

# Comparison of *Glycyrrhiza glabra* Inorabase With Triamcinolone Acetonide Orabase in the Treatment of Oral Lichen Planus

Shamsolmoulouk Najafi,<sup>1,2</sup> Jalil Momen Beytolahi,<sup>2</sup> Nasibeh Aleboye,<sup>3</sup> Narges Gholizadeh,<sup>1,2,\*</sup> and Tayebe Sadegi<sup>4</sup>

<sup>1</sup>Dental Research Center and Oral Medicine, Faculty of Dentistry, Tehran University of Medical Sciences, Tehran, IR Iran

<sup>2</sup>Department of Oromaxillofacial Pain Disease, Tehran University of Medical Sciences, Tehran, IR Iran

<sup>3</sup>Dental Faculty, Tehran University of Medical Sciences, Tehran, IR Iran

<sup>4</sup>Dental Faculty, International Campus, Tehran University of Medical Sciences, Tehran, IR Iran

\*Corresponding author: Narges Gholizadeh, Dental Research Center and Oral Medicine, Faculty of Dentistry, Tehran University of Medical Sciences, Tehran, IR Iran. Tel: +98-2142794000, Fax: +98-2181633501, E-mail: n.gholizadeh88@gmail.com

Received 2014 December 20; Revised 2015 February 17; Accepted 2015 March 08.

## Abstract

**Background:** Lichen planus is a chronic inflammatory mucocutaneous disease that is most commonly found in middle-aged women. A wide spectrum of topical and systemic therapies have been applied for treatment of this condition.

**Objectives:** The aim of this study was to compare the efficacy and safety of 1% *Glycyrrhiza glabra* in orabase with 0.1% Triamcinolone Acetonide paste in treating oral lichen planus (OLP).

**Patients and Methods:** In this study, 22 patients were randomly assigned to one of two equal groups. They received either *Glycyrrhiza glabra* or Triamcinolone Acetonide four times daily for a total of one month and were followed-up for three months. The patients were assessed for painful symptoms, measured by the visual analogue scale (VAS), and lesion size via Thongaprasom. The analysis and comparison of pain scores and the size of the lesions' clinical and symptomatic response rates between the two groups were performed using the Mann-Whitney U-test and SPSS 13.0 computer software.

**Results:** Ten patients in the *Glycyrrhiza glabra* group and 12 patients in the triamcinolone acetonid group completed the four-month trial course. Both *Glycyrrhiza glabra* and Triamcinolone Acetonid reduced burning symptoms. Clinical scores in both groups also significantly improved over the one-month treatment period. The difference between the two groups was not statistically significant ( $P = 0.442$ ).

**Conclusions:** This study showed that topical *Glycyrrhiza glabra* appeared to be a promising alternative in the treatment of OLP. Further studies should be conducted to assess the long-term effects of *Glycyrrhiza glabra*.

**Keywords:** Oral Lichen Planus (OLP), Triamcinolone Acetonide, *Glycyrrhiza glabra*

## 1. Background

Lichen planus is a chronic inflammatory immunological disease (1) that typically can involve the skin, mucous membranes, and nails (2). Lichen planus has an unknown etiology, but it seems that it is an immunological process with a delayed hypersensitivity reaction, in microscopic views (3). Due to having symptoms of irritation and pain, especially in erosive and atrophic form, and the risk of malignancy, the treatment of these lesions is of the utmost importance (2).

The incidence of squamous cell carcinoma (SCC) in five years is variable, from 0.4% to 2% between the cases (3). Currently, no treatment is known for OLP, but controlling the symptoms is helpful in treating the patients. Corticosteroids are very valuable and successful in controlling the

symptoms. Considering that even the topical type of corticosteroids such as triamcinolone have side effects such as atrophy, fragility, telangiectasia, weakening the immune system, and increasing the susceptibility to various infections, such as candidiasis, and the common occurrence of recurrent lesions after discontinuing the treatment (4), we decided to use an herbal medicine, such as *Glycyrrhiza glabra*, with fewer side effects and more efficacy on OLP. We compare it with the more common treatment, Triamcinolone.

Licorice plant, which is made from a dried root crop (*Glycyrrhiza glabra*) from the pea family (*Leguminosae*) contains minimally 4% glycerizine. It has anti-inflammatory, anti-allergic, and anti-radical activity and a protective effect against the peroxidation of liposomal membranes (5, 6).

In addition to its anti-inflammatory mechanisms, glycerizine has anti-radical activity and a protective effect against the peroxidation of liposomal membranes (7). Licorice plants have anti-inflammatory effects similar to steroids, including cortisone. It also plays an anti-inflammatory role by inhibiting the activity of A2 phospholipase, which is an important enzyme in beginning the inflammatory process (8).

## 2. Objectives

The aim of this study was to compare the efficacy and safety of 1% *Glycyrrhiza glabra* in orabase with 0.1% Triamcinolone Acetonide paste in treating oral lichen planus (OLP).

## 3. Patients and Methods

This study was a randomized control, double-blind clinical trial. Twenty-two patients with keratotic and atrophic/erosive OLP were selected from those referred to the department of oral medicine, faculty of dentistry, Tehran University of Medical Sciences. Inclusion criteria consisted of clinical and histopathological diagnosis of OLP patients receiving immunosuppressive, immunomodulatory treatments, or local drugs were eliminated. Participants demonstrating histological signs of dysplasia; lichenoid drug reactions; drug consumption in the past month; lesions such as azathioprine, cyclosporine, PUVA, UVA, UVB; pregnant, or breast-feeding women; uncontrolled diabetes; hypertension; kidney failure and liver cancer; recurring infections; an oral history of susceptibility to viral infections; a history of allergies to herbal medicines; immunodeficiency; or HCV infection was excluded from the study sample.

In this study, 22 patients were randomly divided into two groups (intervention and control), according to block randomization ([www.randomization.com](http://www.randomization.com)). Twelve patients in the control group received 1% triamcinolone acetonide or Adcortyl, and 10 cases were in the intervention group and received 1% *Glycyrrhiza glabra*. According to our design conditions, and one-way ANOVA tests and taking  $\alpha = 0.01$  and  $\beta = 0.20$  (5), the minimum sample size required in each group was 10 persons.

### 3.1. Directions

The patients were instructed to apply the medication to their lesions four times daily for four weeks (one month) (9). They were advised not to eat or drink for at least an hour before or after the drug administration.

All patients were assessed at the end of the second week, after the first month (at the end of the drug's administration), and at the second and fourth month (follow-up).

This study presents the results of an approved investigation project conducted at Tehran University of Medical Sciences, ID No. 4541 2/8/1387. All patients provided their written consent and completed a questionnaire that included data about their age; gender; medical history; symptoms; type, size, and location of lesions; pain; and burning.

The lesions size (sign) were scored from 0 (no lesion) to 5 (large lesion) (Table 1).

**Table 1.** Sign and Stage by Thongprasom

Stage	Sign
Score 0	No lesion, normal mucosa
Score 1	Mild white striae, no erythematous area
Score 2	White striae with atrophic area less than 1 cm <sup>2</sup>
Score 3	White striae with atrophic area more than 1 cm <sup>2</sup>
Score 4	White striae with erosive area less than 1 cm <sup>2</sup>
Score 5	White striae with erosive area more than 1 cm <sup>2</sup>

Table 1 shows the scores, which ranged from 0 to 5 according to the criteria set by Thongprasom et al. (9). A scaled tongue Blade (a wooden tongue blade divided into equal 5-cm sections) was used to assess the size of the lesions, and the visual analogue scale (VAS) was used for the assessment of pain (a symptom). Pain scores or symptom stages were used to rank the severity of the subjects' pain and discomfort, which ranged from 0 (showing no pain) to 100 mm (demonstrating extreme pain) (Table 2).

**Table 2.** Symptoms Stage or Pain Score

Stage	Symptoms
0	Asymptomatic pain (no pain)
25	Low level of symptoms, does not interfere with usual daily activity (mild)
50	Symptoms interfere with regular daily activity (moderate)
75	Sore and painful; greatly interferes with regular daily activity (severe)
100	Impossible to live with such severe symptoms (very severe)

In this study, both the patients and the examiner were blind. Patients were divided into four groups based on their recovery:

1- No improvement, 2- Partial improvement, 3- salient improvement, 4- Full improvement. The criteria for partial

improvement was a 50% decrease in lesion size, in comparison with the initial extent. For salient improvement, it was more than a 50% decrease, but not completely. For full recovery, all the clinical symptoms were recovered.

Initial measurements were recorded on the patient's information form. On the third visit (one month after the drug's administration), after completing the questionnaire related to the visit, the patient was recommended not to use any medication for OLP.

The final follow-up examination was done by examining the patient and completing a final questionnaire at the end of the fourth month of the study.

Analyses and comparisons of pain scores, the size of the lesions, and the clinical and symptomatic response rates between the two groups were performed using the Mann-Whitney U-test and SPSS 13.0 computer software.

### 3.2. Manner of Blinding

The drugs were poured into same-color and same-shape glasses, and their differences were distinguished based on the code and a list, provided to a third person, and subject to decoding. The examiner and analyzer did not know anything about the drug.

### 3.3. Preparing the Base for Orabase

The first step in making the base for the mucosa adhesive paste was preparing the plastibase. Plastibase gel was made by quick freezing warm 5% polyethylene in liquid paraffin, as described below:

The polyethylene was added to a beaker, and then 80°C liquid paraffin was added, as much as twice the weight of the polyethylene.

The above mixture was stirred at 80°C until it became a viscous gel. Then, the leftover liquid paraffin was added to the mixture and stirring continued until the liquid paraffin was finished.

After one hour of stirring and mixing, the mixture was added to a special bowl, which was made of tin foil, and cooled with ice and salt, in order to cause the mixture to cool quickly. The final product was a Plastibase gel.

The formula for the base for mucosa adhesive:

The known formula consists of 16.6% gelatin, 16.6% pectin, 16.6% cellulose sodium carboxy methyl, and plastibase up to 100% (10).

At first, the gelatin powder, pectin powder, and cellulose sodium carboxy methyl were strained through a 200-mesh strainer.

The best way to make mucosa adhesive paste is to slowly add cellulose sodium carboxy methyl and then pectin powder and gelatin powder to the base of plastibase. The mixture must be stirred continuously to reach a

homogenbase. In the end, the extract of licorice was added to the mixture with a proportion of 1%.

## 4. Results

Of all 22 patients being studied, there were five women (50%) and five men (50%) in the licorice group, and they had a mean age of  $43/4 \pm 17/19$ . The triamcinolone group consisted of seven women (3/58) and five men (7/41), with a mean age of  $50/67 \pm 12/24$ . No statistically significant differences were observed between the groups regarding the distribution of males and females ( $P = 0.623$ ). No statistically significant differences were observed between the groups regarding the difference in sample size ( $P = 0.786$ ). Both drugs reduced the extent of the lesions, but between the two groups, the difference was not statistically significant ( $P = 0.872$ ).

In addition, burning sensations in all patients (five in the control group and four in the experimental group) were fully mitigated after using both drugs.

In terms of recovery improvement, both groups had recovered after the one-month treatment period, but the difference was not statistically significant ( $P = 0.442$ ).

Regarding the 95% confidence interval calculation for the mean difference between lichen planus lesion surfaces, it can be said that the mean of the decreases in lichen planus' surfaces after consumption of triamcinolon acetone was 3.909, and in consumers of *Glycyrrhiza glabra*, it was 4.102 ( $P = 0.872$ ) (Table 3).

Table 3. Two Drug Groups

Drug Groups	Mean Difference (95%)	P Value
triamcinolone acetonide	-3.91 (-5.48 - 2.34)	0.74
Glycyrrhizaglabra 1%	-4.10 (-5.83 - 2.38)	0.82

No adverse effects of irritation, infection, or altered sense of taste were found in any of the groups.

Based on the results of the variance analysis, the type of drug, gender, drug interaction with gender, and age had no effect on the recovery rate of LP in the studied population ( $P = 0.865$ ,  $P = 0.623$ ,  $P = 0.082$ , and  $P = 0.129$ , respectively).

## 5. Discussion

In this study, 1% licorice extract was compared with the common steroid triamcinolone acetone for the treatment of oral lichen planus.

There was no restriction on the type of lichen planus (keratotic, erosive, or atrophic) examined in our study.

The research conducted here is the first double-blind, randomized clinical trial to investigate the efficacy of licorice in comparison with triamcinolone acetonide (the conventional therapy) in the treatment of oral lichen planus.

In 2008, Choonhakarn et al. (11) evaluated the effect of aloe vera gel compared with a placebo for the treatment of oral lichen planus in a double-blind clinical trial study.

Based on that study's results, we know that the effect of aloe vera gel on the treatment of oral lichen planus is significantly more effective than a placebo.

However, we used the commonly used drug instead of a placebo in our control group, resulting in a higher recovery rate among that group. Further, Choonhakarn et al.'s study (11) contained more women with oral lichen planus than men. In our study, the number of women in the control group was greater than the number of men.

According to Choonhakarn et al.'s findings, most of the lesions in the subjects were erosive and ulcerative, and the most common site of the lesions was the lower lip. Nine patients (33%) in their experimental group and one patient (4%) in their control group showed recovery in burning sensation by the end of treatment. On the contrary, in the present study, keratotic lesions were more prevalent, and they were more often observed on buccal mucosa. All the patients with burning sensation (five in the control group and four in the experimental group) recovered after the treatment.

In some studies, no side effects were reported in treatment with *Glycyrrhiza glabra* (12, 13), and no side effects were observed in our study. It should be said that use of triamcinolone acetonid for an extended period of time will leads to side effects such as atrophy, fragility, telangiectasias, weakening of the immune system, and increased susceptibility to various infections, including candida. In this study, both *Glycyrrhiza glabra* and triamcinolone acetonid had similar effects in reducing the symptoms of burning and improvement in the extent of disease and recovery within one month of treatment.

Although some patients expressed that the use of the drug in orabase form was difficult, it had a more positive effect because of its insolubility.

Because of the limited number of patients, the classification of OLP according to subtypes was not possible, and this is a limitation of this study. We hope that this may be considered in our next investigations.

### 5.1. Conclusions

This study showed that the topical application of *Glycyrrhiza glabra* had a significant effect on oral lichen planus and, since people are often attracted to using herbal

medicine, it can be a suitable substitution for the treatment of lichen planus.

### Acknowledgments

The authors of this article acknowledge all of the participants and organizations in this study, particularly Tehran University of Medical Sciences.

### Footnote

**Authors' Contribution:** Dr. Shamsolmoulouk Najafi, conductor; Dr. Jalil Momen Beytollahi, data analysis; Dr. Narges Gholizadeh, corresponding author.

### References

- Gholizadeh N, Mehdipour M, Najafi S, Bahramiyan A, Garjani S, Khoeini Poorfar H. Evaluation of the Serum Zinc Level in Erosive and Non-Erosive Oral Lichen Planus. *J Dent Shiraz Univ Med Sci*. 2014;**15**(2):52-6.
- Hall R, Wartman D, Jellinek N, Robinson-Bostom L, Telang G. Lichen planus of the nail matrix with predominant plasma cell infiltrate. *J Cutan Pathol*. 2008;**35** Suppl 1:14-6. doi: [10.1111/j.1600-0560.2007.00965.x](https://doi.org/10.1111/j.1600-0560.2007.00965.x). [PubMed: [18544055](https://pubmed.ncbi.nlm.nih.gov/18544055/)].
- Greenberg MS, Glick M, Ship JA. Burket's oral medicine. 11 ed. B.C Decker Inc; 2008.
- Passeron T, Lacour JP, Fontas E, Ortonne JP. Treatment of oral erosive lichen planus with 1% pimecrolimus cream: a double-blind, randomized, prospective trial with measurement of pimecrolimus levels in the blood. *Arch Dermatol*. 2007;**143**(4):472-6. doi: [10.1001/archderm.143.4.472](https://doi.org/10.1001/archderm.143.4.472). [PubMed: [17438179](https://pubmed.ncbi.nlm.nih.gov/17438179/)].
- Boms S, Gambichler T, Freitag M, Altmeyer P, Kreuter A. Pimecrolimus 1% cream for anogenital lichen sclerosis in childhood. *BMC Dermatol*. 2004;**4**(1):14. doi: [10.1186/1471-5945-4-14](https://doi.org/10.1186/1471-5945-4-14). [PubMed: [15485581](https://pubmed.ncbi.nlm.nih.gov/15485581/)].
- Gupta VK, Fatima A, Faridi U, Negi AS, Shanker K, Kumar JK, et al. Antimicrobial potential of *Glycyrrhiza glabra* roots. *J Ethnopharmacol*. 2008;**116**(2):377-80. doi: [10.1016/j.jep.2007.11.037](https://doi.org/10.1016/j.jep.2007.11.037). [PubMed: [18182260](https://pubmed.ncbi.nlm.nih.gov/18182260/)].
- Fiore C, Eisenhut M, Krausse R, Ragazzi E, Pellati D, Armanini D, et al. Antiviral effects of *Glycyrrhiza* species. *Phytother Res*. 2008;**22**(2):141-8. doi: [10.1002/ptr.2295](https://doi.org/10.1002/ptr.2295). [PubMed: [17886224](https://pubmed.ncbi.nlm.nih.gov/17886224/)].
- Okimasu E, Moromizato Y, Watanabe S, Sasaki J, Shiraishi N, Morimoto YM, et al. Inhibition of phospholipase A2 and platelet aggregation by glycyrrhizin, an antiinflammation drug. *Acta Med Okayama*. 1983;**37**(5):385-91. [PubMed: [6689106](https://pubmed.ncbi.nlm.nih.gov/6689106/)].
- Cilurzo F, Gennari CG, Selmin F, Epstein JB, Gaeta GM, Colella G, et al. A new mucoadhesive dosage form for the management of oral lichen planus: formulation study and clinical study. *Eur J Pharm Biopharm*. 2010;**76**(3):437-42. doi: [10.1016/j.ejpb.2010.07.014](https://doi.org/10.1016/j.ejpb.2010.07.014). [PubMed: [20708076](https://pubmed.ncbi.nlm.nih.gov/20708076/)].
- Alsadat Hashemipour M, Borna R, Gandjaliphan Nassab A. Effects of mucoadhesive paste of chlorhexidine and betamethasone on oral ulcer recovery process in rats. *Wounds*. 2013;**25**(4):104-12. [PubMed: [25868058](https://pubmed.ncbi.nlm.nih.gov/25868058/)].
- Choonhakarn C, Busaracom P, Sripanidkulchai B, Sarakarn P. The efficacy of aloe vera gel in the treatment of oral lichen planus: a randomized controlled trial. *Br J Dermatol*. 2008;**158**(3):573-7. doi: [10.1111/j.1365-2133.2007.08370.x](https://doi.org/10.1111/j.1365-2133.2007.08370.x). [PubMed: [18093246](https://pubmed.ncbi.nlm.nih.gov/18093246/)].

12. Iino S, Tango T, Matsushima T, Toda G, Miyake K, Hino K, et al. Therapeutic effects of stronger neo-minophagen C at different doses on chronic hepatitis and liver cirrhosis. *Hepatol Res.* 2001;**19**(1):31-40. [PubMed: [11137478](#)].
13. Tsubota A, Kumada H, Arase Y, Chayama K, Saitoh S, Ikeda K, et al. Combined ursodeoxycholic acid and glycyrrhizin therapy for chronic hepatitis C virus infection: a randomized controlled trial in 170 patients. *Eur J Gastroenterol Hepatol.* 1999;**11**(10):1077-83. [PubMed: [10524635](#)].