Effectiveness of tea tree oil versus chlorhexidine in the treatment of periodontal diseases: a systematic review

Niharika Singh,[1] Lakshmi Puzhankara,*[1] Madhurya N. Kedlaya[1] and Venkitachalam Ramanarayanan[2]

Key points

- Tea tree oil is an effective agent for reducing gingival inflammation.
- The anti-plaque effect of tea tree oil is inferior to that of chlorhexidine.
- In conjunction with the conventional mechanical plaque control measures, tea tree oil is an effective alternative to chlorhexidine in non-surgical periodontal therapy.

Abstract

Background Plaque biofilm that adheres to tooth surfaces and gingiva is the main aetiology of periodontitis. Chlorhexidine (CHX) is considered as a gold standard anti-plaque and anti-gingivitis agent but it has side effects such as permanent staining of teeth and dysgeusia. Tea tree oil (TTO) is an essential oil extracted from the leaves of *Melaleuca alternifolia.* Many studies have reported that TTO exerts strong antibacterial, antifungal, antiviral and anti-inflammatory activities.

Primary study objective The review aims to answer the question of whether TTO (intervention) is a viable alternative to CHX (comparator) for the management of gingival and periodontal disease (outcomes) in adolescents and adults (population).

Methods/design The following search terms were used in PubMed, Scopus, Proquest, Web of Science, EBSCO (dentistry and open access), Cochrane database, Clinical.gov.org and ctri.nic.in to search for relevant articles: patients with periodontal disease; OR periodontitis; OR gingivitis; OR gingival inflammation; AND essential oil; OR tea tree oil; OR Melaleuca alternifolia; AND chlorhexidine; AND reduction in gingival index; OR reduction in plaque index; OR reduction in bleeding from gums. The initial check for the title and abstract screening followed by removal of duplicates in Mendeley Reference Manager (version 1.19.4) based on the inclusion and exclusion criteria were performed.

Primary outcome measures Parameters such as plaque index (PI), plaque surface score, gingival index (GI), bleeding index or bleeding as measured by % of sites with bleeding on probing (BOP) or bleeding scores, papillary bleeding index (PBI), were the primary outcomes considered.

Results TTO is found to be superior to CHX in reducing signs of gingival inflammation; however, CHX is superior to TTO in inhibiting plaque formation, probably due to its increased substantivity.

Conclusion TTO may be used as an alternative to CHX for reduction of gingival inflammation in conjunction with efficient plaque control measures.

Introduction

Periodontitis is a major public health problem and a significant burden to the healthcare economy.[1] In total, 54 billion USD/year is the global cost of lost productivity due to severe periodontitis.[2] It is characterised by inflammation of the supporting structures of the teeth with resulting bone and soft tissue loss and eventual tooth loss if left untreated.[3] The prevalence of periodontal disease in India has been estimated to be in the range of 86.5–100%.[4] Moreover, periodontal disease can impact systemic health through several direct and indirect pathways.[5,6] Management of periodontal disease is thus a critical element for maintaining overall health and reducing the economic and disease burden worldwide. Bacterial colonisation forming a biofilm that adheres to tooth surfaces and gingiva is the main aetiology of periodontitis.[7] Gram-negative anaerobic bacteria, such as *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, *Fusobacterium nucleatum* and *Treponema denticola* are some of the pathogens present in the biofilm that are implicated in the aetiology of periodontal disease.[8] Thus, periodontal therapy primarily involves the removal of the plaque microbiota and balances the inflammatory response in the periodontal tissues.[9] Mechanical plaque control with or without adjunctive use of chemical plaque control agents constitutes one of the initial steps of the etiotropic phase of periodontal therapy.[10]

Several chemical plaque control agents have been in use and chlorhexidine (CHX), which is a broad spectrum antiseptic agent, is considered as a gold standard anti-plaque and anti-gingivitis agent. It acts as an antibacterial agent through disruption of the bacterial cell membrane, increasing

[1]Department of Periodontology, Manipal College of Dental Sciences, Manipal Academy of Higher Education, Manipal, Karnataka, India; [2]Department of Public Health Dentistry, Amrita School of Dentistry, Amrita Vishwavidyapeetham, Kochi, Kerala, India.
*Correspondence to: Lakshmi Puzhankara
Email address: lakshmi.puzhankara@manipal.edu

Submitted 27 July 2021
Accepted 23 September 2021
Published 12 July 2022
https://doi.org/10.1038/s41432-022-0259-6

the permeability of the cell membrane and resulting in cell lysis. It can be either bacteriostatic or bactericidal, depending on the dose. The side effects like permanent staining of teeth and dysgeusia have been noticed associated with CHX.[11] Although non-staining CHX has been researched upon, diversification of research has delved into the use of alternate anti-plaque and anti-gingivitis agents and the search has extended into the field of herbal medicine also.

Studies have shown that traditional herbal medicines and fruits can be used in the prevention or treatment of oral disease due to their ability to inhibit the adhesion of pathogenic biofilms in the oral cavity.[12] Extracts of *acacia catechu*, *aloe vera*, *azadirachta indica*, *glycyrrhiza glabra*, *cinnamomum zeylanicum*, *allium sativum*, *propolis, mikania laevigata, mikania glomerate*, *drosera peltata*, *helichrysumitalicum, coptidis rhizoma*, *piper cubeba*, *azadirachta indica*, *syzygium aromaticum* and tea tree oil (TTO) are some of the herbal medicines used in the treatment of periodontal therapy.[13] TTO is an essential oil extracted from the leaves of Melaleuca alternifolia,which belongs to the family Myrtaceae. Many studies have reported that TTO exerts strong antibacterial, antifungal, antiviral and anti-inflammatory activities (Fig. 1). It contains α-terpineol and terpinen-4-ol, which have been shown to inhibit the growth of *Staphylococcus aureus* and *Escherichia coli*. Terpinen-4-ol and 1,8-cineol have also been shown to inhibit the adhesion of P. gingivalis and reduce inflammation in oral tissue. Thus, TTO has the potential to treat gingivitis.[13] According to a study conducted by Abdul Gani Soulissa *et al.*, the *P. gingivalis* and *A. actinomycetemcomitans* colony counts on enamel surfaces treated with all concentrations of TTO were lower than those in the negative control. These results indicated that TTO inhibited the adhesion of *P. gingivalis* and *A. actinomycetemcomitans* biofilms to enamel surfaces significantly.[14] It has also been observed that the local delivery of TTO gel in case of chronic periodontitis may have some beneficial effects to augment the results of conventional periodontal therapy. It can result in enhanced clinical results without any systemic side effects and bacterial resistance.[15]

Although TTO is seen to be efficacious in controlling periodontal inflammation and plaque formation, there is still no evidence that confirms if it can be an alternative to CHX for the management of periodontal diseases. Therefore, the present review aims to systematically appraise whether TTO can be used as an alternative to CHX to effectively limit plaque accumulation and maintain periodontal health. This review consolidates the existing evidence to show if TTO can be a viable alternative for managing periodontal diseases.

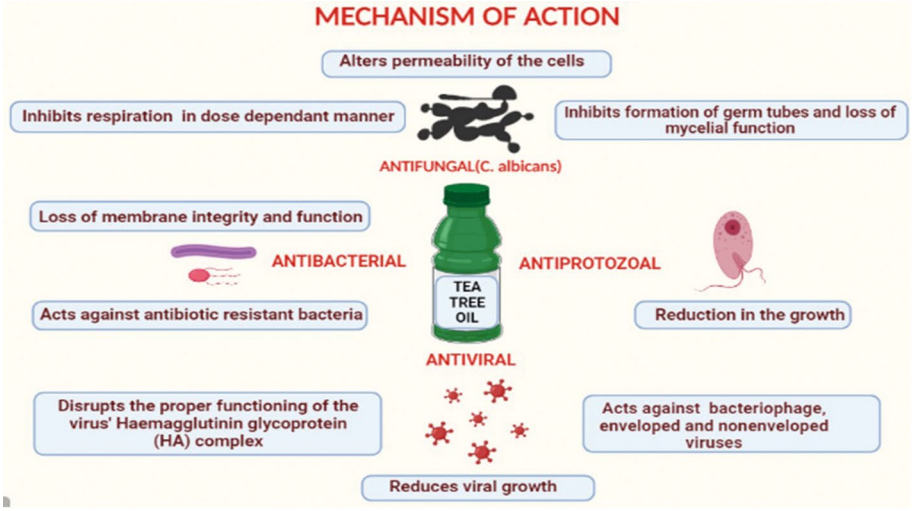


Fig. 1 Mechanism of action of tea tree oil

Method

Protocol and registration

The systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). This systematic review was registered with PROSPERO (#CRD42021241323).

Focus question

The review aims to answer the question of whether TTO (intervention) is a viable alternative to CHX (comparator) for the management of gingival and periodontal disease (outcomes) in adolescents and adults (population). The main objective of this review is to answer the following questions:

- Can TTO be used as an alternative to CHX for controlling gingival inflammation?
- Can TTO be used as an alternative to CHX for controlling biofilm formation?

Search strategy and keywords

The following keywords were used: patients with periodontal disease; OR periodontitis; OR gingivitis; OR gingival inflammation; AND essential oil; OR tea tree oil; OR *Melaleuca alternifolia*; AND chlorhexidine; AND reduction in gingival index; OR reduction in plaque index; OR reduction in bleeding from gums, in PubMed, Scopus, Proquest, Web of Science, EBSCO (dentistry and open access), Cochrane database, Clinical.gov.org and ctri.nic.in to search for relevant articles on 7 March 2021. Additionally, hand searching and snowballing were performed to identify relevant articles. The references in the included studies were checked for additional records. All published articles were included for screening. The grey literature (Google scholar) was also searched along with hand searching for relevant articles in the *Journal of Periodontology*, *Journal of Clinical Periodontology*, *Journal of Periodontal Research*, *Journal of Dental Research*. Open grey literature of any unpublished trials and registry of clinical trials (https://clinicaltrials.gov/) were searched for trial protocols.

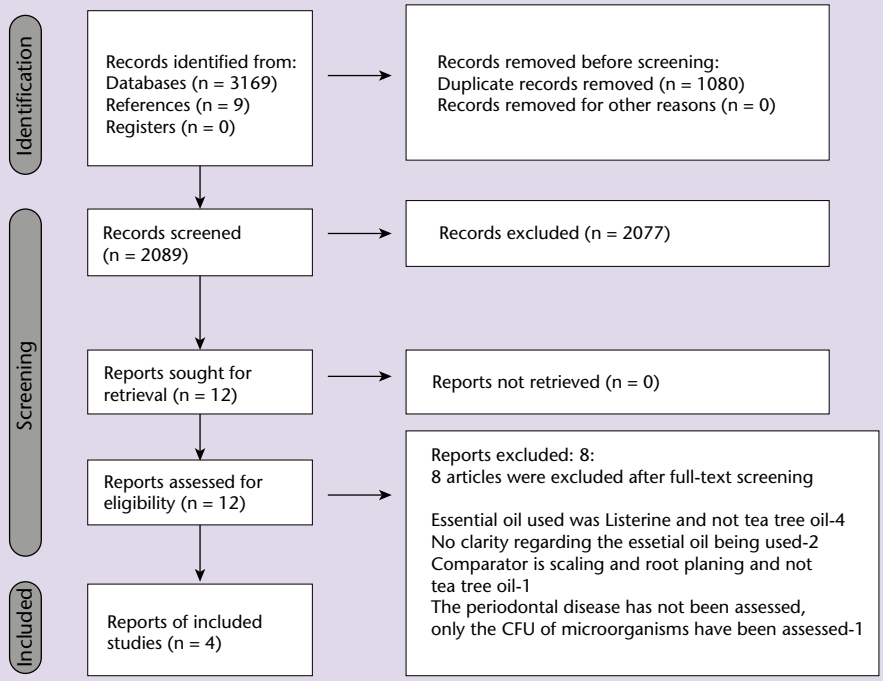
Articles written in English were reviewed and included. Two reviewers (NS and LP) independently performed the searches in different databases. The initial check for the title and abstract screening followed by removal of duplicates in Mendeley Reference Manager (version 1.19.4) based on the following inclusion and exclusion criteria were performed.

Inclusion and exclusion criteria

Types of participants/disease

The studies conducted among patients aged between 12–75 years suffering from any of the periodontal diseases as classified by American Academy of Periodontology classification 1999 were included.[16] Studies with systemically healthy patients without

Fig. 2 PRISMA flow chart



any medical or drug history were included.

Trials including participants without a baseline assessment and more than 50% of the patients who were lost to follow-up were excluded. Studies where patients reported the presence of any oral abusive habit, such as smoking, tobacco chewing or use of any form of tobacco, areca nut, or supari were excluded. Studies with participants undergoing chemotherapy or radiation therapy and pregnant and lactating people were excluded. All studies where TTO was used for the treatment of diseases other than periodontal disease were excluded.

Types of interventions

All patients where TTO was given as an adjunct to non-surgical periodontal therapy (scaling and root planing) were considered. TTO in any concentration and delivery systems were considered.

Type of comparator

CHX, in any concentration and form, prescribed for the treatment of periodontal disease was considered.

Types of outcome measures

The following primary and secondary outcomes were considered for inclusion:

- Primary outcomes: clinical parameters such as plaque index,[17] plaque surface score, gingival index (GI),[17] bleeding index or bleeding as measured by % of sites with bleeding on probing (BOP) or bleeding scores and papillary bleeding index (PBI)[18] were the primary outcomes considered
- Secondary outcomes: dental staining, taste perception, gingival recession (in mm), periodontal inflamed surface area index (in mm^2), alveolar bone loss (in mm or%) and radiographic changes (bone gain in mm or%) were considered.

Study design

All randomised, quasi-randomised and non-randomised clinical trials evaluating the efficacy of TTO compared to CHX were included. We considered studies with a minimum follow-up of 14 days from the start of the intervention or randomisation.

All *in vitro* and animal studies, letters to editors and commentaries and narrative and systematic review articles were excluded. Any study where TTO was not compared to CHX was excluded.

Data collection and analysis

Selection of studies

The results of the searches run on different databases were compiled in the Mendeley Reference Manager (version 1.19.4) and duplicates were removed. For those articles that fulfiled the eligibility criteria, the full articles were retrieved. A sample (that is, 20%) of the retrieved articles was screened by another team member (MK) to ensure a consistent application of the eligibility criteria. Any disagreements were mutually discussed between the two reviewers (NS and LP) and a consensus was reached by arbitration by the third reviewer (MK) if required. The process of study selection is reported using the PRISMA flowchart (Fig. 2).

Data extraction and management

Data extraction was performed on a pilot-tested spreadsheet by two authors (NS and LP) independently. The following data was captured: author details; journal; country of origin; methodology of the study; sample size; type of periodontal disease and its diagnostic criteria; characteristics of the study population; nature of intervention and comparator group; method of randomisation; allocation concealment; blinding; number of follow-up/recall visits; and primary and secondary outcomes. All the data collected was switched among reviewers to check for any discrepancy. In case of any discrepancy, a third reviewer (MK) was consulted and final data was recorded after mutual consensus (Table 1). One reviewer (LP) transferred the data into the Review Manager 5.4 (Review Manager 2020) file.

Assessment of risk of bias in included studies

Two review authors (MK and LP) independently assessed the risk-of-bias (RoB) for each study according to the Cochrane risk-of-bias tool (RoB2).[19] Any disagreement was resolved by involving another review author (VR). RoB was done within and across studies. In the assessment of the RoB, a score of low, high, or unclear was assigned for each included study. The overall quality of each study was then assessed by grading the seven bias categories.[20]

Data synthesis

While the risk of bias was minimal within and across the studies, a quantitative synthesis could not be performed due to the following conditions:

1. The total number of studies were only four. Among them, one study expressed the results in the form of a figure and did not explicitly mention the outcome values. Attempts to contact the author of the study failed
2. Of the three studies, there was considerable clinical heterogeneity, especially with regard to the variation in

Table 1 Characteristics of included studies

Serial no.	Author/ country/ year	Study type	Type of randomisation	Type of disease	Duration of disease	Diagnostic criteria for the disease	Groups/intervention/control			TTO (y/n) (type of TTO)	Comparator CHX (type of CHX)	Sample size	Mean age group	Female to male ratio	Primary outcome	Secondary outcome	Time points of parameter assessment
1	Ripari *et al.*, Italy, 2020	Pilot, randomised, double blinded clinical trial	Computer-generated randomisation list	Dental plaque-induced gingivitis	-	1<GI<3 1<PI<3 BOP, no attachment loss, mobility, periodontitis	Group A: 100% TTO mouthrinse diluted in 100 ml of water	Group B: CHX 0.12% mouthrinse		100% TTO mouthrinse	0.12% CHX mouthrinse	42	18–60 years	30 women and 12 men	• GI (Sillness and Loe) • PI (Sillness and Loe), (O Leary) • Bleeding index (Ainamo and Bay) • Presence of dental dyschromia, taste perception and breath		Day 0 and day 14
2	Soukoulis *et al.*, 2004, Adelaide	Double-blind, longitudinal non-crossover	Not clear	Moderate to severe plaque-induced gingivitis		GI (score of 2–3 in a minimum of one tooth in each quadrant)	Test group: TTO (2.5% TTO-containing gel)	A positive control group; CHX (0.2% CHX gel (Periogard, Colgate, NSW, Australia)	A negative control group (placebo gel identical to the test agent but not containing TTO)	2.5% TTO-containing gel	0.2% CHX gel	49	45.59	25 men and 24 women	GI, 19 PBI and PSS		Week 0, week 4, week 8
3	Elmehy *et al.*, 2018, Tanta	Prospective randomised trial	Random number table	Patients were treated with fixed orthodontic appliances in the upper and lower arches and suffered from chronic gingivitis	-	Not given	Group I (Control group – 20 patients) SRP alone	Group II (Test group – 20 patients) SRP +0.2% CHX mouthrinse twice daily for 2 min with 15 ml	Group III (Test group – 20 patients) 1% TTO mouthrinse twice daily for 2 min with 15 ml	1% TTO mouthrinse twice daily for 2 min with 15 ml	0.2% CHX mouthrinse twice daily for 2 min with 15 ml	60	12–30 years	21 men and 39 women	• PI according to Silness & Loe (1964) • GI according to Loe & Silness, (1963) • PBI according to Mühlemann (1977) • ISI according to Loebene *et al.* (1989)		Baseline 1, 3 and 6 months after treatment
4	Veera Reddy *et al.*, 2020, India	Randomised comparative study	Simple random method (lottery)	Moderate to severe plaque-induced gingivitis	-	PI (Silness and Loe) and GI (Loe and Silness) were used to assess the plaque accumulation and gingivitis	Group A: TTO (0.2%) 10 ml	Group B: CHX (0.12%)	Group C: placebo 10 ml	0.2% TTO mouthrinse 10 ml	0.12% CHX mouthrinse 10 ml	90	12–16 years of age	43 men and 47 women	PI (Silness and Loe) and GI (Loe and Silness)		Baseline, 7 and 15 days

Key:
CHX = Chlorhexidine
TTO = Tea tree oil
PI = Plaque index
GI = Gingival index
PBI = Papillary bleeding index
ISI = Intensity stain index
PSS = Plaque surface score
SRP = Scaling and root planing
BOP = Bleeding on probing

Fig. 3 Risk of bias graph

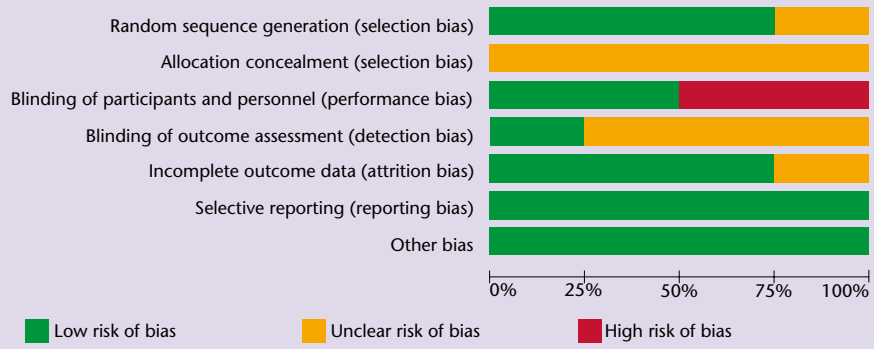


Fig. 4 Risk of bias summary

that terpinen-4-ol suppressed N-formyl-methionyl-leucyl-phenylalanine (fMLP) and lipopolysaccharide (LPS) but not phorbol 12-myristate 13-acetate (PMA)-stimulated superoxide production, while a-terpineol effectively suppressed fMLP-, LPS- and PMA-stimulated superoxide production so that an excessive superoxide activity is inhibited.[33] The antibacterial effect of the TTO has been postulated to result from its ability to disrupt the permeability barrier of the microbial membrane.[15] This in turn results in the loss of membrane integrity and function with leeching of intracellular material and an inability to maintain microbial intracellular homeostasis.[34] In the study by Soukalis *et al.*, there was a greater reduction in GI in the CHX group as compared to the TTO group. This was the only study included in this review in which gel forms of both the agents have been used. In this study, 2.5% TTO has been compared with 0.2% CHX. It may be assumed from the findings of this study that 0.2% CHX is superior to 2.5% TTO in reducing the GI which is contradictory to the findings of the other included studies. However, a systematic review by Supranoto *et al.* has shown that CHX gel is inferior in its ability to control plaque as compared to CHX mouthrinse.[35] Furthermore, in the study by Taalab *et al.* local delivery of 5% TTO gel has resulted in the improvement of pocket probing depth (PPD), clinical attachment loss (CAL), GI and BOP.[36] The variation in the behaviour of the two agents in the included studies may be explained on the basis of the difference in the concentration of the agents used.

CHX has been found to be more effective than TTO in achieving plaque control.[29,30,31] The efficacy of TTO as an antibacterial agent has been shown in several studies.[15,34] Hence, the inferior anti-plaque activity of TTO as compared to CHX might be explained as due to a reduced substantivity or a reduction of its antibacterial properties in comparison to CHX once bounded to oral tissues.[37] TTO has been shown to produce less staining[29,30] and alteration in taste sensation as compared to CHX.[30] Similar results have been observed in other studies.[37]

This review shows that the effect of TTO in reducing gingival inflammation is comparable to that of CHX but its ability to reduce plaque is less. The limitation of the review is that the strength of evidence obtained from this systematic review is based on the limited number of studies with wide clinical heterogeneity. The studies differed in the mode and dose of administration of CHX and TTO, outcome assessment using multiple indices and duration of follow-up visits. Periodontal disease parameters such as PPD and CAL have not been assessed in the included studies. Another limitation was that meta-analysis could not be conducted due to the considerable clinical and methodological heterogeneity. It is recommended that more standardised randomised controlled trials with definite diagnostic criteria for periodontal disease and uniform trial protocol for the administration of TTO and CHX may be conducted to support or refute the evidence on the use of TTO as a replacement for CHX in the management of periodontal diseases.

Conclusion

TTO as a replacement of CHX would be beneficial while considering the adverse effects of CHX on taste perception and staining of teeth. TTO can improve gingival inflammation, reduce BOP and control plaque. TTO is found to be superior to CHX in reducing signs of gingival inflammation elicited through indices such as GI and PBI; however, CHX is superior to TTO in inhibiting plaque formation, probably due to its increased substantivity. Thus, with

existing evidence, it can be concluded TTO may be used as an alternative to CHX for reduction of gingival inflammation in conjunction with efficient plaque control measures.

Ethics declaration

The authors declare no conflicts of interest.

Author contributions

Niharika Singh contributed to conception and design of the work, data collection, drafting the article, critical revision of the article and gave final approval of the version to be published. Lakshmi Puzhankara contributed to conception and design of the work, data collection, data analysis and interpretation, drafting the article, critical revision of the article and gave final approval of the version to be published. Madhurya N. Kedlaya contributed to drafting the article, designing images in the article, critical revision of the article and gave final approval of the version to be published. Venkitachalam Ramanarayanan contributed to data analysis and interpretation, drafting the article, critical revision of the article and gave final approval of the version to be published.

References

1. Batchelor P. Is periodontal disease a public health problem? *Br Dent J* 2014; **217:** 405–409.
2. Tonetti M S, Jepsen S, Jin L, Otomo-Corgel J. Impact of the global burden of periodontal diseases on health, nutrition and wellbeing of mankind: A call for global action. *J Clin Periodontol* 2017; **44:** 456–462.
3. Könönen E, Gursoy M, Gursoy U K. Periodontitis: A Multifaceted Disease of Tooth-Supporting Tissues. *J Clin Med* 2019; **8:** 1135.
4. Janakiram C, Basapathy R, Taha F, Venkitachalam R, Akalgud H, Kadanakuppe S. Equity in Oral Healthcare in India: A Review on Health System Analysis. *Econ Polit Wkly* 2017; **52:** 82.
5. Andriankaja O, Trevisan M, Falkner K *et al.* Association between periodontal pathogens and risk of nonfatal myocardial infarction. *Community Dent Oral Epidemiol* 2011; **39:** 177–185.
6. Nobre M D A, Maló P. Prevalence of periodontitis, dental caries, and peri-implant pathology and their relation with systemic status and smoking habits: Results of an open-cohort study with 22009 patients in a private rehabilitation centre. *J Dent* 2017; **67:** 36–42.
7. Chandki R, Banthia P, Banthia R. Biofilms: A microbial home. *J Indian Soc Periodontol* 2011; **15:** 111–114.
8. Torrungruang K, Jitpakdeebordin S, Charatkulangkun O, Gleebbua Y. Porphyromonas gingivalis, aggregatibacter actinomycetemcomitans, and Treponema denticola/Prevotella intermedia Co-Infection Are Associated with Severe Periodontitis in a Thai Population. *PLoS One* 2015; DOI: 10.1371/journal.pone.0136646.
9. Cekici A, Kantarci A, Hasturk H, Van Dyke T E. Inflammatory and immune pathways in the pathogenesis of periodontal disease. *Periodontol 2000* 2014; **64:** 57–80.
10. Figuero E, Nóbrega D F, García-Gargallo M, Tenuta L M A, Herrera D, Carvalho J C. Mechanical and chemical plaque control in the simultaneous management of gingivitis and caries: a systematic review. *J Clin Periodontol* 2017; DOI: 10.1111/jcpe.12674.
11. Balagopal S, Arjunkumar R. Chlorhexidine: The Gold Standard Antiplaque Agent. *J Pharm Sci Res* 2013; **5:** 270–274.
12. Palombo E A. Traditional Medicinal Plant Extracts and Natural Products with Activity against Oral Bacteria: Potential Application in the Prevention and Treatment of Oral Diseases. *Evid Based Complement Altern Med* 2011; DOI: 10.1093/ecam/nep067.
13. Eid Abdelmagyd H A, Ram Shetty D S, Musa Musleh Al-Ahmari D M. Herbal medicine as adjunct in periodontal therapies – A review of clinical trials in past decade. *J Oral Biol Craniofacial Res* 2019; **9:** 212–217.
14. Soulissa A, Afifah J, Herryawan, Widyarman A. The effect of tea tree oil in inhibiting the adhesion of pathogenic periodontal biofilms *in vitro. Sci Dent J* 2020; **4:** 88–92.
15. Elgendy E A, Abdel-Moula Ali S, Zineldeen D H. Effect of local application of tea tree (Melaleuca alternifolia) oil gel on long pentraxin level used as an adjunctive treatment of chronic periodontitis: A randomized controlled clinical study. *J Indian Soc Periodontol* 2013; **17:** 444–448.
16. Armitage G C. Development of a classification system for periodontal diseases and conditions. *Ann Periodontol* 1999; **4:** 1–6.
17. Löe H. The Gingival Index, the Plaque Index and the Retention Index Systems. *J Periodontol* 1967; **38:** 610–616.
18. Engelberger T, Hefti A, Kallenberger A, Rateitschak K-H. Correlations among Papilla Bleeding Index, other clinical indices and historically determined inflammation of gingival papilla. *J Clin Periodontol* 1983; **10:** 579–589.
19. Sterne J A, Hernán M A, Reeves B C *et al.* ROBINS-I: A tool for assessing risk of bias in non-randomised studies of interventions. *BMJ* 2016; DOI: 10.1136/bmj.i4919.
20. Viswanathan M, Patnode C D, Berkman N D et al. Recommendations for assessing the risk of bias in systematic reviews of health-care interventions. *J Clin Epidemiol* 2018; **97:** 26–34.
21. Alshehri M, Alshail F, Aldosary K M, Alamri A A. Comparison of an essential -oil -based oral rinse and chlorhexidine as adjuncts to scaling and root planing in the treatment of periodontal inflammation. *Interv Med Appl Sci* 2015; **7:** 78–84.
22. Charugundla B R, Anjum S, Mocherla M. Comparative effect of fluoride, essential oil and chlorhexidine mouth rinses on dental plaque and gingivitis in patients with and without dental caries: a randomized controlled trial. *Int J Dent Hyg* 2015; **13:** 104–109.
23. Cortelli S C, Cortelli J R, Holzhausen M *et al.* Essential oils in one-stage full-mouth disinfection: double-blind, randomized clinical trial of long-term clinical, microbial and salivary effects. *J Clin Periodontol* 2009; **36:** 333–342.
24. Kulkarni P, Singh D K, Jalaluddin M, Mandal A. Comparative Evaluation of Antiplaque Efficacy between Essential Oils with Alcohol-Based and Chlorhexidine with Nonalcohol-Based Mouthrinses. *J Int Soc Prev Community Dent* 2017; DOI: 10.4103/jispcd.JISPCD_131_17.
25. Tumer H, Berberoglu A, Caygur A, Yilmaz H G. Clinical Evaluation of Chlorhexidine and Essential Oils' Adjunctive Effects in Subgingival Ultrasonic Instrumentation on Periodontal Parameters and Halitosis. *J Essent Oil-Bearing Plant* 2019; **22:** 169–175.
26. Yilmaz H G, Bayindir H. Clinical evaluation of chlorhexidine and essential oils for adjunctive effects in ultrasonic instrumentation of furcation involvements: a randomized controlled clinical trial. *Int J Dent Hyg* 2012; **10:** 113–117.
27. Siddabasappa K G, Vandana L. Effect of Tea Tree Oil in Chronic Periodontitis Patients: A Clinical and Microbiological Study. *CODS J Dent* 2019; **11:** 26–31.
28. Shetty S K, Sharath K, Shenoy S, Sreekumar C, Shetty R N, Biju T. Compare the efficacy of two commercially available mouthrinses in reducing viable bacterial count in dental aerosol produced during ultrasonic scaling when used as a preprocedural rinse. *J Contemp Dent Pract* 2013; **14:** 848–851.
29. Elmehy G, Abo-Shady T. Comparison Between Tea Tree Oil and Chlorhexidine Mouth Rinse in Treatment of Gingivitis Induced by Orthodontic Treatment: A Randomized Control Clinical Study. *Egypt Dent J* 2018; **64:** 249–256.
30. Ripari F, Cera A, Freda M, Zumbo G, Zara F, Vozza I. Tea Tree Oil versus Chlorhexidine Mouthwash in Treatment of Gingivitis: A Pilot Randomized, Double Blinded Clinical Trial. *Eur J Dent* 2020; **14:** 55–62.
31. Soukoulis S, Hirsch R. The effects of a tea tree oil-containing gel on plaque and chronic gingivitis. *Aust Dent J* 2004; **49:** 78–83.
32. Reddy V, Bennadi D, Satish G, Divya, Guruprasad, Reddy C V K. Effectiveness of tea tree oil and chlorhexidine as mouth rinse in the control of dental plaque and chronic gingivitis – A comparative study. *Eur J Mol Clin Med* 2020; **7:** 1576-1582.
33. Brand C, Ferrante A, Prager R H *et al.* The water-soluble components of the essential oil of Melaleuca alternifolia (tea tree oil) suppress the production of superoxide by human monocytes, but not neutrophils, activated *in vitro. Inflamm Res* 2001; **50:** 213–219.
34. Carson C F, Hammer K A, Riley T V. Melaleuca alternifolia (Tea Tree) oil: a review of antimicrobial and other medicinal properties. *Clin Microbiol Rev* 2006; **19:** 50–62.
35. Supranoto S C, Slot D E, Addy M, Van der Weijden G A. The effect of chlorhexidine dentifrice or gel versus chlorhexidine mouthwash on plaque, gingivitis, bleeding and tooth discoloration: a systematic review. *Int J Dent Hyg* 2015; **13:** 83–92.
36. Taalab M R, Mahmoud S A, Moslemany R M El, Abdelaziz D M. Intrapocket application of tea tree oil gel in the treatment of stage 2 periodontitis. *BMC Oral Health* 2021; DOI: 10.1186/s12903-021-01588-y.
37. Rahman B, Alkawas S, Al Zubaidi E A, Adel O I, Hawas N. Comparative antiplaque and antigingivitis effectiveness of tea tree oil mouthwash and a cetylpyridinium chloride mouthwash: A randomized controlled crossover study. *Contemp Clin Dent* 2014; **5:** 466–470.