***Review Article***

# Evaluation of the effectiveness of herbal and non-herbal oral formulations for the prevention of oral diseases in children: A systematic review and meta-analysis

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## Introduction

"An ounce of prevention is worth a pound of cure"; this statement by Benjamin Franklin eloquently signifies maintaining good oral hygiene as a part of our daily routine. Good oral health is essential for overall physical and psychological well-being. While mechanical tooth brushing and dental flossing are necessary, they may not be sufficient for many children due to factors such as lack of dexterity, motivation, and parental supervision, which can limit their effectiveness[1]. The use of chemotherapeutic agents in mouth rinses can aid in mechanical plaque removal and promote an oral environment free of dental caries and periodontal disease in children[2]. Parents and caregivers should consult with their child's dentist to identify appropriate auxiliary oral care products tailored to the child's individual needs.

Among various antimicrobial delivery systems, mouth rinses are considered one of the safest and most effective options, especially for children above 7 years, as they can deliver therapeutic ingredients to all accessible surfaces in the mouth, including interproximal surfaces[3]. Chlorhexidine mouth rinse is a widely used chemo-mechanical adjunct that is considered the gold standard due to its ability to reduce plaque accumulation and gingival inflammation[4]. However, it has drawbacks, including altered taste sensation, brown staining of teeth, tongue sensitivity and unpleasant taste, which limit its long-term use[5]. Mouth rinses should not be used alone for oral care but should be used in conjunction with mechanical means such as dentifrice, toothbrush, or flossing to control dental caries and plaque[6]. Dentifrice plays a crucial role in reducing the microbial count when used with a toothbrush[6]. Fluoride-containing dentifrice has been proven effective in reducing the microbial count[7].

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The health risks associated with fluoride toxicity from accidental ingestion have increased interest in exploring plant-based antimicrobial agents. Patients prefer safer, healthier products without synthetic or toxic ingredients. Medicinal plants have been used for centuries to treat oral or systemic diseases with oral manifestations. Herbal mouth rinses and dentifrices are popular as they contain no alcohol or colours and provide effective antimicrobial and anti-inflammatory effects through phytochemicals[5,8]. They are cost-effective, easily accessible, and have no side effects[9]. Commonly used herbal mouth rinses include neem, pomegranate, guava, tulsi, propolis, and green tea[10,11]. The literature reveals the antimicrobial and anti-inflammatory efficacy of both herbal and non-herbal oral formulations among the adult population[4]. However, a comprehensive study of the herbal mouth rinses and dentifrices for their antimicrobial and anti-inflammatory efficacies in children is sparse. Thus, this study will be the first to assess the effectiveness of herbal mouth rinses and herbal dentifrices in children.

## Focused question

Are the herbal oral formulations (mouth rinse and dentifrice) effective in reduction of microbial count over the non-herbal commercially available oral formulations in children?

## PICOST format

**P** (Population) - Children under 15 years of age
**I (**Intervention) – Herbal oral formulations (mouth rinse and dentifrice)
**C** (Comparison)– Non-herbal commercially available oral formulations (mouthrinse and dentifrice)
**O** (Outcome) –

1. Reduction of microbial count in children.
2. Reduction of gingival inflammation.
3. Reduction of plaque accumulation.

**S (**Study design) – Randomized control trials, Quasi-controlled trials and Control clinical trial.
**T** (Time frame) – Data collection from past 20 years.

## Objectives

1. To evaluate and compare the efficacy of herbal and non-herbal oral formulations in reduction of microbial count.
2. To evaluate and compare the efficacy of herbal and non-herbal oral formulations in reduction of gingival inflammation.
3. To evaluate and compare the efficacy of herbal and non-herbal oral formulations in reduction of plaque accumulation.

**Method**

***Protocol and registration:*** The review has been registered in PROSPERO international prospective register of systematic reviews funded by National Institute of Health Research and produced by Centre for Reviews and Dissemination, an academic department of the University of York (registration number CRD42022318648 and can be accessed at:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022318648[12].

***Inclusion criteria:***

1. Study setting should be *in vivo*.
2. Study design should be randomized control trials, quasi-randomized, and control clinical trial.
3. Study population should be children under 15 years of age.
4. Study evaluating the microbial count.
5. Study published from 1st January 2000 to 1st January 2023.
6. Studies written in English and studies written in any other language but are possible to get translated into English.

***Exclusion criteria:***

1. Articles reported as an *in vitro* study or a review article.
2. Studies including children with medical conditions and children with special health care needs.

**Search strategy:** Literature search strategy was developed using keywords related to mouthwash, dentifrice, herbal, chlorhexidine, fluoride, commercially available, oral hygiene aid, microbial count, plaque, gingivitis and children. Data were searched through the databases PubMed, Google scholar, Web of science, and Cochrane from 1st January 2000 to 1st January 2023. Cross references were checked; grey literature and hand searching of articles was done when full texts of the relevant studies were unavailable through electronic database.

**Study selection:** Two review authors (BB and SMH) independently screened the titles and abstracts and included them if they met inclusion criteria. Later, full texts of all included studies were obtained and entirely read. Whenever there was uncertainty regarding any study, the problem was resolved by discussing it with another review author (NK). For inclusion of articles for meta-analysis the quality assessment of each article was done by both reviewers independently and later it was cross checked by other reviewers. Finally, the search yielded 42 studies to be included in the systematic review. All the excluded studies were recorded with reason for exclusion for each study (Figure 1).

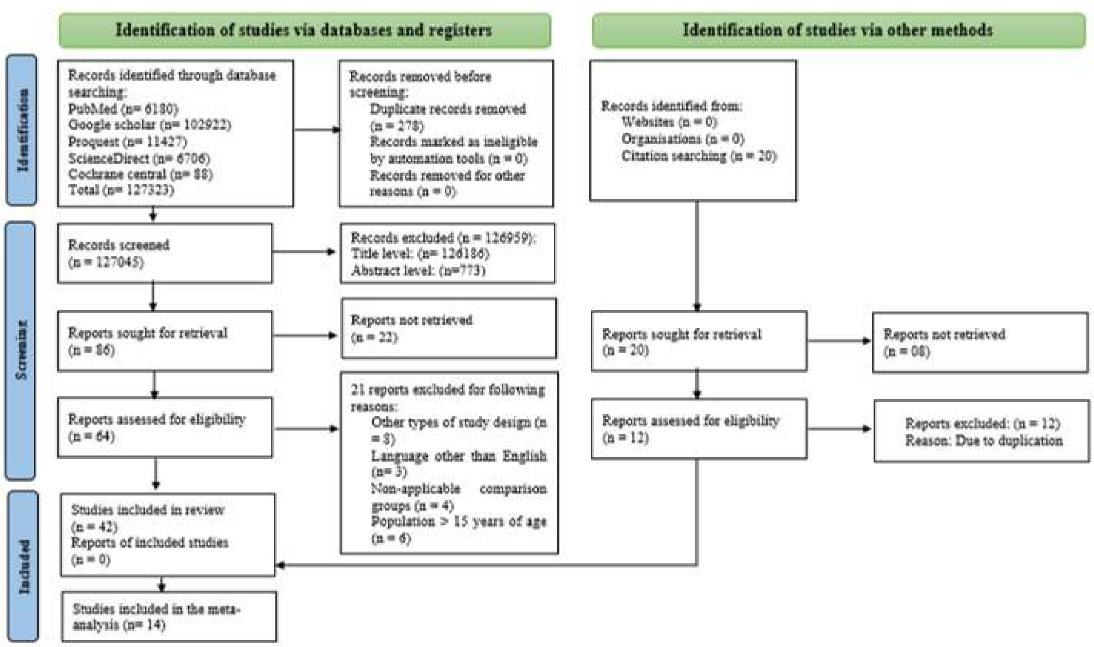


**Figure 1:** ***PRISMA 2020 flow diagram depicting the process of selection and exclusion of articles at each step***

***Data extraction:*** This was performed using a standardized outline. Study characteristics like author and year of publication, study design, age group, control group, test group, any other groups evaluated, follow-up interval, method of outcome assessment, author conclusion were all tabulated for the selected studies (Table 1).

**Table 1: *Qualitative analysis of the studies selected for the systematic review***

| Sl. No | Author and year | Study design | Age group (yrs) | Control group (n) | Test group (n) | Other groups assessed (n) | Follow-up interval (weeks) | Method of assessment | | Author conclusion |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | Primary (microbial) | Secondary (clinical) | |
| 1 | Bajaj *et al* 2011 | RCT | 8 -12 | CHX (440) | Herbal (Triphala extract) (457) | DW (412) | B, 26, 39 | Culture | PI (Silness & Loe) and GI (Loe and Silness) | No significant difference between herbal and CHX mouth rinse group. |
| 2 | Babu *et al* 2011 | RCT | 6-10 | CHX (25) | Herbal (Cacao bean extract) (25) | - | B, 1, 4, 8 | Culture | - | No significant difference between herbal and CHX mouth rinse group. |
| 3 | Mehta *et al* (2013) | RCT | 8-14 | CHX (20) | Herbal (Freshol) (35) | - | NR | Culture | PI (Silness & Loe) and GI (Loe and Silness) | Freshol was better than CHX in reducing microbial count and equi-effective to CHX in altering plaque and gingival scores. |
| 4 | Lobo *et al* (2014) | RCT | 6-12 | CHX mouth rinse | Herbal (LSO mouth rinse) | CHX gel, Herbal (LSO toothpaste), Herbal (LSO gel) | B, 4, 8, 25, 52 | Culture | - | LSO toothpaste demonstrated most long-lasting microbial reduction, whereas other LSO formulations did not effectively reduce microbial levels. |
| 5 | Mishra *et al* (2014) | RCT | 6-14 | CHX (20) | Herbal (20) | Probiotic mint with water (20) | B, 4 | Culture | PI | Herbal rinse proved equally effective as CHX in reducing *S. viridans* counts and plaque accumulation |
| 6 | Jaidka *et al* (2014) | Non-RCT | 7-14 | CHX (10) | Herbal (10) | Xylitol (10) | B, 4 | Culture | PI (Silness & Loe) and GI (Loe and Silness) | Maximum antiplaque, anti-gingivitis and antibacterial activity was displayed by herbal mouthwash followed by xylitol mouthwash and minimum was shown by CHX mouth rinse |
| 7 | Jauhari *et al* (2015) | RCT | 6=12 | NaF (13) | Herbal (*Salvadora persica* extract) (13) | Oil pulling (13) | B, 2 | Culture | - | Efficacy of fluoride and herbal mouth rinses was found to be comparable in reducing bacterial colonization of an individual. |
| 8 | Bhat *et al* 2017 | RCT | 8-14 | CHX (10) | Herbal (Mango extract) (10) | - | - | Culture | PI (Silness & Loe) and GI (Loe and Silness) | Higher reduction in microbial count and better plaque control and gingival health seen in CHX group. |
| 9 | Somaraj *et al* (2017) | RCT | 12-15 | NaF (80) | Herbal (Freshol) (80) | Placebo (80) | B, 26, 39 | Culture | | Both herbal and fluoride mouth rinses were equally effective |
| 10 | Sharma *et al* (2018) | Non-RCT | 6-12 | CHX (15) | Herbal (Hiora) (15) | NaF (15) | B, 2 | Culture | - | Hexidine and fluoritop both showed equal efficacy in reducing *S. mutans* levels but Hiora was inferior to both hexidine and fluoritop |
| 11 | Shah *et al* (2018) | RCT | 7-8 | CHX (15) | Herbal (Oratreat) (15) | DW (15) | B, 2 | Culture | - | Oratreat herbal mouthwash proved to be better compared to 0.2% chlorhexidine mouthwash. |
| 12 | Kamath *et al* (2018) | RCT | 7-10 | CHX (45) | Herbal (*Camellia sinensis*) (45) | DW (45) | B, 2 | Culture | - | CHX mouth rinse in comparison with Camellia sinensis extract or DW was found to be more effective. |
| 13 | Padiyar *et al* (2018) | RCT | 9-12 | CHX (15) | Herbal (Triphala extract) (15) | Herbal (Garlic extract) (15), DW (15) | B, 2, 4 | Culture | PI (Turkesky PI) | CHX was the most effective followed by Triphala and Garlic extracts in antimicrobial effect. |
| 14 | Oznurhan (2018) | RCT | 10-13 | CHX (30) | Herbal (Licorice) (30) | NS (30) | B, 5min, 60 min | Culture | - | No significant differences between CHX and licorice |
| 15 | Hassan *et al* (2018) | RCT | 7-12 | NaF (11) | Herbal (*C. sinensis extract*)(11) | Herbal (Guava extract) (11), NS (11) | - | Culture | - | Green tea extract more effective than guava extract on *streptococcus mutans* in comparison to fluoride |
| 16 | Megalaa *et al* (2018) | RCT | 6-12 | NaF (20) | Herbal (Tulsi extract) (20) | Herbal (Black myrobalans) (20) | B, 1 | Culture | - | NaF showed minimal reduction when compared to herbal extracts; Tulsi leaf extract showed more reduction than black myrobalans. |
| 17 | Kamath *et al* (2019) | RCT | 8-14 | CHX (18) | Herbal (Aloe vera) (25) | Herbal (Tea tree oil) (19), Placebo (27) | B, 2, 4 | Culture | PI (Silness & Loe) and GI (Loe and Silness) | Difference in variables between groups using aloe vera, Tea tree oil and CHX was not statistically significant. |
| 18 | Mon *et al* (2019) | RCT | 10-12 | CHX (25) | Herbal water (25) | Oaonated water (25), DW | B, 2, 4 | Culture | - | CHX was more effective in reducing *S. mutans* count followed by herbal water and ozonated water. |
| 19 | Ali *et al* (2019) | RCT | 5-6 | CHX (14) | Herbal (Green tea) (14) | Placebo (14) | B, 2 | Culture | - | No statistically significant difference between the two groups |
| 20 | Ismail *et al* (2020) | RCT | 8-12 | CHX (20) | Herbal (*S acmella*) (20) | - | B, 2 | Culture | - | Reduction in CHX group was greater compared to *S. acmella* group. |
| 21 | Vilela *et al* (2020) | RCT | 5-12 | CHX (15) | Herbal (EGCG Green tea) (15) | Herbal (*Camellia sinensis*) (15), DW (7) | - | Culture | - | Microbial reduction by EGCG solution was higher than green tea and DW, but less than CHX. |
| 22 | Havale *et al* (2020) | RCT | 8-12 | NaF (15) | Herbal (Coriander) (15) | DW (15) | B,1,2 | Culture | - | Coriander seed oil mouthwash showed equivalent and significant reduction compared to NaF mouthwash |
| 23 | Kamath *et al* (2021) | RCT | 8-12 | CHX (25) | Herbal (Green tea extract) (25) | - | B, 2 | Culture | - | No statistically significant difference in reduction of *S. mutans* count between CHX and green tea mouth rinse group. |
| 24 | Okasha *et al* (2021) | Non-RCT | 6-12 | CHX (20) | Herbal *(R. officinalis*) (20) | - | B, 2 | Culture | - | No statistically significant difference in reduction of *S. mutans* count between CHX group & R. officinalis mouth rinse group. |
| 25 | Bersy *et al* (2021) | Non-RCT | 6-12 | CHX (20) | Herbal (Cinnamon) (20) | - | B, 2 | Culture | - | No statistically significant difference in reduction of *S. mutans* count between CHX group and Cinnamon mouth rinse group. |
| 26 | Mukherje *et al* (2021) | RCT | 6-12 | NaF (30) | Herbal (Triphala, green tea, neem) (30) | Combination (Tulsi 4% with NaF) (30) | B, 1 | Culture | | No statistically significant reduction in *S. mutans* count among groups after 1 week interval. |
| 27 | Sruthi *et al* (2021) | RCT | 12-15 | CHX (30) | Herbal (manuka honey) (30) | - | B, 1, 2 | Culture | PI (Silness & Loe) and GI (Loe and Silness) | No statistically significant difference in *S. mutans* count and plaque and gingival scores between groups at baseline, 7th day, and 14th day. |
| 29 | Bhor *et al* (2021) | RCT | 14-15 | CHX (36) | Herbal (Triphala) (36) | - | B, 4, 12 | Culture | PI (Silness & Loe) and GI (Loe and Silness) | Triphala and CHX had similar inhibitory effect on plaque accumulation, gingivitis, and growth of *S. mutans*. |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 30 | Mohamed *et al* (2021) | Non-RCT | 6-12 | CHX (20) | Herbal (10% Pomegranate peel) (20) | Herbal (10% guava leaves) (20)<br>Herbal (15% pomegranate peel) (20),<br>Herbal (15% guava leaves) (20) | B, 2 hrs | Culture | | Lowest *S. mutans* count recorded with CHX group followed by 15% and 10% pomegranate peel extract groups while lowest performance observed in guava leave extract 15% and 10% groups. |
| 31 | Sajadi *et al* (2021) | RCT | 4-6 | CHX (30) | Herbal (Thyme) (30) | Herbal (Chamomile) (30) | B, 1 | Culture | - | Lowest rate of elevation in the *S. mutans* level after one week was related to chamomile, thyme and CHX |
| 32 | Sajadi *et al* (2022) | RCT | 4-6 | CHX (30) | Herbal (Teucrium polium) (30) | Herbal (Camelia Sinesis) (30) | B, 1 | Culture | - | Teucrium polium and guava leaves significantly more effective compared to CHX. Among the two herbals, Teucrium polium was more effective. |
| 33 | Farrag *et al* (2022) | Non-RCT | 7-12 | CHX (20) | Herbal (Grape seed) (20) | - | B, 1 | Culture | - | No statistically significant difference between the two groups at different time intervals |
| 34 | Havale *et al* (2022) | RCT | 8-12 | NaF (15) | Herbal (Rice husk) (15) | DW (15) | B, 1, 2 | Culture | - | Rice husk mouthwash showed equivalent, significant, and effective reduction in *S. mutans* count similar to NaF mouth rinse. |
| 35 | Kamble *et al* (2022) | RCT | 6-14 | CHX (25) | Herbal (Hiora) (25) | Oral probiotics | B, 2,3 | Culture | - | Oral probiotics showed similar efficacy as CHX in reduction of *S. mutans*. Herbal mouth rinse not as effective as oral probiotics or CHX in reducing *S. mutans* count |
| 36 | Shah *et al* (2022) | RCT | 7-11 | CHX (30) | Herbal (Hiora) (30) | | B, 1 | Culture | - | Reduction of *S. mutans* count in herbal mouth rinse as compared to CHX mouth rinse was statistically significant. |
| 37 | Shankarguru *et al* (2022) | RCT | 6-9 | NaF (30) | Herbal (Virgin coconut oil) (30) | - | B, 4 | Culture | - | NaF group exhibited a higher reduction of *S. mutans* count compared to Virgin coconut oil. |
| 38 | Patil *et al* (2010) | Non-RCT | 4-6 | NaF (50) | Herbal (Himalaya Herbal dental cream) (50) | - | B, 2, 4, 12, 21 | Culture | - | No significant difference in the bacterial count between both groups |
| 39 | Bhati *et al* (2015) | RCT | 6-12 | NaF (15) | Herbal (Aloe vera) (15) | Herbal (Meswak) (15),<br>Placebo (15) | B, 4 | Culture | - | No statistically significant difference in the bacterial count among all groups |
| 40 | Shetty *et al* (2017) | Non-RCT | 9-12 | NaF (20) | Herbal (Munident) (20) | - | B, 4 | Culture | - | Munident dentifrice showed better efficacy compared to NaF dentifrice but not statistically significant. |
| 41 | Patel *et al* (2018) | Non-RCT | 5-10 | NaF (20) | Herbal (Babool) (20) | - | B, 2 | Culture | PI (Silness & Loe) | No significant difference between the two dentifrices. |
| 42 | Chandhru *et al* (2020) | Non-RCT | 3-6 | NaF (10) | Herbal (Coconut Oil) (10),<br>Herbal (Aloe Dent) (10) | Herbal (Patanjali dant kanti junior) (10),<br>Colgate Kids (10),<br>Crest pro-health (10),<br>DW | - | Culture | - | NaF dentifrice showed maximum antifungal activity and Aloe Dent children's dentifrice showed minimum antifungal activity. |
| 43 | Usha *et al* (2021) | RCT | 14-15 | NaF (28) | Herbal (Tulsi) (28) | Placebo (28) | B, 1 | Culture | - | Tulsi extract dentifrice showed maximum reduction in *S. mutans* count for a period of 7 days when compared to fluoridated dentifrice |

*RCT: Randomised control trial, CHX: Chlorhexidine, NaF: sodium fluoride, DW: Distilled water, B: Baseline*

***Risk of bias:*** Risk of bias within each study is mentioned in the form of a figure and the studies are categorized into high (red), some concerns (yellow) and low (green) risk bias according to Risk-of-Bias Visualization (ROBVIS) tool. Most trials were at low risk of bias in the five domains i.e., random sequence generation and allocation concealment, performance bias for blinding of participants and personnel, detection bias for blinding of outcome assessment, attrition bias for incomplete outcome data and reporting bias for selective reporting that we assessed. Summary of the risk of bias for individual study as well as the judgments of the risk of bias for each domain is mentioned (Figures 2 and 3).

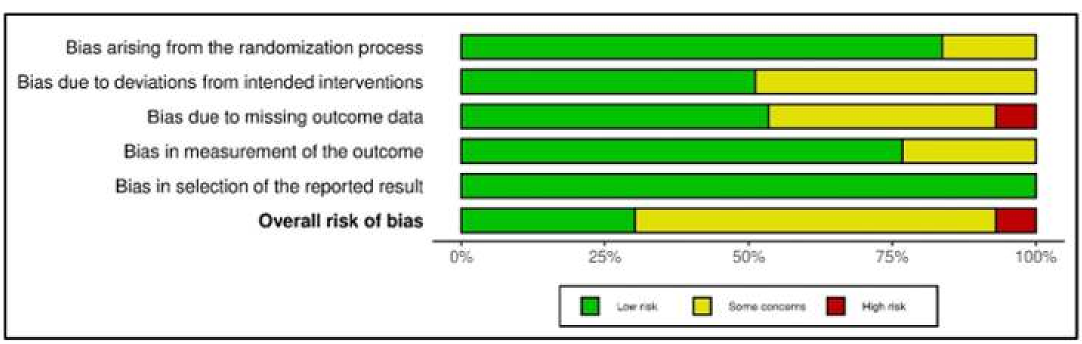


**Figure 3:** ***Graph showing risk of bias: Review authors' judgements about each risk of bias item presented as percentages across all included studies***

**Figure 2:** *Graph showing summary of risk of bias: Review authors' judgements of each risk of bias item for each study*

**Results**

Total articles yielded after the search were 127,323. After screening through titles 126,959 articles were excluded because they were not related to the objectives of the systematic review. Remaining articles were screened for duplicates through Endnote Software Version X7 and 278 articles were found to be duplicates; 86 articles which remained after screening abstracts were sought for retrieval, out of which 22 articles were not retrieved. Thus, they were excluded. Finally, 64 articles were screened for full text. Out of these 64 studies, 21 were excluded the reasons being; 8 articles had other types of study design, three articles were in language other than English, four studies did not have applicable comparison groups and six articles had their study population above 15 years of age. At the end, 42 studies were selected which were then qualitatively analysed after which they were included in the systematic review.

**Meta-analysis**

For quantitative measures, 42 articles were reviewed and 14 of them were selected for meta-analysis. These articles were statistically evaluated using Statistics and Data software (STATA). Forest graph was plotted while comparing the herbal and commercially available mouth rinses.

Meta-analysis was carried out using studies conducted by Babu NSV, *et al*[13] (Study 1), Mehta S, *et al*[14] (Study 2), Jauhari D, *et al*[15] (Study 3), Mon J, *et al*[16] (Study 4), Ali AM, *et al*[17] (Study 5), Havale R, *et al*[18] (Study 6), Kamath S, *et al*[19] (Study 7), Mukherjee A, *et al*[10] (Study 8), Bhor K, *et al*[20] (Study 9), Sruthi KS, *et al*[21] (Study 10), Elkarkhy Y, *et al*[11] (Study 11), Sajadi FS, *et al*[22] (Study 12), Havale R *et al*[23] (Study 13) and Kamble A, *et al*[24] (Study 14).

Forest plot showing pooled data was obtained which showed high heterogeneity among the studies suggesting that studies differed in their sample size. This heterogeneity can also be attributed to smaller number of studies included in the meta-analysis. However, the reason behind small selection was that studies were strictly chosen in accordance with the selection criteria laid down for the study. In our systematic review, we have chosen 14 studies for meta-analysis to evaluate and compare the effectiveness of herbal and commercially available oral formulations in the reduction of microbial count in children. Random effect model was used to plot the graphs. Both groups showed reduction in microbial count in children who used mouth rinse. In our study, the diamond is crossing the line of no effect and is lying on the right side of the line which suggests that the commercially available aids were found to be more effective in reduction of microbial count in children and the difference was statistically significant (p = 0.01) (Figure 4).

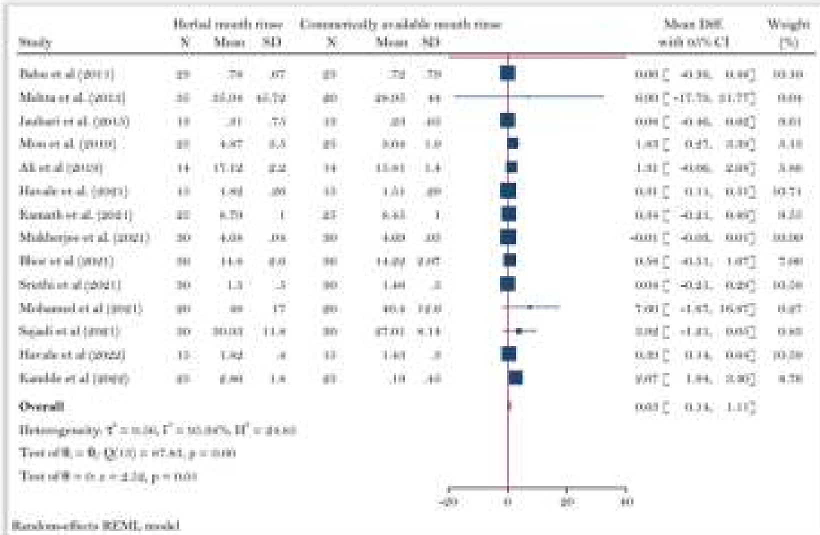

**Figure 4:** ***Forest plot showing pooled data obtained from herbal and commercially available mouth rinse***

Another forest plot was plotted to show the pooled data obtained from meta-analysis of herbal and commercially available mouth rinse based on duration of follow-up. The studies which had short-term follow-up, that is less than or equal to two weeks, showed an equi-effective reduction of microbial count in children in both groups. However, studies which had long-term follow-up, that is more than two weeks, showed that commercially available oral formulations were more effective in reduction of microbial count in children which could be because of the substantivity of chlorhexidine, which allows it to bind to soft and hard tissues in the mouth, enabling it to act over a long period after use. However, the difference between the groups did not show any statistically significant difference (p = 0.10) (Figure 5).

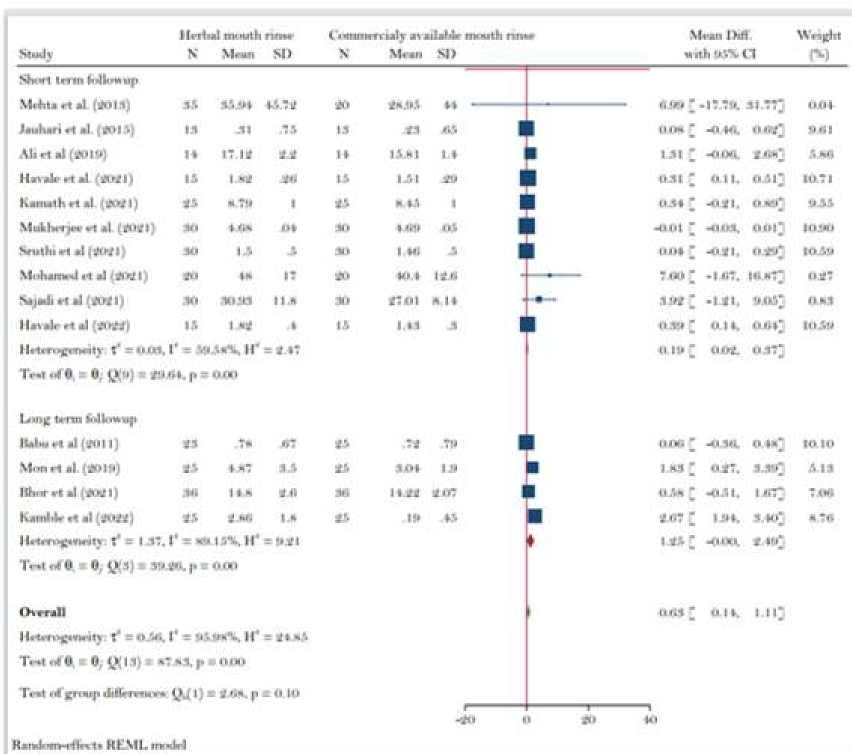


**Figure 5:** ***Forest plot showing pooled data obtained from meta-analysis of herbal and commercially available mouth rinse based on duration of follow-up***

Another 2 forest graphs were plotted while comparing the plaque index and gingival index to evaluate the effectiveness of herbal and commercial oral formulations. (Figures 6 and 7). Plaque index was taken for assessing the reduction of plaque accumulation whereas gingival index was taken to evaluate the efficacy of oral formulations in reduction of gingival inflammation.

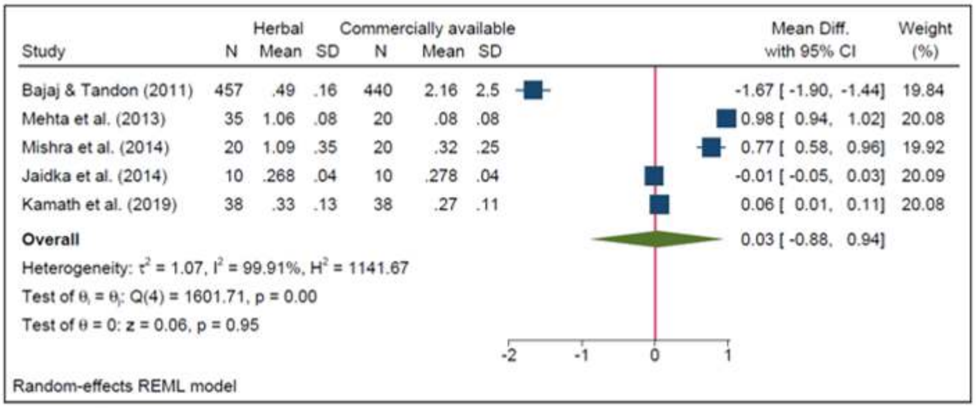


**Figure 6:** ***Forest plot showing pooled data obtained from meta-analysis of plaque index of herbal and commercially available mouth rinse***

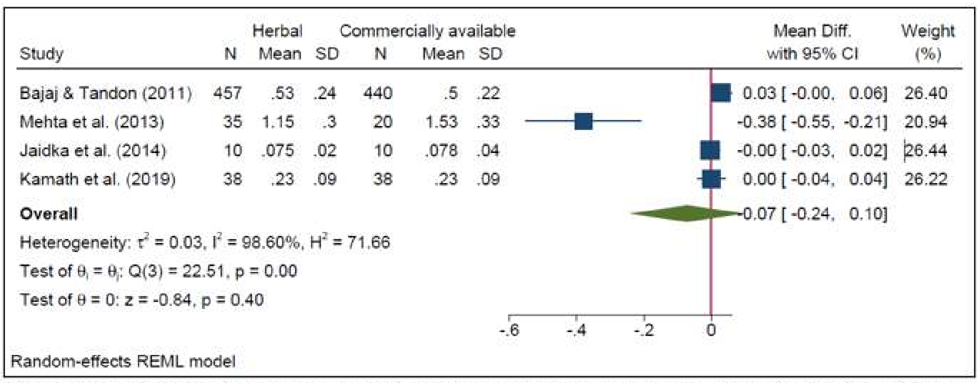


**Figure 7:** ***Forest plot showing pooled data obtained from meta-analysis of gingival index of herbal and commercially available mouth rinse***

In our systematic review, we have chosen 5 studies for meta-analysis for assessing the scores in plaque index and 4 studies for assessing the scores in gingival index. For the plaque index, both groups of oral formulations showed reduction in plaque accumulation in children who used mouth rinse. The pooled estimate showed the central distribution of result which suggests there was no statistically significant difference among herbal and commercially available mouth rinses, as the overall mean difference with 95% confidence interval showed 0.03 value. For the gingival index, herbal mouth rinses showed better results as compared to commercially available mouth rinses; however, it was not found to be statistically significant ($p > 0.05$). None of the studies in dentifrice had assessed plaque and gingival index component for evaluation, hence they were not considered for meta-analysis.

The overall results are also depicted by the diamond which sits on the value of overall effect estimate and the width depicts the overall CI as the left and right ends of the diamond correspond to the lower and upper bounds of 95% CI. Here it was seen that the diamond is crossing the line of no effect and is lying on the right side of the line for the evaluation of microbial count and for plaque index it is merely crossing the line of no effect on the right side, whereas it is lying on the left side of the line for gingival index and it can be interpreted that the calculated difference between the intervention and control groups can be considered statistically significant for microbial reduction and statistically non-significant for gingival and plaque index. This implies that the control group which is the commercially available oral formulations are more effective in reduction of microbial count and equi-effective for plaque accumulation as compared to the experimental herbal group in children. On the other hand, herbal group is more effective in reduction of gingival inflammation among the mouth rinses in children.

***Certainty of evidence:*** Table 2 presents a summary of the findings based on the GRADE approach. In the present review, the outcome of short-term and long-term follow-up assessed was attributed to low certainty and very low certainty of the evidence, respectively.

**Table 2:** ***Table showing GRADE summary of findings***

| Certainty assessment | | | | | | | No. of patients | | Effect | | Certainty | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **No. of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Publication bias** | **Intervention** | **Control** | **Relative (95% CI)** | **Absolute (95% CI)** | | |
| **Short term follow-up** | | | | | | | | | | | | |
| 10 | RCT | Not serious | Serious [a] | Not serious | Not serious | Very serious [b] | 287 | 272 | | SMD 0.19 SD higher (0.02 higher to 0.37 higher) | ⊕⊕◯◯ Low | Critical |
| **Long term follow-up** | | | | | | | | | | | | |
| 4 | RCT | Serious | Serious | Not serious | Not serious [c] | Very serious [d] | 109 | 111 | | SMD 1.25 SD higher (0 higher to 2.49 higher) | ⊕◯◯◯ Very low | Critical |

*CI: confidence interval; SMD: standardized mean difference*

[a] *See Figurr 5, substantial statistical heterogeneity: $I^2$ = 59.58%, p < 0.001. Therefore, inconsistency was downgraded by one level.*

[b] *Presence of publication bias. Therefore, publication bias was downgraded by one level.*

[c] *Small-sample size and hence not enough power to attain reliable level of certainty. Therefore, imprecision was downgraded by one level.*

[d] *Presence of publication bias. Therefore, publication bias was downgraded by one level.*

## Discussion

In modern dentistry, preventive measures that target the causative factors of oral diseases have become increasingly important. In particular, controlling microbial count, gingival inflammation, and plaque accumulation is of primary concern. Natural antimicrobial mouth rinses have been shown to complement mechanical plaque removal which aid in preventing oral diseases[25]. Given the recent trend towards using 'herbal' medicine, the purpose of this study is to investigate the efficacy of herbal oral formulations compared to commercially available non-herbal oral formulations, such as chlorhexidine and sodium fluoride.

When long-term use of mouth rinse is necessary, it is important to consider chlorhexidine substitutes due to the adverse effects associated with its prolonged use. Hence, the US Food and Drug Administration recommended limiting the use of chlorhexidine rinses to 6 months, but the World Health Organization (WHO) has also advised investigating the possible use of natural plants and herb extracts[26].

The current review included 42 randomized control trials which were eligible for the outcomes intended to evaluate. It was observed that the sample size was low for the majority of studies. Low sample size can affect the outcome of the meta-analysis. Nonetheless, differences in the quality of the study designs, populations, percentage of dropouts, and reported loss to follow-up were revealed in further data analysis. We cannot solely conclude that the product investigated is beneficial in reducing plaque and gingivitis. Different formulations of test and control group have different active agents which may have different levels of efficacy and would have affected intervention effects.

In our study for better understanding, we have classified oral formulations into 3 broad categories as per the following: a) Natural herbal extracts; b) Commercially available herbal agents; c) Commercially available non-herbal agents. Among the natural herbal extracts, Triphala, Cacoa bean, *Salvadora persica*, *C. sinesis*, Manuka honey, *Glycyrrhiza glabra*, *Ocimum sanctum*, *T. chebula*, *Aloe babadensis*, *Corriandum sativum*, *Cinnamomum zeylanicum* and *R. officinalis* were found to be equi-effective to the commercially available non-herbal agents. whereas, *Cocos nucifera*, *Magnifera indica*, *Allium sativum*, *Psidium guajava* and *Spilanthes acmella* were found to be less effective compared to the commercially available non-herbal agents. Among the commercially available herbal agents Munident, Babool, Freshol, Hiora and Himalaya were found to be superior or equi-effective to the commercially available non-herbal agents.

One suggested mechanism of action for the active ingredients in herbal agents is the ability to penetrate the biofilm and prevent plaque accumulation[27]. This action has the potential to hinder the colonization of oral bacteria on tooth surfaces, which may contribute to better oral health. Herbal agents contain natural compounds with potential antibacterial and anti-inflammatory properties that may help prevent plaque accumulation and inhibit the growth of oral bacteria[28]. Some of the commonly used herbal agents include tea tree oil, neem extract, and aloe vera[6,10]. Tea tree oil, neem extract, and aloe vera are herbal ingredients with antimicrobial and anti-inflammatory properties that can improve oral health and reduce the risk of dental problems[6,10]. They have demonstrated efficacy in reducing the number of bacteria in the mouth, preventing plaque buildup, and reducing inflammation[6,10]. However, further research is necessary to fully understand the effectiveness and mechanisms of action of these natural remedies.

Since the results of the study indicate significant antimicrobial properties of herbal and commercially available non-herbal oral formulations, herbal oral formulations can be considered as a viable alternative as a daily rinse when desired. Additionally, herbal mouth rinses are suitable for children and individuals with special needs who run the risk of accidentally ingesting chemically formulated mouth rinse solution or fluoridated dentifrice. It is also an affordable choice for patients of low socio-economic status. Collectively, herbal mouth rinse is an option that can improve the oral health-related quality of life of individuals of different ages, socioeconomic background, and medical conditions.

The study had some limitations. During the literature search of our systematic review, we encountered a few lacunae. The heterogeneity observed between studies might have resulted from different methodologies followed, study designs and small sample sizes in the individual studies. Heterogeneity was overcome by the use of random effects instead of fixed effects analysis. Further high-quality long-term randomized controlled clinical trials of more than six months with larger sample sizes are recommended, particularly in children. Also, there is a need to conduct more systematic reviews including studies in language other than English since language was a limitation in our study. Also, there is a need for reporting guidelines for standard herbal concentrations which would enhance the knowledge of the research evidence into policy.

**Conclusions**

Although the herbal oral formulations showed suboptimal effectiveness to the gold standard commercially available non-herbal ones in relation to microbial reduction, it is still an effective alternative that can be used especially in children for long-term use due to its efficacy, safety and cost-effectiveness among children.

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