

Clinical Study Report

Clinical Efficacy of the e-Bright Tooth Whitening Accelerator Home Edition: a randomized placebo controlled clinical trial

(Clinical Study Protocol Number: **EBRIGHT-2007-01**)
Study Sponsored by Beyond Dental and Health

Report prepared by

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Study Objective

The objective of this study is to assess the tooth whitening efficacy of an over-the-counter tooth whitening product (e-Bright Tooth Whitening Accelerator Home Edition) versus a placebo control.

Methods

Subjects: This study is a stratified, double-blind, randomized, and parallel design. All subjects must meet the following inclusion/exclusion criteria:

Inclusion Criteria:

1. Male or female volunteers between 18 – 65 years of age
2. Good general health
3. Must sign the informed consent form.
4. Must have a shade of: A3 or darker on teeth #7-10 on a VITA shade guide arranged according to VITA order.
5. Must have a professional prophylaxis within the past 6 months
6. Must have the following natural (uncrowned) teeth for shading: #7, 8, 9, 10 (upper front teeth)
7. No history of allergy to personal care consumer products, or their ingredients, relevant to any ingredient in the test products as determined by the dental professional monitoring the study.

Exclusion Criteria:

1. History of allergy to Hydrogen Peroxide.
2. Medical condition which requires premedication prior dental procedures/visits
3. Current use of antibiotics for any purpose
4. Subjects unable or unwilling to sign the informed consent form.
5. Acute gingivitis with hyperemic gingival tissues.
6. Untreated dental decay on teeth #7, 8, 9, 10 (upper front teeth).
7. Other disease of the oral mucosal or alveolar tissues.
8. Presence or use of an orthodontic appliance on teeth #7, 8, 9, 10.
9. Tooth discoloration associated with intrinsic stain (e.g., tetracycline, fluorosis)
10. Restorations or crowns that would interfere with color measurements on teeth: #7, 8, 9, 10
11. Pregnant or nursing women.
12. Participation in any other clinical study or test panel within 2 weeks prior to enrollment into this study.
13. Smoking.
14. Subjects who must receive dental treatment during the study dates.
15. History of allergy to common whitening ingredients.

16. Immune compromised individuals (Immuno-suppressive drug therapy, etc.)

Study Procedures:

Screening: An initial screening was conducted to ascertain the suitability of the subject to take part in the study. All subjects were asked for medical history including allergies to ingredients contained in tooth whitening products. A VITA shade assessment on teeth #s 7, 8, 9, 10 was carried out to determine the eligibility of each subject to enter the study.

Enrollment: Subjects with teeth # 7 to 10 A3 or darker were invited to participate in the present study. All subjects completed the Informed Consent Form prior to being allocated to use the test products. All subjects had received an evaluation of their oral soft tissues by the clinical examiner, including an assessment of the soft palate, hard palate, gingival mucosa, buccal mucosa, mucogingival fold areas, and tongue, sublingual and submandibular areas and salivary glands. The results from this evaluation were recorded on the Study Initiation Form.

Washout: At the beginning of the study all subjects were provided with Colgate Regular toothpaste and they were instructed to brush twice daily (unsupervised) for one week prior to the start of the study. A Colgate adult, soft bristle toothbrush and floss was also provided for each subject during the 'washout' periods. Subjects were instructed to not use any other oral hygiene devices or products.

Baseline evaluation: Subjects will return to the Eastman Dental Center dental clinic for a tooth color measurement using the Vita Shade Guide and X-Rite ShadeVision System (a colorimeter designed for dental applications) and for a brief oral assessment including plaque index (PI) and gingival index (GI). The medical history and medications will be updated. The subject will then receive the test article that has been randomly assigned to them and will be instructed in its use.

Randomization and treatment assignment: Treatment assignment was determined using a computer generated random table and the subjects were randomized into 2 treatment groups (XX and YY), stratified based on the VITA shades of teeth # 7 to 10.

Treatment: After the baseline examination, subjects were given a demonstration on how to use the assigned products with the assistance of picture charts and DVD movies. Subjects were asked to use the products once daily for 20 minutes. A written instruction was given and the subjects were instructed to record any sensitivity or discomfort and to avoid use any other tooth whitening products during the study period. They were provided with Colgate regular toothpaste and toothbrushes.

Day-7 and Day-90 evaluations: Subjects will return to the clinic for a tooth color measurement using the Vita Shade Guide and ShadeVision System at day-7 and day-90 after the whitening procedure and for a brief oral assessment including PI and GI. The medical history and medications will be updated and any adverse effects will be recorded.

Final evaluation: This visit will occur on the 180th day from baseline. Subjects will return to the dental clinic for a tooth color measurement using the Vita Shade Guide and the ShadeVision System and for a final oral health exam, including PI and GI. The medical history and medications will be updated and any adverse effects will be recorded. The whitening product (used and unused) will be returned by the subject on this visit. At the conclusion of the study, all subjects also received an oral hard and soft tissue evaluation, including an assessment of the soft palate, hard palate, gingival mucosa, buccal mucosa, mucogingival fold areas, and tongue, sublingual and submandibular areas and salivary glands. The results from this evaluation were recorded on the Study Termination Form.

Adverse reaction report:

Any adverse reaction reported by subjects or observed clinically was recorded on the Adverse Reaction Report form. Tooth sensitivity was evaluated as none, mild, moderate or severe based on the subject's report.

Statistical analyses:

Changes in VITA shade from baseline to Day-7, Day-90 and Day-180 post-treatment were calculated for each subject for each treatment cell. The non-parametric Mann-Whitney U tests were used to compare the VITA shade scores between the groups at baseline, and Day-7, Day-90 and Day-180. Changes in VITA shades from baseline at Day-7, 90 and -180 evaluations were also compared between the treatment groups. A difference between treatments will be considered significant if a 95% confidence level is achieved.

Changes in the three coordinates of CIELAB color space L^* , a^* and b^* (ΔL^* , Δa^* , and Δb^*) were compared between the two treatment groups at Day-7, -90, and -180 using t-tests. The L^* values represent the lightness of the color ($L^* = 0$ yields black and $L^* = 100$ indicates diffuse white). The a^* values represent color positions between red and green (a^* , negative values indicate green while positive values indicate magenta). The b^* values represents color positions between yellow and blue (b^* , negative values indicate blue and positive values indicate yellow). The overall color change (ΔE^*) was calculated using the formula $\Delta E^* = \sqrt{\Delta L^{*2} + \Delta a^{*2} + \Delta b^{*2}}$ and compared between groups at Day-7, -90 and -180 using t-test.

Changes in PI and GI were compared between baseline and different evaluation stages using paired t-test.

Results

To achieve the enrollment target of a minimum of 25 subjects in each group and to account for potential dropouts, 60 eligible subjects were enrolled into 2 treatment groups after initial screening. One subject in Group XX and one in Group YY dropped out of the study before the end of the study for reasons not related to the product use. The data was analyzed using the intention-to-treat principle.

Changes in VITA shades:

The median VITA shade rankings and their inter-quartile ranges in each treatment period using XX and YY are presented in Table 1. The median ranking dropped from 10 to 9 in the XX group and from 10 to 7 in the YY group at the Day-7 evaluation. Product YY showed a consistently lower value in median shade rankings till 6 months after the whitening treatment.

Table 1: VITA shade scores of teeth #s 7, 8, 9 and 10 (median and inter-quartile range) using XX and YY

	Baseline		Day 7		Day 90		Day 180	
	Median	IQR	Median	IQR	Median	IQR	Median	IQR
XX	10	5	9	3	9	5	9	8
YY	10	4	7	4	7	4	6	4
Z*	-0.266		-3.053		-2.920		-2.129	
p	0.7901		0.0023		0.0035		0.0333	

*Mann-Whitney U test, two-tailed

As shown in Table 2, product YY resulted in significant reductions in VITA shade scores when compared between baseline and Days 7, 90 and 180. No significant change was observed in the product XX group. The changes in VITA shades were statistically significant between the XX and YY groups throughout the evaluation period (Mann-Whitney test, $p < 0.01$). The shade change in the YY group remained stable at the conclusion of the study.

Table 2: Changes in VITA shade scores at Day-7, -90, -180 as compared to baseline (median and inter-quartile range) using XX and YY

	Day 7		Day 90		Day 180	
	Median	IQR	Median	IQR	Median	IQR
XX	0.0	2.0	0.0	1.0	-0.5	3.0
YY	-4.0	3.0	-3.5	4.0	-4.0	3.0
Z*	-4.169		-3.896		-3.186	
p	<0.0001		<0.0001		0.0012	

*Mann-Whitney U test, two-tailed

Changes in CIE L*a*b* values:

Changes in CIE L*a*b* (ΔL^* , Δa^* , and Δb^*) and overall color (ΔE^*) are listed in Tables 3 through 5 for evaluations at Day-7, -90 and -180. There were statistically significant differences between the XX and YY groups in lightness, red-green and blue-yellow dimensions of tooth color in the 3 coordinates of CIE L*a*b* color space. After whitening treatments, tooth color in the YY group showed significant increase in lightness (positive ΔL^*), decrease in redness (negative Δa^*), and decrease in yellowness (negative Δb^*) as compared to the XX group. There were slight regression towards baseline values in lightness and yellowness of the teeth as shown by the diminishing ΔL^* and Δb^* values with time in the YY group. But such changes were not statistically significant and did not result in discernable changes in overall color as show by ΔE^* .

Table 3. Changes in CIE L*a*b* and overall color at Day-7as compared to baseline (mean and standard deviation) using XX and YY

	ΔL^*		Δa^*		Δb^*		ΔE^*	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
XX	-0.00	1.10	-0.03	0.85	-0.40	0.91	1.41	0.93
YY	2.05	2.99	-0.57	0.79	-2.64	2.24	4.21	2.85
t	-3.517		2.472		5.033		-5.087	
p	0.0009		0.0165		<0.0001		<0.0001	

t-test, two-tailed

Table 4. Changes in CIE L*a*b* and overall color at Day-90 as compared to baseline (mean and standard deviation) using XX and YY

	ΔL^*		Δa^*		Δb^*		ΔE^*	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
XX	0.30	1.95	-0.50	0.81	0.35	1.29	1.99	1.57
YY	1.92	3.61	-1.00	0.72	-1.67	2.06	3.98	3.03
t	-2.137		2.478		4.475		-5.087	
p	0.0371		0.0163		<0.0001		<0.0001	

t-test, two-tailed

Table 5. Changes in CIE L*a*b* and overall color at Day-180 as compared to baseline (mean and standard deviation) using XX and YY

	ΔL^*		Δa^*		Δb^*		ΔE^*	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
XX	-0.05	1.45	-0.39	0.79	0.62	1.85	2.13	1.41
YY	1.27	2.62	-0.97	0.85	-1.51	2.81	3.75	2.45
t	-2.370		2.579		3.407		-3.103	
p	0.0213		0.0126		0.0012		0.0030	

t-test, two-tailed

Changes in PI and GI:

There were statistically significant reductions in PI and GI at Day 7 evaluation as compared to the baseline in both groups. The improvement in PI and GI remained in both groups at Day 180 evaluation.

Tooth sensitivity:

There was no report of sensitivity related to treatment with either XX or YY.

In summary, the results of this study indicated that product YY significantly improved tooth shade after 20 minutes of treatment daily for 5 days. The treatment effect remained 6 month after treatment. The tooth color change was largely due to an increase in lightness and a decrease in yellowness as measured by colorimeter. Whitening treatment had a positive effect on gingival health as indicated by decreases in PI and GI scores.

Conclusions

The testing products were decoded after completion of the data analysis. Product YY is the testing product, while product XX is the identical placebo without the active ingredients (6% hydrogen peroxide).

1. The e-Bright tooth whitening accelerator home edition is effective in whitening teeth by increasing the lightness and decreasing the yellowness of the teeth. The median shade change is 4.0 on the VITA shade guide. The mean color change is $\Delta E^* 4.0$ on the CIE $L^*a^*b^*$ color space.
2. The e-Bright tooth whitening accelerator home edition is safe. No subjects reported sensitivity or other adverse effects.
3. Whitening treatments have a positive effect on gingival health. This effect is not likely related to the active ingredients but likely a sign of Hawthorne Effect.