

CLINICAL EVALUATION OF *ZATARIA MULTIFLORA* ESSENTIAL OIL MOUTHWASH IN THE MANAGEMENT OF RECURRENT APHTHOUS STOMATITIS

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ABSTRACT

The purpose of this study was to evaluate the efficacy of the topical use of 0.2% oral mouth wash of essential oil of *Zataria multiflora* in the control of recurrent aphthous stomatitis (RAS). In this double-blind, randomized study each of 60 patients with RAS was assigned to one of the 2 management modalities. Those in group A received an oral rinse solution of *Zataria multiflora* essential oil, 3 times a day for 4 weeks and those in group B received placebo 3 times a day for 4 weeks. The patients were monitored two times weekly. A statistical Chi-Square test was performed to analyze the data. *Zataria multiflora* oral rinses was shown to be more efficacious than placebo in the treatment of patients with RAS.

Keywords: Redurrent aphthous stomatitis (RAS), *Zataria multiflora*, Essential Oil, Clinical trials

INTRODUCTION

Recurrent aphthous stomatitis (RAS) is a chronic inflammatory disease characterized by recurrent painful single or multiple, necrotizing ulceration of the oral mucosal tissue. Its clinical course is essentially unaltered by modern medical and dental therapy (1-4). The exact prevalence of RAS is unknown; however, RAS is a common disease affecting 10-20% of the general population and reaching as high as 50% in selected groups such as university students (3-6). Several treatment modalities have been used in order to eliminate recurrence and to reduce the duration of aphthous ulcerations. The therapeutic rationale was based on the following factors: efficiency of agents to serve as either immunosuppressive, immunostimulator, antibiotic or to provide relief from pain and discomfort. The therapeutic value of many of these modalities remains unproven or even disproved (1).

Zataria multiflora Boiss (labiatae) is widely distributed in the central and southern parts of Iran. It is renowned for its medical uses based on its antiseptic, analgesic and carminative properties in folk medicine (7,8). The composition of essential oil of *Zataria multiflora* has been reported (9). The main constituents, of this oil are thymol, carvacrol, *p*-cymene, linalool and γ -terpinene. The essential oil of *Zataria multiflora* showed antimicrobial

activity (10). One study noted the inhibitory activity of thymol, carvacrol on oral bacteria in vitro (11). Herewith we conducted a prospective, placebo controlled, double-blind clinical trial in order to assess the efficacy of essential oil of *Zataria multiflora* in the treatment of RAS.

MATERIAL AND METHODS

Patients and samples

Sixty patients with RAS, who did not have any systemic diseases and did not received any other drugs during the study, received either treatment with *Zataria multiflora* essential oil or essential oil-free placebo mouthwash. The study group consisted of 31 men and 29 women, their mean age was 33 (range 9-63) years.

When topical *Zataria multiflora* essential oil treatment was started, all the lesions were untreated, newly formed and old lesions were classified as minor aphthae. The diagnosis was made on the basis of clinical appearance, location, history and the absence of other pathogens or pathogenic processes that cause oral ulcers (12,13). Table 1 summarizes the patients characteristics. All patients agreed to self-treatment of 1 to 10 aphthae with one solution (A or B) for at least one month. The two solutions were arbitrarily coded A and B. 30 ml of clear solutions in identical dark bottles were used. The patients were instructed to

use the mothwash three times a day with routine care. The solutions were given randomly. Solution A consisted of 30 ml of an aqueous-alcoholic solution of 60 mg of essential oil of *Zataria multiflora* and solutions B was a liquid placebo of essential oil free aqueous alcohol (50:50).

None of the patients received any other medication during the study. A special sheet was assigned to each RAS patient, in which a detailed clinical history of aphthous lesions developed in the preceding one year was recorded. This included the frequency, duration number, degree of pain of aphthous lesions and location of aphthae (Table 2). These records served as the internal control data for patients without *Zataria multiflora* essential oil treatment. The patients were monitored two times a week by an experienced dermatologist from the

Department of skin diseases. At the end of the treatment period, improvements in the relief of pain and shortening of the healing time were compared between the two groups of the study. Statistical analysis by means of a chi-square test was performed on the resulting data.

RESULTS AND DISCUSSION

Eighty-three percent of the patients responded well to the essential oil formulation. Whereas only 17% reported deterioration of their symptoms whilst receiving the drugs.

For those receiving placebo, 13% was improved and 87% deteriorated. These differences were statistically significant (P<0.001). Table 3 summarizes the relief of pain in two groups, namely group A and B.

Table 1. Patient characteristics

Age range (years)	Male		Female		Total	
	Number	(%)	Number	(%)	Number	(%)
0-10	1	3	1	3	2	3
11-20	3	10	4	14	7	12
21-30	8	26	6	21	14	23
31-40	12	39	11	38	23	38
41-50	6	19	6	21	12	20
51-60	1	3	0	0	1	2
61-70	0	0	1	3	1	2
Total	31	100	29	100	60	100

Total number of men 31, women 29, total =60, average mean age 33.

Table 2. Number of ulcers in respect to localization

Location	Number	%
Tongue	46	36.2
Gingiva	29	22.8
Buccal & floor of the mouth	33	26
Soft plate	15	12
Hard plate	4	3
Total	127	100

Table 3. The relief of pain as clinical comparison in two groups A and B

Healing time		Shortened		Long	Total
		0-2 (days)	2-7 (days)	>7 (days)	
A	Number of patients	10	15	5	30
	%	33	50	17	100
B	Number of patients	2	2	26	30
	%	7**	7**	86**	100

Group A consisted of 30 ml of an aqueous-alcoholic solution of 30 mg of essential oil of *Zataria multiflora*. Group B was a liquid placebo of essential oil-free aqueous-alcohol (50:50) ** P<0.01.

Favorable and immediate response to the treatment was noted in 33% of the drug group and 7% of the placebo group. Improvement of the ulcers after 2-7 days of treatment was achieved in 50% and 7% of drug and placebo groups respectively. Shortening of the healing time was also different between the 2 groups. It was found that the healing time of the placebo group (9.1 days) was 4.6 days more than that of the drug group (4.5 days). Therefore, compared with the internal control data we found a significant clinical improvement including less pain and shorter duration in RAS patients of *Zataria multiflora* essential oil treatment.

The etiology of RAS is still not well understood. Some genetic, immunopathogenic and microbial possibilities have been reported (14-17); however, these are neither sufficiently convincing nor particularly helpful in exploring RAS treatment. The uncertain pathogenesis has led to many clinical trials of therapeutic drugs.

Many drugs, such as chlorhexidine, corticosteroids, levamisole, colchicine, and others have been applied to RAS with some degree of improvement (18-24). However, these agents have not specifically been developed for RAS and their effects do not seem to be long-lasting in RAS therapy. Thymol and carvacrol has a proven antiseptic value in the inhibition of oral bacteria in vitro (11). The current study represents the first randomized double-blind placebo controlled trial. The phenol like structure of thymol and carvacrol

suggest its possible antimicrobial and antifungal properties (7,8). In our study 83% of patients experienced a beneficial effect on their symptoms in the short term (prompt relief of pain and reduction in healing time). There was one pemphigus patient who had many aphthae at the back of his lip. After three days using the drug all of the aphthae disappeared. However, in the oral bechcet's aphthae the drug had no beneficial effect. In comparison with other trials using other drugs we concluded that the *Zataria multiflora* essential oil had a good beneficial effect. In 80% and 25% of those treated with sucralfate and Al-Mg antacid, respectively, the healing time was shortened (25). For levamisole, duration of ulcers is 7 days after 2 and 4 months treatment and 5 days after 6 months treatment (26).

In another report, aqueous chlorhexidine 0.2% mouthwash did not appear to improve any aspect of the pattern of ulceration and benzydamine hydrochloride 0.15% mouthwash was no more effective than aqueous chlorhexidine 0.2% mouthwash in control of minor RAS (27). The result of the current study establishes that the aqueous alcoholic essential oil of *Zataria multiflora* can be effectively used in treatment of RAS.

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