

Anti-Inflammatory Effect of Sage (*Salvia officinalis*) Extracts on Oral Health

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ABSTRACT

The aim of the study is to show the anti-inflammatory effect of sage (*Salvia officinalis*) extract as mouthwash on treating the infected gums (gingivitis) and mouth ulcers (minor aphthous ulceration).

Methods and materials: sixty (60) patients (50% female and 50% male) 30 patients had RAU (minor aphthous ulceration) according to clinical presentation and 30 patients had gingivitis according to gingival index of loe and Silness. Sage mouthwash was extracted from the plant *Salvia officinalis*. The patients of the study group were demonstrated to how they made the mouth wash. Patients with minor aphthous ulceration of study and control group were included in the post-treatment daily observations of the ulcer on [first, third and sixth day] and we looked for pain relief, reduction of intensity of pain, reduction in size of ulcers, and complete healing.

Results: Analysis of gingival scores by gingival index of loe and silness of sage mouthwash individually showed a statistically highly significant improvement and healing of gingivitis (decreased mean value) from the first day to the sixth day. Analysis of gingival scores by gingival index of loe and silness of normal saline mouthwash showed a statistically significant results from the first day to the sixth day but there was no complete healing. Minor aphthous signs and symptoms of the study group in comparison with control group showed a statistically significant improvement in daily observations.

Conclusions: Sage extract was found to be effective as anti-inflammatory product against gingival inflammation and mouth ulcers and present study confirmed the efficacy of the plant.

KEY WORDS

Sage, *Salvia officinalis*, Gingivitis, RAU, herbal extracts.

المستخلص:

خلفية البحث: إن تأثير عشبة الميرمية المضاد للبكتيريا قد اثبت بالتجارب. اوراق عشبة الميرمية المجففة قد استعملت لعلاج عدة امراض وهي واحدة من اشهر الاعشاب استعمالا في مجال الطب. وقد لوحظ ان لها طيف علاجي واسع كمضادات للبكتيريا والفطريات وايضا مضادات للاكسدة ولذلك استعملنا هذه العشبة لتحديد تأثيرها على صحة الفم. هذه العشبة تعود الى عائلة النباتات العطرية ذات الزيوت الطيارة وتنتشر في منطقة حوض البحر المتوسط وقد استخدمت كعشبة منكهة وكذلك كعلاج عشبي.

اهداف البحث: لبيان تأثير مستخلص عشبة الميرمية المضاد للالتهابات اذا ما استعملت كغسول فموي لعلاج الالتهاب اللثوي وتقرحات الفم.

المواد والطرق: اختييار المرضى: تم اختيار 60 مريضا 30% اناثا و 30% ذكور اعمارهم تتراوح بين (20-40) سنة من فرع طب الفم وعيادة الفحص في كلية طب الاسنان /الجامعة المستنصرية للفترة من اذار - نيسان 2016

30 مريضا كانوا يعانون من تقرحات الفم و 30 مريضا كانوا يعانون من التهاب اللثة. تحضير الغسول الفموي: قطعت اوراق الميرمية الى اجزاء صغيرة ومن ثم جففت ثم تم تعليم المرضى على تحضير الغسول بوضع ملعقة صغيرة من اوراق الميرمية المجففة في كوب واحد من الماء الساخن المغلي وتركها لمدة 20 دقيقة.

النتائج: ستون مريضا قد شاركوا في هذه الدراسة (30 ذكرا و 30 انثى) وكانت نسبة الاستجابة للدراسة 100%. ان التحليل الاحصائي لقراءات اللثة حسب معيار اللثة ل (loe و silness) اظهر انخفاض واضح في القراءات اللثوية في مجموعة غسول الفم الميرمية من (2,05 ± 0,48) في اليوم الاول للدراسة (الخط الاساس) الى (0,82 ± 0,21) في اليوم السادس للدراسة (p-value > 0,05). اما المشاركون في الدراسة والذين استعملوا الماء كغسول للفم كان التحليل الاحصائي لقراءات اللثة لديهم يظهر بان هنالك تحسن قليل لديهم فكانت قراءات اللثة لديهم (2,02 ± 0,67) في اليوم الاول (الخط الاساس) الى (1,35 ± 0,57) في اليوم السادس للدراسة (p-value > 0,05) أي ان المرضى لازالوا يعانون من التهاب اللثة. كما ان الملاحظة السريرية لتقرحات الفم للمجموعة الاولى الذين استعملوا غسول الفم الميرمية اظهرت تحسن واضح للمجموعة من اليوم الاول للدراسة فان شدة الالم قد قلت لديهم وحجم القرحة الفموية بدأ بالنقصان بصورة تدريجية وصولا الى الشفاء الكامل لقرح بعض المرضى في اليوم السادس.

الاستنتاجات: مستخلص عشبة الميرمية اثبتت فعالية كغسول مضاد للالتهابات في علاج تقرحات الفم والتهاب اللثة.

INTRODUCTION

The global need for alternative prevention and treatment options and products for oral diseases that are safe, effective and economical comes from the rise in disease incidence (particularly in developing countries), increased resistance by pathogenic bacteria to currently used antibiotics and chemotherapeutics, opportunistic infections in immune-compromised individuals and financial considerations in developing countries (1).

Herbal medicine is both promotive and preventive in its approach. It is a comprehensive system, which

uses various remedies derived from plants and their extracts to treat disorders and to maintain good health.

The major strength of these natural herbs is that their use has not been reported with any side-effects till date (2). A number of herbs and medical plants have been found to be evaluated against oral microbes in vitro. Some of the plant extracts showed promising antimicrobial effects both in vitro and in vivo (3).

Recurrent aphthous stomatitis (RAS), or recurrent aphthous ulcer (RAU), is one of the most common oral diseases, with an estimated prevalence of 25% (4). Many factors may be involved in its progression,

such as genetic predisposition, immunological abnormalities, microbial infection, psychological stress, and hormonal state⁽⁵⁾. Since the etiology and pathogenesis of RAS remains unclear, there is currently no consensus regarding a definitive curative therapy. The commonly accepted treatment strategy is to lessen the pain and duration of lesions⁽⁶⁾. longer treatment and frequent exposure to these medications may cause fungal infection and drug resistance, which may further lead to more severe adverse effects or even life-threatening complications⁽⁷⁾.

The condition ranges in severity from minor recurrent aphthous stomatitis; it is characterized by self-limited ulcerations, to a very debilitating form, and is called major recurrent aphthous stomatitis. A third and much less common form of the condition is herpetiform aphthous ulceration^(8,9). Natural herbal medicines as an alternative therapy for RAU have been widely used in many countries for decades^(8,10). Clinical studies on the use of such remedies have reported favorable benefits to patients by reducing the discomfort and duration of ulcers^(9,10). All herbal mouth rinses do not contain alcohol, sugar, artificial color artificial sweetener (such as saccharine), stannous fluoride (processed form of fluoride that can stain teeth) and acetylpyridinium chloride that can also cause staining. Thus, by use of an herbal mouth rinse, we can avoid these ingredients and get better oral hygiene⁽¹¹⁾.

Antimicrobial effect of sage (*Salvia officinalis*) extract has been shown experimentally^(12, 13). Dry sage leaves were used in folk medicine for a variety of disorders. Today, sage is also used as a traditional remedy for many diseases⁽¹⁴⁾. *Salvia officinalis* is one of the most commonly used herbs in traditional medicine. It has been popularly referred to as "Sage". It has been reported that sage exerts a range of therapeutic activities including antibacterial, antiviral, antifungal, and antioxidant effects^(15, 16, and 17). It would be of interest to determine if such an herb could also have a beneficial effect on oral health. The genus *Salvia*, commonly known as **sage**, is the largest member of Lamiaceae or mint family^(18, 19). The plants are mostly aromatic and perennial, with flowers in different colors. Many species of *Salvia*, including *Salvia officinalis* (common sage), are native to the Mediterranean region and some of the *Salvia* species have been used worldwide as flavoring spices as well as traditional herbal medicine⁽²⁰⁾.

Sage is also a natural source of flavonoids and polyphenolic compounds (e.g., carnosic acid, rosmarinic acid and caffeic acid) possessing strong

antioxidant, radical-scavenging, and antibacterial activities⁽²¹⁾. The majority of the phenolic acids in *Salvia* species are derivatives of caffeic acid which is the building block of a variety of plant metabolites⁽²²⁾. Caffeic acid plays a central role in the biochemistry of the Lamiaceae plants, and occurs mainly in a dimer form as rosmarinic acid. Carnosic acid and rosmarinic acid, which are present at high concentrations in the extract of sage plants, have shown strong antioxidant properties⁽²²⁾. Ursolic acid, also a component of sage, has strong anti-inflammatory properties, and in sage preparations, it is considered as a quality control measurement for the anti-inflammatory effects of different solutions⁽²⁴⁾.

Salvia species may represent a natural, safe, and effective treatment for many diseases and their symptoms. In recent decades, with the increase in pharmacological knowledge about the beneficial effects of sage, especially *S. officinalis*, these herbal medicines with antibacterial, antioxidant, anti-inflammatory, free radical scavenging, and antitumor activities have been found to be very effective in the development of novel natural drugs to prevent, control, and treat many minor health problems as well as more serious and complicated diseases⁽²⁵⁾. Sage tea has been traditionally used for the treatment of digestive and circulation disturbances, bronchitis, cough, asthma, angina, mouth and throat inflammations, depression, excessive sweating, skin diseases, and many other diseases^(26, 27, and 28).

The aim of this study is to show the Anti-inflammatory effect of sage (*Salvia officinalis*) extract as mouthwash on treating the infected gums (gingivitis) and mouth ulcers (RAU).

MATERIALS AND METHOD

Patients selection: sixty (60) patients (50% female and 50% male) in age range (20-40) years with mean age (30) years were randomly selected from Oral medicine Department and oral diagnosis clinic (College of Dentistry \ Al-Mustansiriya University), and seen in period of 2 months (Mar. 2016 to Apr.2016), 30 patients had RAU (Minor aphthous) and 30 patients had gingivitis. Complete medical history and full history of present illness was obtained, physical examination and laboratory investigations were carried out to assess patient's condition. These sixty patients were equally divided into 2 groups; study group 30 patients (15 patients with gingivitis and 15 patients with RAU) and control group 30 patients (15 patients with gingivitis and 15 patients with RAU).

Exclusion criteria were: patients with major

aphthous and herpetiform aphthous ulceration, wearing a denture, wearing orthodontics appliance, receiving medications for RAU and inflammatory and allergic conditions, smoking, pregnancy, estimation of poor cooperation during the study. Informed consent was taken for each participant. Sage mouthwash preparation: Sage mouthwash was extracted from the plant *Salvia officinalis*. Leaves of the plant were chopped, fragmented, and broken into small pieces and then dried. The patients of the study group were demonstrated to how they made the mouth wash by Steep one teaspoon of dried herb (sage) in one cup of boiling water for 20 minutes. The gingival condition of patients with gingivitis were examined and calculated according to the method given by (GI) of Loe and Silness⁽²⁹⁾.

The study group patients were instructed to continue their usual oral hygiene measures and use herb (sage) mouthwash for the duration of the study. The subjects were demonstrated to use the mouth wash for 60 seconds, twice daily (once taken at night just before the bed time) over the 6-days study period. The control group was given normal saline mouthwash (placebo with no active ingredient) over the duration of the study with same instructions of using sage mouthwash. The gingival condition of gingivitis patients for both study and control group were examined according to gingival index of Loe and Silness at the first and the sixth day of the study period.

The patients with RAU for both study and control group were undergo daily observation of the ulcer on [first, third and sixth day] and we looked for pain relief, reduction of intensity of pain, reduction in size of ulcers, and complete healing. Statistical analysis was carried out by SPSS version 16. Paired comparison tests and chi-square test were used to confirm the results with p-value set at < 0.05. Mean and standard deviation was calculated using the

paired t test and mean difference was calculated to yield significant results.

RESULTS

Sixty patients (30 females and 30 males) participated in the study and the response rate to the study was 100%. Analysis of gingival scores by gingival index of loe and Silness of sage mouthwash individually showed a statistically highly significant improvement from the first day to the sixth day. The reduction in gingival index scores in sage mouthwash group was 2.05 ± 0.48 to 0.82 ± 0.21 (from baseline 1st day to 6th day) respectively with p-value set at < 0.05 (Table 1).

Analysis of gingival scores by gingival index of loe and Silness of normal saline mouthwash showed a statistically significant improvement from the first day to the sixth day. Although there was reduction in gingival index scores 2.02 ± 0.67 to 1.35 ± 0.57 (from baseline 1st day to 6th day) respectively with p-value set at < 0.05 but patients still had gingival inflammation (Table 2).

Post-treatment daily observation of the clinical signs and symptoms of RAU on (first and sixth day) we looked for pain relief, reduction in the intensity of pain, reduction in size of ulcers, and complete healing. Both groups were included in the post-treatment observation. RAU patients of the study group in comparison with RAU patients of the control group in the 1st day showed significant pain relief in one patient with (p-value=0.001) and significant reduction in pain intensity in three patients with (p-value=0.005), in the 3rd day RAU patients of the study group showed significant reduction in pain intensity in seven patients with (p-value=0.005) while in the 6th day thirteen patients showed significant pain relief with (p-value=0.005) and three patients showed complete healing of ulceration with (p-value=0.02), the other daily observations showed no significant differences as shown in (Table 3).

Table (1): The gingival index score for the sage mouthwash group

GI Study group*	Mean of first day	Mean of sixth day	t-test	SD±	Sig.
No. 15	2.05	0.82	12.06	0.39	0.000

Table (2): The gingival index score for normal saline mouthwash group

GI control group*	Mean of first day	Mean of sixth day	t-test	SD±	Sig.
No. 15	2.02	1.35	10.23	0.25	0.000

Table (3): Post treatment observation of the clinical sign and symptoms for the study and control groups

variables	Clinical observation	1 st day	3 rd day	6 th day
Study group (RAU patients no. 15)	Pain relief	1*	5	13**
	Reduction of intensity of pain	3**	7**	15
	Reduction of size of ulcer	0	2	11
	Complete healing of ulcer	0	0	3***
Control group (RAU patients no. 15)	Pain relief	0	1	5
	Reduction of intensity of pain	0	2	5
	Reduction of size of ulcer	0	2	7
	Complete healing of ulcer	0	0	0

*p value=0.001, **p value=0.005, ***p value=0.02

DISCUSSION

Salvia officinalis is one of the most commonly used herbs in traditional medicine⁽³⁰⁾. It has been popularly referred to as “Sage”. It has been reported that sage exerts a range of therapeutic activities including antibacterial, antiviral, antifungal, and antioxidant effects⁽¹²⁾. It would be of interest to determine if such an herb could also have a beneficial effect on oral health. Several herbs have been studied for their effect on oral health⁽¹⁵⁾. Studies on the *Salvia* species rich in essential oils (such as *S. officinalis*) with volatile monoterpenoid as their major constituents are reported to be effective antibacterial⁽¹⁷⁾. Sage contains the constituent alpha- and beta-thujone, camphor, and cineole. It also contains rosmarinic acid, tannins and flavonoids. In modern European herbal medicine, a gargle of sage tea is commonly recommended to treat a sore throat, inflammations in the mouth, and gingivitis. Sage extracts has antibacterial, antifungal, and antiviral activity, which may partially explain the effectiveness of sage for these indications.^(31, 32)

Sage containing anti-microbial effects and being of an astringent nature, it reduce swelling in the mouth tissues, and has anti-inflammatory action. Thus, sage mouthwash can be used for sore mouth concerns alike. Rinse with sage mouthwash two times daily to soothe irritated gingival and mucosal tissues and to reduce swelling as the result of this study show a significant decrease in the gingival inflammation on patients with gingivitis in the study group. RAU is one of the most common oral disorders and its etiology is not well understood. Its management is mainly directed toward symptomatic, supportive treatment⁽⁶⁾. Therefore, corticosteroids and analgesics serve as the first choice for RAU patients⁽³³⁾. However, longer treatment times and frequent exposure to such drugs may induce severe complications, such as secondary fungal infections and drug resistance⁽³⁴⁾. There has been

a long history of the use of natural herbal medicines for various disorders, including RAU, worldwide and such remedies have been studied both in clinic trials and experimental studies⁽³⁵⁾. In this study, we focused on the efficacy and safety of the topical application of natural herbal *Salvia officinalis* (sage) for the treatment of RAU and gingival inflammation.

Natural herbal *Salvia officinalis* (sage) greatly improved the patients’ symptoms by reducing ulcer size, shortening ulcer duration, and relieving pain without severe complications. However, only a weak conclusion can be drawn due to several limitations. Sample size, experiment duration and the laboratory requirement for making the natural herbal medicines and extracts. The natural course of an untreated ulcer was 9.5 ± 1.3 days⁽¹⁶⁾ and the duration of herbal medicine treatment was 5.21 ± 1.73 days and that was compatible with present study (36,37) It is therefore suggested that the experimental period should exceed 7 days to avoid missing valuable data. Moreover, follow-up is highly recommended.

CONCLUSIONS

Sage extract was found to be more effective as anti-inflammatory product against gingival inflammation and mouth ulcers. This study has confirmed the anti-inflammatory effect and the efficacy of the plant, thus supporting the applications that used the sage as a preventive remedy for various oral infections. Emergence of multidrug resistant strains, significant side effects of existing chemical drugs and their limited options are unsolved problems even today. Herbal products have shown promising results with minimal side effects. Also, their additional effect on inflammatory pathways and antioxidant potential, make them eligible to be used as effective agents to maintain oral health and the integrity of oral cavity.

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