©Operative Dentistry, 2003, **28-3**, 236-241

Clinical Research

In Vivo Kinetics of Bleaching Gel with Three-Percent Hydrogen Peroxide Within the First Hour

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Clinical Relevance

The results of this study showed that hydrogen peroxide has an overall similar kinetics curve as carbamide peroxide, yet, it has a faster degradation rate. Therefore, hydrogen peroxide is indicated for daytime application; however, since hydrogen peroxide is used for shorter time periods, the results are still not conclusive since the duration of this study is only one hour.

SUMMARY

This *in vivo* study determined the kinetics of 3% hydrogen peroxide in a bleaching gel within the first hour. The material used in this study was 3% hydrogen peroxide gel (Perfecta 3/15, Premier Dental Products Co) and the study involved 10 subjects who met the inclusion and exclusion criteria. Each subject wore the tray with gel six different times on separate days. Evaluation of remaining amount of hydrogen peroxide was calculated by the method stated in US Pharmacopoeia. The study results indicate that the mean percentage of hydrogen peroxide recovered for 5, 10, 20, 30, 45 and 60 minutes was 61, 56, 49, 44, 38 and 32, respectively. The amount of hydrogen peroxide in the saliva sample after one hour was 0.42 mg. Excluding the first 10 minutes, the kinetics of hydrogen peroxide in the tray and teeth sample was exponential.

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INTRODUCTION

The appearance of an individual's teeth is a prime concern. Therefore, it is not surprising that tooth discoloration has been the subject of studies for many years. A healthy smile improves self-image and confidence and projects an aura of health to others.

During the past decade, the demand for cosmetics dentistry has grown dramatically, which has been fueled, in part, by different bleaching techniques. Based on current clinical studies, at-home bleaching is a safe, effective technique for whitening teeth. The kinetics cycle, according to the ADA (American Dental Association, 1998), is an important issue that determines the safety and effectiveness of at-home bleaching materials that are used during the day or at night. Nighttime bleaching agents use carbamide peroxide as the active agent, whereas, daytime bleaching agents use hydrogen peroxide (HP). There are studies that report the kinetics of carbamide peroxide (Gaiao, 1997; Wattanapayungkul & others, 1999; Matis & others, 2002); however, information regarding the kinetics of

hydrogen peroxide in bleaching agents is limited. The only published data is for the degradation of 10% hydrogen peroxide, which showed that only 50% of the hydrogen peroxide was recovered after 30 minutes (Clinical Research Associates, 1997), with a very small amount present in the tray after two hours. This *in vivo* study determined the kinetics of 3% hydrogen peroxide in a bleaching gel within the first hour.

METHODS AND MATERIALS

Patient Selection

This study was presented to the Institutional Review Board of Indiana University Purdue University Indianapolis. Upon approval, 10 human subjects were enrolled in the study. Tables 1 and 2 list the inclusion and exclusion criteria.

Table 1: *Inclusion Factors*

1. Presence of six caries-free maxillary anterior teeth that have not been restored facially.
2. No significant periodontal disease Gingival Index <1.0 (Loe and Silness, 1963)
3. Crown of the right central incisor at least 9 mm in length and 8 mm in width.
4. Patient agrees not to smoke during the study period.
5. Patient has the ability to return for periodic examinations.
6. Patient is willing to sign consent form.

Table 2: *Exclusion Factors*

1. History of any medical disease that may interfere with the study or require special consideration such as prescribing premedication before dental procedures.
2. Pregnant or lactating women.
3. Younger than 18 years of age.
4. Patient has smoked 15 days prior to being evaluated for acceptance into the study.

Methodology

Qualified subjects received a dental prophylaxis treatment with a rubber cup and pumice at least one week but no more than two months prior to the study. During the same visit, an alginate impression (Jeltrate Plus, Caulk Division Dentsply International Inc, Milford, DE, USA) of the upper arch was taken for each subject. The impression was then poured with Super Die fast-setting stone (Whip Mix Corp, Louisville, KY, USA). From this cast, a customized vacuum-formed tray was made with 0.035-inch soft vinyl sheets (Premier Dental Products Company, King of Prussia, PA, USA). The margins of the tray were trimmed with the Tray Magic Trimmer (Premier Dental Products Company) 1 mm short of the gingival margins. There were no reservoirs in the fabrication of the trays, according to the manufacturer's instructions.

The clinical procedure required a strip of 3% hydrogen peroxide (HP) bleaching gel (Premier Dental Products Company) be placed on the facial surfaces of the six maxillary anterior teeth spaces in the vacuum-formed tray. The filled tray was weighed on an analytical balance with +/- 0.1 mg sensitivity (Mettler AE100, Mettler Instrument Corp, Hightstown, NJ, USA). The tray was then placed into the subject's mouth and seated. Each subject wore the tray with the 3% hydrogen peroxide (HP) bleaching gel on separate days for 5, 10, 20, 30, 45 and 60 minutes. During tray use, the participants were asked to refrain from eating, drinking and speaking. They were provided a beaker for collecting their salivary secretions (saliva sample). The saliva was analyzed to evaluate the amount of hydrogen peroxide each subject would probably have swallowed. At the end of each evaluation period, the bleaching agent was retrieved from: 1) the tray (tray sample), 2) the teeth, by scraping the gel off with a spatula (tooth sample) and 3) the mouth, by having the subject rinse four times with deionized water and collecting the expectorant in a beaker (rinse sample).

Chemical Analysis

The method stated in United States Pharmacopeia (2000) and used in previous studies (Gaiao, 1997; Wattanapayungkul & others, 1999; Matis & others, 2002) was used to determine the amount of peroxide in each sample.

A solution of 0.025N sodium thiosulfate was used to determine the amount of hydrogen peroxide in each sample. Each ml of 0.025N sodium thiosulfate is equivalent to 1.7 mg of hydrogen peroxide. Therefore, the amount of recovered hydrogen peroxide could be identified by determining the volume of sodium thiosulfate used in triturating.

The concentration of hydrogen peroxide (wt %) for tray and teeth samples was determined by the following formula:

$$\text{Concentration of hydrogen peroxide} = \frac{V\,(0.025)\,(1.7)}{W}$$

V = volume of sodium thiosulfate (ml)

W= weight of the sample (milligrams of a recovered sample that incorporates gel and saliva into it)

The amount of hydrogen peroxide recovered in milligrams of HP present in the recovered sample was calculated using the following formula:

Amount of HP = V (0.025) (1.7)

V = the volume of sodium thiosulfate (ml). This formula was applied to the three samples.

The concentration of recovered gel was determined by calculating the percentage of the total physical amount of gel recovered from the tray, teeth and rinse samples compared to the initial amount of gel delivered:

$$\frac{\text{Concentration of HP at time}}{\text{initial gel delivered}} = \frac{\text{total gel recovered x100}}{}$$

The kinetics of hydrogen peroxide with each time was calculated from the ratio:

$$\frac{\text{Concentration of Hydrogen peroxide (t)}}{\text{Initial concentration of hydrogen peroxide}} \times 100$$

The initial concentration of bleaching gels was analyzed in triplicate by testing both pretreatment and post-treatment to determine the amount of hydrogen peroxide percentage at those times.

Statistical Analysis

A previous study (Gaiao, 1997) showed excellent within-subject repeatability. As a result, each subject wore the tray with bleaching agent only once for each specified time. The mean, standard deviation, standard error, range, 95% confidence interval for the mean concentration of hydrogen peroxide and percentage of hydrogen peroxide recovered were reported for each wearing time both for the total sample and the component tray, teeth and rinse samples. Regression analyses with a means to correlate the multiple measurements from each subject was used to model the degradation curves. A 5% significance level was used for all statistical comparisons.

RESULTS

The weight of gel delivered averaged 194.7 mg and ranged from 132.1 mg to 321.8 mg.

The amount of HP delivered averaged 6.04 mg and ranged from 4.10 mg to 9.98 mg.

The change in HP concentration in the tray and teeth samples (Figure 1) was 8.5 (p=0.0001) and 4.5 (p=0.0002) times greater, respectively, from five to 10 minutes compared to 10 to 60 minutes. The change in the amount of HP in the rinse and tray samples (Figure 2) was 28 (p=0.0004) and 4.0 (p=0.0012) times greater, respectively, from five to 10 minutes compared to 10 to 60 minutes. The amount of HP in the teeth sample (Figure 2) was relatively constant over time (p=0.2169). The change in the total amount of HP (Figure 2) was 5.9 times greater between five and 10 minutes compared to 10 and 60 minutes (p=0.0001). The amount of HP in the saliva sample increased over time (p=0.0212) but did not increase at a consistent rate (Figure 2).

The total percentage of HP recovered (Table 3, Figure 3) at 5, 10, 20, 30, 45 and 60 minutes was 61, 56, 49, 44, 38 and 32, respectively. All samples showed an exponential degradation of hydrogen peroxide after 10 minutes.

DISCUSSION

Tooth discoloration can be emotionally traumatic for people in a society that places a high value on appearance. Therefore, mastering using current at-home vital bleaching products allows the dentist to offer a reasonable treatment option along with other esthetic restorative options.

The term "kinetic cycle" means the degradation rate of bleaching-active agent at a specific time. The ADA has established the document *Acceptance Program Guidelines for Home-Use Tooth Whitening* (American

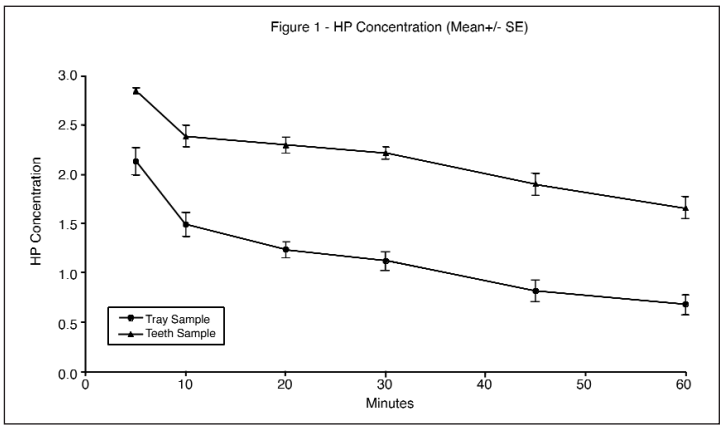

Figure 1. *HP Concentration (Mean +/- SE).*

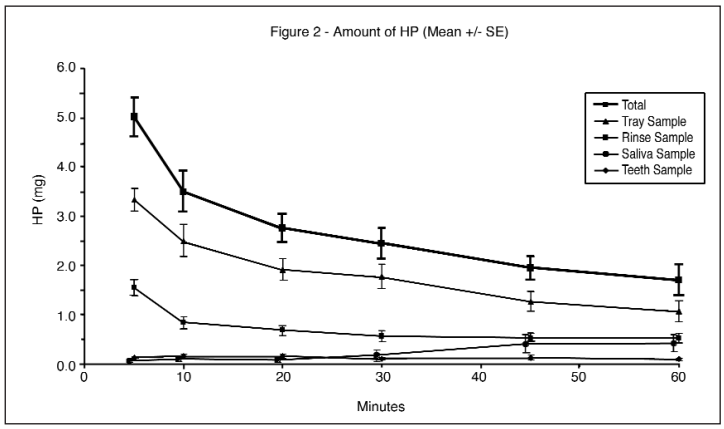

Figure 2. *Amount of HP Concentration (Mean +/- SE).*

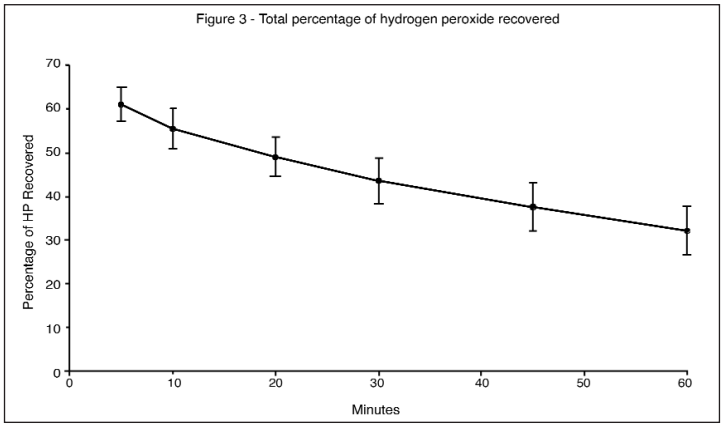

Figure 3. *Total percentage of hydrogen peroxide removed.*

Table 3: *Total Percentage of Hydrogen Peroxide Recovered*

Minutes	N	Mean	SD	SE	Min	Max	95% CI for MEAN	
5	10	61.12	12.23	3.87	44.52	80.11	52.37	69.87
10	10	55.62	14.62	4.62	32.62	79.97	45.17	66.07
20	10	49.01	14.39	4.55	30.58	75.77	38.72	59.30
30	10	43.55	16.34	5.17	20.24	72.38	31.86	55.24
45	10	37.64	17.19	5.44	15.78	69.18	25.33	49.95
60	10	32.23	17.53	5.54	7.43	66.85	19.70	44.76

Dental Association, 1998). Section "8D" of that document states that manufacturers must supply the ADA with the "Kinetics of active ingredient release." The word "kinetics" was chosen instead of "degradation," because the rate of physical loss of peroxide from the tray and the rate of peroxide lost from the chemical breakdown are combined to determine the amount of active agent remaining at different time intervals. Therefore, "kinetics" appears to be a better term for this study than "degradation."

To grant their seal of approval, the ADA requires information about the kinetics of an at-home bleaching product. This information is essential to understanding the pattern of degradation and achieving ultimate results with limited side effects and recommended application time.

The methodology used in this study simulates the clinical situation for at-home vital bleaching. To facilitate the collection of the remaining gel, only six upper anterior teeth were selected for gel retrieval. For this study, subjects with large, caries-free teeth with no restoration on the facial surfaces were selected. Subjects with periodontal diseases were excluded to avoid any variable that might affect the kinetics of the bleaching gel by potential reaction with large numbers of microorganisms (Gurgan, Bolay & Alacam, 1996).

Trays were filled with a strip of bleaching gel, Perfecta 3/15 (Premier Dental Products Company), which was placed on the facial surfaces of the six anterior teeth as recommended by the manufacturer. A pilot study was conducted in an attempt to prevent under- or overfilling of the tray with bleaching gel. Underfilling could produce voids that might reduce the reaction of bleaching gel with the tooth surface, while overfilling could cause physical loss of the material.

The rapid kinetics in the first 10 minutes might be due to the saturation or diffusion of hydrogen peroxide into the tooth (Wattanapayungkul & others, 1999). Once hydrogen peroxide contacts the tooth, it breaks down to oxygen and water.

There is a significant difference between the kinetics of the tray and teeth samples. The kinetics of the teeth sample is significantly slower than the tray sample. Two factors could contribute to this result. First, the teeth sample was relatively non-contaminated since the gel was retrieved by scraping off just the incisal half of the anterior teeth where there would be a minimum of saliva. Second, saliva was present on the outside of the tray sample, with some occasionally found inside the tray. When the tray was removed from the subject's mouth and weighed, the weight included the gel recovered from the tray and the weight of the saliva contaminant. Therefore, a lower concentration would be obtained when the weight is greater. The concentration of hydrogen peroxide in the tray and the teeth samples did not reveal the exact kinetics process but gave a general predication for it. On the other hand, the total percentage obtained from the total amount of hydrogen peroxide retrieved from the tray, teeth and rinse samples provided precise kinetics information.

The results of this study agree with the hypothesis that the kinetics of hydrogen peroxide and carbamide peroxide are similar in the first hour in that, after a fast degradation, they decayed in an exponential manner.

In this study, the mean percentage of hydrogen peroxide recovered at one hour was 32.23 (Table 2, Figure 3). Fifty percent of the active agent was recovered in this study after 20 minutes in the mouth. Gaiao (1997) found that the kinetics of carbamide peroxide in trays with reservoirs after five minutes is exponential and the mean percentage of carbamide peroxide recovered at one hour is 63%; approximately half (52%) of the active agent was recovered after two hours in the mouth. Wattanapayungkul and others (1999) found that the kinetics of carbamide peroxide after five minutes is exponential and the mean percentage of carbamide peroxide recovered at one hour is 54%. Matis and others (2002) found that the kinetics of carbamide peroxide after two hours of bleaching using gel in trays with facial reservoirs was 52%; while the percentage of bleaching gel in trays without facial reservoirs was 23%. However, products tested with and without reservoirs had the same kinetics rate. These differences relate to tray design and possibly system components. In some studies using carbamide peroxide, trays with facial reservoirs were used. By using reservoirs, the amount of bleaching gel physically lost during active treatment is decreased by approximately 50% after two hours. In this study, trays with no reservoirs were used.

Carbamide peroxide is hydrogen peroxide coupled with urea. Urea and its byproducts appear to slow the kinetics of carbamide peroxide.

A study by Mokhlis and others (2000) found that teeth lightened with 20% carbamide peroxide were significantly lighter than teeth lightened with 7.5% hydrogen peroxide at one and two weeks but no significant difference was found at the end of 12 weeks. A study by Panich (1999) compared 15% carbamide peroxide with 5.5% hydrogen peroxide used in trays with reservoirs for 30 minutes twice a day. No significant difference in tooth whitening was found between them. However, Mokhlis and others (2000) noted that tooth lightening did not occur in the Panich study to the degree that it had in other overnight studies using 10% carbamide peroxide. On the other hand, the reversal was also much less. Kowitz and others (1991) compared 3% hydrogen peroxide to 10% carbamide peroxide *in vivo*. After four weeks, there was no significant difference between the whitening effects of the two products tested.

Saliva was collected from a patient's expectorate during the clinical procedure. This saliva was analyzed to determine the approximate amount of hydrogen peroxide that the subject might have swallowed during the bleaching treatment. In this study, the amount of hydrogen peroxide in the saliva sample after one hour was 0.42 mg (Figure 2). This is a significantly lower amount than the maximum amount ingested that could result in serious side effects. In addition, if a patient would wipe off the excess gel, expectorate and saliva and brush after the procedure, the amount of gel swallowed would be reduced even more.

Matis (1999) studied the degradation of whitening gel in saliva. He found that each patient's saliva degraded the whitening gel at a specific rate. A similar result was found in this study. Therefore, there are variants that affect the individual's kinetics rate. A possible factor that could be responsible for this individual variation is salivary antioxidants. Salivary antioxidants are essential for peroxide decomposition and are present intra- and extra-cellularly. There are factors that might affect the secretion level of salivary antioxidants and their ability to decompose peroxide. Attin & Hellwig (1996) found that dentifrices caused an elevated level of fluoride ions in saliva after tooth brushing. Larsen & others (1999) found that intraoral pH varies among individuals. Hannuksela & others (1994) observed that decreased pH and elevated fluoride ion concentration in saliva inhibit the activity of salivary antioxidants. This inhibition was observed only at a pH of less than 6.5 and with fluoride concentrations equal to or greater than 20 mM. Abbeele, Pourtois & Courtois (1992) found that salivary antioxidant activity was reduced to less than 40% of its initial activity value when fluoride concentration was equal to or greater than 0.1 mm. A study evaluating the effects of using different fluoride-containing products on the kinetics of peroxide gel would serve as a valuable contribution to the scientific literature.

CONCLUSIONS

This study concluded that:

1. Half or 50% of the active agent was recoverable after 20 minutes of tray use.
2. At one hour, the average of the total remaining hydrogen peroxide was 32.23%.
3. For one hour of bleaching treatment, the average concentration of hydrogen peroxide in collected saliva was 0.42 mg/100ml.
4. The kinetics rate was higher in the first 10 minutes for tray, teeth and rinse samples.

(Received 7 May 2002)

References

Abbeele A, Pourtois M & Courtois P (1992) Fluoride inhibition of SCN- and Cl- peroxidase activities in whole saliva and recombinant myeloperoxidase: Influence of pH and hydrogen peroxide concentration *Journal of De Biologie Buccale* **20(4)** 219-224.

American Dental Association (1998) Acceptance program guidelines for home-use tooth whitening products Council on Scientific Affairs Chicago, IL.

Attin T &Hellwig E (1996) Salivary fluoride content after tooth brushing with a sodium fluoride and an amine fluoride dentifrice followed by different mouthrinsing procedures *Journal Clinical Dentistry* **7(1)** 6-8.

Clinical Research Associates (1997) Tooth bleaching, state-of-art '97 *Clinical Research Associates Newsletter* **21(4)** 3.

Gaiao U (1997) A Clinical study of 10-percent carbamide peroxide degradation in bleaching trays [Thesis] Indianapolis: Indiana University School of Dentistry.

Gurgan S, Bolay S & Alacam R (1996) Antibacterial activity of 10 percent carbamide peroxide bleaching agent *Journal of Endodontics* **22(7)** 356-357.

Hannuksela S, Tenovuo J, Roger V, Lenader-Lumikari M & Ekstrand J (1994) Fluoride inhibits the antimicrobial peroxidase system; in human whole saliva *Caries Research* **28(6)** 429-434.

Kowitz GM, Rustogi KN, Wong R, Curtis JP &Wieckowski SE (1991) *In vivo* effect of peroxide on tooth coloration *Journal of Dental Research* Abstract #424, p 70.

Larsen MJ, Jensen AF, Madsen DM & Pearce EI (1999) Individual variation of pH, buffer capacity, and concentrations of calcium and phosphate in unstimulated whole saliva *Archives of Oral Biology* **44** 111-117.

Loe H & Silness J (1963) Periodontal disease in pregnancy: Prevalence and severity *Acta Odontologica Scandinavica* **21** 533-551.

Matis BA (1999) Degradation of whitening gel in saliva Personal Communication.

Matis BA, Yousef M, Cochran MA & Eckert GJ (2002) Degradations of nine bleaching gels after two hours *in vivo* *Operative Dentistry* **27(1)** 12-18.

Mokhlis GA, Matis BA, Cochran MA & Eckert GJ (2000) A three-month clinical evaluation of 20% carbamide peroxide and 7.5% hydrogen peroxide whitening agents during daytime use *Journal of the American Dental Association* **131** 1269-1277.

Panich M (1999) *In vivo* evaluation of 15% carbamide peroxide and 5.5% hydrogen peroxide whitening during daytime use [Thesis] Indianapolis: Indiana University School of Dentistry.

United States Pharmacopeia (2000) The National Formulary United States Pharmacopeial Convention, Inc, Rockville, MD.

Wattanapayungkul P, Matis BA, Cochran BA & Moore BK (1999) A clinical study of the effect of pellicle on the degradation of 10% carbamide peroxide within the first hour *Quintessence International* **30(11)** 737-741.