500 mg/kg) was found to have a strong hepatoprotective effect in rats suffering from paracetamol-induced liver damage. Histopathological tests revealed that rats given paracetamol had significant congestions, hydropic degeneration, and occasional necrosis, whereas rats given leaves had less hepatocyte damage. Paracetamol-induced alterations in serum proteins, bilirubin, cholesterol, and triglycerides, as well as paracetamol-induced changes in serum ALT, AST, alkaline phosphatase (ALP), LDH, and GGT, were all returned to normal levels with the leaf powder.

Methanol extract of leaves and chloroform extract of roots of *E. alba* demonstrated significant reductions of lysosomal enzymes in serum from the increased levels caused by carbon tetrachloride in CCl4-induced hepatotoxicity in rats. With the injection of both extracts, CCl4-induced increased serum GOT, GPT, ALP, and bilirubin levels were likewise brought back to normal.

In rats administered ethanol for 21 days, the hepatoprotective effect of an ethanol extract of *E. alba* entire plants was investigated. Histopathological alterations, a rise in thiobarbituric acid-reactive substances (TBARS), a decrease in reduced glutathione (GSH), superoxide dismutase (SOD), and catalase (CAT), and an increase in glutathione peroxidase (GPx) in the liver were all observed after ethanol administration. In alcohol-treated mice, histopathological alterations revealed hepatocytic necrosis and inflammation in the centrilobular area, as well as portal triaditis. With the addition of ethanol to the extract, the harmful effects were reversed.

Hepatoprotection against paracetamol-induced liver damage has been discovered using an aqueous extract of the plant's leaves. The aqueous extract reduced paracetamol-induced increases in TBARS and restored paracetamol-induced decreases in GSH. Catalase was likewise reduced in paracetamol-treated groups, but this was reversed when the extract was given together.

Hepatoprotective effect of the alcoholic and aqueous extracts of *E. alba* leaves against paracetamol-induced liver injury in albino rats was investigated. Hepatoprotective benefits of the alcoholic extract were found to be significant. When compared to the paracetamol-treated group, the alcoholic extract-treated rats showed remarkable hepatoprotection, with significant (P 0.01) reductions in SGOT, SGPT, ALP, total bilirubin, and direct bilirubin and a significant (P 0.01) increase in total protein and albumin.

In male albino rats, the aqueous leaf extract (85%) of *E. alba* was tested for hepatoprotective properties in CCl4-induced hepatotoxicity. CCl4 caused oxidative stress in rats, which resulted in oxidative damage as seen by increased TBARS and hydroperoxides, as well as increased blood AST, ALT, and ALP levels. SOD, CAT, GPx, and glutathione-S-transferase levels were all decreased at the same time (GST).

These effects were reversed and returned to normal levels when the aqueous extract was given at a dose of 250 mg per kg body weight. The findings imply that oxidative stress plays an important role in the progression of hepatic damage, which can be alleviated by administering an aqueous extract of the leaves.

A polyherbal formulation (Ayush-Liv.04) including *E. alba* (together with Clitoria ternatea, Asparagus racemosus, Alpinia galanga, and milk tuttam, *i.e.*, copper bearing stone) demonstrated hepatoprotective effect in rats when exposed to CCl4 and ethanol. Serum AST, ALT, ALP, acid phosphatase, and bilirubin levels were considerably reduced in rats given the polyherbal formulation.

In male albino rats, the ethanolic extract of a polyherbal formulation containing *Melia azadirachta* leaves, *Piper longum* seeds, and whole plants of *E. alba* was tested for hepatoprotective properties against CCl4-induced liver injury. The extract restored the significantly lowered levels of SOD, CAT, GPx, GST, and glutathione reductase (GR) caused by CCl4.

In a model of CCl4-induced acute hepatotoxicity in albino rats, the hepatoprotective properties of an ethanolic extract of *E. alba* leaves and leaf callus were investigated. Serum markers such as GOT, GPT, ALP, albumin, and total protein, as well as histological investigation, were used to determine liver damage. Hepatoprotective properties were proven by restoring serum parameters to near normal levels and relieving liver lesions produced by carbon tetrachloride after oral administration of the extract at 250 and 300 mg/kg, respectively.

4.2. Hair Growth Promoting Activity

Albino rats were given petroleum ether and ethanol extracts of *E. alba* to see if they could promote hair growth. The extracts were mixed into an oleaginous cream (water in an oil cream base) and applied topically to male albino rats' shaved denuded skin. When compared to non-treated control animals, the extracts cut hair growth time in half. Quantitative study of hair growth after treatment with petroleum ether extract (5%) revealed a higher number of hair follicles in the anagenic phase (69 4) than the control (47 13).

The efficacy of the plant's methanol extract in boosting hair development in pigmented C57/BL6 mice preselected for their telogen phase of hair growth has also been studied. The truncal epidermis in these species is devoid of melanin-producing melanocytes, and melanin production is tightly linked to the anagen phase of hair growth. Following topical administration of the extract, the telogen to anagen transition was examined. Following extract treatment, a dose-dependent transition from telogen to anagen phase of hair growth was observed; with an extract dose of 3.2 mg/15 cm2, 87.5 percent of the animals showed anagen phase of growth, whereas with an extract dose of 1.6 mg/15 cm2, 50% of the animals showed the transition from telogen to anagen phase.

In Wistar albino rats, a polyherbal formulation containing *E. alba*, *Hibiscus rosa-sinensis*, and Nardostachys jatamansi showed good hair growth activity. Hair growth initiation time and total hair growth time were both dramatically lowered. In the anagenic phase, treatment with the formulation resulted in a higher number of hair follicles.

4.3. Antidiabetic Activity

The plant's anti-diabetic properties have been documented. In streptozotocin- (STZ-) induced diabetic male CF strain rats, an Ayurvedic formulation containing *Withania somnifera, Tinospora cordifolia*, *Eclipta alba*, *Ocimum sanctum, Picrorhiza kurroa,* and shilajit at doses of 100 and 200 mg/kg, p.o. administered once daily for 28 days induced a

dose-related decrease in STZ hyperg It's been claimed that the STZ-induced hyperglycemia was caused by a reduction in islet SOD.

Oral administration of *E. alba* leaf suspension (2 and 4 g/kg body weight) for 60 days in alloxan-diabetic rats resulted in a significant reduction in blood glucose (from 372.0 33.2 to 117.0 22.8), glycosylated haemoglobin HbA (1)c, a decrease in the activities of glucose-6 phosphatase and fructose 1,6-bisphosphatase, and an increase in the activity of liver hexokin
In STZ-diabetic rats, the anti-diabetic action of *E. alba* ethanolic extract was studied for putative benefits against hyperglycemia and diabetic nephropathy. At a dose of 250 mg/kg, a single dose of the extract was observed to lower blood glucose levels by 17.6% after 5 hours of oral administration.

Treatment of STZ-diabetic mice with the aforesaid dose level for 10 weeks considerably lowered raised blood glucose, percent HbA1C, urea, uric acid, and creatinine levels while also dramatically increasing depressed serum insulin levels. The extract had a noncompetitive inhibitory impact on -glucosidase, with an IC50 of around 54 g per mL, and was found to be inhibitory to eye lens aldose reductase, having an IC50 of around 4.5 g per mL. The other reported effects were thought to be caused by inhibition of -glucosidase and aldose reductase. Four echinocystic acid glycosides were isolated using a bioactivity-guided isolation technique based on -glucosidase inhibition, with eclalbasaponin VI being the most potent (IC50 54.2 1.3 microM).

4.4. Analgesic and Anti-Inflammatory Activities

In rats and mice, the analgesic efficacy of an alcoholic extract of *E. alba* was tested using tail flick, hot plate, and writhing procedures. The extract had significant analgesic and antinociceptive effects in all three techniques at a dose of 200 mg/kg.
At a dose of 200 mg/kg p.o., a hydroalcoholic extract of the plant demonstrated considerable antinociceptive action in acetic acid-induced writhing tests in a mouse model. In formalin tests, the extract had analgesic effects, with inhibition occurring in the second part of the response.

Using conventional experimental paradigms such as the tail clip method, the tail flick method, and the acetic acid induced writhing reaction, the analgesic activity of an ethanol extract of *E. alba* entire plants as well as a total alkaloid fraction was seen in albino mice.

In all of the numerous models of analgesia studied, both the ethanol extract and the whole alkaloids produced good analgesic action, according to the findings. The analgesic activity of the whole alkaloid fraction was higher than that of the ethanolic extract.

Carrageenan, mediators such as histamine and serotonin produced paw oedema, and cotton pellet induced granuloma tests were used to assess the plant's anti-inflammatory activity in acute and chronic phase inflammation models in rats. The results showed that the plant has substantial anti-inflammatory effect in all of the animals studied. Overall, the evidence suggests that the plant could be useful as a central and peripheral analgesic.

4.5. Skin Diseases

In Trinidad and Tobago, the leaves of *E. alba* are used to treat ectoparasites in dogs. An Ayurvedic formulation using *E. alba* powder was proven to produce complete remission to 22.6 percent of patients and to prevent disease recurrence in 89.5 percent of "Vicharchika" patients (eczema).

The antioxidant and protective effects of an *E. alba* water extract against UV-irradiation-induced damage have been studied. The extract was effective at scavenging 2,2-diphenyl-1-picrylhydrazyl (DPPH), superoxide radicals, and ferrous ion chelation, with IC50

values of 0.23 mg/mL, 0.48 mg/mL, and 1.25 mg/mL, respectively. The extract has a total phenol content of 176.45 mg gallic acid equivalents. The extract was also found to absorb UVA and UVB irradiation and to protect HaCaT human keratinocytes and mouse fibroblasts 3T3 cells from UVB-induced cytotoxicity in a dose-dependent manner. A synergistic interaction between chlorogenic acid and vitamin E was shown to protect skin cells from harm.

4.6. Neuropharmacological Activities

At dosages of 150 and 300 mg/kg, p.o., the aqueous and hydroalcoholic extracts of *E. alba* were tested for sedative, muscle relaxant, anxiolytic, nootropic, and antistress properties. The aqueous extract (300 mg/kg, p.o.) and its hydrolyzed fraction (30 mg/kg, p.o.) were found to have nootropic activity. The aqueous extract and hydrolyzed fraction were found to protect against stomach ulcer formation caused by cold constraint and to normalise white blood cell count in a milk-induced leukocytosis challenge animal.

The memory-enhancing properties of an aqueous extract of *E. alba* leaves have been investigated. Rats were given doses of 100 and 200 mg of extract suspension in water (per kg body weight) to test transfer latency (TL) in an elevated plus maze. This method determines how well a person learns to acquire and retrieve information. Mice were subjected to spatial habitual learning tests at the two doses specified.

Mice were placed in the centre of an open-field apparatus to test spatial habitual learning, and were observed for 20 minutes for rearing and 30 minutes, 24 hours, 96 hours, and 144 hours for time spent during rearing. The extract significantly reduced TL in rats and the amount of rearing in mice at both doses. The presence of luteolins in the extract was found to cause an improvement in cognitive capabilities, which was linked to the findings.

Foot shock-induced aggression and water competition tests were used to see if an aqueous extract of *E. alba* could lessen aggression. At doses of 100 and 200 mg/kg, the extract was found to reduce aggression in both tests.

In a rat model of Alzheimer's disease, a methanolic extract of *E. alba* whole plant was demonstrated to alleviate oxidative stress-induced mitochondrial dysfunction (evaluation of short-term memory using elevated plus maze model). The MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] test was used to measure mitochondrial function. MTT reduction was significantly reduced in synaptosomal fractions of scopolamine hydrobromide-treated rats, which was reversed by the extract at a dose of 200 mg/kg. Scopolamine caused a substantial increase in transfer latency in rats, indicating amnesia or memory impairment. The extract reduced transfer latency in rats using the elevated plus maze paradigm in a dose-dependent manner (reversing the scopolamine-induced increase), indicating a gain in memory. The extract had a significant amount of phenolic and flavonoid compounds, which may have helped to reduce oxidative stress.

4.7. Antioxidant Activity

Both *in vitro* and ex vivo models have been used to investigate the antioxidant activity of *E. alba* methanol and hydrolyzed extract. The antioxidant activity of 2,2-diphenyl-1-picrylhydrazyl (DPPH) was measured *in vitro* using free radical scavenging and nitric oxide radical inhibition. The ex vivo antioxidant activity was assessed using the thiobarbituric acid-reactive substances (TBARS) method on mice liver homogenate to determine lipid peroxidation inhibitory action. Both the methanolic extract and the hydrolyzed extract demonstrated strong antioxidant activity in models, scavenging DPPH free radicals and nitric oxide radicals while also inhibiting lipid peroxidation. The plant's ethanol extract has also

been shown to have antioxidant activity as measured by DPPH free radical scavenging techniques.

In hydrogen peroxide scavenging assays, total antioxidant capacity, and a reducing ability testing, methanolic and aqueous extracts of *E. alba* displayed antioxidant activity. DPPH free radical scavenging and 2,2′-azinobis-(3-ethylbenzthiazoline-6-sulfonic acid) (ABTS) tests were used to demonstrate the antioxidant capability of the plant methanolic extract. In DPPH and ABTS experiments, the ethanolic extract of the plant also showed antioxidant activity. In the ferric thiocyanate method, ethanol and ethyl acetate extracts of the plant's leaves showed antioxidant activity; aqueous and hexane extracts also showed antioxidant activity, but to a lesser extent than ethanol and ethyl acetate extracts. In rats with global cerebral ischemia, the putative cerebroprotective and antioxidant effects of *E. alba* hydroalcoholic extract were investigated. Occluding bilateral common carotid arteries (BCCA) for 30 minutes, followed by 4 hours of reperfusion, resulted in worldwide cerebral ischemia-reperfusion damage. In the brain, BCCA induced a significant decrease in superoxide dismutase (SOD), glutathione peroxidase (GPx), reduced glutathione (GSH), catalase (CAT), glutathione-S-transferase (GST), and glutathione reductase (GR), as well as an increase in malondialdehyde (MDA). When compared to the ischemia control group, pretreatment with hydroalcoholic extract significantly reversed the levels of biochemical markers and significantly reduced edoema and cerebral infarct size.

4.8. Antimicrobial Activity

Various solvent extracts of *E. alba* were reported to be active against clinical isolates from oral cancer cases (petroleum ether, benzene, chloroform, acetone, methanol, and aqueous). Bacteria such as *Staphylococcus aureus, Escherichia coli, Staphylococcus epidermis, Pseudomonas aeruginosa, Klebsiella pneumoniae, Proteus mirabilis*, and *Proteus vulgaris,* as well as fungi such as Candida albicans and *Aspergillus fumigatus*, were among the isolates.

Ethanol and ethyl acetate extracts of the plant's leaves have been reported to be efficacious against *E. coli, K. pneumoniae, Shigella dysenteriae, Salmonella typhi, Pseudomonas aeruginosa, Bacillus subtilis*, and *Staphylococcus aureus,* with MICs ranging from 4.5 to 90 L/mL. *S. aureus, Bacillus cereus, E. coli, S. typhi, K. pneumoniae, Streptococcus pyogenes*, and *P. aeruginosa* were all found to have antibacterial activity in hexane extracts of the plant's aerial parts, while acetone, ethanol, methanol, and aqueous extracts had intermediate activity against *S. aureus, B. cereus, E. coli S. pyogenes, B. cereus, E. coli,* and *P. aeruginosa* were all resistant to the aqueous extract.

The well diffusion method was used to investigate the susceptibility of several *E. alba* extracts against nine distinct test organisms. *B. cereus, B. subtilis, C. albicans, Erwinia carotovora, E. coli, K. pneumoniae, P. aeruginosa, S. typhi*, and *S. aureus* all demonstrated inhibitory effect against the n-butanol extract. Some of these microbes were inhibited to varied degrees by petroleum ether, dichloromethane, methanol, and aqueous extracts.

Aqueous extracts of *E. alba* leaves, stems, and flowers were tested for inhibitory action against a variety of test organisms. *Enterobacter cloacae* and *K. pneumoniae* were resistant to leaf extract; *E. cloacae, Enterococcus faecalis, K. pneumoniae,* and *Staphylococcus saprophyticus* were resistant to stem extract; and *P. vulgaris, S. aureus*, and *S. saprophyticus* were resistant to flower extract. When evaluated using the agar plate disc diffusion method, aqueous and ethanolic extracts of leaves allegedly showed moderate inhibitory activity against *S. aureus, E. coli, P. vulgaris, P. aeruginosa, Candida albicans*, and *Aspergillus niger.*

Petroleum ether, ethyl acetate, ethanol, and an aqueous extract of *E. alba* were tested for inhibitory efficacy against *B. subtilis, S. aureus, P. mirabilis, B. cereus, E. coli, Salmonella enterica serv. typhi, P. aeruginosa, S. epidermis,* and *C. albicans* using the agar well diffusion method. The ethyl acetate fraction inhibited the most organisms examined, with zones of inhibition ranging from 11 1 mm to 22 1 mm, with greatest activity against *B. cereus*. Against *E. coli*, the ethanol extract had the highest inhibitory efficacy. Only *B. cereus* was inhibited by petroleum ether extract, whereas *B. subtilis, B. cereus, S. aureus,* and *C. albicans* were all inhibited by aqueous extract.

The disc diffusion method was used to test the antibacterial activity of methanol, acetone, and aqueous extracts of leaves from three morphotypes of *E. alba* against Gram positive bacteria *S. aureus* and *B. subtilis*, as well as Gram negative bacteria *K. pneumoniae, E. coli,* and *P. aeruginosa.* The extracts were shown to be inhibitory to all bacteria except *P. aeruginosa*. The least effective extract was determined to be aqueous extract.

The acetone extract has higher antibacterial activity than the methanol extract against S. aureus, *E. coli*, and *K. pneumoniae*. The methanol extract has the highest antibacterial activity against *B. subtilis.*

The agar plate disc diffusion method revealed that an aqueous extract of *E. alba* leaves inhibited the fungus Fusarium oxysporum. *S. epidermis, S. aureus*, and *Salmonella typhimurium* were all inhibited by a methanolic preparation of the plant's aerial portions. The antibacterial activity of wedelolactone, which was isolated from the ethyl acetate fraction of aerial parts, was increased, suggesting that it could be the cause of the observed antimicrobial effects. Another phytochemical ingredient of the plant, eclalbasaponin, has been found to be responsible for the plant's inhibitory activity against *B. subtilis* and *P. aeruginosa*. This inhibitory activity has been linked to bacterial cell membrane rupture, which results in bacterial cell death.

4.9. Antimalarial Activity

In mice, the antimalarial activity of *E. alba* leaf extract was investigated against Plasmodium berghei ANKA strain. During early and established infection, the methanolic leaf extract (250–750 mg/kg) had a dose-dependent chemosuppressive or schizontocidal effect, with high mean survival time (m.s.t.) values, notably in the group given 750 mg/kg/day of extract. Repository activity was also seen in the plant extract.

The mosquito larvicidal and ovicidal properties of crude hexane, ethyl acetate, benzene, chloroform, and methanol extracts of *E. alba* leaves were investigated against *Anopheles stephensi* (Liston) early third-instar larvae (Diptera: Culicidae). Larval mortality was detected 24 hours after exposure to the extract. Methanol extract had the largest larval mortality (LC50 = 112.56 ppm, LC90 = 220.68 ppm). The percent hatchability was likewise discovered to be inversely proportional to the extract concentration. With methanol extract at 200 ppm, 100% mortality was achieved. As a result of its larvicidal and ovicidal properties, this plant may be effective in the fight against malaria.

The activity of benzene, hexane, ethyl acetate, methanol, and chloroform leaf extract of *E. alba* against the dengue vector, Aedes aegypti, were also investigated. The methanol extract has the highest larvicidal activity. Benzene, hexane, ethyl acetate, methanol, and chloroform extract of *E. alba* had LC50 values of 151.38, 165.10, 154.88, 127.64, and 146.28 ppm, respectively, against early third-instar larvae of Aedes aegypti. The methanol extract was shown to be the most efficient against Aedes aegypti in terms of ovicidal action. At 300 ppm, the methanol extract caused 100% mortality (zero hatchability).

Crude hexane, ethyl acetate, benzene, chloroform, and methanol extracts of *E. alba* leaf were tested for their adulticidal and repellant effects against two significant vector mosquitoes, *Culex quinquefasciatus* and *Aedes aegypti* (Diptera: Culicidae). *Wuchereria bancrofti*, avian malaria, and arboviruses such as St. Louis encephalitis virus, Western horse encephalitis virus, and West Nile virus are all spread by *C. quinquefasciatus*. All of the extracts had a mild adulticide activity. The extracts also demonstrated mosquito repellent properties that were concentration dependant. In comparison to benzene, hexane, ethyl acetate, and chloroform extracts, the methanol extract of *E. alba* leaves allegedly displayed the most adulticidal and repellant properties against A. stephensi.

4.10. Cardiovascular Effects

In moderate hypertensive patients, the effects of using dry *E. alba* leaf powder (3 g per day) were examined. For 60 days, subjects were given six capsules (500 mg powder per capsule) in three dosages. When compared to placebo-treated control groups, the *Eclipta*-supplemented group had a 15% reduction in mean arterial pressure, a 24% reduction in total cholesterol, a 24% reduction in low-density lipoprotein fraction, a 14% reduction in triglycerides, a 14% reduction in very-low-density lipoprotein fraction, and a 14% reduction in plasma lipid peroxides (18 percent). In the *Eclipta*-treated group, urine volume increased by 34%, urine sodium increased by 24%, serum vitamin C increased by 17%, and serum tocopherols increased by 23%. The findings showed that leaf powder has diuretic, hypotensive, and hypocholesterolemic characteristics, and that it can help hypertensives avoid oxidative stress-related problems. In isolated frog hearts, an ethanolic extract of *E. alba* leaves and leaf calluses was tested for cardiac inhibitory action. The extracts had negative ionotropic and chronotropic effects, as well as lowered cardiac output. At 20 mg doses, callus extract had a stronger cardiac inhibitory effect than leaf extract. The effects of adrenaline were also found to be counteracted by the callus extract.

4.11. Immunomodulatory Effects

The immunostimulatory effects of feeding aqueous extract of *E. alba* leaves to tilapia fish have been investigated (*Oreochromis mossambicus*). Fish were fed diets containing extract at concentrations of 0, 0.01 percent, 0.1 percent, and one percent. Nonspecific humoral (lysozyme, antiprotease, and complement) and cellular (myeloperoxidase content, generation of reactive oxygen and nitrogen species) responses to Aeromonas hydrophila were measured after each week. Gram-negative straight rods with rounded ends (bacilli to coccobacilli form) are pathogens in both fish and humans. After feeding fish with aqueous extract for 1, 2, or 3 weeks, lysozyme activity rose dramatically. After one week of feeding with aqueous extract, reactive oxygen species generation and myeloperoxidase concentration both increased significantly. When fish were fed the extract and then challenged with the pathogen, the percent mortality decreased dramatically.

Using carbon clearance, antibody titer, and cyclophosphamide immunosuppression parameters, the immunomodulatory responses of methanol extract of whole plant of *E. alba* (containing 1.6 percent wedelolactone) were assessed at five dose levels (dose-response relationship) ranging from 100 to 500 mg/kg body wt. The phagocytic index and antibody titer were both dramatically raised by *E. alba* extract. The phagocytic index and white blood cell (WBC) count F ratios were also significant.

4.12. Antiepilepsy Activity

The antiepileptic effect of methanol extraction of *E. alba* leaf powder was tested in rats using the Maximal Electroshock Test (MES). Rats were given the extract orally for 7

days at dosages of 50, 100, and 200 mg per kg body weight. Seizures were generated in rats one hour after the last treatment by using an electro convulsiometer to deliver 150 mA for 0.2 seconds through a pair of ear clip electrodes. Anticonvulsant action was measured by a decrease in the time of hind leg extension. In a dose-dependent way, rats given extract at various doses showed a significant decrease in the duration of time spent in the extensor phase when compared to controls. Wedelolactone, luteolin, and -amyrin, all included in the extract, were found to have antiepileptic action.

Using pentylenetetrazole and picrotoxin-induced seizure models in mice and guinea pigs, the anticonvulsant efficacy of methanol extract of *E. alba* leaves was investigated. The process was further explained by looking at the extract's GABAA receptor modulatory activity as well as its influence on GABA (-amino butyric acid) levels in the brains of mice. The extract showed potent anticonvulsant efficacy when given at doses of 10–200 mg/kg with a saturation threshold of 50 mg/kg. Positive modulatory actions on GABAA receptors were found to be responsible for the anticonvulsant effect. The extract's wedelolactone and luteolin were suspected of being responsible for the observed impact. GABAA receptor malfunction, in particular, has a role in epileptogenesis. Wedelolactone has been shown to bind to the BZD (benzodiazepine) binding site on GABAA receptors with selectivity and affinity. Luteolin also has neuroprotective properties and binds to the BZD binding site on GABAA receptors.
In rats, ethanolic leaf extracts of *E. alba* was tested for anticonvulsant and muscle relaxant activity in the maximal electroshock-induced seizures (MES), rotarod, and traction tests at dosages of 50, 100, 200, and 400 mg/kg, p.o. The extract reduced seizures generated by MES, shortened the duration of tonic hind limb extension (THLE) (by 76.2 and 89.8%, respectively), and decreased motor coordination at dosages of 200 and 400 mg/kg, indicating anticonvulsant and muscle relaxant action. At doses of 200 and 400 mg/kg, *E. alba* ethanolic leaf extract has been demonstrated to cause thiopental sodium-induced sleeping time in rats and to lengthen the duration of sleep. In rats, the extract at 400 mg/kg reduced locomotor activity, indicating a sedative effect. The extract contains ursolic and oleanolic acids, which can act as GABAA agonists, and this feature may be responsible for the CNS depressive action. Methanolic extract of Ipomoea aquatica leaves has been shown to have CNS depressive and antiepileptic properties.

4.13. Snake Bite

Crotalus durissus terrificus venom phospholipase A2 activity has been reported to be inhibited by extract of *E. alba*. The extract's inhibitory effect has been related to the presence of coumestans, wedelolactone, and demethylwedelolactone.

4.14. Anticancer Activity

The anticancer potential of *E. alba* hydroalcoholic extract has been studied. The extract suppressed cell proliferation in HepG2, A498, and C6 glioma cell lines in a dose-dependent manner, with IC50s of 22 2.9, 25 3.6, and 50 8.7 g/mL, respectively. Matrix metalloproteinases (MMP) 2 and 9 expression was dramatically reduced. Additionally, nuclear factor B (NFB) was shown to be downregulated. Following 72 hours of extract treatment, DNA damage was identified, leading to apoptosis. In multidrug-resistant DR-HepG2 cells, a hepatocellular carcinoma cell line, a hydroalcoholic extract of the plant showed antiproliferative activity.

E. alba juice has been demonstrated to stop HCC-S102 (hepatocellular carcinoma) cells from migrating. The juice reduced migration of multiple human cancer cell lines from various tissue sources (liver, lung, and breast) with IC50 values ranging from 31–70 g/mL. As

a result, the plant may be useful in avoiding cancer spread. The juice has also been shown to have antiangiogenic properties.

The MTT assay was used to test the inhibitory effects of ethyl acetate, methanol, and aqueous extracts of whole dried plants of *E. alba* on the human lung epithelial adenocarcinoma cell line (HCC-827). All three extracts showed dose-dependent reductions in viable cell count, with the ethyl acetate extract having the maximum efficacy. Apoptosis was elicited in cancer cells by all extracts.

Ethinylestradiol is a hormone that is found in a variety of contraceptives and is also used to treat metabolic and sexual diseases. It's also a genotoxic and tumor-inducing substance. The combination of 10 mM ethinylestradiol and 1.02 104, 2.125 104, 3.15 104, and 4.17 104 g/mL acetone extract of *E. alba* leaves resulted in a considerable dose-dependent reduction in the genotoxic effects generated by the administration of 10 mM ethinylestradiol. The development of colon cancer cells was inhibited by a crude methanol extract of *E. alba*. The methanolic extract of the plant's aerial portions inhibited the proliferation of hepatic stellate cells, also known as HSCs. Five oleanane-type triterpenoids were isolated using activity-guided fractionation: echinocystic acid, eclalbasaponin II, eclalbasaponin V, eclalbasaponin I, and eclalbasaponin III, all of which are echinocystic acid derivatives. Echinocystic acid and eclalbasaponin II, two of the five echinocystic acid derivatives identified, strongly suppressed HSC proliferation in a dose- and time-dependent manner.

4.15. Antiulcer Activity

The antiulcer effects of an ethanolic extract of *E. alba* have been studied in different ulcer models in rats, including cold resistant stress (CRS) and pylorus ligation (PL). The extract was observed to diminish ulcerative lesions dose-dependently and considerably when given orally twice daily at doses of 50, 100, and 200 mg/kg. Simultaneously, extract administration resulted in a considerable reduction in lipid peroxidation and an increase in catalase activity. When compared to control (non-extract) rats, the extract's antisecretory efficacy was demonstrated by a considerable reduction in stomach volume, acid output, and gastric pH.

In ulcers generated in 36-hour fasting Sprague Dawley rats by aspirin or ethanol or pylorus ligation + aspirin treatment, the methanolic extract of *E. alba* showed antiulcer action. When compared to the control groups, the group receiving *E. alba* oral administration prior to ulcer induction exhibited a highly significant reduction in the incidence of gastric ulcers as well as stomach inflammation (after 4 hours of treatment). The activity of the extract was comparable to that of the proton pump inhibitor rabeprazole.

4.16. Anthelmintic Activity

At dosages of 25–100 mg/mL, the methanol extract of the whole plant of *E. alba* was tested for its anthelmintic activity against the earthworm *Pheretima posthuma*. The extract caused worms to be paralysed at doses of 50, 75, and 100 mg/mL, and death at doses of 75 and 100 mg/mL. Antihelmintic action was also found in the ethanol and aqueous extracts against P. posthuma.

5. Pharmacological Activity Reports on *E. alba* Phytoconstituents

5.1. Wedelolactone

Wedelolactone has been shown to inhibit 5-lipoxygenase *in vitro*. The two-step conversion of arachidonic acid to leukotriene A4 is catalysed by 5-lipoxygenase (5-LO) (LTA4).

The parent compound and most of the wedelolactone derivatives significantly protected primary cultured liver cells from the toxicity of CCl4, galactosamine (Galc), and phalloidin, and strongly inhibited the activity of 5-lipoxygenase in porcine leukocytes, according to a study using synthetically prepared wedelolactone and derivatives. In isolated nuclei from hepatocytes, the synthetic wedelolactone was discovered to have a stimulatory effect on RNA production.

When combined *in vitro* before i.p. injection into adult Swiss mice, an ethanolic extract of the aerial portions of *E. alba* was demonstrated to counteract the fatal activity of the venom of the South American rattlesnake (Crotalus durissus terrificus). Wedelolactone (0.54 mg/animal), sitosterol (2.3 mg/animal), and stigmasterol (2.3 mg/animal), three phytoconstituents extracted from the plant, were able to counteract three deadly dosages of the venom. The release of creatine kinase from isolated rat muscle subjected to crude venom was suppressed by aqueous preparations of the plant. When the venom was preincubated with the extract before injection into animals, this protection was also found *in vivo*.

The ability of *E. alba* and three of its constituents, wedelolactone, sitosterol, and stigmasterol, to protect against myotoxicity caused by crotalid venoms (*Bothrops jararaca, Bothrops jararacussu,* and *Lachesis muta*) and purified myotoxins (bothropstoxin, BthTX; bothropasin; and crotoxin) has been investigated *In vitro* myotoxicity of crotalid venoms and myotoxins was neutralised more effectively by wedelolactone than by sitosterol or stigmasterol. Preincubation with wedelolactone neutralised the *in vivo* myotoxicity of venoms and myotoxins. Wedelolactone was given intravenously to reduce the rise in plasma CK activity caused by subsequent intramuscular injections of crotalid venoms or myotoxins.

Wedelolactone decreased the hemorrhagic effect of *B. jararaca* venom, as well as the crotoxin's phospholipase A2 activity and *B. jararaca* venom's proteolytic activity. The components' antiproteolytic and antiphospholipase A2 actions are thought to be responsible for these effects. Wedelolactone also inhibited the myotoxic action of venoms from Crotalus viridis viridis and Agkistrodon contortrix laticinctus in mice, as well as two phospholipase A2 myotoxins derived from them, CVV myotoxin and ACL myotoxin.

By reducing NF-B-mediated transcription, wedelolactone has been reported to reduce lipopolysaccharide (LPS)-induced caspase-11 (an inflammatory caspase) production in cultured cells. Wedelolactone has also been demonstrated to be an inhibitor of IKK (IB, a component of the upstream NF-B signal transduction cascade), a kinase that is required for NF-B activation through regulating IB phosphorylation and degradation.

In LPS-stimulated RAW 264.7 cells, wedelolactone reportedly inhibited the protein expression levels of iNOS (inducible nitric oxide synthase, produced after activation by endotoxins or cytokines and generating copious amounts of NO) and COX-2 (cyclooxygenase-2 converts arachidonic acid to prostaglandins, resulting in pain and inflammation), as well as the downstream products, including NO (Wedelolactone also reduced LPS-induced NF-B p65 activation by degrading and phosphorylating IB- and preventing the NF-B p65 subunit from being translocated to the nucleus. This shows that the chemical could be utilised to treat inflammation.

Six compounds were isolated from *E. alba* extract using bioassay-guided fractionation for anti-HIV-1 (human immunodeficiency virus 1) integrase activity. 5-hydroxymethyl-(2,2′:5′,2″)-terthienyl tiglate, 5-hydroxymethyl-(2,2′:5′,2″)-terthienyl agelate, 5-hydroxymethyl-(2,2′:5′,2″)-terthienyl acetate, ecliptal, orobol, and wedelolactone were found as the compounds. With an IC50 value of 4.0 ± 0.2 microns, wedelolactone showed the most anti-HIV-1 integrase inhibitory efficacy. This research backs up the use of *E. alba* in individuals with acquired immunodeficiency syndrome (AIDS).

The androgen receptor (AR) stimulation of transcription from the prostate-specific antigen promoter in prostate cancer (PCa) cells has been reported to be modulated by wedelolactone, which was derived from Wedelia chinensis. Wedelolactone's anticancer efficacy was also demonstrated in androgen receptor-negative MDA-MB-231 breast cancer cells, where it inhibited proliferation and promoted apoptosis. With the generation of DNA damage, cells were arrested in the S and G2/M phases of the cell cycle. Wedelolactone was discovered to interact with dsDNA and limit DNA topoisomerase II function.

Wedelolactone, in combination with LPS and polyI:C (polyinosinic: polycytidylic acid), was found to induce apoptosis in Chlamydia trachomatis-infected HEp-2 cells (human epithelial type 2 cells, thought to originate from a human laryngeal carcinoma), resulting in *Chlamydia trachomatis* viability being reduced.

The asthma medications cromolyn disodium and nedocromil sodium have been demonstrated to target G protein-coupled receptor-35 (GPR35). Wedelolactone, an antiallergic, has been discovered to be a powerful -arrestin-biased GPR35 agonist and could be used to treat asthma.

Adipocyte hyperplasia is linked to obesity and occurs when local multipotent stem cells in the vascular stroma of adipose tissue and distant stem cells from other organs differentiate into adipocytes. The adipogenic differentiation of human adipose tissue-derived mesenchymal stem cells has been reported to be inhibited by wedelolactone (hAMSCs). This process has been demonstrated to be mediated by the ERK (extracellular signal-regulated kinase) pathway.

Arachidonic acid metabolism via the 5-lipoxygenase pathway has been found to have a significant role in prostate cancer cell survival. Wedelolactone has been discovered to induce apoptosis in both androgen-sensitive and androgen-independent prostate cancer cells, killing them in a dose-dependent way. c-Jun N-terminal kinase (c-JNK) and caspase-3 were required for wedelolactone-induced apoptosis. Apoptosis was induced by inhibiting protein kinase C but not Akt (protein kinase B), implying that a novel mechanism is at work. JNK modulates the activity of mitochondrial pro- and antiapoptotic proteins through different phosphorylation processes, which is important in death receptor-initiated extrinsic as well as mitochondrial intrinsic apoptotic pathways. Caspase-3 is a death protease that plays an important role in apoptosis. Downregulation of protein kinase C has also been demonstrated in glioma cells activated with tumour necrosis factor-related apoptosis inducing ligand (TRAIL); however, in this case, lower expression of Akt was also observed.

Wedelolactone has been shown to trigger apoptosis in tumour cells when combined with interferon- (IFN-). Through specific inhibition of T-cell protein tyrosine phosphatase (TCPTP), an important tyrosine phosphatase for STAT1 dephosphorylation, the compound increased IFN-signaling by inhibiting STAT1 (signal transducer and activator of transcription 1 protein) dephosphorylation and prolonging STAT1 activation. Following stress-induced responses, STAT1 has been linked to the modulation of pro- and antiapoptotic genes.

On the human hepatic stellate cell line LX-2, wedelolactone has been shown to have antifibrotic properties. LX-2 cellular viability was lowered by the chemical in a time and dose-dependent manner. Wedelolactone increased apoptosis in LX-2 cells by lowering antiapoptotic Bcl-2 expression and boosting proapoptotic Bax expression. The authors ascribe the inhibition of LX-2 cell activation to a variety of factors, including increasing Bcl-2 family-related apoptosis, upregulating phosphorylated state of ERK and JNK expressions, and suppressing nuclear factor-B (NF-B) mediated activity.

Overall, the chemical appears to have antiinflammatory, hepatoprotective, snake venom neutralising, anti-HIV, anticancer, and antiasthmatic properties, according to several researches.

5.2. Eclalbasaponins

It has previously been reported that eclalbasaponin isolated from *E. alba* has an antiproliferative impact on hepatic stellate cells. Eclalbasaponin, which I extracted from the plant's aerial parts, apparently suppressed the proliferation of hepatoma cell smmc-7721 in a dose-dependent manner, with an IC50 value of 111.1703 g/mL. Eclalbasaponin VI, which was isolated from *E. alba*, was found to have -glucosidase activity. Antibacterial activity has been demonstrated for Eclalbasaponin, which was isolated from *E. alba*.

In RAW 264.7 macrophages, echinocystic acid extracted from the ethyl acetate fraction of the plant's 70 percent ethanol extract reduced LPS-induced generation of nitric oxide and cytokines such as tumour necrosis factor- and interleukin-6. The chemical also suppressed LPS-induced inducible nitric oxide synthase protein expression and mRNA expression of inducible nitric oxide synthase (iNOS), tumour necrosis factor (TNF), and interleukin-6 (IL-6) as well as LPS-induced iNOS promoter binding activity. Echinocystic acid also inhibited nuclear factor-B transcriptional activity generated by LPS by preventing p65 nuclear translocation. As a result, this molecule can be considered a powerful anti-inflammatory agent.

Eclalbasaponins have anticancer and anti-inflammatory properties when combined.

5.3. *α*-Amyrin

There are limited publications on -amyrin; however, there are multiple reports on the pharmacological effects of a mixture of - and -amyrin (ABA) as well as -amyrin derivatives. -Amyrin acetate has been shown to have antilipoxygenase activity, suggesting that it may have a therapeutic role in arthritis. -amyrin palmitate induced increases in serum hyaluronate and blood granulocytes toward nonarthritic levels in adult male Wistar rats made arthritic by subplantar injection of complete Freund's adjuvant, and rectified the moderate anaemia of adjuvant arthritis. The triterpenes -amyrin and its palmitate and linoleate esters inhibited the growth of rat osteosarcoma cells and inhibited the digestion of type I (bone) native collagen by tadpole collagenase. The antiarthritic action has been related to the suppression of joint deterioration by triterpenes. ABA, isolated from *Protium kleinii* resin, caused dose-dependent and significant antinociception against visceral pain in mice caused by (intraperitoneal) i.p. injection of acetic acid; ABA given by i.p., p.o., intracerebroventricular (i.c.v.), or intrathecal (i.t.) routes inhibited both neurogenic and inflammatory phases of overt nociception caused by intraplantar In addition, i.p. ABA therapy reduced nociception generated by 8-bromo-cAMP (8-Br-cAMP) and 12-O-tetradecanoylphorbol-13-acetate (TPA) as well as glutamate-induced hyperalgesia.

The capacity of -amyrin isolated from P. kleinii to suppress both ear edoema and polymorphonuclear cell inflow in response to topical application of 12-O-tetradecanoylphorbol-acetate (TPA) in mice ears has been observed. Amyrin also blocked IB degradation, phosphorylation of p65/RelA, and activation of NF-B. Furthermore, ERK, p38 mitogen-activated protein kinase (MAPK), and protein kinase C (PKC) were all inhibited by -amyrin. Suppression of COX-2 expression by inhibition of ERK, p38MAPK, and PKC, as well as preventing NF-B activation, has been postulated as an anti-inflammatory strategy. Cerulein-induced acute pancreatitis in mice was greatly reduced by ABA extracted from Protium heptaphyllum. With the injection of ABA, the cerulein-induced elevations of tumour necrosis factor TNF-, interleukin-6, lipase, amylase, myeloperoxidase (MPO), and TBARS were reduced. Furthermore, ABA reduced pancreatic edoema, inflammatory cell infiltration,

acinar cell necrosis, and TNF and iNOS expressions. A similar protective effect of ABA was reported in rats with acute pancreatitis caused by L-arginine.

Antinociceptive activity of ABA (3–100 mg/kg) isolated from Protium heptaphyllum resin against subplantar (1.6 g) or intracolonic application of capsaicin in mice has been reported; antinociceptive activity of ABA has also been reported in mice for cyclophosphamide-induced bladder pain and intracolonic administration of mustard oil.

In Swiss male mice, the preventive effect of ABA against trinitrobenzene sulphonic acid (TNBS)-induced colitis has been established. The findings suggest that ABA reduces the levels of inflammatory cytokines and COX-2 through inhibiting the NF-B and CREB signalling pathways. The anti-inflammatory action of ABA against dextran sulfate-induced colitis in mice has also been reported; the cannabinoid system is thought to be involved. The chemical was likewise found to be effective in KCl-induced contractions, with an EC50 of (72 3) 10(5) M. As a result, the chemical may be useful in the treatment of gastrointestinal illnesses such as diarrhoea and dysentery.

In normoglycemic mice, ABA, extracted from Protium heptaphyllum resin, had a hypolipidemic impact and lowered high plasma glucose levels during oral glucose tolerance testing. When STZ-induced diabetic mice were given ABA, their blood glucose (BG), total cholesterol (TC), and serum triglycerides (TGs) all decreased significantly. Histopathological studies revealed that ABA helps to maintain -cell integrity in the pancreas. The HFD-associated rise in serum TC and TGs was much reduced in mice fed a high fat diet (HFD), especially at a dose of 100 mg/kg. At this dose, very low-density lipoprotein (VLDL) and low-density lipoprotein (LDL) cholesterol levels were much lower, but high-density lipoprotein (HDL) cholesterol levels were significantly higher. ABA also dramatically lowered the atherogenic index.

In STZ-induced diabetic rats and db/db diabetic mice, -amyrin acetate, isolated from aerial roots of Ficus benghalensis, was shown to lower hyperglycemia and ameliorate diabetic conditions.

Amyrin from *Rhaponticum carthamoides* has been demonstrated to increase the proliferation of human keratinocytes (HaCaT) by 18%. Adult female A. stephensi mosquitoes died 76.9% of the time when exposed to amyrin acetate at a concentration of 1.6 percent. *In vivo* treatment of mosquitos to the chemical increased mean probing time, decreased blood engorgement time and feeding rate, and decreased fecundity, all of which reduced the malaria vector Aedes stephensi's overall survival and reproductive potential.

When examined in mice using the open-field, elevated plus maze, rotarod, forced swimming, and pentobarbital-induced sleeping time, ABA, derived from the stem bark resin of Protium heptaphyllum, demonstrated anxiolytic and antidepressant effects. Anxiolytic effects may be mediated by benzodiazepine-type receptors, while antidepressant effects may be mediated by noradrenergic pathways.

In mice, ABA has been shown to have a hepatoprotective effect against acetaminophen-induced liver injury. ABA was extracted from Protium heptaphyllum trunk wood resin. Acetaminophen (500 mg/kg, p.o.) produced fulminant liver injury with centrilobular necrosis and inflammatory cell infiltration, increased serum ALT and AST activity, decreased hepatic glutathione (GSH), and 50% mortality. Pretreatment with ABA (50 and 100 mg/kg, i.p. 48, 24, and 2 hours before acetaminophen) reduced the acetaminophen-induced acute increase in serum ALT and AST activity, raised depleted hepatic GSH, and reduced histopathological changes significantly. Furthermore, ABA increased the sleeping time of pentobarbital (50 mg/kg, i.p.). The findings suggest that ABA's hepatoprotective

effects were due to suppression of hepatic cytochrome P450, as well as a reduction in oxidative stress and toxic metabolite production in the liver.

In mice, ABA, which was extracted from Protium heptaphyllum resin, was found to have a gastroprotective action against ethanol-induced stomach mucosal injury. In mice with their sensory afferents chemically ablated by a neurotoxic dose of capsaicin, maximum gastroprotection was obtained with a 100 mg/kg dose of ABA, which was nearly abolished in mice with their sensory afferents chemically ablated by a neurotoxic dose of capsaicin. It's been claimed that ABA's gastroprotective mechanism involves the activation of capsaicin-sensitive primary afferent neurons, at least in part.

The scratching behaviour caused by dextran T40 and compound 48/80 in mice was allegedly considerably reduced by ABA, which was extracted from Protium heptaphyllum resin. A stabilising effect on the mast cell membrane is thought to be the cause of the inhibition.

According to the available scientific literature, -amyrin and derivatives, either alone or in combination with other -amyrins, have a wide range of pharmacological activities, including antiarthritic, analgesic, anti-inflammatory, antispasmodic, antidiabetic, cholesterolemic, antimalarial, anxiolytic, antidepressant, hepatoprotective, gastroprotective properties, or may also be beneficial for pancreatitis and pruritus.

5.4. Miscellaneous Phytochemical Constituents of *E. alba*

Several phytochemical elements of *E. alba* have been linked to a wide range of pharmacological effects, which will be briefly discussed. Oleanolic acid has anti-diabetic and anti-cancer properties. It has the ability to directly influence enzymes involved in insulin production, secretion, and signalling. Many of its actions are mediated by the transcription factor Nrf2 being activated (nuclear factor erythroid 2-related factor 2). Nrf2 has the ability to regulate the expression of over 200 genes involved in drug and toxin metabolism, oxidative stress and inflammation protection, and protein stability and degradation. Nrf2 has the ability to interact with the tumour suppressor protein 53 (p53) and hence regulate the cell cycle and NF-B. Nrf2 protects against several age-related disorders, including cancer and neurodegeneration, as well as improving longevity, through these interactions.

The compound can modulate multiple signalling pathways in tumour cells, including NF-b, AKT, signal transducer and activator of transcription 3, mammalian target of rapamycin, caspases, intercellular adhesion molecule 1, vascular endothelial growth factor, and poly (ADP-ribose) polymerase, according to a recent review. As a result, oleanolic acid has the potential to be both a preventative and therapeutic agent for cancer.

Ursolic acid has been demonstrated to have antioxidative, anticancer, and anti-inflammatory activities in numerous studies, yet a recent review pointed out that the chemical has also been proven to have proinflammatory properties in normal cells and tissues. Ursolic acid has been demonstrated to have anticancer, cytotoxic, antitumor, antioxidant, anti-inflammatory, anti-wrinkle, anti-HIV, acetyl cholinesterase, -glucosidase, antibacterial, and hepatoprotective properties in a number of studies.

Hepatoprotective, anti-inflammatory, and antihyperlipidemic effects have been described for oleanolic and ursolic acids. Neurodegenerative diseases such as Alzheimer's disease may benefit from oleanolic and ursolic acids. According to a review study, ursolic acid's anticancer effects include DNA protection, inhibition of the epidermal growth factor receptor/mitogen-activated protein kinase signal or FoxM1 transcription factors, antiangiogenesis (which can inhibit tumour cell growth), inhibition of tumour cell migration and invasion, and induction of apoptosis in cancer cells. The forkhead transcription factor

FoxM1 has been found to bind to and regulate a collection of genes involved in late cell cycle events in the G2 and M phases. Breast cancer cells' proliferation and anchorage-independent growth have been reported to be reduced when FoxM1 expression is inhibited. Lutein has been shown to have antioxidant, anti-inflammatory, and antiallergic properties. It's also possible that the chemical has a cardioprotective effect. Luteolin has also been shown to limit the growth of cancer cells *in vitro* and *in vivo* by providing protection against carcinogenic stimuli, reducing tumour cell proliferation, and inducing cell cycle arrest and/or apoptosis.Furthermore, luteolin can sensitise cancer cells to therapeutic-induced cytotoxicity through a variety of mechanisms, including suppressing cell cycle pathways like PI3K/Akt, NF-B, and X-linked inhibitor of apoptosis protein (XIAP) and stimulating apoptosis pathways like those that induce the tumour suppressor p53. Modulation of reactive oxygen species (ROS) levels, inhibition of topoisomerases I and II, reduction of NF-B and AP-1 activity, stabilisation of p53, and inhibition of PI3K, STAT3, insulin-like growth factor 1 receptor (IGF1R), and human epidermal growth factor receptor 2 (HER2) have all been proposed as reasons for luteolin's cancer chemopreventive and chemotherapeutic potential. Overexpression of HER2 has been linked to the development of certain aggressive forms of breast cancer.

Following ischemia-reperfusion, luteolin has been found to protect cardiomyocytes, implying that the substance could be used to prevent and cure cardiovascular disorders.

Apigenin is a chemopreventive agent that has been described. Antioxidant and anti-inflammatory effects are also present in the molecule. The chemical could also help people with cardiovascular and neurological problems. Apigenin can decrease cancer cell proliferation, sensitise cancer cells to apoptosis, and prevent the creation of blood vessels to serve the growing tumour, according to a recent review. Apigenin inhibits cancer cell glucose uptake, extracellular matrix remodelling, cell adhesion molecules involved in cancer growth (such as VCAM-1), and chemokine signalling pathways that direct metastasis to other sites. Apigenin, for example, has been demonstrated to inhibit transformed cell motility and invasion by downregulating C-X-C chemokine receptor 4 expressions. All of these actions work together to prevent cancer growth and spread. Apigenin may reduce GLUT-1 expression in malignancies of the head and neck.

6. Conclusion

Traditional medical practitioners see *E. alba* as a valuable medicinal plant for the treatment of liver illnesses, gastrointestinal disorders, respiratory tract disorders, hair loss, skin disorders, and fever. Most ethnomedicinal claims, including the treatment of snake bites with the herb, have been supported by scientific research. The plant has yielded a number of significant phytochemicals, which have been separated and identified. Wedelolactone, eclalbasaponins, -amyrin, ursolic acid, oleanolic acid, luteolin, and apigenin are some of these chemicals. According to existing scientific data, these chemicals have the potential to become the next generation of medications for the treatment of cancer, arthritis, liver illnesses, hair loss, and snake bites.

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