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Therapeutic effects of *Zataria Multiflora* essential oil on recurrent oral aphthous lesion

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ABSTRACT

Background: Aphthous lesions are one of the most common diseases of the oral cavity. They can cause severe pain, and there is no definite treatment. The purpose of this study was to determine the efficacy of *Zataria multiflora* (ZM, a thyme-like plant) essential oil for the control and treatment of aphthous lesions.
Materials and Methods: This Triple blind clinical trial study was performed on 28 patients who were divided into two groups (eight men and six women in each group) and given ZM or placebo (control). The healing time, pain intensity, and aphthous zone diameter were recorded for each patient and followed for 6-month. Data were analyzed using Mann–Whitney and Friedman tests ($P < 0.05$).
Results: After 6-month of follow-up, 4 patients in the placebo group and 6 patients in the ZM group suffered from recurrent aphthous lesions. The average complete healing time and duration of burning sensation were significantly lower in the ZM group ($P < 0.05$). Significant difference was observed between the two groups with regard to the diameter of lesions and halo of the lesions ($P < 0.05$).
Conclusion: Within the limitations of this study, ZM shortened the healing period compared to placebo.

Key Words: Aphthous stomatitis, therapeutics, multiflorol

INTRODUCTION

Recurrent aphthous stomatitis (RAS) is the most common recurrent lesion of the oral epithelium.[1,2] The prevalence of RAS was reported to be 40% in a population of children of the United States.[3] A prevalence of 31-36% has been reported for RAS among medical and dental students, compared with 10-20% in the general population.[4] Although few data are available regarding the etiologies and management of aphthous lesions, factors such as inheritance,[5] hormonal effect[6] and immunological factors[7] have been considered. Lesions usually begin due to local trauma, stress, certain foods or drugs, hormonal fluctuations or deficiencies in the Vitamin B group, folate or iron.[8-11] Apart from the different causes and predisposing conditions affecting the disease, pain, recurrence, self-limitation and epithelial damage are present in almost all lesions.[12]

Recurrent aphthous lesions are divided into three groups including: Minor, major and herpetiform, based on the clinical appearance and prognosis of the disease.[10] There is no firmed treatment option

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available to prevent or cure aphthous lesions. All the existing treatment options are based on symptomatic management, lesion count reduction and/or extending the lesion-free periods.[13] Prior to any treatment, patients should be screened for all predisposing factors. Blood samples should then be assessed for deficiencies in serum iron, folate, ferritin and Vitamin B12. Most patients suffering from minor aphthous lesions need no special treatment or only local treatment to adequately reduce their symptoms or lesion counts as well as to increase the interval between aphthous episodes.[13]

In patients suffering from major aphthous lesions or in those susceptible to numerous minor lesions that are resistant to local treatment, systemic treatment should be considered. The administration of local antibiotics such as tetracycline was effective in aphthous lesion management, probably due to a secondary decrease in infection and the clinical improvement of lesions.[1] Most therapeutic approaches are based on palliative rather than curative therapy, and none of them could prevent the recurrence of the symptoms. *Zataria multiflora* (ZM) with the common Persian name "Avishan-e Shirazi" is a thyme-like essential oil (EO)-bearing plant that belongs to the Lamiaceae family and grows extensively wild in the central and southern parts of Iran, Pakistan, and Afghanistan.[14] The dry aerial parts of the plant have been used for their flavor and preservative properties in the food products industry.[15] In Iran, ZM is mainly used in traditional folk remedies for its antiseptic, analgesic, and carminative (antiflatulence and intestine-soothing) properties.[14] It also has been reported that the EOs and extracts of ZM can stimulate innate immunity[16] and have antibacterial and antifungal activities.[17-20] Thus, the present study was aimed to investigate the therapeutic effects of ZM for treatment of oral aphthous lesions.

MATERIALS AND METHODS

This triple blind clinical trial was performed on 28 patients who were randomly selected from all patients suffering from recurrent aphthous lesions who were admitted to the Department of Oral Medicine, Faculty of Dentistry, Babol University of Medical Sciences in the North of Iran. The study protocol was approved by research review board and research Ethics Committee of Babol University of Medical Sciences and we registered the protocol in the Iranian Clinical Trials registry (IRCT201408076926N2). The inclusion criteria were as follows:

1. Presence of a minor solitary aphthous lesion in labial or buccal epithelium.
2. No usage of other treatments for aphthous lesions.
3. No reduction in pain, pain intensity or burning sensation at the time of admission compared to the 1st days of the occurrence of the lesion.
4. Willingness to participate in the study.
5. Age between 18 and 40 years.

All the eligible patients were interviewed. The exclusion criteria were: Patients with any systemic diseases or special syndrome that aphthous ulcer is one of its symptoms (Behcet's syndrome); pregnant patients; those with aphthous lesions older than 4 days, patients subjected to any other treatment for at least 4 weeks before the start of the study and those who declined entering the study. Diagnosis of minor aphthae was made on the basis of the patient's health history, clinical examination and the presence of a well demarcated painful ulcer on the smooth unattached oral mucosa, which is surrounded by a light red areola.

After explaining the objectives of the study, all the participants were given written informed consent prior to the clinical examination. After that, the eligible participants were divided into ZM- and placebo-treated groups randomly.

The patients received a bottle of 0.5% ZM EO or a bottle of placebo (distilled water with a cap scented with ZM EO). Standard ZM essence was obtained from Barij Essence Pharmaceutical Company (Kashan, Iran).

All bottles were coded by a third person who did not involve in the project, so that the contents of the bottles remained unknown to the researchers and patients throughout the study. To administer the drug or placebo, 15 drops of drug/placebo were diluted into one half cup of cold water and used as a mouthwash for 2 min 3 times a day, once after each meal. This therapy was continued until complete healing (no ulcer and no burning sensation) was obtained. Patients were examined by the clinician on the 1st, 5th and 7th days of treatment. The pain intensity was measured using a scale, which the patients completed every day for 10 days (before and after treatment). The lesion and halo diameters were measured using a ruler with 0.1-mm accuracy.

Statistics

Statistical analysis was performed using SPSS 18 (Chicago, IL, USA). Data were analyzed using Mann–Whitney and Friedman tests. $P < 0.05$ was considered as the level of statistical significance.

RESULTS

In total of 14 participants in each group (eight men and six women), all of them finished the study. A history of aphthous lesions was reported for 3 patients in the placebo group and 7 patients in the ZM group ($P = 0.236$). During the 6-month follow-up, recurrence had occurred in 4 and 6 patients in the placebo and ZM groups, respectively.

The mean (±standard deviation) treatment durations were 8.5 ± 1.2 and 8.4 ± 1.2 days in the placebo and ZM groups, respectively ($P = 0.765$). Complete healing and burning sensation cut-off times (the time in which the patient had no pain thereafter) were significantly decreased in the ZM group compared to the placebo group [Table 1]. There were also significant differences between the lesion and halo diameters in the two groups [Tables 2 and 3]. As illustrated in Figure 1, the peak pain score occurred between days 3 and 5.

Table 1: Mean (±SD) complete healing and burning sensation cut-off times (days) in the placebo and ZM groups

Time	Placebo	ZM*	*P*
Complete healing	8.43±1.29	6.50±1.30	<0.0001
Burning sensation cut-off	6.14±0.99	3.57±0.49	<0.0001

*ZM: *Zataria multiflora*. SD: Standard deviation.

Table 2: Mean (±SD) halo diameters (mm) in the placebo and ZM groups

Time	Placebo	ZM	*P*
Day 1	5.29±1.91	6.7±1.49	NS*
Day 5	5.07±1.03	2.86±2.23	<0.01
Day 7	3.5±1.45	1.50±1.55	<0.005

*Not significant. ZM: *Zataria multiflora*; SD: Standard deviation.

Table 3: Mean (±SD) lesion diameters (mm) in the placebo and ZM groups

Time	Placebo	ZM	*P*
Day 1	3.86±1.60	4.29±2.23	NS
Day 5	3.36±1.04	1.93±1.53	0.039
Day 7	1.92±1.00	1.00±1.07	0.011

NS: Not significant; ZM: *Zataria multiflora*; SD: Standard deviation.

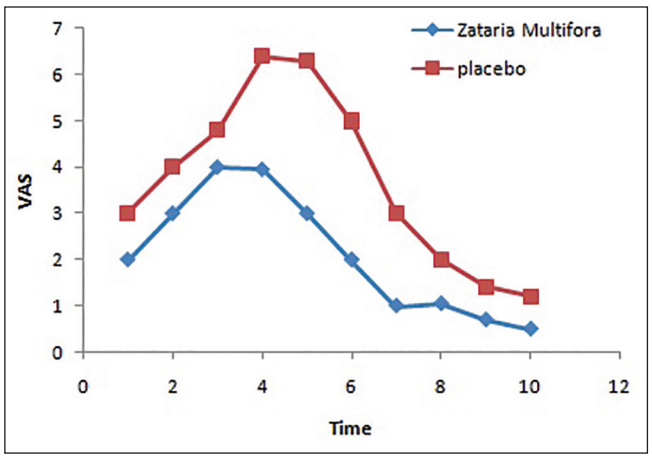

Figure 1: Mean (±standard deviation) pain intensity according to officinale in the placebo and *Zataria multiflora* groups.

DISCUSSION

Our findings revealed that the management of RAS lesion with ZM could indicate a significant decrease in the characteristic of the lesion (diameter of the lesion and halo), complete healing time and burning sensation of the patients.

RAS is a common oral disorder of uncertain etiopathogenesis, and presently, its management is largely focused on symptomatic treatment.[2,21] RAS causes considerable pain and distress for patients and presents a difficult management challenge for clinicians.[22] Different classes of chemical and biochemical products have been reported to be of some benefit in the management of RAS, but no definitive treatment is yet available. Management of the pain of RAS using various herbal preparations has also been reported.[23-27] ZM EO has been reported to have antibacterial, antiviral, antioxidant, and anti-inflammatory properties.[14-20]

This study was undertaken to evaluate the therapeutic effects of ZM EO for treatment of recurrent aphthous lesions. The results of the study showed that the complete healing time in the drug group was significantly shorter than that in the placebo group. In other words, using ZM led to a reduction in the time required for the lesions to heal. A review of the literature yielded few reports on the effectiveness of ZM EO in treating oral aphthous lesions.[28,29] The mechanism of action that play the major role in the healing process of these lesions may due to its anti-microbial role and ant-oxidative effect on the aphtous reactivity.[30-32]

Nevertheless, there are many reports on the efficacy of other herbal drugs for treatment of the disease.[23-25] In a study by Mansoori *et al.*, ZM EO

effectively resulted in a faster pain relief and shorter healing period.[29] In a study conducted by Jafari *et al*. ZM extract was a more effective treatment than *Myrthus communis*, which is reported to be effective in the treatment of RAS. It was concluded that ZM extract was an effective treatment for the management of minor aphthae.[28] Antimicrobial and anti-oxidant activities of four Tai plants (*Quercus infectoria*, *Kaempferia galanga*, *Coptis chinensis* and *Glycyrrhiza uralensis*) for aphthous ulcers were shown by Mekseepralard *et al*.[33] Previous studies have evaluated the therapeutic effects of *Satureja khuzestanica* extract for the treatment of aphthous lesions of the oral epithelium. These studies have demonstrated the extract to be more effective than placebo in reducing the duration of suffering from pain and burning sensation as well as the time needed for complete clinical resolution.[34] It has also been shown that myrtle is an effective treatment in terms of size change, pain severity, the level of erythema and exudation in RAS.[23] Moghadamnia *et al*. evaluated the efficacy of licorice bioadhesive hydrogel patches for controlling the pain and reducing the healing time of recurrent aphthous ulcers. They found that licorice bioadhesive can be effective in the reduction of the pain and of the sizes of the inflammatory halo as well as the necrotic center of aphthous ulcers.[25] In another clinical trial using herbal options muco-bioadhesive containing ginger officinale extract was indicated relieving pain of RAS but had no efficacy on ulcer diameter, inflamed halo and healing time when compared to a placebo.[24]

Our study's limitation was the small sample size and the fact that we were not completely sure whether the patients consumed the ZM as any form (mouthwash or food ingredient) in the follow-up period or not. Within these limitations, our results provided evidence that ZM mouthwash is an effective treatment modality for RAS. Herbal medicines provide a wider range of treatment options for patients and practitioners. They have limited complications and can be useful alternatives to chemical medicines.

CONCLUSION

According to our findings, ZM can reduce the RAS symptoms and characterisitic of the aphthous lesions compared to the placebo group. Future studies with larger sample sizes are suggested examining the role of ZM in the management of RAS.

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Conflict of interest

The authors of this manuscript declare that they have no conflicts of interest, real or perceived, financial or non-financial in this article.

REFERENCES

1. Barrons RW. Treatment strategies for recurrent oral aphthous ulcers. Am J Health Syst Pharm 2001;58:41-50.
2. Porter SR, Scully Cbe C. Aphthous ulcers (recurrent). BMJ Clin Evid 2007;2007. pii: 1303.
3. Shulman JD. Prevalence of oral mucosal lesions in children and youths in the USA. Int J Paediatr Dent 2005;15:89-97.
4. Rees TD, Binnie WH. Recurrent aphthous stomatitis. Dermatol Clin 1996;14:243-56.
5. McCullough MJ, Abdel-Hafeth S, Scully C. Recurrent aphthous stomatitis revisited; clinical features, associations, and new association with infant feeding practices? J Oral Pathol Med 2007;36:615-20.
6. Scully C, Porter S. Oral mucosal disease: Recurrent aphthous stomatitis. Br J Oral Maxillofac Surg 2008;46:198-206.
7. Natah SS, Häyrinen-Immonen R, Hietanen J, Malmström M, Konttinen YT. Immunolocalization of tumor necrosis factor-alpha expressing cells in recurrent aphthous ulcer lesions (RAU). J Oral Pathol Med 2000;29:19-25.
8. Carrozzo M. Vitamin B12 for the treatment of recurrent aphthous stomatitis. Evid Based Dent 2009;10:114-5.
9. Kozlak ST, Walsh SJ, Lalla RV. Reduced dietary intake of vitamin B12 and folate in patients with recurrent aphthous stomatitis. J Oral Pathol Med 2010;39:420-3.
10. Scully C, Gorsky M, Lozada-Nur F. The diagnosis and management of recurrent aphthous stomatitis: A consensus approach. J Am Dent Assoc 2003;134:200-7.
11. Vucicevic Boras V, Savage NW. Recurrent aphthous ulcerative disease: Presentation and management. Aust Dent J 2007;52:10-5.
12. Porter SR, Hegarty A, Kaliakatsou F, Hodgson TA, Scully C. Recurrent aphthous stomatitis. Clin Dermatol 2000;18:569-78.
13. Ship JA. Recurrent aphthous stomatitis. An update. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1996;81:141-7.
14. Shafiee A, Javidnia K. Composition of essential oil of *Zataria multiflora*. Planta Med 1997;63:371-2.
15. Gandomi H, Misaghi A, Basti AA, Bokaei S, Khosravi A, Abbasifar A, *et al*. Effect of *Zataria multiflora* Boiss. essential oil on growth and aflatoxin formation by *Aspergillus flavus* in culture media and cheese. Food Chem Toxicol 2009;47:2397-400.
16. Shokri H, Asadi F, Bahonar AR, Khosravi AR. The role of *Zataria multiflora* essence (Iranian herb) on innate immunity of animal model. Iran J Immunol 2006;3:164-8.

17. Gandomi H, Misaghi A, Basti AA, Hamedi H, Shirvani ZR. Effect of *Zataria multiflora* Boiss. essential oil on colony morphology and ultrastructure of *Aspergillus flavus*. Mycoses 2011;54:e429-37.
18. Mahboubi M, Bidgoli FG. Antistaphylococcal activity of *Zataria multiflora* essential oil and its synergy with vancomycin. Phytomedicine 2010;17:548-50.
19. Parsaeimehr M, Basti AA, Radmehr B, Misaghi A, Abbasifar A, Karim G, *et al.* Effect of *Zataria multiflora* Boiss. essential oil, nisin, and their combination on the production of enterotoxin C and alpha-hemolysin by *Staphylococcus aureus*. Foodborne Pathog Dis 2010;7:299-305.
20. Simbar M, Azarbad Z, Mojab F, Majd HA. A comparative study of the therapeutic effects of the *Zataria multiflora* vaginal cream and metronidazole vaginal gel on bacterial vaginosis. Phytomedicine 2008;15:1025-31.
21. Ship JA, Chavez EM, Doerr PA, Henson BS, Sarmadi M. Recurrent aphthous stomatitis. Quintessence Int 2000;31:95-112.
22. Porter S, Scully C. Aphthous ulcers: Recurrent. Clin Evid 2002;8:1397-403.
23. Babaee N, Mansourian A, Momen-Heravi F, Moghadamnia A, Momen-Beitollahi J. The efficacy of a paste containing *Myrtus communis* (Myrtle) in the management of recurrent aphthous stomatitis: A randomized controlled trial. Clin Oral Investig 2010;14:65-70.
24. Haghpanah P, Moghadamnia AA, Zarghami A, Motallebnejad M. Muco-bioadhesive containing ginger officinale extract in the management of recurrent aphthous stomatitis; a randomized clinical study. Caspian J Intern Med 2015;6:3-8.
25. Moghadamnia AA, Motallebnejad M, Khanian M. The efficacy of the bioadhesive patches containing licorice extract in the management of recurrent aphthous stomatitis. Phytother Res 2009;23:246-50.
26. Burgess JA, van der Ven PF, Martin M, Sherman J, Haley J. Review of over-the-counter treatments for aphthous ulceration and results from use of a dissolving oral patch containing glycyrrhiza complex herbal extract. J Contemp Dent Pract 2008;9:88-98.
27. Ramezani M, Hosseinzadeh H, Samizadeh S. Antinociceptive effects of *Zataria multiflora* Boiss fractions in mice. J Ethnopharmacol 2004;91:167-70.
28. Jafari S, Amanlou M, Bohran-Mojabi K, Farsam H. Comparative study of *Zataria multiflora* and *Anthemis nobelis* extracts with *Myrthus communis* preparation in the treatment of recurrent aphthous stomatitis. DARU 2003;11:23-7.
29. Mansoori P, Hadji Akhoondi A, Ghavami R, Shafiei A. Clinical evaluation of *Zataria multiflora* essential oil mouthwash in the management of recurrent aphthous stomatitis. DARU 2002;10:74-7.
30. Bazargani-Gilani B, Tajik H, Aliakbarlu J. Physicochemical and antioxidative characteristics of Iranian pomegranate (*Punica granatum* L. cv. Rabbab-e-Neyriz) juice and comparison of its antioxidative activity with *Zataria multiflora* Boiss essential oil. Vet Res Forum 2014;5:313-8.
31. Kavoosi G, Teixeira da Silva JA, Saharkhiz MJ. Inhibitory effects off *Zataria multiflora* essential oil and its main components on nitric oxide and hydrogen peroxide production in lipopolysaccharide-stimulated macrophages. J Pharm Pharmacol 2012;64:1491-500.
32. Sajed H, Sahebkar A, Iranshahi M. *Zataria multiflora* Boiss. (Shirazi thyme) — An ancient condiment with modern pharmaceutical uses. J Ethnopharmacol 2013;145:686-98.
33. Mekseepralard C, Kamkaen N, Wilkinson JM. Antimicrobial and antioxidant activities of traditional Thai herbal remedies for aphthous ulcers. Phytother Res 2010;24:1514-9.
34. Amanlou M, Babaee N, Saheb-Jamee M, Salehnia A, Farsam H, Tohidast Akrad Z. *Satureja khuzistanica* extract and its essential oil preparations in the management of recurrent aphthous stomatitis. DARU 2007;15:231-5.