

***In Vivo* Study of Two Carbamide Peroxide Gels with Different Desensitizing Agents**

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Clinical Relevance

Under the conditions of this study, 15% carbamide peroxide with potassium nitrate and fluoride exhibited greater bleaching potential but exhibited no difference in sensitivity compared to 16% carbamide peroxide with amorphous calcium phosphate.

SUMMARY

This study evaluated tooth whitening and sensitivity that occurred during and after 14 days of overnight bleaching with 15% carbamide peroxide gel with potassium nitrate and fluoride (Opalescence 15% PF, OP) and 16% carbamide peroxide with amorphous calcium phosphate (Nite White 16%, NW). Thirty-two subjects

bleached their teeth using custom trays. The subjects had a baseline evaluation and returned after 7, 14, 21, 35 and 90 days for subjective and objective color evaluations. The subjects also recorded daily tooth and gingival sensitivity. The treatments were compared for differences in mean L*, a*, b* and shade guide rank order at baseline and each appointment thereafter, using repeated measures analysis of variance (ANOVA). OP and NW showed significant tooth whitening. Subjects using OP were significantly lighter in b* and E* than those using NW, while exhibiting no difference in tooth or gingival sensitivity overall or during any evaluation.

INTRODUCTION

White teeth are believed to be associated with health and beauty; lighter colored teeth have become desirable. Vital tooth whitening, the most conservative treatment for discolored teeth, can be performed with a high rate of success and less expense to the patient than restorative treatments, such as porcelain veneers, crowns or composite bonding.¹

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At-home vital tooth bleaching has become commonplace in dentistry.²⁻⁵ The main types of bleaching agents currently used are hydrogen and carbamide peroxide and are used in a variety of concentrations. Dental tissue sensitivity during bleaching is a common side effect⁶⁻⁸ and varies from patient to patient. Usually, the sensitivity is reversible and resolves itself over time or with the help of a desensitizing agent.⁹

As the popularity of tooth bleaching has increased, improvements have been made to bleaching products. Currently, many different compounds have been added to tooth whitening gels to improve them. Of these newer agents, potassium nitrate¹⁰ and amorphous calcium phosphate (ACP)¹¹ have been identified as agents that are thought to decrease sensitivity. It is believed that potassium nitrate reduces dental sensitivity by decreasing the ability of nerve fibers in the dental pulp to re-polarize after an initial depolarization due to pain sensation. Fluoride is added to potassium nitrate, because it is believed that fluoride aids in the reduction of sensitivity by blocking the dentin tubules, thus reducing fluid flow to the pulp chamber.¹⁰ It is also believed that ACP reduces sensitivity by blocking tubules and surface defects with hydroxyapatite crystals that form from the interaction of ACP and carbonate.¹¹ There are limited studies comparing how or if the addition of these agents affects the tooth whitening potential of whitening gels.

This study evaluated the amount of tooth whitening and sensitivity that occurred during and after 14 days of overnight bleaching with 15% carbamide peroxide gel with potassium nitrate and fluoride and 16% carbamide peroxide gel with amorphous calcium phosphate. The amount of rebound that occurred up to three months post-bleaching was also measured. This study utilized a split-mouth design, the effectiveness of which has been described in other studies.¹²⁻¹⁸ The null hypotheses are that there will be no difference between either bleaching product with regard to 1) lightening of the teeth, 2) color rebound or 3) tooth/gingival sensitivity.

METHODS AND MATERIALS

The materials used in this study were Opalescence 15% carbamide peroxide gel with potassium nitrate and fluoride (OP) (Ultradent Products, Inc, South Jordan, UT, USA) and Nite White 16% carbamide peroxide with amorphous calcium phosphate (NW) (Discus Dental Inc, Culver City, CA, USA).

This study received approval from the Indiana University Purdue University Indianapolis Institutional Review Board. Thirty-two subjects, 16 female and 16 male with a mean age of 57 years, were recruited through advertisements and met the Inclusion/Exclusion criteria.

The inclusion criteria required that the patient have all six maxillary anterior teeth, have no maxillary anterior teeth with more than 1/6 of the labial surface of their natural tooth covered with a restoration, be willing to sign a consent form, be at least 18 years of age, be able to return for periodic examinations, be willing to refrain from the use of tobacco products during the study period and have maxillary anterior teeth that are shade B54 or darker on the Trubyte Bioform Color Ordered Shade Guide (Dentsply/Trubyte, York, PA, USA).

The exclusion criteria included a history of any medical disease that could interfere with the study or require special considerations, any use of tobacco products within the past 30 days, any current or previous use of professionally applied or prescribed "in-office" or "at-home" bleaching agents, gross pathology in the oral cavity (excluding caries), a gingival index score greater than 1.0, any pregnant or lactating women or tetracycline-stained teeth.

Each participant received, read and signed a consent form. Additionally, the subjects received a complete oral prophylaxis with a dental prophylaxis paste containing fluoride, which was used to remove extrinsic stain from the teeth in a period no greater than two months but no less than two weeks prior to the start of the study. A maxillary arch impression was taken with Jeltrate Plus (Dentsply LD Caulk Division, Milford, DE, USA) from which a study model was made from Microstone (Whip Mix Corp, Louisville, KY, USA).

Prior to the baseline evaluations and tray manufacture, the products were randomly assigned to different halves of the subject's maxillary arch. This was accomplished before the baseline evaluation, because the manufacturer's instructions state that reservoirs are required for OP but are not needed for NW. The products were used in custom trays, which were trimmed just shy of the gingival margins.

At the baseline appointment, the surrounding tissues were visually examined for gingival health using the Loe-Silness Gingival Index.¹⁹ The color evaluations were performed by subjective shade guide matching of the maxillary anterior teeth using the Trubyte Bioform Color Ordered Shade Guide (Dentsply/Trubyte) arranged by value order and by using a colorimeter (Chroma Meter CR-321, Minolta, Osaka, Japan). Clinical photographs were also taken with a digital camera (Nikon S2Pro, Tokyo, Japan). The subjects were then required to return at 7, 14, 21, 35 and 90 days after baseline for subjective and objective color evaluations. The same procedures were repeated at each subsequent appointment. The evaluations were conducted in the same geographic location and under color corrected overhead lighting, with the same examiner per-

forming all of the evaluations. The evaluator was blind as to the product used.

The colorimeter used a color system that was defined by the International Commission on Illumination in 1967 and is referred to as CIELAB.²⁰ The color system is based on the following values: L^* , which represents the value (lightness or darkness); a^* , which represents the measurement along the red-green axis and b^* , which represents the measurement along the yellow-blue axis. Total color differences or distances between two colors (ΔE^*) were calculated using the formula: $\Delta E^* = [(\Delta L^*)^2 + (\Delta a^*)^2 + (\Delta b^*)^2]^{1/2}$.¹⁸ For a darker tooth color that was not present on the Trubyte shade guide, color tab B90 was recorded when the color of the tooth was darker than the darkest shade tab, B85. There were only two cuspids that were darker than the darkest available shade tab.

The treatments were compared for differences in mean L^* , a^* , b^* and shade guide rank order at baseline and at each return visit, using repeated measures analysis of variance (ANOVA). Terms included in the ANOVA were treatment, tooth type and the treatment-by-tooth type interaction. The repeated subject effect was used to model correlations between teeth. Change in colorimeter measurements and shade guide assessments were computed by subtracting the baseline measurements from the follow-up measurements. The treatments were compared for differences in mean ΔL^* , Δa^* , Δb^* , ΔE^* and Δ shade guide rank order using repeated measures ANOVA. Terms included were for treatment, tooth type, time and all interactions in-between the three factors. Baseline measurements were included as covariates. The repeated subject effect was used to model correlations between teeth and correlations over time.

The subjects were asked to brush their teeth at least twice a day with a non-whitening toothpaste (Crest Cavity Protection, Procter & Gamble, Cincinnati, OH, USA) to standardize oral hygiene. They were also given a sheet on which to record daily any tooth and/or gum sensitivity on their right or left side using a five-point scale where: 1 = none, 2 = mild, 3 = moderate, 4 = considerable and 5 = severe. Subjects who experienced more than a moderate degree of sensitivity on either side of their mouth were asked to return to the dental school to receive potassium nitrate desensitizing gel. The sheets containing the daily recordings were returned to the examiner at the two-week evaluation.

The treatments were compared for differences in daily gum and tooth sensitivity assessments using ANOVA, with terms for treatment, day and the treatment-by-day interaction and random subject effects to correlate the sensitivity values within and between days.

RESULTS

Color Changes

The baseline mean measurements for the OP group were: $L^*=49.19$, $a^*=-0.053$, $b^*=4.18$ and shade guide value=20. The baseline mean measurements for the NW group were: $L^*=49.08$, $a^*=-0.55$, $b^*=4.14$ and shade guide value=20. There were no significant differences between the two groups for any of the baseline measurements.

The data for ΔL^* , Δa^* , Δb^* , ΔE^* and Δ shade guide value mean and standard deviation at all time measurements are displayed in Tables 1 through 5 and are graphically represented in Figures 1 through 5.

OP had a significantly higher ΔL^* than NW at days 7, 14, 21 and 35 and was marginally higher at 90 days. OP had a significantly higher Δa^* than NW at days 7, 14 and 21 and was marginally higher at week 35. OP had a significantly higher Δb^* than NW at days 7, 14, 21, 35 and 90. OP had a significantly higher ΔE^* than NW at days 7, 14, 21, 35 and 90. OP had a significantly higher Δ shade guide value than NW at days 7, 14 and 21. Significant color change was still occurring between day 35 and 90

Table 1: Mean Change and SD of ΔL^* for All Time Periods

	Day	OP		NW		p value
		Mean	SD	Mean	SD	
Delta						
L^*	0	0.00	0.00	0.00	0.00	---
	7	6.28	2.76	5.07	2.36	0.0001†
	14	7.05	3.08	5.99	2.95	0.0017†
	21	5.04	2.54	3.76	2.55	0.0002†
	35	2.38	1.23	1.96	1.42	0.0136†
	90	2.08	1.13	1.84	1.07	0.0577††

† - indicates statistical significance

†† - indicates marginally significant

Table 2: Mean Change and SD of Δa^* for All Time Periods

	Day	OP		NW		p value
		Mean	SD	Mean	SD	
Delta						
a^*	0	0.00	0.00	0.00	0.00	---
	7	-0.78	0.57	-0.59	0.58	0.0001†
	14	-1.22	0.56	-1.06	0.54	0.0012†
	21	-0.97	0.55	-0.76	0.58	0.0001†
	35	-0.76	0.56	-0.69	0.61	0.0846
	90	-0.71	0.50	-0.68	0.50	0.4196

† - indicates statistical significance

for both products. Both groups had significant mean changes from the baseline to 14 days post-bleaching for ΔL^* , Δa^* , Δb^* , ΔE^* and Δ shade guide values.

Table 3: Mean Change and SD of b^* for All Time Periods

Day		OP Mean	SD	NW Mean	SD	<i>p</i> value
Delta b*	0	0.00	0.00	0.00	0.00	---
	7	-4.75	1.48	-3.64	1.46	0.0001†
	14	-5.84	1.58	-4.76	1.61	0.0001†
	21	-4.77	1.55	-3.60	1.58	0.0001†
	35	-3.51	1.08	-2.84	1.22	0.0001†
	90	-3.18	0.79	-2.67	1.00	0.0001†
† - indicates statistical significance						

Table 4: Mean Change and SD of E^* for All Time Periods

Day		OP MeanSD		NW MeanSD		<i>p</i> value
Delta E*	0	0.00	0.00	0.00	0.00	---
	7	8.10	2.80	6.49	2.45	0.0001†
	14	9.57	2.71	8.04	2.82	0.0001†
	21	7.24	2.69	5.56	2.72	0.0001†
	35	4.53	1.37	3.84	1.48	0.0002†
	90	4.08	1.02	3.61	1.06	0.0001†
† - indicates statistical significance						

Table 5: Mean Change and SD of Shade Guide Value at All Time Periods

		OP		NW		
Day		Mean	SD	Mean	SD	<i>p</i> value
Delta shade guide	0	0.00	0.00	0.00	0.00	---
	7	-12.19	3.66	-11.05	3.63	0.0010†
	14	-16.08	3.80	-15.21	3.84	0.0010†
	21	-14.33	3.84	-13.77	3.80	0.0279†
	35	-13.03	3.80	-12.83	3.82	0.4186
	90	-12.30	3.79	-12.18	3.81	0.6876
† - indicates statistical significance						

Table 6: Mean Change and SD of Gingival and Tooth Sensitivity Scores at 5, 10, 15 and 20 Days

Day	Gingival Sensitivity				Tooth Sensitivity			
	OP		NW		OP		NW	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
5	1.16	0.51	1.16	0.45	1.34	0.65	1.34	0.55
10	1.28	0.73	1.22	0.49	1.34	0.65	1.34	0.60
15	1.00	0.00	1.00	0.00	1.22	0.49	1.16	0.37
20	1.00	0.00	1.00	0.00	1.00	0.00	1.00	0.00

Sensitivity

Tooth sensitivity comparisons were only possible through day 17 due to a lack of significant sensitivity after day 17. OP and NW were not significantly different overall ($p=0.9773$) or at any day (Figure 6). Additionally, gingival sensitivity comparisons were only possible through day 14 due to a lack of significant sensitivity after day 14. OP and NW were not significantly different overall ($p=0.3321$) or on any particular day (Table 6, Figure 6).

DISCUSSION

Dental bleaching has become popular because it is an easy, inexpensive way to improve a patient's smile. Many effective bleaching products can be found on the current market. However, as one of the side effects of bleaching is sensitivity, manufacturers have started to add desensitizing agents to bleaching products, two of which include potassium nitrate and amorphous calcium phosphate (ACP). There is little prior research comparing the effectiveness of bleaching and the reduction of sensitivity between products with desensitizing agents. However, other comparisons have been made that are clinically relevant.

Tam²¹ compared 10% carbamide peroxide (CP) and 10% CP with potassium nitrate and fluoride (PF). A split-mouth study design was used on 21 subjects to determine the whitening ability and sensitivity from those two agents. Tam concluded that the addition of PF made no difference in the whitening ability of 10% CP but noted that it significantly reduced the amount of sensitivity.²¹ A study conducted by Giniger and others²² compared the differences between a 16% CP product and a 16% CP product with ACP added. These authors determined that the addition of ACP caused

a statistically significant decrease in sensitivity and a statistically significant increase in whitening ability.²²

In addition to whitening ability and sensitivity, bleaching agents can also be

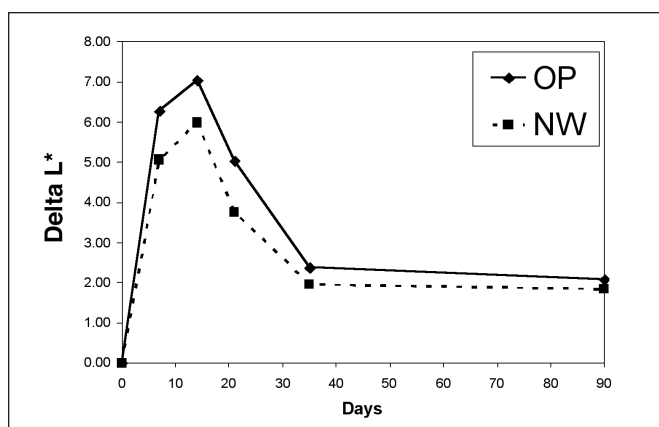


Figure 1: Change in mean L* scores.

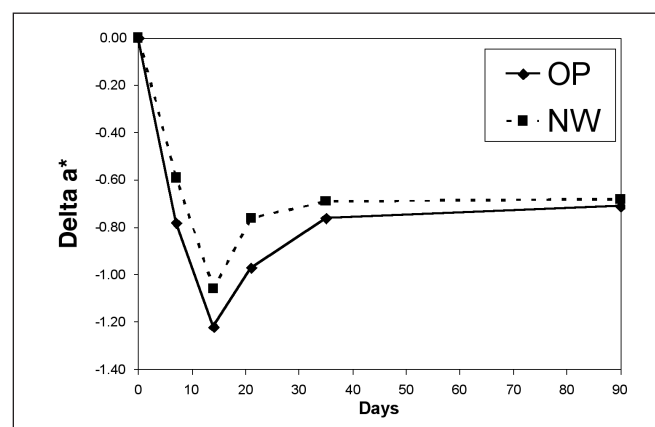


Figure 2: Change in mean a* scores.

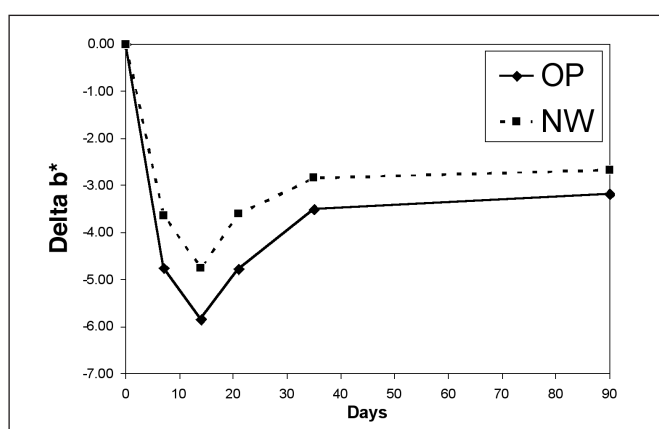


Figure 3: Change in mean b* scores.

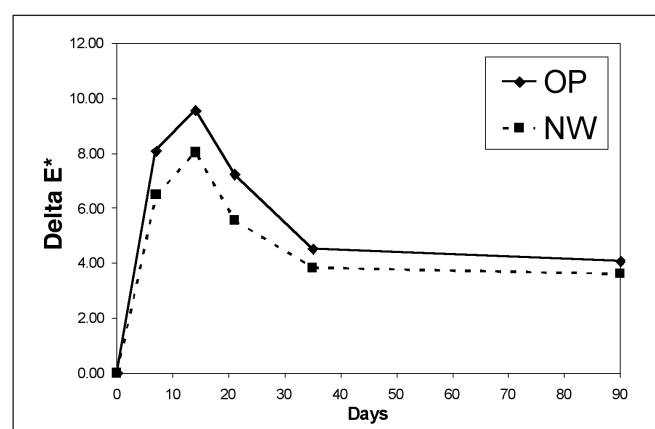


Figure 4: Change in mean E* scores.

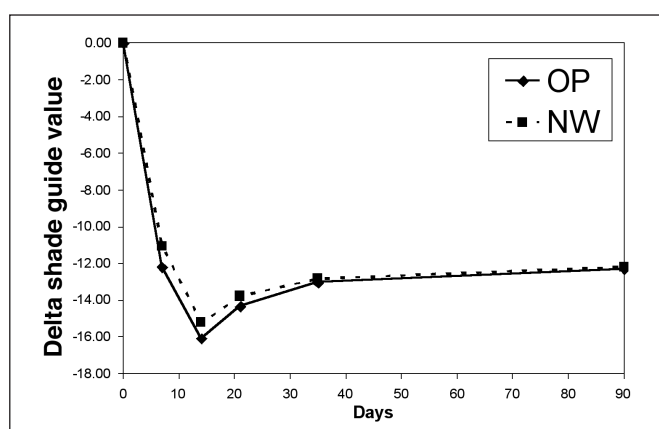


Figure 5: Change in mean shade guide values.

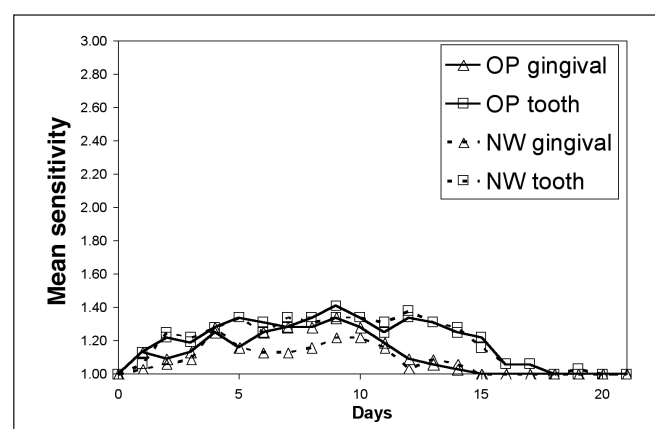


Figure 6: Change in mean tooth and gingival scores.

compared using the microhardness of enamel. Although hardness was not measured in this study, this method of assessment can be used to determine the similarity of the products. In a recent study, it was determined that the use of 20% CP with PF eight hours a day for 42 days actually increased the microhardness of enamel as compared to baseline values.²³ Cimilli and

Pameijer found no significant differences in the hardness values of teeth treated six hours a day for five days with 15% and 16% CP without any desensitizing agents.²⁴

The colorimeter measured color based on CIELAB values. It has been determined that successful dental bleaching will induce a positive change in L* (an

increase in value or “lightness”), a negative change in a^* (a decrease in chroma or “intensity” of red) and a negative change in b^* (a decrease in chroma or the “intensity” of yellow).⁶ The current study found results that met these color shifts (Figures 1 through 3). Color evaluation also occurred with the Trubyte Bioform Color Ordered Shade Guide (Dentsply/Trubyte). This guide is organized with higher value (lighter) tabs on the lower end of the scale and lower value (darker) tabs on the higher end of the scale.

The current study compared 15% CP and PF (OP) with 16% CP with ACP (NW), which had not been accomplished previously. This study demonstrated that the reduction in sensitivity was similar between OP and NW. However, it was demonstrated that OP had a statistically significant improvement in some lightened areas over NW. It must be noted that this study did not take into account the other differences in composition of the bleaching agents, which might have had an effect. Additionally, the addition of fluoride in OP was not addressed. It has been theorized that fluoride improves the whitening effect and effectiveness of bleaching agents.²³ Further research should be conducted to determine if this same effect is exhibited with differing concentrations of CP or if there is a difference if the bleaching agent used is hydrogen peroxide.

CONCLUSIONS

- Both OP and NW demonstrated significant tooth whitening at the end of 14 days of bleaching and at the end of the three-month study.
- Subjects using OP were significantly lighter in tooth whitening than those who used NW in b^* and E^* overall and at each visit.
- Subjects using OP were significantly lighter in tooth whitening than those who used NW in L^* , a^* and shade guide overall at some follow-up visits.
- OP and NW were not different in tooth or gingival sensitivity overall or at any visit.

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