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# Comparison of clinical indices and therapeutic effect of a mucoadhesive system containing Melissa 1% and triamcinolone 0.1% on lichenoid reactions

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## ABSTRACT

**Background:** Lichenoid reaction (LR) is a relatively common mucocutaneous disease with an unknown etiology. Since the cause of the LRs is unknown, many drugs have been studied to palliate the symptoms. Previous studies reported that corticosteroids are often effective in the management of several oral inflammatory diseases. The aim of the present study was to compare the effect of Melissa gel and triamcinolone 0.1% paste on clinical indices of oral LRs.

**Materials and Methods:** In this randomized clinical trial, sixty patients with erosive oral LRs were randomly divided into two groups, and each group was treated with Melissa gel or triamcinolone acetonide 0.1% paste, three times a day, for 4 weeks. The recovery rate and severity of pain and burning sensation were assessed after 2 and 4 weeks. Finally, the obtained data were analyzed using SPSS software (version 20, IBM Corp., Armonk, NY, USA) and repeated measures ANCOVA, Mann–Whitney test, Chi-square test, paired *t*-test, and survival analysis.($\alpha$ = 0.05).

**Results:** The Visual Analog Scale scores for recovery rate, pain, and burning mouth sensation and objective scoring for oral lichen planus were significantly improved at 2 and 4 weeks in both the groups. However, the pain intensity decreased significantly in the Melissa group, as compared to the triamcinolone 1% group.

**Conclusion:** In general, we showed that Melissa gel has a better effect than triamcinolone on pain intensity. Although Melissa gel is effective in reducing lesion size, triamcinolone significantly showed better results.

**Key Words:** Lichenoid eruptions, *Melissa*, triamcinolone acetonide

## INTRODUCTION

Lichenoid reactions (LRs) are a set of disorders with similar clinical presentations but various causes. These reactions are divided into such subtypes as lichen planus, drug-induced lichen planus, contact LRs, and LRs due to graft-versus-host disease. Oral lichen planus (OLP) is a rather common and chronic oral disease that mostly affects the oral mucosa.[1]

LRs are common oral mucosal lesions, which the most significant factor to distinguish from OLP is

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their atypical location and unilaterality. Although the primary cause of this disease is unknown, recent studies have shown different immune complexes along with responding cells for inflammatory structures and chronic lesions.[2]

Most of the patients with lichen planus are middle-aged women.[3] The prevalence of lichen planus has been reported to be 1%–1.5%, and in 80%–90% of cases, it affects buccal mucosa.[4,5]

OLP has six different subtypes but is mainly seen as reticular and erosive forms, the most common of which is reticular form.[6]

Oral LRs also can be induced by drugs such as thiazides, nonsteroidal anti-inflammatory drugs, and angiotensin-converting enzyme inhibitors; systemic diseases like diabetes; and allergic reactions to metals such as amalgam and food supplies.[7-9]

The discomfort and pain associated with these lesions can affect the normal function of the mouth, increase the risk of infection, and to some extent, reduce the patients' quality of life.[10]

The management of such lesions first requires the identification of the triggering factors.[11] The main treatment for LRs is the administration of systemic and local corticosteroids. Its local and potent type such as triamcinolone has increasingly been used for the treatment of LR.[12] Adverse effects of using corticosteroids include secondary candidiasis, adrenal suppression, increased blood pressure, and becoming prone to infections.[13,14]

Another treatment for lichen planus is medicinal plants such as *Melissa officinalis* which its extract is used in Melissa gel. Melissa gel, offered by Goldaru Pharmacy Co. in Iran, includes 1% gel-based balm mint (*M. officinalis*) dried extract, standardized by 0.23% tannic acid.[15] Melissa is used for local treatment of gingival inflammatory, microbial and painful complications, and oral lesions. It includes antimicrobial, antifungal, antivirus, anticancer, and anti-inflammatory properties and can reduce salivary and sweat secretion.[16-18]

As long as LRs are currently one of the common oral lesions and using prolonged corticosteroids as main treatment have shown various complications, this study was conducted to analyze the effect of Melissa gel comparing to triamcinolone paste among the patients with LRs.

## MATERIALS AND METHODS

In this randomized clinical trial, 60 patients (29 females and 31 males) aged between 20 and 60 years (59.8 ± 14.3) who referred to the department of oral and maxillofacial medicine with at least one clinically and histopathologically proven erosive oral LR in buccal mucosa and having Thongprasom score[19] more than 1 were included. The exclusion criteria were as follows: patients with allergy to botanical products, the presence of any malignant or viral involvements in the mouth, history of receiving topical therapy for oral LRs in the last 2 weeks or systemic therapy in the last 4 weeks, histopathological sign of dysplasia, history of allergy to corticosteroids, life-threatening and systemic diseases such as increased blood pressure and diabetes, pregnancy, and lactation. Informed consent was obtained from the patients before the study initiation. This study was approved by the Isfahan University of Medical Sciences Ethics Committee and conducted according to the Declaration of Helsinki.

Patients were randomly divided into two groups either take Melissa or triamcinolone 0.1% according to a list made by block randomization. Group A was instructed to apply and spread a 1-cm layer of Melissa gel (Melissan 5gr gel, Goldaru Corporation, Isfahan, Iran), and Group B was instructed to apply and spread a 1-cm layer of triamcinolone acetonide 0.1% paste (Teriadent 0.1%, Raha Pharmaceutical Corporations, Isfahan, Iran) on the oral lesions, three times a day, for 4 weeks. The patients were asked to use the medication after eating and washing their mouth and not to eat, drink, or smoke for at least 30 min. The assessment was performed at weeks 0, 2, and 4 by a clinician who was blind to patients' allocated groups.

The lesion size was measured by a scaled tongue blade and the recovery rate was evaluated in each visit according to the Thongprasom criteria[19] [Table 1].

Patients ranked the severity of pain and burning sensation on a 10-cm Visual Analog Scale (VAS) from 0 (no pain) to 10 (extreme pain) at the beginning and each visit. The patients were asked to draw a vertical line on the VAS horizontal ruler and score their intensity of pain.

In each visit, patients were asked about any side effects such as ulcer, burning sensation or pain during eating and drinking, dry mouth, and numbness after

taking the prescribed drugs. Any use of products such as caffeine, tobacco, and alcohol was also recorded in the patients' questionnaires.

The obtained data were analyzed by SPSS software (version 20, IBM Corp., Armonk, NY, USA). Repeated measures ANCOVA test was used to compare the analyzed data between groups at different intervals and the Mann–Whitney test was administered to compare two groups. Chi-square test, paired *t*-test, and survival analysis were performed as well.

## RESULTS

Enrollment into the study began in March 2016 and ended in April 2017. Sixty patients, 29 females and 31 males with the age range of 20–60 years and a mean age of 59 years, referred to the Department of Oral and Maxillofacial Medicine, Isfahan University of Medical Sciences, were included in this study. There were thirty patients in each group. The demographic characteristics are listed in Table 2.

There were no significant differences between the two groups for baseline characteristics including age, sex, baseline lesion size, and pain intensity (VAS) ($P > 0.05$).

In the first visit (week 2), the mean and standard deviation of VAS among the Melissa group were 2.4 and 1.35 and 3.4 and 1.31 for the triamcinolone group. VAS index between the two groups showed significant differences in the 2$^{nd}$ and 4$^{th}$ weeks ($P = 0.018$, $P = 0.001$).

As demonstrated in Table 3, comparing VAS values at different visits revealed a significant difference for Melissa before treatment and in 2 and 4 weeks after treatment. In the triamcinolone group, the same results were reported based on the paired sample *t*-test.

To compare the clinical index of LR in the study groups, findings showed no significant difference between the groups in terms of the lesion extension before and 1 weeks after treatment, but there was a significant difference between the two groups after 4 weeks and triamcinolone was better in reducing lesion size ($P = 0.003$) [Table 4].

**Table 1: Thongprasom criteria**

| Score | Clinical signs |
|---|---|
| 0 | No lesion, normal mucosa |
| 1 | Mild white striae, no erythematous area |
| 2 | White striae with an atrophic area <1 cm$^2$ |
| 3 | white striae with atrophic area >1 cm$^2$ |
| 4 | white striae with an erosive area <1 cm$^2$ |
| 5 | white striae with erosive area >1 cm$^2$ |

**Table 2: Demographic characteristics of the studied patients**

| Demographic characteristics | Melissan | Triamcinolone |
|---|---|---|
| Age (mean±SD), years | 60.36±15.33 | 59.36±13.52 |
| Male (%) | 13 (43.3) | 18 (60) |
| Female (%) | 17 (56.7) | 12 (40) |

SD: Standard deviation

**Table 3: Comparison of the pain at baseline (Visual Analog Scale) between Melissa and triamcinolone groups**

| Treatments | Melissan | | Triamcinolone | | Total (*P*) |
|---|---|---|---|---|---|
| | Mean±SD | *P* | Mean±SD | *P* | |
| Baseline | 7.0±2.51 | - | 6.9±2.36 | - | 0.777 |
| 2 weeks | 2.4±1.35 | 0.000 | 3.4±1.61 | 0.000 | 0.018 |
| 4 weeks | 0.6±0.67 | 0.008 | 1.3±0.88 | 0.010 | 0.010 |

SD: Standard deviation

**Table 4: Comparison of the clinical index between the Melissa and triamcinolone groups**

| Treatments | Mean±SD | | *P* |
|---|---|---|---|
| | Melissan | Triamcinolone | |
| Baseline | 3.86±1.00 | 3.80±0.96 | 0.745 |
| 2 weeks | 2.56±1.07 | 2.26±0.94 | 0.281 |
| 4 weeks | 2.0±1.14 | 1.16±0.79 | 0.003 |

SD: Standard deviation

## DISCUSSION

LRs are common oral lesions caused by numerous factors.[20,21] Therefore, it seems necessary to make an effort to treat and eliminate the factors associated with the disease to prevent the following complications such as possible malignant changes. Corticosteroids like triamcinolone are effective to treat LRs, but medicinal plants have also shown to be effective with minimum adverse effects.[10,22-24]

This study was carried out to evaluate the effect of Melissa gel compared to triamcinolone paste on patients with LRs, and it demonstrated that Melissa gel was more effective than triamcinolone in terms of reducing pain in 4 weeks. Birdane *et al*. also investigated the effect of Melissa in rodents, and similarly, it indicated antinociceptive effects.[25] Evaluating the effect of Melissa in recurrent herpes labialis, Ahadian *et al*. concluded that Melissa gel

is more able to decrease the pain than acyclovir.[15] Melissa contains flavonoids, polyphenolic ingredients, and essences such as limonene, citral, and citronella. Since flavonoids and limonene have shown analgesic and anti-inflammatory effects, it is appropriate to use Melissa gel to decrease the pain.[26,27]

Although Melissa gel was more effective than triamcinolone in reducing pain in 4 weeks, the short-term effect of triamcinolone was more than Melissa gel between 2 and 4 weeks. Similar to our study, Hasanein and Riahi *et al*. in an animal model of diabetic hyperalgesia demonstrated that long-term oral administration of *M. officinalis* has antinociceptive effects on painful diabetic neuropathy. The possible cause of these results may be rosmarinic acid which is the major phenol constituent of *M. officinalis* and possesses a strong antinociceptive and antioxidant effect.[28,29]

The results of our study also showed that Melissa gel decreased the size of the lesion at each visit compared to baseline. The results of Koytchev *et al*. were similar to ours and established that *M. officinalis* can significantly reduce the intensity of symptoms of herpes labialis such as the number and size of the affected area.[30] These results may be due to the inflammatory effect in phenolic compounds such as flavonoids and rosmarinic acid and essential oil in *M. officinalis*.[31]

The results also indicated that although there was no significant difference between the two groups before and 2 weeks after treatment, triamcinolone was significantly more effective in reducing lesion size in 4 weeks. In contrast to our results, an *in vivo* study in rats demonstrated that *M. officinalis* causes a significant reduction and inhibition of paw edema induced by carrageenan and experimental trauma in rats.[24]

Medicinal plants have been used successfully to treat oral diseases. For instance, Das *et al*. reported the positive effects of licorice biofilm in the treatment of radiotherapy-induced mucositis.[32] Furthermore, Sookto *et al*. showed that *M. officinalis* had anti-Candida properties and prevented the connection of this fungus.[33]

Moreover, Martin *et al*. investigated the effect of oral patches containing licorice extract in the treatment of aphthous ulcers and reported positive effects in the size of the lesion and patient's pain.[34] Another nonpharmacologic and nonsteroidal therapy used for the treatment of lichenoid diseases was the use of topical retinoic acid in comparison with topical fluocinolone acetonide, and the topical fluocinolone acetonide was more effective to reduce the severity of lichen planus.[12]

The limitations of this study included a lack of comprehensive control over the use of drugs and small sample size. Future studies are recommended to recruit a larger study sample, compare different herbal compounds, use herbal complexes, and make use of topical corticosteroids and herbal medicines alternatively to obtain more accurate results.

## CONCLUSION

Melissa gel performed better than triamcinolone in decreasing pain intensity, however, triamcinolone was more effective in reducing lesion size.

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### Conflicts of interest

The authors of this manuscript declare that they have no conflicts of interest, real or perceived, financial or non-financial in this article.

## REFERENCES

1. Neville B, Douglas D, Allen C, Bouquot JE. Oral and Maxillofacial Pathology. 3rd ed. Philadelphia: Saunders Co.; 2009. p. 470-1.
2. Regezi JA, Sciubba JJ, Jordan CK. Oral Pathology Clinical Pathologic Correlations. 5th ed. Philadelphia: Saunders; 2008. p. 127-9.
3. Edwards PC, Kelsch R. Oral lichen planus: Clinical presentation and management. J Can Dent Assoc 2002;68:494-9.
4. Gorouhi F, Davari P, Fazel N. Cutaneous and mucosal lichen planus: A comprehensive review of clinical subtypes, risk factors, diagnosis, and prognosis. ScientificWorldJournal 2014;2014:742826.
5. Mostafa B, Ahmed E. Prevalence of oral lichen planus among a sample of the Egyptian population. J Clin Exp Dent 2015;7:e7-12.
6. Casparis S, Borm JM, Tektas S, Kamarachev J, Locher MC, Damerau G, *et al.* Oral lichen planus (OLP), oral lichenoid lesions (OLL), oral dysplasia, and oral cancer: Retrospective analysis of clinicopathological data from 2002-2011. Oral Maxillofac Surg 2015;19:149-56.
7. Fortuna G, Aria M, Schiavo JH. Drug-induced oral lichenoid reactions: A real clinical entity? A systematic review. Eur J Clin Pharmacol 2017;73:1523-37.
8. Serrano-Sanchez P, Bagan J, Jimenez Y, Pérez MG. Drug-induced oral lichenoid reactions. A literature review. J Clin Exp Dent

2010;2:71-5.
9. Janardhanan S, Ananthalakshmi R, Sathiya Jeeva S. Oral lichenoid reaction – An overview. J Med Dent Sci 2016;15:56-8.
10. Carrozzo M, Gandolfo S. The management of oral lichen planus. Oral Dis 1999;5:196-205.
11. Dunsche A, Kästel I, Terheyden H, Springer IN, Christophers E, Brasch J. Oral lichenoid reactions associated with amalgam: Improvement after amalgam removal. Br J Dermatol 2003;148:70-6.
12. Ismail SB, Kumar SK, Zain RB. Oral lichen planus and lichenoid reactions: Etiopathogenesis, diagnosis, management and malignant transformation. J Oral Sci 2007;49:89-106.
13. Beigom Taheri J, Anbari F, Maleki Z, Boostani S, Zarghi A, Pouralibaba F. Efficacy of *Elaeagnus angustifolia* topical gel in the treatment of symptomatic oral lichen planus. J Dent Res Dent Clin Dent Prospects 2010;4:29-32.
14. Boorghani M, Gholizadeh N, Taghavi Zenouz A, Vatankhah M, Mehdipour M. Oral lichen planus: Clinical features, etiology, treatment and management; a review of literature. J Dent Res Dent Clin Dent Prospects 2010;4:3-9.
15. Ahadian H, Hasan Akhavan Karbassi M, Ghaneh S, Hakimian R. Therapeutic effect of melissa gel and 5% acyclovir cream in recurrent herpes labialis: A double-blind randomized clinical trial. Jundishapur J Nat Pharm Prod 2015;10:e26160.
16. Chizzola R, Lohwasser U, Franz C. Biodiversity within *Melissa officinalis*: Variability of bioactive compounds in a cultivated collection. Molecules 2018;23:294.
17. Aslani A, Zolfaghari B, Fereidani Y. Design, formulation, and evaluation of a herbal gel contains melissa, sumac, licorice, rosemary, and geranium for treatment of recurrent labial herpes infections. Dent Res J (Isfahan) 2018;15:191-200.
18. Miraj S, Rafieian-Kopaei M, Kiani S. *Melissa officinalis* L: A review study with an antioxidant prospective. J Evid Based Complementary Altern Med 2017;22:385-94.
19. Buajeeb W, Kraivaphan P, Pobrurksa C. Efficacy of topical retinoic acid compared with topical fluocinolone acetonide in the treatment of oral lichen planus. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1997;83:21-5.
20. Schlosser BJ. Lichen planus and lichenoid reactions of the oral mucosa. Dermatol Ther 2010;23:251-67.
21. Kamath VV, Setlur K, Yerlagudda K. Oral lichenoid lesions - a review and update. Indian J Dermatol 2015;60:102.
22. Ghahremanlo A, Boroumand N, Ghazvini K, Hashemy SI. Herbal medicine in oral lichen planus. Phytother Res 2019;33:288-93.
23. Lee YC, Shin SY, Kim SW, Eun YG. Intralesional injection versus mouth rinse of triamcinolone acetonide in oral lichen planus: A randomized controlled study. Otolaryngol Head Neck Surg 2013;148:443-9.
24. Bounihi A, Hajjaj G, Alnamer R, Cherrah Y, Zellou A. *In vivo* potential anti-inflammatory activity of *Melissa officinalis* L. essential oil. Adv Pharmacol Sci 2013;2013:101759.
25. Birdane Y, Buyukokuroglu M, Birdane F, Cemek M, Yavuz H. Anti-inflammatory and antinociceptive effects of *Melissa officinalis* L. in rodents. Rev Med Vet (Bogota) 2007;158:75-81.
26. Bahmani M, Shirzad H, Majlesi M, Shahinfard N, Rafieian-Kopaei M. A review study on analgesic applications of Iranian medicinal plants. Asian Pac J Trop Med 2014;7 Suppl 1:S43-53.
27. Aleebrahim-Dehkordy E, Tamadon MR, Nasri H, Baradaran A, Nasri P, Beigrezaei S. Review of possible mechanisms of analgesic effect of herbs and herbal active ingredient. J Young Pharm 2017;9:303-6.
28. Hasanein P, Riahi H. Antinociceptive and antihyperglycemic effects of *Melissa officinalis* essential oil in an experimental model of diabetes. Med Princ Pract 2015;24:47-52.
29. Bisset NG, Wichtl M. Herbal Drugs and Phytopharmaceuticals. 3rd ed. Stuttgart and Boca Raton: Medpharm GmbH Scientific Publishers and CRC Press; 1994. p. 91-5.
30. Koytchev R, Alken RG, Dundarov S. Balm mint extract (Lo-701) for topical treatment of recurring herpes labialis. Phytomedicine 1999;6:225-30.
31. Shakeri A, Sahebkar A, Javadi B. *Melissa officinalis* L. – A review of its traditional uses, phytochemistry and pharmacology. J Ethnopharmacol 2016;188:204-28.
32. Das D, Agarwal SK, Chandola HM. Protective effect of Yashtimadhu (Glycyrrhiza glabra) against side effects of radiation/chemotherapy in head and neck malignancies. Ayu 2011;32:196-9.
33. Sookto T, Srithavaj T, Thaweboon S, Thaweboon B, Shrestha B. *In vitro* effects of Salvia officinalis L. essential oil on Candida albicans. Asian Pac J Trop Biomed 2013;3:376-80.
34. Martin MD, Sherman J, van der Ven P, Burgess J. A controlled trial of a dissolving oral patch concerning glycyrrhiza (licorice) herbal extract for the treatment of aphthous ulcers. Gen Dent 2008;56:206-224.