

Review Paper

## Approach of *Eucalyptus globulus* plant parts for Human Health Safety and Toxicological Aspects

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### ABSTRACT

In traditional medicine, *Eucalyptus globulus* (eucalyptus) was used for the treatment of common infections such as bronchial affections, cough, asthma, pharyngitis, cold, fever and wound. It is used internally for the treatment of asthma, fever, flu, whooping cough, loss of appetite, dyspeptic complaints, inflammatory and infectious diseases of kidneys and bladder, diabetes, rheumatic complaints. It is used externally for wounds, acne, poorly healing ulcers, stomatitis, bleeding gums, rheumatism, neuralgia, gonorrhoea. Traditional use for the treatment of several medical conditions has been reported. Some of the cited therapeutic indications are insufficiently described and supported by scientific data, thus it is recommended to list only the indications that are appropriate for traditional use without the supervision of a medical practitioner for diagnostic purposes or for prescription or monitoring of treatment. It is effects on ecological system through directly or indirectly exposure to the environment.

**Keywords:** Eucalyptus globules, Leaf extract, Bio-safety, Bio-pesticide, Eco-toxicology.

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## Introduction

Eucalyptus plant belongs to the Myrtaceae (Myrtle) family. Commonly known as Safeda in Hindi. The products of this tree have multifold uses i.e. medicinal as well as insecticide/herbicide/pesticides, but due to harmful side effects of synthetic products and the fact that plants are easily accessible, interest in drugs of herbal origin has significantly increased. Scientific research is being conducted all over the world to determine whether plants that are traditionally used to treat various diseases are actually appropriate for their intended use. Eucalyptus leaf extract, a natural food additive, is commercially available as steam distillate, or an ethanol extract of eucalyptus (*Eucalyptus globulus*) leaf and is officially approved in the "Lists of Existing Food Additives in Japan"(Sakai et al., 2006).

Eucalyptus is a tall evergreen tree native to Australia, nowadays found around the world. It now grows in almost all tropical and subtropical areas and is cultivated in many other climates. Much research has been conducted on the medicinal properties of *Eucalyptus* spp. of the different species, *E. globulus* has been the most widely studied. The ecological effects of eucalypt plantations on the water cycle, the local or regional climate, the microclimate within the forest, surface run-off of water (which may affect water quality and the amount of erosion); soil moisture content, and the recharge of aquifers (M.E.D. Poore et al., 1985). The toxic effects are caused by reactive species called "oxygen radicals". Some of the reactive oxygen species (ROS), including hydrogen peroxide, singlet oxygen, hydroxyl and superoxide radicals, have positive roles in energy production in In-vivo systems, phagocytosis, intercellular signal transfer, regulation of cell growth and the synthesis of important biological compounds. The defense systems that work to prevent ROS damage in the body are called antioxidant defense systems (Basak et al., 2010).

*Eucalyptus globulus* in order to show that plant waste stem bark, which is shed periodically can be utilized as food dye with high antioxidant activity (Vankar et al., 2006). The oral administration of the eucalyptus leaf extract caused a significant reduction of serum triglyceride and cholesterol on diabetic rat (Eidi et al., 2009).

Several hundred species of *Eucalyptus* contain volatile oils which are classified into three types; medicinal, perfumery and industrial. Some studies have demonstrated that leaf extract and essential oil of *Eucalyptus* spp. have antifungal, repellent, antibacterial, analgesic and anti-inflammatory activities (Boland D. J. et al., 1991). In India, the leaf essential oil is traditionally used externally as a mosquito repellent and as an insecticide. In addition to the target pathogen, pesticides may also kill various beneficial organisms and their toxic forms can persist in soil (Hayes & Laws 1991).

## Review of Literature

The eucalyptus tree that grows in Southern Anatolia is known as 'Adana eucalyptus'. Eucalypts must have been the very early European explorers and collectors, no botanical collections of them are known to have been made until 1770 when Joseph Banks and Daniel Solander arrived at Botany Bay with Captain James Cook. There they collected specimens of *E. gummifera* and later, near the Endeavour River in northern Queensland, *E. platyphylla*; neither of

these species was named as such at the time. Eucalyptus is used to treat many human ailments and some livestock ailments. Eucalyptus extracts, oils, or fresh leaves are used in steam inhalation treatments, consumed in teas, or used in bathing. While Eucalyptus trees are well known for their medicinal properties and their strong fragrance, they are best known as the feed source for koala. The koala only eats a few species of Eucalyptus. However, there are over 500 species of the tree.

The material used in our study is the leaf of *Eucalyptus camaldulensis* Dehnh. (Myrtaceae). Its leaves are 15-30 cm long, 2-5 cm wide, hard, crisp and yellowish green in color (Yang, et al., 2004). The Eucalyptus genus is the most cultivated worldwide. The preferred choices for companies and forest farmers due to its growth potential and pathology resistance and high economic value and consolidated silvicultural practices and great potential for phytoremediation and waste disposal and also tolerance to the presence of chromium in the soil (H.N. Cipriani et al., 2012).

Eucalyptus Plants have been used for the treatment of diseases for a very long time. The leaves and oil of the eucalyptus plant are used for medicinal purposes. Eucalyptus oil consists of the volatile oil distilled from the fresh leaves and branch tops of the eucalyptus plant. Topical ointments containing eucalyptus oil have been used in traditional Aboriginal medicines to heal wounds and fungal infections. Teas containing eucalyptus leaves were also used to reduce fevers. The therapeutic uses of eucalyptus soon spread to other traditional medicine systems, including Chinese, Indian (Ayurvedic), and Greco-European (Trivedi & Hotchandani, 2004). In vitro cytotoxicity of all the six extracts (n-hexane extract, chloroform extract, ethyl acetate extract, ethanolic extract, 50% ethanolic extract and aqueous extract) of leaf parts of *Eucalyptus citriodora* was estimated against three human cancer cell lines. Growth inhibition in a dose dependent manner was observed in all the cell lines by all the extracts (Bhagat et al., 2009).

Efficiency of Eucalyptus extract was examined as an acceptable alternative for chemical control. Both seed extract and leaf extract were screened in laboratory conditions (Shereen M. Elbanna 2006). Extracts (aqueous or oil) of some plant materials are toxic to some species of insect pests of crops and others are less toxic. These extracts with lethal activity on insects may be applied single or in mixtures with less toxic plant extracts to ascertain their complimentary or synergistic attributes in the management of crop pests. (Oparaeke A.M et al., 2005)

The ability of toxic compounds to penetrate the fungal or bacterial cell wall is also likely to be an important factor. Chemotherapeutic agents, used topically or systemically for the treatment of microbial infections of humans and animals, possess varying degrees of selective toxicity. An increasing public awareness of 'green issues', plant volatile oils, including those from Eucalyptus, offer a more eco-friendly alternative to conventional formulations in a number of sectors where antimicrobial action is desirable (EMA, 2012). The antibacterial activity of the leaf extracts of *Eucalyptus camaldulensis* was studied against *Klebsiella* spp, *Salmonella typhi*, *Yersinia enterocolitica*, *Pseudomonas aeruginosa* (Gram-negative), *Staphylococcus aureus* and *Bacillus subtilis* by the agar diffusion method. (Ayepola & Adeniyi 2008). The administration of aqueous extract of eucalyptus induced undesired

behavior and external features include general weakness, decrease in physical activities and loss of body furs, ruffle fur and changing in white coat color which were more pronounced in most mice and also decrease blood glucose level (Aglal A. Alzergy et al., 2010).

The effect of eucalyptol on the liver microsomal enzyme activity of foetal and newborn rats was studied in Sprague-Dawley rats. A dose-related effect of body weight gain and absence of a normal degree of hepatic centrilobular cytoplasmic vacuolization was observed in male rats (EC 2002). Sucrose is more lipogenic than starch, and the extreme ingestion of sucrose induces adiposity and obesity. A rat fed a high-fructose diet, the plasma and hepatic triacylglycerol concentrations were significantly decreased by ELE. Which is inhibits the intestinal fructose absorption, can suppress adiposity in rats that ingest large amounts of sucrose or fructose (Sugimoto K. et al., 2005). The hematological & biochemical changes and histopathological effects were founded of the essential oils from Eucalyptus Eucalyptus globules L. on liver and kidney of albino rats. A significant increase of WBC counts and decrease of hemoglobin concentration and platelets counts as well as RBC counts and serum GOT & GPT enzymes were a significantly increase. In this study was founded of histopathological changes in liver as congestion of the blood vessels and inflammatory infiltration and desquamation of the epithelial cells of the renal tubules (Shehata E. M. Shalaby et al., 2011).

The antimicrobial agent poses a serious problem for physicians, and necessitates ongoing development of new antimicrobial agents that can inhibit the growth of or kill resistant organisms. Eucalyptal (1, 8-cineole) is the active ingredient of eucalyptus oil that is responsible for its various pharmacological activities. Eucalyptus species are effective against a range of pathogens, non-pathogens and spoilage organisms. The antibacterial effects of Eucalyptus globulus leaf extract against pathogenic bacteria isolated from patients with respiratory tract infection (Salari et al., 2006). The effects of repeated administration of varying concentrations of the aqueous extract of Eucalyptus globulus leaves on some biochemical parameters of rat liver has also been studied. The activities of acid phosphatase (ACP), alkaline phosphatase (ALP), superoxide dismutase (SOD) and the level of malondialdehyde (MDA) were determined in the liver and serum (Arise et al., 2009). Studies using clonal pancreatic cells showed that aqueous extract of Eucalyptus leaf extract a dose-dependent stimulatory effect on insulin secretion. Eucalyptus administration significantly improved the hyperglycemia, polydipsia, polyphagia, and it also compensated weight loss of diabetic rats (Bokaeian M. et al., 2010). Eucalyptus globulus leaf extract (ELE) suppresses the postprandial elevation of serum fructose concentrations in the portal, cardiac and peripheral blood after sucrose ingestion. ELE potentially prevent and treat disorders induced by excessive fructose intake (Sugimoto K. et al., 2010).

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 activity (Dahanukar et al., 2000). The reduction in both weeds caused by leaf residues of E. globules ranged from 53 to 68.6 % at 70 DAS. Phenol contents in foliage and rhizomes of both Cynodon dactylon and Echinochloa colonum were increased with increasing the residue concentrations. A high-

performance liquid chromatography analysis showed that the following acids; caffeic, ferulic, benzoic, chlorogenic, hydroxybenzoic and cinnamic were present in *Eucalyptus globulus* extract (El-Rokiek, Kowthar G. et al., 2011). The essential oils of *Eucalyptus g.* stood out promoting adults *S. zeamais* mortality, however at low levels of efficiency. *Eucalyptus globules* in the stored corn grain protection against *S. zeamais*, through the determination of mortality effect on exposed individuals to treated grains (Singh A. et al., 2012) as a potential bio-pesticide. Eucalypts are used for pulp and rayon industries. They are reducing stream discharge, reduce soil fertility and cause soil toxicity. So, they are concerned with the negative effects of eucalyptus plantation and consume more water (R.M. Palanna, 1996).

### Chemical Compounds

*E. globulus* is the one of the most important species of *Eucalyptus*. Within species the quantity of essential oil and the specific compounds in the essential oil and extracts of dry and fresh leaves, buds, mature fruit, and bark vary with the origin of the tree and the age of the leaves. The essential oil in the leaves is commonly used for medicinal purposes. The quantity of essential oil ranges from less than 1.5 to over 3.5%. On average, between 70 and 95% of the oil is 1,8-cineole (eucalyptol). *Eucalyptus globulus* contain of 1,8- cineol, its cause drowsiness, ataxia, seizures, nausea, vomiting, coma (Woolf 2003). The pharmacological activity of eucalyptus is related to the content of several classes of secondary metabolites such as essential oils, tannins, flavonoids, sterols, carotenoids, tannins, saponins, triterpene alcohols, polysaccharides, it has been found that stem bark of eucalyptus contains 3-O-methylellagic acid 3'-O- $\alpha$ - 3''-acetylramnopyranoside, 3-O- methylellagic acid 3'-O- $\alpha$ - 2''-acetylramnopyranoside. The important compounds found in the leaves, buds, branches and bark of *E. globulus* include taxifolin and eriodictyol (antioxidants), rutin, tannins, gamma-terpinene and terpineol. *Eucalyptus spp.* contains high levels of phenolics and terpenoids which can be toxic (Whitman and Ghazizadeh, 1994). Five major compounds were purified from "Eucalyptus leaf extract" by the preparative HPLC. Each component was identified as gallic acid, quercetin 3-O- $\beta$ -D-glucuronide, kaempferol 3-O- $\beta$ -D- glucuronide, 2,4-dihydroxy-3-(3-methyl-1-butenyl)-5-methylbenzaldehyde 6-O-b-D-glucopyranoside, named globuluside and macrocarpal I by NMR and FAB-MS (Sakai et al., 2006).

It was observed that the highest yield of oil was 3.5% achieved in the month of July on 01.07.08 among 1-30 days after 10 days interval. But the yield of the oil was decreased gradually during the months of August, September, October, November and the lowest yield of oil was 0.08% found in the month of December on 30.12.08. The yield of oil depends on season (A. M. Khan et al., 2012). Some of these properties have been related to the action of these compounds as antioxidants, free-radical scavengers, quenchers of singlet and triplet oxygen. Antioxidant activity of phenolic compounds is correlated to some structure-activity relationships, such as redox properties and the number and arrangement of the hydroxyl groups. *Eucalyptus* is a tree of ancient medicinal repute. It grows as a wild and common tree throughout India and other tropical climate. Activities contributed to this compound include:

anesthetic, antibronchitic, anticatarrh, antilaryngitic, antipharyngitic, antiseptic, CNS-stimulant, fungicide, hepatotonic, herbicide, hypotensive, pesticide, and sedative (Ponte et al., 2008).

## Medicinal Uses

Eucalyptus has been used traditionally medications. Today, eucalyptus is commonly used in remedies to treat coughs and the common cold. It can be found in many lozenges, cough syrups, rubs, and vapor baths. Herbalists recommend the use of fresh leaves in teas and gargles to soothe sore throats and treat bronchitis and sinusitis. Ointments containing eucalyptus leaves are also applied to the nose and chest to relieve congestion. Eucalyptus oil helps loosen phlegm, so many health care providers recommend inhaling eucalyptus vapors to help treat bronchitis, coughs, and the flu. On the skin, eucalyptus oil has been used to treat arthritis, boils, sores and wounds. Eucalyptus oil is also rich in cineole (a potent antiseptic that kills bacteria responsible for bad breath. Eucalyptus leaves contain tannins (which are believed to help reduce inflammation), flavonoids (such as quercetin, which has antioxidant properties), and volatile oils. Eucalyptus oil is a rich source of the antiseptic substance cineole (sometimes referred to as eucalyptol).

Eucalyptus oil is also useful for Alertness, antibacterial, antifungal, anti-inflammatory, antimicrobial, antioxidant, antiviral, aromatherapy, arthritis, astringent, back pain, bronchitis, burns, cancer prevention, cancer treatment, chronic obstructive pulmonary disease (COPD), deodorant, diabetes, diarrhea, ear infections, emphysema, fever, flavoring, fragrance, herpes, hookworm, inflammation, influenza, insect repellent, leukemia, liver protection, muscle/joint pain (applied to the skin), muscle spasm, nerve pain, parasitic infection, rheumatoid arthritis (applied to the skin), ringworm, runny nose, scabies, shingles, sinusitis, skin infections in children, skin ulcers, snoring, stimulant, tuberculosis, urinary difficulties, urinary tract infection, whooping cough, wound healing (Angela E. Sadlon and Davis W. Lamson (2010).

Some contents tannins, flavonoids and phenolic acids are particularly attractive as they are known to exhibit various beneficial pharmacological properties such as vasoprotective, anticarcinogenic, anti-neoplastic, anti-viral, anti-inflammatory, as well as anti-allergic and anti-proliferative activity on tumor cells (Vankar et al., 2006).

Eucalyptus extract was found to significantly reduce the blood glucose level in diabetic animals but failed to restore the liver glycogen level, whereas insulin lowered blood glucose and restored liver glycogen to high concentration. Eucalyptus extract appears to exert an antioxidative activity demonstrated by the increase of catalase, superoxide-dismutase and glutathione-peroxidase activities in liver and kidney, and a lowering of lipids peroxidation level in these organs (Khaled et al., 2009). The plant has widespread application as a medicinal plant. In Nigeria and some parts of sub – Saharan Africa, its medicinal uses include the use of its oil as a remedy for cough and cold. The gum when boiled with water and sugar, become a liquid drink used to treat pulmonary complaints and as a general anesthetic for tooth ache (Imam, A.A. and Wudil, A.M., 2011).

## Future Aspects

Many researchers have been done and will be continuing in future on this. Natural products are widely using by humans worldwide because these products does not have any side effect. Eucalyptus leaf extracts are such a wide spread area in field of medical and science. Eucalyptus leaf extracts contain tannins, flavonoids, sterols, carotenoids, tannins, saponins, triterpene alcohols, polysaccharides and many other important compounds and these compounds show very useful and important properties such as anti-diarrheal, anti bacterial, anti cancer, anti microbial, anti malarial, hepatoprotective effect, anti-oxidant, anti allergic, anti glyceic, anti inflammatory, wound healing, analgesic and many more.

Information pertaining to general aspects of Eucalyptus is available on literature, books and journals, news papers, internet med line etc. Lot of work has been done on Eucalyptus products. But there is lack of information on bio-safety studies in laboratory animals which are chosen as experimental model for human being and Eco-toxicological aspects.

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