

## Efficacy of Olive Leaf Extract in the Treatment of Minor Oral Aphthous Ulcers

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**Abstract:** This research is a double blinded clinical study that tries to assay the therapeutic effects of olive leaf extract on the oral minor aphthous ulcers in comparison with dexametasone mouth wash. The statistical society of the study was 80 patients which were equally divided into 2 groups. One group received olive leaf extract and the other group received dexametasone mouth wash (elixir 0.1%). The diameter of ulcers measured by periodontal prob(Williams) and the amount of pain determined by visual scale analysis. The data were collected on the first, third and fifth day after beginning of the treatment. The result showed that there is no significant difference between two groups based on size and pain reduction ( $p>0.05$ ). The results were statistically analyzed by Greenhouse Geisser Test and Q square ( $p<0.05$ ). The project was also approved by ethic committee of Kerman University of Medical Sciences (No.10/61/10241).

**Key words:** Olive leaf extract, oral aphthous ulcers, mouth wash, dexamethasone, clinical study.

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### INTRODUCTION

Recurrent aphthous stomatitis (RAS) is a disorder with recurrent oral ulcer in person who does not have other sign of sickness<sup>[1]</sup>.

RAS is a multifactorial disorder which is common in 20% of society. Study on the different social and ethnic groups has shown that incidence varies between 5-50%<sup>[1,2]</sup> and it is more common in females than males. The disorder occurs more in winters and springs<sup>[2,3]</sup>. RAS is seen in three forms: minor, major and herpetiform. The minor ulcer is 80 percent composed of the cases which are ulcers with less than 1 cm in diameter, painful and are cured without scar<sup>[1]</sup>. RAS occurs in second decay and nowadays it is believed that RAS is a clinical syndrome which is affected by different etiology but the important factors are heredity, hematological deficiency and immunological deficiency. This disorder is self-cure but may cause problems in chewing and swallowing and speech<sup>[1,2,3]</sup>. The goal of treatment is to decrease the disability and uncomfotability of patient<sup>[1, 2]</sup>. Depending on the severity and the size of ulcer, different treatments have been reported: *i*-Antibiotics, *ii*-anti inflammatory, *iii*-immunological mediators, *iv*-topical anesthetic, and *v*-alternative<sup>[4]</sup>.

Therefore, finding the suitable drugs with fewer side effects is the goal of many researches. Between chemical drugs, steroid (topical and oral) is golden standard for RAS but, systemic absorption of local steroids have undesirable influence on immunologic system and may lead to secondary infections<sup>[5]</sup>.

Because of the side effects of the chemically synthesized drugs, trends are toward the use of naturally made ones. Due to a phenolic component (oleuropin), antioxidant particles of olive leaf extract, and antiviral and antimicrobial activity that has been established for olive leaf extract (OLE)<sup>[6,7,8,9,10]</sup>, it was considered in this study as a treatment for aphthous ulcer. In addition, olive leaf extract is traditionally used in some regions of Iran as aphthous ulcer treatment. The study emphasis on the possible advantage of OLE in treatment of RAS over the Dexamethasone mouth washes which is considered as golden treatment for RAS.

### MATERIALS AND METHODS

*Preparation of OLE:* After gathering the olive leaves from some regions of Kerman province (Iran), the leaves were washed and dried. The leaves were then powdered and passed through mesh 20 (ASTM) to increase their contact with solvent in the solvent-extraction process. The powder was macerated and then extracted using ethanol: water (50:50) as extracting solvent. The mixture was vacuum-filtered, pressed and maintained for 5 days at 150 °C. The solution was then rotary-evaporated at 30 °C to obtain a solution containing 2% OLE. The product was packed in 60ml dark bottles for further experiments<sup>[10]</sup>.

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**Dexamethasone Elixir:** To provide Dexamethasone Elixir, dexamethasone disodium phosphate dissolved in deionized water and added to potassium dihydrogen phosphate to adjust its pH to 6-7. Saccharin as sweetener and 0.1% methyl paraben 0.01 propyl paraben as preservatives were added to solution. Adding deionized water the volume of the solution reached 100ml. It was then passed through a membrane filter (22% micron) in sterile condition to be sterilized. The solution of 0.1% was then packed in 60ml dark bottles for further experiments [11].

**Clinical method:** After taking clinical permission from ethic committee of Kerman University of medical sciences (NO.10/61/10241) and regulating the permit paper for every patient, drugs in equal amounts were packed and randomly coded and were kept unknown until the last step. It was described to the patients that they may receive chemical or herbal mouth wash by a probability of 50%. The patients were also informed about the instruction of use and the time of the next visit. The patients were requested to use 1 teaspoonful of the mouth wash for 2 minute, 4 times a day and then drop it out [1]. In the first, third, and sixth day after receiving the drug, the patients referred to the clinic. The diameter of ulcers was measured by periodontal probe (Williams) and amounts of pain measured by visual scale analysis [11]. Each patient used mouthwash until their ulcer cured and in the case of recurrence, they received more drug, but were not considered as new cases in the study.

In this research only patients were entered who:

- 1) had only a minor aphthous ulcer
- 2) their ulcers diameter were less than 1cm
- 3) were not receiving any other drug
- 4) did not have a systemic disorder or behcet syndrome
- 5) it had not been passed more than 4 days from beginning of their ulcer.

All the steps were carried out by instructed dental students in the clinics of Kerman (Iran) as double blinded trial. The results were then statistically analyzed by Greenhouse Geisser Test and Q square ( $p < 0.05$ ).

## RESULTS AND DISCUSSION

Eighty patients were entered into this study. The patients were randomly divided equally into 2 groups (40 patients in each group). The youngest one was 10 and the oldest one was 80 years old. During the study 25 patients were omitted as they did not follow the investigation process carefully. Comparison between diameter mean of ulcer in different days showed that generally there was no significant difference between 2

groups ( $p < 0.05$ ), although diameter of ulcer in the group A (Dexamethasone) in the first day decreased more than group B (olive leaf extract) (Fig.1).

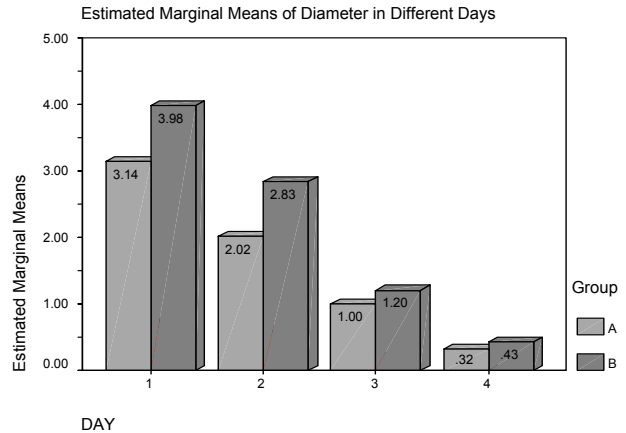


Fig. 1: Marginal diameter of ulcers in different days for both groups

The results of the measured pain among the patients showed no significant difference between two groups ( $p < 0.05$ ) (Fig. 2).

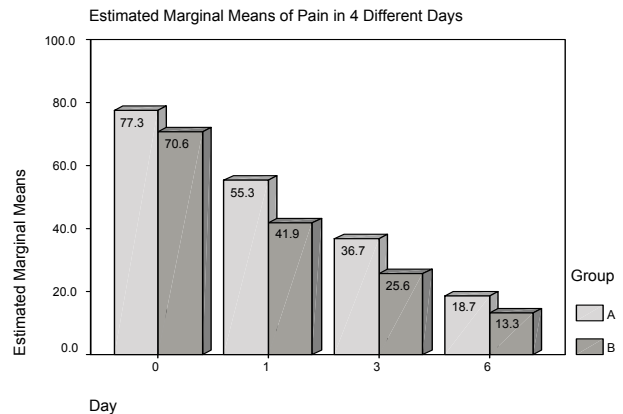


Fig. 2: Pain measured in different days for both groups

The healing period from first day of the appearance of clinical signs, up to the complete cure also showed no significant difference between two groups.

Analysis of different factors such as patient age, incidence, age and recurrence rate, healing period and also qualitative factors such as sex, patient history, past drug use, aphthous history, relation with food, stress, menstruation, and illness showed no significant difference between 2 groups. Results of the size of ulcer in 0, 1, 3, 6 day, showed that the size of ulcers decreased in both groups. Only in the first day the size of ulcers in group A had more reduction. The results

also confirmed that the effects of olive leaf extract on the oral aphthous ulcers healing compare favorably with the standard dexamethasone mouth wash.

The goals of therapy are three fold: *i-* control the pain of the ulcer, *ii-* promote ulcer healing, and *iii-* prevent recurrence [5]. Olive leaf extract can provide first two items. The extract contains phenolic compounds which have anti-oxidant, anti-viral, and anti-microbial effects [6-10]. Therefore, the healing properties of the extract could be related to the aforementioned properties, especially the anti-microbial, of the extract composition. Furthermore, olive leaf extract shows no specific adverse drug reaction and the administration of the extract is not cumbersome and discomfort which corticosteroids, for example, may do. In addition, the preparation process of the extract is not complicated and the product is not expensive.

The authors could not find any similar studies regarding the use of olive leaf extract to be compared with this study. Matsuda et.al. in 2003 studied the efficacy of rabapimide extract and De Armas et.al. in 2005 studied the efficacy of Rhizophora mangle aqueous bark extract [12,13]. In these two studies a reduction in pain and size of ulcers was also observed which may confirm our findings.

### CONCLUSION

These observations demonstrate that olive leaf extract reduced the amount of pain and the size of ulcers. There was no evidence of any adverse side effects. This is the first time that the olive leaf extract has been reported to have oral aphthous ulcers healing properties.

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