

A COMPREHENSIVE REVIEW: EHRETIA LAEVIS ROXB

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Abstract: *Ehretia laevis* Roxb. (Boraginaceae) has been extensively used as a traditional remedy for the treatment of a various range of ailments related to the gastrointestinal tract, the reproductive system, respiratory system and against several diseases. This review critically assesses and documents, for the first time, the fragmented information on *E. laevis* roxb including its botanical description, plant profile, geographical distribution, bioactive phyto -metabolites and pharmacological activities. *E. laevis* showed the presence of important phytoconstituents such as alkaloids, aliphatic alcohols, hydrocarbons, amino acids, pentacyclic triterpenoids, phenolic acids, flavonoids, fatty acids, steroids, carbohydrates, vitamins and minerals. *Ehretia laevis* Roxb. exhibit broad spectrum of therapeutic activities viz., anti-inflammatory, antiulcer, antidiarrheal, antidysenteric, antioxidant, antiarthritic, antidiabetic, antivenom, wound healing and anti-infective activities.

Keywords: *Ehretia laevis* Roxb, Pharmacological activities,

01 INTRODUCTION

Ehretia laevis is a rapidly growing medium sized tree of the Boraginaceae. The genus *Ehretia* contains more than 150 species. The plant is primarily distributed throughout tropical and subtropical regions of Asia, Africa and Australia. *E. laevis* is the most popular member of its genus and is commonly known by more than 120 names in diverse languages in English it is called as *Ehertia*, In Gujarati its *Vadha vardi* , In Hindi it's called *Bhairi*, *chamror*, *Konkani*, *Kalo gamdo*, in Marathi it's called *Datrangi*, *Ajanvruksha*, In Tamil its called *Kuruviccai*, *Kalvirasu* and In telugu it's called *Tellajuvvi*, *Paldattam*. It has a religious important among Hindus it found near The Dnyaneshwar temple in Alandi and it's have a several medicinal u. In India the plant is mainly found in the Northern parts of the country (e.g., in Bengal, Maharashtra and Rajasthan). The plant has also been documented in the traditional system of medicine (e.g., Ayurveda and Siddha).

It has a religious important among Hindus it found near The Dnyaneshwar temple in Alandi and it's have a several medicinal uses this is very spiritual plant as Santa Dnyaneshwar Maharaj from Alandi Pune has taken Samadhi at the base of this plant. *E. laevis* is shown to be an excellent potential source

of drugs for the mitigation inflammation, liver problems, jaundice, asthma, dysentery, ulcers, diarrhea, ringworm, eczema, diabetes, fissure, syphilis, cuts and wounds venereal and infectious disorder.

Ehretia Laevis Roxb. plant has many compounds useful in wound healing, fractures, UTI, aphrodisiac, headache, anthelmintics, diuretic, demulcent, expectorant, RTI, fever, fungal infections, hepato-protective, cytotoxic, insecticidal, anti-inflammatory, anti-apoptotic, anti-carcinogenic, weight gain, diabetes, muscles wasting, anti-viral activity, psychiatric disorders, collagen formation, reduce the recurrence, severity, healing period of herpes simplex virus infections, it also acts as painkiller and also used in fingerprinting healing period of herpes simplex virus infections, calcium absorption, muscle protein, postsurgery recovery, sports injuries, hormones, aging, used in psychotropic drugs for the purpose of extraction the Soxhlet extraction and rotary evaporator is used.

The advantages and uses of folklore herbs have been acclaimed and executed from ancient times in India. The use of these Folklore remedial herbs for therapeutic applications is contributing to maintenance of human health. The ancient literature, i.e., Ayurveda and Unani, also describes the global usage of herbal medicine for treatment, and its formulation's concoction for prevention of various diseases.

Ehretia laevis is a conventional therapeutic herb from ancient times, frequently designated as Khandu Chakka by local people in Maharashtra. *E. laevis* leaves are used in the treatment of skin infections, fungal infections, mouth blisters, eczema, cuts and wounds, diabetes, asthma, fever and joint pain etc. The leaf of this plant contains abundant therapeutically beneficial secondary metabolites besides primary metabolites.

02 PLANT PROFIL

Ehretia laevis is a rare Indian medicinal plant used from the ancient period, it belonging to a member of the Boraginaceae or Borage family, and is native to India, Pakistan, Laos, Myanmar, Vietnam, China, and Bhutan. The *Ehretia laevis* Roxb. Is high valued medicinal plant and becoming rare in the state of Maharashtra. It has religious importance among Hindus. It is growing luxuriantly growing at Alandi near the Dnyaneshwar temple. The use of medicinal plants is increasing worldwide. The general information of *Erthia laevis* given below



Figure No.1: Ehretia Laevis plant

Table NO. 1: Taxonomical classification of Ehretia Laevis

Kingdom	Plantae
Division	Tracheophyta
Family	Boraginaceae
Order	Boraginales
Genus	Ehretia
Species	Ehretia Laevis (Roxb.)
Botanical name	Ehretia Laevis (Roxb.)
Synonyms	Khanduchakka
Fruits	A small drupe.

2.1 DISTRIBUTION

Ehretia Laevis is a medium sized tree reaching up to height of 12 m (Fig-1). Its drooping branches bear dark green colour leaves with varied size 2-7.8 cm in length and 1.2-3.8 cm in width. The shape of leaves is obtuse; with 5-7 lateral veins on each side of the mid rib with the slender 2-3 cm long petiole. The bark of the plant is irregular and light grey. The flowers are white, with round orange fruits when ripe or mature.



Fig no.: 02 A) Ehretia Laevis Fruit B) Ehretia Laevis Flower

2.2 GEOGRAPHICAL DISTRIBUTION

E.laevis is mainly cultivated in India, China, Pakistan, Shrilanka, Africa, Bhutan, Nepal, Burma and Australia. The plant is mainly located in hilly forest and on hilly slopes.

3) CHEMICAL CONSTITUENT

Phytochemical investigations had led to the extraction and isolation of secondary metabolites along with the primary metabolites from petroleum ether, Chloroform and Methanolic extract of its barks and leaves. These are pentacyclic Triterpenoids, Flavonoids, Alkaloids, Tannins, Phenolic components, Phenolic acids, Hydrocarbons, Aliphatic alcohols, Fatty acids, Ascorbic acids, Amino acids, Carbohydrates, Benzoquinolins, Vitamins and minerals.

Lupeol

Lupeol (lup-20(29)-en-3 β -ol) is abundantly found in medicinal plants and has been reported to possess an array of pharmacological activities, including antiangiogenic, Antiinflammatory, Anticancer, and arthritis, antidiabetic, cardiovascular and Antioxidant activities. Lupeol is one of the potential anticancer biomarkers.

Ursolic Acid

Ursolic acid (3 β -hydroxy-urs-12-ne-28-oic acid) is a wellknown pentacyclic terpenoid of Plant origin exhibiting a wide range of pharmacological activities, eg, antiviral, anti-ulcerosos, anti-inflammatory and anticancer activities.

α -Amyrin

α -Amyrin (3 β -hydroxy-urs-12-en) is the precursor of ursolic acid and predominantly Found in plant origin exhibiting an array of pharmacological activities, eg, anxiolytic, antidepressant anti-inflammatory, anti-hyperglycemic and hypolipidemic activity.

β -Sitosterol

The physteron β -sitosterol (3 β -stigmast-5-en-3-ol) is one of the important active principles of many plants. It is also used as one of the potential plant biomarkers for the treatment and Prevention of cancer.

Flavonoids

Flavonoids are a group of natural products, which are ubiquitously present in plants (fruits, vegetables and also in certain beverages) They are associated with various ther-apeutic activities and are present in a variety of medicinal, nutraceutical, pharmaceutical, and cosmetic preparations. The basic structures of these compounds are often character-ized by a fifteen-carbon skeleton as a common phenyl benzopyrone linkage ($C_6-C_3-C_6$) in their structures Flavonoids are a promising class of natural products sub-divided into flavonols (quercetin and kaempferol), flavones (luteolin and apigenin), flavanones (hesperetin and naringenin), flavan-3-ols (catechin and epicatechin) isoflavones (genistein), and flavanones.

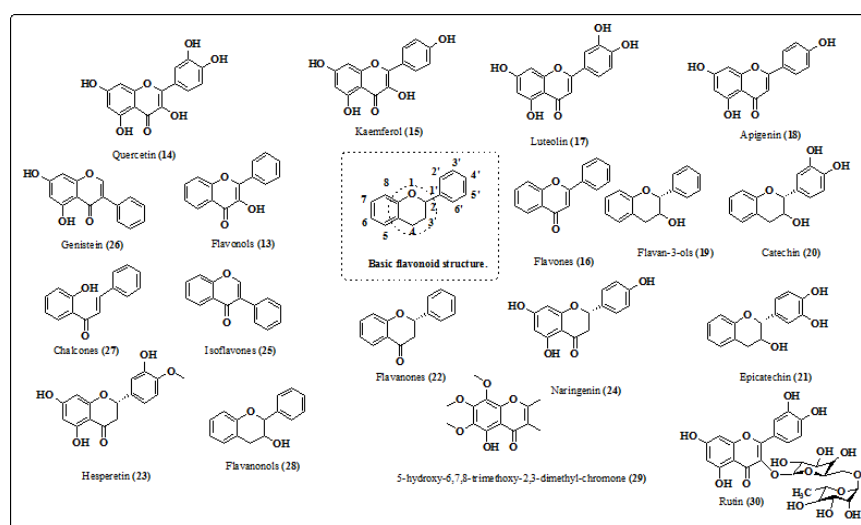


Fig.no -03 structure of Flavonoids compound.

Quercetin

Quercetin (3,3',4',5',7-pentahydroxyflavone) is a citrus polyphenolic flavonoid abundantly present in vegetables and fruits, e.g., black grapes, onion and tea. It was the first known tyrosine kinase inhibitor in the phase-I human clinical trials. Recent studies have reported for its broad spectrum of activities, including against cancer, cardiovascular diseases, inflammatory and CNS disorders. Quercetin exhibits its significant antioxidant activity by sustaining oxidative balance

Kaempferol

Kaempferol (3,4,5,7-tetrahydroxyflavone) belongs to the flavonol class of flavonoid. It is abundantly found in tea, beans, apple, strawberries and spinach [94–96]. Recently, numerous investigations established its diverse pharmacological activities, e.g., cardioprotective, hepatoprotective, anti-inflammatory, antioxidant, anticancer, neuroprotective and antidiabetic properties. Kaempferol was found to be effective against various types of cancers, including skin, colon and hepatic cancer.

Luteolin

Luteolin (3,4,5,7-tetrahydroxyflavone) is a flavone present in a wide variety of fruits, vegetables and in medicinal plants. Vegetables including celery, parsley, onion leaves, broccoli, peppers and carrots are rich in luteolin. Luteolin shows an array of biological properties, including antioxidant, antimicrobial, anticancer and estrogenic regulator properties. Luteolin has the ability to induce apoptosis and produce anticancer effects by causing cell cycle arrest in human oral squamous cancerous cells, human esophageal, colon, lung and liver cancers.

Apigenin

Apigenin (4,5,7-trihydroxyflavone) is predominantly found in everyday diet. Out of all the classes of flavonoids, apigenin is ubiquitous in the plant kingdom. It is rich in tea, oranges, onion, celery, parsley, beer and wines. Apigenin attracts researchers and has been recommended in nutraceuticals because of its numerous benefits and low toxicity. Apigenin exhibits a broad spectrum of activities and is used in the cure of amnesia, depression, stroke, diabetes and cancer. Numerous in vitro and in vivo studies support the therapeutic potential of apigenin as antioxidant, anti-inflammatory and anticancer

Gallic acid

Gallic acid (3,4,5-trihydroxybenzoic acid) is a naturally-occurring plant phenol obtained by the hydrolysis of tannins. Gallic acid is known for its diverse biological activities such as, hepatoprotective, anticancer, antimicrobial and gastroin-testinal disorders. Oxidative stress results in an accumulation and overproduction of free radicals, and is the foremost origin of several degenerative diseases such as cardiovascular system (CVS) diseases, atherosclerosis, cancer and inflammatory diseases. Gallic acid is a low molecular weight compound readily available in fruits, vegetables and medicinal plants. It has the ability to induce apoptosis and also acts as a strong antioxidant. It has been found in the methanolic extract of leaves of *E. laevis*

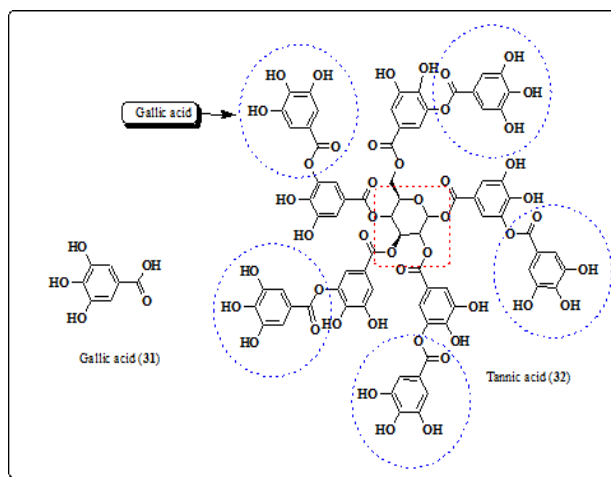


Fig.no-04- structure of polyphenolic compound.

Phenolic Acids and Tannins

Plant phenolic acids are a fundamental human dietary component and are well renowned for their pharmacological actions such as antioxidant, anticancer, antiallergic, antimicrobial and anti-inflammatory properties. The antioxidant potential of a particular phenolic acid depends on the number of hydroxyl groups present as well as their position on the molecule. Tannins belong to the class of polyphenols. Tannins are water soluble compounds, are present in many plants and have the ability to precipitate proteins

Naringenin

Naringenin [5,7-dihydroxy-2-(4-hydroxyphenyl) chroman-4-one] belongs to the flavanone series of flavonoids and is predominantly found in citrus fruits like oranges, lemons, grapes and tomatoes. It is a common polyphenolic dietary component and is derived from the hydrolysis of narirutin or naringenin-7-rutinoside. The scientific community pays considerable attention to this flavonoid because of its therapeutic potential, including its antioxidant, antidiabetic, and anti-inflammatory properties and potential against malignancies and neurodegenerative diseases. Naringenin exerts its antioxidant effects by scavenging free radical generation and enhancing several antioxidant enzyme levels such as glutathione peroxidase, catalase and superoxide dismutase.

Rutin

Rutin (3,4,5,7-tetrahydroxyflavone-3-rhamnoglucoside) is abundantly available as a flavonol of plant origin. The compound is abundantly present in fruit skin, buckwheat and potato skin of this plant. It exhibits various pharmacological activities including neuroprotective, cardioprotective, antidiabetic, anticarcinogenic, anti-inflammatory, and antioxidant. It scavenges free radicals and inhibits the lipid peroxidation. It is also reported to act as a hepatoprotective agent.

Table no : -02 chemical content present in plant and its medicinal uses.

SR. NO	PART	CHEMICAL CONTENT	MEDICINAL USES
1	LEAVES	Naphthoquinone derivative Minerals such as Na, NH ₃ , Fe, Mn, K, P, Zn, Cu, Si, Mg, Ca, Gallic acid, Tannic acid, Rutin, Vitamin, ascorbic acid, Phytol, Piperazine, Betulin & Betulinic acid, Lupeol.	Antibacterial, antifungal, antiviral, insecticidal, cytotoxic, anti-inflammatory, antipyretic, antiparasite analgesic, obesity, diabetes mellitus, heart disease, brain and liver disease, immune system.
2	FRUITS	Decanoic acids, phthalic acid, phytol, amyryn, piperazine, phenylephrine. Benzoquinones: - 1,4naphthoquinone lewisone, Bauerenol, Bauerenol acetate, $\hat{\pm}$ -amyryn, Betulin.	Antiseizure, Larvicidal activity, antinociceptive, Antioxidant, anticancer, immune-enhancing effects, inhibitcellular senescence, arthritis, asthma, mosquito repellent, useful for malaria antitumor, anti-viral, antibacterial, anti-inflammatory and antimalarial.
3	BARK	Tanins Tanic Acid, Baurinol, Pythol, Phenilepherin	Bacteria, fungi, yeasts, growth is prohibited by tannins, Clotting of blood, reduce hyper tension, control lipid level, causes liver necrosis and improve immune response.

Table no: - 03 Ethnobotanical uses

Sr.NO	ETHANOBOTANICAL	USES
1.	AYURVEDIC SYSTEM	Appetizer, anthelmintic, skin related diseases, psoriasis, herpes, allergies, rashes, hemorrhoids, restore normal color of the skin, wound healing, reduce itching, menorrhagia, irregular menstrual cycle, habitual abortion, strengthens the uterus, use in urinary tract infection, cooling effect, reduce inflammation
2.	UNANI SYSTEM	Laxative, emetic, carminative, coolant, heart tonic, use in grippe in children, pain, expectorant, brain tonic, emmenagogue, inflammation
3.	TRADITIONAL SYSTEM	Diarrhea, dysentery, wounds, hemorrhages, cancer, epilepsy, snakebites, calculus, dropsy, sores, carbuncle, cramps, eye diseases, dandruff, fever, measles, leukoderma, hysteria, bronchitis

4) PHARMCOLOGICAL ACTIVITY

4.1 Anti-inflammatory activity

The inflammatory process may be outline a sequence of events that occurs in response to noxious stimuli, infection, or trauma. The classic sign of inflammation are redness, heat, swelling, pain and loss of function. The issue of inflammation that underlines these manifestations are induced and regulate by a large number of chemical mediators including eicosanoids, kinins, complement proteins, histamine and monokines.

Phytoconstituents like hexadecanoic acid (palmitic acid), oleanolic acid, and other fixed oils were suggested to be responsible for its antiarthritic actions. Although systematic scientific studies are still lacking, forthcoming work will probably produce interesting consequences and may provide a prospective remedial candidate from *E. laevis* for the treatment of inflammatory disorders

4.2 Antimicrobial activity

E. laevis has been employed as an ethnic medicine for the treatment of several infectious diseases, including those of viral, fungal, protozoal and bacterial origin. Several investigations have been performed in the recent past years to authenticate the antimicrobial Potential of *Elaevis*. For example, the plant has been tested against different Gram-positive and Gram-negative bacterial strains. There is always tremendous demand for antimicrobial agents due to the speedy development of microbial resistance. The bioactive constituents of this plant could be excellent lead compounds in the search of new potential antimicrobial agents.

Recently, the antimicrobial activity of isopropanol and acetone extracts of *E. laevis* leaves have been evaluated against *Pseudomonas aeruginosa*, *Escherichia coli* and *Staphylococcus aureus*. The results established that the extract was considerably effective towards *S. aureus* and *E. coli*. The antimicrobial potential was found in terms of minimum inhibitory concentration (MIC) using agar broth dilution assay

4.3 Anti-allergic activity

Allergic disorders such as rhinitis, sinusitis, atopic dermatitis, asthma, and food allergy are the most common cause of human disease. There are a number of pharmacological agents available for the treatment of allergic conditions such as asthma and allergy rhinitis. Some species of *Ehretia* genus have compounds such as dimeric prenylbenzoquinones, nitrile glucosides, rosmarinic acid shows anti-allergic effects.

4.4 Anti-bacterial activity

All extracts of *E. laevis* leaves (methanol, chloroform and aqueous solvent) have revealed excellent anti-bacterial activity. When compared to methanol, chloroform and aqueous methanolic extract showed the high anti-bacterial activity on Gram-positive and Gram-negative bacteria, aqueous extracts show the high anti-bacterial activity on Gram-negative than Gram-positive. Some other species also shows positive response against anti-bacterial activity.

4.5 Anti-oxidant activity

Several studies suggest the antioxidant potential of plant *E. laevis*. Antioxidants are the substances which have capacity to inhibit or delay the oxidation process under the Influence of either reactive oxygen species or environmental oxygen. Antioxidants are compounds which protect living organisms from damage caused by concomitant? Lipid peroxidation, protein damage, uncontrolled ROS production and breaking of the Deoxyribonucleic acid (DNA) strand.

In Ayurveda, there are many plants that possess antioxidant potential and can be used against diseases in which free radicals and ROS play an important role. In another study, the methanolic extract of *E. laevis* fruits was reported for antioxidant effects. The plant displayed its antioxidant effects due to the presence of phyto molecules Such as flavonoids, tannins, ascorbic acid and phenolic acids. The antioxidant potential of various other parts of *E. Laevis* needs to be explored.

4.6 Wound healing property

A tribe of wardha district of Maharashtra, India used *E. laevis* for the management of wound healing and found interesting results. Similarly, folklore practitioners of Garasia community of district Sirohi, Rajasthan also recommended the paste prepared from leaves of plant for early healing of cuts.

Thakre et al. reported the wound healing Activity of paste made from leaves of *E. laevis*. Recently, a case report had been published on the local application of *E. laevis* (Khanduchakka Ghrit) in the treatment of anal fissure (Parikartika) A broad antimicrobial spectrum of barks and Leaves can be a probable rationale for its wound healing property. Till now, no investigational work is presented on the wound healing activity as well as in the management of Anal fissures. So, there could be a wide scope for future research to figure out the possible mechanism and possible phytoactive metabolites for wound healing effects.

4.7 Dental Carries

Dental caries is a format health trouble of oral cavity. Dental caries is situated by the interaction of microbes on the tooth enamel. It is anticipated that about 2.3 billion Inhabitants suffer from dental caries globally. According to the World Health Organization (WHO) the incidences of dental caries are constantly increasing It affects all races, genders and age groups The prevalence of caries is about 49% before the age of 12 years, while it progressively increases from 15 years (60%) and peaks at the age group of 60-74 (84%) All these documental reports validate the traditional uses of *E. laevis* towards Microbial diseases of oral times.

4.8 Antitrypanosomal and antiprotozoal activity

Sleeping sickness, leishmaniasis, Chagas disease, and malaria are infectious diseases caused by unicellular eukaryotic parasites “protozoans.” The available drugs for the treatment of trypanosomiasis and protozoans are old, expensive, and less effective, associated with severe adverse reactions and face the problem of drug resistance. This situation underlines the urgent need for the development of new safe, cheap, and effective drugs for the treatment of parasitic disease. The search for new

antitrypanosomal and antiprotozoal agents in this study is based on ethnomedicine. *E. amoena* show weak antitrypanosomal potential with ethanol extract of leaves, bark, and root. *E. acuminata* show antiprotozoal activity with methanol extract of leaves.

4.9 Antidiabetic activity

Diabetes mellitus, one of the fastest-growing health problems, is concerned about the use of antihyperglycemic drugs because of undesirable pathological conditions, for example, the adverse effect of metformin is gastrointestinal discomfort, pioglitazone with bladder cancer and heart failure, and sulfonylureas with hypoglycemia and weight gain. There are the ethnobotanical studies of medicinal plants used in the treatment of diabetes mellitus in many countries. A lot of genus have already reported for effective respond of antidiabetic

4.10 Anti-snake venom activity

Snakebite is an important cause of morbidity and mortality and is one of the major health problems in India and other Asian countries. *Ehretia genes* claimed to be useful in treating snake poison. The present study evaluated the potential antivenom effect *Ehretia* genus. A compound ehretianone has isolated from MeOH extract from *E. genes* is responsible for anti-snake venom activity

4.11 Antitubercular activity

In human being, tuberculosis is a contagious infectious disease primarily caused by *Mycobacterium tuberculosis*. Although regimens exist for treating tuberculosis, they are far from ideal. Development of efficient strategies for the treatment of human tuberculosis has posed a challenge, considering the increase in infections associated with the human immunodeficiency virus and immunocompromised patients. Phytoconstituents have been used in traditional treatment of many diseases; however, careful investigation of these constituents has not been undertaken with respect to treatments of tuberculosis. Two compounds ehretiolide and prenylhydroquinone have extracted from root of *Ehretia genus* are responsible for antitubercular activity

4.12 Antiarthritic Activity

Arthritis is an inflammatory disorder involving damage of joints. There are over a hundred different forms of arthritis, of which rheumatoid arthritis, osteoarthritis, and psoriatic arthritis are the most common. The treatment of any systemic disorder with allopathic drugs causes moderate-to-severe adverse effect that could cause death. Hence, alternative systems of medicine are being explored to treat diseases. *E. laevis* treatment supports antiarthritic activity. Of the three parts such as stem, leaf, and bark and fruit employed, the leaf extract was the most effective. This antiarthritic respond may be due to the presence of active constituents such as hexadecanoic acid (palmitic acid), oleanenic acid, and other fixed oils

4.13 TOXICOLOGY

The therapeutic perspective of the plant or isolated molecule is considered commendable when it is devoid of any sign of adverse effects or toxicity. It is well acknowledged that toxicity studies are of most imperative for natural products and also for their isolated compounds. Even though numerous pharmacological activities of *E. laevis* have been established to support its pervasive traditional and customary use of the plant as antioxidant, analgesic, anti-inflammatory, antimicrobial, antiarthritic, and also used in several liver, skin, inflammatory, dysentery, infectious, and dental problems. None of the research groups approved any toxicity of the plant. Moreover, the plant is widely accepted as food, as its ripened fruits are eaten by tribal people. Only one report on acute oral toxicity study has been performed as per the organization for economic cooperation and development (OECD) guidelines 423. All the methanolic extracts of leaves, stems and fruits were considered safe at the dose of 2000 mg/kg. Assessment of body weight and behavioral changes were also observed. There was no sign of toxicity (mortality), as all these three extracts showed no neurotoxic effects and were found to be safe.

Discussion

E. laevis is one of the famous plants used by various tribes of tropical Asia, Africa and Australia in ethnomedical treatment of jaundice, diarrhea, cough, syphilis, dysentery, asthma, fissure, dental, skin, infectious and liver disease. Pharmacological investigations carried out on various plant parts, crude extracts/fractions and isolated molecules of *E. laevis* grant a realistic support for its conventional uses. Recent studies have been paying attention to the investigation of antioxidant, analgesic, anti-inflammatory, antiarthritic, antimicrobial, wound healing activities.

Conclusion This review presents the bioactive phytometabolites, pharmacological and ethanopharmacological which uses fascinating therapeutic perspectives. The available literature also reveals that this plant is use for variety of purpose including cosmetics, pot herbs, wood, stone dye and ornaments and the inner bark is use as a food. The plant has also been documented in the traditional system of medicine due to its extensive uses to treat respiratory system disease, gastrointestinal tract infection and endocrine system disease.

MARKETED PRODUCT

Fig no: - 05 Khandu chakka oil

Khandu chakka oil is an ayurvedic medicine formulated with the natural ingredients to provide effective pain relief. It is powerful blend of herbs and oils that works synergistically to alleviate various types of pain.

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