



## Review Paper

# An approach on phytochemistry and pharmacological studies of *Eucalyptus globulus* plant parts

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Available online at: [www.isca.in](http://www.isca.in), [www.isca.me](http://www.isca.me)

Received 2<sup>nd</sup> May 2017, revised 6<sup>th</sup> July 2017, accepted 14<sup>th</sup> July 2017

## Abstract

The medicinal plants played an importance role throughout world and primarily used against for the treatment and prevention of number of diseases. Among the medicinal plants, *Eucalyptus globulus*, a diverse genus of flowering trees and shrubs belongs to the family Myrtaceae, commonly known as blue gum, cultivated in palni, Nilgiris, shimla hills, Punjab etc. This plant contains phytochemical constituents which contain tannins, alkaloids, terpenoids and propanoids, which are present in the leaves, root and stem of the plants. From ancient, *Eucalyptus globulus* was used for the treatment of some common infections such as cough, cold, asthma, bronchial affections, fever, pharyngitis, stomatitis, neuralgia, bleeding gums, gonorrhoea and wounds. Various types of chemical constituents such as (+)-oleuropeic acid, Isoleptospermone, Sideroxylonal C, cypellogins A, B and C, cypellocarpins A, B and C, grandinol, essential oils and many others have been isolated from the *Eucalyptus globulus* plant. Many compounds from *Eucalyptus globulus* exhibit the many interesting pharmacological activities such as antiviral, antimicrobial, antitumor, antioxidant activities and so on. This present review reveals that all information on phytochemical and pharmacological activity of the *Eucalyptus globulus* has been performed by different methods.

**Keywords:** *Eucalyptus globulus*, phytochemistry, pharmacological activities, Antiviral, Antibacterial.

## Introduction

Nature is a great source of medicinal agents and various modern natural drugs has been isolated from natural sources and these isolated compounds have been used as traditional medicine<sup>1</sup>. The ancient Egyptians were aware of the usefulness of medicinally important herbs in the treatment of various chronic diseases. In India also there exists a vast literature which provides the information, knowledge and benefits for health care of drugs which includes the systems like Siddha, Tibetan, Ayurveda, Homeopathy and Unani on one hand. In addition of this, the earliest treatment system of India, the Charaka Samhita (1000 B. C.) reveals that about 2000 herbs were used for medicinal purposes<sup>2,3</sup>.

Among the whole population, large proportions used traditional medicines due to very much cost and unpleasant side effects of orthodox medicines<sup>4</sup>. It is also believed worldwide that natural shrubs are safer and lesser side effects to human body than synthetic drugs, so natural herbs provided us the very valuable life saving natural drugs used in the armamentarium of modern science<sup>5</sup>.

Traditional medicinal system of India comprises herbal shrubs for the treatment of various types of chronic diseases but also further investigation of the chemical constituents and pharmacological analysis of the plants provide us the basis for the development of novel agents<sup>6</sup>.

In the tradition of India, all the believed to have medicinal properties as:

“Jagatyevamanoushadham na kinchit vidyate dravyam yoga yoh”

This means “in the whole world, no any plant is non-medicinal”. It is recorded that about 19,000 odd angiosperm plants have medicinal importance. It was observed that the number of medicinal plants which are in use have no any single short consolidated list on the subject, but there is a consolidated list of medical plants for region wise is available for few states that are Himachal Pradesh, South West Bengal, Gujarat, shivalik Ranges in Haryana and Chhattisgarh and a full consolidated list of medicinal plants across the whole country under the All India Coordinated Study on Ethnobotany, is still in progress. Phyto remedies extracted from medicinal plants were utilized for the treatment of infectious diseases including viral infections<sup>3</sup>. Various studies have been already done on the extraction of various natural products for phytochemical and pharmacological screening of various medicinal plants but presently attention has been focused on the one of the medicinal plant *Eucalyptus*.

Abundant species of *Eucalyptus* (Myrtaceae family) are cultivated in subtropical and Mediterranean areas<sup>7</sup>. *Eucalyptus* trees are cultivated in whole world due to its rapid growth and also remarkable due to its many species have great height.

Among the *Eucalyptus* species, *Eucalyptus amygdalin* (Labille) having the great height which is near to 480 feet and even beyond to big tree (*Sequoia gigantea*) in height the Californian. Genus *Eucalyptus* comprising more than 600 species, *Eucalyptus globulus* (Figure-1) is used traditionally for the treatment of common infections. *Eucalyptus globulus* is used internally for the treatment of flu, fever, loss of appetite, dyspeptic complaints, asthma, diabetes, inflammatory and infectious diseases of kidney and bladder, rheumatism complaints and also used externally as for acne, wounds, bleeding gums, neuralgia, poorly healing ulcers, stomatitis, and gonorrhea<sup>8,9</sup>.



**Figure-1:** *Eucalyptus globulus* plant.

The island of Tasmania where *Eucalyptus globulus* was firstly discovered by French explorers in 1792, Tasmania forest of the primeval eucalypt was the tallest forest among the world and the height of *Eucalyptus globulus* up to 101 m was recorded. In addition of this, 60-90 m heighted trees were regularly harvested from the Tasmania forest and shipped for wharf piles throughout the world<sup>10</sup>.

*Eucalyptus globulus*, also called blue gum and it was known as fuel tree in India in 1843. This plant grows well in Nilgiris of height 5000-8300 feet, Annamalai and Pillani hills of height 4000-7000 feet in the south to Shimla hills in Himachal Pradesh and Shilong in the east of India. Raniket, Kullu, Kangra, Chamba, Punjab are the other places where this plant has been cultivated<sup>11</sup>.

The present review contains the medicinal importance of *Eucalyptus globulus* with its phytochemistry and pharmacological activities.

#### Plant profile

##### Classification

Kingdom: Plantae  
Superdivision: Spermatophyta  
Division: Flowering plants  
Class: Dicotyledons

Order: Myrtales  
Family: Myrtaceae  
Genus: *Eucalyptus*  
Species: *Eucalyptus globulus* Labill.

#### Common Names

In India, depending upon the language and geographical regions, this plant is recognized by different names, for example  
Hindi: Neelgir, Safeda  
English: Eucalyptus, Blue Gum, Fever Tree  
Urdu: Nilgiri  
Marathi: Nilgiri  
Kannad: Nilgiri  
Gujrati: Harit Parn  
Sanskrit: Sugandh patra

#### Botanical descriptions

**Leaf:** *Eucalyptus globulus* tree is an evergreen but some of the species at tropical regions in the end of the dry seasons lost their leaves (Figure-2). The leaves of the tree on the juvenile shoots are sessile, opposite, cordateovate and covered with the bluish white bloom and leaves on an adult stage are yellowish petioate 1.4-5 cm long, narrowly lanceolate, acute at base, thick, entire, glabrous, leathery, alternate, glossy or waxy dark green and also the leaves on seedlings are quadrangular and glaucous<sup>12-14</sup>.



**Figure-2:** Leaves of *Eucalyptus globules*<sup>12</sup>.

**Bark:** The bark (Figure-3a, 3b, 3c) of *Eucalyptus globulus* is dark grey, smooth to slightly fissured, deciduous, and detaching in long strips; fissures are usually longitudinal and narrow. In addition of this the length, color, thickness and hardness of bark varies with the plant age. The different types of barks on the basis of are explained as - i. **Stringybark:** long and thick fibres with a spongy texture usually. ii. **Ironbark:** is rough, hard and deeply furrowed and also dark red or even black color of bark is due to dried sap discharged by the tree. iii. **Tessellated bark:** is broken up into many distinct flakes and flakes are like cork which can flake off. iv. **Box:** Short fibres. v. **Ribbon:** this bark is coming off in long thin pieces and these pieces can be long ribbons, firmer strips or twisted curls<sup>15</sup>.



**Flowers and Fruits:** *Eucalyptus globulus* have distinctive flowers and fruits (capsule or gumnuts). The flowers (Figure-4a) at leaf base of more than 5 cm across, buds appear top to-shaped (12-15 mm long and 12-25 mm wide) and several white fluffy stamens (12 mm long). Stamens are numerous, threadlike, white, anthers opening in broad slits with round gland; pistil with interior ovary of 3-5-celled and long stout style and stamens enclosed in a cup described as an operculum that is composed of fused sepals of both. When flower expands, the operculum is thrown off, split the cup like membrane of the flower. Fruit (Figure-4b) is enclosed by a cup shaped receptacle, by a woody and having numerous minute seeds<sup>16,17</sup>.

## Phytochemistry

Numerous studies of the phytochemistry of *Eucalyptus globulus* have been carried out and which provide a valuable informatory report on the isolation of various phytoconstituents from different plant parts. As explained below -

**Phyto-components of the leaves:** Leaves of *Eucalyptus globulus* have been reported that the essential oils posses several volatile compounds and the essential oil from the leaves of the plant has been collected by steam distillation (Figure-5). The qualitative and quantitative analysis of the essential oil is done

by GC/MS and direct compared with MS databases attached to the instruments.

The essential oil mainly constituted by oxygenated sesquiterpenes, oxygenated monoterpenes, and monoterpenes. Essential oil contains constituents such as  $\gamma$ -cadiene,  $\alpha$ -gurjuene, linalool oxide,  $\alpha$ -pinene,  $\beta$ -pinene, aromadendrene,  $\gamma$ -elemene, 1,8-cineole, globulol, pipertone,  $\alpha$ - $\beta$ - and  $\gamma$ -terpinen-4-ol, fenchol, linalool, boreneol, caryophyllene, citronellal, Cuminaldehyde, citral, geranyle acetate, cinnamic acid, eudesmyl acetate, geranyl acetate, epi-globulol, ledol, S-guaiazulene, quercetin, rutin, caffeic,  $\alpha$ -pinocarvone, viridifloral, homoserin, cyanin, chrysanthemin, malvidin, peonin,  $\beta$ -selinene, delphindin, cis-pinocarveol, lycoricyanin, cynaidin, peonin, 8-demethylsideroxylin, quercetol, alloaromadendrene, d-myrtanal, ferulic, gallic, keracyanin, gentisic and protocatechic acids<sup>18-20</sup>.

The leaf wax contains the constituents such as 16-hydroxy-18-tritricotanone, 4-hydroxytritricotan-16, 18-di-one and a novel antioxidant compound such as ntritricotan-16, 18-dione isolated. Moreover, the compounds which are biological active such as phloroglucinol based derivatives with an attached terpene moiety, flavonoids and tannins, 1,8-oleanolic and masinic acid has been isolated from the leaves<sup>12, 21-24</sup>.



Figure-3a: Colored Bark<sup>3</sup>.



Figure-3b: Bark<sup>3</sup>.



Figure-3c: White box Bark<sup>3</sup>.



Figure-4a: Flower of Eucalyptus globules<sup>59</sup>.



Figure-4b: Fruit of Eucalyptus globules<sup>60</sup>.

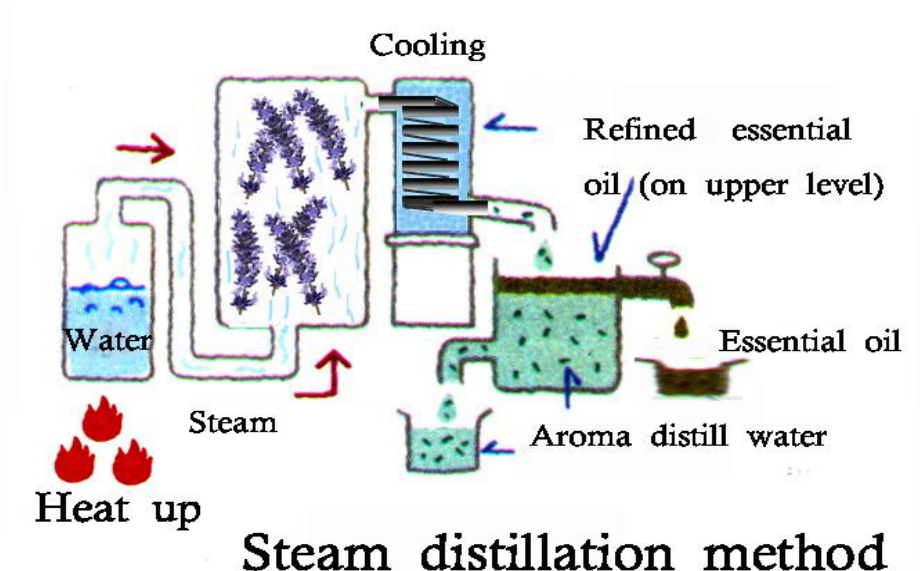


Figure-5: Steam distillation process for extraction of essential oil<sup>61</sup>.

**Phyto-components of the bark and wood:** Constituents of *Eucalyptus* wood have been isolated as sterol, phloroglucin derivatives, ellagitannin, 8-methoxy elagic acid-2-rhamnoside, syrigaldehyde, p-hydroxybenzaldehyde, vanillin, esters, steroid ketones, fatty acids, triglycerides and hydrocarbons. Major constituents are fatty acids, sterols, sterol esters, hydrocarbons, sterol ketons and triglycerides and minor components are waxes, tocopherols, fatty alcohols, mono- and diglycerides are isolated from wood of the plant. These constituents were fractionated by lipid extract by using Solid-Phase extraction and the resulting fractions were analyzed by GC/MS technique having high temperature capillary columns. Hetroxylan compounds of galactosyl, 4- Omethyi-glucuronosyll and xylosyl have been isolated from wood<sup>25-28</sup>.

The major constituents have been isolated from the stem bark such as ellagic acid rhamnopyrosides which are 3-O-nethylellagic acid 3'-O-3'-acetylramnopyrosides, 3-O-methyl ellagic acid 3'-O- $\alpha$ -rhamnopyranoside, 3'-Omethylellagic acid 3'-O-4'-Oacetylramnopyrosides and 3-Onethylellagic acid 3'-O-2-Oacetylramnopyrosides and also three triterpinoids as methyl 11 $\alpha$ -methoxy-3-aqetoxysursolate methyl cis-p-methoxy cinnamoyl urosolate; and methyl cis-pmethoxy cinnamoyl oxyoleanolate have been isolated from the plant. Steroidal lactone of withanolides and a series like areinclude (+)-6 $\alpha$ ,7 $\alpha$ -epoxy-5 $\alpha$ - hydroxy-1-oxo- 2,24-dienolide as a major component and structrully similar steroidal lactone as the minor one has been isolated from the supercritical fluid extract of bark<sup>29-32</sup>.

**Phyto-components of the flowers and fruits:** Several constituents isolated from the flowers and fruits of *Eucalyptus globulus* such as bornylacetate, caproic acid, borneol, betasitosterol, stigmasterol, citral, fenchone, macrocarpal, 2a-Hydroxybetulinic acid, euscaphic acid, p-menthane, betulinic acid, myrtenol, thymol, camaldulenside, macrocarpal A,

macrocarpal B, verbinone, 3,4,3'-O-trimethylellagic acid, cysteine, glutamic acid, ellagic acid, norvaline, glycine, gallic acid, 3- O-methylellagic acid-4'-O- $\alpha$ -L-rhamnppyranside, 3-O-methylellagic acid 4'-O-2 (2''-O-acetyl)- $\alpha$ -L-rhamnopyranoside, theonine, 3-O-methylellagic acid, oleanolic acid, ornithine, cypellocarpin C, heteroxylan and eucalyptone have been found in the fruit of the plant.

The compounds isolated from the fruits have been isolated such as caproic acid, fenchone, borneol, isoamylalocohal, myrecene, eudesmol, sabinene, p-menthane, trans-pinocarveol, camphene, myrtenol, bornylacetate, thymol, transverbinol,  $\alpha$ -and  $\beta$ -thujone,  $\alpha$ -terpineol, citral, glutamic acid, cysteine, asparagine, verbinone, ornithine, glycine, norvaline, theonine and dextrin, sucrose, eucalyptol and forming acid have been isolated from buds<sup>33-36</sup>.

## Pharmacological activities

*Eucalyptus* is the most important and widely planted throughout the world after *Acacia*. Due to the presence of secondary metabolites, various studies on *Eucalyptus globulus* have been done to possess diverse pharmacological properties. Additionally, *Eucalyptus* is a folk remedy for the treatment of burns, cough, cancer, fever, cold, malaria, dysentery, wounds, tumors, spasms, tuberculosis, arthritis, abscess, miasma, dyspepsia, sorethroat, diabetes, tumors, worms and vaginitis<sup>37-39</sup>. Several properties have been exhibited by plant including antiphlogistic, astringent, deodorant, inhalant, rubefacient, insect repellent, vermifuge etc.

**Antibacterial and antifungal activity:** The antibacterial activity of essential oil has been examined against the Gram (+) *Staphylococcus aureus* and Gram (-) *Escherichia coli* bacteria and essential oils showed an excellent inhibitory effect on *Staphylococcus aureus* than that of *Escherichia coli*<sup>40</sup>. The

antifungal activity of essential oil has been examined against fungi *Aspergillus flavus* and *Aspergillus parasiticus*. It is reported that 1,8-cineole is the major component showed partial inhibition at the highest level of 1.3492 mL and also observed that at 200 mL dose of the essential oil reduces Aflatoxin B1 production in headspace and partial inhibition<sup>41</sup>. Essential oil of *Eucalyptus globulus* has a strong antimicrobial activity, especially against *Streptococcus pyogenes*, *Candida albicans*, *Escherichia coli*, *Klebsiella pneumoniae*, *Staphylococcus aureus*, and *Acinetobacter baumannii*. MIC (minimum inhibitory concentration) values revealed the lowest activity against *Salmonella infantis* and *Pseudomonas aeruginosa* (3.13 mg/ml) while the highest activity was against *S. aureus*, *S. pyogenes*, *E. coli*, and (0.09 mg/ml)<sup>42</sup>. The antibacterial activity of leaf extract of *Eucalyptus globulus* against 25 isolates of *Streptococcus pyogenes*, 56 isolates of *Staphylococcus aureus*, 12 isolates of *Streptococcus pneumoniae* and 7 isolates of *Haemophilus influenzae* was checked from 200 patients with respiratory tract infection and MIC values for these species were calculated 64, 32, 16 and 16 mg/L respectively. These results clarify that the treatment of respiratory tract infection with this plant extract are warranted<sup>43</sup>.

**Antioxidant activity:** Fruit crude extract of *Eucalyptus globulus* was screened to check antioxidant properties in vitro and antioxidant activity was measured by two methods- lipid peroxidation inhibition and reducing power. The extract of *Eucalyptus globulus* exhibited moderate inhibition of lipid peroxidation of linoleic acid emulsion ( $51.34 \pm 0.72\%$ ) and high reducing power ( $IC_{50} = 39.52$  g/mL). These results suggest that fruits of *Eucalyptus globulus* have interesting antioxidant activities<sup>44</sup>. Nitric oxide free radical and 2, 2-Diphenyl-1-picrylhydrazyl radical (DPPH) were also used to check antioxidant activity of eucalyptus oil (essential oil) extracted from the leaves of *Eucalyptus globulus*. The free radical scavenging activity of the essential oils was checked against different concentrations of the leaf oil (10, 20, 40, 60 and 80% (v/v) in DMSO) and the activity was increased by increase of concentration of leaf oil and was observed that the oil in 80% (v/v) concentration exhibited  $79.55 \pm 0.82\%$  and in nitric oxide radical scavenging method, it was found that 80% (v/v) concentration exhibited  $81.54 \pm 0.94\%$  inhibition. It was concluded that leaf oil is potent inhibition of free radicals<sup>12</sup>. The potential of antioxidant properties of methanolic, water and supercritical fluid extract (SCF) of eucalyptus stem bark in a concentration range of 0.10–0.90 mg/ml, was evaluated by free-radical species: 2,2-diphenyl-1-picrylhydrazyl free radical (DPPH) and  $\beta$ -carotene lineolate radical using electron spin resonance (ESR) spectroscopy. Usually, methanolic extracts having better scavenging and antioxidant activity than water extracts, while SCFE extracts exhibited lower activities than methanolic extracts. The ESR data demonstrate that SCF, methanolic and water extracts of eucalyptus having similar free radicals scavenging and antioxidative activity higher than synthetic antioxidants BHT. The SCF extract is also shown to be a good antioxidant activity<sup>45</sup>.

**Anti-inflammatory:** A strong inhibitor of cytokines is 1, 8-cineole which is a major constituent from the *Eucalyptus globulus*, and is considered to be better for the long term treatment of bronchial asthma and other steroid-sensitive problems. Acetic acid-induced writhes in mice and hot plate thermal stimulation in rats test models have been employed to check analgesic action of essential oils of *Eucalyptus globulus* and which showed that the essential oils of *Eucalyptus globulus* induced analgesic effects in both models, suggesting peripheral and central actions while the anti-inflammatory effects of essential oils was checked by the carrageenan-induced rat paw edema and xylene-induced ear edema tests which revealed that vascular permeability induced by carrageenan and histamine and also by inhibition of rat paw edema induced by carrageenan and dextran, neutrophil migration into rat peritoneal cavities induced by carrageenan<sup>46</sup>. NO production induced by lipopolysaccharide (LPS) and interferon- $\gamma$  (IFN- $\gamma$ ) in the murine macrophage cell line J774A.1 was also affected by essential oils. In addition, cell viability, scavenging activity and inducible nitric oxide synthase (iNOS) mRNA expression of plant extract was evaluated which showed significant scavenging of NO radicals released by an NO donor, PAPANONOate<sup>47</sup>.

**Antidiabetic (antihyperglycemic):** *Eucalyptus globulus* is a traditional medicine to treat the diabetes. Aqueous ethanolic leaf extracts of *Eucalyptus globulus* of doses 200 to 400 mg/kg were separately administered orally to groups of glucose loaded rats and which was compared to glibenclamide 10 mg/kg in fasted normal rats. This was observed that there was a reduction in blood glucose levels which was most significant at the dose 400 mg/kg. The median lethal g/ml for *S. aureus* for *E. globulus*; 37.20  $\mu$ g concentrations LC<sub>50</sub> in brine shrimps was 55.95<sup>48</sup>. It was also observed that the hyperglycemia level reduces by the incorporation of eucalyptus in the diet (62.5 g/kg) and drinking water (2.5 g/L) and associated weight loss of streptozotocin-treated mice. An aqueous extract of eucalyptus enhanced 2-deoxy-glucose transport by 50%, glucose oxidation by 60% and incorporation of glucose into glycogen by 90% in mouse abdominal muscle<sup>49</sup>.

**Larvicidal:** Essential oils of *Eucalyptus globulus* were screened for their larvicidal activity against three mosquito larvae *Culex quinquefasciatus* (Say), *Aedes aegypti* (L.) and *Anopheles stephensi* (Liston). The effect of different concentration of the Plant oil formulation 25, 50, 100, 200 and 400 ppm on the Larvicidal activity against *Aedes aegypti* LC<sub>50</sub> 68.18 and LC<sub>90</sub> 248.37. Larvicidal activity against *Anopheles stephensi* LC<sub>50</sub> 56.83 and LC<sub>90</sub> 208.30. 50 90 50 90 Larvicidal activity against *Culex quinquefasciatus* LC<sub>50</sub> 70.80 and LC<sub>90</sub> 234.15<sup>50</sup>.

**Antimalarial:** Both aqueous and chloroform extracts and hexane leaf extract of *Eucalyptus globulus* leaf extract did not inhibit the growth of *O. gallinaceum* and *plasmodium berghei* respectively. The growth of *p. falciparum* was inhibited by ethanol-water extract of leaves in vitro at a concentration of 75 mg/ml<sup>51</sup>.



**Antiplateque:** *Eucalyptus globulus* has an important source which is the useful in inhibiting the dental plaque formation<sup>52</sup>.

**Anticancerous:** Anticancer activity against MCF-7 breast cancer cell lines was checked by using methanolic crude extracts of *Eucalyptus globulus* leaves. It was observed that the cytotoxicity of individual plant extracts grown in polluted area was more than that of plants grown in natural conditions investigated at final concentration of 200µg/ml. The cell inhibition of combined extracts of polluted area 81.2% and natural area 84% having IC50 values 82.400 µg/mL, 91.980 µg/mL respectively.

The plants grown in industrial polluted area showed the better activity against MCF – 7 cell lines, further it could be recommended to study the pure components and their anticancer affectivity for the substitution of synthetic drugs<sup>53</sup>.

**Antitumor:** *Eucalyptus globulus* has been used to treat tumor, Antitumor- promoting activity of Euglobals 1a 1, 1a 2, 1b, 1c, 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). The nuclear translocation of NF-kappa B induced by LPS in tHP-1 cells was inhibited by essential oils<sup>54</sup>.

**Antihistaminic:** The IgE dependent histamine release from RBL- 2H3 cells inhibited by hexane and ethanol extract of leaves, ethanol extract of fruit of *Eucalyptus globulus*<sup>55</sup>.

**Antiseptic, stimulant and rubefacient activity:** The essential oils of *Eucalyptus globulus* broadly used in cough drops, antiseptic, rubefacient, and stimulant<sup>56, 39</sup>.

**Anthelmintic activity:** Essential oils and chloroform extract has been used as one of the remedies in the tropic for hookworm, due to the presence of cineol, linalool, borneol, saffrol, gernayl acetate and antheol exhibits anthelmintic activity and also used for the treatment of pulmonary infections<sup>57</sup>.

**Antiviral:** From *Eucalyptus globulus*, twelve euglobals has been isolated which played a vital role in the antiviral activity and euglobals having monoterpene structure and euglobal-III<sup>58</sup>.

**Anti HIV:** Constituents like terpenoids, macrocarpals (A- E) has anti-HIV effect. Among these, macrocarpal B played a potent role in the treatment of HIV. In this procedure adult and mixture of plant extract like *Annona squamosa*, *Cymbopogon citrate* and *Centella asiatica* etc. were found to be most effective.

Numerous other pharmacological activities such as nerve blocker, UTI and RTI, wound healing activity of *Eucalyptus globulus* has been studied due to the presence of active constituents.

## Conclusion

It is concluded from the literature that *Eucalyptus globulus* is an evergreen tree and an important plant due to the presence of active constituents. Over the past decades, herbal medicines paid much attention with both medicinal and economic implications. *Eucalyptus globulus* has been used for various activities such as antiviral, antifungal, antimalarial, antibacterial, anti-inflammatory, antitumor, anticancer etc. Present review has been made to cover phytochemical, botanical, pharmacological and ethno pharmacological information of *Eucalyptus globulus*.

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