Antimicrobial activities of citronella (*Cymbopogon nardus*) essential oil against several oral pathogens and its volatile compounds

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ABSTRACT

Introduction: *Cymbopogon nardus* is a strong aromatic plant with relevant medicinal properties due to its essential chemical compounds and its potential therapeutic effects. This study was aimed to evaluate the antimicrobial activities of citronella essential oil against several oral pathogens and to identify the volatile compounds. **Methods:** The essential oil of *C. nardus* was purchased from Excellent Wisdom Sdn. Bhd., Malaysia. The source of raw material was collected from Malacca, the southern region of Malaysia, and the company made its taxonomic identification. An experimental in-vitro study was conducted on the essential oil processed from *C. nardus* genus Cymbopogon of Poaceae family. The in-vitro antimicrobial activities of *C. nardus* essential oil were evaluated against *Streptococcus mutans* (ATCC 25175), *Streptococcus sobrinus* (ATCC 33478), and *Candida albicans* (ATCC 10231) using agar well diffusion assay. The identification of the volatile compounds was performed using gas chromatography-mass spectrometry (GC-MS). **Results:** The *C. nardus* essential oil exhibited inhibitory activity against *C. albicans* at the concentration of 6.25%, whereby the inhibitory activity against *S. mutans* and *S. sobrinus* began at the concentration of 25%. The antimicrobial activity of *C. nardus* essential oil was statistically significant at the concentration of 50% in all tested pathogens. The GC-MS analysis of the *C. nardus* essential oil revealed the presence of few constituents, which include monoterpenes, diterpenes, sesquiterpenes and phenolic compounds. Monoterpenes were the major identified terpenoids and contributed to 54.45% of the total volatile composition. The main identified monoterpenes were citronellal (11.35%), z-Citral (11.34%), ß-Myrcene (6.70%), and ß-Trans-ocimene (6.03%), which was the first time ß-Myrcene and ß-Trans-ocimene was found in high percentage. **Conclusion:** *C. nardus* essential oil is an active antibacterial agent against several oral pathogens, and the percentages of active volatile compounds are different within different origins.

Keywords: Antimicrobial, *Cymbopogon nardus,* essential oil, GC-MS, oral pathogens.

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INTRODUCTION

Cymbopogon nardus (*C. nardus*), commonly known as citronella grass, is a perennial grass of the Poaceae grass family. It is a tall herb and can grow up to 1 to 1.5 m. In Malaysia is called as "Serai wangi" due to its aroma which is stronger than the lemongrass. *C. nardus* is distributed throughout the tropical region of Asia such as India, Burma, Malaysia Peninsular, Sri Lanka, and Indonesia.

It is a rugged plant and able to adapt to different types of soil and climate. In Malaysia, it is usually planted at the house backyard, and since the past ten years, it has been cultivated in large quantities in Malaysia for extracting the valuable essential oil.

C. nardus is traditionally used as a mosquito repellent, household fumigant, and as a fragrance of cosmetics. The properties of *C. nardus* have been extensively investigated and showed a varied range of antimicrobial effects including antibacterial, antifungal, and antiparasitic properties.[1-3] However, its antimicrobial activity against oral pathogens remains unknown. Despite the commonly used of standard antibacterial agents including 0.2% chlorhexidine and triclosan in oral care products, finding an alternative natural source antibacterial agent is a top priority because adverse effects such as emerging multidrug-resistant pathogens in the environment by the latter.[4] Microbes such as *Streptococcus mutans* and *Streptococcus sobrinus* are endogenous bacteria in pathogenesis of dental caries. While *Candida albicans* have been implicated in oral diseases as the most common opportunistic oral fungus.[5,6]

Therefore, the present study was aimed to investigate the antimicrobial effects of the *C. nardus* essential oils against *S. mutans*, *S. sobrinus* and *C. albicans* and identified of its volatile components were investigated using agar well diffusion method and gas chromatography-mass spectrometry (GC-MS).

METHODS

This study was an experimental and in-vitro study of antimicrobial properties of the commercialised *C. nardus* essential oil. The extract was chosen due to its abundance of resource locally and recent enthusiasm in natural products and medicinal plants for its biological activities and therapeutic potential.

Sample of C. nardus essential oil

Sample of *C. nardus* essential oil was purchased from Excellent Wisdom Sdn. Bhd., Malacca, Malaysia. The raw materials were extracted from *C. nardus* genus Cymbopogon of Poaceae family, which were commercially cultivated in the same region of Malacca, Malaysia.

Organism testing

In the current study, the microorganisms *S. mutans* (ATCC 25175), *S. sobrinus* (ATCC 33478) and *C. albicans* (ATCC 10231) were obtained from the Craniofacial Laboratory, School of Dental Sciences, Universiti Sains Malaysia, Kelantan, Malaysia. The media used in this study were purchased from Oxoid Ltd., UK.

Determination of antimicrobial activity

C. nardus essential oil was tested for antimicrobial activity at different concentration (50, 25, 12.5 and 6.25%) using agar well diffusion method. This method will determine the ability of *C. nardus* essential oil at a different concentration to inhibit the formation of new bacterial and fungal colonies through the formation of an inhibition zone. Each bacterium was suspended in 2 ml of peptone water whereas *C. albicans* was suspended in 2 ml of sterile saline. The turbidity of this suspension was adjusted to a 0.5 Mc Farland standard by using turbidimeter. A sterile cotton swab was dipped into the inoculum suspension, and a lawn was made on Mueller-Hinton agar (*S. sobrinus*), Mueller-Hinton blood agar (*S. mutans*) and Sabouraud dextrose agar (*C. albicans*) plates. The sterile well was impregnated with 100 µl of *C. nardus* essential oil at different concentration. Well infused with 100 µl chlorhexidine 0.2% and dimethyl sulfoxide (DMSO) were used as positive and negative controls, respectively. These plates were then incubated at 37°C for 24 to 48 h, and the zone of inhibition was measured. This experiment was performed in triplicates. Diameter of the inhibition zone (the clear area around each well) was measured with a digital calliper in millimetres. Data collection was conducted on each plate after 24 to 48 h.

Gas Chromatography Mass Spectrometry (GC-MS) analysis

The GC-MS analysis of *C. nardus* essential oil was performed by GC-MS (Hewlett Packard 6890 Gas Chromatograph with 5973N Mass Selective Detector). The column was fused silica capillary, HP-5 column (30 m x 0.25 mm i.d x 0.25 µm film thickness) (Agilent Technologies, USA). The carrier gas was helium at the flow rate of 1.0 ml/min. The column temperature was maintained at 50W°C for 2 min, then programmed at 20°C/min to 280°C and waited for 10 min. The injection and interface temperatures were set at 250°C and 280°C, respectively. One µl sample was injected in splitless mode and analysed in MS full scan mode (*m/z* 40-650). The electron ionization was fixed at 70eV. The solvent delay was 4 min. Acquisition of data was performed using Chemsation software. The identification of the peaks was based on computer matching of the mass spectra with the National Institute of Standards and Technology (NIST02) and Wiley 275 libraries (≥ 80% matching). The percentage compound was calculated from the summation of the peak areas of *C. nardus* compounds.

Statistical analysis

Results were expressed as Mean ± SD for illustration. Statistical analysis was performed using a statistical package, SPSS Statistics Campus Edition version 24.0 by applying values to determine the effect between different concentrations of *C.nardus* essential oil against tested microorganisms.

Statement of human and animal rights

This study did not involve human or animal subjects performed by any of the researchers.

RESULTS

The antimicrobial study of *C. nardus* essential oil exhibited antibacterial and antifungal properties against all tested microorganisms at a concentration of at least 25%, as shown in Table 1. The *C. albicans* were the most sensitive to the *C. nardus* essential oil at the concentration of 6.25%, whereby S. mutans and S. sobrinus were sensitive to the *C. nardus* essential oil at the concentration of 25%. These results showed that the antimicrobial activities of the *C. nardus* essential oil varies with different concentrations. At the concentration of 25 and 50%, there is an antimicrobial activity of the essential oil towards all the tested pathogens. Results of the GC-MS analysis of *C. nardus* essential oil cultivated in Malacca, Malaysia, are shown in Table 2. A total of 35 volatile compounds were identified, including 13 monoterpenes, 2 diterpenes, 9 sesquiterpenes, 2 phenolic compounds, and 9 others. Monoterpenes were the dominant class in the *C. nardus* essential oil, and they accounted for 54.45% of the total volatile composition. The main identified monoterpene was citronellal (11.35%), followed by z-Citral

Table 1. Antimicrobial activity of C.nardus essential oil

Tested microorganism	Inhibition zone diameter (mm)									
	C. nardus essential oil concentration								Chlorhexidine concentration	
	6.25%		12.5%		25%		50%		0.2%	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
S. sobrinus					19.34	0.85	42.20	2.82	29.39	0.46
S. mutans					23.56	2.92	32.83	2.52	27.52	0.08
C. Albicans	22.80	0.57	22.83	0.44	26.02	0.24	26.70	0.50	23.84	0.26

***The experiments were performed in triplicate and the results are presented in the median values, with 0.2% chlorhexidine used as positive (+) control**

(11.34%), β-Myrcene (6.70%), β-Trans-ocimene (6.03%), geranyl acetate (3.82%), limonene (3.50%), and citronellol (3.22%).

After monoterpenes, sesquiterpenes were the dominant constituent in the citronella oil with a total percentage of 5.20%. Nine sesquiterpenes were identified with β-Caryophyllene (1.55%) as the most abundant. The other minor compounds identified from *C. nardus* essential oil were diterpenes and phenolic compounds which respectively contributed in as many as 0.29 and 3.79% to the total volatile compositions.

Table 2. Volatile compounds of *C. nardus* essential oil

Compounds	Composition (%)
Monoterpenes	
1R-α-Pinene	2.72%
Camphene	1.47%
β-Phellandrene	0.47%
β-Myrcene	6.70%
β-trans-Ocimene	6.03%
Linalool	0.52%
(ñ)-Limonene	3.5%
Citronellal	11.35%
Citronellol	3.22%
Z-Citral /cis-Citral	12.49%
cis-Geraniol	2.08%
Geranyl acetate	3.82%
Geraniol	0.08%
Diterpenes	
Geranyl linalool isomer	0.11%
Geranyl geraniol	0.18%
Sesquiterpenes	
β-Caryophyllene	1.55%
α-Humulene	0.72%
α-Muurolene	0.53%
Caryophyllene oxide	0.85%
γ-Eudesmol	0.21%
.tau-Muurolol	0.25%
β-Eudesmene	0.60%
β-Elemene	0.21%
Farnesol isomer A	0.28%
Phenolic compounds	
Methyleugenol	2.04%
Trans-methyl iso-eugenol	1.75%
Others	
Tricyclene	0.44%
6-methyl-5-hepten-2-one	0.61%
4-Nonanone	1.65%
3,5-Heptadienal,2-ethylidene-6-methyl-	0.55%
Bicyclo(3.1.1)hept-2-ene,2,6-dimethyl-6-(4-methyl-3-pentenyl)-	0.84%
α-Amorphene	2.43%
Elemol (others)	1.35%
Neophytadiene	0.11%
6,11-Dimethyl-2,6,10-dodecatrien-1-ol	0.24%

DISCUSSION

The essential oil from *C. nardus* exhibited antimicrobial properties towards *C. albicans* at all concentration ranges. This result showed that *C. albicans* was the most susceptible towards citronella essential oil compared to the other microbes. This condition is partly due to in its planktonic form the *C. albicans* virulence potential decreases.[7] They are commonly considered as harmless commensals and are isolated from the vagina, mouth and gastrointestinal tracts. When the host-fungus interactions become unbalanced, the fungus can initiate infection and cause disease.[8] *C. albicans* are commonly isolated from immunocompromised patients such as HIV patients.[8]

However, no inhibitory effects were detected by the agar well diffusion method at the concentration of 6.25 and 12.5% for *S. mutans* and *S. sobrinus*. Both of these microorganisms were shown to be associated with the pathogenesis of dental caries.[9] Compared to *S. sobrinus*, *S. mutans* plays a more vital role in producing major caries associated microbial virulence factor in caries pathogenesis.[10] Presence of the high-level of *S. mutans* in the oral cavity is correlated with high caries risk.[11] They adhere to the tooth surface facilitated by extracellular polysaccharides and form a biofilm which then uses as a sugar substrate in the diet for bacterial metabolism producing an acidic environment which promotes demineralisation.[12] They are Gram-positive bacteria and has a thick cell wall which would explain the need for a higher concentration of the essential oil to assert its effect.[13]

In the present study, *C. nardus* essential oil at the concentration of 25 and 50% showed antimicrobial activity towards all tested pathogens. The antimicrobial activities of the *C. nardus* essential oil at different concentrations were compared with 0.2% chlorhexidine which acted as the positive control. Chlorhexidine

digluconate (CHX) is from biguanide group and used for plaque prevention and disinfection in dentistry due to its good antimicrobial activity apart from its staining effect and increase of calculus deposits in prolonged use.[14,15] Thus, these results show that *C. nardus* essential oil had antimicrobial effect properties towards the tested microorganisms when compared to chlorhexidine. These results also showed that *C. nardus* essential oil has the potential of antimicrobial agent for use in dentistry.

It is known that microorganisms have different characters in planktonic form compared to biofilm form.[16] From the findings of the current experiment, there was a requirement to carry out an additional investigation on the antimicrobial properties of the essential oil with a condition which imitates the oral condition to strengthen the study. Further studies, especially cytotoxicity and genotoxicity tests, are a necessity to determine whether *C. nardus* essential oil can be used safely in the oral cavity.

The antimicrobial activity of the *C. nardus* essential oil could be due to terpenoids and phenolics compounds. Monoterpenes are the major compounds identified. The main identified monoterpene was citronellal (11.35%), followed by z-Citral (11.34%), ß-Myrcene (6.70%), ß-Trans-ocimene (6.03%), geranyl acetate (3.82%), limonene (3.50%), and citronellol (3.22%). A similar finding was observed from the previous study on *C. nardus* cultivated from the state of Kelantan in Malaysia.[17] This present study showed that citronellal (29.6%) was the primary compound identified.[17] However, the other compounds have differed. Only six compounds identified in *C. nardus* cultivated from both areas were the same, which were citronellal, caryophyllene, citronellol, limonene, geraniol and geranyl acetate.

Interestingly, previous studies of *C. nardus* cultivated from other countries such as Brazil[18], Togo[19] and Benin[3] also showed that citronellal was the main identified volatile compound. However, the other compounds also differ. Therefore the significant difference in the GC–MS profiles of the *C. nardus* essential oil collected from different locations is consistent with the fact that plants often produce different amounts of phytochemicals when grown in different geographical origins.

On the other hand, a study of *C. nardus* essential oil that obtained from the other state in Malaysia, which was Selangor, found that the age of *C. nardus* leaves influences the composition of essential oils or volatile compounds.[20] They found that citronellal (39.66%) was the main volatile compound identified from younger leaves, while geraniol (46.10%) was the main volatile compound identified from older leaves.[20] In the current study, *C. nardus* that obtained from Malacca, Malaysia showed that geraniol composition was only 0.08%.

In contrast, *C. nardus* cultivated from two regions in Thailand showed that geraniol was the main identified volatile compound.[2,21] However, the authors did not mention the age of the *C. nardus* leaves. Thus, the differences in volatile compounds of the *C. nardus* could be attributed to the different regions, soil and age of the leaves.

After monoterpenes, sesquiterpenes were clearly the dominant constituent in the citronella oil with total percentage of 5.20%. Nine sesquiterpenes were identified and ß-Caryophyllene (1.55%) was the most abundant. ß-Caryophyllene was also identified in *C. nardus* cultivated from Thailand[2,21] and other regions in Malaysia[17] which ranged from 0.8 to 6.5%. In contrast, ß-caryophyllene or caryophyllene was found in trace amount (0.1%) in *C. nardus* cultivated from Benin[3] and absent in *C. nardus* cultivated from Togo[19], Brazil[18] and other regions in Malaysia.[20]

Terpenoids are well known to possess various pharmacological effects. Studies on citronellal, showed that this compound has antibacterial activities against both Gram-positive (*Staphylococcus aureus*) and Gram-negative (*Escherichia coli*) bacterial.[22] Antifungal activities also have shown against several species of Aspergillus, Penicillium and Eurotium.[2] z-Citral, which was known to have antibacterial activity against a wide range of Gram-positive and Gram-negative bacterial.[23] The other main compounds identified were ß-Myrcene, limonene and citronellol. Both studies of ß-Myrcene[24] and limonene[25] demonstrated anti-ulcer properties. ß-Myrcene was also had neuroprotective effects.[26] Study on the citronellol compound showed that this compound had antidiabetic and antinociceptive effects.[27,28]

CONCLUSION

C. nardus essential oil shows active antibacterial properties against several oral pathogens, and the percent-ages of active volatile compounds are different from other origins.

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