



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

Moumita Das^{ID}, Nihar Ranjan Panda^{ID}, Ruchi Bhuyan^{ID}, Sanat Kumar Bhuyan^{ID}

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.

Please cite this paper as: Das M, Panda NR, Bhuyan R, Bhuyan SK. *Moringa oleifera* and its application in dental conditions: A systematic review and meta-analysis. J Herbmed Pharmacol. 2023;12(3):331-336. doi: 10.34172/jhp.2023.35.

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, antiulcer, 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

*Corresponding author: Ruchi Bhuyan,
Email: ruchibhuyan@soa.ac.in

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 *I*² 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

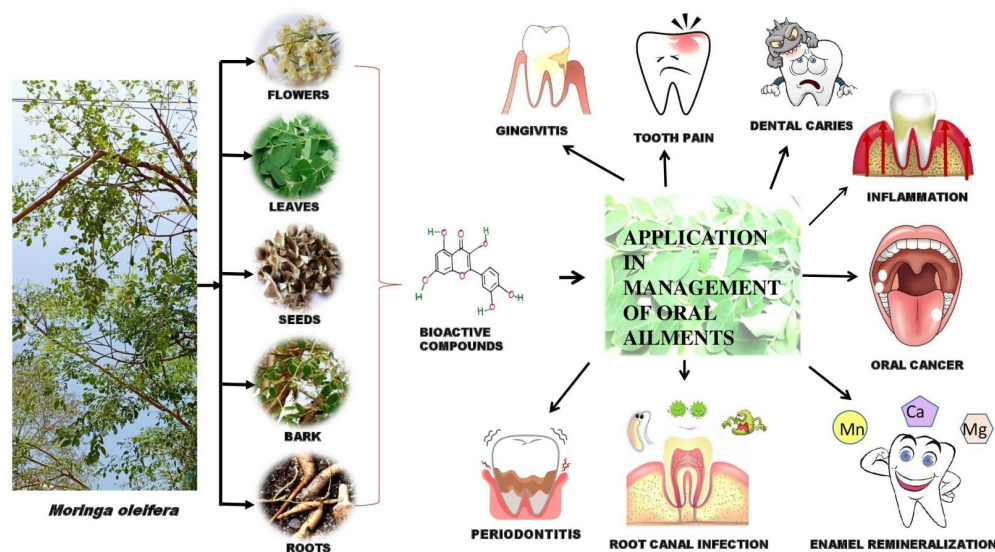


Figure 1. Application of *Moringa oleifera* in management of oral ailments.

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

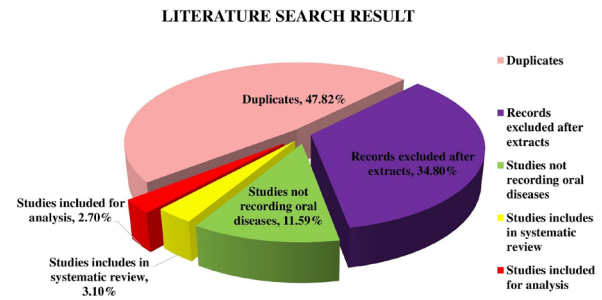


Figure 2. Graphical representation of articles retrieved from literature search.

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 (I^2 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 (I^2 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

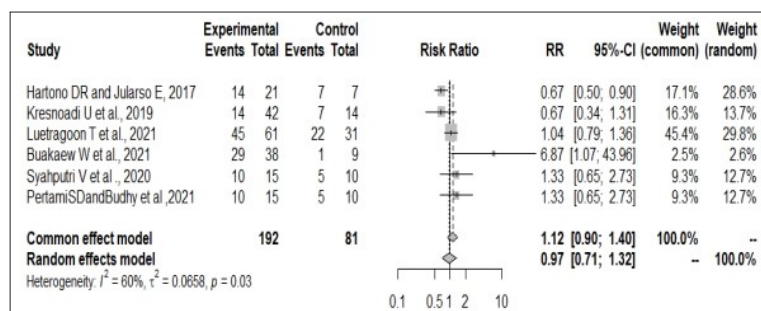


Figure 3. Meta-analysis comparing the effect of *Moringa oleifera* among treatment and control groups, *in vivo*.

Table 1. The summary characteristics of studies included in meta-analysis

Author (Reference)	No. of participants (studies)	Parts used	Plant used	Control	Preparation	Route of administration	Duration	Oral diseases treated
Elgamily et al (18)	324 microbes	Leaves, roots, seeds	400 mg/mL	Only toothpaste base	Ethanolic, acetone, acetate	Toothpaste, mouthwash	24 hours	Control of oral pathogens
Nagib et al (16)	50 (posterior teeth)	Leaves	-	Only etched teeth	Solution	Solution	7 days	Enamel and dentin remineralization and prevent erosion
Hartono and Jularso (12)	28 (rats)	Leaves	3.125%, 4.6875%, 6.25%	Placebo	Extract	Intraorally by means of insulin sonde	20 days	Oral cancer
Kresnoadi et al (15)	56 (Cavia cobaya)	Leaves	0.1 mL	PEG	Crude extract	Injection	30 days	Preservation of tooth extraction sockets.
Syahputri et al (13)	25 (rats)	Leaves	3.125%, 6.25%, 9.375%	Placebo	Extract	Intraorally by means of insulin sonde	1 month	Oral cancer
Younis et al (17)	75 (premolars)	Leaves	50 mg/mL, 200 mg/mL	No treatment	Lyophilized extract	Directly applied by composite bond brush	14 days	Surface enamel remineralization
Luetragoon et al (9)	93	Leaves	145.86 mg	Placebo	Crude extract	Lozenge	4 weeks	Gingivitis, Periodontitis, oral inflammation
Buakaew et al (10)	47	Leaves	0.02%	Placebo	Crude extract	Mouthwash	14 days	Dental plaque and gingivities
Pertami and Budhy (14)	25 (rats)	Leaves	3.125%, 6.25%, 9.375%	Placebo	Extract	Intraorally by means of insulin sonde	1 month	Oral cancer

PEG, polyethylene glycol

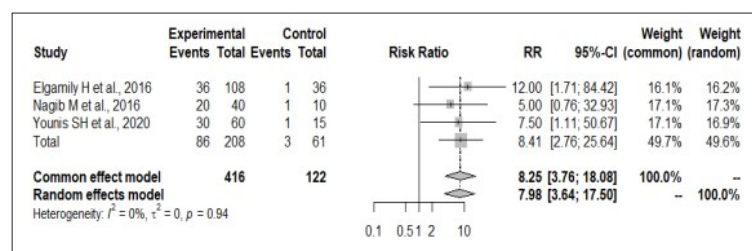


Figure 4. Meta-analysis comparing the effect of *Moringa oleifera* among treatment and control groups, *in vitro*.

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, oral cancer, 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

on *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. Gangadhar 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

1. Benzian H, Watt R, Makino Y, Stauf N, Varenne B. WHO calls to end the global crisis of oral health. *Lancet*. 2022;400(10367):1909-10. doi: 10.1016/s0140-6736(22)02322-4.
2. Peres MA, Macpherson LMD, Weyant RJ, Daly B, Venturelli R, Mathur MR, et al. Oral diseases: a global public health challenge. *Lancet*. 2019;394(10194):249-60. doi: 10.1016/s0140-6736(19)31146-8.
3. Mohanty M, Mohanty S, Bhuyan SK, Bhuyan R. Phytoperspective of *Moringa oleifera* for oral health care: an innovative ethnomedicinal approach. *Phytother Res*. 2021;35(3):1345-57. doi: 10.1002/ptr.6896.
4. Bhattacharya A, Tiwari P, Sahu PK, Kumar S. A review of the phytochemical and pharmacological characteristics of *Moringa oleifera*. *J Pharm Bioallied Sci*. 2018;10(4):181-91. doi: 10.4103/jpbs.jpbs_126_18.
5. Liu R, Liu J, Huang Q, Liu S, Jiang Y. *Moringa oleifera*: a systematic review of its botany, traditional uses, phytochemistry, pharmacology and toxicity. *J Pharm Pharmacol*. 2022;74(3):296-320. doi: 10.1093/jpp/rgab131.
6. Anzano A, Ammar M, Papaiani M, Grauso L, Sabbah M, Capparelli R, et al. *Moringa oleifera* Lam.: a phytochemical and pharmacological overview. *Horticulturae*. 2021 Oct;7(10):409. doi: 10.3390/horticulturae7100409.
7. Popoola JO, Aworunse OS, Oyesola OL, Akinnola OO, Obembe OO. A systematic review of pharmacological activities and safety of *Moringa oleifera*. *J Herbmed Pharmacol*. 2020;9(3):174-90. doi: 10.34172/jhp.2020.24.
8. Noushad MC, Ashraf K, Suneetha MP. Antibacterial efficacy of muringa seed extract and potato peel extract against *Enterococcus faecalis*. *Contemp Clin Dent*. 2020;11(4):327-31. doi: 10.4103/ccd.ccd_223_19.
9. Luetragoon T, Sranujit RP, Noysang C, Thongsri Y, Potup P, Somboonjun J, et al. Evaluation of anti-inflammatory effect of *Moringa oleifera* Lam. and *Cyanthillium cinereum* (Less) H. Rob. lozenges in volunteer smokers. *Plants (Basel)*. 2021;10(7):1336. doi: 10.3390/plants10071336.
10. Buakaew W, Sranujit RP, Noysang C, Sangouam S, Suphrom N, Thongsri Y, et al. Evaluation of mouthwash containing *Citrus hystrix* DC., *Moringa oleifera* Lam. and *Azadirachta indica* A. Juss. leaf extracts on dental plaque and gingivitis. *Plants (Basel)*. 2021;10(6):1153. doi: 10.3390/plants10061153.
11. Chiricosta L, Gugliandolo A, Diomedea F, Pizzicannella J, Trubiani O, Iori R, et al. Moringin pretreatment inhibits the expression of genes involved in mitophagy in the stem cell of the human periodontal ligament. *Molecules*. 2019;24(18):3217. doi: 10.3390/molecules24183217.
12. Hartono DR, Jularso E. The potential effect of *Moringa oleifera* leaves extract on vascular endothelial growth factor expression in Wistar rat oral cancer cells. *Dent J*. 2017;52(2):71-5. doi: 10.20473/j.djmk.v52.i2.p71-75.
13. Syahputri V, Budhy TI, Sumaryono B. The potential of ethanolic extract of *Moringa oleifera* leaves on HSF1 expression in oral cancer induced by benzo [a] pyrene. *Dent J*. 2020;53(2):107-10. doi: 10.20473/j.djmk.v53.i2.p107-110.
14. Pertamina SD, Budhy TI. The role of *Moringa oleifera* L. leaves extract in increasing caspase 3 expressions in carcinoma of oral squamous cells. *Malaysian J Med Health Sci*. 2021;17(Suppl 2):95-8.
15. Kresnoadi U, Rahmania PN, Caesar HU, Djulaeha E, Agustono B, Ari MDA. The role of the combination of *Moringa oleifera* leaf extract and demineralized freeze-dried bovine bone xenograft (xenograft) as tooth extraction socket preservation materials on osteocalcin and transforming growth factor-beta 1 expressions in alveolar bone of *Cavia cobaya*. *J Indian Prosthodont Soc*. 2019;19(2):120-5. doi: 10.4103/jips.jips_251_18.
16. Nagib AM, Amin LE, Khalaf EA, Ibrahim FM. Biological effects of topical applications of *Moringa oleifera* extract versus fluoride on uremic patients extracted teeth. *Int J Adv Res*. 2016;4(9):1513-20. doi: 10.21474/ijar01/1648.
17. Younis SH, Obeid RF, Ammar MM. Subsurface enamel remineralization by Lyophilized *Moringa* leaf extract loaded varnish. *Heliyon*. 2020;6(9):e05054. doi: 10.1016/j.heliyon.2020.e05054.
18. Elgamily H, Moussa A, Elborae A, El-Sayed H, Al-Moghazy M, Abdalla A. Microbiological assessment of *Moringa oleifera* extracts and its incorporation in novel dental remedies against some oral pathogens. *Open Access Maced J Med Sci*. 2016;4(4):585-90. doi: 10.3889/oamjms.2016.132.
19. Vázquez-León LA, Páramo-Calderón DE, Robles-Olvera VJ, Valdés-Rodríguez OA, Pérez-Vázquez A, García-Alvarado MA, et al. Variation in bioactive compounds and antiradical activity of *Moringa oleifera* leaves: influence of climatic factors, tree age, and soil parameters. *Eur Food Res Technol*. 2017;243(9):1593-608. doi: 10.1007/s00217-017-2868-4.
20. Vergara-Jimenez M, Almatrafi MM, Fernandez ML. Bioactive components in *Moringa oleifera* leaves protect against chronic disease. *Antioxidants (Basel)*. 2017;6(4):91. doi: 10.3390/antiox6040091.
21. Leone A, Spada A, Battezzati A, Schiraldi A, Aristil J, Bertoli S. Cultivation, genetic, ethnopharmacology, phytochemistry and pharmacology of *Moringa oleifera* leaves: an overview. *Int J Mol Sci*. 2015;16(6):12791-835. doi: 10.3390/ijms160612791.
22. Sujatha BK, Patel P. *Moringa oleifera*—nature's gold. *Imp J Interdiscip Res*. 2017;3(5):1175-9.
23. Fahal EM, Rani BM, Aklakur MD, Chanu TI, Saharan N. Qualitative and quantitative phytochemical analysis of *Moringa oleifera* (Lam) Pods. *Int J Curr Microbiol Appl Sci*. 2018;7(5):657-65. doi: 10.20546/ijcmas.2018.705.080.
24. Gopalakrishnan L, Doriya K, Kumar DS. *Moringa oleifera*: a review on nutritive importance and its medicinal application. *Food Sci Hum Wellness*. 2016;5(2):49-56. doi: 10.1016/j.fshw.2016.04.001.
25. Oladeji OS, Odelade KA, Oloke JK. Phytochemical screening and antimicrobial investigation of *Moringa oleifera* leaf extracts. *Afr J Sci Technol Innov Dev*. 2020;12(1):79-84. doi: 10.1080/20421338.2019.1589082.
26. Saad MA, Elkhtab ES. Antimicrobial activity of *Moringa oleifera* leaves extract and its effect on the shelf life and quality of yoghurt. *Egypt J Dairy Sci*. 2019;47:91-9.
27. Brilhante RSN, Sales JA, Pereira VS, Castelo-Branco D, de Aguiar Cordeiro R, de Souza Sampaio CM, et al. Research advances on the multiple uses of *Moringa oleifera*: a sustainable alternative for socially neglected population. *Asian Pac J Trop Med*. 2017;10(7):621-30. doi: 10.1016/j.apjtm.2017.07.002.