



# An Overview on Clinical Effectiveness of Curcumin in Oral Submucous Fibrosis

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## Abstract

Oral submucous fibrosis (OSMF) is the condition affecting the oral health characterized by restricted mouth opening. This condition greatly interferes with the patient's quality of life. It is becoming a major health issue in Indian population mainly due to the habit of areca nut chewing. Some cases of OSMF have the tendency to progress into malignancy. No definitive treatment is available for this condition at present. The objective of this study was to analyse the clinical efficacy of curcumin in OSMF based on the available literature. The articles published in PubMed and Cochrane from the duration of 2011 to 2021 were searched and reviewed for the expected outcome. The review was suggestive of the significant result of the curcumin in oral submucous fibrosis especially in symptoms like restricted mouth opening and burning sensation. Multicentric studies with large sample size and long duration of follow ups are needed to emphasize the effect of curcumin in OSMF.

**Keywords:** Turmeric, OSMF. Oral health, restricted mouth opening

## 1. Introduction

Oral submucous fibrosis is the condition of buccal mucosa characterized by abnormal collagen deposition causing ulceration, burning sensation, xerostomia and restricted mouth opening. It is becoming a major health issue in India having prevalence rate of 6.42 per 1000.<sup>[1]</sup> There are multiple causative factors for OSMF like areca nut chewing spicy food consumption, especially chilly, nutritional deficiencies etc.<sup>[2]</sup> Chewing betel nut

and tobacco together increases the incidence of OSF.<sup>[3]</sup> In Indian population this combination is frequently consumed now a days causing the increase in cases of OSMF. 1.5 to 15% cases of OSMF progress to malignancy hence indirectly contribute to significant mortality.<sup>[4]</sup> There is no definite treatment for OSMF at present. Various medical therapies are tried by different researchers like fibrinolytic agents, systemic, topical and intralesional vasodilators, enzymes, anti-oxidants, multivitamins, immunomodulators etc.<sup>[5]</sup> Various herbal medicines are used for the treatment of OSMF. Considering the pathophysiology of the disease, the herbs having anti-inflammatory, fibrinolytic, anti-oxidant and anti-cancer properties must be used to get the expected result. Curcumin has a promising result in OSMF due to all the above mentioned properties.

### 1.1 Properties of curcumin

Curcumin is a polyphenol compound which is isolated from ground rhizomes of the *curcuma longa* plant of *Zingiberaceae* family found in South Asia.<sup>[6]</sup> Curcumin reduces inflammation by lowering histamine levels and increasing the production of natural cortisone by adrenal gland.<sup>[7]</sup> Some researchers have shown that curcumin has a strong capability for scavenging superoxide radicals, hydrogen peroxide and nitric oxide from activated macrophages, reducing iron complex and inhibiting lipid peroxidation. It also has been shown to scavenge various reactive oxygen species produced by macrophages (including superoxide anions, hydrogen peroxide and nitrite radicals). These are the mechanisms by which curcumin exhibits its anti-oxidant properties.<sup>[8]</sup> Curcumin inhibits lipid peroxidation and checks cellular proliferation, hence reduces the rate of collagen synthesis. This mechanism acts as a fibrinolytic property.<sup>[9]</sup> Curcumin increases levels of vitamin C and E thus prevents lipid peroxidation and DNA damage by decreasing the oxidation stress, hence has an anti-cancerous effect.<sup>[10]</sup> Curcumin has been used by many researchers to treat OSMF and found a significant result in various symptoms like burning sensation, restricted mouth opening etc.

This review has been done to analyse the clinical effectiveness of curcumin in oral submucous fibrosis.

## 2. Methodology

Literature search was done on the databases PubMed and Cochrane with the terms curcumin in oral submucous fibrosis. The articles published in the duration from 2011 to 2021 in English language are selected.

### 2.1 Inclusion criteria

Only randomized control trials on use of curcumin in OSMF were included for this review.

## 2.2 Exclusion criteria

Case reports, case series, observational studies, systemic reviews and meta-analysis were excluded from the study

## 2.3 Selection of studies

After screening of the articles, full texts of all the selected articles were read and after excluding some articles as per eligibility criteria few articles were selected for quality assessment

## 2.4 Quality Assessment

Quality assessment of selected articles was done by the quality assessment tool designed by Effective Public Health Practice Project.<sup>[11]</sup> which consists of six components – selection bias, study design, confounders, blinding, data collection method, withdrawal and dropouts

## 2.5 Outcome Assessed

The primary outcomes, like burning sensation, mouth opening and cheek flexibility were assessed.

## 3. Result

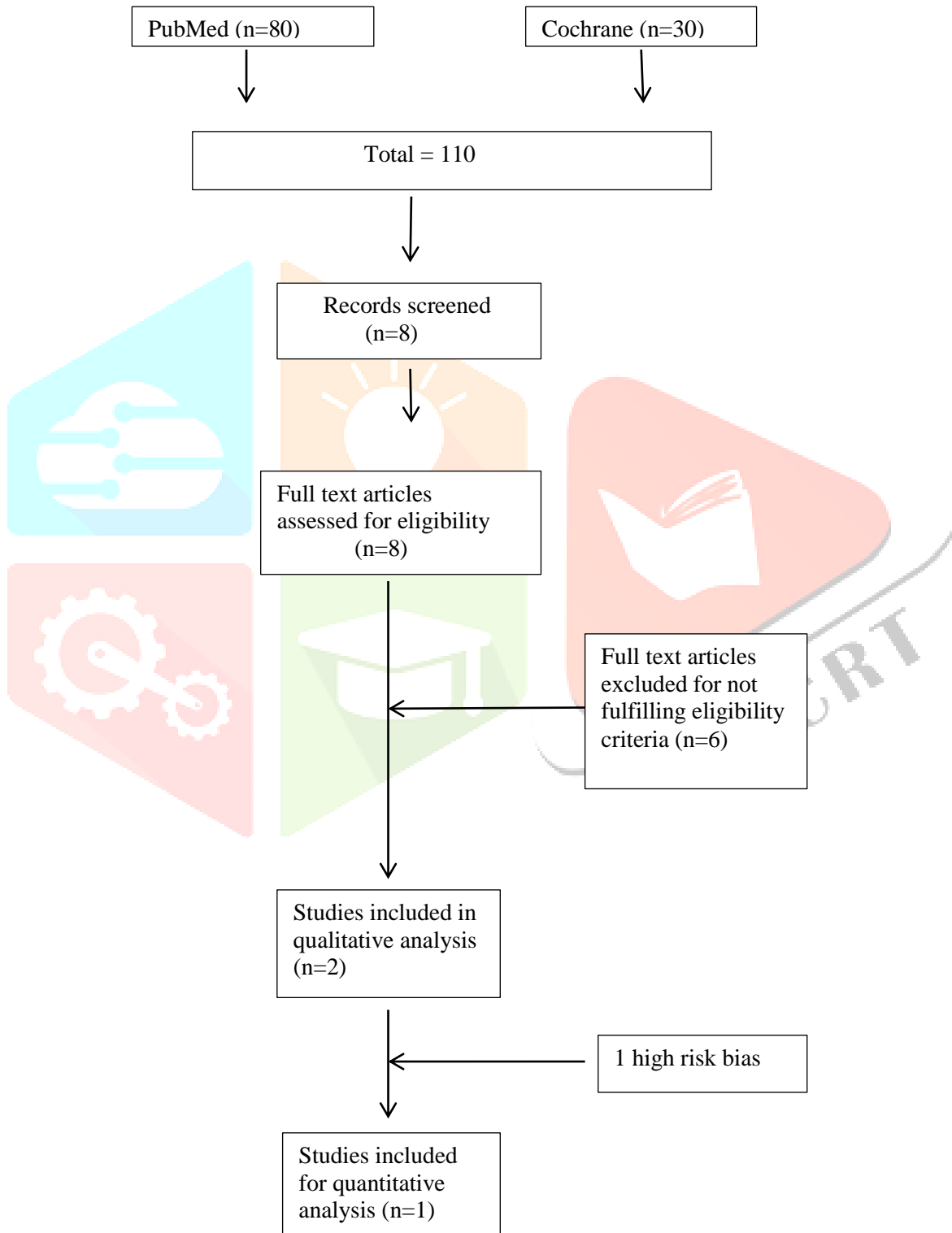
Total 110 studies were found relevant after searching in PubMed and Cochrane database out of which 80 were from PubMed and 30 were from Cochrane. After screening title and abstract total 8 studies were assessed for eligibility. Out of these studies 6 were excluded on the basis of not fulfilling eligibility criteria. Reasons for exclusion are summarized in **Table 1**. 2 studies finally selected for the qualitative analysis of the result. Quality assessment of the included studies is shown in **Table 2**. Out of these 2 studies 1 was found having high risk. At last only 1 study was found suitable for the quantitative synthesis of the result. The quantitative synthesis of the result is done as shown in **Table 3**. Data extraction is shown in **Figure 1**.

### 3.1 Quantitative Analysis

In the given study total 90 patients were included in age group ranging from 17 – 60 years out of which 70 were males and 30 were females. Patients were divided in 3 groups containing 30 patients each. Group A was given Tab Curcumin 300 mg twice a day. Group B was given Cap Lycopene 8 mg twice daily. Group C was given Placebo once a day. The duration of treatment was 6 months. After 3 months follow up was taken and no malignant transformation was observed during follow up. Assessment was done on the parameters like – burning pain, mouth opening and cheek flexibility. Burning pain was calculated on VAS (visual analogue

scale). It was seen that mean was seen that curcumin group had significant improvement in these parameters as compared to the placebo group. (Table 4)

**Figure 1: Flowchart of data extraction**



**Table1. Excluded studies with reasons**

Author name & year	Title of the study	Reason for exclusion
Ashwini et al, 2021 <sup>[12]</sup>	A comparative study to evaluate efficacy of curcumin and aloe vera gel along with oral physiotherapy in the management of oral submucous fibrosis: A randomised clinical trial	Both groups were experimental, i.e. no placebo group was included
Lanjekar et al, 2020 <sup>[13]</sup>	Comparison of efficacy of topical curcumin gel with triamcinolone-hyaluronidase gel individually and in combination in the treatment of oral submucous fibrosis	All the three groups were experimental, i.e. no placebo group was included
Rai et al, 2019 <sup>[14]</sup>	Comparative evaluation of curcumin and anti-oxidants in the management of submucous fibrosis	All the three groups were experimental, i.e. no placebo group was included
Saran et al, 2018 <sup>[15]</sup>	A comparative study to evaluate the efficacy of lycopene and curcumin in oral submucous fibrosis patients: A randomised clinical trial	Both groups were experimental, i.e. no placebo group was included
Hazarey et al, 2015 <sup>[16]</sup>	Efficacy of curcumin in the treatment for oral submucous fibrosis- A randomised clinical trial	The study was not randomised and Both groups were experimental, i.e. no placebo group was included
Yadav et al, 2014 <sup>[17]</sup>	Comparison of curcumin with intralesional steroid injections in oral submucous fibrosis- A randomised open label interventional study	Both groups were experimental, i.e. no placebo group was included

**Table 2 : Quality assessment**

Study	Overall quality assessment	Selection Bias	Study design	Confounders	Data collection	Blinding	Withdrawal and dropout
Shah et al <sup>[18]</sup>	+	++	+	+++	+	+	+
Piyush et al <sup>[19]</sup>	+	+	+	+	+	+	+

Low +, Moderate ++, High +++

**Table 3 : Study included for quantitative synthesis of result**

Author	Study groups (no. of participants)	Age (Mean/range)	Gender	Duration	Follow up months	Variables evaluated
Piyush et al, 2019	Gr. A : Curcumin tablet 300 mg twice daily (n=30)  Gr. B : Lycopene capsule 8 mg twice daily (n=30)  Gr. C : Placebo capsule once daily (n=30)	32(17-60)	M-70 F-20	6 months	3 months	Burning sensation, Mouth opening, Cheek flexibility

**Table 4 – Quantitative Analysis**

	P value for difference of burning pain (VAS*)	P value for difference of mouth opening	P value for difference of cheek flexibility
<b>Group A &amp; Group C</b>	<b>0.0001</b>	<b>0.023</b>	<b>0.03</b>

\*VAS – Visual analogue scale

#### 4. Discussion

Oral submucous fibrosis is a precancerous condition of buccal mucosa characterized by the restricted mouth opening. It is mainly associated with the habit of betel nut chewing mixed with tobacco and mainly affect the male population of low socioeconomic group in India. It affects the quality of life by hampering the activities like eating, swallowing and pronation due to fibrosis of oral mucosa. It also causes difficulty in brushing hence affects the oral hygiene causing other infective orodontal diseases. Various treatment modalities are opted for OSMF, but no definitive cure is found till date. Hence there is tremendous scope for research in this topic. Various studies have been carried out to prove the efficacy of curcumin in OSMF.

This review has searched many randomised control trials on use of curcumin in OSMF and after data extraction only one study was found to be eligible for the quantitative analysis. It is evident from the result of this study that the use of oral curcumin 600 mg daily has significant improvement in mouth opening, burning sensation and cheek flexibility in comparison to the placebo.

The possible properties by which curcumin is effective in OSMF is anti-fibrotic, anti-inflammatory, antioxidant and anti-carcinogenic.

It is suggested to perform more RCTs (randomised control trials) with large sample size and long duration of follow up to reach on the firm conclusion.

#### 5. Conclusion

It is concluded from the result that oral curcumin is safe and effective treatment is oral submucous fibrosis.

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