Original Research Article

Evaluation of an Ayurvedic toothpaste in a diabetic population

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ABSTRACT

Background: Diabetes mellitus is a chronic disease that is present in almost every country around the world. Diabetics are known to suffer more from gingivitis/periodontitis than the general population. The projected increase in the diabetic population will only lead to an increase in oral diseases, such as gingivitis in this population.

Aim: This study evaluates an Ayurvedic toothpaste for the control of gingivitis in a diabetic population.

Materials and Methods: In vitro and in vivo evaluations were performed on this Ayurvedic toothpaste. The in vitro study used a well known anaerobic biofilm model. In the in vivo clinical studies, diabetic subjects were evaluated for plaque and gingivitis using classical methods. The subjects were also evaluated using traditional Ayurvedic endpoints, namely *Raktasrava* (gum bleeding), *Shotha* (inflammation), and *Dantamamsa mriduta* (sponginess of gums).

Results: The results of these evaluations demonstrate that the Ayurvedic toothpaste has antibacterial efficacy against anaerobic bacteria. Its use by diabetic subjects resulted in a reduction in plaque and gingival indices in two separate studies lasting up to 6 months. In addition, there was an improvement in the Ayurvedic endpoints in these clinical studies as well.

Conclusions: This study demonstrates that an Ayurvedic toothpaste has a positive oral health benefit in diabetic subjects who suffer from gingivitis.

Key Messages: The research reported within demonstrates that this Ayurvedic toothpaste has a positive oral health benefit in diabetic subjects who suffer from gingivitis. It has also shown effectiveness against anaerobic bacteria that are responsible for periodontal infections.

1. Introduction

Diabetes mellitus is a chronic disease that is present in almost every country around the world. A recent publication from the International Diabetes Foundation, estimates that globally 463,000,000 individuals are living with diabetes and that this number is projected to increase to 578,000,000 in 2030 and 700,000,000 in 2045.[1] Furthermore, they report that India has the second largest diabetic population estimated at 77,000,000 in 2019 rising to 101,000,000 in 2030 and 134,000,000 in 2045. Two recent publications have estimated the overall prevalence of diabetes within the Indian population to be between 7.3%[2] and 7.7%,[3] and this percentage is only expected to increase. Lamster et al. surveyed the literature and identified a number of oral health conditions that are impacted by diabetes. Among these are dental caries, salivary dysfunction, gingivitis, and periodontitis.[4] A more recent review concluded that there is a clear correlation between diabetes and periodontal disease.[5] Diabetics are known to suffer more from gingivitis/periodontitis than the general population.[6,7] The projected increase in the diabetic population will only lead

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to an increase in oral diseases, such as gingivitis in this population.

There are many clinical studies in which oral care products, such as toothpastes and mouthrinses, have been evaluated for their efficacy against various oral health conditions,[8–13] but only a few were conducted in diabetic subjects. In a 3-month clinical study, Raslan et al. determined daily use of a mouthrinse containing essential oils after ultrasonic debridement benefited diabetic and non-diabetic patients in terms of reductions in plaque index and gingivitis index.[14] Additionally, an herbal mouthrinse containing *Punica granatum* (Golnaar) was compared to one containing 0.2% Chlorhexidine (CHX) in diabetic subjects. After 2-weeks of use, the Golnaar mouthrinse showed a statistically significant reduction in mean gingival index as compared to the CHX mouthrinse.[15]

Ancient classical Ayurvedic texts contain detailed descriptions about the causes, symptoms, and management of diabetes – known as *Prameha* in Ayurveda.[16] Various single herbs, formulations of multiple herbs, and herbo-mineral formulations have been prescribed in these texts along with life-style modifications including diet and exercise.[16] Globally, individuals with diabetes have been known to be 1.6 times more likely to use Complementary and Alternative Medicine (CAM) than non-diabetics.[17] In India too, many diabetics continue to seek Ayurvedic interventions for managing diabetes.

In recent times, there has been a significant interest in corroborating the experiential knowledge contained in the Ayurvedic texts by applying modern research methodologies.[18] While this is a welcome development, it is a challenge to holistically capture and substantiate the nuances of Ayurvedic epistemology through the use of modern research methodologies.[19]

Several research papers have been published on herbal medicines wherein the primary focus has been on studying the anti-hyperglycemic activity. Papers elucidating the mechanisms of action of these herbs in diabetes are fewer.[19] Several plants such as *Curcuma longa* (turmeric), *Phyllanthus emblica* (*amla*), *Eugenia jambolana* (black plum or *jamun*), *Momordica charantia* (bitter gourd or *karela*), *Gymnema sylvestre* (*gurmar*), *Ocimum sanctum* (holy basil or *tulsi*), *Trigonella foenum-graecum* (fenugreek, *methi*), *Coccinia indica* (ivy gourd, *kunduru*), *Aegle marmelos* (*bel*), *Pterocarpus marsupium* (*vijayasara*), and *Azadirachta indica* (neem) have been studied for their anti-diabetic activity.[16,19] Systematic reviews or meta-analysis are available on few plants such as *Gymnema sylvestre*,[20] *Aloe vera*,[21] *Momordica charantia*,[22] *Nigella sativa*,[23] and Berberine[24] (a constituent from *Berberis aristata*).

In recent times, there have been studies conducted on certain herbs such as *Gymnema sylvestre* (Gurmar) on its efficacy on dental caries.[25] Further, Gurmar and some other herbs have also shown significant anti-inflammatory, immunomodulatory and antioxidant activity.[26,27]

This observation led to the hypothesis that an Ayurvedic oral care formulation containing proven herbs which possess anti-inflammatory, immunomodulatory and antioxidant activity may provide benefits in periodontitis in diabetics which may even lead to better holistic management of diabetes. Hence, this unique toothpaste formulation, containing Yashad Bhasma (Zinc oxide), Madhunashini (*Gymnema sylvestre*), Surya Kshar (Potassium nitrate), Amalaki (*Emblica officinalis*), Nimba (*Azadirachta indica*), and Jamun (*Eugenia jambolana*), was developed and evaluated to test its efficacy in both in vivo and in vitro studies.

The Ayurvedic parameters used in the clinical studies for the assessment of gum health are similar to those used in modern medicine in terms of gum bleeding, sponginess of the gums and inflammation.

The ecosystem of germs is continuously in flux on the tooth surface and along the gum line. This complex structure is called biofilm, which provides protective environment for bacteria residing in the biofilm relative to their planktonic counterparts, which makes the chemotropic effect of active ingredients on the bacteria more difficult. This is especially true for anaerobic bacteria. Biofilm formed by these anaerobic bacteria are responsible for gingival and periodontal infections. The in vitro research reported within evaluated the antibacterial efficacy of the Ayurvedic toothpaste against anaerobic bacteria.

2. Materials and Methods

In vitro method,[28] in which biofilm was grown in an anaerobic chamber on hydroxyapatite (HAP) discs. HAP discs are the experimental equivalent of human tooth enamel as they bear the same inorganic structure of tooth enamel. Saliva collected from four healthy volunteers was pooled together and used as an inoculum. The HAP discs were immersed in a mixture of human saliva and artificial saliva in 1:1 proportion. The HAP discs were incubated for 24h allowing the biofilm to develop.

The discs were treated with 1:2 toothpaste to water slurry. Each sample was treated in triplicate twice a day for 8 days. Recovery and quantification of biofilms on HAP discs was done after 16 treatments to measure viable bacteria using the BacTiter-Glo[TM] Microbial Cell Viability Assay (Promega Corp., Madison WI, USA). Three toothpastes were compared in this study, Regular Fluoride Toothpaste, Ayurvedic toothpaste and a positive control toothpaste, known for its effectiveness in this model.

The following applied to both the 12-week clinical study and the 6-month clinical study, except as noted. The test products used were as follows:

2.1. Test

An ayurvedic toothpaste containing Yashad Bhasma (Zinc oxide), Madhunashini (*Gymnema sylvestre*), Surya Kshar (Potassium nitrate), Amalaki (*Emblica officinalis*), Nimba (*Azadirachta indica*), and Jamun (*Eugenia jambolana*) in a flavoured calcium carbonate/fluoride base (Colgate-Palmolive Company, Mumbai, India).

2.2. Negative control

A commercially available fluoride toothpaste in a calcium carbonate base (Colgate-Palmolive Company, Mumbai, India).

A commercially available soft-bristle toothbrush was provided to the panelists for use during the study.

Healthy adult male and female subjects aged 25-70 years from New Delhi that had an initial gingivitis index (GI) score ≥1.5 and a certified A1C level at least 6% but no more than 8% within 3 months prior to the study start were eligible for enrolment. The studies were approved by the Good Society Ethical Research Institutional Review Board, and all patients signed an Informed Consent.

The sample size of 50 per group was determined based on a standard deviation for the response measure of 0.58, a significance level of $\alpha = 0.05$, a 10% attrition rate and an 80% level of power. The study was powered to detect a minimal statistical difference between the study group means of 15%. The sample calculation utilized historical data from previous studies. Subject-wise scores were calculated by summing all scores for all sites and dividing by the total number of sites scored.

Gingivitis Assessments for both the clinical studies (12-week and 6-month studies) were performed. The degree of gingival inflammation was scored at 6 sites (disto-, mid-, mesio-buccal and disto-, mid, mesio-lingual) of each tooth according to the criteria of the Gingival Index system.[29]

Dental Plaque Assessments for only 6-month study was performed. The dentition was disclosed with disclosing solution and plaque scored at the disto-, mid-, mesio-buccal and disto-, mid-, mesio-lingual surfaces of each tooth according to the criteria of the Quigley and Hein Index.[30]

Ayurveda assessments (12-week and 6-month studies) were conducted by a licensed Ayurveda physician and evaluated the following attributes: *Raktasrava* (gum bleeding), *Shotha* (inflammation) and *Dantamamsa mriduta* (sponginess of the gums).[31,32] A Visual Analog Scale (VAS) was used to evaluate each attribute with a score of 0 representing an absence of an attribute and a score of 10 representing a severe presentation of an attribute.[33]

The 12-week clinical study enrolled 104 subjects and ended with 92 subjects. Panelist disposition is shown in Diagram 1. Qualifying subjects were randomized to one of two treatment groups based on their initial gingivitis scores. Subjects were instructed to brush twice daily (morning and evening) for two minutes with their assigned toothpaste for 12-weeks. Oral soft and hard tissue assessments, as well as, gingival inflammation, bleeding, and Ayurveda evaluations were conducted at baseline and 12-weeks. Statistical analyses were performed separately for the Gingival, Gingival Severity, Gingival Interproximal, and the Ayurveda assessments (Raktasrava, *Shotha* and *Dantamamsa mriduta*). Comparison of the treatment groups with respect to gender were performed using a Chi-Square analysis and for age an Independent t-test. Comparisons of the treatment groups with respect to baseline-adjusted gingival indices and the Ayurveda assessments at 12-weeks were performed using analyses of covariance (ANCOVA). All statistical tests of hypotheses were two-sided and employed a level of significance of $\alpha = 0.05$.

The 6-months clinical study enrolled 110 subjects and ended with 90 subjects. Panelist disposition is shown in Diagram 2. Qualifying subjects were randomized to one of two treatment groups. Subjects were instructed to brush twice daily (morning and evening) for two minutes with their assigned toothpaste for 6-months. Oral soft and hard tissue assessments, as well as, gingival, gingival severity, gingival interproximal, plaque, plaque severity and plaque interproximal index scores along with Ayurveda evaluations were conducted at baseline and 6-months. Statistical analyses were performed separately for the Gingival, Gingival Severity and Gingival Interproximal indices via Löe-Silness Gingival Index and Plaque, Plaque Severity and Plaque Interproximal indices via Quigley-Hein Plaque Index and Ayurveda assessments (*Raktasrava*, *Shotha* and *Dantamamsa mriduta*). Comparison of the treatment groups with respect to gender were performed using a Chi-Square analysis and for age an Independent t-test. Comparisons of the treatment groups with respect to the baseline-adjusted gingival indices and plaque indices as well as the Ayurveda assessments at 6-months were performed using ANCOVA's. All statistical tests of hypotheses were two sided and employed a level of significance of $\alpha = 0.05$.

3. Results

The results from the in vitro anaerobic biofilm study are shown in Figure 1. The results show that the Ayurvedic Toothpaste performed statistically significantly better than the Negative Control Toothpaste and equivalent to the positive control toothpaste in terms of viable bacteria as measured by ATP using relative light units (RLU). The Ayurvedic toothpaste reduced viable bacteria by over 40% compared to the Negative Control Toothpaste. Significant reductions (ANOVA) in the viability of the bacterial biofilms (as measured in RLU) were observed for Ayurvedic toothpaste in comparison to negative control (p<0.05).

For both clinical studies, no adverse events were observed by the Investigator or reported by the subjects when questioned.

In the 12-week clinical study, there were no differences between the two treatment groups with respect to gender or age. The subject-mean baseline values for all indices are shown in Table 1 for those subjects that completed the 12-week study. There were no statistical differences between the two treatment groups for any of these indices. After 12-weeks of product use, each treatment group exhibited a statistically significant reduction from baseline for each indice or assessment. As seen in Figure 2, subjects assigned to the Ayurvedic Toothpaste Group exhibited statistically significant reductions (p<0.001) after 12-weeks of use of 21.9% in gingival index, 51.5% in gingival severity index, and 22.5% in gingival interproximal index as compared to subjects assigned to the Negative Control Group. Finally, as seen in Figure 3, subjects assigned to the Ayurvedic Toothpaste Group exhibited statistically significant reductions (p<0.001) after 12-weeks of use of 29.7% in *Raktasrava* (gum bleeding), 34.5% in *Shotha* (inflammation), and 38.0% in *Dantamamsa mriduta* (sponginess of gums) as compared to subjects assigned to the Negative Control Group.

In 6-months clinical study, there were no differences between the two treatment groups with respect to gender or age. The subject-mean baseline values for all indices are shown in Table 2 for those subjects that completed the 6-month study. There were no statistical differences between the two treatment groups for any of these indices. After 6-months of product use, each treatment group exhibited a statistically significant reduction from baseline for each indice or assessment. As seen in Figure 4, subjects assigned to the Ayurvedic Toothpaste Group exhibited statistically significant reductions (p<0.001) after 6-months of use of 14.0% in gingival index, 32.9% in gingival severity index, and 14.8% in gingival interproximal index as compared to subjects assigned to the Negative Control Group. As seen in Figure 5, subjects assigned to the Ayurvedic Toothpaste Group exhibited statistically significant reductions (p<0.001) after 6-months of use of 7.6% in plaque index, 21.9% in plaque severity index, and 7.2% in plaque interproximal index as compared to subjects assigned to the Negative Control Group. Finally, as seen in Figure 6, subjects assigned to the Ayurvedic Toothpaste Group exhibited statistically significant reductions (p<0.001) after 6-months of use of 35.7% in *Raktasrava* (gum bleeding), 38.7% in *Shotha* (inflammation), and 41.6% in *Dantamamsa mriduta* (sponginess of gums) as compared to subjects assigned to the Negative Control Group.

4. Discussion

Gum inflammation (gingivitis) is caused by bacterial biofilm (dental plaque)and is the mildest and reversible form of periodontal disease. Left untreated, chronic periodontitis can develop, resulting in the loss of connective tissues,
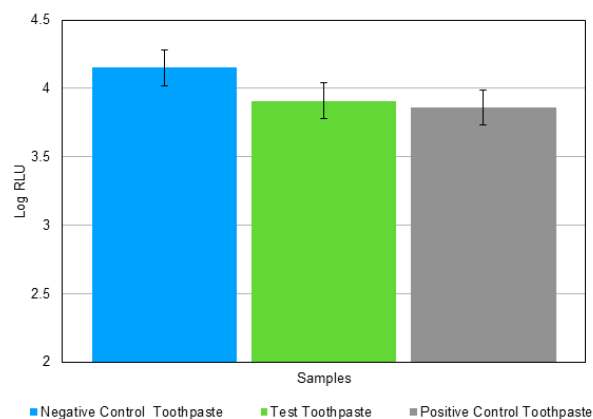

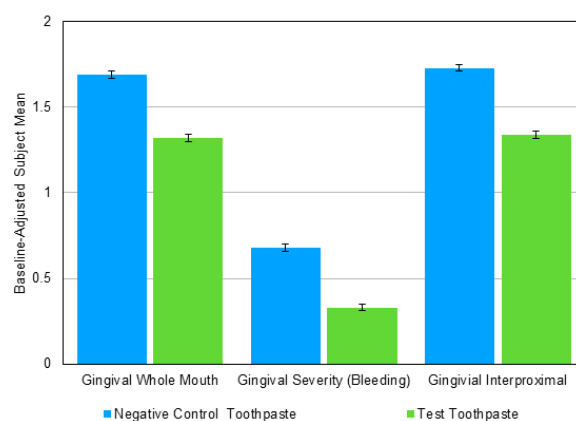**Fig. 1:** Viable bacteria measured as ATP (RLU)

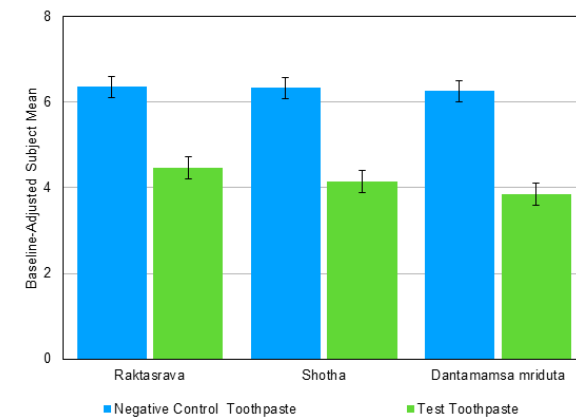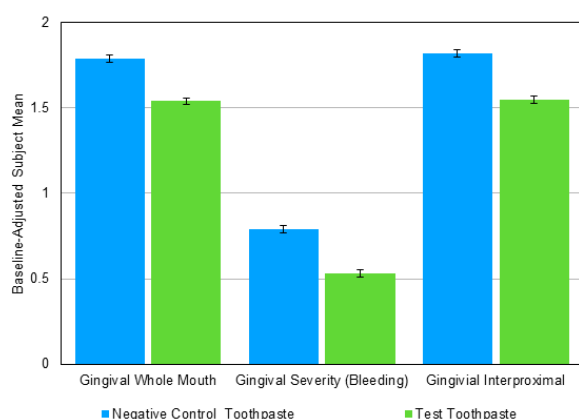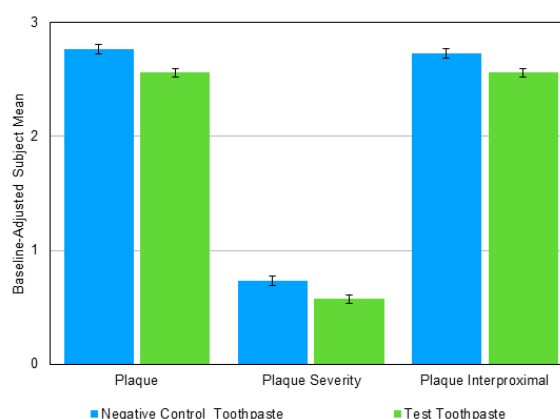**Fig. 2:** Baseline-adjusted subject mean scores for gingival indices at 12-weeks

Fig. 3: Baseline-adjusted subject mean scores for Ayurvedic indices at 12-weeks

Table 1: Subject mean values (±S.D.) for all clinical and Avuryeda indices at baseline for subjects who completed the 12-week clinical study (p< 0.001).

Index	Ayurvedic Toothpaste Group (n=43)	Negative Control Group (n=49)
Gingival (Whole Mouth)	1.85±0.12	1.88±0.12
Gingival Severity (Bleeding)	0.83±0.10	0.85±0.09
Gingival Interproximal	1.92±0.11	1.95±0.11
Raktasrava (Gum Bleeding)	6.84±0.66	6.80±0.66
Shotha (Inflammation)	6.91±0.68	6.91±0.72
Dantamamsa mriduta (Sponginess of Gums)	6.98±0.71	6.94±0.84

Table 2: Subject mean values (±S.D.) for all clinical and Avuryeda indices at baseline for subjects who completed the 6-month clinical study (p< 0.001)

Index	Ayurvedic Toothpaste Group (n=43)	Negative Control Group (n=49)
Gingival (Whole Mouth)	1.96±0.15	2.00±0.14
Gingival Severity (Bleeding)	0.88±0.10	0.91±0.09
Gingival Interproximal	2.03±0.14	2.07±0.14
Plaque	3.00±0.24	2.97±0.20
Plaque Severity	0.83±0.18	0.82±0.14
Plaque Interproximal	2.94±0.22	2.91±0.18
Raktasrava (Gum Bleeding)	5.92±0.84	5.88±0.67
Shotha (Inflammation)	5.72±0.92	5.59±0.73
Dantamamsa mriduta (Sponginess of Gums)	5.61±0.96	5.61±0.76

Fig. 4: Baseline-adjusted subject mean scores for gingival indices at 6-months

Fig. 5: Baseline-adjusted subject mean scores for plaque indices at 6-months

bone support and even teeth.[34] It has been established that the incidence and prevalence of gingivitis and chronic periodontitis is higher in diabetics than non-diabetics.[35,36] It has been postulated that diabetes and periodontitis have a bi-directional relationship in that individuals with diabetes are more likely to have periodontitis and patients with periodontitis were more likely to develop diabetes.[37] Preemptive measures via the use of effective oral care products to control gingivitis may be viable approach to prevent the more serious condition of periodontitis.

One study compared a herbal toothpaste to a triclosan-containing toothpaste. The herbal toothpaste containing chamomile, sage, myrrh, and eucalyptus, was shown to be statistically equivalent to the triclosan toothpaste in the reduction of plaque and gingivitis after 21 days of use.[38] There have also been two studies in which an Ayurvedic medicinal toothpaste containing a mixture of nine herbs was shown to be more effective as compared to a placebo toothpaste. A 12-week study demonstrated a significant reduction in plaque and bleeding on probing (gingival severity) for the Ayurvedic toothpaste,[39] and a 24-week study demonstrated a significant reduction in plaque, bleeding on probing (gingival severity), and periodontal pocket depth for the Ayurvedic toothpaste.[40]
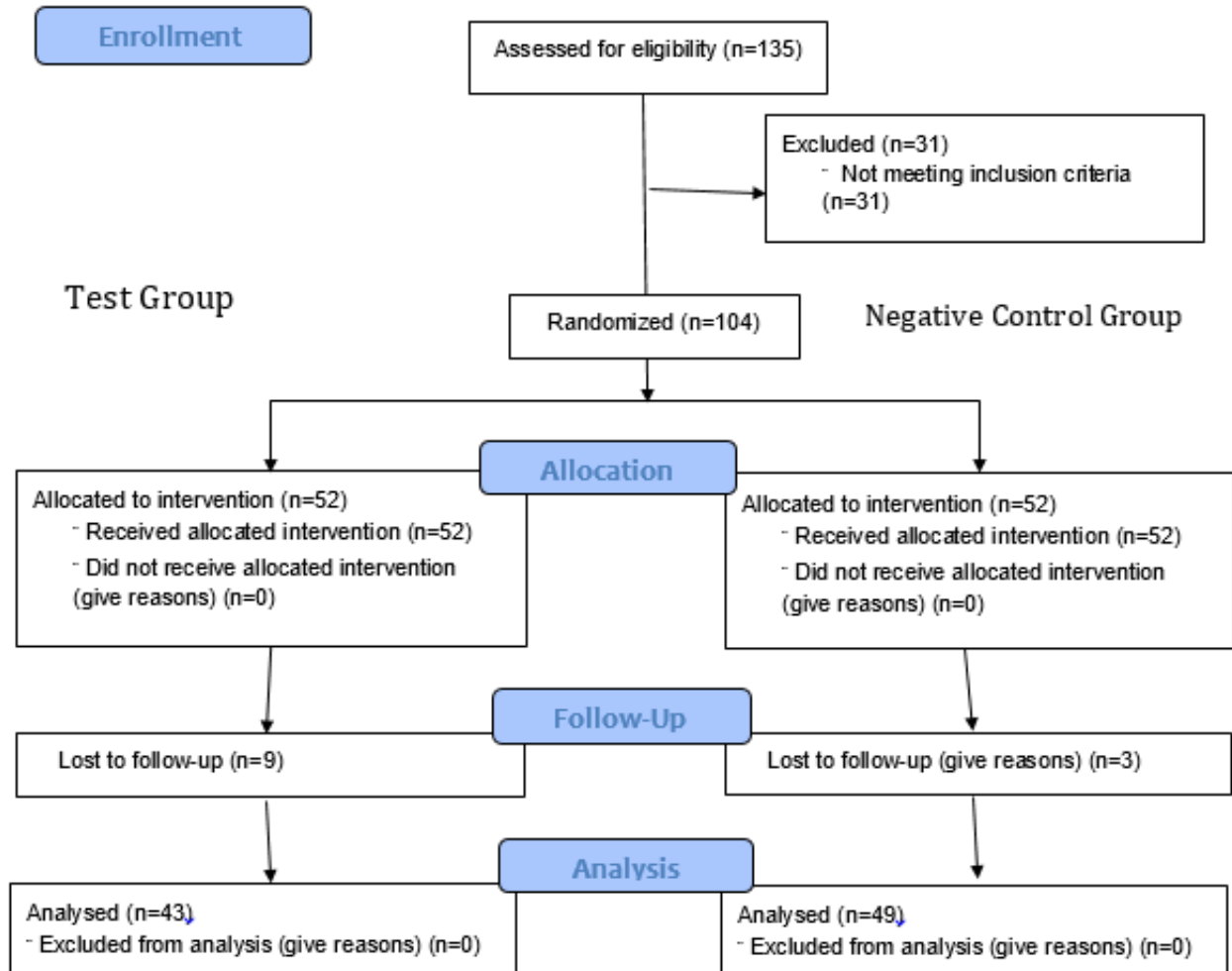
Diagram 1: Consort flow diagram for 12-week study

The result of the research, to our knowledge, is the first evidence for treatment of gingivitis by an Ayurvedic toothpaste in a diabetic population. The in vitro research demonstrated that the Ayurvedic toothpaste has significantly reduced anaerobic bacteria as compared to negative control toothpaste in a biofilm model that has been used previously. This efficacy against oral bacteria was confirmed in two clinical studies looking at the impact of the toothpaste on reductions in plaque and gingivitis in the target population of diabetics. A truly effective therapeutic toothpaste has the ability to demonstrate improvement in measures related to gingival health, such as the plaque index and the gingival index. Additionally, it should demonstrate efficacy relating to severity (bleeding) and hard-to-reach places (interproximal). To that end, the Ayurvedic toothpaste demonstrated efficacy in as little as 12-weeks, with statistical significant reductions in gingival index, gingival severity index, and gingival interproximal index as compared to the Negative Control Toothpaste. These findings were further expanded and corroborated in a 6-month study that evaluated plaque as well. In the longer study, the Ayurvedic toothpaste demonstrated statistically significant reductions in gingival index, gingival severity index, and gingival interproximal index as compared to the

CONSORT
TRANSPARENT REPORTING of TRIALS

CONSORT 2010 Flow Diagram

Enrollment

Assessed for eligibility (n=132)

Excluded (n=22)
- Not meeting inclusion criteria (n=21)
- Declined to participate (n=1)

Randomized (n=110)

Test Group   Negative Control Group

Allocation

Allocated to intervention (n=56)
- Received allocated intervention (n=56)
- Did not receive allocated intervention (give reasons) (n=0)

Allocated to intervention (n=54)
- Received allocated intervention (n=54)
- Did not receive allocated intervention (give reasons) (n=0)

Follow-Up

- Lost to follow-up (n=12)
- Discontinued intervention (n=1)

- Lost to follow-up (n=7)

Analysis

Analysed (n=43)
- Excluded from analysis (give reasons) (n=0)

Analyzed (n=47)
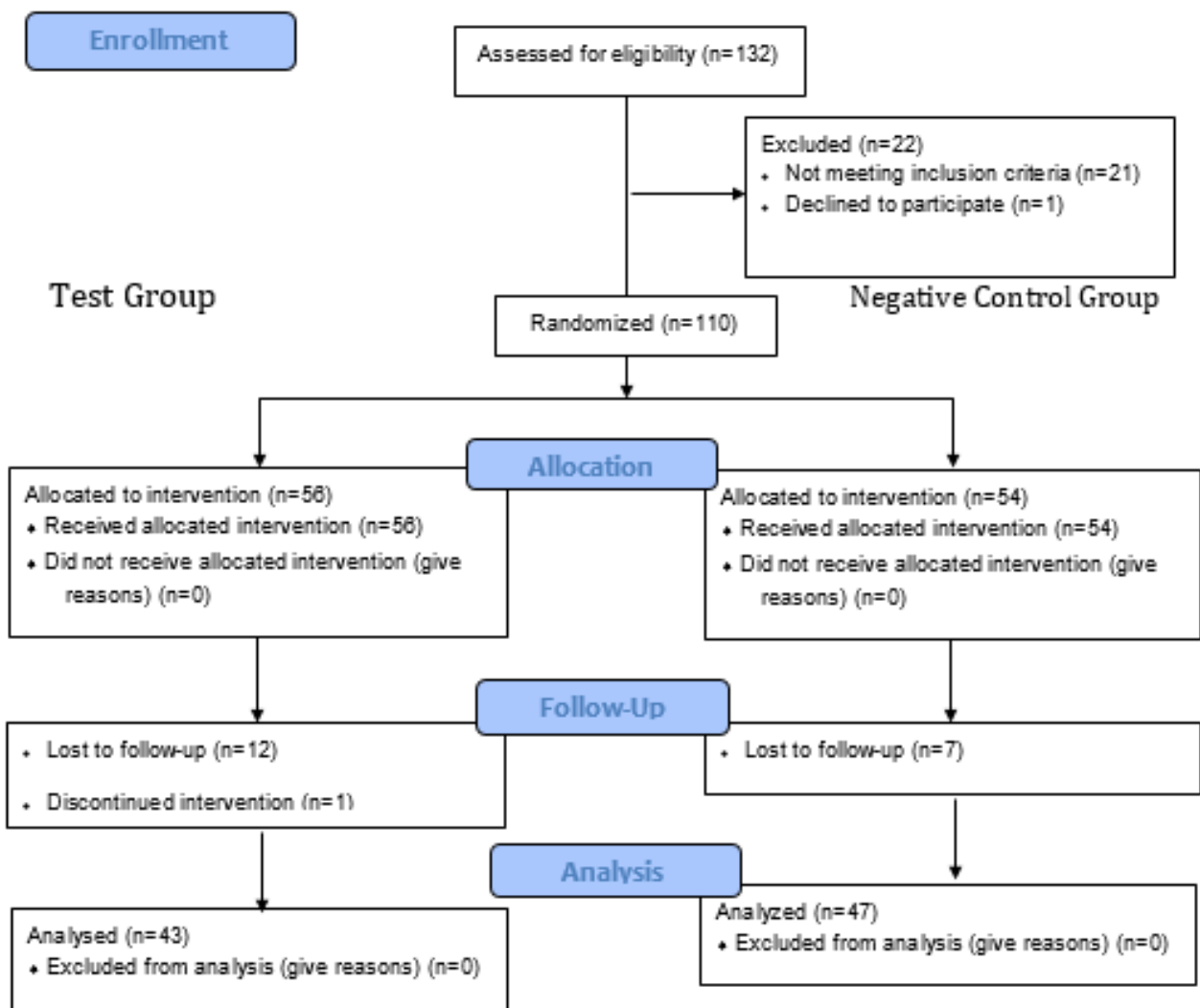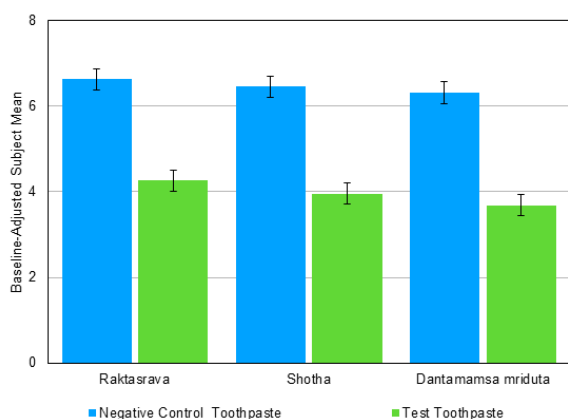- Excluded from analysis (give reasons) (n=0)

Diagram 2: Consort flow diagram for 6-months study

Fig. 6: Baseline-adjusted subject mean scores for Ayurvedic indices at 6-months

Negative Control Toothpaste.

Additionally, statistically significant reductions in plaque index, plaque severity index, and plaque interproximal index were observed for the Ayurvedic toothpaste as compared to the Negative Control Toothpaste in the 6-month study.

Gingivitis has been well-recognized in Ayurveda. It has been broadly covered under the description of the condition called as *Sheetada* and is characterized by spontaneous bleeding from the gums without any injury, halitosis, blackish discoloration of gums, etc.. It can progress into periodontitis – the disease in which the firmness, contour, and position of the gums are altered and teeth become mobile. [32,41–43] Some important clinical signs and symptoms that have been identified in Ayurveda for this condition include *akasmata raktasrava* (bleeding gums), *shotha* (inflammation), *siryamana dantamamsa* (gingival recession), *krisnata* (discoloration of gums), *daurgandhya* (halitosis), *vedana* (pain), *dantamamsa mriduta* (sponginess of the gums), *dantamamsa klinnata* (deposition of wastes on the gums), *paka* (pus discharge), and *chaladanta* (tooth mobility). [32]

While the basic principles of clinical evaluation remain identical, the evaluation by the licensed Ayurvedic Physician provided additional affirmation of the findings of the study from the Ayurvedic point of view. As is evident from the results of the clinical studies, in addition to the improvement in Löe-Silness Gingival Index, the subjects assigned to the test product showed statistically significant improvement (within-product comparison) in rating scores for *raktasrava* (gum bleeding), *shotha* (inflammation), and *dantamamsa mriduta* (sponginess of gums). Similar results were observed in between-product comparisons as well.

The above results clearly indicate that the Ayurvedic Toothpaste provides statistically significant benefit not just in reducing the symptom scores as per the Löe-Silness Gingival Index, but also as per the criteria laid down in Ayurvedic medicinal literature. The findings of this study further support the hypothesis that Ayurvedic herbs/actives/formulations which also possess antimicrobial, anti-inflammatory, immunomodulatory and antioxidant activities, are effective in providing oral care benefits in the sub-set of adult population with type 2 diabetes in terms of preventing gingivitis, thereby providing benefits in holistic management of diabetes.

The Ayurvedic toothpaste formula contains the ingredients known for anti-inflammatory, immunomodulatory, antimicrobial and antioxidant activity. The results of the study demonstrates the benefits of the product formula towards gingivitis in type 2 diabetics. This study thus opens up the possibilities for further studies to explore the synergistic effect for the above mentioned properties.

5. Conclusions

These results support the efficacy in a diabetic population of an Ayurvedic toothpaste, containing Yashad Bhasma (Zinc oxide), Madhunashini (*Gymnema sylvestre*), Surya Kshar (Potassium nitrate), Amalaki (*Emblica officinalis*), Nimba (*Azadirachta indica*), and Jamun (*Eugenia jambolana*) in a flavoured calcium carbonate/fluoride base by providing a significantly greater reduction in anaerobic bacteria, as well as improvements in plaque indices, in gingival indices, and in Ayurvedic endpoints as compared to a commercially available fluoride toothpaste in a calcium carbonate base.

6. Source of Funding

7. Conflict of Interest

The authors declare that there is no conflict of interest.

8. Acknowledgement

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