

Evaluate the Efficiency of Sage (*Salvia Officinalis*) and Curcumin Mouthwash in the Treatment of Recurrent Aphthous Stomatitis (Comparative Study)

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Abstract: *Recurrent Aphthous Stomatitis (RAS) is a common oral disorder that the clear etiology is un known. These ulcers are painful and caused serious complications in eating, talking and swallowing that make an individual requires treatment to relieve these symptoms. Corticosteroids and analgesics considered the first choice for RAS patients. Some of these drugs lead to many complications; so many therapies have been tried to find alternative modalities. Natural herbs and plants gain global interest due to their distinct properties, recently they are directed to be employed in medicine and dental care. Sage (*Salvia officinalis*) and curcumin are among the most prominent herbal substances that have been used in medicine and dentistry. The present study was carried out to evaluate the efficacy of a mouthwash containing Sage (*Salvia officinalis*) with curcumin extracts as natural herbal medicine in treating recurrent aphthous stomatitis (RAS).*

Method: *The study was carried for the period of (November 2019-January 2020), where 74 patients visited a consultant educational clinic of Al-Mustansiriyah University, Collage of Dentistry complaining of minor oral ulcers. A special questionnaire was designed for the purpose of data collection. Criteria in this study include the evaluation of ulcer size, remission of pain, and time needed for complete healing. Two study groups were included, the first group uses Sage mouthwash and second group curcumin mouth wash, both groups rinse for 1 minute five times for five days, the comparisons were based on the results of statistical analysis conducted by SPSS.*

Results: *Through statistical comparison between the two studied groups, the pain mean of aphthous ulcer in the second visit was 3.93 ± 1.52 sage group that is less than the pain mean in the curcumin group 4.73 ± 1.2 , and it was significant as for the third visit. Decrease in the pain mean of the sage group compared with the curcumin group 0.81 ± 1.09 and 2.77 ± 1.59 respectively, highly significant difference between the two groups (($t = -6.257, P = 0.000$). The mean of healing duration was 5.32 ± 1.65 in the sage group, while in the curcumin group was 4.56 ± 1.20 , there was a significant difference between the two studied groups. ($t = -2.010, P = 0.048$).*

Conclusion: *Herbal medicine can be acknowledged as a promising therapy. There is some confirmation of the potential utilization of the natural herbal medicines according to improved RAS outcome measures.*

Recommendation: *More studies should be conducted with promising natural herbs which deals with more benefits and achievements in the dental field.*

Keywords: Recurrent aphthous stomatitis, herbal, sage (Salvia officinalis), curcumin

تقييم فعالية غسول الفم بالميرمية والكرمين في علاج حمى الفم القلاعية المتكررة (دراسة مقارنة)

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المستخلص

مقدمه: حمى الفم القلاعية هو اضطراب فموي شائع مسبباته غير واضحة، هذه القرحة مؤلمة وتسبب مشاكل حقيقيه في الأكل والكلام والبلع مما يجعل الفرد يطلب علاج لتخفيف هذه الأعراض، تعتبر الكورتيكوستيرويدات والمسكنات الخيار الأول لهذه الفئه وقد تؤدي بعض هذه الأدوية إلى العديد من المضاعفات ، لذا فقد تم تجربة العديد من العلاجات لإيجاد طرق بديلة ، اكتسبت الأعشاب والنباتات الطبيعية اهتمامًا عالميًا نظرًا لخصائصها المميزة ، مؤخرًا أصبح هناك توجه لاستعمالها في الطب والعناية بالأسنان. تعتبر الميرمية و الكركمين من أبرز المواد الطبيعية المستخلصة والتي تم استخدامها في هذا المجال ، وقد أجريت هذه الدراسة لتقييم فعالية هذه المستخلصات كأدوية عشبية طبيعية (غسول الفم) في علاج التهاب الفم القلاعي المتكرر

طرائق البحث: نفذت الدراسة في الفترة (نوفمبر 2019- يناير 2020) حيث قام 74 مريضاً بزيارة العيادة التعليمية بكلية طب الاسنان/ المستنصرية، المرضى يعانون من قرح الفم الطفيفة، تم تصميم استبيان خاص لغرض جمع البيانات المطلوبة تشمل المعايير في هذه الدراسة تقييم حجم القرحة ، وتهديئة الألم ، والوقت اللازم للشفاء الكامل ، وقد تم تضمين مجموعتين دراسيتين متساويتين، المجموعة الأولى تستخدم غسول الفم الميرمية والمجموعة الثانية غسول الفم الكركمين ، كلتا المجموعتين غسلت الفم لمدة دقيقة واحدة وتكرر خمس مرات لمدة خمسة أيام ، وسجلت التغيرات المرتبطة بمعايير الدراسة، و استندت المقارنات الى نتائج التحليل الاحصائي للمجموعتين باستخدام برنامج SPSS.

الاستنتاجات: يمكن الاعتراف بالأدوية العشبية كعلاج واعد حيث هناك بعض التأكيد على الاستخدام المحتمل للميرمية والكرمين كأدوية عشبية طبيعية وفقاً لمقاييس نتائج التحسن لحمى الفم القلاعية

التوصيات: إجراء المزيد من الدراسات حول الأعشاب الطبيعية الواعدة التي تتعامل مع المزيد من الفوائد والإنجازات في مجال طب الاسنان

الكلمات المفتاحية: التهاب الفم القلاعي المتكرر، عشبي، ميرمية (سلافيا أوفيسيناليس)، الكركمين

Introduction

RAS remains a common oral mucosal disorder in most communities of the world, with an estimated prevalence of 25% [1], minor aphthous ulcer makes up more than 80% of all cases of RAS. Its precise etiology remains unclear, no particular cause has ever been demonstrated of RAS [2, 3]. Due to inadequate understanding of RAS etiologic factors, studies failed to introduce a definite treatment [4]. These sores are painful and adjust the life nature of patients by trouble in eating, talking, and swallowing [5] that make an individual seek treatment to relieve these symptoms. Thus, the primary goals of RAS therapy are focused on sign and symptomatic management such as palliation of pain, a reduction in number, size, recurrence, duration of ulcers, and healing promotion Topical anti-inflammatory, antihistaminic, analgesics, anesthetics agents, immunosuppressant's, as well as steroids agents are prescribed based on the severity of RAS [6], Some of these drugs lead to

many symptoms or bothersome responses or even life-threatening complications such as osteoporosis, hyperglycemia, hypertension, adrenal suppression, and immune system suppression [7], there is no agreement in the treatment of RAS, so many therapies have been tried to find alternative modalities, employment of natural herbal agents in medication and dentistry picking up importance around the world. Herbs and plants gain global interest due to their remarkable properties, they are increasingly used day by day, and they are more employed in medicine and dental care. Several herbs have been studied for their effect on oral health [8].

Curcumin is created by a plant that has a bright yellow-orange chemical material and maintains pharmacological properties. The methoxy group in the phenolic structure of curcumin is mainly responsible for its anti-inflammation action and antioxidant activity, It is a natural phenolic compound that has a potent antitumor, analgesic, antiseptic activity, and anti-carcinogenic properties [9], it is ten times more active as an antioxidant than vitamin E due to the presence of effective enzymes such as superoxide. Curcumin is thought to be suppressed the activation of NF- κ B, an inducible transcription factor that adjusts the expression of a host of genes involved in inflammation. Cellular proliferation, and cell survival Inflammation is inhibited by curcumin in other pathways associated with arachidonic acid, prostaglandin E₂ synthesis through direct inhibition of microsomal prostaglandin synthesis [10] and by inhibiting the formation of inflammatory interleukin molecule such as IL-1, IL-2, -6,-8,-12, and chemokine's[11] moreover, Curcumin defeats the growth of several bacteria like staphylococci, streptococcus, and lactobacillus ,the combination of Curcumin with some antibiotics such as ampicillin, oxacillin, norfloxacin gives a synergetic effect against (MRSA) Methicillin-resistant Staphylococcus aureus strain [12].The anti-inflammatory qualities of curcumin were used to treat sprain and muscle pain in addition to various diseases such as Alzheimer's, cardiovascular, diabetes, asthma, inflammatory, arthritis, pancreatitis, and renal diseases, as for the uses of curcumin in dentistry incorporate its utilization as pit and crevice sealant, mouthwashes, dental plaque detection, subgingival irritant, intracanal medicament and healing effects on ulcers at an earlier stage of the application[13],Waghmare et al. conducted a study to compare chlorhexidine and turmeric mouthwash, which was prepared by dissolving 10 mg of curcumin extract in 100 ml of distilled water, they observed the depletion of total microbial count for both groups [14,15].

Salvia officinalis or popularly sage is one of the common herbs in customary medication. It has been prevalently alluded to as "Wise", it has been applied scope of restorative activity including antibacterial, antiviral, antifungal, and cancer prevention agent influence [16]. Numerous types of *Salvia*, including *Salvia officinalis*, are native to the Mediterranean area, and have been utilized worldwide as seasoning flavors just as conventional home grew medication, sage is additionally a characteristic wellspring of flavonoids and polyphenolic mixes (e.g. caffeic acid, carnosic acid, and rosmarinic acid) caffeic acid is the building block of a variety of plant metabolites, it assumes a focal part in the natural chemistry of the Lamiaceae plants and appears predominantly in a dimer structure. Carnosic and rosmarinic acid which are available at high establishing in the concentrate of sage plants, having potent antioxidant, radical-scavenging, antibacterial efficacy and have strong cancer prevention agent properties [17]. Stomach and circulation disturbances, cardiorespiratory diseases, mouth and throat aggravations, skin infections, and numerous different illnesses have been treated with sage extract [18]. In traditional medicine, various herbs sage tea, thyme, and peppermint have been used as a mouth rinse against oral mucositis and for the prevention of oral cancer [19]. In Iraq there is insufficient attention to the effect of herbal compounds in dealing with many malady and with the development in pharmacological information about the effect of sage, particularly *S. officinalis*, these locally grown drugs with antibacterial, anti-oxidant, calming, free radical rummaging, and antitumor activities have been found to be exceptionally compelling in the advancement of new characteristic medications to prevent, control, and treatment numerous of medical issues just as more real and bewildered sicknesses [20].

Materials and method

The study was carried in the period of (November 2019-January 2020), where 74 patients (37 male, 37 female) visited a consultant educational clinic of Almustansiriyah university collage of dentistry complaining minor oral ulcers, Ages of the patients range from 15-50 years, exclusion patterns incorporate systemic disease, inflammatory and allergic conditions, individuals wearing a denture or using orthodontics appliance, patient receiving medications for RAU, pregnant women, and smoking people. The medical history of the patient, the clinical examination, and the presence of a well-defined painful ulcer of less than 1 cm in diameter was thoroughly diagnosed, the main outcome criteria in this study include the evaluation of ulcer size, remission of pain, and time needed for complete healing. Patients were asked to record aphthous pain level on first, third, and fifth day according to the Visual Analogue Scale (VAS) using a grade from 0 to 10 to follow pain remission and elimination.

Two equal study groups were included, the first group uses Sage mouthwash, which was extracted from the plant *Salvia officinalis*, leaves of the plant were cut into small pieces and then dried, the patients were directed to make the mouth wash by one teaspoon of dried herb (sage) only in one cup of boiling water for 20 minutes, the second group consists of 1% curcumine extract as a mouthwash, the plant preparation is made from mixing curcumin extract with hot water and used after cooling to be taken as a mouthwash, both groups rinse for 1 minute and repeated five times for five days, the two groups receive natural herbal medicines without combining topical or systemic medication. Assessment under the daily observation process of the ulcer on the first, third, and fifth day for pain relief, decrease of pain intensity, reduction in the size of ulcers, and a complete healing duration were established ,all patients were informed about this treatment and their agreement was taken. The comparisons were based on the results of statistical analysis conducted by SPSS test.

Results

The present work is a comparative study that included 74 patients were suffering from minor ophthous ulcer 37 received sage mouthwash treatment, an equal number of the study participants received curcumin mouth wash treatment. General characteristics of the study population are illustrated in Table (1). The age and gender were matched between two groups to standardize the circumstances of the study. The mean age of the sage group was 29.00±9.2 years, and 27.97±9.06 years among the curcumin group (P>0.05). Regarding gender, the number of males 14 (37.8%)and female 23 (62.2%) in the sage group while male 7 (18.9%) and female numbers were 30 (81.1%) in the curcumin group, there was no statistically significant difference (P>0.05) according to age and gender.

Table (1): General characteristics of study population

General characteristics		Sage (n=37)	Curcumin (n=37)	Statistical test		
				t	χ ²	P-value
Age (years)	Mean±SD (Min-max)	29.00±9.2 (16-48)	27.97±9.06 (15-49)	0.484		0.630
Gender	n (%) Male Female	14 (37.8) 23 (62.2)	7 (18.9) 30 (81.1)		3.258	0.071

Table (2) clarify medical characteristics of ulcer among the study population. Analysis of the aphthous ulcer shape of the sage group patients showed that 4 (10.8%) and 5 (13.5%) were irregular shape, 5 (13.5%) and 5 (13.5%) were oval shape of ulcer ; 28 (75.7%) and 30(81.1%) were round shape of ulcer, in the two studied groups respectively without statically significant

differences ($\chi^2=0.736$, $P=0.692$) between sage and curcumin group. Concerning of ulcer site, 4 (10.8%) and 7 (18.9%) ; 28 (57.1%) and 7 (18.9%) were alveolar sulcus; anterior tongue were 7 (18.9%) and 5 (13.5%) , buccal mucosa were 5 (13.5%) and 13 (35.1%), labial mucosa were 12 (32.4%) and 8(12.6%), labial sulcus were 5(13.5%) and 2 (5.4%), lateral tongue 4 (10.8%) and 2 (5.4%) in the two studied groups sage and curcumin respectively , and was statistically significant ($\chi^2=13.174$, $P=0.040$).

Table (2): Medical status of ulcer among study population according to treatment type

Variables	Sage (n=37) n (%)	Curcumin (n=37) n (%)	χ^2	P-value
Ulcer shape				
Irregular	4 (10.8)	2 (5.4)	.736	0.692
Oval	5 (13.5)	5 (13.5)		
Round	28 (75.7)	30(81.1)		
Ulcer site				
Alveolar sulcus	4 (10.8)	7 (18.9)	13.174	0.040
Anterior tongue	7 (18.9)	5 (13.5)		
Buccal mucosa	5 (13.5)	13 (35.1)		
Labial mucosa	12 (32.4)	8(12.6)		
Labial sulcus	5(13.5)	2 (5.4)		
Lateral tongue	4 (10.8)	2 (5.4)		

Table (3) points out that the mean aphthous size were decreased in the three patients visits among two studied groups received sage and curcumin treatment as follow (4.0 ± 1.15 vs. 3.87 ± 1.35 ; 3.14 ± 1.53 vs 3.15 ± 1.34 ; 0.7 ± 0.85 vs 0.97 ± 0.67) respectively in visit 1,2 and 3 between two studied groups. This change was not statistically significant ($P > 0.05$) among follow-up visits.

Table (3): Comparison between sage and curcumin according to aphthous size in patients visits among study groups

Variables	Sage (n=37) Mean \pm SD	Curcumin (n=37) Mean \pm SD	Statistical test t	P-value
Aphthous size in visit (1)	4.0 \pm 1.15	3.87 \pm 1.35	0.437	0.663
Aphthous size in visit (2)	3.14 \pm 1.53	3.15 \pm 1.34	-0.012	0.990
Aphthous size in visit (3)	0.7 \pm 0.85	0.97 \pm 0.67	-1.511	0.135

Table (4) points out that the pain mean of aphthous ulcer in the three follow-up visits. In the first visit pain mean were 6.91 ± 1.03 and 6.63 ± 0.98 in sage and curcumin group, there was no significant difference between two groups in the first visit ($t=1.159$, $P>0.05$); while pain mean in the second visit were 3.93 ± 1.52 sage group and less than pain mean in curcumin group 4.73 ± 1.2 and there was significant ($t= -1.511$, $=0.014$). As for visit three there were obvious decrease in the pain mean of sage group in comparison with curcumin group 0.81 ± 1.09 and 2.77 ± 1.59 respectively and highly significant between two groups ($t=-6.257$, $P=0.000$).

Table (4): Comparison between sage and curcumin according to pain in patients visits among study groups

Variables	Sage (n=37) Mean±SD	Curcumin (n=37) Mean±SD	Statistical test t	P-value
Pain in visit (1)	6.91±1.03	6.63±0.98	1.159	0.250
Pain in visit (2)	3.93±1.52	4.73±1.2	-1.511	0.014
Pain in visit (3)	0.81±1.09	2.77±1.59	-6.193	0.000

As illustrated in Table (5) mean of healing duration were 5.32 ± 1.65 in the sage group, while in curcumin group the mean of healing duration 4.56 ± 1.20 and there was significant difference ($t=-2.010$, $P=0.048$) between two studied groups.

Table (5): Comparison between sage and curcumin according to aphthous healing duration among study groups

Variables	Sage (n=37) Mean±SD	Curcumin (n=37) Mean±SD	Statistical test t	P-value
Healing duration (Min-max)	5.32 ± 1.65 3-7	4.56 ± 1.20 3-7	2.010	0.048

Discussion

RAS is a common oral disorder that the clear etiology is not precisely known and the management is coordinated particularly toward supportive symptomatic, treatment, corticosteroids and analgesics considered the best option for RAS patients, extreme complications may occur with frequent exposure to those drugs, such as secondary fungal infections and drug resistance, furthermore, an allergic reaction, loss of taste sensation, and staining of teeth may occur by continuing using chemical mouth wash in a few individual [21]. Nowadays patients tend to use natural medicine to avoid the side effects of synthetic drugs. Most of studies have reported favorable results related to herbal medicine and several effects have been recognized, this study proposed to evaluate the diverse effects of sage (*Salvia officinalis*) and the curcumin extract as mouth wash on curing minor aphthous ulcer as an substitute favorable natural herbal medicine.

Current data show the benefits of the topical treatment mouthwash sage and curcumin in decreasing the size of the ulcers. Statistical analysis of data reveal the aphthous ulcer as for the third visit was an obvious decrease in the pain, and confirmed by the highly significant difference between the two groups specified in Table (4), from both the biological and chemical point of view, sage contain anti-inflammatory properties that help to decrease inflammation and healed ulcers in general, it is rich in antioxidants that help to improve the rate of oxygen in the blood, which works to repair damaged cells, thus it protects against various types of ulcer [22,23], additionally Ursolic acid is the component of sage, that has a strong anti-inflammatory effect [24], this support the results illustrated in table (5) that expose remarkable improvement in the sage group, one further conceivable clarification of the improvement of the sage group may be attributed to the effect of the phenolic and flavonoid compounds which are mainly responsible for the antioxidant influences of the sage leaves that play a major role in protecting the body against the oxidative stress and free radical that may induce damages [18], these observations were confirmed and validated by the outcomes of this study, and in agreement with other researches employment of sage herbs in previous studies reported the tensile strength of the healing wound was promoted through higher cross-linking of collagen, as well as faster re-epithelialization process. The sage extract was found to be more effective as an anti-inflammatory product against gingival inflammation and mouth ulcers [25].

According to Wagner H. et al., many herbal agents contain a mixture of active pharmaceutical ingredients that are blended based on either their additive or synergistic properties [26], this agrees with the outputs of this study which demonstrate the outstanding therapeutic activity of the herbal sage as an antimicrobial and a defensive remedy for various oral infections and disorders [27].

Turmeric contains an essential ingredient known as curcumin, that provides the required antioxidant, antimicrobial and anti-inflammatory agents, several studies record a statistically significant reduction of the ulcer size in patients receiving curcumin herbal therapy, It has a wide spectrum of biological functions as healing depends on vascularization and the capacity to create collagen, so it promotes the formation of new cells and helps transport nutrients and oxygen, leads to earlier resolution of ulcers, Saldanha et al. assessed the viability and wellbeing of curcumin mouthwash in correlation with other types of mouthwashes such as chlorhexidine and normal saline in handling the oral mucositis, curcumin mouthwash was more viable in terms of rapid wound healing and better patient compliance without complication, this finding is confirmed by the present study [28], the result of the utilizing curcumin mouthwash group could be best explained by its anti-inflammatory features, the possible mechanism of curcumin role in RAS treatment include decreased release and metabolism of arachidonic acid, , It considered as an immune-modulating agent, and suppresser inflammation [29,30] that cause re-epithelization and accelerated the healing process which provides validation to this study, never the less insufficient number of participants is a concern and suggests the need for further researches. More studies should be conducted with promising natural herbs which deals with more benefits and achievements.

Conclusion

The current study revealed promising benefits of the topical treatment of RAS with natural herbal medicines. The outcomes of this investigation contribute a positive proof of the remarkable role of the sage and curcumin mouthwash in reducing the severity of the oral ulcer. The present study has supported the use of sage in dentistry on a large scale due to its unique properties.

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Ethical Clearance: the article has not considered for publication in another journal

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