

Comparative Effectiveness of Herbal versus Commercial Toothpaste on Salivary pH and Streptococcus mutans Count: A Randomized Crossover Clinical Trial

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Abstract

Objectives: Enhancing dental health and oral hygiene is essential for preventing dental caries. Recently, there has been significant interest in using natural ingredients in oral care products. This study aimed to compare the effects of herbal toothpaste containing Saqqez oleo-gum resin essential oil with Sensodyne toothpaste on the colony count of Streptococcus Mutans (*S. mutans*) and salivary pH levels.

Methods: A randomized double-blinded clinical trial with a crossover design was conducted with 40 students aged 18-35 years who were caries-free. Initially, unstimulated saliva samples were collected to determine the baseline mutans streptococci count and salivary pH levels. In the first phase, participants were randomly divided into two groups: Group I received herbal toothpaste containing Saqqez oleo-gum resin essential oil, while Group II used Sensodyne toothpaste. After supervised tooth brushing, saliva samples were collected again to assess pH levels and *S. mutans* counts. Following a 72-hour washout period, the procedures were repeated with the groups switching toothpastes according to the crossover design. Data were analyzed using the Mann-Whitney U test and Wilcoxon matched pairs signed-rank test, at a significance level of $p < 0.05$.

Results: A significant reduction in the *S. mutans* colony count and a significant increase in salivary pH levels were observed in both groups compared to their baseline values ($P < 0.05$). However, no significant difference was found between the efficacy of the two toothpastes ($P > 0.05$).

Conclusion: The effect of herbal toothpaste containing Saqqez essential oil on salivary pH and *S. mutans* level was comparable to that of commercial toothpaste evaluated in this study.

Keywords: Cross-Over Design; Streptococcus mutans; Salivary pH; Toothpaste

How to cite:

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Introduction

The oral microbiome is highly diverse, comprising over 700 distinct bacterial species.¹ The oral cavity, being warm and moist, provides an ideal environment for the growth of a wide variety of bacteria, fungi, viruses, and protozoa.^{1,2} Saliva constantly removes dietary carbohydrates and microorganisms from the oral cavity, playing a crucial role in maintaining oral homeostasis and symbiosis.³ It maintains the oral pH at a relatively persistent level by buffering acids produced by bacterial fermentation.⁴ The normal saliva pH is essential for the maintenance and promotion of the healthy microbial population.⁵ The overgrowth of aciduric and acid-tolerating bacteria results in increased carbohydrate fermentation and acid production, raising the risk of tooth demineralization and dental caries.¹

Dental caries is a multifactorial condition and ranks among the most common infectious diseases worldwide. Studies indicate that nearly 60 to 90% of school-aged children and nearly all adults will experience dental caries at some point in their lives.⁶ *S. mutans* is identified as the primary cause of dental caries. Its virulence factors, including its ability to adhere, produce acid, and tolerate acid, play crucial roles in

its colonization on dental surfaces.⁷

Given the broad side effects associated with conventional chemical drugs, natural products have increasingly been explored for the prevention and treatment of infectious diseases in recent years. The Baneh tree, scientifically known as *Pistacia atlantica* subsp. *kurdica*, is a medicinal and edible plant from the Anacardiaceae family. Native to and growing wild in Iran, particularly in the Kurdistan province of western Iran, this tree produces a resin known as Saqqez. This oleo-gum resin, extracted from the tree's trunk, has been found to possess a wide range of therapeutic properties.⁸

Saqqez has been reported to exhibit a bacteriostatic effect in the oral cavity.⁹ Previous studies have demonstrated that essential oil derived from Saqqez possesses significant antimicrobial activity against *S. mutans*, both in vitro and in vivo.¹⁰ Saqqez is used in the production of various products, including xylitol-containing mastic chewing gums, pure mastic chewing gums, and more recently, herbal toothpaste containing Saqqez essential oil (SEO) derived from *Pistacia atlantica* subsp. *kurdica*. Due to the high absorbent capacity of the oral cavity, some chemical ingredients in commercially available oral health products may pose

potential risks.¹¹

As this product is new, there has yet to be an evaluation of the effects of herbal toothpaste containing Saqqez essential oil (SEO) on cariogenic bacteria and salivary pH. This study aimed to compare the effects of herbal toothpaste containing SEO and Sensodyne toothpaste on salivary *S. mutans* counts and saliva pH levels. Sensodyne toothpaste, approved by the Food and Drug Administration in Iran, is widely available in Iran and many other countries.

Methods

Study design

A randomized double-blinded crossover clinical trial was conducted to evaluate the effects of herbal and Sensodyne toothpastes on salivary *S. mutans* levels and pH. The study involved 40 healthy students (21 females and 19 males) from the Faculty of Dentistry at Kurdistan University of Medical Sciences, Sanandaj, Iran, aged 18 to 34 years, who voluntarily participated. The participants were in good general health and maintained good oral hygiene, with no signs of dry mouth or salivary gland disorders. Exclusion criteria included untreated dental caries, special healthcare needs, systemic diseases, recent or current use of antibiotics, orthodontic treatment, smoking, gingivitis, periodontitis, or other medical conditions such as hypertension or diabetes. The study protocol was approved by the Ethics Committee of Kurdistan University of Medical Sciences (Ethical Code: IR. MUK.REC.1398.280) and registered in Iranian registry of clinical trials (IRCT) under the code #IRCT20201213049704N1. The study was performed in accordance with the ethical guidelines of the World Medical Association (Declaration of Helsinki). All participants signed a written informed consent form before participating. The sample size was calculated based on previous reports, considering an effect size of 0.5574, a significance level of $\alpha = 0.05$, and 90% power. The required sample size was determined to be 36, which was increased to 40 to account for a 10% potential sample loss during phase 2 of the study.

Clinical trial

The trial was conducted between 2 and 4 pm, two hours after the participants had eaten lunch. In Phase 1 of the trial, participants were numbered from 01 to 40 and randomly assigned to two groups (N=20 in each) using generated random numbers: Group I was supposed to use herbal toothpaste containing SEO, and Group II the Sensodyne toothpaste. Baseline unstimulated saliva was first collected by instructing the participants to use the noninvasive spitting method described by Navazesh.¹² The participants were asked to sit comfortably and tilt their heads slightly downward without swallowing for at least five minutes. Then they expectorated saliva into a sterile dispensing cup.

The samples were immediately coded and sent to the microbiology laboratory.

Each participant was provided with an adult-sized toothbrush (Oral B Pro Expert, Procter & Gamble, United States) and either herbal toothpaste (Zhiran Darou Co, Sanandaj, Iran) or Sensodyne toothpaste (Sensodyne Multi-Action, GlaxoSmithKline Co, UK) based on the group. The toothpastes were placed in identical tubes coded A and B to ensure blindness. Participants were instructed on how to brush consistently using the Bass technique. This method requires aligning the brush head parallel to the occlusal plane, covering approximately 3-4 teeth, and starting from the distal-most teeth of the arch. Participants were instructed to apply a pea-sized amount of toothpaste to the toothbrush and brush their teeth for three minutes. The amount of toothpaste was visually checked by a research assistant. Following this, saliva samples were collected for five minutes, providing stimulated saliva samples, which were then sent to the microbiology laboratory.

After a 72-hour washout period, Phase 2 of the trial was conducted. The same procedure was repeated with the groups interchanged: Group I used Sensodyne toothpaste, and Group II used the herbal toothpaste. The codes were maintained by an independent assistant, ensuring that the primary investigator, participants, and research assistants were blinded to the interventions.

In all laboratory procedures, *S. mutans* was cultured in the mitis salivarius bacitracin agar (MSBA, HiMedia) media. Saliva samples (0.5 mL) were serially diluted, and 25 μ L of 10-fold diluted saliva was plated. The plates were then incubated for 72 hours at 37°C under 5% CO₂. Colony counts for each plate were recorded, and the mean colony-forming units (CFU/mL) were determined.¹³ The pH of the saliva samples was measured immediately after each sampling using a pH meter (BASIC 20+, pH range: 5.00-9.00 \pm 0.01, Crison Co).

Statistical Analysis

The data were recorded in Excel spreadsheet (Microsoft Excel, 2016) and presented as Mean \pm SD and interquartile range. The normality of the data was assessed using the Shapiro-Wilk test, which revealed that the data were non-normally distributed. The Wilcoxon signed-rank test was used to investigate the effect of each toothpaste on *S. mutans* colony count and salivary pH. The Mann-Whitney U test was used for intergroup comparisons. Statistical analysis was conducted using STATA 14.0 (Stata Corporation, USA), with $P \leq 0.05$ considered significant.

Results

Forty dental students (21 females, 19 males) participated in this study, with an average age of 24.6 \pm 2.21 years. There was no significant difference in age and gender distribution

between the two groups ($p>0.05$) (Table 1). No participants dropped out of the study.

Variable	Group I	Group II	p-value
Gender	8 12	11 9	0.9
Age(min-max, mean)	22-29, 24.75	22-34, 24.45	0.47

Table 2 presents the interquartile range (IQR) of *S. mutans* colony counts and salivary pH at different time points. Within-group comparisons showed that both toothpastes

significantly decreased the number of *S. mutans* colonies immediately after brushing compared to baseline ($P < 0.05$ for both toothpastes). Additionally, salivary pH significantly increased after brushing with both toothpastes ($P < 0.05$) (Figure 1).

Parameter	Group	N	Mean \pm SD	p-value ^a
Salivary pH	Herbal	Baseline	6.96 \pm 0.47	0.035
		After brushing	7.06 \pm 0.33	
	Sensodyne	Baseline	6.79 \pm 0.47	< 0.001
		After brushing	7.13 \pm 0.39	
<i>S. mutans</i> colony count	Herbal	Baseline	82.22 \pm 71.13	0.03
		After brushing	67.37 \pm 54.83	
	Sensodyne	Baseline	80.5 \pm 62.26	<0.001
		After brushing	57.1 \pm 49.12	

^a Wilcoxon signed-rank test

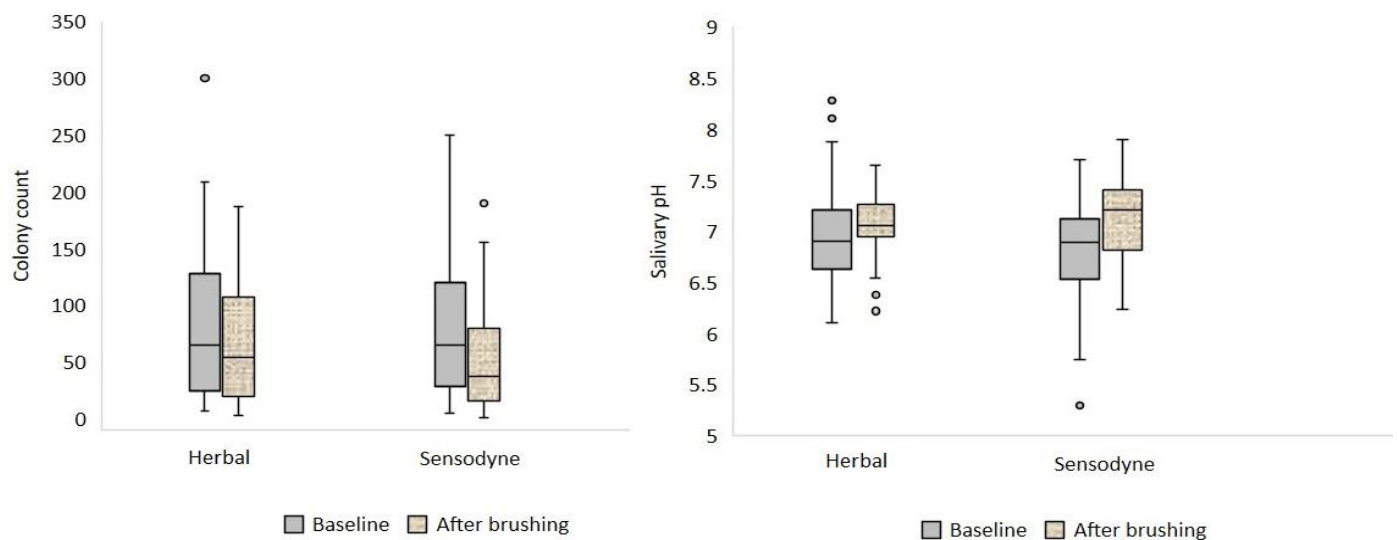


Figure1: Changes in *S. mutans* colony count and salivary pH after brushing with herbal and Sensodyne toothpastes

The intergroup comparison between the two toothpastes found no statistically significant difference at baseline salivary pH ($p=0.544$) (Table 3). However, the median (IQR) salivary pH in Sensodyne 7.21 (6.8-7.4) was higher than that of herbal toothpaste 7.05 (6.9-7.2) after brushing, though the difference was not statistically significant ($p= 0.351$). Likewise, no statistically significant difference was found at

baseline *S. mutans* colony count for Sensodyne and herbal toothpaste ($p=0.919$). Similarly, the median (IQR) colony counts in Sensodyne 37 (14.5-80) were lower than that of herbal toothpaste 54.5 (20-110) after brushing, however the difference was not statistically significant ($p= 0.425$).

Table 3 - Comparative evaluation of the salivary pH and *S. mutans* colony count between herbal and Sensodyne toothpastes

Parameter	Time period	Group	N	Mean ± SD	p-value ^a
Salivary pH	Baseline	Herbal	40	6.96±0.47	0.23
		Sensodyne	40	6.79±0.47	
	After brushing	Herbal	40	7.06±0.33	0.16
		Sensodyne	40	7.13±0.39	
<i>S. mutans</i> colony count	Baseline	Herbal	40	82.22±71.13	0.99
		Sensodyne	40	80.5±62.26	
	After brushing	Herbal	40	67.37±54.83	0.35
		Sensodyne	40	57.1±49.12	

^a Mann–Whitney U test

Discussion

Dental caries is a multifactorial oral disease characterized by localized destruction and demineralization of dental tissues resulted from plaque accumulation on tooth surfaces.¹⁴ *S. mutans* is recognized as the most prevalent cariogenic bacterial species found in human dental plaque. Various oral health products, including toothpastes, are used to enhance natural antimicrobial defenses and prevent tooth decay.¹⁵ The use of chemical toothpastes is linked to various side effects, including tooth surface discoloration, altered taste perception, soft tissue irritation, and a burning sensation.¹⁶ The World Health Organization encourages researchers to explore the potential use of herbal products and plant extracts. There has been a notable shift towards using herbal products that feature safe ingredients and minimal side effects.¹⁷ The antibacterial properties of herbal products are due to bioactive compounds that disrupt bacterial cell walls, inhibit bacterial enzymatic activity, and reduce bacterial adhesion to tooth surfaces.¹⁸ The success in caries prevention relies predominantly on oral hygiene measures and selection of toothpastes with active ingredients and antibacterial efficacy.¹⁹

While laboratory findings are informative, clinical trials are necessary to confirm the efficacy and practicality of newly developed herbal products. This study investigated the antibacterial effects of two toothpastes (herbal and control) against *S. mutans*, a key pathogenic bacterium that plays a crucial role in the development of dental caries.⁷ The high bacterial count in the saliva is an indicator of caries development.²⁰ The present results showed significant inhibitory activity of both toothpastes against the *S. mutans* ($P < 0.05$). Different concentration of ingredients and components in the toothpastes affect their efficiency. For example, Golfeshan et al. (2021), compared the effectiveness of theobromine and caffeine toothpastes on enamel microhardness. Their study revealed significant differences in microhardness values on demineralized enamel surfaces depending on the type of toothpaste used.²¹ Likewise,

Prasanth (2011) assessed the antibacterial efficacy of various toothpastes and found that those containing triclosan were more effective in controlling oral microflora compared to toothpastes without triclosan.²²

Saqez contains natural components with minimal side effects, and previous studies have demonstrated the significant advantages of mastic gum over synthetic products.²² Azeez et al. (2019) observed that the α -pinene, as a main component of SEO has significant antimicrobial properties.²³ Similarly, the study by Biria et al. (2014) demonstrated that a three-week regimen of mastic gum significantly reduced salivary *S. mutans* colonies²² which is consistent with the present findings. The primary components of mastic gum include pinene, terpineol, limonene, terpinene, verbenol, caryophyllene, camphene, linalool, and myrcene.²⁴ The active ingredients of Sensodyne toothpaste include Potassium nitrate 5% w/w and sodium fluoride 0.254% w/w (fluoride 0.115% w/w). The Sensodyne toothpaste was chosen as the control for current study because it is one of the popular brands used in the country.

Virulence factors of *S. mutans* such as bacterial adhesion, biofilm formation, and acid tolerance are associated with cariogenicity.²⁵ Previous study revealed that Chrysanthemum boreale essential oil, which contains pinene, downregulated the virulence factors of on *S. mutans* in a dose dependent manner.²⁵ Further investigations have demonstrated that α -pinene effectively prevents acid production, growth, and biofilm formation by *S. mutans*. The antibacterial action of phenolic compounds, such as α -pinene, in essential oils involves disrupting essential biological pathways in microorganisms, inhibiting protective enzymes, or altering cellular wall functions.²⁵ α -Pinene has also shown antibacterial activity against *Campylobacter jejuni* by inhibiting microbial efflux, compromising membrane integrity, and disrupting metabolic processes.²⁶

In the present study, the impact of the two toothpastes on salivary pH was also evaluated. Low pH levels contribute to tooth enamel demineralization and the development of dental caries, as *S. mutans* metabolizes dietary sugars to produce

organic acids.²⁵ Therefore, an increase in pH is used as an indicator of the effectiveness of anticariogenic agents. In this study, salivary pH increased in both groups immediately after brushing. This increase can be attributed to enhanced salivary secretion from the stimulation of parotid glands, the release of calcium and phosphorus ions from the toothpastes, and the antibacterial effects of toothpastes against acid-producing bacteria in the saliva.²⁷ The increase in pH levels was equal between Sensodyne and herbal toothpaste. This suggests that the herbal toothpaste may prevent dental caries by inhibiting acid production.

This study had several limitations, including the relatively small sample size and the immediate evaluation of the salivary changes. Follow-up studies with an extended duration of toothpaste use are recommended to confirm the findings, similar to the method used in a recent clinical trial by Biria et al. on another Iranian herbal toothpaste type.²⁸ Additionally, natural biases inherent in community-based intervention studies should be considered when interpreting the results. Further research is also recommended to explore the potential benefits of herbal toothpastes on other aspects of oral health.

Conclusion

This study found that herbal toothpaste containing SEO demonstrated promising antimicrobial activity against *S. mutans*. Additionally, it was highly effective in increasing salivary pH. The herbal toothpaste was as effective as Sensodyne, a commercially available conventional toothpaste.

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Supplementary Materials: None.

Author Contributions:

Concept and design: M.R.K. and H.S. Data collection: RE and HP. Data analysis: S.J.E. and R.E. Writing—original

draft preparation: S.J.E; writing—review, and editing: M.R.K., H.P and S.J.E. Supervision: MRK. All authors approved the final manuscript and agreed to be accountable for all aspects of this research.

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Ethical Approval Code:

This study was approved by the Institutional Review Board (IRB) of Kurdistan University of Medical Science, and the protocols used in the study was approved by the Ethics Committee of the Kurdistan University of Medical Science. A total of 40 healthy dental students voluntarily participated in the clinical trial at the School of Dentistry. The participants were informed consent forms according to institutional guidelines and the study was approved by IRB protocols of Kurdistan University of Medical Science.

Informed Consent Statement:

The informed consent form provided to the volunteers at the beginning of the study contained:

1. A statement of activity.
2. The purpose of the activity.
3. Procedures.
4. Risks to the participant.
5. Benefits to the participant.
6. Cost of participation.
7. Confidentiality.
8. Voluntary participation.

All volunteers participated in the study have read the Consent and Authorization form. All volunteers have had the opportunity to ask, and have received answers to, any questions they had regarding the study and the use and disclosure of information about them. All volunteers understood that their participation is voluntary and that they are free to withdraw at any time, without giving a reason and without cost. All volunteers agreed to take part in the study as a research participant.

Data Availability Statement:

The data supporting the findings are available from corresponding author upon reasonable request.

Conflict of Interest

No Conflict of Interest Declared ■

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