

## Effectiveness of herbal medicine as an alternative therapy for burning mouth syndrome: a systematic review

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BMS; Herbal Medicine;  
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### ABSTRACT

**Background:** Burning mouth syndrome (BMS) is characterized by a burning sensation or dysesthesia of the oral mucosa without accompanying abnormal clinical or laboratory findings. Management of BMS is very important to reduce pain, support nutrition and improve patients' quality of life. Various studies on BMS therapy have been carried out, one of which is by using alternative materials derived from nature known as herbal ingredients. The objective of this systematic review is to review the effectiveness of herbal medicine to reduce pain in BMS patients.

**Methods:** This systematic review was conducted using the Preferred Reporting Items for Systematic Review and Meta-analyses (PRISMA) guidelines. Article searches were conducted through Pubmed, Scopus, Science Direct, Cochrane, and Springer Link published from 2012 to 2022 with specific keywords. The search for articles was limited to human studies and randomized controlled trial (RCT), papers written in English and availability of full text. The risk assessment of bias uses the Modified Jadad Scale.

**Results:** Seven articles with good eligibility that meet the inclusion criteria were analyzed. The herbal medicine reviewed were capsaicin (two articles), *Aloe vera*, *catuama*, capsaicin, virgin olive oil, chamomile and crocin (one article for each herbal medicine). All of the herbal medicine reviewed were proven to reduce pain in BMS patients, but capsaicin and *catuama* showed significant differences with the comparison group. Minimal side effects were also observed with capsaicin and *catuama*.

**Conclusion:** Herbal medicinal ingredients have been proven to be effective, useful and safe alternative therapies for BMS patients.

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## INTRODUCTION

Burning mouth syndrome (BMS) was first mentioned and later described in 1803.<sup>1</sup> The International Classification of Headache Disorders Third Edition (ICHD-3) defines BMS as an intraoral burning or dysaesthetic sensation, recurring daily for more than two hours each day over more than three months, without clinically evident causative lesions.<sup>2,3</sup> This condition is also known as burning mouth disease, stomatodynia, burning tongue syndrome, stomatopyresis, glossopyresis, glossodynia, and oral dysphasia.<sup>4,5</sup> The prevalence of BMS varies throughout the world with an estimation in the general population, based on various study designs and diagnostic criteria, of around 0.7-15%. The highest prevalence is found in Europe, which reached 7%, while Asia and America showed lower numbers, reaching 2-3% and 0.7%, respectively.<sup>6-8</sup> The peak prevalence is found between the fourth and sixth decades of life, whereas children, adolescents, and young adults are rarely affected.<sup>1,9</sup>

The etiopathogenesis of BMS is still unclear, but possibly very complex and multifactorial between somatic and psychiatric comorbidities.<sup>10,11</sup> Another hypothesis states that neurology, endocrine, and genetics contribute to the tissue in increasing pain sensation.<sup>12</sup> The clinical manifestations of BMS vary, which usually consist of three cardinal symptoms, i.e., burning pain in the oral, dysgeusia, and xerostomia, occurring 3 to 12 years after menopause.<sup>1,4,9</sup> The patient describes pain sensations similar to burning, scalding, itching, tingling, stabbing, numbness and uncomfortable.<sup>4,10</sup> These sensations can be intermittent or constant and increase in the afternoon and evening.<sup>4,5</sup> Pain intensity varies

from mild to severe, similar to dental pain with an average VAS of 3.1-5.1/10.<sup>4</sup> This symptom is usually bilateral and localized in the anterior two-thirds of the tongue (71-78%). However, other sites such as hard palate, lips, buccal mucosa, gingiva, floor of the mouth, and oropharynx can also be involved.<sup>2,4,10</sup>

BMS treatment is important to reduce pain, support nutrition, and improve quality of life.<sup>2,13</sup> Various studies on BMS therapy have been conducted, some of which used natural products known as herbal medicine.<sup>2,5,14</sup> Along with the back-to-nature trend, the potential of using medicinal plants, both topical and systemic, is growing not only in Indonesia but also in Asia, even the world. According to data from the WHO, between 40 and 59% of Indonesians and 88% of all nations worldwide have utilized various natural products as traditional treatments. Herbal ingredients are known to be cost-effective and easy to obtain.<sup>15,16</sup>

Based on the search conducted to date, there has been no systematic review concerning herbal medicine as BMS therapy with RCT design, even though the use of herbal medicine may be applicable in Indonesia. Therefore, the author is interested to conduct this systematic review to investigate the effectiveness of various herbal medicine as an alternative therapy to BMS. This systematic review is expected to be a scientific fundamental and scientific information update on herbal medicine to aid in the management of BMS.

## RESEARCH METHODS

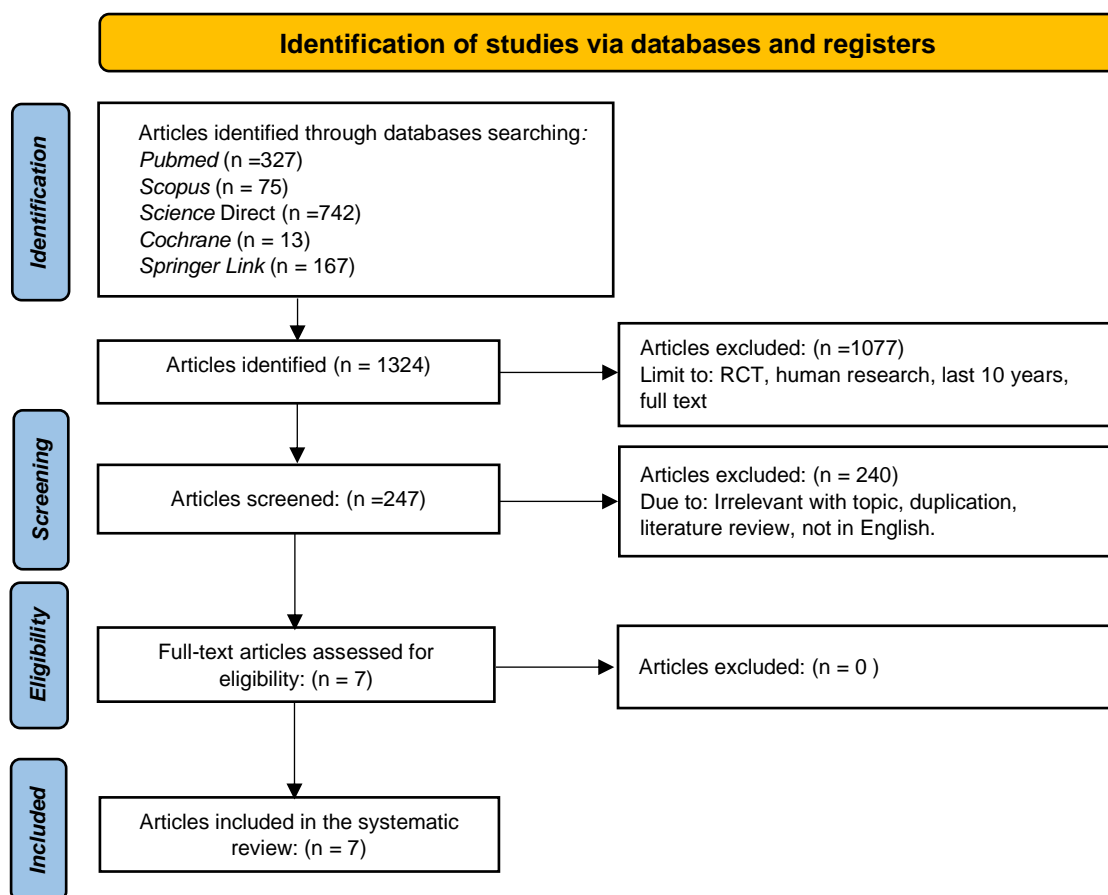
This systematic review used The Preferred Reporting Items for systematic review and meta-analyses (PRISMA) guidelines. This systematic review's theme was arranged using population, intervention,

comparison, and outcome (PICO) framework. The PICO criteria were as follow: 1) Population: patients with BMS without distinguished type of BMS, ages and genders. 2) Intervention: the use of herbal medicine for BMS therapy. 3) Comparison: the positive or negative control group. 4) Outcomes: The effectiveness of the intervention group in the form of changes in the pain intensity of BMS patients as a clinical parameter of therapy

Several databases were used in the electronic literature search, including Pubmed, Scopus, Science Direct, Cochrane, and Springer Link. The following keywords are combined to carry out the article search process: (burning mouth syndrome OR stomatopyrosis OR glossalgia) AND (herbal medicine OR medicinal herbs OR medicinal plants). A manual hand-searching of the

reference lists of relevant studies was also performed. The search focused on papers published between 2012 and 2022, and was performed on September 1, 2022.

After searching the five databases using the selected keywords, a total of 1324 papers were retrieved. The inclusion criteria in this study were limited to a RCT study design with the topic of the use of herbal medicine for BMS therapy, human study, full paper available and published in the past ten years (range between 2012-2022). The exclusion criteria were excluded for duplication and irrelevant with the topic; articles with a non-RCT design (case report, study in vivo and in vitro, pilot study and literature review); and not presented in English. The flow chart of article searching process in this systematic review is based on the PRISMA guidance shown in Figure 1.



**Figure 1.** Flowchart of article searching based on the PRISMA guidelines.

The article selection process was conducted by two reviewers (NTP and NN). The abstracts and titles of the reviewed articles were screened to ensure that they were relevant to the aim of the study. Information on population, intervention, comparison group, and the outcome was also extracted. Both authors (NTP and NN) discussed the extracted data and proceed to make decisions for final recommendations in this study, as well as for assessment risk of bias or article qualities. Differences in opinions were discussed and decided to obtain mutual agreement. There was no difference to decide the eligible articles for review, the extracted data, and the risk of bias assessment.

The Modified Jadad Scale quality scoring system was used for assessing the quality of articles or the risk of bias in the methodology used in the articles. The instrument included eight item scale to assess randomization, blinding processes, withdrawals and dropouts that occurred, inclusion or exclusion criteria, adverse effects, and statistical analysis. The conclusion of the article's quality assessment refers to the total score of each article. The articles are given a score ranging from 0 (the lowest quality) to 8 (the highest quality). High quality is shown by scores of 4 until 8, meaning between good and excellent, while low quality is expressed by scores of 0 until 3.<sup>17</sup> The details of quality assessment for 7 selected articles, detailed in table 1.

**Table 1.** Assessment of the risk of bias and quality for the reviewed articles using the Modified Jadad Scale.

	Risk assessment of bias and quality (Answer formulation)	Authors						
		López et al. <sup>18</sup>	Spanemb erg et al. <sup>19</sup>	Silvestre et al. <sup>20</sup>	Cano et al. <sup>21</sup>	Jørgensen et al. <sup>22</sup>	Valenzuela et al. <sup>23</sup>	Pakfetrat et al. <sup>24</sup>
1	Was the study described as random? (Yes: 1, No: 0)	1	1	1	1	1	1	1
2	Was the randomization scheme described and appropriate? (Yes: 1, No: 0, No described: -1)	1	1	1	1	1	1	1
3	Was the study described as double-blind? (Yes: 1, No: 0; double-blind: 1; single-blind 0.5)	1	1	1	1	1	1	1
4	Was the method of blinding appropriate? (Yes: 1, No: -1, No described: -1)	1	1	1	1	1	1	1
5	Was there a description of withdrawals and dropouts? (Yes: 1, No: 0)	1	1	1	1	1	1	1
6	Was there a clear description of the inclusion/exclusion criteria? (Yes: 1, No: 0)	1	0	0	1	1	1	1
7	Was the method used to assess adverse effects described? (Yes: 1, No: 0)	1	1	1	1	1	1	1
8	Was the method of statistical analysis described? (Yes: 1, No: 0)	1	1	0	1	1	1	1
	<b>Score</b>	8	7	6	8	8	8	8
	<b>Result</b>	High range of quality	High range of quality	High range of quality	High range of quality	High range of quality	High range of quality	High range of quality

## Results

This systematic review described the results of the risk of bias assesment, distribution of research subjects by country,

herbal ingredients used, average age, a number of patient, research study design and parameters to asses the effectiveness of herbal medicine in BMS. All of the studies used an

RCT study design with an appropriate blinding process. The detail of the assessment score for the quality of the seven chosen articles is presented in Table 1. A general summary of the information on population, such as author name, year, country, study design, population age, number of samples, number of groups, and herbal medicine intervention can be seen

in Table 2. Effectiveness of herbal medicine for BMS therapy can be seen in Table 3. The table describes ingredients, preparation, the procedure of administration, intervention dose, and comparison used, instruments as effectiveness parameters, and outcome from herbal medicine on BMS

**Table 2.** General summary of the reviewed articles

No	Authors (Year)	Country	Herbal Medicine	RCT's Blinding Type	Average Age (decade)	Age Range (year)	Number of patient	Number of groups
1	López et al. (2012) <sup>18</sup>	Spain	<i>Aloe vera Barbadosensis</i>	Double	6	30-84	75	3
2	Spanemberg et al. (2012) <sup>19</sup>	Brazil	<i>Catuama</i>	Double	6	41-79	60	2
3	Silvestre et al. (2012) <sup>20</sup>	Spain	Capsaicin	Double	7	40-90	30	2
4	Cano-carillo et al. (2014) <sup>21</sup>	Spain	<i>Lycopene-enriched virgin olive oil</i>	Double	6	NM	60	2
5	Jørgensen et al. (2016) <sup>22</sup>	Denmark	Capsaicin	Double	6	34-70	22	2
6	Valenzuela et al. (2016) <sup>23</sup>	Spain	Chamomile ( <i>Chamaemelum nobile</i> )	Double	6	NM	62	2
7	Pakfetrat et al. (2019) <sup>24</sup>	Iran	Crosin ( <i>Crocus sativus</i> L.)	Double	5	NM	47	2

Notes: RCT: Randomized Controlled Trial, NM: No mention

**Table 3.** Effectiveness of herbal medicine for BMS therapy

No	Reference	Intervention	Control	Instrumen dan Outcome
1	López et al. (2012) <sup>18</sup>	Tongue protector (15 min) + 0,5 ml <i>Aloe vera barbadensis</i> gel 70% applied for 12 weeks, three times every day. (n=25)	-Tongue protector alone (15 min) for 12 weeks, three times every day. (n=25) -Tongue protector (15 min) + 0,5 ml placebo gel applied for 12 weeks, three times every day. (n=25)	The VAS score decreased for the intervention group compared to baseline but without statistically significant differences. There was no significant differences in VAS scores between the three groups (p=0,210).
2	Spanemberg et al. (2012) <sup>19</sup>	Herbal <i>Catuama</i> capsules 310 mg was composed of four extracts of medicinal plants: <i>Paullinia cupana</i> 125 mg, <i>Ptychopetalum olacoides</i> 87,5 mg, <i>Trichilia catigua</i> 87,5 mg, and <i>Zingiber officinalis</i> 10 mg. Two capsules was given orally each day for 8 weeks. (n=30)	Two placebo capsules was given orally each day for 8 weeks. (n=30)	The effect of <i>catuama</i> administration significantly reduce VNS score (p<0,001) compared to baseline and there was a significant difference in VNS between <i>catuama</i> and placebo (p=0,003) (p=0,001)
3	Silvestre et al. (2012) <sup>20</sup>	Capsaicin rinse 0,02% administered 15 ml for one week, three times every day. (n=12)	Placebo rinse formulation administered 15 ml for one week, three times every day. (n=11)	The effect of capsaicin rinse administration significantly reduce VAS score compared to baseline (p morning=0,003 & p afternoon=0,002) and there was a significant difference in VAS between capsaicin rinse and placebo (p=Nm).
4	Cano-carillo et al. (2014) <sup>21</sup>	Lycopene-enriched virgin olive oil (lycopene-enriched VOO) 300 ppm was sprayed then swallowed 1,5 mL three times a day for 12 weeks. (n=30)	Placebo solution was sprayed then swallowed 1,5 mL three times a day for 12 weeks. (n=30)	The effect of lycopene-enriched VOO administration significantly reduce VAS score compared to baseline (VAS pain: p=0,000; VAS burning: p=0,003). There was no significant differences in VAS scores between lycopene-enriched VOO and placebo. (VAS pain: p=0,574; VAS burning: p=0,992).
5	Jørgensen et al. (2016) <sup>22</sup>	I: Capsaicin oral gel 0.01% applied three times daily for two weeks then wash-out for two weeks. Furthermore, cross-over capsaicin 0,02% applied three times a day for two weeks and then wash-out for two weeks. (n=11)	II: Capsaicin oral gel 0,02% applied three times daily for two weeks then wash-out for two weeks. Furthermore, cross-over capsaicin 0,01% applied three times a day for two weeks and then wash-out for two weeks. (n=11)	Both concentrations of capsaicin gels significantly reduce VAS score compare to baseline (p=0,002). There was no significant differences in VAS scores between group I and group II (p=0,27).

6	Valenzuela et al. (2016) <sup>23</sup>	Chamomile ( <i>Chamaemelum nobile</i> ) gel 2% applied 0,5 ml in 30 seconds, twice a day for 1 month. (n=31)	Placebo gel applied 0,5 ml twice daily for 1 month. (n=31)	The effect of Chamomile gel application significantly reduce VAS compared to baseline ( $p<0,001$ ). There was no statistical difference in VAS score between the chamomile and placebo ( $p=0,847$ ).
7	Pakfetrat et al. (2019) <sup>24</sup>	Crocins from saffron ( <i>Crocus sativus</i> L.) tablets 15 mg was given orally twice daily for 11 weeks. (n=26)	Citalopram was given orally, once daily with an initial dose of 10 mg that increased to 20 mg after a week for 11 weeks. (n=21)	In both groups, VAS score at the end of the study was significantly lower as compared to the beginning of the trial ( $p<0,001$ ). There was no significant difference in VAS score between crocin and citalopram ( $p>0,05$ ).

Notes: VAS: Visual Analogue Scale, VNS : Visual Numeric Scale, NM: No Mention

**Table 4.** Comparison of VAS scores for BMS therapy using herbal medicine

No	Reference	Herbal Medicine	Parameters	VAS Score on week													
				0	1	2	3	4	5	6	7	8	9	10	11	12	
1	López et al. (2012) <sup>18</sup>	<i>Aloe vera</i>	VAS	9													5
2	Spanemberg et al. (2012) <sup>19</sup>	<i>Catuama</i>	VNS	6,8				4,6					3,3				3,3
3	Silvestre et al. (2012) <sup>20</sup>	Capsaicin	VAS (Morning)	6	5												
			VAS (Night)	6	4												
4	Cano-carillo et al. (2014) <sup>21</sup>	<i>Lycopene-enriched VOO</i>	VAS (Pain)	9													6
			VAS (Burning)	5													
5	Jørgensen et al. (2016) <sup>22</sup>	Capsaicin 0,01;0,025	VAS	6,4	4,7	5,9	5,1	6,0									
		Capsaicin 0,025;0,01	VAS	4,6	3,6	3,5	3,0	3,2									
6	Valenzuela et al. (2016) <sup>23</sup>	<i>Chamomile</i>	VAS	7,4	6,7	6,7											
7	Pakfetrat et al. (2019) <sup>24</sup>	<i>Crosin</i>	VAS	8,9		5,6					2,9						1,1

Detailed results of clinical assessment for the intervention group in the form of a pain scale before and after herbal medicine therapy in BMS patients are shown in Table 4. The severity of BMS was assessed with a standard instrument to determine the pain scale. Six out of seven articles used visual analogue scale (VAS), while one article from Spanemberg, et al. used visual numeric scale (VNS) as parameter in determining pain. The majority of pain scores in the intervention group that used herbal medicine showed a decrease in line with intervention duration.<sup>18-24</sup>

The results of pain score assessment before and after herbal medicine intervention showed

that six out of seven articles had a significant decrease in pain score, while one article from Lopez et al. showed a similar decrease in pain score, albeit insignificant. Two out of seven articles stated a significant difference between the intervention group and control group, i.e., Spanemberg et al., (2012) and Silvestre et al., (2012), while five other articles showed an insignificant difference. Three articles from Spanemberg et al., (2012), Silvestre et al., (2012) and Jørgensen et al., (2017) showed adverse effects from the use of herbal medicine of capsaicin solution and gel and *catuama*.<sup>18-24</sup>

## DISCUSSION

BMS is a puzzling, idiopathic, chronic, and painful clinical entity that does not have a validated and standardized definition, diagnostic criteria, or classification. BMS causes significant discomfort to patients with chronic continuous symptoms that linger for a varied time period from months to years, reducing the quality of life.<sup>25</sup> A lot of types and variations of therapies have been used on BMS patients. However, there is no certain effective therapy. The existing treatment only aims to eliminate symptoms, which is a challenge. The suggested choices of therapy for BMS include pharmacological and non-pharmacological therapies.<sup>2,29,30</sup> Furthermore, the use of herbal medicine is also started to be suggested and investigated as an alternative therapy for BMS.<sup>10,26</sup> Herbal medicine is known to be used from the early days to prevent and cure various diseases.<sup>27</sup> Herbal extract have a lot of benefits in oral medicine as antiseptic, antioxidant, antifungal, antibacterial, antiviral, and analgesic, and also improves immunity.<sup>27-29</sup>

This systematic review was carried out on articles related to alternative therapies using natural ingredients on BMS patients published between 2012 to 2022. Seven articles were reviewed and analyzed. Assessment on risk of bias and method quality of the articles with RCT designs was carried out using the Modified Jadad Scale. Table 1 concluded that all articles had high quality. High-quality articles are used for qualitative analysis and treatment recommendations.<sup>17-24</sup>

Information on population and intervention in Table 2 indicated six types of herbal ingredients from seven articles, including capsaicin (two articles), *Aloe vera*, *catuama*, capsaicin, virgin olive oil, chamomile, and crocin (one article each). The table also showed that herbal medicine studies on BMS were conducted in several countries, with the majority of Spain, which comprises four studies. Most articles are derived from Europe, which is the continent with the highest prevalence of BMS. All studies used a double-blind RCT method with various sample sizes. The average age of the samples is within the fifth and seventh decades, with the majority within the sixth decade, which is the peak prevalent age.<sup>18-24</sup>

The article summary in Table 3 showed various herbal medicines given as an intervention to BMS patients. High heterogeneity appears in this systematic review as shown by the formula of herbal ingredients, method of application, and various intervention duration. The therapeutic activities of herbal medicine and its products are validated through laboratory test, ethnopharmacological surveys and clinical trials are regarded as the gold standard for analyzing therapeutic intervention.. Reviewed herbal medicines are proven to be beneficial and effective to reduce pain in BMS patients, thus increasing the quality of life of the patients.<sup>18-24,29</sup> According to Table 4, herbal medicine therapy decreased the severity and pain score in BMS, which also improved the patient's quality of life. The VAS has already been used for the intensity of symptoms pain and burning sensation in numerous studies.

The majority of people use VAS for assessing the severity of BMS. Patients assessed the severity of oral symptoms on a scale from 0 to 10, with 0 denoting no symptoms and 10 denoting unbearable pain symptoms intensity.<sup>30</sup>

Capsaicin (*Capsicum frutescens* L) is an active component found in chilies and is considered a potential herbal therapy for BMS.<sup>20,31,32</sup> Capsaicin has analgesic, anti-inflammatory effects on sensory neurons and salivary glands then increases saliva production.<sup>37</sup> The application of topical capsaicin can activate the Transient Receptor Potential Vanilloid-1 (TRPV-1) and modulate the transmission of nociceptor to release neuropeptides such as P substance, neurokinin A (NKA), calcitonin-gene-related peptide (CGRP), resulting in pain, thermal and mechanical sensitivity (hyperalgesia). The activation of TRPV-1 produces pain. However, repeated application makes the receptor not sensitive, thus blocking the signal to the primary afferent. This is estimated due to the mechanism of depleting neuropeptides, loss of membrane potential and inability of axonal transportation from the nerve terminal.<sup>20,22,26</sup> The studies by Petruzzi et al. (2004), Marino et al. (2010), and Eipsten et al. (1994) showed that capsaicin given topically and systemically can reduce the symptoms of BMS.<sup>31-33</sup>

*Catuama* is a Brazilian herbal product that has been used for more than 30 years to overcome mental and physical fatigue. It is derived from a mixture of four plant extracts, i.e., *Paullinia cupana* (guarana), *Trichilia catigua* (catuaba), *Zingiber officinalis* (ginger), and *Ptychopetalum olacoides*

(*muirapuama*).<sup>19</sup> No previous report is available concerning the use of *catuama* or its extract components in BMS. Separately, the extract components are known to have analgesic, antibacterial, and vasorelaxant effects. Scientific evidence on animals showed that *catuama* acts as an antidepressant, antinociceptive, and vasorelaxant. The working mechanism of *catuama* is not completely known. However, dopaminergic, serotonergic, nitric oxide and opioid pathways might be involved. The current hypothesis showed that *catuama* can reduce the burning sensation in BMS caused by psychological disorders and neuropathic changes.<sup>19,34</sup>

*Aloe vera Barbadosensis* is a member of the family *Liliacea*. The active ingredients in aloe vera are anthraquinones, saponins, glucomannan and acemanan.<sup>18,35</sup> A previous clinical test indicated that topical *Aloe vera* is proven to be beneficial in the healing process of burns, psoriasis, and oral lichen planus (OLP). Topical *Aloe vera* can inhibit the inflammatory process by interrupting an arachidonic acid pathway through cyclooxygenase. Another literature stated that *Aloe vera* also has anti-inflammatory effects by reducing the adhesion level of leukocytes and TNF- $\alpha$ . The combination of tongue protectors also acts in reducing the burning sensation. A tongue protector protects the mucosa from continuous friction to the teeth and/or dentures, isolates the tongue from changes in temperature, taste, and increased salivary flow, and is a reminder for the patient to refrain from engaging in parafunctional habits.<sup>18,36,37</sup>



Lycopene-enriched virgin olive oil (VOO) consists of VOO with the addition of 300 ppm of lycopene. Lycopene is a carotenoid synthesized by plants like tomatoes. Lycopene is known to have anti-inflammatory, antiapoptotic, and antioxidant effects. A previous study showed the benefits of lycopene in oral disease therapy, such as oral cancer, and precancer lesions such as oral submucous fibrosis, oral lichen planus, and leukoplakia. VOO contains various polyphenols and tocopherols useful for oxidative stress. The combination of VOO and lycopene is known to provide a synergic antioxidant effect and improve bioavailability. Topical application of Lycopene-enriched VOO is expected to protect the peripheral neurons of oral mucosa from oxidative stress, while VOO provides a lubricative effect.<sup>21,38</sup>

*Chamamelum nobile* (Chamomile) is a member of the family *Asteraceae* or *Compositae*. Chamomile contains various active flavonoids and terpenoid-rich essential oils such as alpha-bisabolol, azulene, matricin, and chamazulene. The contents provide analgesic, anti-inflammatory, antioxidant, antibacterial, and antifungal effects and improvement to the immune system. Chamazulene has anti-inflammatory effects by inhibiting the synthesis of leukotriene B4 and arachidonic acid peroxidation in neutrophils. Flavonoid also has anti-inflammatory and analgesic effects by inhibiting endogenous prostaglandin E2 in RAW 264.7 macrophages, which is a selective COX-2 inhibitor. A previous study showed that the use of chamomile gargle is effective as therapy for aphthous lesions,

gingivitis, laryngitis, oral mucositis, and periodontal diseases.<sup>23,39</sup>

Crocin is one of the primary substances from the plant *Crocus sativus* L. or saffron. Psychological effects such as depression and anxiety are known to be associated with BMS severity. Various studies showed that saffron extract can significantly reduce symptoms of depression and affect chemical transmitters such as serotonin, norepinephrine, and dopamine. Crocin is a carotenoid substance that produces a dark red color in the crocus flower, which acts as the primary bioactive component for antidepressant. Several tests on animals showed neuroprotective effects from crocin through increased signaling from brain-derived neurotrophic factors and inhibition from serotonin selective reuptake by inhibitors in synapses such as fluoxetine. This is similar to the working mechanism of citalopram.<sup>24,40</sup>

While four of the seven products stated that some patients disobeyed instructions and discontinued their medication because they felt uncomfortable, three of the seven products mentioned patient compliance in finishing treatment with the intervention products given. Several articles stated that the use of lycopene-enriched VOO spray, chamomile gel, aloe vera gel, and crocin tablets had no side effects in their studies. Three articles, however, reported that side effects include burning sensation, nausea, itchy and sore throat from the use of capsaicin gel and rinse furthermore catauma capsule were reported minimum side effect include sleepiness, weight

gain, insomnia, and symptom exacerbation within the first week of intervention.<sup>18–24,29</sup>

Based on the authors' defined the outcome parameters, herbal medicine products has proven to be an effective BMS treatment option. Catuama capsule and capsaicin rinse showed a significant differences in reduce pain. All herbal products showed a decrease in pain scores with the highest reduction in crocin, Aloe vera, and catuama. All articles reviewed in this systematic review have low risk of bias. This showed that plausible bias could not significantly change the results.<sup>18–24,29</sup> The limitation of this review is subjective assessments and the high heterogeneity of studies. This systematic review is expected to be implemented as fundamental information for the development of future studies concerning the use of herbal medicines as an alternative therapy for BMS in the field of oral medicine.

## CONCLUSION

The existence of benefits from the administration of herbal medicine to reduce pain in BMS patients. Minimum side effects were found in capsaicin and catuama. Several pieces of evidence showed that herbal medicine can be used as an effective alternative therapy to improve symptoms of BMS.

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## CONFLICT OF INTEREST

No conflict of interest and financial disclosures were reported by the authors of this systematic review.

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