Original Article

# Efficacy of curcumin in the treatment of denture stomatitis: A randomized double-blind study

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## Abstract

**Background:** The prevalence of denture stomatitis has been shown to vary from 15% to 65% in complete denture wearers. In recent years, a number of studies across the globe have investigated the various biological effects of curcumin, curcumin, a polyphenolic compound derived from dietary spice turmeric, possesses diverse pharmacologic effects including anti-inflammatory, antioxidant, antiproliferative and antiangiogenic activities. The aim of this study was to evaluate the efficacy of curcumin local application with common antifungal agent clotrimazole for the treatment of denture stomatitis.

**Materials and Methods:** A randomised double-blind clinical trial with approval of institutional ethical committee consisting fifty participants divided into two groups (17 men–33 women) with the clinical signs and symptoms of oral candidiasis. The diagnosis was supported by microbiological cultures. Group A patients were prescribed the clotrimazole and Group B patients were prescribed the curcumin ointment which was dispensed in similar amber coloured bottles. Data were analyzed using Chi-squared tests, Wilcoxon's signed rank sum test and Mann-Whitney test.

**Results:** The mean candidal colony counts before treatment in Groups A and Group B were 63.960 and 37.080, respectively. The mean candida colony counts after treatment in both the groups were 14.080 and 3.720, respectively. There was a statistically significant difference between the two groups when mean candida colony counts were calculated before and after treatment. However, intergroup comparison between the two groups considering the mycological eradication showed that there was no statistically significant difference with $P = 0.404$.

**Conclusion:** Topical application of curcumin as a natural ingredient could be an effective agent for the treatment of denture stomatitis as an alternative to regular clotrimazole therapy.

**Keywords:** Clotrimazole, curcumin, denture stomatitis, opportunistic infection, oral candidiasis

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## INTRODUCTION

In recent years, a number of studies across the globe have investigated the various biological effects of curcumin. In addition to its reported cyto-protective effect, curcumin is known to exert an antioxidant effect by removing free radicals and an anti-inflammatory effect by inhibiting the activation of nuclear factor-kappa B.[1]

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Fungal infections, as an opportunistic infection, have increased significantly, contributing to the cause of morbidity. Despite therapeutic progress, opportunistic fungal infectious diseases have increased in the prevalence and still persists an existing problem. Denture stomatitis is the most prevalent and long-standing problem in denture wearers.[2] The etiopathogenesis of denture stomatitis is multifactorial but most common cause was fungal infections. Different classifications have been proposed, but the reference classification for denture stomatitis is the one suggested by Newton in 1962, based exclusively on clinical criteria: Type 1: A localized simple inflammation or pinpoint hyperemia. Type 2: An erythematous or generalized simple type seen as more diffuse erythema involving a part or the entire denture covered mucosa. Type 3: A granular type (inflammatory papillary hyperplasia) commonly involving the central part of the hard palate and the alveolar ridges. Type 3 often is seen in association with Type 1 or Type 2. Type 3 denture stomatitis involves the epithelial response to chronic inflammatory stimulation secondary to yeast colonization and possibly, low-grade local trauma resulting from an ill-fitting denture.[3] The placement of denture produces significant changes in the oral environment and adversely affects the integrity of oral tissues. The combination of entrapment of yeast cells in irregularities in denture-base and denture-relining materials, poor oral hygiene and several systemic factors are the probable cause for the onset of this opportunistic infection.[4]

Early recognition of the potential risk and prophylactic treatment of oral candidiasis may prevent serious morbidity. Oral candidiasis affects 65%–93% of elderly patients wearing dentures.[5]

Localized oral candidiasis should be managed initially with local treatment confined to the site of involvement before systemic antifungal drugs are used. Polyene antibiotics have been the initial choice of antifungal for almost half a century.[6] The azoles have been developed more recently with ketoconazole, itraconazole and fluconazole being used to treat patients with systemic fungal infections. Clotrimazole is known to be effective in the treatment of oral candidiasis.[7]

Curcumin is a yellow—orange polyphenol compound produced by the rhizome of Curcuma longa plants, which is widely used as a spice in Asian cooking. This compound has been shown to possess a wide range of pharmacological activitieswhere antifungal activity was assessed by experiments done with crude extracts of C. longa. Curcumin was able to inhibit the adhesion of Candida Species to human buccal epithelial cells being more potent than the commercial antifungal drugs.[8]

There is a need exists to compare the clinical efficacy of commonly used antifungal agent like clotrimazole and curcumin as a local application in the treatment of denture stomatitis.

## MATERIALS AND METHODS

### Study population and design

This was a randomized double-blind clinical trial with approval of institutional ethical committee consisting fifty participants divided into two groups (17 men and 33 women) with the clinical signs and symptoms of oral candidiasis.

Patients using denture with a history of denture stomatitis are included in the study and study was explained and who are willing to participate are informed to signed in written consent forms for enrolling in the study. Medical histories were obtained and all the patients underwent a physical examination before initiation of the therapy. Previous episodes of oral candidiasis and recent use of antifungal drug therapy were excluded from the study. Information about medical status was obtained from their physician and hospital records. Patients were excluded from the study if they were pregnant or lactating; had used any other antifungal agent during the past 10 days; were taking barbiturates or anticoagulants; had a known sensitivity to polyenes or the azole group of antimycotics; had a history of alcoholism, drug abuse, psychiatric disorder, or any other problem that might invalidate informal consent.[7]

### Inoculation, incubation and colony collection

The diagnosis was supported by microbiological cultures; swab was taken from the affected mucosa of the patient. The swab was dipped thoroughly in 1 ml of saline sample and transported immediately to the laboratory where they were cultured with the use of standard techniques. Each specimen was inoculated on Sabouraud's dextrose agar. The plates were then incubated for 24–48 h at 37°C–25°C. After 48 h, the plates were examined and yeast colonies were counted.

Group A patients were prescribed the clotrimazole and Group B patients were prescribed the curcumin ointment which was dispensed in similar amber coloured bottles. Patients were advised to apply the ointment to the affected areas thrice daily after food intake for 2 weeks.

Patients were recalled in weekly intervals on the 7$^{th}$, 14$^{th}$, 21$^{th}$, and 28$^{th}$ day to check for clinical signs and symptoms

and mycological assessment was carried out by repeating the oral swabs from the same site of the lesion. Side effects associated with both the curcumin and the clotrimazole were noted.

### Data analysis

Data were analyzed using the SPSS software for Windows (v. 18) Curenext oral gel, abbolt brand name, Maharastra, India. The distributions of all the variables were compared between the treatment groups using the Chi-square test and Wilcoxon's signed rank sum test, Mann–Whitney Test was used for the comparison of mycological cure between the two groups considering $P < 0.001$ as significant.

## RESULTS

All patients of the two study groups were matched in terms of gender, denture usage (years), Newton's type of denture stomatitis, colony count of *C. albicans* on affected mucosa of the patient, duration of denture wearing, removal of denture during at night, distribution of medically compromised patients among both the groups and the mycological cure achieved by the two drugs.

In Group A, five patients were male and 20 were female, whereas in Group B, 12 patients were male and 13 were female, when both male and female patients were statistically analysed Denture stomatitis is more prevalent female patients with $P = 0.037$ which is statistically significant.

In Group A, six patients had a mean duration of denture usage (years) 1–5 years and 13 patients (6–10 years), one patient (11–15 years), two patients (16–20 years) and three patients had (>20 years), whereas in Group B, nine patients had a mean duration of denture usage (years) 1–5 years and seven patients (6–10 years), three patient (11–15 years), three patients (16–20 years) and three patients had (>20 years).when both the groups were analysed $P = 0.463$ which is statistically not significant.

In this study, the most common form of observed denture stomatitis lesions in both groups (study group and controls) was in Newton's Type 2 classification.

In Group A, five patients removed denture during at night, whereas 20 patients were night time denture wearers, whereas in Group B, 11 patients removed denture during at night while 14 patients were night time denture wearers.

Twelve patients in Group A and 10 patients in Group B who were medically compromised, had a history of diabetes mellitus, hypertension, asthma, monoplegia, hypothyroidism and vitiligo.

In Group A, complete resolution of the lesion was seen in 14 days in 12 patients, 21 days in 11 patients and 28 days in two patients [Figure 1], whereas in Group B, 14 days in 14 patients, 21 days in 10 patients and 28 days in one patients [Figure 2]. When both the groups were analyzed $P = 0.765$ which is not statistically significant [Table 1].

The mean Candidal colony counts before treatment in Groups A and Group B were 63.960 and 37.080, respectively. The mean candida colony counts after treatment in both the groups were 14.080 and 3.720, respectively. There was a statistically significant difference between the two groups when mean candida colony counts were calculated before and after treatment [Table 2 and Figure 3].

The mycological eradication for Groups A and Group B was 100%, respectively. However, intergroup comparison between the two groups considering the mycological eradication showed that there was no statistically significant difference with $P = 0.404$ [Table 3 and Figure 4]. Both treatment regimens were well tolerated with no side effects.

## DISCUSSION

Denture stomatitis is an inflammatory process of the oral mucosa associated with the presence of Candida or other microorganisms and factors, such as denture wearing and long term antibiotic therapy. *Candida albicans* represents the most common causative agent of the oral candidiasis.[9]

The factors contributing to denture stomatitis have been shown to be varied and have interaction with local and systemic factors. Oral microorganisms change after wearing the denture and this condition favours the growth of organisms causing denture stomatitis. *Candida albicans* and bacterial interaction have shown to be prominent factors contributing to denture stomatitis. Newton's Type 1 has been shown to be the result of trauma, whereas Newton's Class III has multivariable interaction phenomenon.[10]

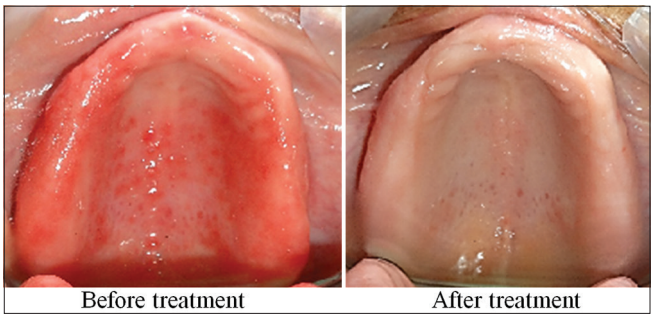


**Figure 1:** Treatment of Type 3 denture stomatitis with clotrimazole

**Table 1: Comparison of baseline characteristics of clotrimazole and curcumin groups**

| Parameter | Clotrimazole | Curcumin | $\chi^2$ | *P* |
|---|---|---|---|---|
| Gender | | | | |
| Male | 5 | 12 | 367 | 0.037* |
| Female | 20 | 13 | | |
| Denture usage (years) | | | | |
| 1-5 | 06 | 09 | 3.600 | 0.463 |
| 6-10 | 13 | 07 | | |
| 11-15 | 01 | 03 | | |
| 16-20 | 02 | 03 | | |
| >20 | 03 | 03 | | |
| Newton's type of denturestomatitis | | | | |
| Type 1 | 11 | 10 | 3.710 | 0.156 |
| Type 2 | 14 | 12 | | |
| Type 3 | 00 | 03 | | |
| Removal of dentureduring at night | | | | |
| Yes | 5 | 11 | 3.309 | 0.069 |
| No | 20 | 14 | | |
| Medically compromised patients | | | | |
| Healthy | 13 | 15 | 8.7814 | 0.190 |
| Diabetes | 04 | 04 | | |
| Hypertension | 06 | 01 | | |
| Asthma | 00 | 02 | | |
| Monoplegia | 00 | 02 | | |
| Hypothyroidism | 01 | 01 | | |
| Vitiligo | 01 | 00 | | |
| Complete resolution of the lesion (weeks) | | | | |
| Within 1 | 00 | 00 | 0.535 | 0.765 |
| Within 2 | 12 | 14 | | |
| Within 3 | 11 | 10 | | |
| Within 4 | 02 | 01 | | |

Chi square test. *Statistically significant

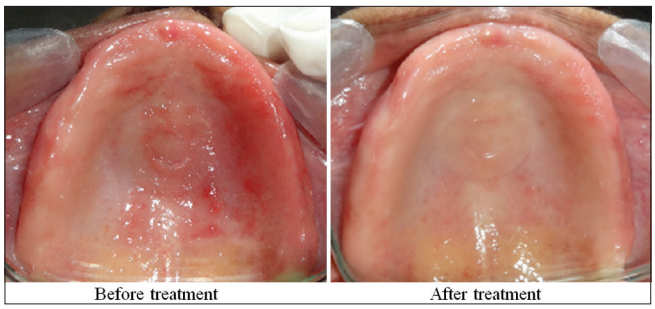


**Figure 2:** Treatment of Type 2 denture stomatitis with curcumin

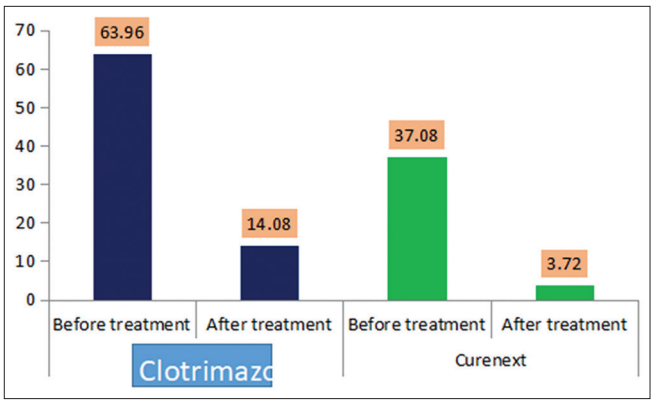


**Figure 3:** Graphical representation showing comparison of colony counts before and after treatment using clotrimazole and curcumin groups

The etiology of denture stomatitis remains controversial as it is of multifactorial nature. Denture trauma, night time denture wearing, denture cleanliness, dietary factors, Candida infections and predisposing systemic conditions have been proposed as associated factors in denture stomatitis.[11]

Denture trauma due to ill-fitting dentures is believed as one of the etiological factors of denture stomatitis. According to Nyquist,[12] trauma caused by dentures was the dominant factor in denture stomatitis. Cawson[13] concluded that the trauma and candidal infection are significant causes of denture stomatitis. Immunohistochemical analysis of the mucosal tissue also has demonstrated a possible role of trauma in denture stomatitis.[14]

Although some earlier investigators linked denture stomatitis with trauma or bacterial infection, others had isolated the strains of the genus candida, in particular candida albicans from the mouths of patients with this condition.[15] It has been recently shown that the presence of *Candida albicans* in denture stomatitis is probably related to an extensive degree of inflammation[16] and that denture stomatitis is usually associated with the detection of candida species while other factors such as denture hygiene habit[15] and trauma[17] are important to the development of the disease. The severity of the denture stomatitis has

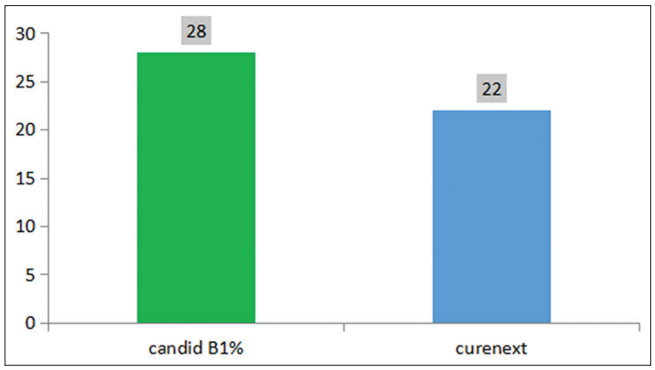


**Figure 4:** Graphical representation showing comparison of colony count reduction between clotrimazole and curcumin groups

been corelated with the presence of yeast colonizing the denture surface.

Denture induced stomatitis or chronic atrophic candidiasis is the commonest form of oral Candidiasis and is present in 24%–60% of denture wearers.[18] Denture stomatitis has been associated with angular cheilitis, atrophic glossitis, acute pseudomembranous candidiasis and chronic hyperplastic Candidiasis and has been found to be more common in females than males.[15] Topical therapy is generally effective in controlling low grade uncomplicated mucosal candidiasis. In cases of severe oral candidiasis, topical therapy in conjunction with systemic therapy may ensure a lower systemic dose and shorten the duration of high-dose systemic antifungal therapy.[7]

In this study control group were given clotrimazole ointment whereas Study group were treated with curcumin ointment and were advised to apply it to the affected areas with the index finger thrice daily for 4 weeks.

The mean candidal colony counts before and after treatment in both study and control groups was statistically significant. The mycological eradication for study and control group was 100%, respectively. However, intergroup comparison between the two groups considering the mycological eradication showed that there was no statistically significant. Both treatment regimens were well accepted with no side effects.

In this study, reduction in the number of Candida and erythematous surface in both of two Groups may be justifiable because of the effect of the standard hygienic recommendations (e.g. cleaning the dentures and denture brushing, removal of denture overnight) during the study which is consistent when compared with previous one.[9]

Clotrimazole has certain side effects that can affect individuals in different ways. The following are some of the side effects that are often associated with the drug: Burning sensation, itching, local mild irritation, hypersensitivity.

Curcumin has been used extensively in ayurvedic medicine for centuries, as it is nontoxic and has a variety of therapeutic properties including antioxidant, analgesic, anti-inflammatory, antiseptic activity and anti-carcinogenic activity. As a natural product, turmeric (curcumin) is nontoxic and has diverse effects in various oral diseases. About 40%–85% of an oral dose of curcumin passes through the gastrointestinal tract unchanged, with most of the absorbed lavonoid being metabolized in the intestinal mucosa and liver. Due to its low rate of absorption, curcumin is often formulated with bromelain for increased absorption and enhanced anti-inflammatory effect.[19]

Due to the increasing resistance of micro-organisms against antifungal agents and their side effects, formation of Candida biofilm and generally positive attitude of patients for natural treatment, novel herbal antifungal therapies with fewer side effects on humans are rational for effective management of candidiasis infections.[20]

The frequent use and misuse of the currently used therapeutic agents has led to the evolution of resistant strains of common pathogens as well as increased incidence of adverse effects associated with their usage. Hence, the search for alternative products continues and natural phytochemicals isolated from plants used as traditional medicines are considered as a good alternative source.[19]

## CONCLUSION

To conclude, curcumin derived from the common food spice turmeric has been used for centuries as a remedy for many ailments and is a nontoxic, highly promising natural antioxidant compound having a wide spectrum of biological functions including antioxidant, analgesic, anti-inflammatory, antiseptic activity and anticarcinogenic activity. Turmeric has been granted "Generally Recognized as Safe" status by the Food and Drug Administration. It is expected that curcumin may find application as a novel drug in the near future to control various diseases, including inflammatory disorders, carcinogenesis and oxidative stress-induced pathogenesis. This study showed that curcumin ointment could be an effective agent for the treatment of denture stomatitis as an alternative to regular clotrimazole therapy. The results of this study can be used as a basis for further studies with a larger sample of patients with oral candidiasis to compare the efficacy of clotrimazole and Curcumin ointment.

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Nil.

## Conflicts of interest
There are no conflicts of interest.

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