Original Article

# Quality evaluation, GC/MS analysis and antimicrobial activities of *Morinda Citrifolia* against oral Microorganisms

**Suparat Jongjai[1], Jongkon Saising[2], Rawiwan Charoensub[1, 3], Pravaree Phuneerub[1, 3]***

[1]Department of Applied Thai Traditional Medicine, School of Integrative Medicine, Mae Fah Luang University, Chiang Rai 57100, Thailand. [2]School of Health Science, Mae Fah Luang University, Muang, Chiang Rai 57100, Thailand. [3]Medicinal Plants Innovation Center of Mae Fah Luang University, Mae Fah Luang University, Chiang Rai 57100, Thailand.

**Correspondence:** Pravaree Phuneerub, Department of Applied Thai Traditional Medicine, School of Integrative Medicine, Mae Fah Luang University, Chiang Rai 57100, Thailand. pravaree.phu@mfu.ac.th

## ABSTRACT

In Thai traditional textbooks, *Morinda citrifolia*. fruit is an antidote to vomiting and cure oral diseases. The current study aimed to develop the standardization parameters, chemical evaluation, and anti-microorganisms activities of *M. citrifolia* fruit extracts against oral microorganisms including *Staphylococcus aureus, Streptococcus mutans,* and *Candida albican. M. citrifolia* fruit (MC) were collected from 15 sources throughout Thailand and then examined the pharmacognostic specification including macroscopic characteristics, microscopic characteristics, and physicochemical parameters. The volatile oils of *Morinda citrifolia* fruit (MCO) were determined by GC/MS. The antimicrobial activity of ethanol extract (MCE), water extract (MCW), and volatile oils (MCO) of *M. citrifolia* fruit were carried out by examining the inhibition areas using the agar well diffusion method, minimal inhibition concentration (MIC), and minimal bactericidal concentration (MBC). The outcome of the study revealed that Physico-chemical identification showing a loss on drying, total ashes, acid-insoluble ashes, and water content should be not more than 10.992, 10.115, 0.973, and 6.882% w/w, respectively. The volatile oil content, water, ethanol, and hexane soluble extractive values should not be less than 0.762, 31.8257, 18.0992, 3.4964 % w/w, respectively. GC-MS analyses of MCO showed the major compound was octanoic acid (84.103%) and hexanoic acid (7.183%). Based on antimicrobial activities, MCE and MCW cannot have antimicrobial activity in the oral cavity. However, MCO was potentially effective in suppressing microbial growth agiant *S.aureus* and *S.mutans,* and *C. albicans*. The volatile oil of *M.citrifolia* fruit may be a beneficial component of oral health care products or drugs for oral disease.

**Keywords:** *Morinda citrifolia*, Antimicrobial activities, Pharmacognostic specification, Chemical analysis

## Introduction

The disadvantaged and poor population groups in both developing and developed countries still have problems about the burden of oral disease, for instance, periodontal disease, dental caries, tooth loss, oral mucosal lesions, and oropharyngeal cancers which had a great impact on general health and life quality [1]. The significance of bacteria strain is the of oral microorganisms including *Enterobacterfaecalis*, *Lactobacillus fermentum*, *Lactobacillus salivarius*, *Streptococcus sobrinus,* and *Streptococcus mutans,* and all of bacteria are Gram positive and cause cariogenic [2]. *Streptococcus mutans* are bacteria that are commonly found in the mouth on the surface of teeth and that are the main cause of dental caries in humans. *S. aureus* (gram-positive bacteria) and *C. albicans* (opportunistic fungal) are the cause of denture stomatitis (DS) and can perform biofilm formation [3]. In addition, *Candida* spp is to be important in the initiation of Oral candidiasis which is a common opportunistic infection of the oral cavity. Nowadays, antibiotics such as vancomycin, teicoplanin (glycopeptide), and linezolid (oxazolidinone) are used to fight this bacterium. However, they have limited available and adverse effects [4].

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*Morinda citriolia* L. is an evergreen shrub or small tree. It is from the Rubiaceae family. It is growing in tropica regions worldwide. It is known as Noni and in Thai called "Yor ban" or "Yor" [5]. *M. citrifolia* is largely used in traditional medicine in primary health care to relieve illness. In Thai traditional textbooks it is stated that the unripe fruit is an antidote to vomiting, the ripe fruit is a woman's menstrual drive and unripe fruit burned into charcoal is mixed with a little salt which is used for treatment swollen gums and gum diseases. In previous studies, *M. citrifolia* extract had significant property concern with antibacterial and antifungal activity against various strains of bacteria and fungi. The ethanol extract of dried noni fruit have displayed significant antibacteria activity against foodborne pathogens such against *S.typhimurium* and *E. coli* [6]. *M.citrifolia* fruit showed antioxidant, anti-inflammatory, liver-protective, and immunomodulatory effects [7]. However, there are no reports about pharmacognostic specification of *M. citrifolia* fruit and lack of evidence about antimicrobial activities against oral microorganisms. Therefore, the purpose of this research is to develop the standardization parameters of *M. citrifolia* crude drug, chemical analysis, and antimicrobial activities against oral microorganisms from MCE, MCW, and MCO to scientific evidence for supporting the use of *M. citrifolia* extract as an alternative treatment in oral diseases.

## Materials and Methods

### Plant materials

Dired MC samples were gathered from 15 different locations in 5 parts of Thailand during August-September 2020 (North, Central, North-East, East, and South) and they were authenticated by the office of the Queen Sirikit National Convention, ChiangMai, Thailand. Hot air oven at 50°C was used to dry the samples and then they were peverized for further investigation.

### Plant extraction

Grinded the dried *M.citrifolia* fruit (MC) from the Supan Buri province of good standardized quality control were macerated with 99% ethanol and water. MC (5 g) were continuously extracted with 99% ethanol until exhaustion using soxhlet apparatus. The extract was filtered and evaporated to be dried under a vacuum. MC (100 g) were continuously macerated with DI water until exhaustion, and then Whatman No. 4 filter paper was used to filter the extract. The water extracts were lyophilized to be dried and stored at -20 °C until being used to reduce the probability of degradation of active compounds.

### Determination of macroscopic and microscopic characteristics

Macroscopic specifications of herbal materials indicate shape, size, color, surface characteristics, texture, fracture characteristics, and appearance of the cut surface and were illustrated by drawing and photograph of the plant. Microscopic characteristics were used for identification and authentication of plant material by cross-section, powder drug by microscope under an OLYMPUS) CX22LED (magnifying lens (4X to 40X), and expressed by drawing and photograph of the plant by the researcher [8].

### Physico-chemical specifications

Loss on drying, total ash, acid-soluble ash, water content, and solvent extractive values were following by World Health Organization guidelines of the Quality control methods for medicinal plant materials [8].

### Determination of volatile oil content

50 gr of powder was poured into round bottom flasks, then 500 ml of distilled water and boiling chips were added and boiled in Clevenger type apparatus for 6 hrs. and volume of the volatile oils was collected and recorded [8]. Each sample was done in three replications. The volatile oil from Supan Buri was used for GC/MS analysis and antimicrobial activities.

### Gas chromatograph mass spectrometer (GCMS)

The volatile oil dissolves in hexane. GC/MS analysis was determined by Agilent 6890 GC with HP-5MS capillary column (30 m × 0.25 mm, 0.25 μm film thicknesses). The oven temperature was ramped from ٦٠°C to 325 °C at a constant rate of 3 °C per minute. The injection port was held 220°C. The gas carrier in this testing was Helium gas with a flow rate of one milliliter per minute and then obtained, analyzed, and compared the mass spectra index of mass spectral of NIST Mass Spectral Library.

### Preparation of microbial strains and growth conditions

Microbial organisms including *S. aureus* (ATCC 25923), *S. mutans* (DMST 1877), and *C. albicans* (ATCC 10231) were collected from STIC, Mae Fah Luang University. *C. Albicans* were cultivated in Brain Heart Infusion Agar (BHA) media and in the dish. And then, they were nurtured for 24 hrs at 37°C. *S. mutans* and *S.aureus* were cultured on Trypticase soy agar (TSA) and Mueller Hinton Agar (MHA), respectively. *S.aureus* was incubated at 37°C for 24 hrs and *S. mutans* was incubated at 37°C for 48 hrs. And then, they were adjusted turbidity equal to McFaLand No. 0.5, then diluted until colony to have approximately to about $1.0\times10^6$ CFU/ml.

### Agar disc diffusion method

Disc diffusion method is generally used to investigate the antimicrobial activity of plants or microbial extracts. This test of antibacterial by agar disc diffusion was adapted from the suggested guidelines and protocols from the Clinical and

Laboratory Standards Institute (CLSI). Sterilized Whatman papers discs (6 mm diameter) were soaked with 10 µl of MCE (2mg/disc), MCW (2mg/disc), MCO (2mg/disc), chloramphenicol (30µg/disc), candixclotrimazole )0.1mg/disc) as positive control, DMSO and tween 20 as negative control. Three organisms was spread on plates by swabed *C.albicans* cultures on BHA plate, *S. mutans* cultured and *S. aureus* cultured on MHA. And then, discs were added. The plates were incubated at 37°C for 18-24 hrs. The diameters of inhibitory zones were measured in millimetres by Vernier caliper [9].

## Specification of MIC, MBC, and MFC

The least inhibitory condensation was specified by broth microdilution technique n 96 well microtiter plate according to the clinical and laboratory standards institute (CLSI). The MCO, chloramphenicol, candixclotrimazole (were dissolved in tween 20), and then dilutions series were prepared in a 96-well plate, ranging from 0.5 µg/ml to 32 µg/ml. 100 µl of extracts or a positive/negative control in broth and 100 µl of inoculate broth were poured into each well and incubated at 37°C, for 24 hours. The least inhibitory condensation was seen at the last well which was indicated in a clear solution. Streaked clear inoculate broth on Mueller Hinton agar (for bacteria) and Sabouraud Dextose - agar (for fungi) then nurtured the agar plate for 24 hours at 37 °C. Minimum bactericidal concentration (MBC) and minimum fungicidal concentrations (MFC) of the extract were investigated from the agar plate with no emerged microbial expansion [10].

## Statistical analysis

The Physico-chemical identification was offered in the Grand mean ± pooled SD values. Antimicrobial activities were done in triplicates and findings are offered as the mean ± standard deviation (SD).


**Figure 1.** Macroscopic evaluation a) Drawing of Composition of *M.citrifolia* Leaves and Cross-section of Fruit, b) Fresh fruit, c) Transverse section of fruit, d) Dried fruits of *M.citrifolia*

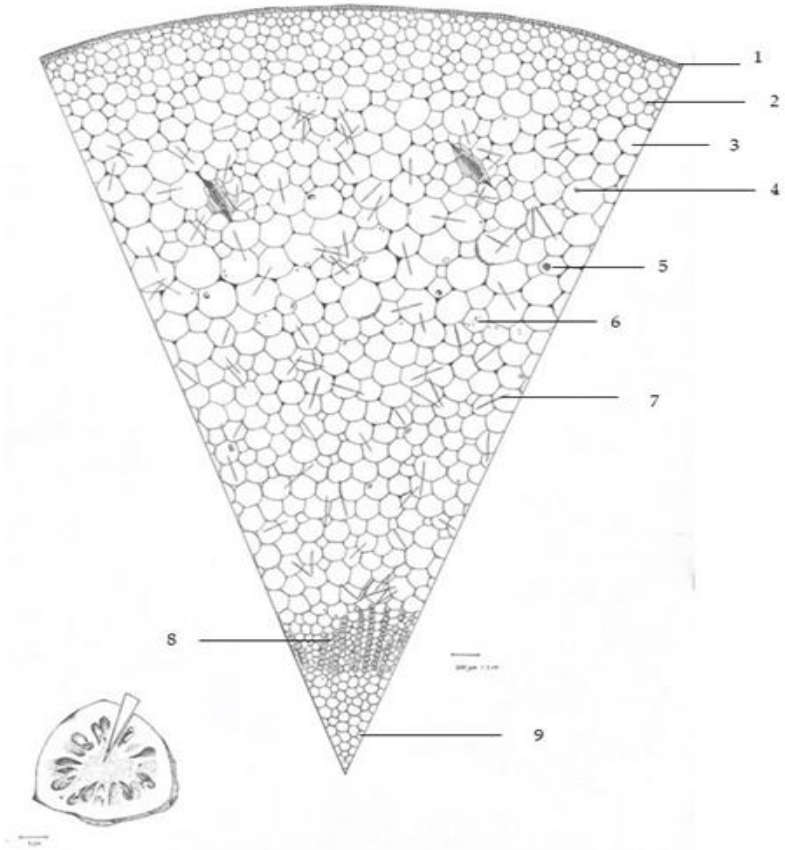


**Figure 2.** Cross-section of *M.citrifolia* Fruit: Thin-Walled Epidermis (1), Collenchyma (2), Parenchyma Cells (3), Prismatic Calcium Oxalate (4), Resin (5), Oils (6), Raphide Calcium Oxalate Crystals (7), Bundle of Spiral Vessel (8), Pith Parenchyma (9)

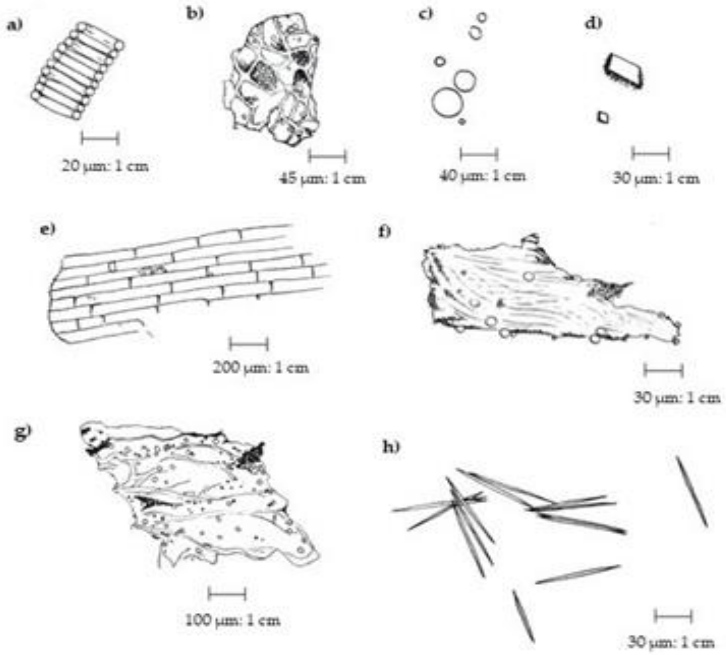


**Figure 3.** Microscopic characteristics of *M.citrifolia* Fruit Was Powder: Reticulated Vessel (a), Parenchyma (b), Oils (c), Prismatic Calcium Oxalate Crystals (d), Longitudinal Parenchyma Wit Oil Gland (e), Oils in Fiber Group (f), Oils with Parenchyma (g), Calcium Oxalate Crystals (Raphide) (h)

**Table 1. Physicochemical Evaluation of *M.citrifolia* Fruit**

| Parameter % (by weight) | Mean ± SD* | Maximum - Minimum |
|---|---|---|
| Loss on drying | 10.992 ± 0.337 | 17.776 - 5.990 |
| Total ash | 10.115 ± 1.812 | 11.849 - 8.321 |
| Acid-insoluble ash | 0.973 ± 0.161 | 1.244 - 0.708 |
| Volatile oil content | 0.762 ± 0.095 | 1.399 - 0.199 |
| Water content | 6.882 ± 1.159 | 9.326 - 2.832 |
| Ethanol-soluble extractive | 18.099 ± 0.668 | 23.889 -3.789 |
| Hexane-soluble extractive | 3.496 ± 0.439 | 4.460 - 0.0002 |
| Water-soluble extractive | 31.826 ± 2.946 | 37.519 - 17.214 |

*Grand mean±pooled SD. The specimen were from 15 various sources throughout Thailand, and each sample was done in triplicate. SD: Standard Deviation

**Table 2. The Chemical Constituents of the Volatile Oil of *M.citrifolia* Fruit Using GC/MS**

| RT | Chemical compounds | Molecular Formula | Molecular weight | Area% |
|---|---|---|---|---|
| 4.3653 | 3-Methyl-3-buten-1-OL | $C_5H_{10}O$ | 86.13 | 0.056 |
| 8.9921 | 2-Heptanone | $C_7H_{14}O$ | 114.19 | 0.047 |
| 10.3651 | Methyl hexanoate | $C_7H_{14}O_2$ | 130.1849 | 0.367 |
| 14.0224 | Hexanoic acid | $C_6H_{12}O_2$ | 116.16 | 7.183 |
| 14.7836 | 2-Pentyne | $C_5H_8$ | 68.12 | 0.050 |
| 18.9745 | Butanoic acid, 2-methyl-, 3-methyl-3-butenyl ester | $C_{10}H_{18}O_2$ | 170.25 | 0.091 |
| 19.5085 | Methyl octanoate | $C_9H_{18}O_2$ | 158.24 | 2.177 |
| 24.3414 | Octanoic acid | $C_8H_{16}O_2$ | 144.21 | 84.103 |
| 25.8362 | Isobutyl 3-methylbut-3-enyl carbonate | $C_{10}H_{18}O_3$ | 186.25 | 0.927 |
| 27.346 | Hexanoic acid, 3-methyl-2-butenyl ester | $C_{11}H_{20}O_2$ | 184.2753 | 0.0928 |
| 28.631 | Decanoic acid, methyl ester | $C_{11}H_{22}O_2$ | 186.2912 | 0.105 |
| 30.7668 | n-Decanoic acid | $C_{10}H_{20}O_2$ | 172.26 | 1.072 |
| 30.9297 | [Dodecanoyl(methyl)amino]acetic acid | $C_{13}H_{25}NO_3$ | 243.3420 | 0.124 |
| 34.3094 | Succinic acid, isobutyl 3-methylbut-3-enyl ester | $C_{14}H_{22}O_4$ | 254.32 | 2.790 |
| 35.6283 | Octanoic acid, 3-methylbut-2-enyl ester | $C_{13}H_{24}O_2$ | 212.33 | 0.277 |
| 39.1784 | Hexyl octanoate | $C_{14}H_{28}O_2$ | 228.37 | 0.058 |
| 42.0099 | Dodecanoic acid, 4-penten-1-yl ester | $C_{17}H_{32}O_2$ | 268.4 | 0.058 |
| 51.2587 | Hexadecanoic acid, methyl ester | $C_{17}H_{34}O_2$ | 270.4507 | 0.131 |
| 56.507 | 9,15-Octadecadienoic acid, methyl ester, (Z,Z)- | $C_{19}H_{34}O_2$ | 294.25588 | 0.165 |
| 56.6972 | 9-Octadecenoic acid, methyl ester, (E)- | $C_{19}H_{36}O_2$ | 296.4879 | 0.099 |
| 62.2251 | 9-Octadecenamide | $C_{18}H_{35}NO$ | 281.5 | 0.028 |

## Results and Discussion

*M.citrifolia* is a small perennial with 2-6 meters in height. Leaves are simple leaves, opposite, with ample large elliptical leaves (5-17 cm length, 10-40 cm width), fresh green young leaves. Flowers are little tubular, white, banded together, and inserted on the peduncle. The petioles leave ring-like marks on the stalks and the corolla is greenish-white. Fruit (3-10 cm length, 3-6 cm width) is ovular and fleshy with an embossed appearance were showed in **Figure 1**. It is somewhat rugged, semi-translucent, and ranges in color from green to yellow to almost white at the time of picking **(Figure 1)**. It is covered with little reddish-brown buds including the seeds [11]. The pulp is juicy and bitter, a light dull yellow or whitish color, and gelatinous. Ripe fruit has many hard triangular reddish-brown pits which are found, each including four seeds (approximately 3.5 mm) [12]. Microscopic characteristics of cross-section and powder of crude drug of MC were illustrated in **Figures 2 and 3**. Microscopic powder features revealed the presence of oil glands, raphide, and prismatic calcium oxalate crystals that were in agreement with the earlier report by Pratima and Shrikanthin in 2015 [13].

Physicochemical evaluation plays an important role in detecting the purity and quality of crude drugs including loss on drying, total ash, acid insoluble ash, volatile oil content, extractive values, and water content parameters. The determination of ash is useful for detecting inorganic materials such as metallic salts, silica, carbonates, calcium oxalate crystals, sandy in crude drug [14]. The physicochemical specifications (% by weight) of the fruit of *M.citrifolia* fruit are demonstrated in **Table 1**. They are evaluated from 15 sources in Thailand. The loss on drying, total ash, acid insoluble ash, volatile oil content, and water content should not be more than 10.992, 10.115, 0.973, and 6.882% w/w respectively. The water, ethanol, and hexane soluble extractive values should not be less than 0.762, 31.826, 18.099, 3.496 % w/w, respectively.

The volatile oil by hydrodistillation method of *M.citrifolia* fruit detected, contained 21 components **(Table 2)**. The major chemical constituents revealed that octanoic acid (84.103%) and hexanoic acid (7.183%) has similarities with previously research [15-17]. In previous study [18] demonstrated that octanoic acid and hexanoic acid showed a strong effect on inhibition of growth of againt *E. coli* and *S. aureus*. According to Bae and Rhee in 2019 [19] have stated that the caprylic acid showed antifungal effects against *C. albicans*. In 2020, Halala *et al.* and Hsieh *et al.* appraised the effect of the capric acid alone and indicated a stronger effect against oral Candida isolates than its combination with common antifungal drugs [20, 21].

The bacteria strain of oral microorganisms *S. mutans* and *S. aureus* as Gram-positive bacteria are the main cause of dental caries and parotitis in humans [22, 23]. Besides, *C. Albicans* is a fungus that is the main causative agent of oral candidiasis [24]. The MCE, MCW, and MCO were investigated the antimicrobial activity by agar disc diffusion method with *S. aureus* and *S. mutans,* and *C. Albicans*. Evaluation of the antibacterial activity of *M. citrifolia* fruit extract was recorded in **Table 3** and **Figure 4**. The results revealed that MCE and MCW extract was not potentially effective in suppressing microbial growth of the oral cavity. However, MCO has potentially inhibited the growth of *S. aureus* and *S. mutans* and *C. albicans* with inhibition zones of 13, 9, and 19 mm, respectively. The minimum inhibitory concentration results, bacterial MICs, and minimal fungicide concentration, MFC with *C. Albicans* showed 2 and 4 µg/ml, respectively. MCO demonstrated strong antimicrobial activity against *C. Albicans*. Similarly, a previous study reported by Luis *et al.* [25] suggested the oil of *M. citrifolia* fruit had potential antifungal activity against fungi *C. Albicans*.

**Table 3. Antimicrobial Screening Test of *M.citrifolia* Fruit Extracts**

| Extract | *S. aureus* | | | *S.mutans* | | | *C.albicans* | | |
|---|---|---|---|---|---|---|---|---|---|
| | Inhibition zones (mm) | MIC (µg/ml) | MBC (µg/ml) | Inhibition zones (mm) | MIC (µg/ml) | MBC (µg/ml) | Inhibition zones (mm) | MIC (µg/ml) | MFC (µg/ml) |
| MCO | 13 | 32 | 32 | 9 | 4 | 32 | 19 | 2 | 4 |
| CP | 27 | 4 | 16 | 24.6 | 2 | 4 | - | - | - |
| CA | - | | | - | - | - | 9.6 | 2 | 4 |

MCO: Volatile Oil of *M. citrifolia* Fruit CP: Chloramphenicol CA: Candixclotrimazole

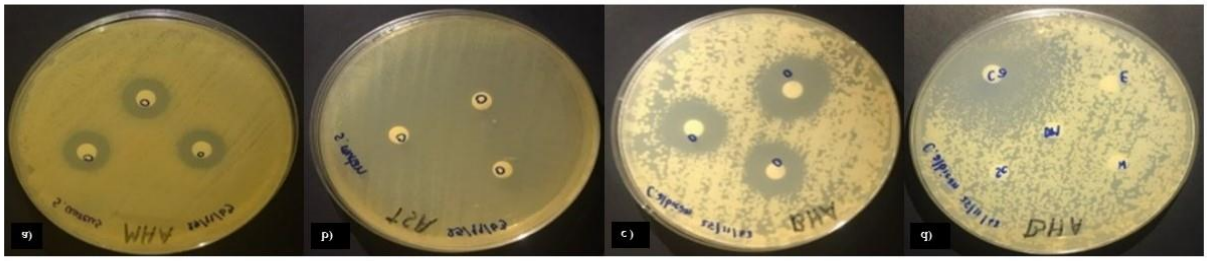

**Figure 4.** Zone of Inhibition of Oral Organisms of Volatile Oil of *M.citrifolia* Fruit (o: Volatileoil of *M. citrifolia* Fruit, DM : (DMSO) Negative Control, and ca (Candix Clotrimazole): Positive Control

## Conclusion

The major component of volatile oils of *M.citrifolia* fruit (MCO) was octanoic acid and hexanoic acid. According to the results obtained in this study for antimicrobial activities, MCO showed effectiveness in suppressing microbial growth in the oral cavity including gram-positive bacteria, *S.aureus* and *S.mutans,* and indicated strongly inhibition to the growth of the fungus is *C.albicans*. It can be further developed into a drug for the alternative treatment of oral candidiasis and maybe a beneficial component of oral health care products.

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**Conflict of interest:** None

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**Ethics statement:** None

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