A study of in vivo degradation of two vital home bleaching gels

Victor ALONSO DE LA PEÑA1, Alfredo RODRIGUEZ CARREIRA2, Rubén CORRAL ANEIROS2, Monica LÓPEZ RATÓN3 and Francisco GUITIÁN RIVERA2

1 School of Dentistry, Faculty of Medicine and Dentistry, Rúa Enterríos, s/n. 15782 Santiago de Compostela, Spain
2 Institute of Ceramics of Galicia, Av. Maestro Mateo, s/n. 15706. Santiago de Compostela, Spain
3 Unit of Biostatistics, Department of Statistics and Operations Research, Faculty of Medicine, Rúa de San Francisco, s/n. 15782, Santiago de Compostela, Spain

Corresponding author, Victor ALONSO DE LA PEÑA; E-mail: victorap@mundo-r.com

This study investigated hydrogen peroxide (H2O2) concentration of two home bleaching gels, in their dispensing syringes and their degradation in vivo in intraoral bleaching trays. Two bleaching gels were studied, 7.5% hydrogen peroxide (HP) and 20% carbamide peroxide (CP). The concentration of H2O2 was determined in dispensing syringes. Twenty individuals were involved in this study. The gels were placed in trays of both arches and their degradation determined at 5, 10, 15, 20, 30, 40, 60 and 75 min. The concentrations of H2O2 in syringes were (HP) 8.12% and (CP) 7.95%. For the HP gel in custom-trays the concentration of H2O2 was 73% at 5 min and 42% after 75 min. In the 20% CP gel it was 75% at 5 min and 39% after 75 min. Activity decreased linearly up to 75 min, where the mean concentration of H2O2 exceeded 35% for the CP and HP gels.

Keywords: Tooth bleaching, Carbamide perixide, Hydrogen peroxide, Degradation

INTRODUCTION

Products used for home dental whitening are hydrogen peroxide (HP) and carbamide peroxide (CP) in different concentrations1-5. They are dispensed in gel form for use in trays1-4. The active substance responsible for dental bleaching is hydrogen peroxide (H2O2). A 10% CP gel (CH6N2O3) decomposes into 3.5% H2O2 and 6.5% urea (CH4N2O)5, although other authors have reported slightly different concentrations6,7. A 3.5% HP has a similar bleaching effect to 10% CP8. A 20% CP breaks down to 7% H2O2, which would be equivalent to a HP gel of 7.5% in bleaching efficiency9.

Recommended daily application times vary according to the concentration of the active ingredient (from 30 min to all night). The recommended duration of treatment ranges from two to four weeks6-10-13. The most common side effects of whitening are tooth sensitivity, which can occur spontaneously or with temperature changes, and gingival irritation14-16.

Easywhite 20 consists of 20% carbamide peroxide by weight, glycérin, aromatics and buffered polycarbon acids. The gels were stored at a temperature of between 6–8 °C from receipt.

The concentration of H2O2 was determined in 19 dispensing syringes of 20% CP gel and in 25 syringes of 7.5% HP. A sample of approximately 0.2 g (±0.05) was taken for analysis directly from the contents of each syringe. The weighing was approximated to avoid extra handling time that could have allowed increased H2O2 degradation.

To determine the degradation of the gel in the tray in the mouth, 20 individuals were selected, 18 women and 2 men, with an age range of 18 to 34 years (25.8±6.8 years) according to the criteria specified in Table 1. All participants were informed of the treatment to be carried out. The protocol was reviewed and approved by the Ethics Committee of the Faculty of Medicine and Dentistry, Santiago de Compostela (Spain). Two weeks before starting the clinical trial, participants underwent a prophylaxis with a Cavitron and Nupro prophyl paste (Dentsply International, York, USA).

Alginate impressions were made of both arches for tray fabrication. The plaster models were cut into a horseshoe shape. Reservoirs of 0.5 mm depth were created on the facial surfaces of the incisors, canines and first premolars in both arches with LC Block-Out Resin (Ultradent, South Jordan, UT, USA). These reservoirs were fabricated by depositing the resin 2 mm from the gingival margin and 1 mm from the incisal, mesial and distal tooth surfaces. The trays were fabricated from 1 mm thick sheets (Mouthguard, Buffalo Dental, NY, USA) that were adapted to the models with a vacuum forming system (Econo-Vac, Dental Buffalo, NY, USA). Trays were cut back 1 mm apical to the gingival

MATERIALS AND METHODS

Two home bleaching gels were studied: Poladay 7.5% (SDI, Victoria, Australia) and Easywhite 20 (Deltamed, Friedberg, Germany). Poladay 7.5%, according to the manufacturers, is composed of 7.5% hydrogen peroxide by weight, glycérin, aromatics and fluoride. While,
Table 1  Inclusion and exclusion criteria

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good general health greater than 18 years of age</td>
<td>Systemic disease. Patients undergoing medical treatment</td>
</tr>
<tr>
<td>Sillnes and Löe index ≤ 1</td>
<td>Pregnancy or breast-feeding</td>
</tr>
<tr>
<td>Twelve caries free maxillary and mandibular anterior teeth without restorations</td>
<td>Root canal filled teeth</td>
</tr>
<tr>
<td></td>
<td>Periapical pathology</td>
</tr>
<tr>
<td></td>
<td>Cervical or incisal abrasion</td>
</tr>
<tr>
<td></td>
<td>Xerostomia. Changes in the oral mucosa</td>
</tr>
<tr>
<td></td>
<td>Structural alteration of the tooth structure</td>
</tr>
<tr>
<td></td>
<td>Orthodontic treatment in progress</td>
</tr>
<tr>
<td></td>
<td>Previous tooth whitening treatment</td>
</tr>
</tbody>
</table>

margin and did not cover the interdental papillae.

The time intervals for which the tray was inserted were 5, 10, 15, 20, 30, 40, 60 and 75 min. Teeth were brushed with water and rinsed with water before each application. The gel was deposited in the deepest part of the tray. After placement of the tray in the mouth of the participant, the excess gel was removed. While the tray was in the mouth, participants did not eat or drink.

All participants received an application of each gel for each time interval and in the maxillary and mandibular arches. One gel, for one time interval, was applied each day. Gel was inserted in the trays from the syringes at each time interval. Thirty-two samples were taken from each participant, one for each time interval (5, 10, 15, 20, 30, 40, 60 and 75 min) in the maxillary tray and the mandibular tray for both gels. After each time interval was completed, and the sample collected, the tray was brushed and washed with water then dried with compressed air. Six hundred and forty samples were collected, 320 from maxillary trays and 320 from mandibular trays. A sample of gel was collected from the trays in the area of the 6 anterior teeth with a small metal spatula. No gel was removed from the surface of the teeth. The measurement of H₂O₂ in the sample was performed immediately after collection.

The same method of analysis was used to determine the concentration of hydrogen peroxide in the dispensing syringes and the samples obtained directly from the trays for the distinct time intervals. All the participants underwent experimentation in the laboratory, allowing immediate measurement after sampling. An experienced researcher undertook all sampling. A chemistry technique was employed as described in the U.S. Pharmacopeia USPXXII NFXXVII, 1995 Hydrogen peroxide assay (17), and previously used in other similar studies (18-20). A hydrogen peroxide assay with potassium permanganate was used. The technique consisted of transferring the sample to a watch glass and weighing it on an analytical balance. The glass with the sample was then placed in an Erlenmeyer flask with 20 mL of deionized water and 20 mL of sulfuric acid 2N. A 20×7 mm teflonated magnet was inserted to stir the mixture.

This volumetric method used the reagent potassium permanganate (K₂MnO₄, 0.1N, Merck Millipore, Darmstadt, Germany), an oxidizing agent that has a purple color and reacts with hydrogen peroxide according to the following equation:

\[
5\text{H}_2\text{O}_2 + 2\text{MnO}_4^- + 6\text{H}^+ \rightarrow 5\text{O}_2 + 2\text{Mn}^{2+} + 8\text{H}_2\text{O}
\]

The reaction starts with a colorless solution that turns a pale pink when there is an excess of reagent (K₂MnO₄) thus indicating the reaction end. The volume of consumed potassium permanganate was recorded and the concentration of hydrogen peroxide was calculated using the following formula:

\[
\%\text{H}_2\text{O}_2 = \frac{1.701 \times 0.1\text{N} \times \text{potassium permanganate volume used (mL)}}{\text{Gel sample weight (grams)}}
\]

The mathematical factor that relates permanganate with hydrogen peroxide is 1.701.

Statistical analysis

A mixed regression model was performed, taking into account the dependence between the observations made over the same patient and allowing the detection of any significant differences in the measurements throughout the time, product and trial. All statistical analyses were conducted with statistical software R version 2.15.0 (R Development Core Team, 2012), using the nlme package for fitting mixed regression models. A p-value less than 0.05 was considered statistically significant.

RESULTS

The concentrations of H₂O₂ obtained from the dispensing syringes were higher than those stated by the manufacturer. In the 25 syringes of 7.5% HP, concentrations of 8.12% (±0.78) were found, while the 19 syringes of 20% CP had a concentration of 7.95% (±0.77). The mean weight of the samples was 0.074 g (±0.035) in the maxillary trays and 0.070 g (±0.035) in the mandibular trays. With the HP gel, a smaller
The H$_2$O$_2$ concentrations found in the samples of both gels are shown in Figs. 1 and 2, and Table 2. The degradation was intense at 5 min, but afterwards linear up to 75 min. The concentrations obtained in the maxillary trays were higher than those in the mandibular trays for both products ($p<0.001$). The degradation of H$_2$O$_2$ was higher in the CP gel, taking into account the results of both arches and for all time periods ($p<0.001$). A more than 50% decline in H$_2$O$_2$ activity was recorded after 60 min for the HP gel and after 40 min for the CP gel.

**DISCUSSION**

In order that the bleaching gels would act only on natural tooth surfaces, no individuals were selected who had restorations in their front teeth. Although not taken into consideration in this investigation, there are studies concerning the degradation of gels, in which selected participants had central incisors with a minimum crown size$^{18-20}$.

The antibacterial properties of whitening gels have been proven$^{21-23}$. For this study, individuals who had a Silness and Löe index$^{24} \geq 1$ were excluded to avoid reactions of H$_2$O$_2$ with microorganisms that cause gingivitis and periodontitis. Brushing with water before inserting the trays aims to avoid the reaction of gel with organic substances of the acquired pellicle and dental plaque$^{25}$. However, other studies state that the pellicle does not affect the degradation of H$_2$O$_2$$^{26,27}$.

Concentrations higher than those given by manufacturers were determined in the gels contained in the dispensing syringes. The H$_2$O$_2$ concentration values obtained for 7.5% HP gel were 8.12% and the 20% CP gel 7.95%. Another study determined the concentrations of various gels used for at-home vital bleaching dispensed by dentists in CP gels of 10% to 22%, they found variations between 2.64% less than what was written on the label up to 0.91% more$^3$. Furthermore, other authors have observed variations ranging from 8.14% to 20.32% in pharmacy dispensed 16% CP$^{28}$. Meanwhile, two in office HP gels of 38% and 35% yielded concentrations of 35.8% and 31.5% respectively$^{29}$.

### Table 2

<table>
<thead>
<tr>
<th>Sample analysis (min)</th>
<th>Hydrogen peroxide 7.5% % H$_2$O$_2$ (SD)</th>
<th>Caramide peroxide 20% % H$_2$O$_2$ (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>73 ($\pm$21)</td>
<td>75 ($\pm$10)</td>
</tr>
<tr>
<td>10</td>
<td>73 ($\pm$18)</td>
<td>69 ($\pm$10)</td>
</tr>
<tr>
<td>15</td>
<td>73 ($\pm$19)</td>
<td>68 ($\pm$13)</td>
</tr>
<tr>
<td>20</td>
<td>66 ($\pm$16)</td>
<td>61 ($\pm$18)</td>
</tr>
<tr>
<td>30</td>
<td>64 ($\pm$15)</td>
<td>60 ($\pm$22)</td>
</tr>
<tr>
<td>40</td>
<td>57 ($\pm$20)</td>
<td>52 ($\pm$15)</td>
</tr>
<tr>
<td>60</td>
<td>51 ($\pm$14)</td>
<td>45 ($\pm$16)</td>
</tr>
<tr>
<td>75</td>
<td>42 ($\pm$13)</td>
<td>39 ($\pm$14)</td>
</tr>
</tbody>
</table>

Concentration over a 75 min period.
Tray contamination with saliva increases the weight of the sample collected from the tray. Therefore, the gel from the 6 anterior teeth was always removed. This would explain the higher concentrations of active ingredient in maxillary trays as they were less contaminated than those of the mandibular. Contamination may also reduce bleaching in the lower arch, although clinical effectiveness studies of whitening gels have only assessed color in the upper arch\textsuperscript{18,25}. The $\text{H}_2\text{O}_2$ has an antimicrobial effect and reacts with oral microorganisms, which are at their highest density during the first hour, explaining the increased degradation over that period\textsuperscript{18,27}.

This study found that the greatest degradation in both products was during the first 5 min. These results are consistent with others where the rate of degradation was also more pronounced in the first few minutes\textsuperscript{18,27,29}. Such degradation could be due to greater diffusion through the tooth in the first few minutes and consequent saturation\textsuperscript{18,25}. The $\text{H}_2\text{O}_2$ has an antimicrobial effect and reacts with oral microorganisms, which are at their highest density during the first hour, explaining the increased degradation over that period\textsuperscript{18,27}.

Hydrogen peroxide concentrations of 42% and 39% were obtained after 75 min for HP and CP respectively. These results, that indicate a similar degradation between both products, may explain the similar degree of whitening obtained when comparing CP and HP bleaching gels with similar $\text{H}_2\text{O}_2$ concentrations\textsuperscript{11,12}.

However, Haywood argued that HP has an activity lower than 10% at 75 min and loses its activity after 90 min. Haywood also stated that the carbamide peroxide gels liberate oxygen more slowly\textsuperscript{30}. In other studies where the same analytical method was used, and a 10% CP gel was investigated, similar results to the present study were obtained. The results of Watanapayuyungkul et al. were 75.7% at 5 min, 74.0% at 10 min, 66.7% at 20 min, 61.1% at 40 min and 55.5% at 60 min\textsuperscript{27}. Matis et al. obtained 41.94% after 1 h\textsuperscript{18}. In another study analyzing 9 CP gels, all had a percentage of active ingredient less than 50% after an hour in the mouth\textsuperscript{29}. Al-Qunaian et al. studied the degradation of 3% HP gel from samples collected from trays and directly from the tooth, and found that the kinetics rate was higher in the first 10 min for tray, teeth and rinse samples. In the trays, 50% of the active ingredient was collected after 20 min\textsuperscript{28}. After this time, in the present study, we had concentrations of 66% and 61% for the HP and CP respectively.

In the clinical studies of at-home bleaching, the daily application time of the bleaching gel in the trays varies from 30 min up to all night\textsuperscript{33,34}. The results from this study could indicate that the recommended application time of the trays should be greater than 30 min. This would be in agreement with the results obtained by Cardoso et al. who stated that the contact time of the gel with the surface of the tooth is important in the efficacy of bleaching, having compared distinct tray application times\textsuperscript{19}.

**CONCLUSIONS**

The concentrations of hydrogen peroxide in the dispensing syringes are greater than those stated by the manufacturer: 7.95% in the 20% carbamide peroxide gel and 8.12% in the 7.5% hydrogen peroxide gel.

The concentration of the active ingredient in both the whitening gels studied was above 40% after an hour of the trays being in the mouth. Concentrations above 35% were still observed at 75 min. The 20% CP and 7.5% HP at-home bleaching gels studied have a similar degradation \textit{in-vivo} in the trays. In both cases, this degradation is greater in the lower arch.

As the concentration of $\text{H}_2\text{O}_2$ in both products is approximately 40% an hour after the trays being in the mouth, studies are needed to determine the most effective daily tray application time.

**REFERENCES**


13) Cardoso PC, Reis A, Loguercio A, Vieira LC, Baratieri LN. Clinical effectiveness and tooth sensitivity associated with