



Phytotherapy efficacy in alleviating burning mouth syndrome symptoms: A systematic literature review

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ABSTRACT

Objectives: To evaluate the efficacy and safety of phytotherapeutics medicines interventions for burning mouth syndrome (BMS) in randomised controlled trials.

Methods: This systematic review, registered in PROSPERO (CRD42023475271), was conducted in accordance with PRISMA guidelines. Search of PubMed, Scopus, Web of Science, Cochrane CENTRAL, BVS/IBECs, BDTD, SciELO, ScienceDirect, and grey literature (final search April 2025). RCTs in adults with BMS testing phytotherapeutics versus placebo/active control were included. Two reviewers extracted data and assessed risk of bias (RoB 2) and certainty of evidence (GRADE). When appropriate, effects were synthesized as between-group differences, otherwise, narrative synthesis was used.

Results: 10 RCTs ($n = 653$) met inclusion criteria. Women are 75.2 % of participants, treatment durations ranged 1–12 weeks. Capsaicin (rinse/gel/capsule), Catuama, and Kampo (Saiboku-to) showed greater pain reduction than control in individual trials. In contrast, chamomile gel, lycopene-enriched olive oil, Aloe vera, and Hypericum did not show superiority to placebo. Adverse events were generally mild.

Conclusions: Evidence for capsaicin (topical/oral) and Catuama is promising but low to moderate certainty due to small samples, heterogeneous formulations, and risk of bias concerns. Controlled studies involving a larger number of patients and longer follow-up are recommended.

Clinical relevance: Selected phytotherapeutics may reduce BMS pain with mostly mild adverse effects, but routine use is premature pending higher quality evidence.

1. Introduction

Burning Mouth Syndrome (BMS) is a chronic condition marked by a bilateral burning sensation in the oral mucosa, predominantly the tongue, palate, and lips, absent any visible lesions. It is classified as either primary, with no apparent cause, or secondary, when linked to local or systemic factors. Its aetiology is complex and multifactorial, it can be involving neuropathic, endocrine, and psychosocial mechanisms (Jääskeläinen and Woda, 2017; Ros Lluch et al., 2008). BMS occurs more

frequently in women, particularly at the postmenopausal age, and is commonly associated with a significant decline in quality of life, including emotional distress, sleep disturbances, reduced self-esteem, and impaired oral function (Aitken-Saavedra et al., 2021; Leuci et al., 2023).

Despite the wide range of pharmacological treatments employed for BMS, such as clonazepam, gabapentin (Neurontin), antidepressants, and antioxidants, the outcomes are inconsistent, with frequent adverse effects and no definitive efficacy across cases (Tan et al., 2022). This

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limited effectiveness has spurred interest in complementary therapies, like photobiomodulation, TENS, acupuncture and other non-pharmacological treatments (Cabras et al., 2021; Camolesi et al., 2022; Medeiros et al., 2023; Tan et al., 2022). Due to its accessibility, low cost, and potential to enhance treatment adherence. Herbal formulations including capsaicin, chamomile, catuama, and others, have demonstrated promising results in preliminary clinical studies (Banik et al., 2023; Spanemberg et al., 2012).

Among the search for less invasive therapies with minimal adverse effects, research into phytotherapeutics medicines for BMS has notably increased. This study aims to conduct a systematic review of the literature to assess the efficacy of medicinal plants in alleviating BMS symptoms, thereby providing scientific evidence to guide its rational use and inform future clinical investigations.

2. Material and methods

This study was conducted in accordance with the PRISMA guidelines (Page et al., 2021) and was prospectively registered on the PROSPERO platform under registration number CRD42023475271. A comprehensive and systematic search was carried out in the multiple electronic databases, including PubMed/Medline (U.S. National Library of Medicine), Scopus, Web of Science (WOS), Cochrane Library (Cochrane Database of Systematic Reviews / CENTRAL), BVS/IBECs (Virtual Health Library/Spanish Bibliographic Index in Health Sciences), BDTD (Brazilian Digital Library of Theses and Dissertations), SciELO (Scientific Electronic Library Online), and ScienceDirect. To enhance the strategy, grey literature was incorporated through manual screening of the first 100 titles in Google Scholar and OpenGrey, along with a bibliographic review of the references cited in the selected studies.

The final search was conducted in April 2025 using MeSH terms and related synonyms, adapted to each database. The following key terms were applied: (phytotherapy) AND (burning mouth syndrome) OR (oral dysesthesia OR stomatodynia OR glossodynia), aiming to comprehensively capture relevant scientific literature on the use of phytotherapy in treating Burning Mouth Syndrome (BMS). No language or publication date restrictions were imposed to maximize the inclusion of pertinent studies. Eligible studies involved patients diagnosed with BMS who had received interventions containing active compounds derived from medicinal plants.

The research question followed the PICO framework: Participants (patients with BMS), Intervention (phytotherapeutic treatments), Comparison (other treatments, placebo, or no treatment), primary outcomes (pain reduction) and secondary outcomes (quality of life and adverse events). Only randomised clinical trials were considered. Data extraction included dosage, route of administration, treatment duration, adverse effects, and follow-up.

Study selection was conducted in multiple stages. Initially, duplicate records were removed using EndNote X9 (Thomson Corporation, USA). Subsequently, titles and abstracts were screened via the Rayyan QCRI™ platform (Qatar Computing Research Institute), where researchers JPAS, JCS, and RSH independently reviewed the entries. Articles meeting the inclusion and exclusion criteria were selected by consensus, after which full texts were retrieved for comprehensive analysis. This systematic review excluded letters to the editor, narrative reviews, case reports, clinical cases, short communications, prospectives or retrospective studies, editorials, books, and manuals, focusing exclusively on studies providing robust clinical evidence on phytotherapeutic treatments for BMS.

During data extraction, key information was recorded for each study, including author, country, year of publication, study design, sample size, mean age, tools used to assess pain and/or depression, treatment duration, follow-up period, outcomes, adverse effects, and conclusions. Data were organized in Microsoft Excel spreadsheets (version 2016, USA), with a distinction between qualitative and quantitative variables.

The methodological quality and risk of bias of the included studies

were independently assessed by two reviewers (JAS and JCS) using the Cochrane Risk of Bias 2 (RoB 2) (Sterne et al., 2019) and the GRADE approach to assess the certainty of evidence (Guyatt et al., 2011). In cases of disagreement, a third reviewer (RSH) was consulted to reach a final decision. This process ensured the rigor and transparency of the evaluation of studies included in this systematic review.

3. Results

3.1. PRISMA flow and study characteristics

The systematic search in the multiple databases identified 2253 records (Fig. 1). Following the application of inclusion and exclusion criteria based on PRISMA guidelines and the PICOS framework (Page et al., 2021), 10 studies met the established methodological standards and were included. A detailed summary of these studies is provided in Table 1 and 2, while excluded studies, along with the reasons for exclusion, are listed in Table 3.

The selected studies, published between 1998 and 2019, originated from three continents: Europe (7 studies), specifically Spain (Cano-Carrillo et al., 2014; López-Jornet et al., 2013; Silvestre et al., 2012; Valenzuela et al., 2016) and Italy (Marino et al., 2010; Petruzzi et al., 2004; Sardella et al., 2008); Asia (2 studies), one from Japan (Bessho et al., 1998) and another from Iran (Pakfetrat et al., 2019); and South America, with a single study from Brazil (Spanemberg et al., 2012).

Regarding methodological design, all included studies were randomised; ten clinical trials (Alajbeg et al., 2024; Bessho et al., 1998; Cano-Carrillo et al., 2014; López-Jornet et al., 2013; Marino et al., 2010; Sardella et al., 2008; Pakfetrat et al., 2019; Silvestre et al., 2012; Spanemberg et al., 2012; Valenzuela et al., 2016) and one pilot trial (Petruzzi et al., 2004).

3.2. Sample characteristics

The total sample size of the studies comprised 653 participants, aged between 22 and 80 years, with mean ages ranging from 54.6 ± 6.1 to 73.45 ± 11.10 years. A marked predominance of females was observed, accounting for 75.2 % of cases (491 women). Pain and burning sensations were primarily localized to the tongue, palate, lips, oral mucosa, gingiva, oropharynx, and floor of the mouth. Symptom duration ranged from 3 months to 5 years and treatment durations ranged from 25 min to 12 weeks.

3.3. Phytotherapy characteristics

Five studies reported a significant reduction in pain symptoms ($p < 0.05$), including the use of capsaicin in capsule, rinse, or gel form (Marino et al., 2010; Petruzzi et al., 2004; Silvestre et al., 2012); catuama capsules (Spanemberg et al., 2012); and Kampo medicine capsules (Bessho et al., 1998). In contrast, five studies, 2 % chamomile gel (Valenzuela et al., 2016), crocin (saffron) (Pakfetrat et al., 2019), *Hypericum perforatum* extract capsules (Sardella et al., 2008), a lycopene-enriched virgin olive oil spray (Cano-Carrillo et al., 2014), and *Aloe vera barbadensis* gel combined with a lingual protector (López-Jornet et al., 2013), showed no significant efficacy (Table 2).

Adverse effects were reported in five studies, including gastric pain (Petruzzi et al., 2004), somnolence and weight gain (Spanemberg et al., 2012), headache (Sardella et al., 2008), and digestive disorders such as loss of appetite and diarrhea (Bessho et al., 1998) (Table 1).

3.4. Quality of life and anxiety

Three of the eleven studies assessed the treatment impact on quality of life using instruments such as the OHIP-14, OHIP-49, DN4, and SF-36 (Cano-Carrillo et al., 2014; López-Jornet et al., 2013; Valenzuela et al.,

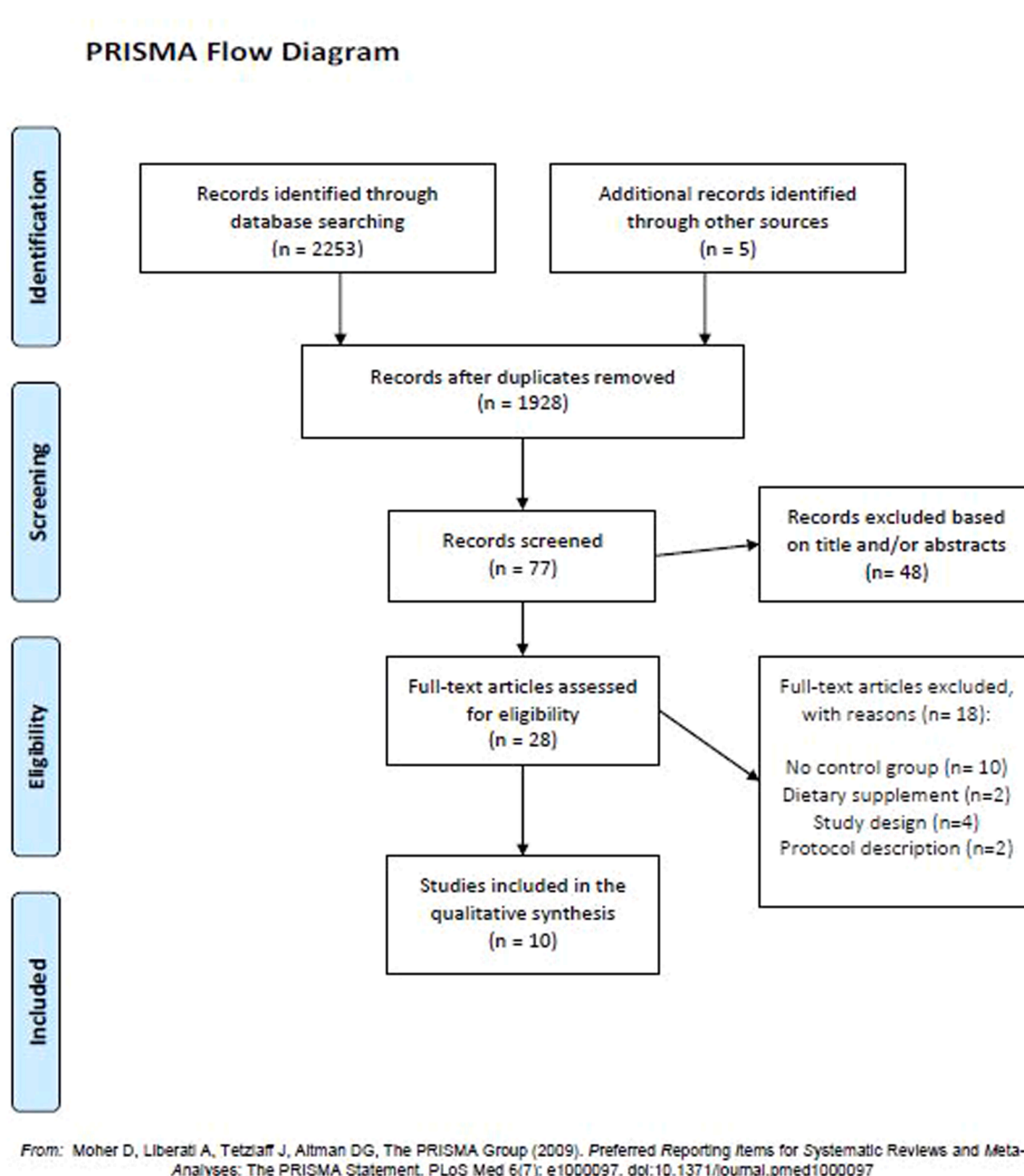


Fig. 1. PRISMA flow diagram.

2016). The Hospital Anxiety and Depression Scale (HADS) was employed in three studies (Cano-Carrillo et al., 2014; López-Jornet et al., 2013; Sardella et al., 2008).

3.5. Study quality and certainty of evidence

The RoB 2 risk assessment, revealing a low risk for 8 of the 10 included studies (Supplementary 1) and the and the GRADE assessment identify 2 studies with low certainty for pain reduction with capsaicin and 1 study for moderate, while for other treatments like Catuama, Kampo (Saiboku-to), chamomile, lycopene-enriched olive oil, Aloe vera, and Hypericum, showed a moderate certainty.

4. Discussion

This systematic review aimed to assess the efficacy of phytotherapy

in alleviating BMS symptoms. This chronic condition of multifactorial origin that markedly impairs quality of life (Carreño-Hernández et al., 2021). Of the patients included, 75.2 % were women with a mean age above 50, predominantly postmenopausal. This finding highlighting the suspected association between BMS and hormonal changes characteristic of this stage (Perdomo Lovera and Chimenos Klistner, 2003). The estrogen and androgen levels decline affects pain modulation by altering hormone receptors located in the oral mucosa and within central and peripheral nociceptive pathways (Seol and Chung, 2022).

The studies reporting significant pain reduction employed various active compounds, each with distinct mechanisms of action. Capsaicin, for instance, activates TRPV1 receptors on nociceptive C fibres, initially triggering the release of substance P and other pro-inflammatory mediators. This is followed by neuronal desensitisation and neurotransmitter depletion, resulting in a transient reduction in pain sensitivity (Epstein and Marcoe, 1994; Ricken et al., 2021; Sharma et al., 2013;

Table 1

Characterization and descriptive results of the articles included. N, Patients number; RCT, Randomised Clinical Trials.

Author, Year; Country	Study design	Treatment	Side effects (N)	Main findings	RoB 2 assessment
Petruzzi M. et al. 2004; Italy	Pilot - RCT	Group 1 = Oral capsaicin 0,25 % capsules; Group 2 = placebo.	Gastric pain (Cabras et al., 2021)	The results for Capsaicin were statistically superior to placebo.	Low
Marino R. et al. 2010; Italy	RCT	Group 1 = capsaicin 250 mg chilli powder / 50 ml oral rise, 3x/day; Group 2 = ALA 400 mg, 2x/day; Group 3 = lysozyme-lactoperoxidase (Biotene®) oral rinse, 5x/day; Group 4 = mouthwash with boric acid 0.05 g dissolved in 100 ml of distilled water, 3x/day.	Not reported	A statistically significant reduction in VAS at the end of the study was found only in group 1. No statistically significant difference in VAS when the four groups were compared with each other.	Low
Silvestre F.J. et al. 2012; Spain	RCT	Group 1 = mouth rinse with 0.02 % of capsaicin, 3 × /day for 30 s at volumes of 15 ml; Group 2 = placebo, 3 × /day for 30 s at volumes of 15 ml.	Burning sensation after using the substance (Jääskeläinen and Woda, 2017)	The results for Capsaicin were statistically superior to placebo.	Low
Spanemberg J.C. et al. 2012; Brazil	RCT	Group 1: herbal drug Catuama (310 mg), 2 × /day; Group 2: placebo (lactose), 2 × /day.	Insomnia (Ros Lluch et al., 2008), drowsiness and weight gain (Ros Lluch et al., 2008).	The results for Herbal drug Catuama was statistically superior to placebo.	Low
Valenzuela S. et al. 2015; Spain	RCT	Group 1: oral gel <i>chamaemelum nobile</i> 2 %, 2 × /day for 30 s.; Group 2: placebo, 2 × /day for 30 s.	Not reported	Symptoms are significantly reduced in both groups. No significant differences found between the groups.	Low
Pakfetrat A. et al. 2019; Iran	RCT	Group 1: oral administration, <i>Crocus sativus</i> L. (saffron) 15 mg, 2x/day; Group 2: Citalopram, first week 10mg/daily and 20mg/daily after a week.	Not reported	Symptoms are significantly reduced in both groups. No significant differences found between the groups.	Low
Sardella A. et al. 2008; Italy	RCT	Group 1: <i>Hypericum perforatum</i> extract, capsules 300 mg, 3 × /day; Group 2: placebo, 3 × /day.	Headache (Ros Lluch et al., 2008)	Symptoms are significantly reduced in both groups. No significant differences found between the groups.	Moderate
Cano-Carrillo P. et al. 2014; Spain	RCT	Group 1: Lycopene-enriched (300 ppm) extra virgin olive oil 1.5 ml spray, 3 × /day Group 2: placebo (water and dye), 3 × /day	Not reported	Symptoms are significantly reduced in both groups. No significant differences found between the groups.	Low
López-Jornet P. et al. 2013; Spain	RCT	Group 1: tongue protector alone, 3 × /day; Group 2: tongue protector + .5 mL of <i>Aloe vera</i> 70 % oral gel, 3 × /day; Group 3: tongue protector + placebo, 3 × /day.	Not reported	Symptoms are significantly reduced in the groups. No significant differences found between the groups.	Low
Bessho K. et al. 1998; Japan	RCT	Group 1: Oral administration Kampo (Sai-boku-to) 2.5 g, 3x/day. Group 2: Oral administration diazepam 2 mg + 3 tablets of vitamin B complex, 3x/day.	Loss of appetite (Aitken-Saavedra et al., 2021) and diarrhea (Ros Lluch et al., 2008)	At the final evaluation the results Kampo was statistically superior to control group.	Moderate

Yang and Zheng, 2017). However, this analgesic effect is reversible, as receptor function is restored upon discontinuation of treatment (Spanemberg et al., 2011). Silvestre et al. (Silvestre et al., 2012) and Marino et al. (Marino et al., 2010) observed a marked improvement in pain scores with capsaicin oral rise when comparing baseline values with those at the end of follow-up, like a Petruzzi et al. (Petruzzi et al., 2004), who reported significant improvement in the capsaicin group compared with the placebo group.

Catuama, is a Brazilian herbal product formulated from medicinal plant extracts: guarana, catuaba, ginger, and muirapuama, act on serotonergic and dopaminergic receptors, improving mood and decreasing pain perception through central modulation of the emotional response to nociceptive stimulus (Linco Olave et al., 2016; Liu et al., 2018). Its effects may parallel those of tricyclic antidepressants, which increase synaptic availability of serotonin and noradrenaline neurotransmitters involved in spinal inhibition of pain signals (Campos et al., 2004). Spanemberg et al. (Spanemberg et al., 2012) reported a significant reduction in pain following eight weeks of treatment, in the comparison between the catuama group and the placebo group.

Other treatments, such as olive oil enriched with lycopene, exert their effects by reducing oxidative stress and local inflammation (Garrido et al., 2013). Lycopene, a carotenoid with potent antioxidant

properties, in conjunction with the polyphenols and tocopherols present in olive oil, neutralises reactive oxygen species that may sensitise nociceptors, particularly within inflamed mucosal tissues (Garrido et al., 2013). Cano-Carrillo et al. (Cano-Carrillo et al., 2014) assessed the efficacy of lycopene-enriched olive oil and reported a significant reduction in pain when comparing baseline and final values, though the intervention failed to demonstrate superiority over placebo in reducing pain or symptoms.

Kampo medicine, a traditional Japanese herbal system originated in China. One of the Kampo formulations, Saiboku-to, have anti-inflammatory and antiallergic properties. Evidence suggests that this formula can inhibit the release of leukotriene C4 (LTC4) by eosinophils, mediators in allergic and inflammatory processes (Hirai et al., 1998). Additionally, Saiboku-to may exhibit anxiolytic properties, contributing to a reduction of anxiety symptoms (Maruyama et al., 1998). A characteristic of Kampo medicine is that its effects tend to manifest gradually. This is because the primary aim of Kampo is to improve the patient's constitution, with symptom relief occurring because of that underlying improvement. This gradual therapeutic response was also observed in the study by Bessho et al. (Bessho et al., 1998), where BMS was treated based on Kampo-specific diagnostic criteria, independent of the pathogenesis as defined by conventional Western medicine, resulting in

Table 2

Statistical results of included studies. M, Men; W, Women; VAS, Visual Analogue Scale; NRS, Numerical Rating Scale.

Author, Year; Country	Patients total	Gender (M:W)	Patients group	Assessment method	Initial symptomatology	Final symptomatology	Treatment duration	Follow-up symptomatology	Time to follow-up	p-value
Petruzzi M. et al. 2004; Italy	50	14:36	Group 1 = 25; Group 2 = 25.	VAS	Group 1: Score 8–10: (15 patients, Score 4–7 (8 patients) and Score 0–3 (2 patients); Group 2: Score 8–10: (13 patients, Score 4–7 (7 patients) and Score 0–3 (5 patients)	Group 1: Score 8–10: (1 patients, Score 4–7 (3 patients) and Score 0–3 (21 patients); Group 2: Score 8–10: (13 patients, Score 4–7 (6 patients) and Score 0–3 (6 patients)	1 month	–	–	0.001**
Marino R. et al. 2010; Italy	56	6:50	Group 1 = 14; Group 2 = 14; Group 3 = 14; Group 4 = 14.	VAS	Group 1 = 6.1 ± 2.2; Group 2 = 5.8 ± 2.2; Group 3 = 5.3 ± 2.0; Group 4 = 4.8 ± 2.3	Group 1 = 2.9 ± 2.6; Group 2 = 3.7 ± 2.5; Group 3 = 3.6 ± 2.4; Group 4 = 5.3 ± 2.2	8 weeks	Group 1 = 2.9 ± 3.0; Group 2 = 4.1 ± 2.9; Group 3 = 4.0 ± 2.8; Group 4 = 5.5 ± 2.4	2 months	0.01*
Silvestre F.J. et al. 2012; Spain	23	4:19	Group 1 = 23; Group 2 = 23.	VAS	–	–	1 week	–	–	0.002*
Spanemberg J.C. et al. 2012; Brazil	60	7:53	Group 1 = 30; Group 2 = 30.	NRS	Group 1 = 6.87 ± 2.16; Group 2 = 7.17 ± 2.0	Group 1 = 3.33 ± 2.56; Group 2 = 5.47 ± 2.76	8 weeks	Group 1 = 3.33 ± 2.49; Group 2 = 5.73 ± 2.71	12 weeks	8 weeks 0.003**; 12 weeks 0.001**
Valenzuela S. et al. 2015; Spain	57	7:50	Group 1 = 31; Group 2 = 26.	VAS	Group 1 = 7.4; Group 2 = 6.9	Group 1 = 6.7; Group 2 = 6.2	1 month	–	–	0.229**
Pakfetrat A. et al. 2019; Iran	47	15:32	Group 1 = 26; Group 2 = 21.	VAS	Group 1 = 8.9 ± 1.20; Group 2 = 9.0 ± 1.30	Group 1 = 1.1 ± 1.57; Group 2 = 1.2 ± 1.67	11 weeks	–	–	0.981**
Sardella A. et al. 2008; Italy	39	4:35	Group 1 = 19; Group 2 = 20.	VAS	Group 1 = 6.8; Group 2 = 7.5	Group 1 = 4.5; Group 2 = 6.2	12 weeks	–	–	0.221**
Cano-Carrillo P. et al. 2014; Spain	50	–	Group 1 = 26; Group 2 = 24.	VAS	Group 1 = 9 (5–10); Group 2 = 9 (6–10)	Group 1 = 6 (3–10); Group 2 = 6 (2–10)	12 weeks	–	–	0.000* 0.574**
López-Jornet P. et al. 2013; Spain	71	8:63	Group 1 = 25; Group 2 = 24; Group 3 = 22.	VAS	Group 1 = 9; Group 2 = 6; Group 3 = 7.75.	Group 1 = 5; Group 2 = 3.25; Group 3 = 6.	3 months	–	12 weeks	0.236* 0.210**
Bessho K. et al. 1998; Japan	200	47:153	Group 1 = 100; Group 2 = 100.	VAS	–	–	3 months	–	–	<0.01*

* p-value of the comparison between baseline vs. final values in the study group (within-group).

** p-value of the final values in the study group vs. control group (between-group). Significant for the study group.

***p-value of the final values in the study group vs. control group (between-group). Significant for the control group.

significant reduction in symptoms and pain compared to control.

Chamomile exerts its effects through GABA-A receptor modulation, producing a calming and anxiolytic response, while flaxseed provides polysaccharides that mimic salivary mucins, thereby reducing friction and mechanical stimulation of the oral mucosa (Aitken-Saavedra et al., 2020; Milani et al., 2018). Although Aitken-Saavedra et al. (Aitken-Saavedra et al., 2020), in a study excluded from this review due to the absence of a control group, reported that chamomile and flaxseed rinses combined anti-inflammatory, sedative, and lubricating properties, Valenzuela et al. (Valenzuela et al., 2016) did not observe a significant reduction in pain compared to placebo.

However, other active compounds, such as 70 % Aloe vera oral gel

(López-Jornet et al., 2013), *Crocus sativus* L. (saffron) (Pakfetrat et al., 2019), and *Hypericum perforatum* (Sardella et al., 2008), failed to demonstrate significant pain or symptom reduction compared to placebo or control group.

Only a few studies conducted follow-up assessments post-treatment, and authors reported a recurrence of symptoms, although with a reduced intensity (López-Jornet et al., 2013; Marino et al., 2010; Spanemberg et al., 2012). This suggests that the therapeutic effect of these substances may be transient. Consequently, the exploration of intermittent or prolonged treatment regimens appears warranted, given the chronic and relapsing nature of BMS.

Recent studies have explored the relationship between the oral

Table 3
Excluded studies. RCT; Randomised Clinical Trial.

Author, Year; Country	Study design	Treatment	Reason for exclusion
León-Espinoza S. et al. 2004; Spain.	Pilot study	Capsaicin 0025 mg, oral gel	- Study design - Without control group
Spanemberg J.C. et al. 2011; Brazil.	Prospective study	Capsaicin 0.02 % mouth rinse	- Study design - Without control group
Jørgense M.R. et al. 2016; Denmark.	RCT - Crossover	Capsaicin 0,01 mg or 0025 mg, oral gel	Without control group
Lauritano D. et al. 2003; Italy.	Short communication	Capsaicin 0,25 mg, capsules	Study design
Scardina G.A. et al. 2006; Italy.	Short communication	Capsaicin topical application	- Study design - Without control group
Azzy L. et al. 2017; Italy.	Short communication	Capsaicin mouth rinse	- Study design - Without control group
Gambino A. et al. 2021; Italy.	Prospective study	Extract 1 g of cannabis in 10 g of olive oil.	Study design
Aitken-Saavedra J. et al. 2020; Brazil.	Preliminary report	Chamomile (<i>Matricaria chamomilla</i> L.) Flower and Flax (<i>Linum usitatissimum</i> L.) mouth rinse	- Study design - Without control group
Milani et al. 2018; Brazil.	Case report	Chamomile (<i>Matricaria recutita</i>) mouth rinse	Study design
Okamoto H. et al. 2013; Japan.	Retrospective study	Kampo medicine	- Study design - Without control group
Hijikata Y. et al. 2008; Japan.	Clinical cases	Kampo medicine	- Study design - Without control group
Okayasu I. et al. 2023; Japan.	Case report	Kampo medicine	Study design
Ayuse T. et al. 2020; Japan.	RCT - protocol description	Kampo medicine - Goreisan	Protocol description
Gao Y. et al. 2024; China.	RCT	Danzhixiaoyao tablets + methylcobalamin tablets	Herbal in combination with dietary supplement
Hato H et al. 2021; Japan	Retrospective study	Rikkosan 2,5 g gargling	- Study design - Without control group
Petrović M. et al. 2021; Serbia	Preliminary report	Organic chokeberry juice (<i>Aronia melanocarpa</i>) mouth rinse	- Study design - Without control group
Ottaviani G. et al. 2019; Italy	Preliminary - RCT	Ultramicronised Palmitoylethanolamide (um-PEA) 600 mg microgranules, sublingual	Dietary supplement with therapeutic properties
Alajbeg I.Z. et al. 2024; Croatia	RCT	Capsaicin powder dissolving in ethanol 96 %. The capsaicin is applied to the dorsal tongue.	Probe pain/opiophin responses, not the therapeutic course.

microbiota and the pathophysiology of BMS. A reduction in bacterial alpha-diversity has been reported, along with an increase in genera such as *Streptococcus*, *Rothia*, *Prevotella*, and *Selenomonas*, which are associated with chronic inflammation, neuropathic pain, and comorbidities such as depression (Nagamine, 2024; Wu et al., 2024). These findings suggest that dysbiosis may contribute to both peripheral and central pain sensitisation. Although this perspective was not addressed in the studies included in this review, it represents an emerging field with therapeutic potential, where strategies such as probiotics or

antimicrobial modulators could be integrated into the management of BMS.

The reported adverse effects highlighting the importance of assessing the safety and tolerability of proposed phytotherapeutic treatments for BMS.

Finally, although three studies evaluated quality of life, no one are demonstrated a significant improvement. Given that BMS is associated with mood disorders, sleep disturbances, fatigue, and low self-esteem (Aitken-Saavedra et al., 2021; Gao et al., 2009), future research should incorporate quality of life as a core outcome in determining therapeutic success.

Using GRADE assessment, the certainty for pain reduction with capsaicin was rated low in 2 studies and moderate for 1 study, reflecting mixed results across small RCTs and imprecision, adverse events were generally mild, with low certainty. Based on singles small RCTs, Catuama, Kampo (Saiboku-to), chamomile, lycopene-enriched olive oil, Aloe vera, and Hypericum, showed a moderate certainty reduction in pain.

Among the limitations of this review, several factors can be highlighted; the variability in studies inclusion criteria, particularly in relation to the use of psychotropic medications and the presence of comorbidities, which complicates the comparison of results, absence of quality of life evaluation. Additionally, some studies do not differentiate between primary and secondary BMS, or do they not apply classifications such as those by Lamey & Lewis (Lamey and Lewis, 1989), limiting the ability to draw robust and generalisable conclusions. Lastly, the small sample size and the short or non-existent follow-up periods in the studies hinder the assessment of the efficacy of the proposed treatments.

5. Conclusión

Although some phytotherapeutics such as capsaicin and catuama, have demonstrated efficacy in pain reduction for BMS patients, their clinical use still requires more robust evidence. In contrast, agents such as chamomile, lycopene, Aloe vera, and Hypericum have not shown superiority over placebo in controlled studies. The absence of standardised protocols, variability in dosages and formulations, and limited regulation hinder their implementation as a valid therapeutic option. Controlled studies involving a larger number of patients are recommended.

CRedit authorship contribution statement

Juan Aitken-Saavedra: Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Data curation, Conceptualization. Gisela Cristina Vianna Camolesi: Writing – review & editing, Resources, Methodology, Data curation. Rachel Estefanía Sánchez Hernández: Writing – original draft, Resources, Methodology, Formal analysis, Data curation. Ana Paula Neutzling Gomes: Writing – review & editing, Conceptualization. Juliana Cassol-Spanemberg: Writing – review & editing, Supervision, Conceptualization.

Declaration of competing interest

The author is an Editorial Board Member/Editor-in-Chief/Associate Editor/Guest Editor for this journal and was not involved in the editorial review or the decision to publish this article.

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Supplementary materials

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