Review

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Review of the Chemical Properties, Pharmacological Properties, and Development Studies of *Cymbopogon sp.*

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Abstract: Cymbopogon is a genus of aromatic plants that famed because of the essential oil production that has many benefit in industrial, daily life, or even for disease treatment. The Cymbopogon genus consists of about 180 plants, including different species, subspecies, varieties, and subvarieties. The aim of this review is to present chemical properties, pharmacological, and development of the Cymbopogon genus from books and research studies. There were many types of research that have been done to prove the benefits of the Cymbopogon genus, including studies about the extract, essential oil, the chemical compound biological activity, and development studies. Some pharmacological studies that have been confirmed are regarding the pharmacological effects of Cymbopogon in the central nervous system, anti-inflammatory, antimicrobial, antioxidant, and anticancer activity. In addition, there have been studied to improve Cymbopogon benefits.

Keywords: Cymbopogon sp.; essential oil; biological activity; chemical properties.

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1. Introduction

Aromatic plants are included in the category of medicinal plants because these plants are widely used as medicine and are used to help maintain health [1]. Gramineae family is a monocot plant which is widely known as a source of essential oils that are widely used both in industry or for daily life [2]. Essential oil is a compound that can be obtained from aromatic plants and has many benefits. In this time, the use of alternative and complementary therapies has been widely developed. Aromatherapy is one of the therapies that use essential oil and has many pharmacological effects. Furthermore, in several countries, *Cymbopogon sp.* is used to treat indigestion, depression, headache, respiratory problems, skin problems, malaria, stomach problem, antihypertension even as a self-treatment for weight loss [3-6]. *Cymbopogon sp.* is also used in daily life as a flavoring agent, antiseptic and deodorant, body cleansing (drink and bath) after menstruation, enemas, and pimples, even for dental hygiene in some countries [7-9].

The Cymbopogon genus from the Graminae family consists of about 180, including different species, subspecies, varieties, and subvarieties. Cymbopogon plants are tall perennial plants with dense and long leaves. Some of the most important aromatic Cymbopogon species in producing essential oils are *Cymbopogon martinii*, *Cymbopogon citratus*, *Cymbopogon flexuosus*, *Cymbopogon westratus*, *Cymbopogon nardus*, and *Cymbopogon winterianus* [2].

Currently, there are many scientific publications that observe regarding pharmacological and composition of Cymbopogon genus plants. Hence this systematic review

intends to discuss and analyze the latest research related to the Cymbopogon genus as a valuable plant that has many benefits.

2. Materials and Methods

This review was performed by analyzing sources from books and articles published in 2016 until 2020 that contain biological activity and chemical properties of Cymbopogon that are indexed by Scopus. The articles choosing based on: (1) article shows the chemical properties of *Cymbopogon sp.*, (2) article that reported the biological testing activity of essential oil, extract, fraction, or pure compound of *Cymbopogon sp.* using *in vitro* or *in vivo* methods, (3) article that reported development studies using *Cymbopogon sp.* Journals published outside of 2016 to 2020 and journals that were not indexed by Scopus were excluded.

3. Results and Discussion

3.1. Chemical properties.

Studies by Gupta *et al.*[10], using GC and GC/MS showed that from 17 different Cymbopogon species, there were many variations in essential oils production (0.4% -1.4%) and significant chemical diversification; most of them consist of neral, geranial, citronellal, and geraniol as the four main components. But plants produce a variety of structurally and functionally different metabolites that can affect the growth and development of these plants. This is influenced by environmental conditions as abiotic and biotic pressures resulting in the chemical properties/active ingredients of the same species of different plants in different diversity zones due to changes in the micro and macro environment of these plants [1,11]. Such as the increase of abiotic stress can increases metabolic production and the quality of essential oils in aromatic plants [12]. Major components of some essential oil of *Cymbopogon sp.* were summarized in Table 1.

There are many factors that can affect the results of essential oils. A previous study demonstrated that the yield of essential oil extracted from different parts of *Cymbopogon winterianus* produces different results, with the leaf parts having the highest yields more than the stem or the whole aerial parts. Moisture content also has been proved a significant effect on oil yield because higher essential oil content was obtained from fresh plants compared to dried plants [21]. The choice of the extracting method also can affect the results of essential oil. *C. nardus* essential oil that was extracted by ohmic-assisted hydrodistillation (OAHD) and hydrodistillation (HD) yielded the same amount of essential oil with similar physical properties but had different activity due to different compound value in the essential oil [22].

3.2. Antimicrobial activity.

Multi-Drug Resistance (MDR) bacteria is a global problem in the world of health, making the development of plant-based antimicrobials is widely studied. The constituents with or without combination with antibiotics can be effective because bacteria, fungi, and viruses may decrease their adapting ability by disturbing processes in the pathogenic process [23].

Table 1. Chemical compounds reported in *Cymbopogon sp* essential oil.

Compound	Species	Percentage (%)	Source	Ref
Elemol	C. winterianus	10.05–15.58	India	[13]
Geranial /citral A	C. citratus	48.18	France	[14]
	C. citratus	42.67	Brazil	[17]

Compound	Species	Percentage (%)	Source	Ref
	C. citratus	53.20	Brazil	[16]
Neral/ citral B	C. citratus	34.37	France	[14]
	C. citratus	33.03	Brazil	[17]
	C. citratus	36.37	Brazil	[16]
Myrecene	C. citratus	5.37	France	[14]
-	C. citratus	10.68	Brazil	[17]
Geraniol	C. citratus	4.99	Brazil	[17]
	C. citratus	2.66	Brazil	[16]
	C. martinii	70.26	Brazil	[18]
Linalool	C. martinii	1.16	India	[19]
	C. martinii	9.59	India	[15]
	C. martinii	1.77	Brazil	[18]
	C. winterianus	16.95-25.81	India	[13]
Limonene	C. giganteus	19.3	France	[14]
	C. nardus	3.5	Brazil	[20]
Mentha-1(7),8-dien-2-ol cis	C. giganteus	17.34	France	[14]
Mentha-1(7),8-dien-2-ol	C. giganteus	13.95	France	[14]
trans				
Trans-Mentha-2,8-diene-	C. giganteus	13.91	France	[14]
para-ol 1				
Mentha-2,8-diene-1-ol, cis-	C. giganteus	8.1	France	[14]
para Trans-geraniol	C. martinii	66.9	India	[19]
Geranyl acetate	C. martinii	7.5	India	[19]
Geranyi acctate	C. martinii	26.71	Brazil	[18]
	C. citratus	1.5	Brazil	[16]
(E,Z)-farnesol	C. martinii	9.43	India	[19]
β-ocimene	C. martinii	0.66	India	[19]
β-caryophyllene	C. martinii	1.36	India	[19]
p-caryophynene	C. citratus	3.91	Brazil	[16]
Trans-nerolidol	C. martinii	1.38	India	[19]
Caryophyllene oxide	C. martinii	0.97	India	[19]
Geraniol hexanoate	C. martinii	8.0	India	[19]
Fernesol acetate	C. martinii	0.68	India	[19]
Geranyl octanoate	C. martinii	1.94	India	[19]
Geranyl octanoate Geranyl proprionate	C. martinii	6.40	India	[19]
Citronellal	C. martinii C. nardus	27.52	Brazil	[20]
Citi diitiiai	C. naraus C. winterianus	16.33–26.83	India	[13]
	C. martinii	2.37	India	[15]
Citronellol	_	25	Brazil	[20]
CIU OHCHOI	C. nardus C. winterianus	14.26–16.30	India	[13]
Nerol	C. nardus	21.89	Brazil	[20]
Citronellyl acetat	C. nardus	5.75	Brazil	[20]
Geranyl acetate	C. nardus	4.53	Brazil	[20]
Geranyi acciaic	C. martinii	14.88	India	[15]
Terpinen-4-ol	C. martinii	11.52	India	
-		7.19	India	[15]
α-Terpineol	C. martinii			[15]
Thymol	C. martinii	6.19	India	[15]
Germacrene D	C. nardus	3.14	Brazil	[20]

The *C. citratus* essential oil has been reported had high antimicrobial activity against gram-positive bacteria such as methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-resistant *Staphylococcus epidermidis* (MRSE), but not significant for most of the Gram-negative bacteria [24]. Citral, one of the major compounds in *C.citratus* essential oil, regulated the proteins involved in transcriptional repression/activation, adhesion, and toxin activity of MRSA [25]. Citral also exposed antimicrobial activity by altering the membrane permeability of *Vibrio alginolyticus*, a Gram-negative marine bacterium [26]. Besides the effect on bacteria, *C. citratus* oil showed an antifungal effect against all *Candida tropicalis* strains with minimum inhibitory concentration (MIC) within the range 2.0 -3.9 µl/ml by inhibiting biofilm [27]. *C. citratus* essential oil also had an effect of inhibiting *Candida albicans*, *Candida krusei*, *Candida glabrata*, *Candida parapsilos*, and *Candida famata* (MIC)

125 to 175 μ g/ml) [28]. In another study *C.citratus* essential oils gave 100% inhibition of *Raffaelea quercus-mongolicae* and *Rhizoctonia solani* (MIC 125 to 175 μ g/ml) in reducing the count of mold, yeast and ethanol content of the silage [29,30]

The other research stated that the essential oil of *C. nardus* (concentrations of 5x and 10x minimum bactericidal concentration) reduced biofilm of *Candida albicans* and *Staphylococcus aureus* compared to the control group that using mouthwashes [20]. An essential oil from *C. nardus* also has a significant inhibitory effect on *Aspergillus niger*, *Aspergillus oryzae*, and *Aspergillus ochraceus* (MIC 1-2 mg/ml) [31].

A previous study expressed that the antimicrobial effect of *Cymbopogon winterianus* Jowitt ex Bor. and *Cymbopogon flexuosus* W. Watson essential oil against *Staphylococcus aureus*, *Micrococcus luteus*, *Bacillus subtilis*, *Escherichia coli*, and *Klebsiella pneumoniae*. MIC of C. *flexuosus* essential oil within the range of 800–1000 μg/ml and the essential oil *C. winterianus* with MIC values lying between 1000–1500 μg/ml [32].

The essential oil of *C.martinii* had many mechanisms for the antifungal activity such as inhibited germination of *Penicillium expansum* (MIC 0.125 or 0.25 g/l), inhibited the growth and production of ochratoxin A (OTA) of *Aspergillus ochraceus*(MIC 1308 \pm 16.69 μ g/ml) and *Penicillium verrucosum* (MIC 964 \pm 18.72 μ g/ml) [15,33]. *C.martinii* essential oil also inhibited toxigenic fungi of *Aspergillus flavus* and *Aspergillus carbonarius* (MIC 3.33 and 1.67 μ l/ml) [34].

3.3. Antioxidant activity.

It has been shown in many studies that essential oil from the Cymbopogon genus had antioxidant activity. Some of the antioxidant activity caused by phenol that known as one of the most famous compounds that have antioxidant activity, but some of them also had antioxidant activity caused by the presence of non-phenolic terpenoid. Several studies have investigated the antioxidant activity of C.citratus and C.giganteus essential oil. Citral, as a major compound of C.citratus essential oil, was statistically equal to the essential oil itself [14]. In addition, citral can reduce oxidative stress, and pro-inflammatory cytokines thus give a protective effect against UV-B -induced carcinogenesis in hairless mice [35]. Another study proved that linalool α -monoterpene that can be found in C.citratus can reduce oxidative stress and mitochondrial dysfunction mediated by glutamate and NMDA toxicity [36].

Research by Kusmardiyani *et al.* [37] used n-hexane, ethyl acetate, and ethanol extracts that prepared using different polarity solvents methods by reflux using herbs of three kinds of lemongrass, which were *C. citratus*, *C. martini* and *C. winterianus*. The samples used to determine antioxidant activity using 2,2-diphenyl-1-picrylhydrazyl (DPPH) and ferric reducing antioxidant power (FRAP) and correlation of total phenolic content (TPC), total flavonoid content (TFC), and total carotenoid contents (TCC) with their inhibitory concentration 50% (IC50) of DPPH and exhibitory concentration 50% (EC50) of FRAP. All samples from three kinds of lemongrass were categorized as a very strong antioxidant by DPPH method with phenolic compounds in *C. citratus* were the major contributor in antioxidant activities by DPPH and FRAP methods; meanwhile, flavonoid compounds were the major contributor in antioxidant activity of *C. martinii* by DPPH assay.

3.4. Antiinflamation activity.

The other research presented some anti-inflammation effects of Cymbopogon essential oils such as *C. citratus* and *C. giganteus* by inhibiting lipoxygenase enzyme that can induce inflammation [14]. Another study revealed that geraniol, one of the monoterpenes in Cymbopogon essential oil, can inhibit Kv1.3 ion channel (voltage-gated potassium channel) with IC₅₀ 0.5 mM. Kv1.3 channel expression is known as an important factor in autoimmune and chronic inflammatory diseases [38].

3.5. Hepatoprotective activity.

C. citratus essential oil significantly reduced 3A and Cytochrome P450 Family 1 Subfamily A Member 1 (CYP1A1) activities and lowered oxidative stress in the liver of rats. Citral as a major component of *C. citratus* essential oil may be the reason for the lowering activity of Cytochrome P450 (CYP) enzyme and oxidative stress in the rats liver [39].

3.6. Insecticide activity.

C. citratus essential oil (at 1%, 1.5%, and 2% concentrations with 100% mortality) and C. nardus essential oil (at 2 % concentration with 66% mortality) gave acaricidal activity against Rhipicephalus microplus larvae, which is a common pest that transmits hemiparasites [40]. C. citratus essential oil also proved insecticidal activity against Ulomoides dermestoides [41]. In addition C. citratus essential oil exhibited insecticidal effect against Phthorimaea operculella, a pest that damages crops such as potatoes, tobacco and tomatoes both stored and field [42].

In another study, *C. flexuous* essential oil significantly affected enzymes that help the organisms to transform or/and eliminate endogenous and exogenous compounds such as acetylcholinesterase (AChE), nonspecific esterases (α -and β -), glutathione S-transferases (GST), and mixed-function oxidases (MFO) in wild *Aedes aegypti* [43].

The other research used essential oil as a repellent against home flies (*Musca domestica*). Tablet combination of essential oil from *C. citratus* and *C. nardus* with essential oil from the clove was the most effective [44].

3.7. Antiparasite activity.

C. citratus essential oil showed trypanocidal activity on parasite *Trypanosoma brucei* using bloodstream trypomastigotes cultures of *T. b. brucei* and also had anthelmintic activity against parasitic plathelminths (monogeneans) in *Colossoma macropomum* (Serrasalmidae) [45,46].

3.8. Anticancer activity.

C. citratus and *C. giganteus* essential oils inhibited the cell growth of human prostate cancer cell lines (LNCaP and PC-3) and human glioblastoma cell lines (SF-767 and SF-763) [14]. The essential oil of *C. flexuosus* reduced the expression of the HSP90 gene significantly in MCF-7 (breast cancer cell lines) compared to HEK-293 [47].

3.9. Antiglycation activity.

Diabetes mellitus has been known to be linked to oxidative stress and nonenzymatic protein glycation. The essential oil of *C. schoenanthus* has moderate glycation inhibitors when compared to aminoguanidine as control [48].

3.10. Influence on the nervous system.

Major compounds of Cymbopogon essential oil such as S-(+)-linalool, one of the major compounds of *C. nardus* showed sedative and anesthetic effects in silver catfish (*Rhamdia quelen*) [49]. Citral also can induce analgesia in arthritic rats by modulating spinal nociceptive signaling [50]. Citronellal and linalool also provided anesthetic efficacy in common carp (*Cyprinus carpio*) by inducing deep anesthesia [51].

Anxiolytics are used to prevent and treat symptoms of anxiety disorders. The essential oil of *C.citratus* at a concentration of 10 mg/l caused significant anxiolysis in zebrafish by increasing the time spent in the light compartment of the tank [52]. Not only the essential oil, but aqueous leaf extract of *C. citratus* also effected neurobehavioral. *In vivo* study with male mice induced by SDS confirmed the effect of *C. citratus* aqueous extracts such as decreasing heightened anxiety, hyperlocomotion, depressive-like symptom, memory deficit, and social avoidance. These studies proved that *C.citratus* aqueous extract modulated modified levels of oxidative stress and acetyl-cholinesterase in SDS-mice [53]. Another study figured the effect of *C. citratus* as neuroprotective. Rats that were treated by AlCl₃ (17 mg/kg/day) showed elevated levels of Aβ peptides, tau proteins, MDA, NF-kB, and IL-6 and altered brain tissues to induce Alzheimer's condition. The rats that treated with AlCl₃ along with aqueous extract (obtained by infusion) and ethanolic extract (obtained by maceration in 90% ethanol) of *C.citratus* has a significant reduction in the hippocampal contents of Aβ peptides and tau protein after administration doses of 250 and 500 mg/kg for aqueous extract or 125 mg/kg for ethanolic extract [54].

Ethanol extract of *C. schoenanthus* that was obtained by macerated dried-air leaves of *C. schoenanthus* in 70% ethanol for 2 weeks had anti-stress potential. Ethanol extract of *C. schoenanthus* had an activity to increase the recovery acetylcholine (Ach) compared to heat-stressed SH-SY5Y cells; thus, this extract can be a new source to treat stress-related diseases [55].

A putative mechanism that could support in treating diarrhea has been studied to butanol and ethanol extracts of *C. schoenanthus* that prepared by liquid-liquid extractions tested on the distal rat colon, on the basal tone, and on KCl- and Ach-induced precontracted preparations. The result exposed that ethyl acetate extract reverted both the KCl- and the Achinduced precontraction of the distal rat colon, but n-butanol extract just affected the Achprecontracted colon probably because there was a distinction in their extract component [56].

3.11. Cymbopogon sp. and nanoparticles.

Nanoparticles are a well-studied delivery system, some of which exist to reducing toxicity, sustained and controlled release, deliver drugs with poor solubility or increase therapeutic targets [57]. Cymbopogon genus that has many benefits is one of the targets of development with nanoparticles. Studies by Jummes *et al.* [18] improved the essential oil from *C. martinii* with the help of poly-e-caprolactone nanoparticles to support and increased the

stability of essential oils. With this nanoprecipitation method, the combination of encapsulated with good stability is proven by the zeta potential and polydispersity index. Encapsulation also has proven to significantly reduce the cytotoxicity of *C. citratus* essential oils tested with human HaCat keratinocytes by WST-1 and LDH assays when encapsulated with PLGA nanoparticle [17]. The use of nanoparticles also helped in the formulation to increase pharmacological effects. *C. citratus* essential oil has been successfully encapsulated with poly nanoparticles (D, L-lactide-co-glycolida) made into hydrogels. This formula prevents the Herpes simplex virus in non-cytotoxic concentrations, 42.16 times lower than free oils without encapsulation, 8.76, and 2.23 times that of nanoparticles and hydrogels that are containing free essential oils [16].

4. Conclusions

This review proved that plants of the genus Cymbopogon are very interesting because Cymbopogon in the extract form or essential oil form has a lot of compounds with plentiful biological activities that are useful for the development of drugs from natural ingredients. Lots of research have been done to prove the benefits of *Cymbopogon citratus* essential oil as one of the commodities that produce essential oils from the Cymbopogon and citral as one of the main components of their essential oils, but there is also a study about the extracts and other Cymbopogon species. Some pharmacological studies that have been confirmed are regarding the pharmacological effects of Cymbopogon in the central nervous system, anti-inflammatory, antimicrobial, antioxidant, and anticancer. In addition, there have been many studies using nanoparticles to improve the deficiency of Cymbopogon essential oil to enhance its pharmacological effects.

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Conflicts of Interest

No conflict of interest was declared by the authors. The authors alone are responsible for the content and writing of this article.

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