

## REVIEW ARTICLE

### Effectiveness of Kampo medicine in the treatment of Glossodynia – A Systematic Review

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#### ABSTRACT:

**Aim:** To assess the effectiveness of Kampo medicine in the treatment of Glossodynia. **Methods:** A systematic review of controlled trials and clinical trials were performed. Thirty-four articles were retrieved from electronic and hand searches, and four studies were included in the systematic review. The systematic review, the intervention and outcomes were assessed in the studies included in the systematic review. In addition, a literature review was performed using Pubmed, PMC, Science Direct, Wiley Online Library, Cochrane Library, and using keywords "Kampo medicine and Glossodynia". According to PRISMA guidelines, the MeSH terms were altered in each search engine. **Result:** In this systematic review, four studies were included: randomized controlled trials and clinical trial studies. They were studies performed in different countries. Among the four trials, three were found statistically significant, but further studies should be done to prove the effectiveness of Kampo medicine and Glossodynia. **Conclusion:** There is a lack of corroboration to show the efficacy of Kampo medicine for Glossodynia. Therefore, further clinical studies and control trials should be done to assess the effectiveness of Kampo medicine for Glossodynia.

**Keywords:** Glossodynia, Kampo medicine, clinical trials

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#### INTRODUCTION

The term "glossodynia" (GD) is derived from the Greek "glossa" for tongue and "odyne" for pain. <sup>[1]</sup> This condition is also called Painful tongue. This is a pathological condition characterized by persistent pain in the tongue not particular to any organic cause. <sup>[2]</sup> Various local and systemic conditions have been associated, like Diabetes, Trigeminal neuralgia, Nutritional deficiencies (Zinc, Iron, Vitamin B12, folate), Hypothyroidism, Periodontal diseases, Xerostomia, and Psychogenic factors. Most cases have been associated with psychogenic factors like emotional disturbance and cancerophobia. In contrast, Temporomandibular joint disorders and electro galvanic discharge occurring between two dissimilar metallic restorations have also been associated in some instances. <sup>[3]</sup> The age of onset is generally between the 5<sup>th</sup> and 7<sup>th</sup> decades of life, rarely seen

before the 4<sup>th</sup> decade and rarely in children and adolescents. <sup>[1]</sup> Clinically, the tissues appear normal, and no visible lesion was present. This condition is mostly described as a symptom.

The primary step in the management of Glossodynia is identifying and correcting the suspected cause. The second step in this direction is to relieve the symptoms. Various therapeutic agents have been used, such as topical anaesthetics, analgesics, smooth- and skeletal-muscle relaxants, sedatives, antibacterial and antifungal agents, antihistamines, vitamins, enzyme digestants, CNS stimulants, salivary stimulants, vasodilators, and sex hormones.

Kampo, the branch of traditional Japanese herbal medicine, is a Kampo, a type of "Oriental medicine" that has been the backbone of Japanese treatment for more than ten centuries. It was introduced to Japan

from ancient China via Korea or directly around 552AD.

The term “Oriental medicine” refers to systems of medicine that originated in Oriental countries, such as Traditional Chinese Medicine, Korean medicine (Koryo medicine), and Ayurveda (traditional Indian medicine). Kampo medicine has been becoming official since the 1970s and is currently used by about 85% of the practitioners in Japan. The main difference between Western and Kampo medicine is the number of active ingredients in a drug. While the former generally comprises a single active ingredient, the latter consists of more than one active ingredient.<sup>[4,5,6]</sup> The working of Kampo medicine is based on the "Yin-Yang Theory", which implies that the world consists of an opposing axis of Yin or "non-resistant" and Yang or "resistant". It is this axis that maintains the balance of the working of nature. When it comes to the body, each internal organ is divided into Yin or Yang, and the patient is treated such that the Ying-Yang balance is achieved, that is, homeostasis.<sup>[7]</sup>

According to Kampo medicine, disease results from a disorder of harmony between the spirit and the body. The various physiological functions that maintain homeostasis are called Shoki or healthy. In contrast, Ki Shoki refers to the body's defence mechanism against various diseases and its healing capacity. Natural healing occurs to seek the harmony of Ki, Ketsu, and Sui (vital energy, blood circulation, and aqua). The factors that disturb homeostasis are Ja or Byoja or stress or pathogen. The origin of a disease can either be endogenous or exogenous.<sup>[8]</sup>

Various studies are being conducted on using Kampo medicine in different dental conditions. According to one such study, around 50-80% of University clinics indicate Kampo medicine for conditions such as Xerostomia, Temporomandibular disorders, Tongue pain, and Oral cancer. In contrast, private clinics prescribe it for gingivitis, toothache, and periodontal diseases. A few of the most frequently used Kampo medicine formulations, especially by private clinics, are Haino-san-kyu-to, Oren-gedoku-to, and Hochu-ekki-to. However, the use of these formulations varies according to the patient's chief complaint.<sup>[9]</sup> Hence, this study aims to assess the treatment for

Glossodynia using Kampo medicine as one of the interventional arms of the studies included.

## **METHODOLOGY**

### **SEARCH STRATEGY**

This systematic review was reported by the Preferred Reporting Items for Systematic reviews and Meta-Analysis.

Published results on the Effectiveness of Kampo medicine in treating Glossodynia, including original articles and research papers in databases such as Pubmed, PMC, Science Direct, Wiley Online Library, and Cochrane Library, were taken into the study. "Kampo medicine AND Glossodynia" were MeSH terms used. According to the PRISMA guidelines, the MeSH terms were altered in each search engine.

### **ELIGIBILITY CRITERIA**

#### **INCLUSION CRITERIA**

- Studies with randomized controlled trials
- Full-text articles
- Studies conducted between 1998-2020

#### **EXCLUSION CRITERIA**

- Pilot studies
- Animal studies
- Studies without articles in the English language.

## **RESULTS**

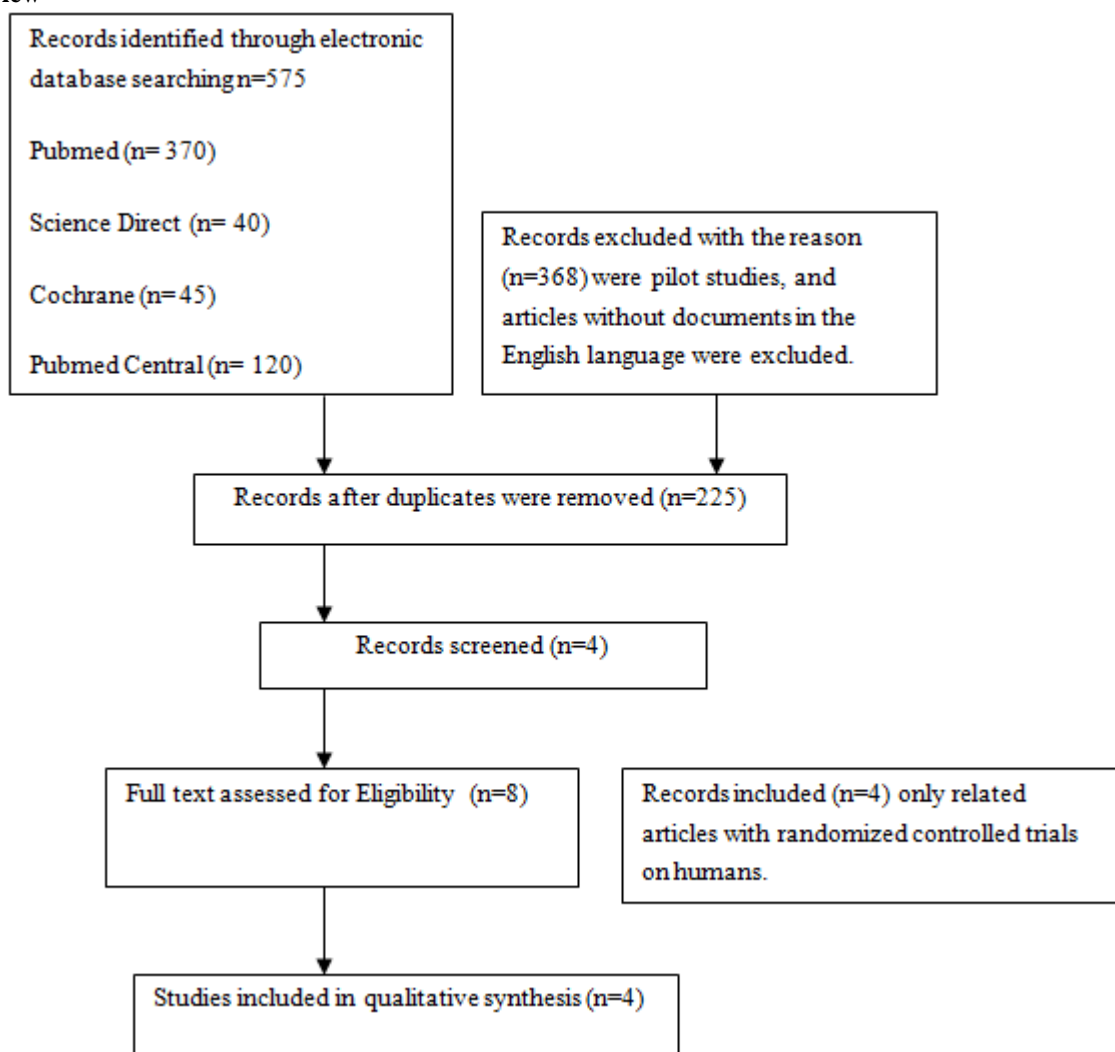
The search yielded 34 articles, and four articles were assessed individually among these eligible articles. Three tables were included. Figure 1 depicts reports identified, screened, assessed for Eligibility, excluded and included for the review.

Table 1 shows the elements of the systematic review. The following characteristics were studied: Author name, year of study, sample size duration and the intervention. The trials either used Kampo medicine with the conventional treatment or Kampo medicine as the only treatment option.

Table 2 depicts the effect measure and results of the trials conducted.

Table 3 shows the bias analysis of the included studies, categorised as high, low and unclear risk of Bias.

**Figure 1: Flow diagram showing the number of studies screened, assessed and identified for systematic review**



**Table I: Characteristics of the treatment in the included studies**

Author	Year	Sample Size	Duration	Interventions
Okayasu et al. <sup>[10]</sup>	2020	15	Seven months	In addition to the current treatment, Goreisan was also administered to patients who provided informed consent to examine the therapeutic effect before and after administration
Ayuse et al. <sup>[11]</sup>	2020	90	12 weeks	Test group: Goreisan will be taken for 12 weeks with conventional treatment. Control group: Received the standard treatment (Western medicine administration).
Bessho et al <sup>[12]</sup>	1998	200	3months	Test group: Oral administration of 2.5 g of Sai-Boku 3 times per day (before meals) for three months was prescribed. Control group: Oral administration of 2 mg of diazepam with three tablets of vitamin B complex daily (after meals) for three months was prescribed.
Hideki Okamoto <sup>[13]</sup>	2013	90		Five years The majority of the 39 patients stopped conventional medications based on Kampo treatment, and the remaining patients' medications were not changed.

Table I shows the characteristics of the studies chosen for the systematic review. The following characteristics were studied: Author name, year of study, sample size duration and the intervention. The trials either used Kampo medicine with the conventional treatment or Kampo medicine as the only treatment option.

**Table II: Characteristics of outcome and effect measures**

Author Name	Year	Effect Measure	Results
Okayasu et al. <sup>[10]</sup>	2020	self-assessed Visual Analogue Scale (VAS) and a tongue perception test (QST)	A total of 57% of patients (8/14) demonstrated an "improved" result after two weeks of Goreisan administration.
Ayuse et al. <sup>[11]</sup>	2020	Visual analogue scale (VAS)	The degree of pain was evaluated using VAS. The verdict for VAS based on subjective symptoms, which is reduced by 20% or more, is "improved," and the others are "non-improved."
Bessho et al <sup>[12]</sup>	1998	Visual analogue scale (VAS)	The effective rate at the various term points for the Kampo group was as follows: 70% after one month, 85% after two months, and 92% after three months; for the control group, the rates were 74% after one month, 71% after two months, and 69% after three months,
Hideki Okamoto <sup>[13]</sup>	2013	" (NRSI)The 11-Point Numerical Rating Scale for Pain Intensity "	Out of 39 patients, 27 (69.2%) had their Glossodynia severity which was reduced by 20% or more, and 23 (59.0%) had their severity reduced by half or more (high responders)."Twelve (30.8%) patients had no improvement (non-responders),

Table II shows the characteristics of the outcomes and effect measures of the studies, included the systematic review. The following characteristics are mentioned: Author name, year, effect measure and results.

**Table III: Characteristics of bias in different studies taken for review**

Author Name	Random Sequence Generation	Allocation Concealment	Blinding Of Outcome	Incomplete Outcome (?)	Selective Bias
Okayasu et al. <sup>[10]</sup>	-	?	-	+	+
Ayuse et al. <sup>[11]</sup>	+	+	+	+	?
Bessho et al <sup>[12]</sup>	-	+	?	+	+
Hideki Okamoto <sup>[13]</sup>	-	?	-	+	+

+: Low risk of Bias; -: High risk of Bias; ?: Unclear risk of Bias

Table III shows the Bias in the study, which was categorized as high-risk Bias, low-risk Bias and unclear risk bias. According to Cochrane, the risk of Bias for randomized controlled trials was used for bias assessment.

**DISCUSSION**

Glossodynia, also known as Burning mouth syndrome, is a chronic or recurring burning sensation in the mouth that has no obvious cause. The tongue, gums, lips, inside of your cheeks, roof of your mouth (palate), or large areas of your mouth may be affected. The burning sensation can be as intense as scalding your mouth.

In this systematic review, four studies were considered to assess Kampo medicine's effectiveness in treating Glossodynia. Korean, Saibokuto, and Kampo decoction were utilized in these studies. Various scales, such as VAS, NRSI, and QST, were used in multiple studies to assess pain relief. Okayasu et al. conducted a randomized controlled trial with 15 patients for seven months. In addition to their current

treatment, Goreisan was also administered. 57% of patients reported a reduced burning sensation in the mouth after two weeks of Goresian administration.<sup>[10]</sup> Ayuse et al. <sup>[11]</sup> conducted a multicenter, randomized controlled trial with 90 patients for 12 weeks. In the experimental group, Goreisan was taken for 12 weeks in combination with conventional treatment. In the control group, patients received Western medicine administration. According to the evaluation of the Visual analogue scale, 20% of patients' pain was reduced after 12 weeks of Goreisan administration. The present study's main role was to assess Kampo medicine's effectiveness in relieving pain or burning sensations in patients. Compared with other interventions, Kampo medicine was the better administration for Glossodynia.<sup>[9]</sup>

Bessho et al. [12] conducted a randomized controlled trial with 200 patients for three months. For the patients in the Kampo group, oral administration of 2.5 g of Sai-Boku-to 3 times per day (before meals) for three months was prescribed. According to the Visual Analog Scale, the effective rate for the Kampo group was 70% after one month, 85% after two months, and 92% after three months. Comparison of Kampo medicine with other interventions resulted in statistically significant Kampo medicine reducing pain.

Hideki Okamoto [13] reported treating Glossodynia with Kampo medicine for nine patients. Only 69.2% of patients had reduced the severity of Glossodynia. The results should prompt with treatment outcomes was compared between the three studies statistically significant was noted in reducing the burning sensation.

In this systematic review, all four studies recommended that patients with Glossodynia should be given a course of Kampo medicine combination of many interventions for 12 weeks. Improvement was seen in all the levels of Glossodynia.

## CONCLUSION

The present systematic review reported that Kampo medicine might be capable of treating Glossodynia without any side effects. Most of the included studies exposed the improvement of relieving the burning sensation for patients with Glossodynia. Kampo medicine revealed statistically significant improvement in pain reduction and decreased burning sensation for glossodynia patients. Further clinical studies and control trials should be done to assess the efficacy of Kampo medicine for Glossodynia.

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