**Moringa oleifera** and its application in dental conditions: A systematic review and meta-analysis

Moumita Das, Nihar Ranjan Panda, Ruchi Bhuyan, Sanat Kumar Bhuyan

Department of Medical Research, IMS and SUM Hospital, Siksha ‘O’ Anusandhan (Deemed to be University), Bhubaneswar, India

**ARTICLE INFO**

**Article Type:** Review

**Article History:**
Received: 3 November 2022
Accepted: 26 February 2023

**Keywords:**
Ethnomedicine
Drumstick plant
Oral cancer
Periodontitis
Dental caries
Gingivitis

**ABSTRACT**

*Moringa oleifera* is a considerable ethnomedical herb with various bioactive compounds. This study aimed to analyze the efficacy of *M. oleifera* in the prevention and management of various oral conditions. A thorough search was conducted on the Web of Science, Scopus, PubMed, and PubMed Central databases. After screening the data on the basis of inclusion and exclusion criteria, 9 studies were considered for further meta-analysis. The analysis was performed on R programming software (version R-4.0.2) and the results were represented by a forest plot. The estimate obtained via common and random effects model for *in vitro* studies was statistically insignificant ($I^2$ test $P > 0.05$) with risk ratios of 8.25 (95% CI: 3.76-18.08) and 7.98 (95% CI: 3.64-17.50) and for *in vivo* studies were statistically significant ($I^2$ test $P < 0.05$) with risk ratios of 1.12 (95% CI: 0.90-1.40) and 0.97 (95% CI: 0.71-1.32), indicating the efficacy of *M. oleifera* in oral diseases on animal and clinical trials, whereas it failed to report the efficacy on *in vitro* level. Future research has to be done to come up with new and more phytoactive compounds from all parts of the plant with proper extraction procedures. The effectiveness of the compounds has to be validated first on *in vitro* scale followed by clinical trials so that *M. oleifera* can be used as therapy in preventing and managing oral ailments.

**Implication for health policy/practice/research/medical education:**
This meta-analysis demonstrated that *Moringa oleifera* had applications in different oral conditions like periodontitis, root canal infection, gingivitis, dental caries, oral cancer, etc.


**Introduction**

According to the WHO Global Oral Health Status Report (2022) data, around 2.5 billion people are affected by oral diseases globally (1). A number of health factors contribute to oral conditions, including consuming free sugars, smoking, drinking alcohol, poor oral hygiene, as well as social and commercial factors. On the other hand, the cost of treatment is very high for both the individual and the larger healthcare system (2). Additionally, conventional drugs have harmful side effects that could be successfully countered with an ethnomedical approach using bioactive compounds of plants (3).

*Moringa oleifera* Lam, a potential medicinal plant, native to India, found mainly in the foothills of the Himalayas, has been used as conventional folk medicine for ages (4,5). The presence of diverse classes of secondary metabolites like alkaloids, flavonoids, isothiocyanates, terpenoids, anthocyanins, anthraquinones, saponins, steroids, essential oils, and tannic acids makes it a potential therapeutic drug. Previous studies revealed various bioactivity of *M. oleifera*, including anti-inflammatory, anti-microbial, antioxidant, anticancer, antilucre, neuroprotective, anti-hypertensive, cardio-protective, cytotoxicity etc. (6,7). Few studies have been conducted evaluating the biological activity of *M. oleifera* in relation to oral disorders. *M. oleifera* leaves extracts in form of lozenge or mouthwash successfully reduced root canal infection, inflammation, gingivitis, and plaque (8-10). Isothiocyanate from *M. oleifera* seeds showed inhibitory action against gene expression involved in mitophagy in the stem cell of the human periodontal ligament (11).

Both *in vitro* and clinical trials have proved the effectiveness of *M. oleifera* on a wide range of diseases; several healthcare product companies have already...
incorporated *M. oleifera* in their products. There are some trials conducted to verify the effect of *M. oleifera* on oral health care. However, there is not a single systematic review and meta-analysis summarizing the current evidence. Thus, this study was designed to observe and analyze the efficacy of *M. oleifera* in the prevention and management of various oral conditions.

**Materials and Methods**

This study was conducted with due permission of SRB (Scientific Review Branch) following the population, intervention, comparison, outcome (PICO) method, as applicable in accordance with the topic of the review.

- **Population**: patients and animal subjects of all ages with any type of oral disease.
- **Intervention**: evaluation of the effect of *M. oleifera* on patients suffering from oral diseases.
- **Comparison**: effects on *M. oleifera* ([Figure 1](#)) among *in vivo* and *in vitro* studies.
- **Outcome**: positive effects or reduction in the diseases of oral cavity.
- **Focused question**: Are *M. oleifera* extracts effective in the treatment of oral disease?

**Eligibility criteria**

Studies must meet the following inclusion criteria based on the PICO question:

- Studies reporting the efficacy of *M. oleifera* on oral diseases,
- Clinical trials and *in vitro* studies were considered,
- The comparison group must comprise treatment and control/placebo,

In this study, the evidence provided by the clinical trials allowed for confident inferences to be made. Studies depicting only survey reports with no control and treatment groups were not considered in the analysis.

**Information sources and literature search**

A systematic search was conducted on databases: Web of Science, Scopus, PubMed, and PubMed Central. The key words used for literature search were: “*Moringa oleifera*”, “uses”, “oral diseases”, “dentistry”, “oral cancer”, “dental plaque”, “dental caries”, “gingivitis”, “periodontitis”. Articles scripted in English and relevant to the research question, from the year 2015 were considered. Screening of the articles was based on the clinical trials and *in vitro* studies reporting the effects of *M. oleifera* extracts on oral diseases. In addition, the references of the retrieved articles were reviewed. At first, the articles were screened based on title and abstracts. Next, the full texts of the articles were analyzed. The studies failing to meet the inclusion criteria were eliminated.

**Synthesis of results**

To compare the therapeutic properties of *M. oleifera* to the treatment and control group among the patients suffering from various oral diseases or tested *in vitro* (microbes and extracted tooth) and to maximize the accuracy of the overall estimate of the effect size, data from individual studies were pooled together to perform the meta-analysis. Because of random distribution in individual studies, the mean was obtained to estimate the risk ratios and their 95% confidence interval (Upper and lower confidence intervals). The extracted data were analysed using R programming software version (R-4.0.2). The heterogeneity of the studies was examined using the Tau value, *P* value, and I² statistics. Meta-regression analysis could not be performed as there was a limited number of eligible studies.

**Results**

**Study selection**

The electronic search resulted in the cover of 345 articles...
publications. By screening the titles, authors, and years of the publications 165 articles were excluded as duplicates. Then, 120 articles were excluded after screening the abstracts as they did not meet the inclusion criteria. Out of the remaining 60 articles, 40 did not report oral diseases and 20 studies were included in the systematic review. From these 20 studies, 9 were considered for meta-analysis (Figure 2).

Study characteristics
The relevant characteristics of 9 qualified studies have been summarized in Table 1. The clinical effects compared between the patients treated with M. oleifera extract and control/placebos were evaluated in 6 studies. There were 2 studies reporting the efficacy of M. oleifera extracts on patients affected with gingivitis, periodontitis, dental plaque, and oral inflammation. Crude leaf extract of M. oleifera was administered in the form of lozenge and mouthwash (9,10). Three studies reported the effects of M. oleifera leaf extracts on rats’ oral cancer. The leaf extract was administered intraorally by means of insulin sonde in three different concentrations (12-14). A study reported the efficiency of M. oleifera crude extract in the preservation of tooth extraction sockets among Cavia cobaya when administered by means of injection (15). Another 2 studies reported the potency of M. oleifera in surface enamel and dentin re-mineralization when tested in vitro on the extracted teeth (16,17). M. oleifera leaf extracts in the form of toothpaste and mouthwash acted as antimicrobials when tested in vitro on microbes (18).

Analysis result and co-relation among the selected studies
The result of the analysis generated by R program has been represented in the form of Forest plots for in vitro and in vivo studies.

In vivo
In the 6 pooled in vivo studies involving 192 subjects (including human, rats and guinea pigs) in the treatment group, 122 ones were more likely to experience reduction in the oral ailment that they suffered from in comparison to the control/placebo groups. But there was heterogeneity (60%), although not highly considerable. However, 2 trials did not favour the reduction in oral diseases (RR 0.67). The narrow CI in the forest plot depicted the accuracy of individual studies. The estimate obtained via common and random effects model was statistically significant (I² test P<0.05) with a risk ratio of 1.12 (95% CI: 0.90-1.40) and 0.97 (95% CI: 0.71-1.32) indicating that the incident of oral diseases among the subjects treated with certain concentrations of M. oleifera extract was lower (Figure 3).

In vitro
In 3 collective studies, 208 subjects (extracted human teeth and oral microbes) were administered with M. oleifera extracts in the form of toothpaste or mouthwash or applied directly. Only 86 among them showed positive effects of M. oleifera extract. No heterogeneity among the studies was observed. The estimate obtained via common and random effects model was statistically insignificant (I² test P>0.05) with a risk ratio of 8.25 (95% CI: 3.76-18.08) and 7.98 (95% CI: 3.64-17.50) indicating that the incident of oral diseases among the subjects treated with certain concentrations of M. oleifera extract was higher (Figure 4).

Discussion
The purpose of this meta-analysis was to evaluate the effects of M. oleifera extracts on oral diseases. Our observation from the pooled studies suggests that the M. oleifera extracts are efficient enough for preventing and managing multiple oral ailments. Our analysis included in vivo experiments performed on humans and animals (rats
## Table 1. The summary characteristics of studies included in meta-analysis

<table>
<thead>
<tr>
<th>Author (Reference)</th>
<th>No. of participants (studies)</th>
<th>Parts used</th>
<th>Plant used</th>
<th>Control</th>
<th>Preparation</th>
<th>Route of administration</th>
<th>Duration</th>
<th>Oral diseases treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elgamily et al (18)</td>
<td>324 microbes</td>
<td>Leaves, roots, seeds</td>
<td>400 mg/mL</td>
<td>Only toothpaste base</td>
<td>Ethanolic, acetone, acetate</td>
<td>Toothpaste, mouthwash</td>
<td>24 hours</td>
<td>Control of oral pathogens</td>
</tr>
<tr>
<td>Nagib et al (16)</td>
<td>50 (posterior teeth)</td>
<td>Leaves</td>
<td>-</td>
<td>Only etched teeth</td>
<td>Solution</td>
<td>Solution</td>
<td>7 days</td>
<td>Enamel and dentin remineralization and prevent erosion</td>
</tr>
<tr>
<td>Hartono and Jularso (12)</td>
<td>28 (rats)</td>
<td>Leaves</td>
<td>3.125%, 4.6875%, 6.25%</td>
<td>Placebo</td>
<td>Extract</td>
<td>Intraorally by means of insulin sonde</td>
<td>20 days</td>
<td>Oral cancer</td>
</tr>
<tr>
<td>Kresnoadi et al (15)</td>
<td>56 (Cavia cobaya)</td>
<td>Leaves</td>
<td>0.1 mL</td>
<td>PEG</td>
<td>Crude extract</td>
<td>Injection</td>
<td>30 days</td>
<td>Preservation of tooth extraction sockets.</td>
</tr>
<tr>
<td>Younis et al (17)</td>
<td>75 (premolars)</td>
<td>Leaves</td>
<td>50 mg/mL, 200 mg/mL</td>
<td>No treatment</td>
<td>Lyophilized extract</td>
<td>Directly applied by composite bond brush</td>
<td>14 days</td>
<td>Surface enamel remineralization</td>
</tr>
<tr>
<td>Luetragoon et al (9)</td>
<td>93</td>
<td>Leaves</td>
<td>145.86 mg</td>
<td>Placebo</td>
<td>Crude extract</td>
<td>Lozenge</td>
<td>4 weeks</td>
<td>Gingivitis, Periodontitis, oral inflammation</td>
</tr>
<tr>
<td>Buakaew et al (10)</td>
<td>47</td>
<td>Leaves</td>
<td>0.02%</td>
<td>Placebo</td>
<td>Crude extract</td>
<td>Mouthwash</td>
<td>14 days</td>
<td>Dental plaque and gingivites</td>
</tr>
<tr>
<td>Pertami and Budhy (14)</td>
<td>25 (rats)</td>
<td>Leaves</td>
<td>3.125%, 6.25%, 9.375%</td>
<td>Placebo</td>
<td>Extract</td>
<td>Intraorally by means of insulin sonde</td>
<td>1 month</td>
<td>Oral cancer</td>
</tr>
</tbody>
</table>

PEG, polyethylene glycol
and guinea pigs) and in vitro studies on oral pathogens and teeth extracts. Results from this analysis suggested that *M. oleifera* leaf extract controlled oral conditions effectively. Its leaves were mostly used for their high concentrations of bioactive compounds compared to other parts of the plant, although their contents varied widely depending on climatic factors (19,20). Vitamins, phytates, polyphenol, phenolic acids, flavonoids, alkaloids, carotenoids, glucosinolates, tannins, saponins, oxalates, and glucosinolates are all found in the leaves of the plant (21). The easy availability and accessibility of the leaves make it a better option for pharmaceutical use.

After excluding the studies that did not meet the inclusion criteria, only 9 studies with properly recorded data were taken for further evaluation (6 reported clinical and animal trials (in vivo) and only 3 reported in vitro studies). According to the results of this study, the statistical analysis of clinical trials i.e., in vivo studies showed significant effects of *M. oleifera* extracts on the study subjects suffered with various oral ailments like periodontitis, gingivitis, inflammation, anti-cancer agents, and root canal remineralisation, when administered intraorally through injection or by means of toothpaste and mouthwash. An overall reduction in the occurrence of oral diseases was observed. Because of its anti-cancer, anti-inflammatory, anti-bacterial, anti-fungal, and anti-oxidant properties, *M. oleifera* has proven useful in oral hygiene (22). The therapeutic effects of *M. oleifera* are attributed to its phytochemical components such as tannins, alkaloids, flavonoids, saponins, and sterols (23). Compounds like glucosinolates, glycosides, glycerol-1-9-octadecanoate, and isothiocyanates possess anti-cancerous activities (24). Anti-microbial, anti-inflammatory, and anti-oxidant activities are mostly regulated by phenolic compounds (25,26). The presence of more than 90 different chemical compounds makes this plant a potent herbal medicine (27).

From the forest plot analysis of in vitro studies, the estimate obtained via random effect model was not statistically significant. This might be due to the variance in population type in the included studies or due to less study size. Due to limited data, the efficacy of *M. oleifera* extracts in the management of oral diseases on in vitro level cannot be confirmed. But, since the bioactivity of *M. oleifera* extracts has been confirmed by the analysis done in vivo studies, more research is needed to be done first in in vitro level followed by clinical trials so that *M. oleifera* can be used as therapy for various oral ailments.

**Conclusion**

*Moringa oleifera* leaf extracts appear to be a potent anti-microbial, anti-inflammatory, anti-cancer agents against oral ailments, also having activity in enamel re-mineralisation and preservation of root extraction sockets. The results from our analysis indicate the efficacy of *M. oleifera* in oral diseases on animal and clinical trials whereas it failed to report the efficacy on in vitro level. Hence, future research has to be done to come up with new and more phytoactive compounds from all parts of the plant with proper extraction procedures. Then, the effectiveness of the compounds has to be validated first on in vitro scale followed by clinical trials so that *M. oleifera* can be used as therapy in preventing and managing oral ailments.

**Acknowledgment**

The authors are highly grateful to the Chairman of Siksha ‘O’ Anusandhan (Deemed to be University), Prof. Manoj Ranjan Nayak for providing support during the study. The authors are also thankful to the Dean, IMS and SUM Hospital, Siksha ‘O’ Anusandhan (Deemed to be University), Prof. Gangadahar Sahoo for encouraging and supporting.

**Author’s contribution**

RB and SKB conceived, planned, designed, guided and edited the manuscript. NRP contributed to data analysis. MD collected the materials and drafted the manuscript and interpreted the data.

**Conflict of interests**

The authors declare no conflict of interest, financial or otherwise.

**Ethical considerations**

None to declare. However, the duplication and plagiarism were checked with our Institute’s Turnitin software.

**Funding**

None.
References

Das et al


