The Effectiveness of *Moringa Oleifera Lam* Extract as an Oral Antimicrobial: a Systematic Literature Review

Ratna Kumala Indrastiti, Febrina Rahmayanti*, Yuniardini Septorini Wimardhani**

** Department of Oral Medicine, Faculty of Dentistry, Universitas Indonesia, Jakarta, 10430, Indonesia*

***Correspondence:** ratna.kumala02@ui.ac.id*

Received 24 April 2024; 1st revision 9 June 2024; 2nd revision 5 July 2024; Accepted 29 July 2024; Published online 31 July 2024

Keywords:

Moringa Oleifera, Oral Antimicrobial, Mouthwash

ABSTRACT

Background: *The use of mouthwash to maintain oral hygiene has been carried out for many years. Tooth discoloration, burning sensation and the death of oral microflora can be caused by long-term use of mouthwash. The use of Moringa oleifera lam has been studied as an alternative medicine because of its pharmacological properties and it is hoped to have minimum side effect. In this systematic literature review, we included the studies that have been investigate the antimicrobial capacity of Moringa oleifera lam as a basic knowledge to develop a preparation for oral hygiene maintenance.*

Method: *A thorough search of the literature was conducted utilizing four different electronic databases: PubMed, Scopus, Cochrane library, and EBSCO. Articles included in this study were published from 2013 to September 2023, with broad search criteria comprising MeSH-terms and free-text keywords Moringa Oleifera, Oral Antimicrobial, and Mouthwash.*

Result:*. We have 7 articles as the result after excluding the articles that do not meet PICO criteria.*

Conclusion: *According to the literature review that has been carried out, Moringa oleifera lam has antimicrobial capacity which allows it to be used as a material in medicinal preparations. Further research, both in vitro and clinical research, will determine the effectiveness of Moringa oleifera lam in suppressing microorganisms.*

doi: http://dx.doi.org/10.30659/odj.11.1.39-47
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Odonto : Dental Journal accredited as Sinta 2 Journal (https://sinta.kemdikbud.go.id/journals/profile/3200)
How to Cite: *Indrastiti et al*. The Effectiveness of Moringa Oleifera Lam Extract as an Oral Antimicrobial: a Systematic Literature Review. Odonto: Dental Journal, v.11, n.1, p.39-47, July 2024.

INTRODUCTION

Oral cavity serves as a reservoir for pathogens, appropriate oral hygiene, and includes cleaning and removing of possible bacterial foci, may aid in the management of oral cavity infections.[1] Several methods can be used to maintain oral hygiene: tooth brushing, flossing, tongue scrapping and application of mouthwash containing antiseptics.[2]

The use of mouthwash and antiseptic gels such as 0.12% and 0.2% chlorhexidine gluconate, 1% povidone iodine and sodium bicarbonate have been widely used to maintain oral hygiene.[3] The use of mouthwash derived from natural/herbal ingredients such as aloe vera, chamomile, pomegranate flowers, propolis, etc. has also been developed and can be an alternative in maintaining patient oral hygiene.[4] The adverse events and/or side effect from the use of several mouthrinse were studied by Tartaglia et.al (2019). In this study, cetyl pyridinium chloride (CPC), essential oils, chlorhexidine (CHX), triclosan, diclofenac, fluorides, and delmopinol were studied, and the majority of the studies found in local anatomical of the oral cavity (oral mucosal lesions, staining both in dental and oral mucosa) and functional (alteration of taste and oral sensation) changes. The most often reported adverse event was tooth discoloration, where it is depends on the length of the trial, the longer the trial, the high amount of occurrence and severity were reported.[5]

In studies that have been carried out previously, it is known that various parts of the *Moringa oleifera lam* (MOL) is known to have several chemical compounds and the pharmacological properties as: antioxidant, anticonvulsant, antimicrobial, anticancer, antiviral, and antiinflammation.[6,7] The utilization of MOL properties in dentistry has also been broadly discovered and investigated for its advancement. *Moringa oleifera lam* might be served as an constituent of toothpaste, mouthwash, irrigation material for endodontic tratment, an ingredient to accelerate wound healing after tooth extraction, a treatment for gingival diseases, oral ulcer, and might be beneficial to avoid caries of the tooth because of its antimicrobials characteristics.[8]

Our goal is to determine whether MOL possible to be used as an oral antimicrobial to maintain oral hygiene. To achieve that goal, we carry out a rigorous search strategy to conduct a systematic review of several studies related antimicrobial effect of MOL which can be obtained from various parts of the plant and especially what active ingredients which contain the highest antimicrobial properties.

RESEARCH METHOD

In this review, a systematic search was done according to PRISMA guidelines. We aim to provide information regarding PICO criteria; for the population (P) is patients with oral health problems who used MOL as intervention (I) which will be compared with gold standard mouthwash as the comparison (C) in order to know about the effectiveness of MOL as oral antimicrobial as the outcome (O). A systematic literature search was performed utilizing four electronic databases: MEDLINE via the PubMed search engine, Scopus, Cochrane library, and EBSCO. Articles included in this study were published from 2013 to September 2023, with broad search criteria comprising MeSH-terms and free-text keywords for “moringa oleifera” or “moringa” and oral antimicrobial. The Boolean operators was used to refined the search strategy and get relevant literature.

Study selection

The eligibility criteria of this systematic review were checked and determined based on PICO criteria by all authors. All relevant literature including clinical trials, randomized controlled trials, and in vitro studies were

included to this study. The title and abstract of each citation were reviewed and full-text citations were evaluated to ensure that those articles were appropriate for addition in data synthesis.

Data extraction

The data extraction was done by each author from all included trials. The study team devised simple forms for extracting characteristics from included studies such manuscript's information, sociodemographic, and methodological information.

RESULTS

This systematic review provided an overview on MOL antibacterial properties. In the PubMed, Scopus, Cochrane library, and EBSCO, and we were found 17 studies on MOL's antibacterial activities. The inclusion criteria based on PICO were used to screen these studies. We exclude several studies because of the duplication, there are several studies on a subject other than antimicrobial/antibacterial activity and we also exclude a systematic literature reviews and ongoing studies/protocols.

PRISMA flowchart was used to explain the process of searching and filtering articles (Figure.1)

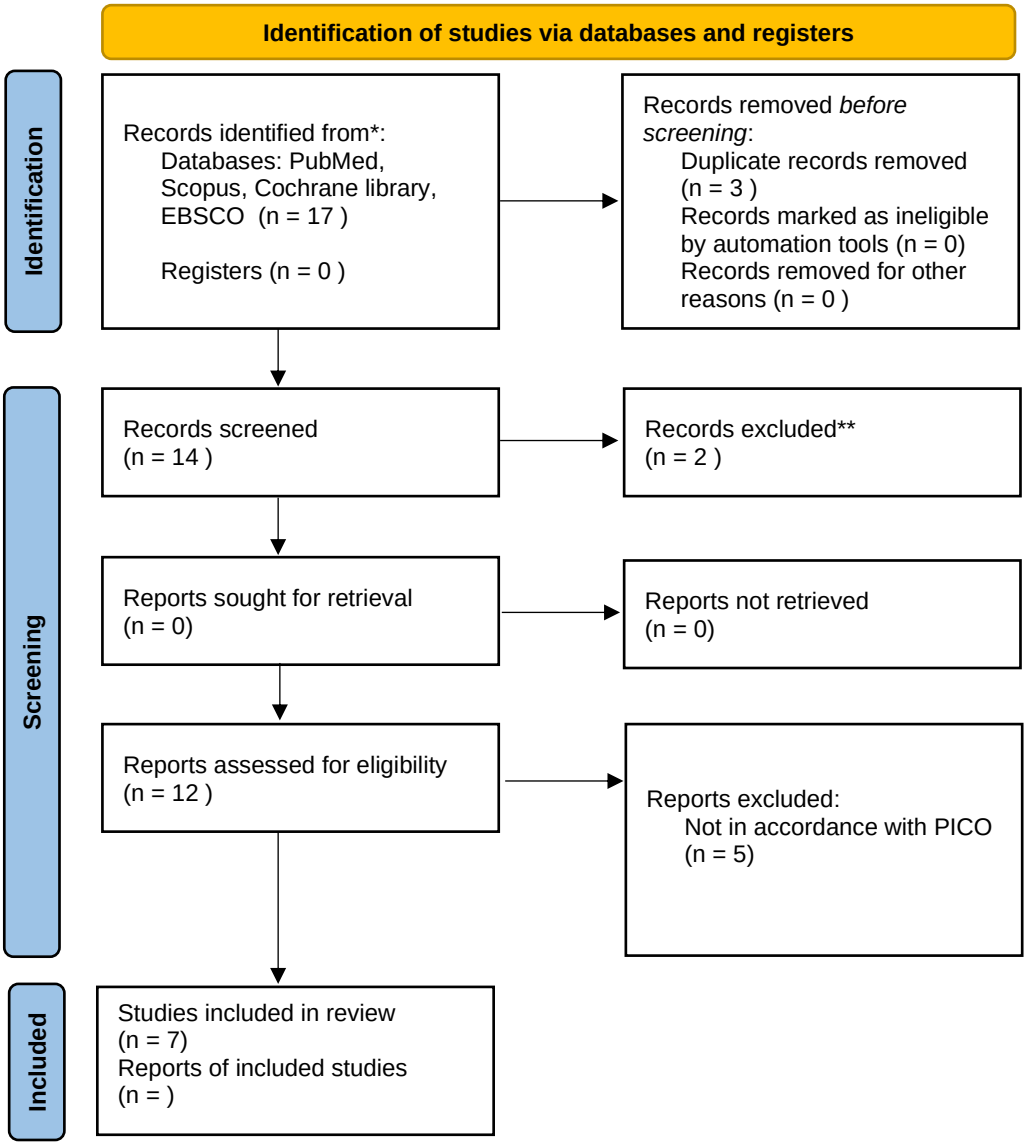

Figure 1. PRISMA Flow Chart

After screening and critical appraisal for the articles that were obtained, we extracted data from the articles and made conclusions from the studies obtained in the following table: (Table.1)

Table 1. Articles of *Moringa Oleifera Lam* as an Antimicrobial

No.	Title	Author & Year of Study	Study Design	Conclusion
1.	Efficacy of *Moringa oleifera* Leaf Extracts against Cariogenic Biofilm	Su-Kyung Jwa. 2019	In-vitro study	• The purpose of this trial was to look into the MOL leaf extracts's antibacterial properties on *S. mutans* and the production of cariogenic biofilm. • The study found that the MOL extracts exhibit antibacterial properties versus bacteria that responsible for cariogenic process and biofilm formation. MOL ethanol extracts seems to be more efficient compared to aqueous extracts.
2.	A Comparative Evaluation of Antibacterial Efficacy of *Moringa oleifera* Leaf Extract, Octenidine Dihydrochloride, and Sodium Hypochlorite as Intracanal Irrigants against *Enterococcus faecalis*: An In Vitro Study	Alharbi et.al.2023	In-vitro study	• The purpose of this study was to observe and compare the microbiological efficacy of MOL leaf extract, octenidine dihydrochloride, Sodium Hypochlorite, and combinations of those materials as intracanal irrigants for *E. faecalis*. • Result of the study indicated a substantial decrease in *E. faecalis* colony number after employing MOL leaf extract as an irrigant.
3.	Microbiological Assessment of *Moringa Oleifera* Extracts and Its Incorporation in Novel Dental Remedies against Some Oral Pathogens	Elgamily et.al. 2016	In-vitro study	• This trial purpose was to evaluate the antibacterial and antifungal properties of various portions of the MOL plant using various extraction technique in order to develop natural dental medicines from the herb. • Results of this study showed that ethanol, acetone, and ethyl acetate from leaf, root, seed that consider of having high antimicrobial activities, and the highest antimicrobial activities is from ethanol extract that obtained from leaves part.
4.	Bactericidal Efficacy of Omega-3 Fatty Acids and Esters Present in *Moringa oleifera* and *Portulaca oleracea* Fixed Oils Against Oral and Gastro Enteric Bacteria	Othman. 2016	In-vitro study	• The purpose of the study was to assess the antibacterial activity of MOL and purslane fixed oils towards various pathogenic bacteria (gram-positive and gram-negative), identify active components and determine the action mechanism. • Results of the study found that purslane was more effective than MOL against *E.coli,* particularly at low doses (20%). The researchers also discovered that the whole strains were unaffected to all dilutions of MOL fixed oil.
5.	*Moringa oleifera* Mouthwash Reinforced with Silver Nanoparticles - Preparation,	Kumar et al. 2022	In-vitro study	• The purpose of this trial was to evaluate the antibacterial activity of 5% MOL oral rinse with silver nanoparticles against oral aerobic microorganisms. • Results of this trial found that 5% MOL-

	Characterization and its Efficacy Against Oral Aerobic Microorganisms - In Vitro Study			silver nanoparticles oral rinse had a greater effect on *S. aureus* and an equal effect on *S. mutans*. The minimum zone of inhibition for *Candida albicans* was 16 mm.
6.	Acute and Sub-Chronic Toxicities and Antimicrobial Profiling of Hydro-Ethanol Extracts of *Moringa oleifera* Seed in Swiss albino mice and Wistar rats	Igbokwe et.al. 2018	In-vivo study	• The purpose this trial was to assess the vulnerability of microorganisms to MOL seed extracts and investigate the safety of utilizing these extracts in experimental animal by using the toxicity indicators. • Results of this study showed that: 1. MOL extract can be categorized as harmless because the LD_{50} per oral was 14.0g/kg body weight (equal to a dose of 980 g in a typical adult male weighing 70kg). This is significantly greater than the WHO toxicity index. 2. Indications that MOL seed extract may increase blood component production, particularly in hypovolemia conditions or anaemia. 3. The extract's adverse effects on the bone marrow may induce the reduction of white blood cells and mean corpuscular volume. 4. The seed extract significantly increased total protein, urea, bilirubin, and creatinine levels ($p < 0.5$), suggesting negative effects on important organs like the liver and kidneys. 5. The seed extract was shown to raise the level of alanine amino transferase (ALT), implying that it had some adverse effects on the liver. A drop in AST and ALP levels, indicating that it may have had a harmful or toxic effect on heart function.
7.	The Effectiveness of Moringa Leaf Extract (Moringa Oleifera)Against Porphyromonas gingivalis Bacteria in Periodontitis Cases Through IL-1 Cytokine Analysis	Rieuwpassa e.al.2022	In-vivo study	• The aim of this research was to establish the effect of MOL leaf on the anti-inflammatory cytokine IL-1. • The result showed that IL 1 levels decreased in both groups, however the decline was faster in the *Moringa* extract group.

DISCUSSION

Moringa oleifera lam is a *Moringa* species with various useful bioactive complexes such as phenolic acids, flavonoids, alkaloids, and phytosterol, which are essential parts of its biological activities.[9] A variety of therapeutic benefits from flavonoids (rutin, quercetin, rhamnetin, kaempferol, apigenin, and myricetin) that can be act as anti-inflammatory, antioxidant, antibacterial, and hypoglycemic properties, as well as assisting in wound healing and tissue regeneration. Additionally, leaves contain a number of phenolic acids, such as caffeic

acid, chlorogenic acid, gallic acid, and others. Tannins are thought to have a role as anticancer, antibacterial, and antihepatotoxic properties.[10]

Flavonoids have antibacterial properties by suppressing virulence factors, cell envelope synthesis, bacterial motility inhibition, biofilm development, efflux pumps, membrane rupture, and nucleic acid synthesis.[11] Plant containing phenolics can have a variety of antimicrobial actions: permeabilization and instability of the plasma membrane or inhibition of extracellular enzymes.[12] Other bioactive compound, tannic acid, belongs to the polyphenolic group and has antiviral effect due to its ability to block receptor binding and impact their activity. It inhibits the attachment of viruses to several types of surfaces by binding to the cell receptor. Furthermore, it prevents the attachment of proteins to cells, which is required for metabolite processing. Tannins' antibacterial potency is explained by their capacity to permeate past the bacterial cell wall and into the interior membrane, causing interference with the cell's metabolism and, as a result, demise.[13]

Several studies in the field of dentistry have been conducted on the use of bioactive compounds from MOL as antimicrobials. Alharbi et al. (2023) conducted research to examine and compare the microbiological efficiency of MOL leaf extract, octenidine dihydrochloride, sodium hypochlorite, and their mixtures as endodontic treatment irrigants against *E. faecalis*. This trial revealed a noteworthy decrease in *E. faecalis* colony counts after MOL utilization. *Moringa oleifera* lam leaf extract's antibacterial action is credited to its ingredients, which include alkaloids, flavonoids, saponins, tannins, triterpenoids and phenolics, all of which have unalike process for bacterial elimination.[14] This result is not in line with study from Natsir et al.2023, whom revealed that NaOCl 50% has the highest effectivity towards *Enterococcus faecalis* and *Streptococcus mutans* compare to 2.5% and 5.0% MOL decoction, although for *Streptococcus mutans*, the inhibition zones of the MOL water extract at 2.5% was significantly different from those of 5.0%.[15]

Elgamily et al. 2016 conducted a microbiological assessment evaluate the antibacterial and antifungal properties of various portions of the MOL using various procedures for extraction in order to develop herbal dental medicines and the result is that the highest antimicrobial activities has gotten from ethanol extract that obtained from leaves part.[16] This result is similar with study from Su Kyung Jwa on 2019 revealed that leaf extracts of MOL have antimicrobial activity against *S. mutans* and biofilm formation. Ethyl alcohol extracts are seems to be more efficient compared to distilled water (DW) extracts.[17] Another trial that held by Kumar et al. (2022) discovered that 5% MOL - silver nanoparticles oral rinse had a robust effect on *S. aureus* and a equal effect on *S. mutans*, though this study did not test its effect on anaerobic bacterial microorganisms.[18] This is similar to the study conducted by Moodley et al. (2018), that is using biosynthesized nanoparticle formulations from leaf extracts of MOL and it shows that the extract is very promising as broad-spectrum antibacterial substances (against *Staphylococcus aureus*, *Enterococcus faecalis*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae*).[19]

Riewpassa et al on 2022 have been done an *in-vivo* study to analyze the effectiveness of MOL leaf extract against *P. gingivalis* bacteria by anti-inflammatory cytokine IL-1 analysis. *Moringa* leaf extract has been proven to decrease pro-inflammatory cytokine IL-1 cells in wistar rats induced with *porphyromonas gingivalis* bacteria on the day of observation (day 0, day 1, day 3, day 5, and day 7).[20] Study from Faisal, Bashir, Sha, and Raad on 2022 was investigate about dissimilar aqueous extracts of MOL (seeds and leaves) and red pomegranate (albedo and seeds) that were tested for antibacterial activity against *porphyromonas gingivalis*. When compared to other extracts, MOL seeds contain more oleic acid (24.6%), Trans-11-Octadecenoic acid

(18%), and hexadecanoic acid (9.4%). Those chemical properties have been proven to have antibacterial effects on *P. gingivalis*, which supports the previous findings. The existence of phenolic substances and fatty acids, particularly oleic acid, which operate by modifying the shape of phospholipid configuration and damaging membrane of the cell and lysis of the cell, was responsible for the antibacterial activity. Furthermore, oleic acid was discovered to suppress the formation of hemagglutinin, a virulence protein that works as an adhesin in *porphyromonas gingivalis*. Furthermore, high levels of 10-trans-11-Octadecenoic acid in *moringa* seeds hinder *porphyromonas gingivalis* survival and proliferation by disrupting their cellular membrane and suppurating messenger ribonucleic acid synthesis.[21]

Slightly different results were obtained from study of Othman on 2016 that compare the antibacterial activity of MOL and *Portulaca oleracea* fixed oils towards some pathogenic bacteria (gram positive and gram negative). This study found that purslane fixed oil is more effective than MOL against *Escherichia coli*, particularly at low doses (20%). The current investigation also found that all of the strains are unaffected to all dilutions of MOL fixed oil.[22] Study from Igbokwe et al on 2018 want to assess the antibacterial effectiveness, acute and sub-chronic toxicity of MOL (seed extracts) in experimental animals. From the results, it shows that the extract demonstrated exceptional antimicrobial activity. In the acute toxicity study, mice fed 15.0 and 20.0 g/kg body weight died within twenty four hours. The lethal dose (LD_{50}) was 14.0 g/kg bodyweight. Body weight, serum electrolytes, and Mean Corpuscular Haemoglobin (MCH) value all increased significantly, but the Mean Corpuscular Volume (MCV) value decreased significantly. Serum liver enzymes were found to be significantly lower, whereas serum protein metabolites were found to be higher. The extract indicates harmful effects on several organs such as kidney, liver and testes. Even though the extracts exhibit a high LD_{50} value (14.0 g/kg) and a strong safety margin, caution should be used in consumption because greater dosages or extended consumption may have negative effects on specific organs.[23]

The literature review that has been carried out has several limitations, such as journal publication sources related to herbal ingredients, which do not appear to be found in many search engines chosen by the author. In the next literature review, it is necessary to search engines for research publications that focus more on herbal materials. Moreover, currently there are so many ongoing research regarding *moringa* implementation in the field of dentistry, so there will be many results and updates related to the use of *moringa* as herbal medicine.

CONCLUSION

Recently, large-scale studies were conducted on the utilization of *Moringa oleifera lam* as an antibacterial agent. According to the literature review that has been conducted, *Moringa oleifera lam* has shown antimicrobial activities which is very promising to be used as a medicinal preparation which is expected to have the same effectivity and lower side effects than existing medicine preparations. Further research, both in vitro and clinical trial, are required to determine the effectiveness of *Moringa* in inhibiting a pathogenic microorganism, especially those that play a role in the existence of disease in the oral cavity, as well as in the whole body. The precise dosage for moringa preparation which has antimicrobial effectiveness must be determined, along with the type of preparation that is proper to use.

CONFLICT OF INTEREST

Author declares no conflict of interest.

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