Treatment of Recurrent Aphthous Ulceration by Mastic Orabase

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ABSTRACT

Background: Recurrent aphthous ulcer is a chronic inflammatory disease of the oral mucosa. Substance P has activity in the inflammatory response. Transforming growth factor beta (TGF-β) as immune-modulators regulates the immune response and has anti-inflammatory, pro-inflammatory effects. Pistacia lentiscus (mastic) of Anacardiaceae family have pharmacological activities like anti-inflammatory, antioxidant, and used in treatment of wound and repair. The aim of this study is to find the safety and efficacy of a new product mastic orabase; experimentally and clinically.

Methods: This research studied two parts: first; experimentally for assessment of mastic orabase effects on rabbit dermal irritation, efficacy of mastic orabase on the induced ulceration, with histopathology of rabbits' tissues, and safety: therapeutic index and safety factor. Second; clinical efficacy of mastic orabase on the healing of RAU by assessment of ulcer size reduction, inflammation, healing time, pain, saliva substance P and TGF-β levels in RAU patients, and monitoring for any adverse effects or adverse drug reactions.

Results: Experimental study of topical mastic orabase treatment showed significant reduction of inflammation and ulcer size, healing time. Safety of mastic orabase was confirmed by no dermal irritation, no toxicity, and wide therapeutic index range. Clinical study showed reduction of inflammation, ulceration, healing in short time, pain was relieved from the first topical dose, and the anti-inflammatory activity of mastic orabase was confirmed by reduction of salivary substance P and TGF-β elevation.

Conclusion: Mastic orabase showed dose-dependent efficacy in the treatment of recurrent aphthous ulceration, short healing time. This may be related to effect of mastic orabase on proinflammatory and anti-inflammatory mediators; substance P and TGF-β.

Key words: Mastic orabase, RAU, substance P, TGF-β. **(J Bagh Coll Dentistry 2017; 29(3):45-53)**

INTRODUCTION

Recurrent aphthous ulcer (RAU) is one of the most painful oral mucosal inflammatory ulcerative conditions and can cause pain on eating, swallowing and speaking [1]. A prodromal localized burning or pain for 24 to 48 hours can precede the ulcers. The lesions are painful, clearly defined, shallow, round or oval, with a shallow necrotic center covered with a yellow-grayish pseudomembrane and surrounded by raised margins and erythematous haloes. The pain lasts for three to four days, at which point early epithelialization can occur [2].

Substance P (SP) is an undecapeptide member of the tachykinin neuropeptide family. It is a neuropeptide, acting as a neurotransmitter and as a neuromodulator [3], it's closely related neurokinin A (NKA) are produced from a polyprotein precursor after differential splicing of the preprotachykinin A gene. The neuropeptide substance P is widely distributed in the central and peripheral nervous system including the skin [4]; it is capable of inducing a number of inflammatory responses including vasodilatation, plasma extravasation, leukocyte activation, endothelial cell adhesion molecule expression, cellular cytokine production, and mast cell activation [5].

These SP pro-inflammatory effects are mediated by the neurokinin receptor 1 (NK1R) [3,4].

Its proinflammatory effects in immune and epithelial cells and participates in inflammatory diseases. Also stimulate cell growth in normal and cancer cell line cultures [6], and it could promote wound healing of non-healing ulcers in humans [7], and its induced cytokines promote multiplication of cells required for repair or replacement, growth of new blood vessels [8]. The TGF-beta superfamily encompasses a diverse range of proteins, many of which play important roles during development, homeostasis, disease, and repair [9].

Mastic is a white, semitransparent, natural resin that is obtained as a trunk exudate from mastic trees. Scientific name is *Pistacia lentiscus*, of the Anacardiaceae family [10]. The essential oil extracted from the aerial parts has been proven to exhibit antioxidant, anti-inflammatory, antimicrobial, antifungal [11] and anti-atherogenic activities [12]. Mastic gum has been used in clinical trials on patients with peptic ulcers; the administration of mastic (1 g daily) relieved the pain and healed the stomach and duodenal ulceration in the majority of the patients within 2 weeks [13].

Mastic gum has bactericidal activity on H. pylori in vivo. Mastic gum kills *Helicobacter pylori*, at concentrations as low as 0.06 mg/mL. The effect of mastic has been studied on

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experimentally induced gastric and duodenal ulcers in rats. Mastic at an oral dose of 500 mg/kg produced a significant reduction of gastric secretions, protected cells, and reduced the intensity of gastric mucosal damage. The in vitro antimicrobial activity of *P. lentiscus* extracts has also been tested on bacteria and fungi [13]. Concerning internal use of mastic oil, tests of repeated toxicity via rectal route, showed that mastic oil is well tolerated with no adverse effect neither on liver nor renal functions; rabbits subjected to six consecutive weeks of oil administration, showed no anatomical or blood biochemical variations of biological signification toxicity [14].In dentistry, mastic acts as an oral antiseptic and tightens the gums, and for that reason it is used in toothpastes and chewing gums. The essential oil of mastic gum is also used in perfumery and in the cosmetic industry (creams and other facial products) [15].

The aims of this study are: 1-Effects of mastic orabase on rabbit dermal irritation. 2-Efficacy of mastic orabase on the induced ulceration. 3-Microscopical histopathology of rabbits' tissues. 4-Safety: therapeutic index and safety factor. 5-Clinical efficacy of mastic orabase on the healing of RAU patients; ulcer size reduction, healing time, pain. 6-Saliva substance P level of RAU subjects: 7-Saliva TGF_beta level of RAU subjects: 8-Adverse effects or adverse drug reactions.

METHODS

The study protocol was approved by the ethics Committee of the College of Dentistry/Hawler Medical University.

Formulation of orabase

The orabase was prepared according to Pharmacopoeia [16] under aseptic conditions. The required weights of dried pectin, sodium carboxymethyl cellulose, gelatin, methyl paraben, and propyl paraben were added gradually to form a homogenous orabase. The measured quantity of mastic oil was added to the orabase gradually with continuous stirring till homogenous orabase was attained. The mastic orabase was poured into the collapsible tubes, closed properly and stored in dry cool place. Placebo was prepared as above but free of the active constituent.

Effects of mastic orabase on rabbit dermal irritation

Primary irritation to the skin was measured by a patch-test technique on the intact skin of the albino rabbit in accordance with the guidelines of the Consumer Product Safety Commission, Title 16, Chapter II, Part 1500. The backs of the rabbits were clipped free of fur with an electric clipper at least 4 h before application of the sample. Introduction under a square patch of surgical gauze measuring 1 inch by 1 inch and two single layers thick, the tests orabase and placebo were applied topically on the back of the animals. The animals were immobilized with patches secured in place by adhesive tape.

The first evaluation was made after 1 h, then the entire trunk of the animal is wrap with a rubberize cloth, for the 24 h period of exposure. After 24 h of exposure, the patches were removed and the resulting reactions were evaluated on the basis of the designated values for erythema and oedema with the Draize scoring criteria. Readings were again made at the end of 48, and 72 h. The Primary Irritation Index (P.I.I.) was calculated following test completion. Material producing a P.I.I. score of greater than or equal to 5.00 was considered positive; the material was considered a primary irritant to the skin.

Efficacy of mastic orabase on the induced ulceration

This study involving animals followed the institutional and national guide for the care and use of laboratory animals. New Zealand albino rabbits (*Oryctolagus cuniculus*) of both sexes were used to assess the efficacy of 3 concentrations (5, 10, and 15%) of mastic orabase (on the induced ulcers. The mucosal injury was performed on both cheek pouches, under ether anaesthesia by two methods (six rabbits for each): in the first method, the buccal surfaces of the animals were exposed for 20 seconds to contact with glacial acetic acid, using a plastic tube of 4 mm in diameter. This produce an immediate mucosal necrosis within the affected area followed 2 days after (designed as ulceration day 0) by the development of a chronic ulcer with a well-define crater, which normally heals within 10 days. In the second method, the ulcer in the buccal mucosa of the rabbit's cheek pouch was induced by surgical incision and exposed for 20 seconds to contact with aspirin (100 mg/kg); chemicals such as aspirin that are held or that come in contact with the oral mucosa may cause tissues to become necrotic and slough off creating an ulcerated surface. The animals were examined by measuring the size of the ulcer using a calibrated probe; signs of inflammation, oedema, and erythema were assessed.

Microscopical histopathology of rabbits' tissues

The cheek pouch was collected and placed in 10% formalin solution for at least 24 hours, then prepared for light microscope examination. The parameters to examine; histopathological alterations, state of epithelial proliferation, type of inflammatory cells, fibrous tissues state, and number of blood vessels in the connective tissue under the microscope.

Safety: therapeutic index and safety factor:

This was assessed by measuring the toxicity and mortality of animals to calculate the therapeutic index (TI) and safety factor using the following formulas:

Therapeutic index= TD_{50}/ED_{50}

Where TD is toxic dose, and ED is effective dose at 50% of animales.

Safety factor = TD_1 / ED_{99}

Where TD is toxic dose at 1%, and ED is effective dose at 99% of animales [17].

Clinical efficacy of mastic orabase on the healing of RAU

This study involving human subjects is in accordance with the Helsinki declaration of 1975 as revised in 2000 and that it has been approved by the relevant institutional Ethical Committee. A prospective randomized double blind; placebo controlled study was performed. The subjects were divided randomly into 2 groups: 3 concentrations of mastic orabase treatment group and a Placebo group. The tests concentrations and placebo were applied topically on the ulcerated areas 3 times daily for 5 days. The assessed parameters were ulcer size reduction, healing time, tolerance, and pain reduction by comparative Pain Scale and memorial pain assessment.

The efficacy indices (EI) of the ulcer size improvement was calculated with the following formula (V4 and V7 refer to the values measured at day 5 visit and day 7 visit, while V1 refers to the baseline value measured before the study entry): EI = ([V4 or V7−V1] / V1) × 100%. The EI were evaluated on a 4-rank scale: [Heal: EI = 100%, Marked improvement: 100% >EI ≥70%, Moderate improvement: 70% >EI ≥30%, No improvement: EI <30%.

Saliva substance P level of RAU patients

Substance P levels in saliva samples were assessed according to kit procedure.

Saliva TGF_beta level of RAU patients

TNF-beta levels in saliva samples were assessed according to kit procedure.

Adverse effects or reaction

Monitoring for the presence of any adverse effects or adverse reaction.

Statistical analysis

Results are presented as mean ± SD or percentage (%). Statistical significance was calculated by comparing results by *t* test or linear regression analysis. ANOVA, Chi-square, fisher exact test. A P value less than 0.05 were considered statistically significant, aided by SPSS software.

RESULTS

Effects of mastic orabase on rabbit dermal irritation

Dermal irritation test of mastic orates showed no erythema or oedema on the intact sites, for placebo group; some animals had very slight erythema after 1, 24 hrs., then disappeared after 48 hrs., and there were no signs of erythema or oedema in all animals after 72 hrs. PII calculation of mastic orabase was 0.00, while in placebo group was the PII was 0.125, as showed in table (1).

Table 1: primary skin irritation test of six rabbits observed at 1, 24, 48, and 72 hrs.

Animal #	Mastic orabase								Placebo							
	Erythema				Oedema				Erythema				Oedema			
	Observation periods (hr.)				Observation periods (hr.)				Observation periods (hr.)				Observation periods (hr.)			
	1	24	48	72	1	24	48	72	1	24	48	72	1	24	48	72
1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Total	0	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0
PII	0.00				0.00				0.125				0.00			

For erythema: 0 = No erythema, 1 = Very slight erythema (barely perceptible), 2 = Well-defined erythema, 3 = Moderate to severe erythema, 4 = Severe erythema (beet redness) to slight eschar formations (injuries in depth). For edema: 0 = No edema, 1 = Very slight edema (barely perceptible), 2 = Slight edema (edges of area well defined by definite raising), 3 = Moderate edema (raised approximately 1 millimeter), 4 = Severe edema (raised more than 1 millimeter and extending beyond the area of exposure). Evaluation of primary irritation index (PII): 0.00 No irritation, 0.04 – 0.99 Irritation barely perceptible, 1.00 – 1.99

Slight irritation, 2.00– 2.99 Mild irritation, 3.00 – 5.99 Moderate irritation, 6.00 – 8.00 Severe irritation.

Effects of mastic orabase on induced ulcer

All rabbits developed erythematous surface and ulceration of 1.5-3.5 mm after 24 hrs. of ulcer induction. There was no differences between the two tested methods used for ulcer induction, after 2 days treatment with mastic orates, there was a significant declined ulcer size and healing in animals of ulcer size range (1.5-2.5 mm), P=0.01. The other animals showed healed ulcers after 3 days of treatment by mastic orabase with ulcer size range (2.6-3.5 mm), P=0.02. Placebo groups showed redness, ulceration along the treatment period (5 days), P=0.6, as showed in figure (1).There was a dose-dependent efficacy of the treatment by three doses of mastic orabase.

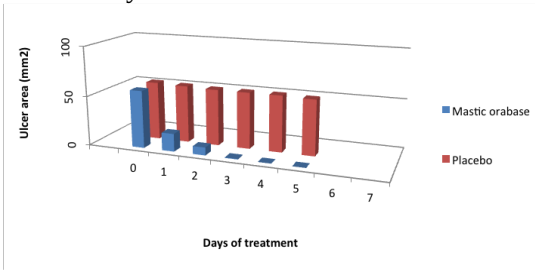

Fig.1: Ulcer area of rabbits' cheek pouches of mastic orabase treated compared to placebo group, level of significance p< 0.05.

Microscopical histopathology study

Histopathology examination of the rabbit's cheek pouch showed no inflammatory cells infiltration and there was re-epithelization, and healing evidence were seen with mastic orabase treated group, while placebo group showed heavy infiltration of acute and chronic inflammatory cells, and fibrous tissues with no evidence of re-epithelization.

Safety/ Toxicity

Rabbits of both sexes showed no signs of toxicity or death during the study& monitoring period (15 days). LD_{50} of mastic was 39±2 ml/kg oral, and 2.9±0.8 I.P., the therapeutic index was 10.9, and safety factor was 0.11 oral. Therapeutic dose: 2 g/ day, toxic dose: 100 mg/Kg, and oral toxic dose: 5 g/ Kg.

Clinical study

Sixty five subjects enrolled were randomized to mastic orabase treatment groups I [35 (53.85%)]; A- 5%, B- 10%, C- 15%, or placebo group II [30 (46.15 %)]. 41 Females (63.08%), and 24 males (36.92%) were participated in this study, mean age was 32, and mean weight was 73 Kg, all enrolled subjects have a minor aphthous ulcer type, table (2) clarified the subjects' characteristics.

Table 2: Subjects' characteristics

No. of Subjects	65
Gender ratio [Female: Male]	41 (63.08%): 24 (36.92%)
Mean Age (year)	32
Mean Weight (Kg)	73
Family history ratio {+ve: -ve}	20 (30.77%): 45 (69.23%)
Mastic orabase treated group	35 (53.85 %)
Placebo group	30 (46.15 %)

All subjects have inflammation and minor aphthous ulceration of 2-3 mm size at baseline, 52.3% (n: 34) of enrolled subjects have 2 mm ulcer size, showed a significant reduction of inflammation and ulcer size, and complete healing within 2 days of treatment (P=0.02), other subjects 47.7% (n: 31) have 3 mm ulcer size, showed a significant reduction of inflammation and ulcer size, and complete healing within 3 days of treatment by mastic orabase (P=0.01). There was no significant difference of inflammation, ulcer size after five days of treatment by placebo compared to baseline (P=0.7), as elucidated in figure (2, 3).

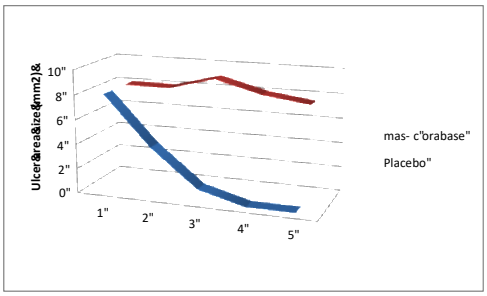

Fig. 2: Ulcer area size (mm^2) with days of trial of mastic orabase and placebo groups.

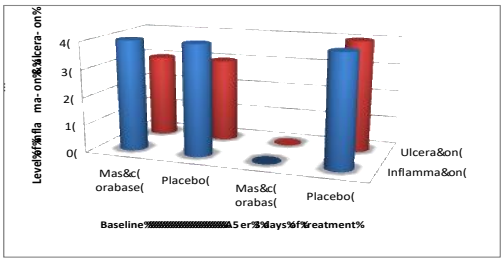

Fig. 3: Level of inflammation and ulceration at baseline and after 3 days of treatment in both groups.

The time needed for diminished the signs of inflammation and healing of ulceration were

faster in mastic orabase treated group than placebo group, as follows: Erythema; mastic orabase 2±0.5, placebo 9±1.5, oedema; mastic orabase 1±0.5, placebo 8±1.8, ulcer healing; mastic orabase 2±0.6, placebo 11±0.7. Pain; mastic orabase 1±0.0, placebo 7±1.5. The efficacy indices (EI) of the ulcer size improvement were 90.8 for mastic orabase treated group, for placebo group EI was 8.2, as elucidated in table (3). Pain was relieved from the first dose in all subjects treated by mastic orates in a significant value (P= 0.02) compared to non-relieved pain in placebo group, as showed in figure (4).

Table 3: Effectiveness index in ulcer size reduction

Grading	Mastic orabase	Placebo	P value
Heal	29	0	
Marked improvement	6	0	
Moderate improvement	0	1	
No improvement	0	16	
% Improvement	100	5.8	0.001
Efficacy index	90.8	8.25	0.0001

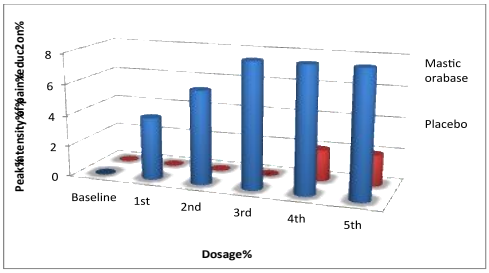

Fig. 4: The peak intensity of pain reduction with the dosage of mastic orabase and placebo groups. {(0= Baseline severe pain, 2= Moderate, 4= Mild, 6= Minimal, 8= No pain), Dose No. was 5 minutes between each}.

Saliva substance P level of RAU subjects

Saliva substance P level was significantly high in both groups at baseline, after 4 days of treatment by mastic orabase showed highly significant reduction, and more reduction after 7 days compared to baseline (P=0.002), while placebo group showed no changes after 4 days of treatment and after 7 days (P=0.6), as clarified in figure (5).

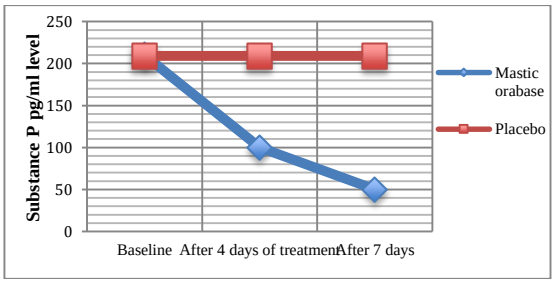

Fig. 5: Saliva substance P values at baseline, 4 days after treatment, and after 7 days for mastic orabase and placebo treated groups.

Saliva TGF_beta level of RAU subjects

Saliva TGF-beta level was low at baseline in mastic orabase, and placebo groups; 139.9±20.8 and 139.8±23.4Pg/ml, respectively. After 4 days of treatment, the level increased significantly in mastic orabase treated group (168.9±22.3Pg/ml) compared to baseline (P=0.01), then the TGF-β level increased significantly to 180±40.7Pg/ml (P=0.02) after 7 days, but placebo group showed no statistical differences after 4 days of treatment, and after 7 days (P=0.8), as showed in figure (6).

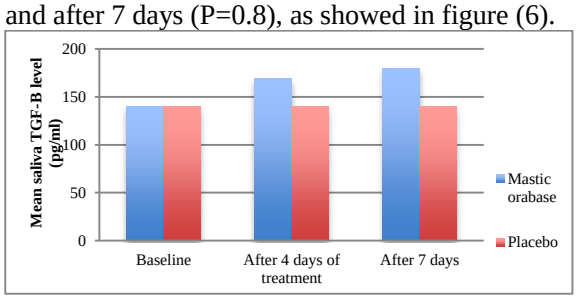

Fig. 6: Mean saliva TGF-beta values for mastic orabase treated and placebo groups at baseline, 4 days after treatment, and after 7 days.

Adverse effects or reaction

There was no adverse effect or reaction noticed during the study period (5 days) and monitoring period (3 weeks) after treatment. No sensitivity or allergy to treatment components was recorded from the usage of mastic orabase.

DISCUSSION

Many studies focused on the causes or factors that lead to RAU, and how is driven by unnatural cytokine responses associated with cellular immunity in oral mucosa. The aim of this study was to study the efficacy of mastic orabase for the first time on the healing process of induced ulcers on animals, and clinically on subjects suffered from RAU. Also for assessment of the levels of salivary cytokine such as substance P, and growth factor such as TGF-beta for the first time.

Mastic oil from Pistacia lentiscus L.

(Anacardiaceae) has been extensively studied for its anti-inflammatory activity attributed to the combination of its bioactive components. It has been widely used since ancient times without any reported toxicity in humans [18]. This study agrees with that.

Analysis of the chemical composition of mastic oil revealed that is a complex mixture of volatile compounds, mainly terpenes, with established beneficial biological properties [15]. The monoterpene perillyl alcohol (POH), which corresponds to 0.84% of mastic oil, is of great clinical interest due to its established chemopreventive and chemotherapeutic potential [19,20]. POH, besides its antitumor effect, acts as an angiogenesis inhibitor [21]. Mastic oil has a wide-range of therapeutic effects: anti-inflammatory, antibacterial, antifungal, antiviral, anticancer, and hypolipidemic activities [22,23]. *Pistacia lentiscus* is also effective in the treatment of functional dyspepsia and gastric ulcer [24], as well as in the healing of burns [14]. Anti-inflammatory properties have been reported from masticadienolic acid, masticadienonic acid, and morolic acid [25].

The dermal irritation test of mastic orabase was performed in this study to ensure the safety usage in humans, the topical application of mastic orabase caused no signs of irritation, neither erythema nor oedema at the intact site, it can be categorized as a non-irritant drug. Mastic orabase is safe and did not exhibit any toxicity during toxicity assessment by LD_{50}, therapeutic index and safety factor on animals, which confirm the safety of mastic orabase, and agrees with studies, which mentioned that mastic agent without substantial side effects in humans and animals [26, 27].

The induced ulcers on animals (by two different methods) were clinically indistinguishable from the spontaneous ulcers of patients, except that the induced lesions were generally smaller and healed more quickly. This study agreed with the previous study [28]. Topical application of mastic orabase showed a significant dose-dependent reduction of the induced ulcer size on animals, which healed between 2-3 days after treatment compared to non-effect by placebo. Mastic orabase has the ability to heal and may protect the induced ulcers, the mechanism that explains this healing activity of mastic orabase can be explained by creating a protective layer on the ulcers and enhancing re-epithelialization and healing of ulcers. Histopathology of the cheek pouch elucidated that there was no inflammation, re-epithelialization, and healing evidence in mastic orabase treated group compared to placebo group, this can be explained by the anti-inflammatory activity of mastic orabase, which help re-epithelialization, and healing of induced ulcer.

Clinical effects of mastic orabase on the inflammation and ulceration in patients suffering from RAU, showed a significant reduction of inflammation, decline ulcer size, and healing of ulcers within 2-3 days of treatment compared to baseline and placebo. The efficacy indices of the ulcer size improvement were higher significantly in mastic orabase group than placebo group. Healing of ulcer was significantly enhanced by the topical application of mastic orabase, so it is considered as an active healing agent.

There is increasing evidence that neuropeptides derived from sensory nerves are important mediators of inflammation in various tissues including the skin. Substance P (SP) has been demonstrated to have a broad range of pro-inflammatory effects in vitro and in vivo by the activation of the NK1R on various immune and non-immune cell types [29,30]. It is a neuropeptide, acting as a neurotransmitter & as a neuromodulator. SP amplifies or excites most cellular processes [32,33]. It is a potent vasodilator, and induced vasodilatation is dependent on nitric oxide release [34]. Substance P released as a response to certain types of infection or injury [35], and initiates expression of almost all known immunological chemical messengers (cytokines) [36-38], most of the cytokines, can induce SP and the NK1 receptor [39,40], which is particularly excitatory to cell growth and multiplication [8]. Treatment by topical mastic orabase in this study showed a highly significant reduction of inflammatory mediator substance P compared to baseline and no effect in placebo group, this confirm the anti-inflammatory activity of mastic orabase.

Release of substance P is induced by stressful stimuli, and the magnitude of its release is proportional to the intensity and frequency of stimulation [6], and it was shown that substance P could promote wound healing of non-healing ulcers in humans [7], and its induced cytokines promote multiplication of cells required for repair or replacement, growth of new blood vessels [41].Ulcer healing in mastic orabase group was faster and complete than that of placebo group, which may explain by the effect on inflammatory mediator substance p.

From Preclinical data, substance P is an important element in pain perception; the sensory function of substance P is thought to be related to the transmission of pain information into the central nervous system, which coexists with the excitatory neurotransmitter glutamate in primary

afferents that respond to painful stimulation [42]. However, if substance P/neurokinin antagonist should have therapeutically useful analgesic activity, substance P release is a primary event, the resultant analgesia correlates to the occupancy of the neurokinin receptor by antagonist. In this study, the pain was relieved significantly from the first topical application of mastic orabase, while placebo no effect on pain, the peak intensity of pain reduction was confirmed by mastic orabase. This may be related to the topical protective coverage of ulcer, and the effects on substance p.

Cytokines are important factors that may induce and determine the type of the immune response in the human body [43], Strong anti-inflammatory effect is contributed to another cytokine called transforming growth factor (TGF)-beta, secreted mainly by the T-regulator lymphocytes [44,45]. It was found that aphthous ulcer develops in response to the enhanced immunologic reaction against particular regions of the oral mucosa, this reaction occurs as a result of initiated cascade of cytokines that activate certain immune processes [2, 45, 46]. Patients with RAU, the immune system's function becomes disrupted in response to some kind of trigger factor, which may include viral and bacterial antigens or stress, and auto immunization [47, 48]. The secretion of anti-inflammatory cytokines TGF-β was significantly decreased in RAS patients compared to the healthy controls [49-51]. This study revealed that mean salivary TGF-β level was significantly decreased in RAU patients at baseline in both groups, which agrees with the above study, then a significant elevation of TGF-β level was seen after topical treatment by mastic orabase in RAU patients, compared to the baseline and no effect on placebo group.

Mastic can affect the function of activated macrophages, inhibited the production of pro-inflammatory substances such as nitric oxide (NO) and prostaglandin (PGE2) by lipopolysaccharide (LPS)-activated mouse macrophage-like cells. Western blot and (RT-PCR) analyses showed that mastic inhibited the expression of inducible NO synthase (iNOS) and COX-2 at both the mRNA and protein level [52-54].

The anti-inflammatory activity of mastic orabase explains its effects on inflammation, and ulcer healing. These activities explain the mechanism of action of mastic orabase in the treatment of aphthous ulceration. Other mechanism of mastic orabase action that may explain its ability to enhance ulcer healing is an immunity enhancer.

Further studies should evaluate the pharmacokinetic effects of mastic orabase and the recurrence of RAU.

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الخلاصة

خلفية: القرحة القلاعية المتكررة هي مرض التهابي مزمن في الغشاء المخاطي للفم. المادة P لديها نشاط في الاستجابة الالتهابية. تحويل عامل النمو بيتا (TGF-β) هو وجهري المناعي ينظم الاستجابة المناعية وله خصائص مضادة للالتهابات، والآثار الموالية للالتهابات. بطم عدسي (المصطكي) من عائلة بطمية لديه أنشطة دوائية مثل المضادة للالتهابات، ومضادات الأكسدة، ويستخدم في علاج وإصلاح الجروح . الهدف من هذه الدراسة للعثور على سلامة وفعالية المستحضر الموضعي الدوائي الجديد المصطكي؛ تجريبيا وسريريا.

طرق العمل: درس هذا البحث قسمين: أولا، تجريبيا لتقييم فعالية المستحضر الموضعي المصطكي على تهيج الجلد للارنب، فعالية المصطكي على القرح المستحدثة، مع دراسة التغيرات في أنسجة الأرانب، وسلامة المستحضر: المؤشر العلاجي وعامل الأمان. ثانيا؛ الفعالية السريرية من المستحضر الموضعي المصطكي على الشفاء من القرحة القلاعية المتكررة عن طريق تقييم للحد من حجم القرحة، وقلة الالتهاب، وتقليل وقت التآم القرحة، و تقليل الألم، قياس مستويات المادة P وعامل النمو التحويلي بيتا في لعاب المرضى الذين يعانون القرحة القلاعية المتكررة ، ورصد أي آثار سلبية أو التفاعلات الدوائية الضارة.

النتائج: أظهرت الدراسة التجريبية لاستخدام العلاج الموضعي المصطكي، انخفاض كبير في التهاب و حجم القرحة، وتضميد الجراح بوقت قصير: وأكد سلامة مستحضر المصطكي بعدم تهيج الجلد، لا سمية، ومستوى واسع للمؤشر العلاجي. أظهرت نتائج الدراسة السريرية الحد من الالتهاب والتقرح، وتضميد الجراح في وقت قصير،الغي الالم من اول جرعة موضعية، والتأكد من وصول النشاط المضادة للالتهابات من استعمال المستحضر الموضعي المصطكي بتخفيض مستوى المادة P وارتفاع مستوى TGF-β في اللعاب.

الإستنتاج: أظهر مستحضر المصطكي الموضعي فعالية تعتمد الجرعة في علاج التقرح القلاعي المتكرر، قصر وقت الشفاء. قد يكون ذلك متعلقا بتأثير المصطكي على العوامل الوسيطة التي تعمل قبل الالتهاب والمضادة للالتهابات. المادة P و TGFبيتا.