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Insights into the phytochemical and pharmacological significance of essential oils present in *Cymbopogon citratus Stapf*

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Abstract
Cymbopogon citratus Stapf is a well-known herb commonly known as Lemongrass or Citronella grass belonging to the family Poaceae (Gramineae). This plant has been recognized for its commercially valuable essential oils and known for its important ethnopharmacological importance and repellent activity. *C. citratus* a fast-growing, perennial aromatic grass is native to South India and Sri Lanka, now widely cultivated in the tropical areas of America and Asia. The freshly cut and partially dried leaves are used medicinally and are the source of the essential oil. The phytoconstituents of essential oil containing a volatile mixture of hydrocarbons with a diversity of functional groups and their activity has been linked to the presence of monoterpenes and sesquiterpenes. The studies indicate that *C. citratus* possesses various pharmacological activities such as anti-amoebic, anti-bacterial, anti-diarrheal, anti-filarial, anti-fungal, anti-inflammatory, anti-malarial, anti-mutagenicity, anti-mycobacterial, anti-oxidant, hypoglycemic, and neurobehavioral activity along with the repellent activity. The results of extensive reported literature review studies about the *C. citratus* are found to be very fruitful / interesting and hence these reveal diverse future potential prospective.

Keywords: *Cymbopogon citratus*, lemongrass, citronella grass, phytochemistry, pharmacology, essential oil

Introduction
Plants are an important group among all living organisms, which serves as a supporting system for humans as well as other living creatures. They have been supporting human civilization through the biologically active phytochemical compounds which they contain. Plants being a source of medicine has been identified and used from ancient times. In the West, the use of plants and herbs as a source of medicine is growing, with approximately 40% of the population are reported to use it for the treatment of many diseases. The officially documented plants with medicinal potential are few but traditional practitioners use more than 6000 plants [1]. Aromatic and medicinal plants form the backbone of the healthcare system for curing various ailments in developing countries including India. Various herbal therapies used in traditional system of medicine possess the benefit of negligible side effects usually associated with the allopathic system of medicine [2].

More than 70% of the Indian population depends on the immortal traditional system of medicine, Ayurveda. The quest for the invention of newer drug research in the phytochemical and pharmacological properties of medicinal plant extracts is a rational approach. The problem with the use of the single isolated compound as a drug is that it may cause various side effects but plant extract possesses a combination of chemicals that counterbalance the side-effects of each other. Therefore, now-a-days current focus of research is on the detailed study of medicinal and aromatic plants so that novel drugs may be synthesized with enhanced physiological actions and minimal side-effects [3]. For the faster investigation of natural compounds, newer sophisticated extraction techniques have been invented for the isolation of bioactive compounds having health benefits [4].

The genus *Cymbopogon* belongs to the family Poaceae (Gramineae). The Poaceae family has about 700 genera and 11,000 species widely distributed in all regions of the world especially in the South-East Asia. *Cymbopogon* is native to warm temperate and tropical regions. The word *Cymbopogon* was introduced by Sprengel in 1815 and at that time the genus consisted of a few species which were then moved to the genus *Andropogon* and it is the sub-type of Gramineae [5]. *Cymbopogon* is a complex genus with its species distribution and is comprised of 144 species. This genus is famous for its high content of essential oils which have been used for cosmetics, pharmaceuticals, and perfumery applications [6]. The commercial value of some *Cymbopogon* species is further enhanced by their ability to grow in moderate and extremely harsh climatic conditions [7]. The name *Cymbopogon* is derived from the Greek words "kymbe" (boat) and "pogon" (beard), referring to the flower spike arrangement [8].

Cymbopogon citratus is a commercially important species of the genus *Cymbopogon.* The present review focuses on the previous research work and information regarding phytochemistry and pharmacological importance of species *C. citratus Stapf* along with repellent activity with future prospective studies.

Ethnobotany and Taxonomy
- **Kingdom:** Plantae
- **Division:** Magnoliophyta
- **Class:** Liliopsida
- **Order:** Poales

- **Family:** Poaceae
- **Genus:** *Cymbopogon*
- **Species:** *citratus*

C. citratus Stapf is popularly known as citronella grass or lemongrass. This plant is a native herb from India and is cultivated in other tropical and subtropical countries. Lemongrass is a tufted perennial grass growing to a height of 1 meter with numerous stiff leafy stems arising from short rhizomatous roots. It has a lifespan for about 5 years with regard to its economic importance [9]. The leaf-blade is tapered at both ends, linear and can grow up to the length of 50 cm and width of 1.5 cm. The leaf-sheath is tubular in shape and acts as a pseudostem. Leaves are long, green, linear tapering upwards and along the margins. After growth and maturation, this plant produces flowers or flowering that has never been observed under cultivation due to rapid harvesting time. The inflorescence is a long spike about 1 meter in length. Flowers are borne on decompound spatheate; panicles 30 to 60 cm long and more. The rhizome produces new suckers that extend vertically as tillers to form dense clumps [10].

Ethnopharmacology

Lemongrass can tolerate a wide range of soils and climatic conditions [11]. However, vigorous growth is obtained on well-drained sandy loam soil with high fertility and exposed to sunlight [12]. Lemongrass has numerous important pharmacological activities which are studied by various researchers in the past [13]. It is reported to possess anti-bacterial, anti-fungal, anti-protozoal, anti-carcinogenic, anti-inflammatory, anti-oxidant, cardioprotective, anti-tussive, antiseptic, anti-rheumatic, inhibit platelet aggregation, treats diabetes, dyslipidemia, gastrointestinal disturbances, anxiety, malaria, flu, fever, and pneumonia, as well as applications in aromatherapy [14-16]. In addition to its therapeutic uses, *C. citratus* is also consumed as a tea, added to non-alcoholic beverages and baked food, and used as a flavoring and preservative in confections and cuisines [17]. In cosmetics, the essential oils are used as a fragrance in the manufacture of perfumes, soaps, detergents, and creams [18].

Traditional uses of lemongrass

- Lemongrass leaves are reported to have a good quantity of oil and this oil has anti-microbial activity.
- Carminative, fungicidal, analgesic, antiseptic, astringent, bactericidal, and anti-depressant properties.
- It can be act as an antibiotic as well as having antiseptic properties and can be used for curing of ringworm and athlete's foot disease.
- Lemongrass possesses good inhibitory activity against methicillin-resistant *Staphylococcus aureus* (MRSA) infection.
- It can be used for colitis indigestion and gastro-enteritis ailments. It helps relieves the symptoms of headache, body ache, nervous exhaustion, and stress-related condition.
- Its infusions are often made useful in infections such as sore throats, laryngitis, bronchitis, etc [19].
- Alves *et al*. reported it is used to cure gastrointestinal problems [20].
- Decoction of lemongrass leaves can be used as diaphoretic in fever [21].
- The studies on lemongrass by researchers have indicated that it can revitalize the body and enhances good health.
- It stimulates digestion and inhibits chemical-induced carcinogenesis by modulating xenobiotic-metabolizing enzymes in the liver and intestine [22].
- Lemongrass tea is commonly used to combat flu, fever, and pneumonia [23].

Phytochemistry of Lemongrass

Most of the biological effects ascribed to *C. citratus* extracts have been attributed to its primary bioactive constituents, derived from its leaves, stem, and roots, and their secondary metabolites. The chemical composition of the essential oil of *C. citratus* varies according to the geographical origin, the compounds as hydrocarbon terpenes, alcohols, ketones, esters, and mainly aldehydes have constantly been registered. Lemongrass contains active ingredients like myrcene, an antibacterial and pain reliever, citronellal, citronellol, and geraniol. The essential oil consists of mainly, citral (3,7-dimethyl-2,6-octadienal), a volatile oil with strong lemon fragrance. Citral is a mixture of two stereoisomeric monoterpene aldehydes; the *trans*-isomer geranial (40-62%) dominates over the *cis* isomer neral (25-38%) and is used in the manufacture of perfumes, colored soaps, and synthesis of vitamin-A [24, 25].

Citral, geranial, and neral form nearly 75 % of the aldehydes present in the oil extracted from lemongrass. These chemicals provide aroma to the plant and help its usage in aromatherapy. Citral-α, citral-β, nerol, geraniol, citronellal, terpinolene, geranyl acetate, myrecene, and terpinol methylheptenone are some of the chemicals that have been extracted from lemongrass parts by various researchers. Two triterpenoids, cymbopogone and cymbopogonol and flavones identified as luteolin and its 6-C-glucoside have also been isolated from leaves of *C. citratus* [26, 27]. Figure 1 comprehensively describes the therapeutically privileged phytochemicals present in the extract.

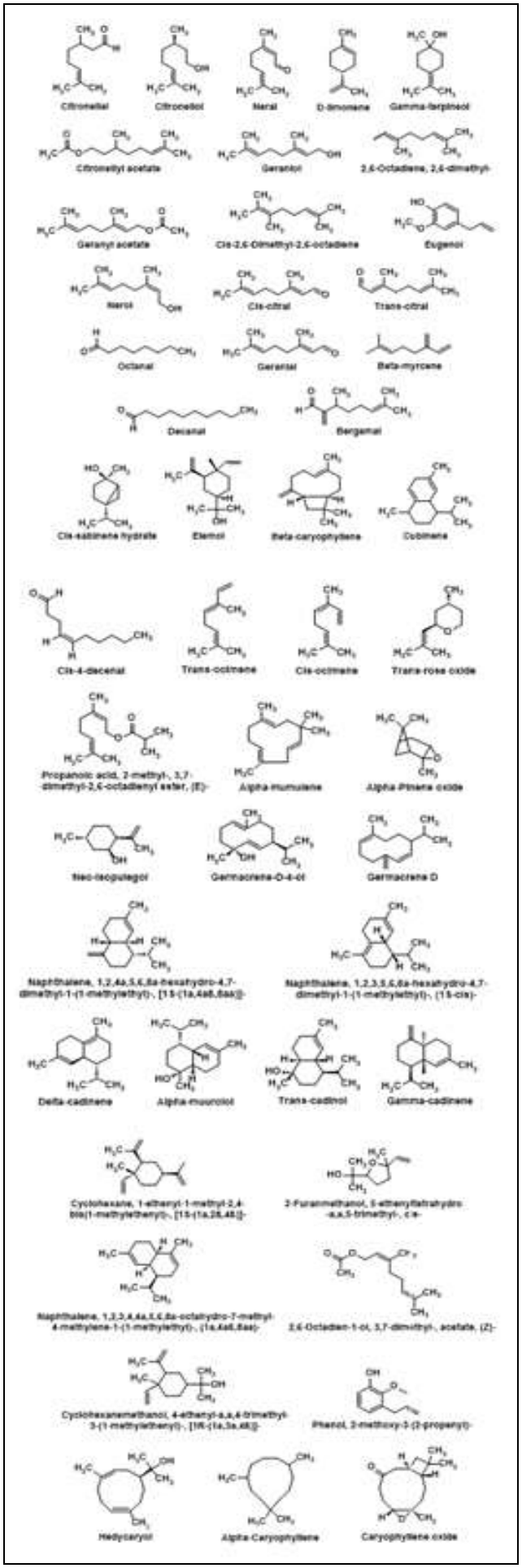

Fig 1: Prominent pharmacologically active phytochemicals found in *C. citratus* extract.

Pharmacological Activities of Lemongrass

Anti-oxidant activity

The antioxidant potential of plants is due to the presence of various phytoconstituents like polyphenols, flavonoids, lignins, alkaloids, terpenoids, carotenoids, vitamins, etc. They help in maintaining the nutritional quality and shelf life of foods by inhibiting lipid oxidation, minimizing rancidity, and removing toxic oxidative products [28, 29]. The phenolic compounds help in scavenging the reactive oxygen species (ROS) which include hydrogen peroxide (H_2O_2), superoxide anion (O^{2-}), and free radicals [30]. These antioxidants offer protective mechanisms against the damaging effects of the oxidation process caused by these radicals. The results of the various studies clearly reveal that the essential oil of lemongrass is effective in scavenging free radicals and has the potential to be good anti-oxidants [31].

Anti-diabetic activity

Various studies have reported that aqueous extract of lemongrass possesses hypoglycemic properties. These properties are due to the presence of flavonoids and alkaloids in the essential oil of lemongrass and its extracts were efficient in reducing cholesterol levels in circulating blood. This activity could be due to the presence of an endogenous ligand of central-type benzodiazepine receptors known as endozepine octadecaneuropeptide (ODN), which are inhibitors of food intake in small animals [31]. β-glucosidase inhibition assay was carried out using an *in-vitro* model for anti-diabetic test and lemongrass stalk essential oil and it showed the highest degree of inhibitory activity (89.63%) [32]. Bharti *et al*. studied the anti-diabetic activities of essential oil obtained by steam distillation of the leaf sheath of *C. citratus* and reported that pharmacological evidence of lemongrass as anti-diabetic mediated by the interaction of various phytoconstituents with multiple targets operating in diabetes mellitus [33].

Anti-inflammatory activity

Boukhatem *et al.* studied the anti-inflammatory and antifungal potential of lemongrass. They found out that lemon grass essential oil (LGEO) (10 mg/kg, administered orally) significantly reduced carrageenan-induced paw edema with a similar effect to that observed for oral diclofenac (50 mg/kg), which was used as the positive control. Oral administration of LGEO showed dose-dependent anti-inflammatory activity. In addition, the topical application of LGEO *in vivo* resulted in a potent anti-inflammatory effect, as demonstrated by using the mouse model of croton oil-induced ear edema. The topical application of LGEO at doses of 5 mL/ear and 10 mL/ear significantly reduced acute ear edema induced by croton oil in 62.5% and 75% of the mice, respectively. In addition, the histological analysis clearly confirmed that LGEO inhibits the skin inflammatory response in animal models [34].

Anti-bacterial activity

The ethanolic extracts of the leaves of lemongrass showed potential antibacterial property against *Staphylococcus aureus* and this activity is attributed to the presence of flavonoids and tannins found in the extract [35]. Umar *et al.* studied the antibacterial activity of the extracts of *C. citratus* against *Escherichia coli*, *Salmonella typhi*, and *S. aureus.* The results of this study showed that ethanol leaf extract was active against all the test organisms at the concentration of 100 mg/ml, 50 mg/ml, and 25 mg/ml. The anti-microbial activity of ethanolic leaf extract was higher than that of acetone and chloroform leaf extracts. This may be due to variable polarity as well as due to the ability of ethanol to extract more of the plant's active components. The highest mean zone of inhibition (23 mm) of *Escherichia coli* by the ethanolic extract was recorded at 100 mg/ml while the lowest (6 mm) was at 25 mg/ml [36].

Anti-fungal activity

Candida albicans is an important pathogen of human infections; moreover, other species can be associated with some infections. The anti-fungal activity of lemongrass and citral against *Candida* species was studied and the study showed that lemongrass oil and citral have a potent *in vitro* activity against *Candida spp*. [37]. Other phytochemicals were analyzed by phenolic extraction, which includes a diverse group of chemical compounds, such as flavonoids, lignins, tannins, phenolic acids, coumarins, phenols, phenylpropanoids, quinines, stilbenoids and xanthones [vermeres]. LGEO exhibited promising antifungal effects against *Candida albicans*, *C. tropicalis*, and *Aspergillus niger*, with different inhibition zone diameters (IZDs) (35-90 mm). The IZD increased with increasing oil volume [34].

Anti-diarrheal activity

Traditionally, the whole stalk and the leaf of lemongrass are boiled and the decoction is drunk to relieve diarrhea. The anti-diarrheal efficacy of *C. citratus* stalk decoction and its main chemical constituent citral, was studied and the results show anti-diarrheal activity [38].

Anti-protozoan activity

The family Trypanosomatidae harbors protozoans that are agents of important illnesses in humans, animals, and plants. This family also includes some lower trypanosomatids such as *Crithidia*, *Blastocrithidia*, and *Herpetomonas*, monoxenous protozoans usually found in insect hosts. The essential oil extracted from *C. citratus* showed anti-protozoan activity against *Crithidia deanei* [39].

Anti-hepatotoxic activity

The aqueous leaf extracts of *C. citratus* showed anti-hepatotoxic action against cisplatin-induced hepatic toxicity in rats. Hence, the extracts have the potential to be used for the management of hepatopathies and as a therapeutic adjuvant in cisplatin toxicity [40].

Anti-nociceptive activity

The essential oil of *C. citratus* possesses significant anti-nociceptive activity. On comparing the results obtained with three different experimental models of nociception viz., hot-plate, acetic acid-induced writhing in mice, and formalin test, showed that the essential oil acts both at the peripheral and central levels [41].

Anti-obesity and Anti-hypertensive activities

Lemongrass has been incorporated in hypolipidemic and hypoglycemic drugs. In folk and Ayurvedic medicine, it has been used to regulate glucose, lipid, and fat level in the blood serum which could prevent obesity and hypertension, usually taken as a tea [42]. The plant has been used to maintain blood glucose through the secretion of insulin

(hyperinsulinemia). It reduces blood pressure which could lead to hypertension [43].

Insecticidal activity
Essential oils from *C. citratus* have been applied in the control of pathogens and insects [44]. It has been reported to be effective against *Aedes aegypti* [45].

Anti-malarial activity
Secondary metabolites such as citral, myrcene, and citronellal have been isolated from lemongrass and were characterized as anti-malarial compounds. These isolated compounds show pronounced activity against *Plasmodium* species [46]. Dichloromethane extract of *C. citratus* was tested against *P. berghei* and *P. falciparum* with pronounced activities of 2-10 µg/mL [47]. Ethanolic extracts show pronounced antiplasmodial activities of EC_{50} against two strains of *P. falciparum* (multidrug-resistant (Dd2) (54.84 µg/mL) and CQ-sensitive (3D7) (28.75 µg/mL) [48].

Anti-cancer Activity
The present study shows a novel finding that lemongrass oil has a potent cytotoxicity effect on HTB43 head and neck cancer cells. Lemongrass oil treatment for 72 hrs significantly decreased the percentage of the cell viability with an IC_{50} value of 15.42 µg/mL. In the same experiment, DMSO was used as a solubilizing agent at a concentration of 1% showed no cytotoxic effect on cell proliferation [49]. Our new finding is supported by several previous studies also. Inhibition of the early phase of hepatocarcinogenesis was also observed in *C. citratus* [50].

Mosquito-repellent activity
Lemongrass oil showed good mosquito repellent activity in performed tests. Hence, lemongrass essential oil, alone or in combinations with those obtained from other mosquito repellent plant species, could be potentially used for the preparation of mosquito repellent products. These could be in the form of spray, cream, liquidator, coil, candle, and sticks, and could be prepared using suitable carries/solvents/diluents, to get better protection from mosquito bites. Such formulations could help in reducing the harmful effects of synthetic mosquito repellents on human health. Moreover, the formulation is safe, eco-friendly, cheap, easy to use, and has maximum repellence against mosquitoes. It is clear from the present study that lemongrass oil exhibits significant repellent activity with a combination of other essential oil. Further studies which include simulated and actual field trials required for commercialization of these herbal mosquito repellents [51]. This will helpful for the development of safe natural repellent for humans and the environment as compared to synthetic compounds.

Dermatotoxicity
C. citratus has been used in herbal soap to treat rashes, itchy, and swollen skin. Herbal soap produced from *C. citratus* leaf, tea tree oil, and orange peel was investigated for their dermatoxicity potency using clinical samples. A significant activity of 60% ($p < 0.05$) was observed after 40 days of treatment with the soap [52].

Conclusion
This current appealing review broadly highlighted the in general fundamentals, plant profile (Kingdom, Order, Class, Family, Genus, Species, Distribution, and Varieties), cultivation aspects, ethnotraditional applications, phytochemical present in various parts, imperative pharmacotherapeutic perspectives (anti-oxidant, anti-diabetic, anti-cancer, anti-obesity, anti-bacterial, anti-fungal, anti-inflammatory, anti-diarrheal, anti-nociceptive, anti-hypertensive, anti-hepatotoxic, anti-nociceptive, anti-malarial, anti-protozoan, insecticidal activity, dermatotoxicity, and mosquito-repellent activity) of *C. citratus*. This information will be relatively functional for the excited modern-day investigators of abundant areas (botany, medicine, chemistry, pharmacognosy, natural products, etc.) in producing varied vital formulations for treating numerous disorders of both human and veterinary origin.

Conflict of Interest
The authors declare no Conflict of Interest.

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