

Comparative evaluation of curcumin gel vs chlorhexidine gel in the management of denture induced traumatic ulcers: A randomized trial

Rajveer Singh¹, Deepak Goyal², Yadwinder Kaur Virk³, Kapil Singla⁴, Ruby Singla⁵, Ajay Kumar⁶

¹Department of Pharmacology, Adesh institute of medical sciences, Bathinda

²Department of Prosthodontics, Adesh institute of dental sciences, Bathinda

³Immunohematology and blood transfusion, Adesh institute of medical sciences, Bathinda

⁴Department of Prosthodontics, Adesh institute of dental sciences, Bathinda

⁵Department of Periodontology, Adesh institute of dental sciences, Bathinda

⁶Department of Human Genetics and Molecular Medicine, Central University of Punjab

Corresponding author: Deepak Goyal, Goyal.drdeepak@gmail.com

Abstract: Introduction: Denture induced traumatic ulcers are very common in elderly individuals who wear removable dentures. It can negatively affect the patient's acceptance to wear dentures, causes pain, ulceration and there are only few treatment strategies available despite its high prevalence. Therefore, there is need for developing drugs with high efficacy and safety for the management of these ulcers.

Aim: To compare the clinical and biochemical efficacy of Curcumin gel with Chlorhexidine gel in patients with denture induced traumatic ulcers.

Material and Methods: The randomized, open labeled, prospective study was conducted on 60 patients allocated to two treatment groups curcumin gel group I (n=30) and chlorhexidine gel group II (n=30) each at Adesh Institute of Dental Sciences and Research, Bathinda, after obtaining ethical approval. For the estimation of clinical parameters pain scores (NRS 0-10), ulcer size (mm²), erythema (modified Greer scale 0-3) were assessed at baseline, 3rd day and 6th day. For biochemical parameter estimation TNF- α levels were measured at baseline and 6th day using ELISA. Data were analyzed using Mann-Whitney U test, independent t-test, paired t-test and Friedman test wherever applicable.

Results: In this study both the curcumin and chlorhexidine gels caused reduction in pain scores, erythema scores and ulcer size over six day period ($p < 0.001$). But there was no significant difference observed between the groups. Salivary TNF- α levels decreased in both groups ($p < 0.001$), with curcumin showing greater reduction in salivary TNF- α levels as compared to chlorhexidine (-20.44 ± 4.47 vs. -13.55 ± 5.27 pg/mL, $p < 0.01$). However, both of these gels were effective in the treatment of denture induced traumatic ulcers.

Conclusion: Curcumin gel is as effective as chlorhexidine gel on clinical parameters in the treatment of denture induced traumatic ulcers with a superior reduction of TNF- α levels with potent anti-inflammatory action.

Keywords: curcumin, chlorhexidine, ulcers, TNF- α , wound healing

1. Introduction

Localized lesions of the oral mucosa resulting from chronic mechanical irritation are termed as traumatic ulcers [1]. Among this denture induced traumatic ulcers represent a significant complication in prosthodontic practice characterized by painful mucosal disruption at sites of continuous friction or pressure [2]. Several etiological factors contribute to this repeated tissue trauma, including ill fitting denture bases, flanges, borders, clasps and occlusal irregularities [3]. These ulcers are prevalent in considerable proportion of patients during the initial post-insertion examination, conducted 3-4 days after denture placement [4]. It can also manifest in long term denture wearers due to ridge resorption, denture instability or wear related defects.



Clinical studies have reported 76-87% of patients presenting with traumatic mucosal lesions require denture adjustment within the first week of denture wear [5], underscoring the critical need for post-insertion follow-up and timely modification of prosthesis. Patients with denture induced traumatic ulcers typically experience sharp localized pain that intensifies during functions such as mastication and speech often leading to dietary modification avoiding hard, rough or thermally hot foods [6].

Histologically, these ulcers exhibit epithelial loss accompanied by fibrinopurulent membrane and mixed inflammatory infiltrate [7]. Clinically, they present as solitary, well defined lesions with a yellowish base and an erythematous halo located on alveolar ridge, vestibular sulcus or palate directly corresponding to denture irritation point [8]. The primary management strategy involves removal or correction of traumatic stimulus which initiates healing within 1-2 weeks [9]. Topical agents are commonly used as adjunct to provide symptomatic relief from pain, inflammation and secondary infections during this healing phase.

Chlorhexidine is a broad spectrum antimicrobial agent which is widely used in oral ulcer management due to its potent and sustained duration of action [10]. Its mechanism is concentration dependent: at bacteriostatic levels it causes disruption of bacterial cytoplasmic membrane leading to leakage of cytoplasmic components while, at higher concentrations it exerts a bactericidal effect through the irreversibly precipitation of intracellular ATP and nucleic acids [11,12]. However, long term chlorhexidine use is associated with significant side effects including acute hypersensitivity reactions, tooth staining, alteration of taste and mucosal irritation [13].

Curcumin, a naturally occurring polyphenolic compound derived from rhizomes of *Curcuma longa* offers a promising alternative due to its potent anti-inflammatory, antioxidant, antimitotic and wound healing properties [14]. Its primary mechanism involves inhibiting NF- κ B activation and suppressing pro-inflammatory cytokines such as TNF- α , IL-6 and IL-1 β [15]. Multiple randomized controlled trials have confirmed the efficacy of topical curcumin gel formulations against various oral lesions including aphthous ulcer, oral submucous fibrosis, candida infections, oral lichen planus and denture stomatitis [16]. Owing to its favorable safety profile, lack of mucosal irritation and natural origin curcumin presents as an attractive therapeutic agent.

While existing studies have evaluated curcumin in *Candida* associated denture stomatitis and aphthous ulcers, its role in mechanically induced denture related traumatic ulcers, particularly in the post adjustment healing phase remains unexplored. Furthermore, comparative trials of topical preparations for denture injuries have rarely incorporated biochemical markers such as TNF- α , a key mediator of inflammation, immunity and cell proliferation that directly reflects the severity of traumatic mucosal inflammation. Therefore, this study is undertaken to compare the effectiveness of topical curcumin gel with chlorhexidine gel in patients with denture induced traumatic ulcers, while also using biomarker levels to support the findings.

2. Material and Methods

The randomized, open labeled, prospective study was conducted at Adesh Institute of Dental Sciences and Research, Bathinda, after obtaining ethical approval from the Institutional ethics committee. The study conducted in accordance with the Declaration of Helsinki (1975, revised in 2000 and 2008). Patients willing to participate and complaining denture induced traumatic ulcers were included in this study.

2.1 Inclusion Criteria

1. Patients with age 18 or above willing to provide informed consent
2. Completely edentulous patients reporting for fabrication of new complete dentures
3. Patients with diagnosis of Denture induced traumatic ulcers

2.2 Exclusion criteria

1. Patients with known hypersensitivity to curcumin or chlorhexidine
2. Patients with any oral malignancy
3. Pregnant or lactating women
4. Patients with any systemic disease that can affect ulcer healing (e.g., diabetes, immunosuppression)
5. Patients with ulcer of other etiologies (e.g., aphthous ulcer, drug induced stomatitis, trauma from teeth or herpetic origin)

A total of 60 patients with 30 allocated to each group were enrolled in this study after meeting the inclusion exclusion criteria. Group A was treated with chlorhexidine gluconate gel (Hexigel 1% W/W, IPCA Laboratories) whereas Group B received Curcumin gel (Curesure 2%, Snehal Pharma and Surgicals limited).

2.3 Study Design

A total of 60 patients were enrolled with Denture induced traumatic ulcers in this study. After initial evaluation and diagnosis, patients were divided into two groups: Group A (30 patients) received chlorhexidine gluconate gel, and group B (30 patients) received curcumin gel. Patients were instructed to apply a thin smear of the gel to the affected area four times daily in the morning after brushing, after lunch, after dinner, and before bed time. Ulcer size was measured in diameter (mm²) using a William calibrated periodontal probe (Hu-Friedy, USA) at baseline (day 0), day 3 and day 6. When multiple ulcers were present only the largest lesion was selected in the same arch for evaluation. Pain was assessed using a Numerical Rating scale (NRS) from 0 to 10. Erythema was evaluated using a 4-point modified Greer scale (0-3). Followup visits were scheduled on 0, 3rd and 6th day with the recording of clinical data. For the estimation of TNF- levels unstimulated saliva (4 ml) was collected from each patient at baseline and day 6 between 9.00-11.00 AM. Patients were refrained from eating, drinking or brushing for 1 hour prior to sample collection. Samples were centrifuged at 3000 rpm for 10 minutes at 4°C and the supernatant was stored at -80°C for further analysis. Salivary TNF-α levels were measured using commercially available ELISA kit (Abclonal) following the manufacturer's instructions. To facilitate the mucosal healing patients were instructed to remove their dentures on the day of adjustment and next day.

Statistical analysis

All the statistical analysis were performed using SPSS version 26.0 (IBM corp, Armonk, NY, USA). All data were expressed as Mean ± SD, Shapiro-Wilk test was used to assess normality of the continuous data. Baseline demographic data (age, height, weight and BMI) between the two groups were compared using independent sample t-test. Chi-square was used to measure categorical variable like sex between two groups. For salivary TNF-α levels which satisfied normality assumptions within group analysis was done using paired sample t-test and in-between group comparisons were made using the independent sample t-test. For the measurement of clinical parameters like pain, erythema and ulcer size which were non-normally distributed between group comparisons were made using Mann-Whitney U test and Friedman test for the within group comparisons on Day 0, Day 3 and Day 6. A p-value <0.05 was considered statistically significant.

3. RESULTS

Baseline demographic characteristics of Curcumin gel (group I) and Chlorhexidine gel (group II) study participants are presented in Table I. The two groups demonstrated no significant differences in mean age 66.63±9.25 years vs 64.70±10.54 years respectively (p= 0.453), sex 13:17 vs 14:16 (p= 0.795), height 161.23±9.20 cm vs 160.57±12.88 cm (p= 0.818), weight 64.03±7.56 kg vs 66.00±14.27 kg (p= 0.507) and BMI (24.75±3.25 kg/m² vs 25.47±4.21 kg/m²) (p= 0.456), indicating that both treatment groups were comparable at baseline, allowing for a valid comparison of the therapeutic effects of curcumin gel against chlorhexidine gel.

Table I. Baseline Demographic characteristics of the study population

Demographic Variable	Group I (n=30)	Group II (n=30)	p-value
Age (years)	66.63±9.25	64.70±10.54	0.453
Sex (M:F)	13:17	14:16	0.795
Height (cm)	161.23±9.20	160.57±12.88	0.818
Weight (kg)	64.03±7.56	66.00±14.27	0.507
BMI (kg/m ²)	24.75±3.25	25.47±4.21	0.456

Values are presented as mean ± standard deviation (SD). Sex distribution was compared using the Pearson's chi-square test. Age, height, weight and BMI were compared using independent samples t-test. p=<0.05 significant

Changes in pain intensity over time was assessed using the Numeric rating scale (NRS 0-10) are shown in Table II. At baseline day (Day 0), the mean pain scores were 5.86 ± 1.00 in the curcumin gel group and 6.13 ± 1.48 in the

chlorhexidine gel group with no significant difference between the groups ($p=0.119$). On day 3 pain scores decreased to 3.13 ± 1.25 and 3.23 ± 1.50 respectively; ($p=0.495$) and by day 6 pain scores further reduced to 0.43 ± 0.56 vs 0.50 ± 0.62 ; ($p=0.727$). Comparison of the pain scores between chlorhexidine and curcumin group was done using Mann-Whitney U test revealed no significant difference at baseline, Day 3 or Day 6 ($p > 0.05$). However, within group analysis using Friedman test revealed a significant reduction in pain scores at all assessment time points in both groups ($p < 0.001$). This shows both curcumin gel and chlorhexidine gel were associated with a significant reduction in pain scores over the study period.

Table II: Comparison of pain scores (NRS 0-10) between curcumin gel and chlorhexidine gel groups over time.

Time point	Curcumin group (n = 30) Mean $\pm$ SD	Chlorhexidine group (n = 30) Mean $\pm$ SD	p-value*
Day 0	5.86 ± 1.00	6.13 ± 1.48	0.119
Day 3	3.13 ± 1.25	3.23 ± 1.50	0.495
Day 6	0.43 ± 0.56	0.50 ± 0.62	0.727
Within group p-value†	<0.001	<0.001	—

Values are presented as mean $\pm$ standard deviation (SD). Between groups comparison was made using Mann-Whitney U test. †Within group comparison was across Day 0, Day 3 and Day 6 was using Friedman test.

Erythema scores over time are presented in Table III. At baseline (Day 0), the mean erythema scores was significantly higher in the curcumin group 2.13 ± 0.571 compared to the chlorhexidine group 1.83 ± 0.531 ($p=0.041$). On (Day 3), mean scores decreased from 1.10 ± 0.548 vs 1.03 ± 0.320 ($p=0.524$). By (Day 6), mean erythema scores decreased from 0.13 ± 0.346 vs 0.07 ± 0.254 respectively ($p=0.393$). Between group comparison was done using Mann-Whitney U test revealed significant difference only at baseline ($p=0.041$) Day 0 with no significant association at Day 3 or Day 6 ($p > 0.05$). The within group analysis using Friedman test demonstrated a significant reduction in erythema scores over time in both curcumin gel and chlorhexidine gel group ($p < 0.001$). This indicated that both the interventions were effective in reducing erythema from baseline to Day 6.

Table III. Comparison of Erythema scores (0 – 3 scale) over time by treatment groups.

Time point	Curcumin group (n = 30) Mean $\pm$ SD	Chlorhexidine group (n = 30) Mean $\pm$ SD	p-value*
Day 0	2.13 ± 0.571	1.83 ± 0.531	0.041
Day 3	1.10 ± 0.548	1.03 ± 0.320	0.524
Day 6	0.13 ± 0.346	0.07 ± 0.254	0.393
Within group p-value†	< 0.001	< 0.001	—

Values are presented as mean $\pm$ standard deviation (SD). Between groups comparison was made using Mann-Whitney U test. †Within group comparison was across Day 0, Day 3 and Day 6 was using Friedman test

Ulcer size over time is presented in Table IV. At baseline (Day 0), the mean ulcer size was 7.67 ± 4.63 mm in the curcumin gel group and 6.72 ± 2.69 mm in chlorhexidine gel group ($p=0.157$). On (Day 3), mean ulcer size decreased to 4.60 ± 4.06 mm vs 3.55 ± 1.66 mm ($p=0.334$). By (Day 6), it further reduced to 0.83 ± 2.17 mm vs 0.27 ± 0.50 mm ($p=0.377$). Between groups comparison was done using Mann-Whitney U test revealed no significant differences at all days ($p > 0.05$). The within group analysis using Friedman test demonstrated a significant reduction in ulcer size (mm) over time in both curcumin gel and chlorhexidine gel group ($p < 0.001$) indicating both interventions were effective in reducing ulcer size from baseline to Day 6.

Table IV. Comparison of ulcer size (mm) over time by treatment groups

Time point	Curcumin group (n = 30) Mean $\pm$ SD	Chlorhexidine group (n = 30) Mean $\pm$ SD	p-value*
Day 0	7.67 $\pm$ 4.63	6.72 $\pm$ 2.69	0.157
Day 3	4.60 $\pm$ 4.06	3.55 $\pm$ 1.66	0.334
Day 6	0.83 $\pm$ 2.17	0.27 $\pm$ 0.50	0.377
Within group p-value†	< 0.001	< 0.001	—

Values are presented as mean $\pm$ standard deviation (SD). Between groups comparison was made using Mann-Whitney U test. †Within group comparison was across Day 0, Day 3 and Day 6 was using Friedman test

TNF- α values at baseline and Day 6 are presented in Table V and Figure I. At baseline (Day 0), the mean TNF- α level was high in curcumin group as compared to chlorhexidine group was 34.06 $\pm$ 3.65 pg/mL vs 29.41 $\pm$ 4.47 pg/mL (p = <0.001). By (Day 6), TNF- α levels decreased to 13.62 $\pm$ 2.70 pg/mL in the curcumin group and 15.87 $\pm$ 2.76 pg/mL in the chlorhexidine group (p = 0.006). The mean reduction in the TNF- α levels from Day 0-6 was significantly greater in the curcumin group -20.44 $\pm$ 4.47 pg/mL compared to the chlorhexidine group -13.55 $\pm$ 5.27 pg/mL (p = <0.01). Within group analysis using the paired t-test revealed a significant reduction in TNF- α levels over time between both groups (p = <0.001).

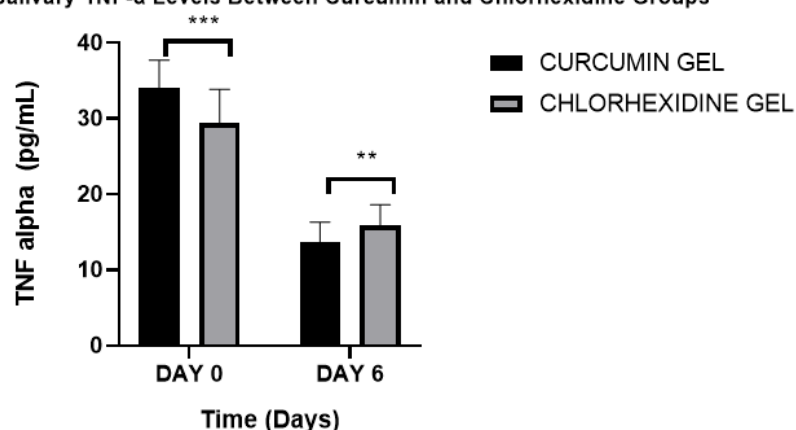
Table V. Comparison of TNF- α levels between curcumin gel and chlorhexidine gel at Day 0 and Day 6.

Time point	Curcumin group (n= 30) Mean $\pm$ SD (pg/mL)	Chlorhexidine group (n= 30) Mean $\pm$ SD (pg/mL)	p-value*
Day 0	34.06 $\pm$ 3.65	29.41 $\pm$ 4.47	< 0.001
Day 6	13.62 $\pm$ 2.70	15.87 $\pm$ 2.76	0.006
Mean change (Day 0-Day 6)	-20.44 $\pm$ 4.47	-13.55 $\pm$ 5.27	< 0.001
Paired t-test value†	< 0.001	< 0.001	—

Values are presented as mean $\pm$ standard deviation (SD). Between group comparison was made using independent samples t-test. Within group p-value† comparison was across Day 0 and Day 6 using the paired t- test.

Figure I. Comparison of salivary TNF- α levels in curcumin gel and chlorhexidine gel groups

Comparison of Salivary TNF- α Levels Between Curcumin and Chlorhexidine Groups



Data expressed as mean $\pm$ SD (pg/mL). Between group comparison by independent samples t-test, error bars represent standard deviation. *** p <0.001, ** p <0.01

4. DISCUSSION

The present study was undertaken to compare the clinical and biochemical efficacy of Curcumin gel with Chlorhexidine gel in patients with denture induced traumatic ulcers over a six day treatment period. In this study both treatment groups demonstrated significant reduction in pain scores, erythema and ulcer healing within each group over time. However, no statistical significance between the groups was observed for any clinical parameters suggesting that both treatment regimens exhibited comparable clinical efficacy.

Demographic parameters included age, sex, height, weight and BMI. These baseline characteristics of curcumin and chlorhexidine gel groups were comparable, with no statistical significance. This baseline comparability strengthens the validity of our findings, as it minimizes the potential influence of confounding demographic factors on the observed clinical outcomes. Pain intensity was assessed using Numeric Rating scale (NRS 0-10). There was a significant and progressive reduction in pain scores from baseline to Day 6 in both curcumin gel and chlorhexidine gel group ($p < 0.001$) confirming that both interventions were effective in reducing pain associated with denture induced traumatic ulcers. By the Day 6 mean pain scores have fallen to near zero level in both groups (0.43 ± 0.56 vs 0.50 ± 0.62) with no statistically significant between group differences observed at any time point suggesting similar analgesic efficacy. The analgesic potential of curcumin can be attributed to its downregulation of the NF- κ B target signaling thereby it suppresses the release of pro-inflammatory mediators such as prostaglandins and cytokines at ulcer site [17]. Chlorhexidine is a potent antimicrobial agent that causes reduction in bacterial load and polymorphonuclear leukocytes (PMN) infiltration at the wound site, thereby reducing the inflammatory response associated with pain [18]. Chlorhexidine can also indirectly reduce the cytokine mediated inflammatory cascade [19].

Erythema scores were assessed on an ordinal scale of 0-3, showed a significant and sustained reduction from baseline to Day 6 within both curcumin and chlorhexidine group ($p < 0.001$). At the baseline levels curcumin gel group showed significantly higher erythema scores compared to the chlorhexidine group (2.13 ± 0.571 vs 1.83 ± 0.531 ; $p = 0.041$) despite random allocation. By the Day 3 and Day 6 erythema scores were comparable between two groups with no statistical significance ($p > 0.05$).

The ulcer size reduction in millimeters in both treatment groups decreased from baseline to Day 6 ($p < 0.001$). At baseline mean ulcer sizes were comparable between the curcumin and chlorhexidine group (7.67 ± 4.63 mm vs 6.72 ± 2.69 mm; $p = 0.157$) whereas on Day 3 and Day 6 no significance was observed. This reflects both gels were effective in promoting ulcer healing. The baseline ulcer dimensions showed considerable variability especially in the curcumin group which may have influenced the between group comparisons. The pathogenesis of denture induced traumatic ulcer is heterogenous and often multifactorial [20]. Although, at no point of time statistically significant differences were observed, suggesting that the therapeutic effects were consistent despite this baseline variation.

This convergence of clinical outcomes may be attributed to the potent anti-inflammatory activity of curcumin. The ability of curcumin to suppress cytokine release, inhibit macrophage driven inflammatory signaling leads to suppression of TNF- α , IL-1 β , prostaglandins and IL-6 promotes ulcer and erythema healing [21]. Curcumin has potent scavenging action on reactive oxygen species (ROS). It also upregulates various antioxidant enzymes at ulcer site like catalase and superoxide dismutase [22]. By reducing this oxidative stress burden it promotes favorable microenvironment for mucosal repair causing clearance of erythema and ulcer healing. In addition it has potent antimicrobial action against various groups of microorganisms. It can cause damage to microbial cell membranes, inhibits microbial biofilm formation at ulcer sites thereby inhibiting secondary microbial colonization [23]. Chlorhexidine can promote ulcer and erythema healing by its potent antimicrobial action producing a clean wound environment throughout the application period [24].

TNF- α is an important pro-inflammatory cytokine which is involved in the pathogenesis of oral ulcers. It is found that TNF- α is upregulated in many inflammatory conditions like aphthous ulcers, denture stomatitis, oral cancers, gingivitis and traumatic ulcers [25, 26, 27]. Salivary TNF- α levels were measured at baseline and Day 6. At baseline day TNF- α levels were significantly higher in curcumin group as compared to chlorhexidine group (34.06 ± 3.65 pg/mL vs 29.41 ± 4.47 pg/mL; $p < 0.001$) indicating a baseline biochemical imbalance inbetween groups despite randomization. This may reflect as inherent inter-individual variability in inflammatory responses among denture wearers and should be considered when interpreting between comparisons. By Day 6, TNF- α levels decreased significantly in both groups (13.62 ± 2.70 pg/mL vs 15.87 ± 2.76 pg/mL; $p < 0.006$). The mean reduction in TNF- α levels were found to be greater in curcumin group vs chlorhexidine group (-20.44 ± 4.47 vs -13.55 ± 5.27 ; $p < 0.001$). This enhanced biochemical response of curcumin is attributed to its direct action on IKK β subunit activity, which blocks the I κ B α phosphorylation and prevents NF- κ B nuclear translocation, blocks MAPK signaling and reduces ROS driven NLRP3 inflammasome activation thereby inhibiting TNF- α gene transcription [28]. These findings indicate

curcumin gel is comparable chlorhexidine gel in clinical efficacy with additional actions at cellular level that may benefit patients with denture induced traumatic ulcers.

5. CONCLUSION

In the present study curcumin gel demonstrated comparable clinically efficacy and biochemically superior reduction in TNF α levels as compared to chlorhexidine gel in the management of denture induced traumatic ulcers. Both gels significantly reduced pain, ulcer size and erythema associated with ulcers over a six day treatment period. The clinical efficacies of both gels were comparable on clinical outcomes. Our findings suggests that curcumin gel on account of its multiple anti-inflammatory mechanisms, easy availability, potent antimicrobial action may serve safe cost effective treatment option for the management of denture induced traumatic ulcers particularly in old denture wearing population where wound healing is impaired with age. Further, large scale, multicenter trials, multiple biochemical markers can further validate these findings and establish long-term clinical utility.

References

1. Budtz-Jørgensen E. (1981). Oral mucosal lesions associated with the wearing of removable dentures. *Journal of oral pathology*, 10(2), 65–80. <https://doi.org/10.1111/j.1600-0714.1981.tb01251.x>
2. Dorey, J. L., Blasberg, B., MacEntee, M. I., & Conklin, R. J. (1985). Oral mucosal disorders in denture wearers. *The Journal of prosthetic dentistry*, 53(2), 210–213. [https://doi.org/10.1016/0022-3913\(85\)90111-8](https://doi.org/10.1016/0022-3913(85)90111-8)
3. Shet R, Shetty SR, M K, Kumar MN, Yadav RD, S S. A study to evaluate the frequency and association of various mucosal conditions among geriatric patients. *J Contemp Dent Pract*. 2013 Sep 1;14(5):904-10. doi: 10.5005/jp-journals-10024-1424. PMID: 24685796.
4. Jainkittivong, A., Aneksuk, V., & Langlais, R. P. (2010). Oral mucosal lesions in denture wearers. *Gerodontology*, 27(1), 26–32. <https://doi.org/10.1111/j.1741-2358.2009.00289.x>
5. Sadr, K., Mahboob, F., & Rikhtegar, E. (2011). Frequency of Traumatic Ulcerations and Post-insertion Adjustment Recall Visits in Complete Denture Patients in an Iranian Faculty of Dentistry. *Journal of dental research, dental clinics, dental prospects*, 5(2), 46–50. <https://doi.org/10.5681/joddd.2011.010>
6. Jovanović, M., Janković, S., Okičić, N., Milojević Šamanović, A., & Milosavljević, M. (2024). Factors affecting the healing of decubital lesions in patients wearing newly made dentures. *Journal of dental sciences*, 19(1), 321–328. <https://doi.org/10.1016/j.jds.2023.03.019>
7. Mubarak, S., Hmud, A., Chandrasekharan, S., & Ali, A. A. (2015). Prevalence of denture-related oral lesions among patients attending College of Dentistry, University of Dammam: A clinico-pathological study. *Journal of International Society of Preventive & Community Dentistry*, 5(6), 506–512. <https://doi.org/10.4103/2231-0762.170525>
8. Mortazavi, H., Safi, Y., Baharvand, M., & Rahmani, S. (2016). Diagnostic Features of Common Oral Ulcerative Lesions: An Updated Decision Tree. *International journal of dentistry*, 2016, 7278925. <https://doi.org/10.1155/2016/7278925>
9. Saraswati, S., Razdan, P., Smita, Aggarwal, M., Bhowmick, D., & Priyadarshni, P. (2021). Traumatic Ulcerations Frequencies and Postinsertion Adjustment Appointments in Complete Denture Patients. *Journal of pharmacy & bioallied sciences*, 13(Suppl 2), S1375–S1380. https://doi.org/10.4103/jpbs.jpbs_207_21
10. Lim, K. S., & Kam, P. C. (2008). Chlorhexidine—pharmacology and clinical applications. *Anaesth Intensive Care*, 36(4), 502–512. <https://doi.org/10.1177/0310057x0803600404>
11. Hibbard, J. S., Mulberry, G. K., & Brady, A. R. (2002). A clinical study comparing the skin antisepsis and safety of Chloraprep, 70% isopropyl alcohol, and 2% aqueous chlorhexidine. *J Infus Nurs*, 25(4), 244–249. <https://doi.org/10.1097/00129804-200207000-00007>
12. Karpanen, T. J., Worthington, T., Conway, B. R., Hilton, A. C., Elliott, T. S., & Lambert, P. A. (2009). Permeation of chlorhexidine from alcoholic and aqueous solutions within excised human skin. *Antimicrob Agents Chemother*, 53(4), 1717–1719. <https://doi.org/10.1128/aac.01289-08>
13. Kotsailidi, E. A., Kalogirou, E. M., Michelogiannakis, D., Vlachodimitropoulos, D., & Tosios, K. I. (2020). Hypersensitivity reaction of the gingiva to chlorhexidine: case report and literature review. *Oral Surg Oral Med Oral Pathol Oral Radiol*, 130(2), 156–160.e151. <https://doi.org/10.1016/j.oooo.2020.04.814>
14. Pawar, R. S., Toppo, F. A., Mandloi, A. S., & Shaikh, S. (2015). Exploring the role of curcumin containing ethanolic extract obtained from *Curcuma longa* (rhizomes) against retardation of wound healing process by aspirin. *Indian J Pharmacol*, 47(2), 160–166. <https://doi.org/10.4103/0253-7613.153422>
15. Zamanian, M. Y., Alsaab, H. O., Golmohammadi, M., Yumashev, A., Jabba, A. M., Abid, M. K., Joshi, A., Alawadi, A. H., Jafer, N. S., Kianifar, F., & Obakiro, S. B. (2024). NF- κ B pathway as a molecular target for curcumin in diabetes mellitus treatment: Focusing on oxidative stress and inflammation. *Cell Biochem Funct*, 42(4), e4030. <https://doi.org/10.1002/cbf.4030>
16. Inchingolo, F., Inchingolo, A. D., Latini, G., Trilli, I., Ferrante, L., Nardelli, P., Malcangi, G., Inchingolo, A. M., Mancini, A., Palermo, A., & Dipalma, G. (2024). The Role of Curcumin in Oral Health and Diseases: A Systematic Review. *Antioxidants (Basel)*, 13(6). <https://doi.org/10.3390/antiox13060660>
17. Zhang, L., Tan, J., Liu, Y., & Luo, M. (2024). Curcumin relieves arecoline-induced oral submucous fibrosis via inhibiting the LTBP2/NF- κ B axis. *Oral Dis*, 30(4), 2314–2324. <https://doi.org/10.1111/odi.14656>

18. Sreenivasan, P. K., & Prasad, K. V. V. (2020). Effects of a chlorhexidine mouthwash on clinical parameters of gingivitis, dental plaque and oral polymorphonuclear leukocytes [PMN]. *Contemp Clin Trials Commun*, 19, 100473. <https://doi.org/10.1016/j.conctc.2019.100473>
19. Stavroullakis, A. T., Carrilho, M. R., Levesque, C. M., & Prakki, A. (2018). Profiling cytokine levels in chlorhexidine and EGCG-treated odontoblast-like cells. *Dent Mater*, 34(6), e107-e114. <https://doi.org/10.1016/j.dental.2018.01.025>
20. Jain, S., Oberoi, N., Kumar, A., Aggarwal, A., & Kaur, K. (2017). A Study to Evaluate the Location and Frequency of Denture-Related Ulcerations and Postinsertion Adjustments in Complete Denture Patients. *Indian Journal of Dental Sciences*, 9(1), 16-21. <https://doi.org/10.4103/0976-4003.201636>
21. Vichare, R., Kulahci, Y., McCallin, R., Zor, F., Selek, F. N., Liu, L., Crelli, C., Troidle, A., Herneisey, M., Nichols, J. M., Shepherd, A. J., Gorantla, V. S., & Janjic, J. M. (2025). Theranostic nanoemulsions suppress macrophage-mediated acute inflammation in rats. *J Nanobiotechnology*, 23(1), 80. <https://doi.org/10.1186/s12951-025-03164-w>
22. Guerrero-Romero, F., Simental-Mendía, L. E., Martínez-Aguilar, G., Sánchez-Meraz, M. A., & Gamboa-Gómez, C. I. (2020). Hypoglycemic and antioxidant effects of five commercial turmeric (*Curcuma longa*) supplements. *J Food Biochem*, 44(9), e13389. <https://doi.org/10.1111/jfbc.13389>
23. Yu, J., Li, X., Fu, X., Wen, J., Jiang, Y., Kuang, Q., Sun, Y., Bai, D., Zheng, C., You, F., & Peng, X. (2026). Targeted repair of oral mucosal injury: emerging applications of biomaterials-based drug delivery systems. *J Nanobiotechnology*, 24(1). <https://doi.org/10.1186/s12951-026-04117-7>
24. Brookes, Z. L. S., Belfield, L. A., Ashworth, A., Casas-Agustench, P., Raja, M., Pollard, A. J., & Bescos, R. (2021). Effects of chlorhexidine mouthwash on the oral microbiome. *J Dent*, 113, 103768. <https://doi.org/10.1016/j.jdent.2021.103768>
25. Chaudhuri, K., Nair, K. K., & Ashok, L. (2018). Salivary levels of TNF- α in patients with recurrent aphthous stomatitis: A cross-sectional study. *J Dent Res Dent Clin Dent Prospects*, 12(1), 45-48. <https://doi.org/10.15171/joddd.2018.007>