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Review article

The effect of herbal medicine in reducing the severity of oral lichen planus: A systematic review and meta-analysis

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ABSTRACT

Background: *Oral lichen planus (OLP) is a chronic autoimmune mucocutaneous disease of unknownaetiology. The reported use of herbal medicines may promote the healing of OLP lesions.* ***Purpose:*** *We aim to determine the effectiveness of herbal medicine to reduce the clinical and pain severity of OLP.* ***Methods:*** *PubMed, Cochrane Library and Wiley Online Library were reviewed according to the inclusion criteria. Risk of bias was performed for the randomised control trial (RCT) and cohort studies to assess the effectiveness of herbal medicinesfor OLP treatment. Outcomes were recorded based on pain severity and the quality of life of patients with OLP. The mean difference and effect size of studies were pooled.* ***Reviews:*** *Out of 1,034 papers, six publications were selected and reviewed. The most common types of OLP lesions were erosive and atrophic and were mainly found at the buccal site. OLP was common in the range of 27–74 years, especially infemales. The herbal medicines used in the publication were curcumin, lycopene, purslane, aloe vera and quercetin. Improvement in quality of life or OLP severity was recorded in the intervention group treated with purslane, curcumin and lycopene (P<0.05) but not in the control group. The total effect of herbalmedicine in reducing pain severity (measured with the Visual Analogue Scale [VAS]) in OLP patients was not significant (mean difference 0.13; 95% CI -0.202 to 0.463; p=0.442).* ***Conclusions:*** *Herbal medicine cannot be used as a single regime to reduce pain severity. Further research is recommended to evaluate cohort design studies to observe the prolonged effect of herbal medicine in OLP lesions. PROSPERO registration number: CRD42021262282 (2021)*

Keywords: *oral lichen planus; herbal medicine; meta-analysis*

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INTRODUCTION

Oral lichen planus (OLP) is a chronic mucocutaneous autoimmune disease with unknown aetiology. Predisposing factors for this disease could be genetics, infection, stress, malnutrition,endocrine gland disorders and a poor immune system.[1] The prevalence of OLP in Indonesia ismore than 10%, and it is mainly found in female patients over 40 years of age.[1,2] Other lesions that resemble OLP clinically and/or histologically have been termed oral lichenoid lesions (OLLs) and oral lichenoid reactions (OLRs).[3,4] In oral mucosa, OLP is commonly found on the buccal mucosa, but the tongue and gingiva may also be involved.[5] Clinically, OLP is categorised into two types: non-erosive (reticular, papular and plaque) and erosive (erosion, atrophic and bullous).[6] Patients with asymptomatic OLP (non-erosive type) usually do not require any treatment.[7]

In symptomatic patients (erosive), topical treatments, such as corticosteroids, calcineurin inhibitors, cyclosporine, retinoids and rapamycin, may relieve pain.[7] Other OLP treatments, such as phototherapy, laser therapy, photodynamic therapy and ultraviolet therapy, have also been reported.[8] Corticosteroids are the main treatment for OLP, but due to their local (burning sensation and irritation) and systemic (immunosuppression) side effects, various studies have been carried out to find alternative treatments, such as herbal medicines,[9] which have been widely used because they are safe, easy to find and low cost.[10] Thus far,

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many studies have shown that herbal medicines may reduce the severity of OLP; for example, Liu Wei Di Huang,[9] Tripterygium glycosides,[9] Zeng Sheng Ping,[9] liquorice,[11] purslane,[12] lycopene,[13] raspberry,[14] propolis,[15] green tea,[16] Ignatia amara,[17] aloe vera,[18] quercetin[19] and Curcuma longa.[20] Different types of herbs have had varied results; for example, curcumin may reduce the inflammatory cytokine response caused by the activity of T lymphocytes in OLP. As OLP treatment originally used corticosteroids, resulting in patients experiencing many side effects, many countries sought alternative approaches using herbal medicine. Until now, there have been limited systematic reviews on the usefulness of these herbs for OLP treatment, although a meta-analysis was conducted on pain severity between intervention and control groups.

This study aims to conduct a systematic review and meta-analysis on the epidemiology and effectiveness of herbal medicine for treating OLP. This review may contribute to the benefits of applying herbal medicine to reduce clinical symptoms in OLP patients.

METHODS

This meta-analysis was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, and it was registered in the PROSPERO database (CRD42021262282).

Selection criteria

A patient/population, intervention, comparison, outcomes and time (PICO(T)) strategy was used to define the following eligibility criteria: (P) patients with OLP and/or OLR/OLL with no histological dysplastic changes; (I) herbal medicine (aloe vera, curcumin, liquorice, green tea, purslane, Liu Wei Di Huang, Zeng Sheng Ping, Tripterygium glycosides, lycopene, raspberries, propolis, quercetin and Ignatia amara); (C) population who received the placebo; (O) epidemiological data of clinical OLP (severity, quality of life and side effects); (T) all literature published up until July 2021.

Inclusion and exclusion criteria

The inclusion criteria were patients older than 18 (as paediatric OLP is very rare) who had been diagnosed clinically and histologically as OLP/OLL/OLR with or without skin lesions, English literature with an RCT study design and a cohort from three database sources (Pubmed, Cochrane Literature and Wiley Online Literature) and OLP patients who experienced dysplastic changes to squamous cell carcinoma and irrelevant conditions/lesions such as OLP with a systemic condition.

Search strategies

Each keyword was determined and the following Boolean words were applied: (“Aloe vera” OR (curcumin OR “Curcuma longa” OR curcuminoids) OR (liquorice OR “Glycyrrhiza glabra” OR glycyrrhizin) OR (“Green tea” OR “Camellia sinensis” OR epicatechin OR epigallocatechin OR “epicatechin 3 gallate” OR “epigallocatechin 3 gallate”) OR (purslane OR “Portulaca oleracea”) OR (“Liuwei dihuang” OR “Liu Wei Di Huang” OR “Six Flavor Rehmanni” OR “Cornus officinalis” OR “Rehmannia glutinosa” OR “Rhizoma dioscoreae” OR “Cortex moutan radicis” OR “Poria cocos” OR “Alisma plantago aquatica”) OR (“Zeng Sheng Ping” OR ZSP OR “Sophora tonkinensis” OR “Polygonum bistorta” OR “Prunella vulgaris” OR “Sonchus brachyotus” OR “Dictamnus dasycarpus” OR “Dioscorea bulbifera”) OR (“Tripterygium glycosida” OR “Tripterygium wilfordii”) OR lycopene OR (raspberry OR “Rubus idaeus”) OR propolis OR (quercetin OR “Ginkgo biloba” OR “Hypericum perforatum” OR “Sambucus canadensis”) OR (ignatia OR “Ignatia amara” OR “Strychnos ignatii” OR strychnine) OR “natural ingredients”) AND (“oral lichenoid reaction” OR “OLP” OR OLR OR “Oral Lichen Planus” OR OLL OR “oral lichenoid lesion” OR “Oral Lichenoid Contact Lesion” OR OLCL OR “Oral Lichenoid Drug Reactions” OR OLDR) AND prevention.

Study selection

After eliminating duplicate studies, the remaining studies were screened based on their titles and abstracts. Then, the studies that were not available in full-text form were excluded. The studies with full texts were evaluated to comply with the inclusion criteria for this review. One investigator (KKV) worked independently to screen the studies using Boolean words and retrieved reports using Microsoft Excel Office 2019. The result was reviewed by all investigators before conducting the risk-of-bias assessment.

Risk of bias assessment

Three reviewers (KKV, IG, RA) independently assessed the risk of bias in the final six studies. The Joanna Briggs Institute (JBI) critical appraisal tools for systematic reviews were used to assess the cohort study, and the Cochrane risk-of-bias tool was used to assess studies with an RCT design.

Data extraction

Three investigators (KKV, IG, RA) extracted data from six studies according to subjects, type of OLP, the severity of OLP, quality of life, types of herbal medicine and side effects.

Data analysis

The outcome variables, such as pain severity taken from the VAS score, were collected and calculated. The mean differences (MDs) were calculated for continuous data. As there was low heterogeneity between the included studies, the fixed-effects model was used to pool the data. The heterogeneity levels of the eligible RCTs were assessed using I^2 statistics. Subgroup analysis was not performed

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because only four studies were included. The study's MD and effect size were pooled using OpenMetaAnalyst for Windows 10 64-bit (CEBM® Brown University). Sensitivity analysis could not be performed as the number of studies included for meta-analysis was low.

RESULTS

Study selection

One independent reviewer selected the studies. The PubMed database provided 234 studies, seven studies were found in Cochrane Literature and 796 studies were from Wiley Online Literature. After removing the duplicates based on their titles, 1,034 studies were obtained. The abstract screening was carried out, and 925 studies were excluded because the abstracts were unavailable and did not discuss OLP, OLL or OLR. Only 91 studies remained out of 109 after full texts were screened. A total of 85 studies were excluded for irrelevant topics, incomplete data (epidemiological data of clinical OLP severity and quality of life) and different study designs. Finally, six studies met the inclusion criteria and were included for the review (Figure 1). Meanwhile, only four studies provided mean VAS scores between the groups, so these studies were used for meta-analysis.

Risk-of-bias assessment

Quality assessment was carried out on the final six studies, five of which were RCTs (Salazar-Sánchez et al.;[18] Amirchaghmaghi et al.;[19] Amirchaghmaghi et al.;[20] Kia et al.;[21] Agha-Hosseini et al.[22]), and only one study was a cohort design (Prasad Kushwaha et al.[23]). Studies conducted by Salazar-Sánchez et al.,[18] Amirchaghmaghi et al.,[19] Amirchaghmaghi et al.,[20] Kia et al.[21] and Prasad Kushwaha et al.[23] had a low risk of bias (Figure 2 and Table 1). In contrast, the study by Agha-Hosseini et al.[22] had a high risk of bias due to unclear allocation concealment and selective reporting, in addition to other sources of bias, including blinding of participants and personnel, blinding outcome assessment and incomplete outcome data (Figure 2). This study was included despite its high risk of bias because of the completeness of data. None of the studies described selective reporting except for Amirchaghmaghi et al.[19]

Data extraction

This research included 212 patients aged 27–74. OLP was found predominantly in females with various types of OLP (erosive, atrophic and reticular). The research results from the six selected reports were based on the severity of OLP and quality of life. The severity of OLP in three reports was measured using the Thongprasom scale and

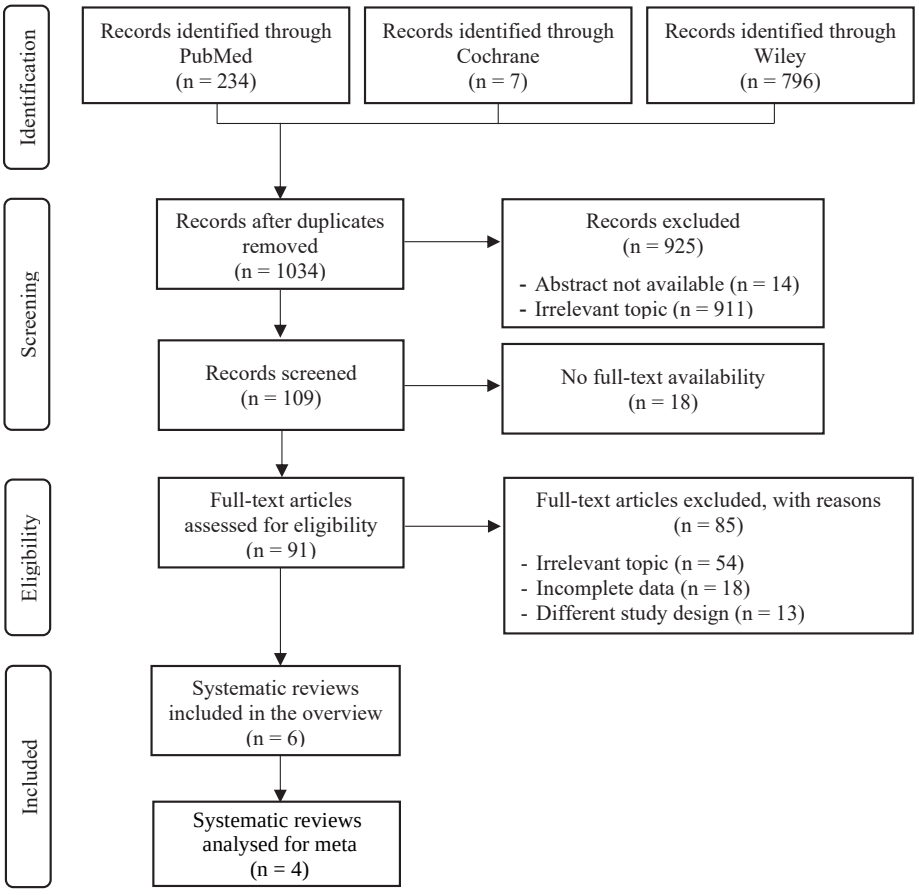

Figure 1. PRISMA flow diagram.

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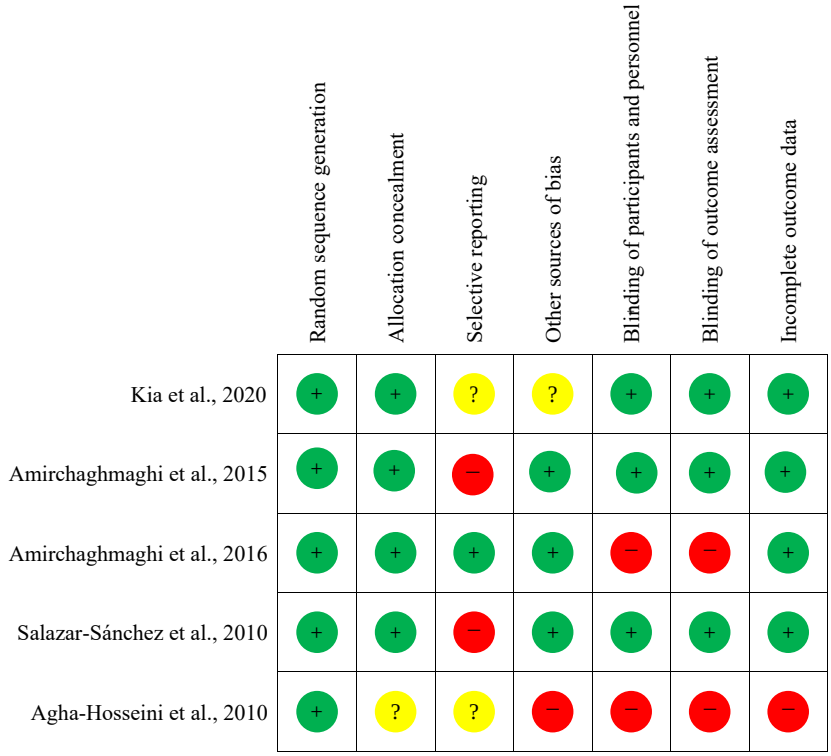

Figure 2. Risk-of-bias assessment for RCT studies.

Table 1. Risk-of-bias assessment for cohort study (Y=yes; N=no)

Author	Design	Score based on appropriate JBI appraisal*										Overall appraisal
		1	2	3	4	5	6	7	8	9	10	
Prasad Kushwaha et al. (2019)	Cohort	Y	Y	Y	N	Y	N	Y	N	Y	Y	Included

Table 2. Studies of herbal medicine for OLP treatment (M=male; F=female; IV=intervention group; C=control group; NA=Not Available)

Studies	Study design	Subjects	OLP type / location	OLP severity	Quality of life	Natural agent	Result
Agha-Hosseini et al. (2010)	RCT	Purslane (IV) = 20 Placebo (C) = 17 16 M, 21 F Age (mean) = 47.4 ± 10.8	Erosive, atrophic, reticular	Tool: Thongprasom scale IV group 4 deg worse = 0 3 deg worse = 0 no change n = 17% 1 deg improvement = 29% 2 deg improvement = 29% 3 deg improvement = 13% 4 deg improvement = 12% C group 4 deg worse = 5% 3 deg worse = 5% no change n = 73% 1 deg improvement = 17% 2 deg improvement = 0 3 deg improvement n = 0 4 deg improvement n = 0	Tool: VAS IV group 1 deg worse = 0 no change n = 0 1 deg improvement = 43% 2 deg improvement = 43% 3 deg improvement = 14% C group 1 deg worse n = 14% no change n = 15% 1 deg improvement n = 71% 2 deg improvement n = 0 3 deg improvement n = 0	Purslane capsule Dosage: 235 mg capsules for 6 months (1x1)	Significant differences in OLP severity and pain score between the purslane group and control group (P<0.001)

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Salazar-Sánchez et al. (2010)	RCT	Aloe vera (IV) = 31 (3 M, 28 F) Placebo (C) = 24 (1 M, 23 F) Age (mean) IV = 62.19 ± 10.45 C = 60.71 ± 12.23	Erosive, atrophic Buccal (n = 52), tongue (n = 38), lip (n = 7), gingival (n = 33), palate (n = 5)	NA	Tool: VAS, OHIP-49, HAD <u>IV group</u> HAD-D Baseline = 6.32 ± 5.77 3 months = 6.19 ± 5.90 HAD-A Baseline = 8.90 ± 4.54 3 months = 7.84 ± 5.10 OHIP-49 Baseline = 40.26 ± 24.60 3 months = 20.35 ± 17.61 VAS Baseline = 5.5 ± 2 12 weeks = 2.5 ± 3.0 <u>C group</u> HAD-D Baseline = 5.83 ± 3.38 3 months = 6.08 ± 3.43 HAD-A Baseline = 10.08 ± 4.03 3 months = 9.42 ± 3.52 OHIP-49 Baseline = 40.75 ± 19.88 3 months = 29.50 ± 20.82 VAS Baseline = 5.8 ± 1.8 12 weeks = 3.7 ± 3.3	Aloe barbadensis gel Dosage: 60ml for 12 weeks (0.4 ml keeping it within the oral cavity for 1 minute) Natural ingredients: aloe vera	There was no significant difference in pain, depression, anxiety or OHIP score between the aloe vera group and the control group; except on OHIP-49 domain psychological disability (P = 0.007) and total score OHIP-49 (P = 0.046)
Amircha-ghmaghi et al. (2015)	RCT	Quercetin (IV) = 15 Placebo (C) = 15 8 M, 22 F Age (mean) IV = 48.26 ± 16.28 C = 44.6 ± 10.22	Erosive, atrophic	Tool: Individual severity index <u>Baseline</u> IV = 9.40 ± 3.16 C = 9.63 ± 3.83 <u>1 week</u> IV = 5.93 ± 3.15 C = 4.63 ± 2.6 <u>2 weeks</u> IV = 4.73 ± 3.23 C = 3.70 ± 2.35 <u>3 weeks</u> IV = 3.70 ± 3.30 C = 2.50 ± 2.45 <u>4 weeks</u> IV = 3.23 ± 3.47 C = 1.33 ± 1.87 <u>8 weeks</u> IV = 2.23 ± 2.93 C = 1.10 ± 2.35	Tool: VAS <u>Baseline</u> IV = 1.92 ± 0.86 C = 1.80 ± 0.77 <u>1 week</u> IV = 1.07 ± 0.95 C = 0.8 ± 0.86 <u>2 weeks</u> IV = 0.53 ± 0.66 C = 0.86 ± 0.91 <u>3 weeks</u> IV = 0.33 ± 0.48 C = 0.66 ± 0.89 <u>4 weeks</u> IV = 0.23 ± 0.43 C = 0.46 ± 0.83 <u>8 weeks</u> IV = 0.46 ± 0.51 C = 0.53 ± 0.91	Quercetin hydrate Dosage: 250 mg capsules 2 times a day	There was no significant difference in clinical and pain severity between systemically administered quercetin and the placebo (P>0.05)

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Amircha-ghmaghi et al. (2016)	RCT	Curcumin (IV) = 12 Placebo (C) = 8 7 M, 13 F Age (mean) IV = 49.42 ± 11.22 C = 52.75 ± 9.43	Erosive, atrophic Buccal (n = 18), gingival (n = 5), tongue (n = 10), lips (n = 2)	Tool: Thongprasom scale <u>Baseline</u> IV = 3.17 ± 1.03 C = 3 ± 1.30 <u>After 4 weeks</u> IV = 1.08 ± 0.66 C = 1.5 ± 1.06	Tool: VAS <u>Baseline</u> IV = 6.5 ± 2.15 C = 4.63 ± 3.20 <u>After 4 weeks</u> IV = 0.33 ± 0.65 C = 0.13 ± 0.35	Curcumin (tablets) Dosage: 500 mg 2x1 for 4 weeks	There was no significant difference in clinical and pain severity between the curcumin group and the control group (P = 0.77)
Prasad Kushwaha et al. (2019)	Cohort	IV = 13 7 M, 6 F Age IV = 27–74 years	Atrophic = 6 Erosive = 4 Reticular= 3 Buccal (n = 25), gingival (n = 6), tongue (n = 3), lips (n = 2), hard palate (n = 1)	Tool: Thongprasom scale <u>Baseline</u> = 2.77 ± 1.74 2 weeks = 2.69±1.65 4 weeks = 2.62±1.66 6 weeks = 1.54±1.19 8 weeks = 0.85±0.37	NA	Lycopene (LycoRed 2mg capsules) Dosage: Lycopene capsules 4mg/day for 8 weeks	Lycopene significantly reduced OLP severity based on the Thongprasom index (P = 0.005) Adverse effects Nausea Mild abdominal pain/cramps Increased appetite Diarrhoea Headaches Dizziness Dry mouth Flatulence
Kia et al. (2020)	RCT	Curcumin (IV) = 29 (4 M, 25 F) Predniso-lone (C) = 28 (5 M, 23 F) Age (mean) IV = 51.86 ± 9.94 C = 52.67 ±8.9	NA	Tool: Thongprasom scale <u>Baseline</u> IV = 3.83 ± 1.17 C = 3.83 ± 1.18 <u>4 weeks</u> IV = 2.34 ± 1.14 C = 1.83 ± 0.92	Tool: VAS <u>Baseline</u> IV = 4.65 ± 3.39 C = 4.89 ± 3.34 <u>1 week</u> IV = 4.38 ± 3.03 C = 4.67 ± 3.45 <u>2 weeks</u> IV = 3.41 ± 2.74 C = 3.28 ± 2.74 <u>4 weeks</u> IV = 2.69 ± 2.89 C = 2.33 ± 2.03	Curcumin (nano-curcumin) micellar soft gel capsule Dosage: 80 mg once daily after breakfast	Curcumin can be an alternative drug for OLP lesions compared to the control group. In the curcumin group, pain decreased significantly at 2 weeks. (P<0.001)

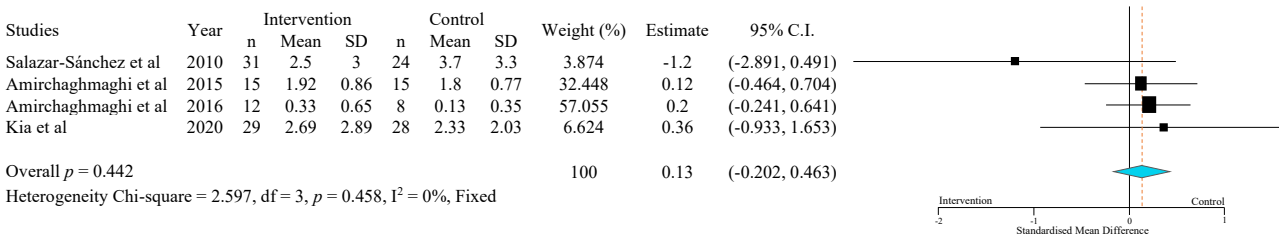

Figure 3. Forest plot of visual analogue scale for pain between intervention group and control group.

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the VAS (Amirchagmaghi et al.;[20] Kia et al.;[21] Agha-Hosseini et al.[22]). The study by Salazar-Sánchez et al.[18] measured quality of life using the VAS, the Oral Health Impact Profile (OHIP-49) and Hospital Anxiety-Depression (HAD) instruments; however, the study did not measure the severity of OLP. Another report by Amirchagmaghi et al.[19] measured the severity of OLP using the individual severity index and measured quality of life using the VAS. Prasad Kushwaha et al.[23] measured the severity of OLP using the Thongprasom scale and did not measure the quality of life (Table 2).

Meta-analysis

Figure 3 depicts the total effect of the VAS in the form of a forest plot, based on the findings of four published studies (Salazar-Sánchez et al.;[18] Amirchagmaghi et al.;[19] Amirchagmaghi et al.;[20] Kia et al.[21]). The forest plot reveals that the heterogeneity of studies was low (chi-squared=2.597, P=0.458, I^2=0%); therefore, a fixed-effect model was utilized for the analysis. The overall pooled effect of the MD VAS score between the intervention and control groups was not significantly different (p=0.442, 95% CI -0.202 to -0.463). The study by Prasad Kushwaha et al.[23] could not be compared because it only had one group, and the researchers did not provide quality-of-life data. Agha-Hosseini et al.[22] could not be compared because the data were presented as a proportion.

DISCUSSION

This systematic review of five RCTs and one cohort study on herbal medicines for OLP treatment found that the general risk of bias was low in all studies, but the resulting meta-analysis performed well. Based on the results of the fixed-effects analysis of four publications,[18–21] herbal medicines may be less effective in reducing the severity of OLP pain, although the results varied between the types of herbal medicine used for treatment. In the study by Salazar-Sánchez et al.,[18] lycopene significantly reduced the severity of OLP pain, but there were some adverse effects. Additionally, Agha-Hosseini et al.[22] stated that purslane had been used as an alternative medicine for treating OLP patients without any side effects.

In this systematic review, OLP was more likely to occur in females (n=161) than males (n=51), as it may be influenced by hormonal cycles, especially during pregnancy, menstruation and menopause. In the perimenopause or menopause phase, the decrease in oestrogen levels can cause physical and emotional symptoms such as depression, irritability, insomnia and fatigue.[24] Oestrogen is a hormone that plays a role in controlling the menstrual cycle, and it can modulate T cells, including CD4+ (Th1, Th2, Th17 and Tregs) and CD8+, which play an important role in the pathogenesis of OLP.[25] Based on six studies, OLP was found to occur from 27–74 years of age. This lesion may be related to decreased immunological reactivity, impaired DNA repair and the atrophy of oral tissues, especially oral epithelium and the salivary glands. Furthermore, at an advanced age, other factors could include systemic diseases, nutritional disorders, the side effects of drugs and the use of ill-fitting dentures.[26] The most studied types of OLP (Salazar-Sánchez et al.;[18] Amirchagmaghi et al.;[19] Amirchagmaghi et al.;[20] Agha-Hosseini et al.;[22] Kushwaha et al.[23]) are erosive and atrophic types because patients often complain about pain, and there have been reports on its potential to become malignant.[27] OLP was most commonly found in the buccal mucosa area, which could be because this area is most susceptible to trauma.[28] Until now, the aetiology of OLP remains unknown, but several factors can trigger its occurrence, including autoimmune disorders, stress, trauma, malnutrition, systemic diseases, and endocrine and salivary gland disorders.[2] In some cases, genetic and viral infections could also trigger the development of OLP.[29] However, none of the six selected studies discussed the predisposing factors of OLP.

Curcumin could decrease the inflammatory response by suppressing the activity of COX-2, lipoxygenase, inducible nitric oxide synthase enzymes (iNOS) as well as inhibiting the production of cytokines that cause inflammation, such as IL-1, IL-2, IL-6, IL-8 and IL-12. Therefore, curcumin was found to effectively reduce the signs and symptoms of OLP such as a burning sensation and the occurrence of erythema and ulceration. However, in its topical use, there were some complaints, such as xerostomia, itching, burning, mild inflammation and the yellowish colour of the gingiva and the surrounding area.[30] Aloe vera is known to inhibit the inflammatory process by interfering with the activity of the arachidonic acid pathway through COX and reducing leukocyte adhesion and tumour necrosis factor (TNF) levels.[31] Due to its properties, aloe vera was found to be effective in reducing the burning sensation and decreasing the healing duration, but the side effects of its topical use may cause allergic reactions.[31,32] Quercetin has anti-inflammatory properties that inhibit cytokines such as IL-12, IFN-γ, IFN-α, IL-8, COX-2 and prostaglandin E. At the same time, its antioxidant content could inhibit free radicals and nitric oxide. Therefore, quercetin was found to reduce pain in OLP patients.[33] Purslane contains melatonin, which is known as an antioxidant agent, and omega-3 fatty acids, which are rich in fatty acids and have anti-cancer and anti-inflammatory effects that have been shown to reduce IL-6 levels. Because of its ingredients, the use of purslane leads to clinical improvements in OLP patients.[9] Lycopene is known to have antioxidants, and immunomodulatory and free radical scavenging properties.[13] It has been shown to reduce the burning sensation in OLP patients and may be used to treat atrophic and erosive types of OLP.[34]

Based on the six journal reports, curcumin is the most studied herbal medicine to reduce the severity of OLP. Curcumin is widely used as the main ingredient in cooking, food colouring and traditional medicine. This natural ingredient originates from India and is widely cultivated in Southern China, Taiwan, Japan, Burma and Indonesia.[35] To

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reduce the severity of OLP, herbal medicines have several ingredients that contain anti-inflammatory, antioxidant and anti-cancer effects.[36] Thomas et al.[33] found that a topical 1% curcuminoid gel reduced signs and symptoms of OLP, although it was not as effective as 0.1% triamcinolone acetonide. Chainani-Wu et al.[37] found that 5% curcumin paste reduced the severity of OLP lesions. No serious effects of herbal medicine were reported, except for lycopene.

Curcumin, aloe vera, purslane, quercetin and lycopene were effective in reducing the clinical severity of OLP. The results of the study by Prasad Kushwaha et al.,[23] found that lycopene can significantly reduce the severity of OLP based on the Thongprasom index (P=0.005), but it had some side effects such as nausea, cramps, diarrhoea, headaches, etc. At the same time, Agha-Hosseini et al.[22] stated that purslane could be used as alternative medicine or a supplement for treatment in OLP patients without side effects. Based on the meta-analysis, a low heterogeneity (p=0.458, I^2=0%) was calculated in four studies with an overall fixed-effect analysis, and herbal medicine had a more negligible effect in reducing pain severity (VAS) against OLP (MD=0.13, p=0.442, 95% CI -0.202 to -0.463). It has been demonstrated that these natural ingredients reduce the inflammatory symptoms of OLP. Since OLP is not only a disease with a chronic inflammatory background, but also an autoimmune disorder, the anti-inflammatory and antioxidant properties of the five natural ingredients are insufficient and have little effect on reducing the severity of OLP.

The limitations and proposed recommendations of this study are: 1) the trend of herbal medicine research reports on a variety of herbs, which may lead to difficulty in comparing the same herbs that have the potential of reducing the severity of OLP, as each study uses different tools to measure lesion severity and the quality of life of OLP patients; 2) most of the studies that examined herbal medicine were conducted over a short period; 3) some studies found improvements in OLP only among baseline data in the intervention group but did not make comparisons with the control group due to the study design. It was sometimes concluded that herbal medicine was effective in treating OLP.

In conclusion, herbal medicine cannot be used as a single regime but might be used as a supplement or additional medicine to reduce the symptoms and severity of OLP lesions. Further research is recommended to evaluate larger cohort design studies to observe the prolonged use of herbal medicine in treating OLP lesions.

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Authors contributions

KKV, IG and RA were responsible for conceptualisation, writing the original draft, and reviewing and editing the manuscript. KKV and IG were responsible for data acquisition and investigation. KKV was also the administrator for projects, resources and the visualisation of charts and tables. IG and RA were responsible for the methodology, supervision and validation of collected data. RBZ was responsible for critically editing the project and manuscript.

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