Safety and efficacy of RF-utilizing toothbrush for the reduction of teeth stains and teeth shade whitening

DO116761A

ToothWave™ (Model H7001) Clinical study report

(Protocol number: DO116028)

ClinicalTrials.gov Identifier: NCT03885609

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1. SUMMARY

Objective:

To evaluate the effect of ToothWave™ a novel RF-utilizing toothbrush on teeth stains and shade as compared to a control standard ADA-approved powered toothbrush.

methods:

This was a single-blind double arm prospective study, including 4 clinical visits that were conducted every two weeks. Subjects were randomized to one of two study groups, receiving either the Silk'n ToothWave™ or control toothbrush, and performed twice daily brushing during a test period of 6 weeks. Teeth stains and shade were assessed using the Lobene stain index and Vita bleachguide 3D Master, at baseline and after 4 and 6 weeks (visits 3 and 4 respectively) of brushing. Results (mean scores) were compared within each group between the different visits and between the groups; delta values (reduction from baseline) of each score were also compared between the groups. Statistical analyses were conducted using the Mann Whitney non-parametric model.

Results:

A total of 84 subjects (41 in the treatment group and 43 in the control) completed the study, having fully evaluable data. At baseline, the test groups did not differ significantly in the efficacy measurements mean scores ($p \geq 0.776$). Following 6 weeks of brushing the test group showed significant reductions in all the tested measures as compared to the control group. In addition, the reduction from baseline of the measured scores were significantly greater in the treatment group as compared to the control ($p \leq 0.001$). Both toothbrushes were well-tolerated and no device related adverse events were reported during the study.

Conclusions:

The ToothWave™ RF-utilizing toothbrush produced significant benefits in reduction of teeth stains and whitening of teeth shade as compared to a control, ADA-approved powered toothbrush.

2. INTRODUCTION

Over the past two decades, tooth bleaching or whitening has become one of the most popular aesthetic dental treatments. The term “bleaching” is permitted for products that contain peroxides and can whiten teeth beyond their natural color. The term “whitening” is used to describe the process of restoring teeth to their natural color by removing stains and debris from the tooth’s surface.

Current tooth bleaching materials are based primarily on either hydrogen peroxide or cabamide peroxide. Both were found to be effective, but raise concerns about the long-term safety of bleaching procedures. Recently, products containing chlorine dioxide were introduced in the United Kingdom, but with no evidence of equivalent efficacy and with additional safety concerns due to low pH of the material [1].

At-home bleaching methods include gels, chewing gums, rinses, toothpastes, paint-on films, and whitening strips. Toothpastes and mouth washes which are advertised as "whitening" rarely contain carbamide peroxide, hydrogen peroxide or any other bleaching agent. These methods are abrasive (usually containing alumina or silica) for the purpose of removing surface stains from the tooth surface. However, in practice, they have not been proven clinically to have a meaningful effect on teeth shade. Further, excessive or long-term use of abrasive toothpastes causes dental abrasion, thinning of the enamel layer, and contributes to a gradual darkening in the appearance of the tooth as the dentin layer becomes more noticeable.

Safety issues have been raised referring to the effects of bleaching on the tooth structure, pulp tissues, and the mucosal tissues of the mouth, as well as systemic ingestion.

Regarding mucosal tissues, safety concerns relate to the potential toxicological effects of free radicals produced by the peroxides used in bleaching products. Free radicals are known to be capable of reacting with proteins, lipids and nucleic acids, causing cellular damage. Because of the potential of hydrogen peroxide to interact with DNA, concerns with carcinogenicity and co-carcinogenicity of hydrogen peroxide have been raised, although these concerns so far have not been substantiated through research [2-10]. However, studies have shown that hydrogen peroxide is an irritant and also cytotoxic. It is known that at concentrations of 10% hydrogen peroxide or higher, the chemical is potentially corrosive to mucous membranes or skin, and can cause a burning sensation and tissue damage [2, 11, 12].

Clinical studies have also observed a higher prevalence of gingival irritation in patients using bleaching materials with higher peroxide concentrations [13, 14]. Regarding hard tissues, transient mild to moderate tooth sensitivity can occur in up to two-thirds of users during the early stages of bleaching treatment [15, 16].

Home Skinovations LTD. (Yokneam, Israel) has developed the Silk'n ToothWave™, a novel toothbrush intended to remove impurities that are attached to the teeth surface, such as plaque, calculus, and extrinsic stains. ToothWave™ utilizes radiofrequency (RF) energy that streams between two electrodes and over a silicon barrier, and reaches the teeth surface during brushing. RF is an alternating electric current that oscillates at radio frequencies in the range of 3kHZ-300GHz. It has been used in medicine for several decades for many different applications, from surgical to aesthetic, providing various effects, depending on the specific parameters of the device in use [17].

Figure 1 below provides a schematic representation of the toothbrush head; ***Figure 2*** exemplifies the process of RF streaming through the toothpaste as it reaches the tooth surface.

The current clinical study aims to evaluate the safety and efficacy of the ToothWave™, as compared to a standard powered toothbrush that is approved by the American Dental Association (ADA).

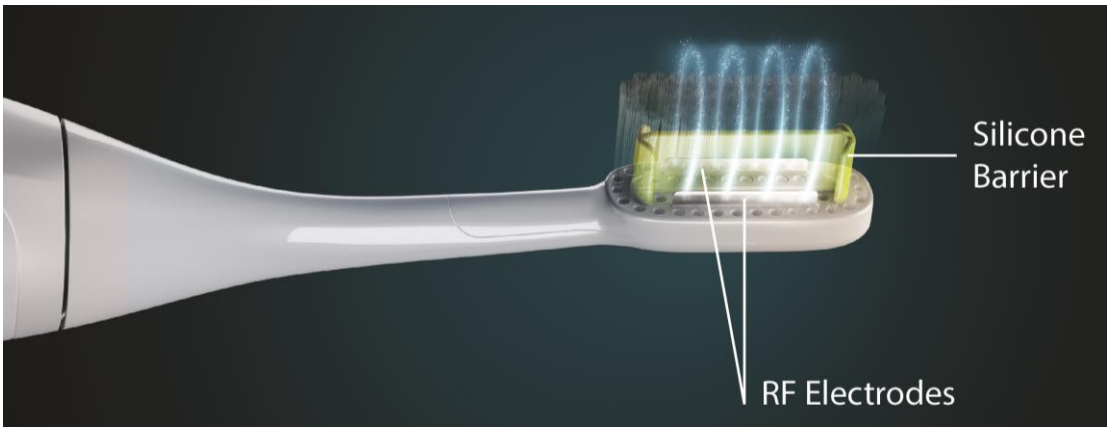

Figure 1 *- a graphic representation of the ToothWave™ brush head*

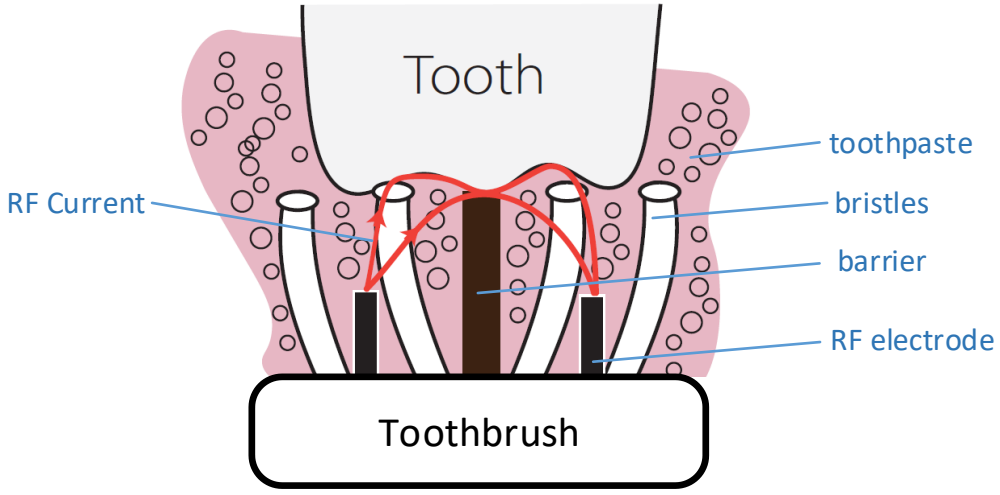

Figure 2 - *schematic representation of the RF current that streams in proximity to the tooth surface*

3. METHODS

A randomized single-blind double arm prospective study was conducted, in order to evaluate the safety and efficiency of the RF-utilizing toothbrush (*ToothWave™, Manufactured by Home Skinovations LTD, Yokneam, Israel*), as compared to a reference powered toothbrush (Smilesonic® Pro Advanced Clean, Manufactured by Ranir, LLC, Grand Rapids, MI 49512). The protocol and consent form were approved by the U.S. Institutional Review Board (U.S.IRB2019SRI/02) before study initiation, and verbal and written consent were obtained from all subjects.

Participants

Screened subjects received an oral soft tissue (OST) examination. Stains and teeth shade were evaluated using the Lobene stain index (LSI) [18, 19] and the Vita bleachguide 3D master.

Recruited subjects were 18-70 years of age, with a total extrinsic facial tooth stain score of at least 1.80, according to LSI. Exclusion criteria were composed of current or history of oral cavity cancer or oropharyngeal cancer, any active electrical implant anywhere in the body, pregnant or nursing, and any active condition or surgery in the oral cavity within 3 months prior to treatment. Regular tobacco smokers and subjects that do not brush regularly were also excluded.

Study procedures

Eligible study participants were provided with regular, marketed Crest® Cavity Protection Cool Mint Gel (0.243% Sodium Fluoride, Procter & Gamble, Cincinnati, OH 45202), and a toothbrush (either the ToothWave™ or control brush). Participants were randomized and assigned to study group in accordance with a randomization schedule generated by an independent statistics agency prior to the start of the study, using validated software (SPSS Version 25.0). Participants were stratified according to their age and ethnicity. Randomization numbers within each stratum were assigned in ascending numerical order according to appearance at the study site on the day participants were randomized. Participating subjects were instructed to brush at home twice-daily (morning and evening) with a full brush head of toothpaste for two timed minutes. The study included 6 weeks of test phase, during which 4 pre-scheduled face-to-face visits were performed every 2 weeks. Each use was recorded in a provided diary.

The first brushing session was carried out under supervision at the study site. Participants brushed for 2 timed minutes in their usual manner with the standard fluoride toothpaste (Crest® Cavity Protection Cool Mint Gel). Participants continued to use their assigned study treatment twice-daily (morning and evening) for the next 6 weeks, recording each brushing in the diary provided. Participants returned to the study site every two weeks over the 6-week study period, bringing their study kit so that the toothpaste be weighed to verify study compliance. Diaries were checked to assess compliance. The participants undertook a supervised brushing during the second visit as was conducted at the first visit, in order to make sure brushing is conducted according to the instructions.

Assessments

Clinical efficacy was evaluated at visits 3 and 4 (following 4 and 6 weeks of brushing, respectively).

Evaluation of stains:

The Lobene stain index was used to measure the intensity and extent of extrinsic stain on the facial surfaces of 12 anterior teeth. Using a provided soft toothbrush, subjects brushed their anterior teeth (with water) for 15 seconds to remove plaque debris and enhance visibility of stain. The facial surface of the selected teeth was divided into two regions, each scored separately:

1. The gingival region which is a crescent-shaped 3 mm wide band adjacent to the gingival margin and extending to the crest of the interdental papillae of the adjacent teeth.
2. The body region which constitutes the remainder of the labial surface of the tooth.

Intensity was scored from 0 (no stain) to 3 (heavy stain; dark brown to black) and extent was scored from 0 (no stain) to 3 (stain covering over two-thirds of the region). Scores were averaged for each subject for intensity (sum of all intensity scores/all sites graded) and extent (sum of all extent scores/all sites graded), and the composite stain score was calculated by multiplying the mean stain intensity by the mean stain extent.

Shade evaluation:

A single examiner performed the visual tooth color assessments under standard lighting conditions. Tooth shade was scored on the selected anterior teeth using the Vita Bleachedguide 3D-Master Shade Guide. The tab marking system includes interpolated shade guide units (sgu), ranging from 1 to 29 sgu. The lightest tab, 0M1, is assigned a rank of 1 and the darkest tab, 5M3 is assigned a rank of 29. Subject shade rank scores were determined for each exam period by calculating the mean across the selected anterior teeth scored.

Safety

For safety, a thorough evaluation of the oral soft tissues was conducted at each visit, by way of a visual examination of the oral cavity, including the gingiva (free and attached), hard and soft palate, oropharynx/uvula, buccal mucosa, tongue, floor of the mouth, labial mucosa, mucobuccal/mucolabial folds, lips, and perioral area. A trained dental evaluator performed intraoral examinations at each study visit. In case an adverse event occurred (AE) it was recorded and monitored throughout the study. Any observed abnormalities noted during the OST examination were transcribed beginning at the screening visit until 5 days after the final use of study product. The investigator determined the causal relationship of each AE using their clinical experience and select the appropriate severity descriptor as mild, moderate, or severe. Treatment-emergent AEs were to be reported for the safety population, which included all randomized participants who received study product.

Data analysis

A sufficient number of participants were to be screened in order to randomize at least 90 participants (approximately 45 to the Test, and 45 to the Control groups) to ensure 84 evaluable participants completed the entire study. The sample size in this the study provided 80% power to detect a significant difference in the scores improvements, with type 1 error of 5%. Safety analysis was carried out on a modified intent-to-treat (ITT) population, defined as all randomized participants who conducted at least one treatment. Efficacy analysis was conducted on the per-protocol (PP) population included all participants in the ITT population who had no protocol deviations deemed to affect efficacy.

Summary statistics (e.g., count, mean & SD, Median, 25th and 75th percentile) of the demographic characteristics and the efficacy measurements were calculated for each group and study visit. Normality distribution of measures was evaluated using Shapiro and Wilk test; as the majority of measures deviate from normal distribution, non-parametric approach was implemented.

Friedman's test followed by Dunn's test was used to evaluate the change over time (the time effect) within each group.

The Mann Whitney test was used to compare the improvement after 4 and 6 weeks between the groups; the improvement was calculated as

$$Delta = Score_{Week_i} - Score_{Baseline}$$

Significance level was defined as α=0.05. Analyses were carried out using SPSS version 25.0.

4. RESULTS

A total of 89 subjects provided informed consent and were enrolled to this study, and 88 of these met the entrance criteria. Two subjects self-selected to withdraw during the first visit, 86 subjects were randomized at baseline to receive either the ToothWave™ or the control powered toothbrush. Two subjects in the treatment group discontinued study participation prior to study end, with 84 subjects (94.38%) completing and deemed fully evaluable at the trial's conclusion. As shown in ***Table I***, the mean age of the randomized study population was 47.8 years, with a range of 18 to 70 years; 58 (69%) of the subjects were female.

Table I exemplifies the demographic baseline values, indicating that the study population was well-balanced with respect to all baseline demographic variables ($p \geq 0.245$).

Efficacy

The treatment and control groups' average baseline scores are shown in ***Table II***. The test groups did not differ significantly in the efficacy measurements mean scores ($p \geq 0.776$).

Figure 3 summarizes the changes in the LSI scores of the treatment and control groups over time, indicating a statistically significant reduction in the treatment group ($p<0.001$), as compared to a significant increase in the control group ($p<0.001$). Moreover, the final LSI scores following 4 and 6 weeks of brushing were significantly lower in the treatment group as compared to the control group ($p<0.001$).

Figure 4 exemplifies the changes in teeth shade index (Bleachguide 3D Master) scores over time, indicating a significantly lower score in the treatment group as compared to the control group following 6 weeks of brushing ($p=0.024$).

Table III summarizes the median delta values, (difference from Baseline) of the efficacy measures, following 6 weeks test phase. Negative delta values represent an improvement in the measured score, having scores that are decreased with time; a greater negative value represents a greater improvement. Statistical analysis indicates that the delta values achieved in the treatment group are significantly lower than those of the control group ($p<0.001$), showing a significantly greater improvement in stain and shade indices in the treatment group as compared to the control group. Moreover, while the treatment group exhibited a significant decrease in stains ($delta<0$, $p<0.001$), the control group showed an increase in stains score ($delta>0$, $p<0.001$) during the test phase of the study.

Safety

Both toothbrushes were well-tolerated and no device-related adverse events or any side effects were reported during the study. There were no medical incidents that led to discontinuation of treatment or withdrawal from the study.

Table I - Demographic characteristics

characteristic		***ToothWave™ N=43***	***control N=43***	***overall***
Sex, n (%)	***Male***	16 (37.2%)	11 (25.6%)	27 (31.4%)
	Female	27 (62.8%)	32 (74.4%)	59 (68.6%)
Race, n (%)	***White/Caucasian/European/ Arabic heritage***	33 (76.7%)	34 (79.1%)	67 (77.9%)
	African American/African heritage	8 (18.6%)	8(18.6%)	16 (18.6%)
	Asian Pacific Islander	1(2.3%)	1 (2.3%)	2 (2.3%)
	Hispanic	1 (2.3%)	0	1 (1.2%)
age	***Mean (SD)***	46.7 (14.1)	49.3 (10.84)	48 (12.6)
	Range	18-70	27-68	18-70

Table II - Baseline efficacy measures

Measure	*Group*	*Mean (SD)*	*Median [25%, 75%]*	*P value**
Stain Index	*Treatment[§]*	*31.5 (14.4)*	*27 [20, 39]*	*0.781*
	Control[£]	*33.1 (16.7)*	*28 [22, 43]*	
Shade index	*Treatment[§]*	*12.4 (5.5)*	*11 [8, 17]*	*0.776*
	Control[£]	*12.1 (5)*	*11 [9, 15]*	

[§]n=41; [£]n=43

* representing significance level, comparing the mean scores of treatment and control at baseline.

Table III - Calculated difference (delta) from baseline after 6 weeks of twice daily brushings

Measure	*Group*	*Median [25 percentile, 75 percentile]*	*Min, Max*	*P value**
Stain Index	*Treatment*[¥]	***-10** [-20, -6]*	*-49, 9*	*<0.001*
	Control[£]	***6** [0, 10]*	*-37, 31*	
Shade Index	*Treatment*[¥]	***-2** [-4, -2]*	*-8, 0*	*<0.001*
	Control[£]	***0** [-2, 0]*	*-4, 3*	

[¥]n=41, [£]n=43

*representing significance level comparing the difference from BL in treatment vs control.

[§]Lobene score index increased in the control group but decreased in the treatment group during 6 weeks of brushing.

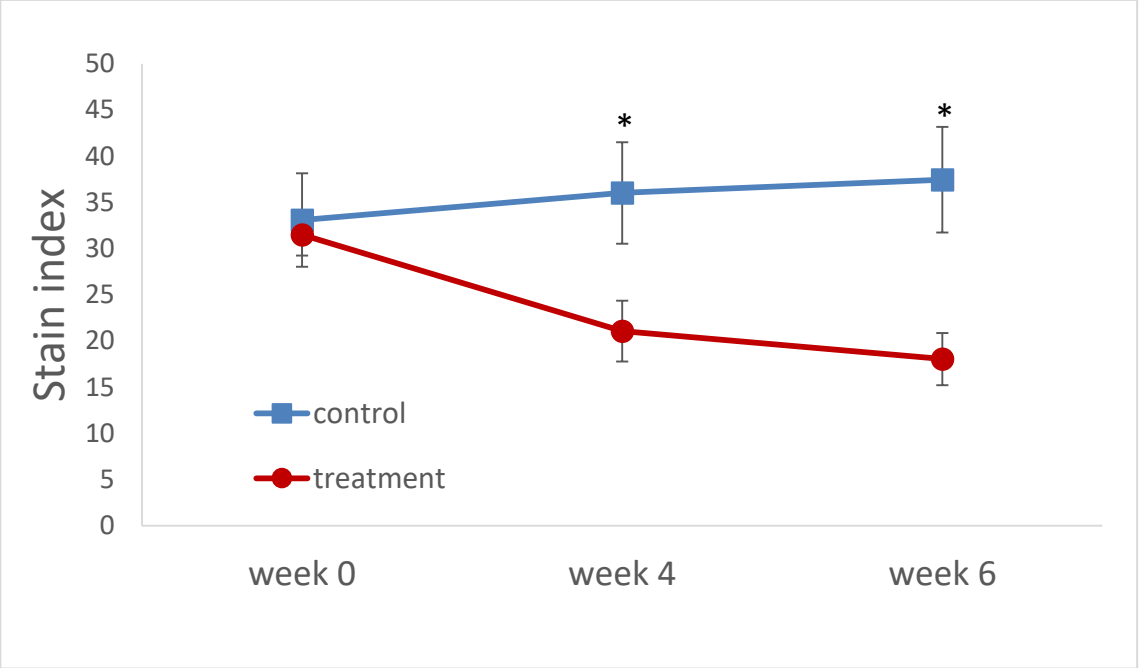

***Figure 3** - LSI scores are significantly lower in the treatment group as compared to the control group following 6 weeks of brushing (*p<0.001)*

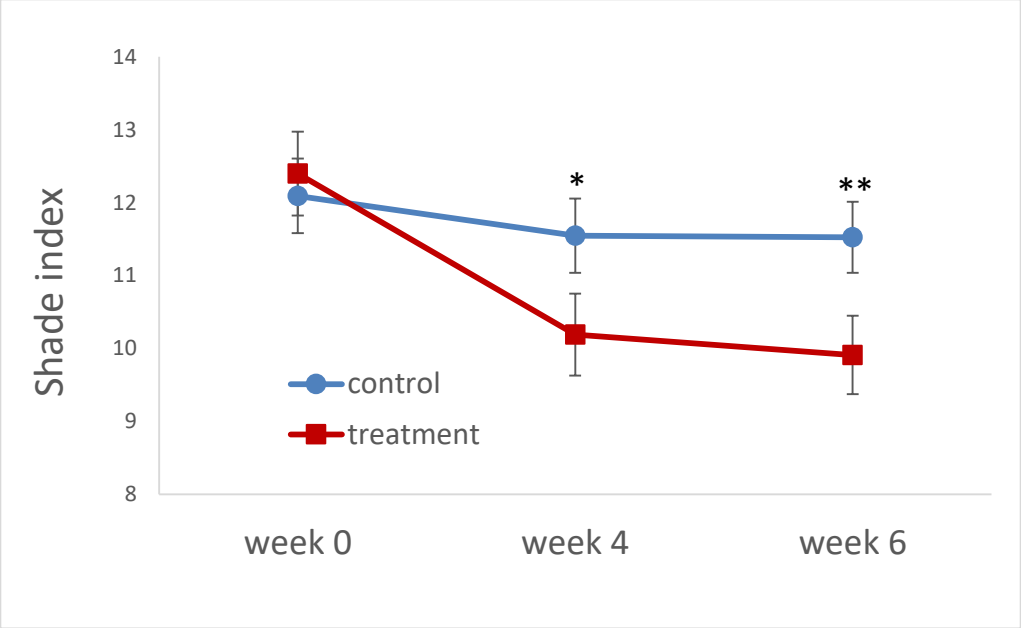

Figure 4 - *Lower shade scores (indicating on a whiter shade) were measured in the treatment group as compared to the control group following 4 and 6 weeks of brushing (*p=0.07, **p=0.024), using the Vita Bleachguide 3D Master scale*

5. DISCUSSION

Stains and impurities that are attached to the teeth surface, can rarely be removed by regular brushing, either with manual or powered toothbrush; however, in the current study we show that the Silk'n ToothWave™ toothbrush provides a significant reduction in stains and whitening of teeth shade. The improvement seen in the efficacy measures was found to be significantly greater in the ToothWave™ group as compared to the control group; and specifically, the significant stains reduction in the treatment group compared to accumulation of stains in the control group.

The Silk'n ToothWave™ utilizes an alternating low power electric current that oscillates at a frequency of 3MHz. During brushing, the current streams through the toothpaste, while air bubbles are formed and increase the surface area available for streaming. RF current tends to flow along the surfaces of electrical conductors, which is known as the "skin effect" [20]. In addition, the Silk'n ToothWave™ includes an electro-mechanical silicon barrier, which is located between the electrodes. Both the "skin effect" and electro-mechanical barrier steer the current to the desired direction and provide alternating current fluency around the tooth. In addition, the electric current is able to effectively reach hidden areas like the ones between the teeth or along the gum line; these areas and surfaces would otherwise be difficult to reach using mechanical means (i.e. powered or manual toothbrush).

Since the alternating current streams close to the tooth, it brings the charged molecules that are present in the toothpaste close to the tooth surface and changes the chemical environment around it. Once charged molecules accumulate near the tooth surface, the chemical balance may be shifted towards the removal of the attached compounds, replacing them by other, non-staining charged substances, which might have greater affinity to the surface area (for instance fluoride).

We hypothesize that by changing the local charges around the tooth the alternating electrical current is able to activate, speed up, or inhibit chemical reactions that could take place at the tooth surface and remove substances (i.e., calculus) that are otherwise attached strongly to the enamel layer.

Our hypothesis is based on the assumption that the electrically charged toothpaste ingredients take part in the process that occurs on the teeth surface. Toothpastes are water based complex mixtures of abrasives and surfactants, humectants, binders, and other active ingredients. All available toothpastes contain charged organic and inorganic molecular compounds that once the RF is activated, act as electrolytes in the medium and stream along the tooth surface, and are able to achieve the desired effect.

6. CONCLUSIONS

The Silk'n ToothWave™ (model H7001) novel toothbrush is shown to produce a significant reduction in stains and to achieve whitening of teeth shade following 6 weeks of brushing. These benefits were shown to be significantly greater as compared to a control powered toothbrush and are attributed to the RF feature that is uniquely utilized by the ToothWave™ brush.

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