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ORIGINAL ARTICALE

A COMPARATIVE ANALYSIS ON EFFICACY OF HERBAL EXTRACTS AND CHLORHEXIDINE ON CLINICAL AND MICROBIOLOGICAL PARAMETERS IN CHRONIC PERIODONTITIS- A SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

Objective: To assess effect of herbal medicines compared to 0.12% chlorhexidine (CHX) in periodontitis

Materials and Methods: Review was adhered with Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines and registered in PROSPERO- CRD42024506918. From January 2000 to January 2025, research on the benefits of herbal medicines vs 0.12% CHX on periodontitis in terms of plaque index (PI), gingival index (GI), clinical attachment level (CAL), deep pocket (PPD), and colony forming unit (CFU) was found by searching electronic databases. Using Review Manager (RevMan) software version 5.3, the Cochrane risk of bias (ROB) -2 tool for randomized controlled trials (RCT) was employed to evaluate quality in all of its domains. The standardized mean difference (SMD) was used as a brief statistic measure with a random effect model ($p<0.05$).

Results: Meta-analysis was suitable for nine out of the fourteen studies that satisfied the criteria for selection in the qualitative synthesis. The quality evaluation determined that the risk of bias was moderate to low. A variety of herbs like Punica granatum, Herborals, Morus alba, Natural curcumin, Salvadora persica, Khadiradi vati, Dashansanskar churana, Neem and Apamarga, Ferula assa-foetida, Aloe vera, tea tree oil, Guava leaf extract, Ocimum sanctum were described. The pooled estimate through SMD suggested that herbal medicines were clinically and statistically superior to 0.12% CHX for parameters assessed at 15th and 30th day ($p<0.05$). There was no asymmetry or heterogeneity in the funnel plot, which suggests that publication bias is not present.

Conclusion: It was observed that herbs showed gradual improvement and are equally effective as CHX and could be used as an excellent adjunct to CHX in treating moderate to advanced periodontitis due to its minimal side effects.

***Keywords*:** Chlorhexidine, Gingivitis, Herbs, Plant extracts, Periodontitis, Systematic review

1.INTRODUCTION

Oral health is considered the mirror to systemic health and mouth is a gateway to person's overall health.[1] Periodontal disease (PD) is a health problem that causes tooth loss.[2] Additionally, it is among the most common oral diseases worldwide.[3] It is commonly known that microbial plaque is the primary risk factor of PD. Therefore, most important principle to control or eliminate it should be to either prevent it or treat it. Plaque control with mechanical devices such as toothbrushes or dental floss is insufficient and not without limitations.[4,5]

For this reason, importance is given to prevention as well as treatment with mouthwashes.[6,7]

Chlorhexidine has come to be a "standard" mouthwash due to its potent antibacterial properties, effectiveness and compatibility.[8] However, prolonged use of chlorhexidine might result in silicate and resin treatment, tooth, tongue, and gum stains, as well as dry mouth, ulcers, and taste alterations. It may also cause situations. Therefore, it cannot be used for daily protection.[9,10]

In recent times people are contemplating medicinal plants as an alternative.

Interestingly, in the field of periodontology, multiple herbs have been successfully utilized to reduce tooth plaque and eradicate oral diseases.[11,12] Patients are worried about their oral cleanliness and health in the modern period in which dentists operate.[13] As a result, there is mounting proof that oral and physical health are related.

Herbs and its "natural" components have long been used to safely and effectively restore health in a minimum hazardous way.[14–16] Herbal plants are both supportive and protective in their own way.[17] Many plants that are medicinal and extracts from them are frequently used to treat diseases and protect health.[18,19]

The main benefit of using these therapeutic plants is that there haven't been any documented negative effects thus far. Furthermore, alcohol and/or sugar, two prevalent constituents in the majority of commercially accessible products, are absent from all herbal products.[20]

Based on available data, no research has offered a thorough, quantitative, and comparative review of how herbal remedies and chlorhexidine affect periodontal diseases. Therefore, we conducted a systematic review and revised our study for pertinent studies in order to assess the efficacy of herbal treatments for periodontitis in contrast to 0.12% chlorhexidine.

2. MATERIAL AND METHODS

The PRISMA statement [21] was followed in this review, which was also filed under the Prospective Registration of Systematic Reviews (PROSPERO) number CRD42024506918.

Study design

The research question “Is there any difference in the efficacy of herbal medicines compared to 0.12% chlorhexidine on periodontitis in terms of reduction in Plaque Index (PI), Gingival Index (GI), reduction in Clinical Attachment Level (CAL), periodontal pocket depth (PPD) and colony forming unit (CFU)?” was put out in the Participants (P), Intervention (I), Comparison and Outcome (O) framework.

Eligibility Criteria

a) Inclusion Criteria:

1) Articles have been selected with no time and language restrictions

2) Studies published till January 2025 and having pertinent information about the effect herbal medicines compared to 0.12% chlorhexidine on periodontitis

3) Research presenting the results with regard to PI, GI, CAL, PPD, CFU

4) Research that displays data as frequency, mean, and standard deviation

5) Comparative studies and randomised controlled trials (RCTs) were included

6) The open access journal articles were selected

b) Exclusion Criteria:

1) Any research done prior to year 2000

2) Articles composed in non-English languages

3) Letters to the editor, editorials, abstracts, reviews, and animal studies were not included.

4) Articles from journals that are not open access

5) Articles that fail to provide the study's mean and standard deviation

Screening Process

Search and screening were done by two authors. The process of choosing of articles was divided into two phases. Two reviewers looked over the titles and abstracts of every article in first round. Articles that didn’t fit into the inclusion were removed. Phase-two, involved independent screening and review of few full papers by the same reviewers. Discussions were held to settle by any disputes. A third reviewer was bought in to make the ultimate decision when two reviewers could not agree upon something. All three authors came to agreement on choice in the end. When more information was needed, the studies corresponding authors were contacted by email.

Screening Process

Two authors conducted the investigation and assessment. There were two stages to the article selection process. In the first stage, two reviewers examined each article's abstract and title. Articles that were deemed unfit for inclusion were eliminated. A limited number of complete submissions were individually reviewed and assessed by identical reviewers in phase two. Any disagreements were resolved through discussions. When two reviewers couldn't agree on anything, the ultimate choice was made by a third reviewer. In the end, each of the three authors agreed with the choice. When more information was needed, emails were sent to the papers respective corresponding authors.

Search Strategy

To discover English-language literature, an electronic

search was conducted until January 2024 utilizing EBSCOhost, Google Scholar, and PubMed databases.

Medical Subject Heading (MeSH) terms and relevant keywords were chosen, and they were merged with Boolean operators such as AND: “herbal medicine” (MeSH term) AND “chlorhexidine” (MeSH term); “gingivitis” (MeSH term) AND “periodontitis” (MeSH term); “plaque index” (MeSH term) AND “gingival index” (MeSH term) AND “clinical attachment level” (MeSH term); “pocket depth” (MeSH term) AND “bleeding index” (MeSH term) AND “microbiological analysis” AND “plaque control” AND “randomized controlled trials” (MeSH term); AND “comparative study”.

Data extraction

Final analysis of each included study comprised the following headings: author(s), study nation, study year, sample size, study design, herbal medications utilized, parameters analyzed, and conclusion.

Assessment of methodological quality

The Cochrane Collaboration Risk of Bias (ROB)-2 tool[22] was used to assess the methodological quality of the included clinical trials or randomized controlled trials (RCT) across its different areas in Review Manager (RevMan) 5.3 software.

Statistical analysis

All statistical analyses were carried out using RevMan 5.3 (Cochrane Collaboration, Software Update, Oxford, UK), with the standardized mean difference (SMD) serving as the summary metric.[23] Less than 0.05 was chosen as the significance level.

Assessment of heterogeneity

Any discrepancies in the estimations of the treatment effects of the various studies were evaluated for significance using the Cochran's test for heterogeneity.[24] If P was less than 0.01, it was decided that heterogeneity was statistically significant.

Investigation of publication bias To evaluate publication bias, Begg's funnel plot was employed. Effect size vs standard error was plotted in a funnel. The asymmetry of the funnel plot may indicate publishing bias.[25]

3. RESULTS

Study Selection

After duplicates were eliminated, 121 studies were eliminated from the reference list of included research. After that, articles with full text had been evaluated for eligibility, and those that didn't fit the requirements were removed. Fourteen studies fulfilled the qualifying criteria and were incorporated into the qualitative synthesis, whereas fourteen studies were incorporated into the meta-analysis, as shown in **Figure 1**.

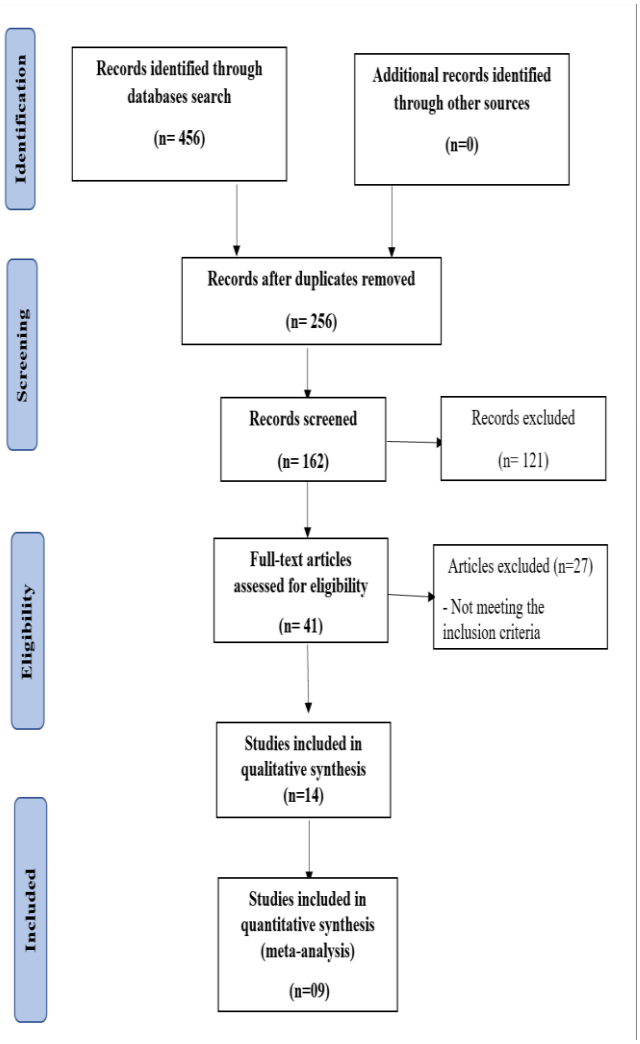

Figure 1. PRISMA Flow Diagram

Study Characteristics

Table 1 displays the results of fourteen research[6, 25–38]that assessed the effectiveness of 0.12% chlorhexidine and a variety of herbal remedies on a total of 1610 teeth. Clinical trial research designs were used in all of the included investigations. Twelve of the included studies[6, 25–29,33,35–38] were carried out in India, one in Malayasia[30], and one in Iran[32]. A variety of herbs has been described which included Punica granatum, Herboral (neem, tulsi, pudina, clove oil, ajwain, triphala), Morus alba, Natural curcumin, Salvadora persica, Khadiradi vati, Dashansanskar churana, Neem and Apamarga, Ferula assafoetida, Aloe vera, tea tree oil, Guava leaf extract, Ocimum sanctum. Various periodontal parameters like GI, PI, CAL, PD, CFU were evaluated between these herbs and 0.12% CHX being followed up for 15th and 30th day. From the results of studies, it was observed that herbs/herbal medicine had better plaque control, showed gradual improvement in controlling gingivitis and are as effective as CHX. The patients accept it biologically, and because it has fewer adverse effects than CHX, it may be a great alternative adjunct for treating intermediate to advanced periodontitis.

Table 1. Showing descriptive study details of included studies

Author, years of study	Country	Study design	Sample size	Herbal medicine used	Parameters evaluated	Follow up duration
Ahuja et al. 2011[25]	India	RCT	20	Punica granatum	GI, PI	15th
Malhotra et al. 2011[6]	India	RCT	50	Herboral (neem, tulsi, pudina, clove oil, ajwain, triphala)	PI	15th day
Gupta et al. 2014[27]	India	RCT	180	Morus alba	PI, GI	15th, 30th day
Anitha et al. 2015[28]	India	RCT	30	Natural curcumin	CAL, PPD	30 day
Prasad et al. 2015[29]	India	RCT	150	Salvadora persica	GI, PI	1st and 5th day
Abdulbaqi et al. 2016[30]	Malaysia	RCT	14	Salvadora persica L	PI	24hrs and 6th day
Mittal et al. 2018[31]	India	RCT	480	Khadiradi vati, Dashansanskar churana, Neem and Apamarga	CPITN	7th day, 30th day and 90th day
Hashemi et al. 2019[32]	Iran	RCT	126	Ferula assa-foetida	PI, GI`	15th day
Kamath et al. 2019[33]	India	RCT	120	Aloe vera, tea tree oil	GI, PI, CFU	30th day
Nayak et al. 2019[29]	India	RCT	60	Guava leaf extract	GI, PI, CFU	30th day
Penmetsa et al. 2019[35]	India	RCT	60	Ocimum sanctum, Aloe vera	GI, PI, BI	15th, 30th day
Saima et al. 2019[36]	India	RCT	90	Herbal rinse	GI, PI	15th day
Siddharth et al. 2020[37]	India	RCT	50	2% curcumin	BI, GI, PI, CAL, PPD	30 day
Gunjal et al. 2024[38]	India	RCT	180	Morus alba	GI, PI, PPD	15th and 30th day

BI: bleeding index; CAL: clinical attachment level; CFU: colony forming unit; CHX: chlorhexidine; CPITN: community periodontal index treatment needs; GI: gingival index; PI: plaque index; PPD: periodontal pocket depth; RCT: randomized controlled trial

Assessment of methodological Quality

Random sequence generation and participant and staff blinding had the highest ROB. The ROB of each included study ranged from moderate to low. The lowest ROB was assigned to the domains of allocation concealment, blinding of outcome assessment, insufficient outcome data, selective reporting, and other bias. **Figures 2 and 3** show ROB for individual studies as well as for other domains.

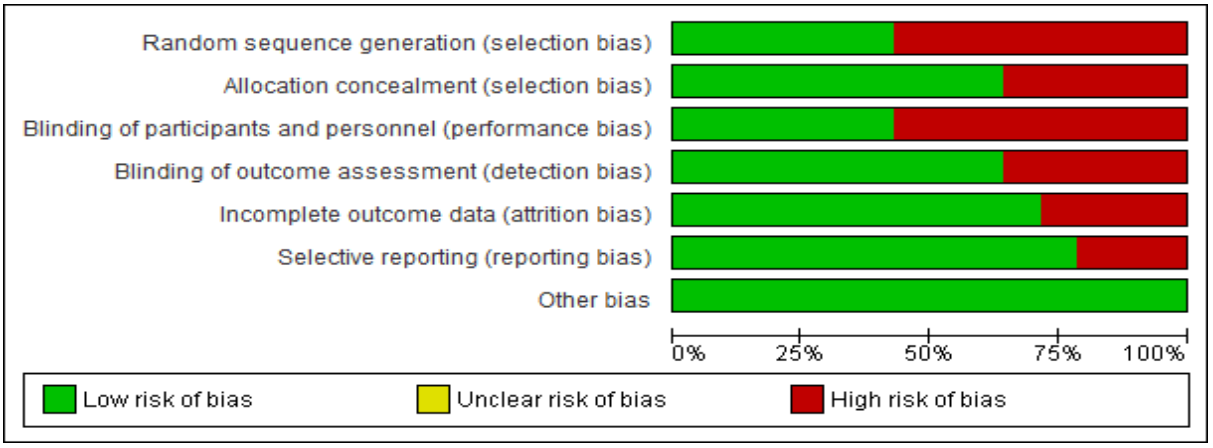

Figure 2. showing ROB graph: presented as percentages across all included studies.

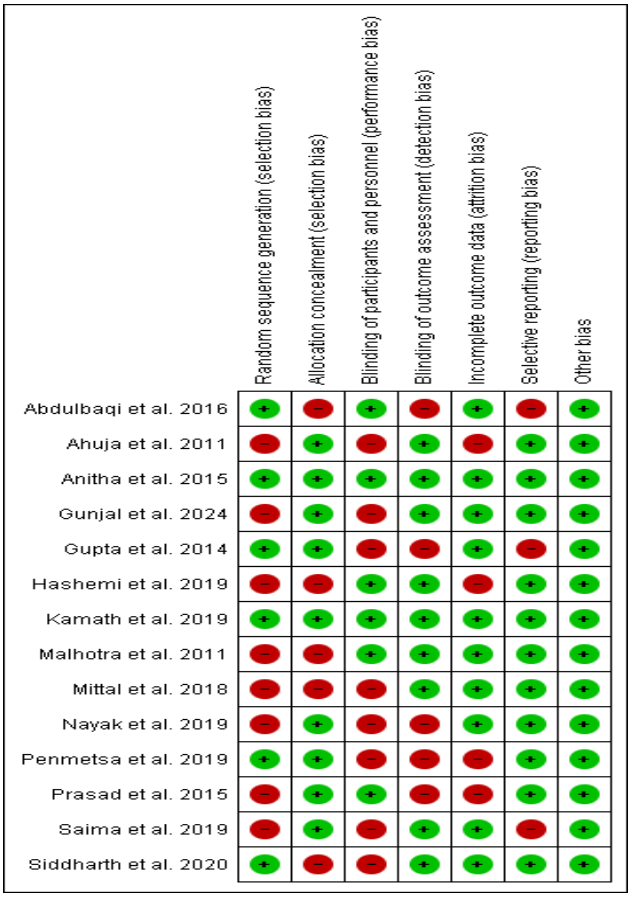

Figure 3. ROB summary: for each included study

Synthesis of results

A meta-analysis was conducted to evaluate the impact of herbs/herbal medicine compared to CHX on various periodontal parameters as shown in figures **4-11.** The parameters were assessed at 15th and at 30th day respectively.

Parameters evaluated at 15th day

Plaque index

Six studies [6, 25–27,32,35,36] with data on 268 patients examined (n=134) patients by CHX 0.12% group and (n=134) patients by herbal group to determine which was more successful in lowering the Plaque Index.

As observed in **Figure 4**, the SMD is 0.83 (-3.69 - 0.03) and the pooled estimates favours the herbal group, indicating that the herbal group has an average reduction in plaque index that is 0.83 times greater (p>0.05).

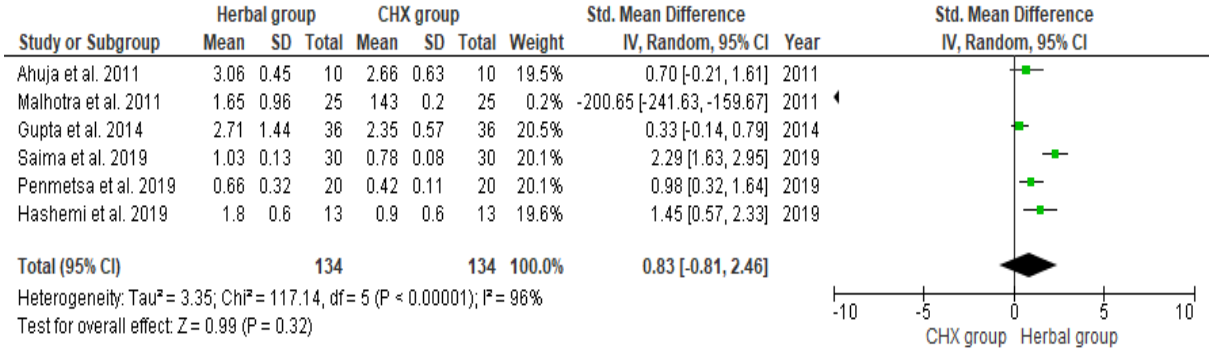

Figure 4. Plaque index between 0.12% CHX and herbal group at 15th day

Gingival index

Five studies had 218 patients in total[25,27,32,35,36] that examined (n=109) patients by CHX 0.12% group and (n=109) patients by herbal group to determine which group was more effective in lowering gingival index. As shown in **Figure 5**, the SMD is 0.68 (0.22 – 1.14) and the pooled estimates favours herbal group signifying that overall greater gingival index reduction on an average is 0.68 times greater in herbal group (p<0.05).

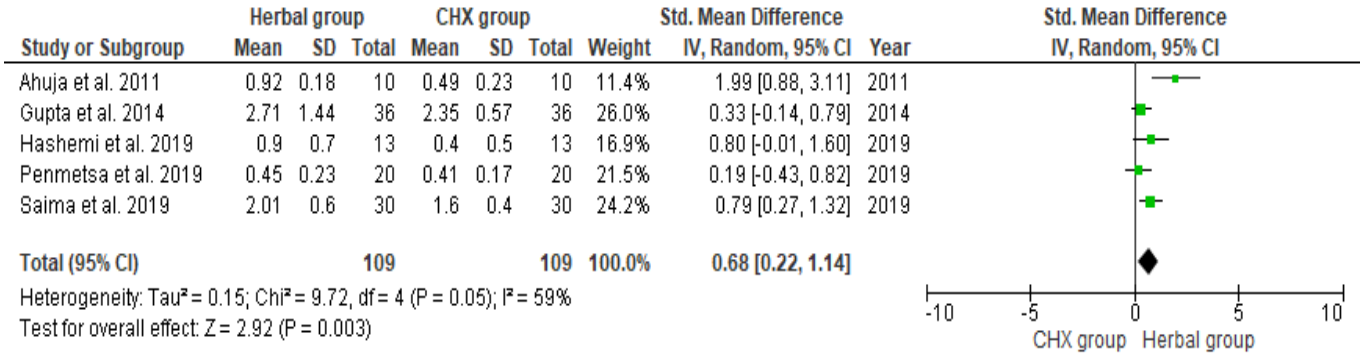

Figure 5. Gingival index between 0.12% CHX and herbal group at 15th day

No asymmetry was visible in the funnel plot, as shown in **Figure 6,** indicating that publication bias did not exist.

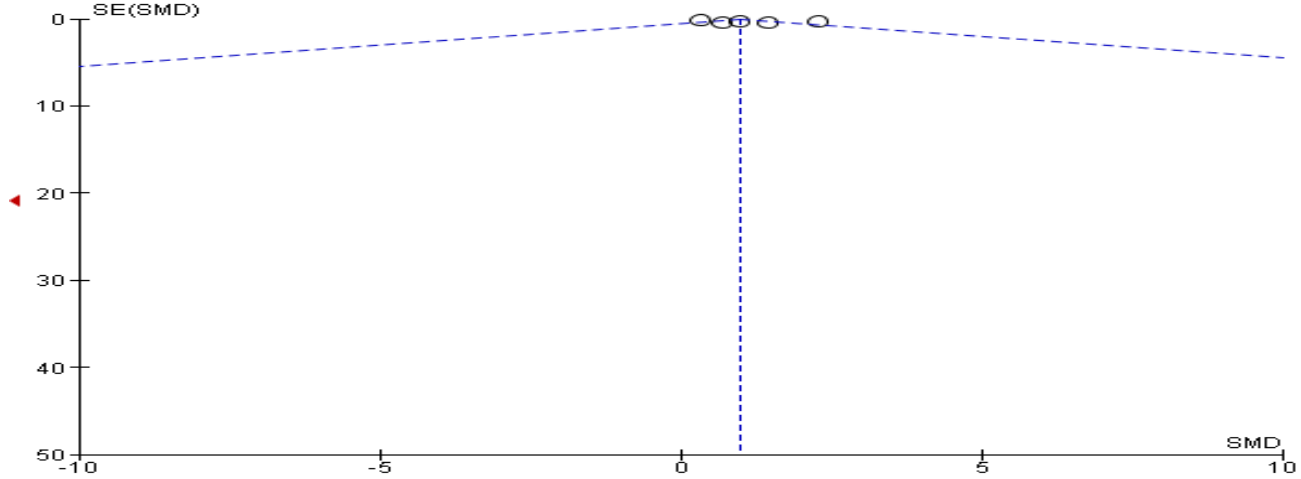

Figure 6. Begg's Funnel plot with 95% confidence intervals showing absence of publication bias

Parameters evaluated at 30th day

Microbial analysis (CFU)

Two studies [33,34] with data on 120 patients tested both the herbal group (n = 60) and the CHX 0.12% group (n = 60) to see which was more effective in reducing colony forming units.

Figure 7 illustrates that the herbal group has a greater overall decrease in colony forming units, with an SMD of 1.87 (01.65 – 5.38), and the pooled estimates favor the herbal group (p>0.05).

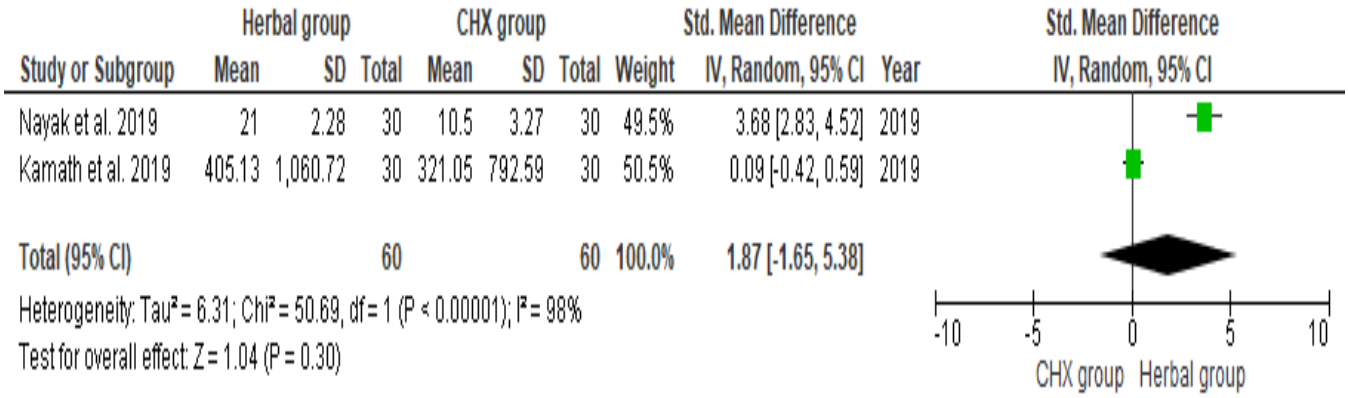

Figure 7. Microbial analysis between 0.12% CHX and herbal group at 30th day

Periodontal Pocket Depth (PPD)

In two studies [28,37] with data on 110 patients,(n= 55) patients were assessed by the CHX 0.12% group and (n=55) patients by the herbal group to determine which was more effective in reducing pocket depth.

As shown in **Figure 8**, the herbal group has a greater overall reduction in pocket depth on average by 1.37 times (p>0.05), with the SMD being -1.37 (-3.20 – 0.45), and the pooled estimates favoring the herbal group.

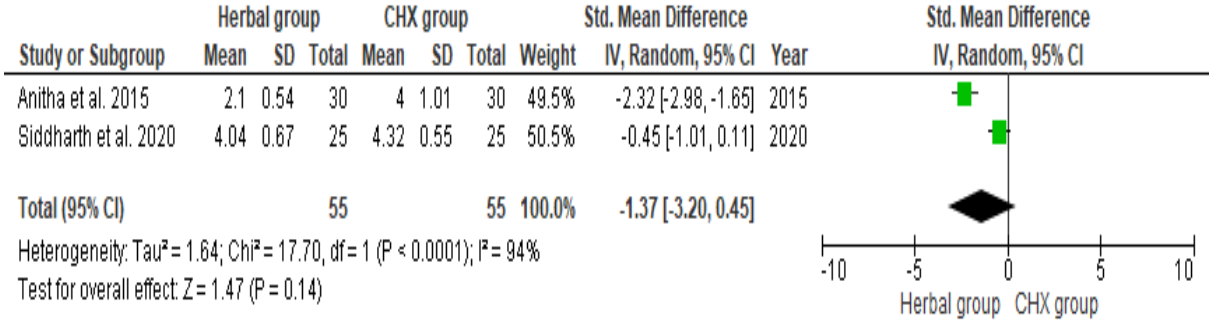

Figure 8. pocket depth between 0.12% CHX and herbal group at 30th day

Clinical Attachment Level (CAL)

Two studies[28,37] including information on 110 individuals, (n= 55) of whom were assessed by CHX 0.12% group and (*n*=55) patients by herbal group in order to evaluate for the better efficacy in lowering the clinical attachment level.

Figure 9 illustrates that the SMD is -1.39 (-3.19 – 0.42) and the pooled estimates favor the herbal group, indicating that the herbal group has an average 1.39-fold larger drop in attachment level (p>0.05).

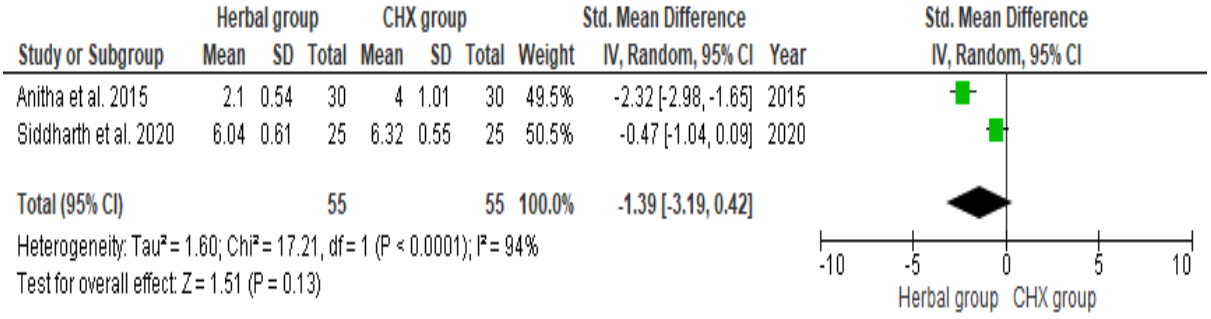

Figure 9. Clinical attachment level between 0.12% CHX and herbal group at 30th day

Gingival Index (GI)

Four studies [27,33–35] including information on 208 individuals, of whom (n=104) were assessed by the CHX 0.12% group and (n=104) by the herbal group to determine which group was more effective in lowering gingival index.

As illustrated in **Figure 10**, the SMD is 2.29 (-0.05 – 4.64), and the pooled estimates favor the herbal group, indicating that the herbal group has an average reduction in gingival index that is 2.29 times greater (p>0.05).

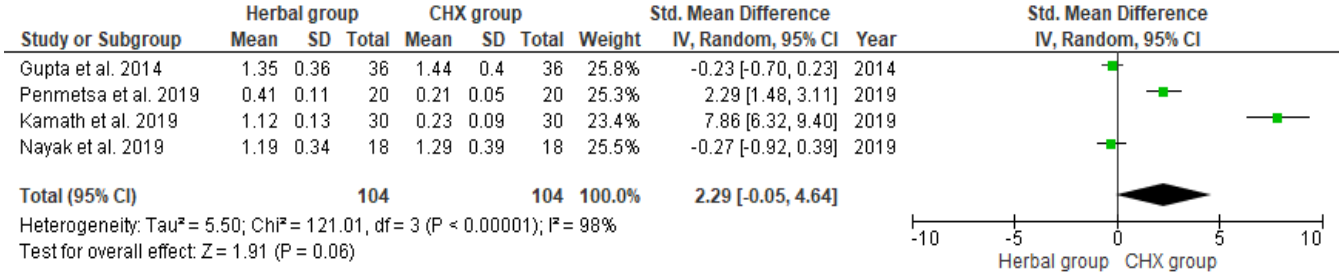

Figure 10. Gingival Index between 0.12% CHX and herbal group at 30th day

Plaque Index PI

Four studies [27,33–35] comprising 208 patient data, of which (n=104) patients were assessed by the CHX 0.12% group and (n=104) patients by the herbal group in order to determine whether group was more effective in lowering it.

Figure 11 illustrates that the SMD is 2.46 (0.55 – 4.37) and the pooled estimates favor the herbal group, indicating that the herbal group has an overall greater reduction in plaque index on average, which is 2.46 times greater ($p<0.05$).

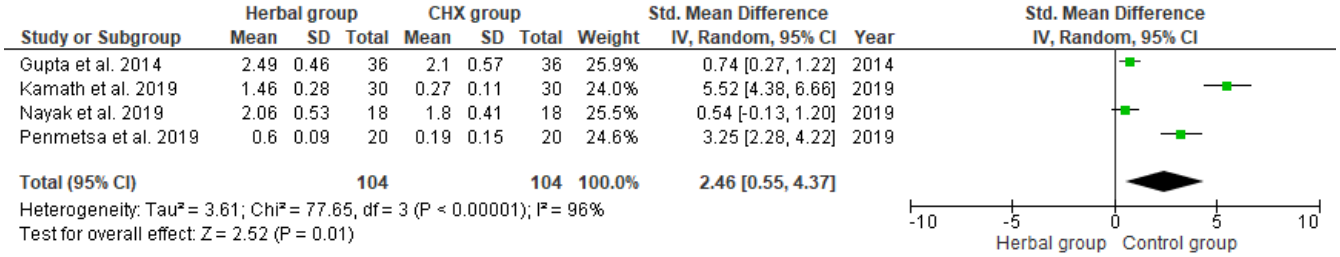

Figure 11. Plaque Index between 0.12% CHX and herbal group at 30th day

There was noticeable asymmetry in the funnel plot, which suggested the existence of publishing bias in **Figure 12.**

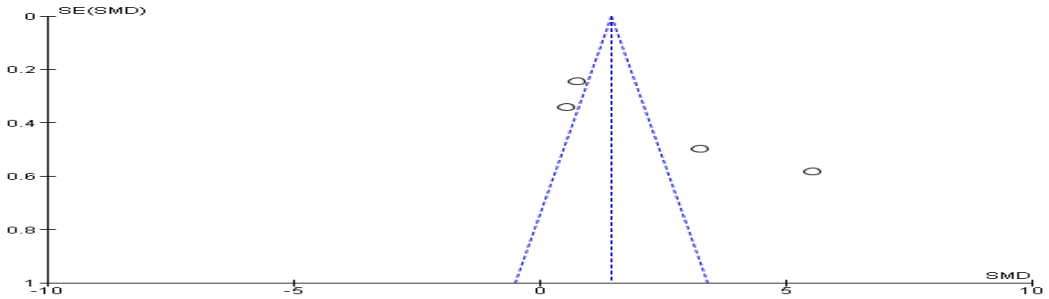

Figure 12. Begg's Funnel plot with 95% confidence intervals presence of publication bias

DISCUSSION

Dos santos et al.[39] performed a systematic review of RCTs with the aim to assess the effect of medicinal plants on dental biofilms. 47 studies were involved in review with herbs like Melaleuca alternifolia, Azadirachta indica and Ricinus communis oil compared against CHX for evaluating parameters like GI, PI and microbial count analysis. Based on the study's findings, it was determined that these herbs work equally as effectively as CHX. and could be a safer treatment for treating periodontal conditions.

The impact of curcumin as an alternate supplement to scaling and root planning was quantitatively analyzed by Zhang et al.[40] in comparison to CHX. Nine RCTs were found when databases were examined till February 2021. PI, GI, CAL, and PPD were evaluated at 3, 4, 6, and 12 weeks. It was observed that no significant difference was seen on reduction in attachment level while effect on GI and PI were similar to that of CHX.

Chatzopoulos et al.[41] observed a systematic review on effectiveness of herbal medicines in patients with periodontitis compared to conventional mode of treatment (scaling and root planning or supragingival debridement). Databases were searched or randomized and non-randomized trial till March 2022. From the finding of the study, it was concluded that herbal products showed better superior and effective clinical periodontal outcomes compared to conventional treatment.

Pasupuleti et al.[42] executed a systematic review on efficacy of herbal medicines within periodontal therapy. Databases were searched till June 2022. 14 studies fulfilled their eligibility criteria, of which eight were original studies and six were review articles. Glycyrrhiza glabra, ficus religiosa, plantago major,

medicago sativa, trifolium pratense, mangifera indica, pongamia pinnata, husk of Cocos nucifera, the root of g. glabra, curcuma longa, leaves of psidium guajava, azadirachta indica, fruits of citrus medica, punica granatum, ocimum moringa oleifera extract, and pomegranate peel extracts were among the various herbs that were included in the review. It was discovered that these herbs' alkaline properties, which have antibacterial properties, stop plaque and calculus from forming. Additionally, because of their anti-inflammatory and antioxidant qualities, these herbs may be used as a supplement to regular oral prophylactics.

This is the novel systematic review and meta-analysis that assesses impact of various herbs and herbal medicines on periodontal diseases and metrics, compared to 0.12% CHX. Databases were searched till January 2024 yielding 14 RCTs assessing the effect of herbal medicines compared to 0.12% CHX on parameters like GI, PI, CAL, PD, CFU at 15th and 30th day. A variety of herbs has been described which included Punica granatum, Organic curcumin, Morus alba, Herboral (neem, pudina, tulsi, clove oil, ajwain, and triphala), Salvadora persica, Khadiradi vati, Dashansanskar churana, Neem and Apamarga, Ferula assa-foetida, Aloe vera, tea tree oil, Guava leaf extract, Ocimum sanctum.

Reviews are widely regarded as the finest available evidence. But the level of quality the incorporated research determines how strong the evidence is. The current evaluation comprised enough studies with an identified risk of bias and a brief observation time.

Therefore, the evidence currently available is enough to provide therapeutic recommendations in answer to the focus issue of the current systematic review.

5. CONCLUSION

It was observed and demonstrated through the meta-analysis that herbal extracts had better plaque control, showed gradual improvement in controlling gingivitis and are as effective as CHX. Patients accept it biologically, and because it has fewer adverse effects than CHX, it may be a great alternative adjunct for treating moderate to advanced periodontitis.

DECLARATIONS

Ethical approval and consent to participate

Not Applicable

Availability of data and material

All data generated or analyzed during this study are included in the published article.

Competing interest

The authors declare that there are no competing interests.

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