

A REVIEW ON PHYTOCHEMICAL AND PHARMACOLOGICAL OF *EUCALYPTUS GLOBULUS*: A MULTIPURPOSE TREE

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ABSTRACT

The phytochemical and pharmacological studies reported in the present review confirm the therapeutic value of *Eucalyptus globulus*. The results of the above studies support the use of these plants for human and animal disease therapy and reinforce the importance of the ethnobotanical approach as a potential source of bioactive substances.

KEYWORDS: *Eucalyptus globulus*, Antibacterial, Anticancer, Antiviral, pharmacological.

INTRODUCTION

Eucalyptus globulus was discovered on the island of Tasmania in 1792 by French explorers and was one of the first eucalypt species to be formally described. The primeval eucalypt forests of Tasmania were amongst the tallest forests in the world and *E. globulus* trees (fig1) up to 101 m in height were recorded. By the late 1800's, trees 60-90 m high were regularly harvested from southeastern Tasmania and shipped throughout the world for wharf piles (100-120 feet in length and 20 inches square). By 1905, four million feet of wharf piles had been supplied for British. The timber was also in great demand for railway sleepers, street paving blocks and mine supports. Various species of *Eucalyptus* are cultivated, particularly in subtropical and warm temperate regions, on account of their economic value. *Eucalyptus* species (Family- Myrtaceae) are remarkable for their rapid growth. Some species of them, in their natural habitat, attain gigantic sizes and are among the tallest trees of the world. Most of the species are popularly called "gum trees" although the exudation from them is not a gum, but an astringent; a tanniferous substance called "kino". There are over 500 species of *Eucalyptus*. Medicinal plants have been used as a source of remedies since ancient times¹⁻²³. The ancient Egyptians were familiar with many medicinal herbs and were aware of their usefulness in treatment of various diseases. Herbal sector has its roots in the very rich and diverse health care traditions of our country that include the codified systems like Ayurveda, Siddha, Unani, Tibetan and Homeopathy on one hand and the largely oral folk traditions on the other.

In Indian traditions, all the plants are considered to have medicinal properties:

"Jagatyevamanoushadham na kinchit
vidyate dravyam vasatnanartha yoga yoh"

Jivaka (*Astanga Hriday* SU. 9-10)

It literally means "there is no plant in the world which is non-medicinal³² or which cannot be used as medicine". This means that all the 19,000 odd flowering plants recorded from India have potential medicinal properties. The major reason for this vast variation in estimates of the number of medicinal plant species in use in the country seems to be mainly due to the lack of any single consolidated list on the subject, even though state-wise or region-wise checklists of medicinal plants are available for a few states viz. Gujarat, Himachal Pradesh, South West Bengal, Shivalik Ranges in Haryana and Chhatisgarh. The consolidated checklist of medicinal plants, enumerated across the country under the All India Coordinated Study on Ethnobotany, is still awaited. Phytomedicines derived from plants have shown great promise in the treatment of intractable infectious diseases including viral infections. Single and Poly herbal preparations have been used numerously throughout

history for the treatment of various diseases. Many studies have been carried out to extract various natural products for screening antimicrobial activity but attention has not been focused intensively on studying the combinations of these products for their antimicrobial activity. One of these medicinal plants, many species of the genus *Eucalyptus* from the Myrtaceae family are used in many parts of the world for the treatment of a wide variety of diseases including microbial infections.

Scientific Classification

Kingdom: Plantae

Subkingdo: Tracheobionta

Superdivision: Spermatophyta

Division: Flowering plants

Class: Dicotyledons

Subclass: Rosidae

Order: Myrtales

Family: Myrtaceae

Genus: *Eucalyptus*

Species: *Eucalyptus globulus* Labill.

Vernacular Names

It has many Indian names, depending on the geographical region or the language, for example: *Eucalyptus globules* (Latin name), Tail Parn, Sugandh Patra (Sanskrit name), Gum Tree, Gum *Eucalypt* (English), Neelgir (Hindi), Nilgiri (Kannad), Harit Parn (Gujrati).

Botanical Descriptions

Leaves: Nearly all *Eucalyptus* are evergreen but some tropical species lose their leaves (fig 2) at the end of the dry season. Although mature *Eucalyptus* trees are usually towering and fully leafed, their shade is characteristically patchy because the leaves usually hang downwards. The leaves on a mature *Eucalyptus* plant are commonly lanceolate, petiolate, apparently alternate and waxy or glossy green. In contrast, the leaves of seedlings are often opposite, sessile and glaucous. But there are many exceptions to this pattern³¹.

Flowers: The most readily recognisable characteristics of *Eucalyptus* species are the distinctive flowers and fruit (capsules or "gumnuts"). Flowers (fig 3) have numerous fluffy stamens which may be white, cream, yellow, pink or red; in bud, the stamens are enclosed in a cap known as an operculum which is composed of the fused sepals or petals or both. Thus flowers have no petals, but instead decorate themselves with the many showy stamens. As the stamens expand, the operculum is forced off, splitting away from the cup-like base of the flower; this is one of the features that unite the genus.

Bark: The appearance of *Eucalyptus* bark (fig 4) varies with the age of the plant, the manner of bark shed, the length of the bark fibres, the degree of furrowing, the thickness, the hardness and the colour. All mature eucalypts put on an annual layer of bark, which contributes to the increasing diameter of the stems. In many species, the dead bark is retained. The extraordinary coloured bark of *Eucalyptus deglupta* native to South East Asia. Bark (fig.5a,5b,5c) consists of long fibres and can be pulled off in long pieces(Stringybark), is hard, rough and deeply furrowed(Ironbark), bark is broken up into many distinct flakes(Tessellated), has short fibres (Box),this has the bark coming off in long thin pieces but still loosely attached in some places(Ribbon).

PHYTOCONSTITUENTS

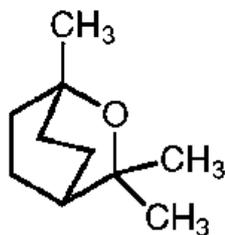
Chemical constituents of the wood of *Eucalyptus globulus*

The composition of lipophilic extractives in the chloroform soluble fraction of the acetone extract from *Eucalyptus globulus* wood has been examined. The lipid extract was fractionated by solid-phase extraction on aminopropyl-phase cartridges into four different fractions of increasing polarity. The total lipid extract and the resulting fractions were analyzed by gas chromatography and gas chromatography-mass spectrometry, using high temperature capillary columns. The main compounds identified included sterols, sterol esters, fatty acids, steroid ketones, hydrocarbons and triglycerides. Minor compounds such as fatty alcohols, mono- and diglycerides, waxes and tocopherols were also identified among the lipids from *E. globulus* wood. Sterols, sterol esters, fatty acids, steroid ketones, hydrocarbons and triglycerides were the major² compounds identified.

Chemical constituents of the leaves of *Eucalyptus globulus*

The isolation of the water-distilled volatile oil from the leaves of *Eucalyptus globulus* Labill, the qualitative examination of the chemical constituents of this essential oil and their quantitative determination by direct comparison with results from MS databases attached to the GC-MS instruments following GC-MS analysis.

The essential oil consisted mainly of oxygenated monoterpenes, monoterpenes and oxygenated sesquiterpenes. Of these, 1, 8-eucalyptol (72.71 %), α -terpineol (2.54 %), terpinen-4-ol (0.34 %), and linalool (0.24 %) were the main oxygenated monoterpenes, while α -pinene (9.22 %), and β -pinene (0.4 %) were the main monoterpenes and α -eudesmol (0.39 %), (-)-globulol (2.77 %), and epiglobulol (0.44 %) were the main sesquiterpene. Several significant compounds were α -terpineol acetate (3.1 %), geranyl acetate (0.71 %), *L*-pinocarveol (0.36 %), β -sabinene (0.25 %), and terpinolene (0.19 %). A portion (0.26 %) of the total constituents remains unidentified³.



1,8-cineole (eucalyptol)

47 constituents of the essential oil from *Eucalyptus globulus* Labill grown in the Cangshan mountain region in the Yunnan Province of China were successfully identified and determined.

Chemical constituents in the fruits of *Eucalyptus globules*:

Fifteen compounds were obtained and identified as beta-sitosterol, betulinic acid, stigmasterol, euscaphic acid, 2 α -Hydroxybetulinic acid, macrocarpal B, macrocarpal A, oleanolic acid, 3,4,3'-O-trimethylellagic acid, 3-O-methylellagic acid 4'-O-(2''-O-acetyl)- α -L-rhamnopyranoside, camaldulenside, 3-O-methylellagic acid 4'-O- α -L-rhamnopyranoside, 3-O-methylellagic acid, ellagic acid and gallic acid⁴.

PHARMACOLOGICAL ACTIVITY

Eucalyptus (Myrtaceae) is one of the world's most important and most widely planted genera. In Australia, this genus is the second largest genus, after *Acacia*, and contains about 750 species. UAs an expectorant for symptomatic treatment of mild inflammation of the respiratory tract and bronchitis. Also for symptomatic treatment of asthma, fever and inflammation of the throat described in pharmacopoeias and in traditional systems of medicine. Treatment of cystitis, diabetes, gastritis, kidney disease (unspecified), laryngitis, leukorrhoea, malaria, pimples, ringworm, wounds, ulcers of the skin, urethritis and vaginitis uses described in folk medicine, but not supported by experimental or clinical data. Myrtaceous plants are known to be rich source of biologically active terpenoids and polyphenols, including flavonoids, phloroglucinol derivatives, and tannins. Previous phytochemical studies on the *Eucalyptus globulus* Labill. one new phloroglucinol derivative named eucalyptone G, together with nine known compounds. The antibacterial activity of the new compound has been studied. Eucalyptone G was found to be active against the Gram-positive *Bacillus subtilis* and *Staphylococcus aureus* and caused an inhibition zone of 16 mm diameter after 24 h of incubation at 37 °C. Also, highly active against Gram-negative *E. coli* with an inhibition zone of 19 mm diameter²².

Anthelmintic activity: The present investigation concludes that *E. globulus* oil has anthelmintic potential due to the presence of borneol, linalool, cineol, geranyl acetate, anethol, saffrol as phytoconstituents. Essential oil from *E. globulus* contains 1,8-cineole as the major component and is used in the treatment of pulmonary infections and also exhibits antibacterial activity⁵.

Wound healing activity: Intra-dermal administration of the essential oils from the leaves of *Eucalyptus* hybrid and seeds of *Seseli indicum* increased cutaneous capillary permeability when tested in Evan's blue treated rabbits. This effect may be beneficial in their probable wound healing activity⁶.

Antibacterial and antifungal activity: A 50% EtOH extract of *Eucalyptus globulus* leaves have antibacterial activity⁷ against oral pathogenic microorganisms with MIC values ranging from 0.20 micrograms/mL to 6.25 micrograms/mL. A 50% EtOH-soluble material was extracted from the dried leaves of *E. globules* shows appreciable antibacterial activity against *S. mutans* Ingbritt and *P. gingivalis* ATCC 33277 (causes dental caries and periodontal disorders) with MICs values 12.5 and 6.25 μ g/ml. Dried residue of methanolic extract of *Eucalyptus globulus* leaves showed antimicrobial activity against *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Candida albicans* with minimum inhibitory concentration of 5.0, 10.0, 10.0, 1.25 mg/ml respectively. Phloroglucinol- sesquiterpene coupled compounds, macrocarpals H, I, and J showed potent antibacterial activity and inhibitory effect of glucosyltransferase²⁶. Freshly prepared camphor oil from *Eucalyptus globulus* with or without glycerol dilutions gave complete cure of human facial demodicidosis with concentrations of 100%, 75% and 50% 40. *Eucalyptus globulus* leaf extracts⁸ and oil showed antifungal property as they progressively inhibited the growth of *Malassezia furfur* on Sabouraud's destrose agar medium.

Antidiabetic (antihyperglycemic): *Eucalyptus globulus* is used as a traditional treatment for diabetes. Incorporation of *Eucalyptus globulus* in the diet (62.5 g/kg) and drinking water (2.5 g/L) reduced the hyperglycemia and associated weight loss of streptozotocin-treated mice. An aqueous extract⁹ of *Eucalyptus globulus* (AEE) (0.5 g/L) enhanced 2-deoxy-glucose transport by 50%, glucose oxidation by 60% and incorporation of glucose into glycogen by 90% in abdominal muscle of mice. In acute, 20 min incubation, 0.25-0.5 g AEE/L evoked a stepwise 70-160% enhancement of insulin secretion from the clonal pancreatic beta-cell line (BRIN-BD11). These data indicate that *Eucalyptus globulus* represents an effective

antihyperglycemic dietary adjunct for the treatment of diabetes and a potential source for discovery of new orally active agent(s) for future therapy.

Antiplateque: *Eucalyptus globulus* may be useful in inhibiting dental plaque¹⁰ formation.

Antitumor: Antitumor-promoting activity of Euglobals Ia1, Ia2, Ib, Ic, IIa, IIb, IIc, III, IVa, IVb, and V and VIII has been tested *in vitro* on 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced Epstein-Barr virus early antigen (EBV-EA) 32 activation test system. Euglobal-III²⁴ showed strong inhibitory activity, followed by euglobals Ib, IIa, Ic, Ia1, Ia2. *Eucalyptus globulus* oil¹¹ inhibits the nuclear translocation of NF-kappa B induced by LPS in THP-1 cells.

Antiviral: Twelve euglobals from *Eucalyptus globulus* and their twenty-six related compounds were examined for their inhibitory effects on Epstein-Barr virus activation by a short-term *in vitro* assay. The results showed that most of the euglobals having monoterpene structures, and euglobal-III had strong inhibitory activity. *Eucalyptus globulus* oil has antiviral¹² activity against herpes simplex virus (herpes simplex virus-1 and -2).

Antihistaminic: Hexane extract of leaves, ethanol extract of fruits and leaves¹³ of *Eucalyptus globulus* inhibited IgE dependent histamine release from RBL-2H3 cells.

Anti-inflammatory: 1,8-cineole, major constituent present in volatile oil of *Eucalyptus globulus* is a strong inhibitor of cytokines, that might be suitable for long term treatment of airway inflammation in bronchial asthma and other steroid-sensitive disorders¹⁴. In addition, essential oil extracts from the *Eucalyptus globulus* produced anti-inflammatory effects, as demonstrated by inhibition of rat paw edema induced by carrageenan and dextran, neutrophil migration into rat peritoneal cavities induced by carrageenan, and vascular permeability induced by carrageenan and histamine¹⁵. *E. globulus* oil has the anti-inflammatory effect on chronic bronchitis induced by lipopolysaccharide in rats and the inhibition effect on hypersecretion of airway mucins¹⁶.

Respiratory Diseases: *Eucalyptus globulus* have been used in traditional medicine in the treatment of bronchitis, asthma and other respiratory diseases¹⁷. Cutaneous application of essential oils of *Eucalyptus globulus* to mice suppressed the cellular inflammation of skin. This suggests that essential oils using in aromatherapy massage may suppresses the inflammatory symptoms related with neutrophil accumulation and edema¹⁸.

Antimalarial: Intragastric administration of a hexane leaf extract to mice (100mg/kg body weight) did not inhibit the growth of *Plasmodium berghei*. Furthermore, administration of an aqueous (3.48 g/kg body weight) or chloroform (264mg/kg body weight) leaf extract to chickens by gastric lavage did not inhibit the growth of *P. gallinaceum*. An ethanol-water extract²⁷ of the leaves inhibited the growth *in vitro* of *P. falciparum* at a concentration of 75mg/ml.

Antioxidant: The methanol extracts of *Eucalyptus globulus* showed efficiency in preventing the oxidation process¹⁹. Hyperglycemia in diabetes has been associated with increased formation of reactive oxygen species (ROS) and oxidative damage to tissue compounds. The aim of this study was to evaluate the effects of eucalyptus in the diet (20 g/Kg) and drinking water (2.5 g/L) on lipid peroxidation, protein oxidation and antioxidant power in plasma and liver homogenate, as well as glycated-Hb (HbA_{1c}) of blood in streptozotocin-induced diabetic rats for a period of 4 weeks. Diabetes induced in rats by a single intraperitoneal injection of streptozotocin (STZ, 65 mg/Kg). At the end of the treatment period, the level of plasma glucose, plasma and liver malondialdehyde (MDA, the main product of lipid peroxidation), protein carbonyl (PC, one of the protein oxidation products) and HbA_{1c} increased and ferric reducing antioxidant power (FRAP) decreased in diabetic rats compared to normal rats. *Eucalyptus* administration for 4 weeks caused a significant decrease in the plasma glucose levels, plasma

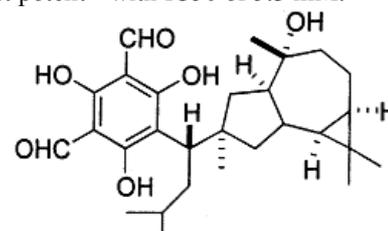
and liver MDA, PC and HbA_{1c}, also a concomitant increase in the levels of FRAP in diabetic treated rats²⁸.

Larvicidal: *Eucalyptus globulus* leaves has potent action against *Culex quinquefasciatus* and *Culex tritaeniorhynchus*²⁰.

Nerve Blocker: Terpeneol, a relatively nontoxic, volatile monoterpene alcohol, is a major component of the essential oil of *Eucalyptus globulus* (*Eucalyptus*), is widely used in folk medicine and aromatherapy. Terpeneol induced a dose-dependent blockade of the compound action potential (CAP) of rat sciatic nerve²¹.

Miscellaneous Activities

A number of macrocarpals (A–E) iso-lated from *Eucalyptus globulus* possessed anti-HIV RTase inhibitory activity, with IC50 ranging from 5 to 12 mM. Amongst these, macrocarpal B was found to be most potent²⁹ with IC50 of 5.3 mM.



The lethality varied in adults and plant extracts of mixture; *Eucalyptus globulus*, *Cymbopogon citratus*, *Artemisia annua*, *Justicia gendarussa*, *Myristica fragrans*, *Annona squamosa*, and *Centella asiatica* were found to be most effective against³⁰ *Anopheles stephensi*.

AYURVEDIC PRODUCTS OF EUCALYPTUS

Prokapha massage oil, Pure essential soap eucalyptus, Cold-pressed body massage oil eucalyptus and black pepper, Amrutanjan pain balm, Dr.kohli's muscle and joint oil. Ayurvedic cleaser for oily skin, Tea tree oil eucalyptus soap etc.

CONCLUSION

The extensive survey of literature revealed that *Eucalyptus* species is an important source of many pharmacologically and medicinally important chemicals, such as Essential oils, terpenoids which have been use in aromatherapy. Various *Eucalyptus* species have also been widely studied for their various pharmacological activities like analgesic, antifungal, anti-inflammatory, antibacterial, antidiabetic, antioxidative, cytochrome p450 enzymes inhibitor²⁵, Antiviral, Antitumor, antihistaminic, anticancer cytochrome p450 inhibitor and hepatoprotective properties. Although aromatherapy is pleasant, inexpensive, and has little side effects (except for rare allergies), there is little evidence that it is effective in patients undergoing medical interventions. Over the past decade, herbal medicine has become an item of global importance with both medicinal and economic implications. In addition pure neelgiri eucalyptus oil used for pain on legs, joints, throat pain, dengue fever, cold and chest congestion. The history of medicine includes many ludicrous therapies, never the less, ancient wisdom has been the basis of modern medicine and will remain as one important source of future medicine and therapeutics. In present review, we have made an attempt to congregate the botanical, phytochemical, pharmacological and ethno pharmacological information on eucalyptus species.

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Fig1. *Eucalyptus* Tree



Fig 2. Leaves of *Eucalyptus*

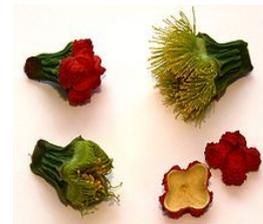


Fig 3 . Flower buds and opercula of *Eucalyptus*



Fig4. *Eucalyptus* bark



Fig5.a]Bark,

Fig5.b] Coloured bark,

Fig 5.c] White Box bark