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Bleaching efficacy, decomposition rate and pH of experimental bleaching gels incorporating bioactive materials

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Aim: To evaluate the bleaching efficacy, decomposition rate, and pH of experimental gels containing 35% hydrogen peroxide (HP) and different concentrations of 45S5-bioglass (BG) or Biosilicate® (BS). **Methods:** Bovine enamel/dentin blocks (n=10) were allocated into the groups HP_BG or HP_BS (2.5, 5, 7.5 and 10 wt%) and HP (35% HP – positive control). The blocks were submitted to three sessions of 40 min and 7-day intervals. During the interval, the blocks were kept in artificial saliva at 37°C. Color change (ΔE_{00}) and whiteness index change (ΔWI_D) were determined after staining with black tea (T_1) and 24 h after the 3rd bleaching session (T_2). HP decomposition rate (%) and pH were evaluated for 40 min. Two-way ANOVA and Tukey analyzed ΔE_{00} and ΔWI_D data, while the Kruskal-Wallis test determined the decomposition rate and pH of the gels. **Results:** There were no differences in ΔE_{00} and ΔWI_D among the experimental bleaching gels containing BG or BS and 35% HP ($p > 0.05$), but BG and BS gels displayed lower HP concentration than 35% HP, regardless of the bioactive material concentration ($p < 0.05$). The experimental BG and BS gels exhibited alkaline pH (ranging from 9.28 to 9.82), which was higher than that of 35% HP ($p < 0.05$). But regardless of the gel, all kept the pH values stable for 40 min. **Conclusion:** The experimental gels containing BG and BS did not hamper the 35% HP bleaching efficacy. Moreover, BG or BS gels decreased the hydrogen peroxide concentration and exhibited alkaline pH values.

Keywords: Bleaching agents. Hydrogen peroxide. Bioglass.

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Introduction

Tooth bleaching is a viable alternative for treating color changes in vital teeth because it is a minimally invasive, low-cost, and effective treatment[1]. The bleaching effect is reported to result from the decomposition of hydrogen peroxide (HP) into reactive oxygen species (ROS) that penetrate enamel and dentin and oxidize the conjugated double bonds of chromophores[2]. Among the possibilities of this treatment, in-office procedures are performed with gels with a high concentration of hydrogen peroxide (35 to 45%), usually carried out in three clinical sessions[3]. Although aesthetic benefits are achieved using different tooth bleaching protocols, several authors demonstrate that HP has a high oxidative power and can promote morphological and structural changes in tooth enamel[4,5].

As a result, alternative protocols have been proposed to enhance safety and reduce the adverse effects of bleaching, including the use remineralizing agents in the bleaching gel's formulation. Particularly, it was noted that incorporating calcium (Ca) and fluoride (F) into 35% HP gels[6] did not compromise the bleaching efficacy, reduced the peroxide diffusion and the enamel microhardness loss[6], and increased the concentration of carbonate and phosphate in enamel[7]. However, while this addition controlled the mineral content on the surface[6,7], it was found to be ineffective in reversing the subsurface demineralization in enamel with initial caries lesions[7]. Other investigations have focused on adding transition metals and oxides, such as TiO_2 into HP bleaching gels, which could optimize the bleaching outcome, allowing low-HP concentrations to be as effective as 35% HP gels[8]. TiO_2 is known for its ability to accelerate chemical reactions and has the potential to accelerate the dissociation of HP into ROS, thus enhancing the bleaching results of low-concentrated gels[8].

Another alternative approach to mitigate the harmful effects observed on tooth enamel's surface after bleaching is the incorporation of bioactive particles into high concentrations of HP gels[9,10]. Among these bioactive particles, 45S5-Bioglass (BG) stands out as a promising bioactive and biocompatible compound. BG is composed of 45% SiO_2, 24.5% Na_2O, 24.5% CaO, and 6% P_2O_5 (wt%)[11]. When in contact with an aqueous medium, it forms hydroxycarbonate apatite (HCA), a mineral structure that resembles the mineral phase of the tooth[11]. It has been previously shown that BG can obliterate the entrance to dentinal tubules and stimulate dentin remineralization[12]. Besides, reports have demonstrated that BG displays excellent bioactive behavior, antibacterial characteristics[13] and the ability to inhibit oxidative stress caused by HP[14]. In previous investigations, BG combined with 30 - 35% HP was found to reduced enamel hardness loss after bleaching without affecting the bleaching efficacy of HP[9,10].

Biosilicate® (BS) is another biomaterial that has proven beneficial effects for dental care. BS is a highly crystallized glass-ceramic (48.5% SiO_2, 23.75% Na_2O, 23.75% CaO, and 4% P_2O_5) that exhibits bioactive, osteoconductive, osteoinductive, non-cytotoxic and antibacterial properties[15]. Similarly to BG, BS forms hydroxycarbonate apatite (HCA) in an aqueous media[15]. BS in tooth bleaching therapy has consistently shown positive outcomes, such as reducing tooth hypersensitivity[16], increasing enamel hardness after tooth bleaching[17], and minimizing pulpal damage when BS is combined with 35% HP bleaching gel[18].

Bearing in mind the possibility of developing remineralizing agents that, in combination with 35% HP, could be safer yet equally effective for in-office bleaching, this study evaluated the color alteration, decomposition rate, and pH change overtime promoted by experimental gels containing different concentrations of BG or BS (2.5, 5, 7.5 and 10 wt%) combined with 35% HP. The research hypotheses were that the bioactive materials BG or BS combined with 35% HP would (1) provide bleaching efficacy similar to the conventional 35% HP bleaching gel, (2) accelerate the decomposition rate of the 35% HP, and (3) keep the pH of the experimental gels stable and close to neutral.

Materials and Methods

Experimental Design. Bovine enamel/dentin blocks (n=10) were randomly divided into nine experimental groups according to the treatments: PC (positive control; commercial gel containing 35% HP - Whiteness HP, FGM, Joinville, SC, Brazil), experimental gels containing Bioglass-45S5 (BG) or Biosilicate® (BS) in the following concentrations: 2.5%, 5%, 5%, 7.5%, and 10% (wt%). During and after bleaching treatments, the color change (ΔE_{00}), whiteness index change (ΔWI_D), decomposition rate of HP, and pH as a function of bleaching time were evaluated. The ΔE_{00} and ΔWI_D data were statistically determined by two-way ANOVA and Tukey post hoc test, and the Kruskal-Wallis test analyzed the decomposition rate (%) and pH values.

Preparation of specimens. Bovine teeth free of defects were selected, cleaned, and disinfected in 0.1% thymol solution (Labsynth, Diadema, SP, Brazil). Initially, the roots were removed below the cementoenamel junction using a diamond saw mounted in a high-precision cutter (Isomet 1000, Buehler, Illinois, USA), under water irrigation. The crowns were cut to obtain enamel blocks (5 × 5 × 3 mm) from the central buccal surface of the crown. The dentin surface of the blocks was flattened with silicon carbide sandpaper (# 400) in a polishing machine (Arotec, São Paulo, SP, Brazil) to allow parallelism with the outer enamel surface. Subsequently, enamel was abraded with silicon carbide sandpaper (# 600 and 1200) and polished with a felt disk and a diamond suspension (with abrasive particles of 1 μm) for 2 min.

Enamel artificial staining. After selection, a thin layer of acid-resistant varnish was applied, except on the surface of the enamel, where the treatments were carried out. The exposed surface of the enamel was immersed for 24 h at room temperature in a buffered black tea solution (Dr. Oetker, SP, Brazil, pH = 7.0), prepared following the protocol of Sulieman et al.[19]. After staining, specimens were kept in artificial saliva (1.5 mM Ca, 0.9 mM P, 150 mM KCl, and 0.1 M Tris, pH 7.0)[20] for 7 days (replaced every 3 days) at 37°C. After color stabilization, post-staining color analysis (T_1) was performed with a digital spectrophotometer (Easyshade 4.0, Vita Zahnfabrik, Bad Säckingen, Germany) to randomize the samples into groups, using the L* parameter to select the specimens with mean values 10% above and below the general mean values[21,22].

Fabrication of 45S5 BG and BS. BG was manufactured using the conventional oxide fusion route[21,22]. Briefly, the raw materials were mixed and homogenized in a jar mill for 24 h, following by melting in a bottom load oven at 1,450°C. The fabricated bioglasses (BG and BS) were grounded in a planetary mill to obtain particles with an average size of 5 mm. The BG and BS powder was vortexed to allow particle dispersion.

The BG and BS particles were weighted according to the concentrations used (2.5, 5, 7.5, and 10 wt%). These concentrations were based on previous reports that indicated a potential to control enamel surface microhardness and surface roughness and reduce pulp cell toxicity[21,22].

Synthesis of experimental bleaching gels. A hydrogel containing BG and BS was prepared using carboxymethyl cellulose (10 wt%) and distilled water. The hydrogel was prepared by weighing the bioactive materials (BG and BS) on a precision analytical balance at the reported concentrations (2.5, 5, 7.5 and 10 wt%), followed by carboxymethyl cellulose and distilled water addition and homogenization in a specific mixer (Speed Mixer, Dac Iso 1. FVZ, Flack Teck, Inc., Hann, Germany). The prepared hydrogel was stored in opaque jars under refrigeration (4°C). Immediately before bleaching, 35% HP was added and homogenized with the BG/BS hydrogel in a 3:2 ratio, maintaining an adequate gel consistency.

Bleaching protocol. The commercial 35% HP bleaching gel was manipulated according to the manufacturer's instructions. The bleaching application protocol was performed in 3 sessions of 40 min each, with an interval of 7 days between sessions, following a protocol previously described[4]. After bleaching, samples were washed abundantly with distilled water and stored at 37ºC in artificial saliva until the next bleaching application.

Color change analysis. Color analysis was performed after staining (T_1) and 24 h after the 3rd bleaching session (T_2) with a digital spectrophotometer (EasyShade, Vita Zahnfabrik, Bad Säckingen, Germany), in the center of the specimen and under controlled ambient lighting conditions. The following color coordinates were obtained: L*, which indicates luminosity (0 to 100 / black to white); a* [green (-) to red (+)] and b* [blue (-) to yellow (+)].

Color change (ΔE_{00}) was evaluated with the CIEDE2000 formula: $\Delta E_{00}\ (T_2 - T_1) = [(\Delta L\times/KLSL)^2 + (\Delta C\times/KCSC)^2 + (\Delta H\times/KHSH)^2 + RT*(\Delta C\times/KCSC)*(\Delta H\times/KHSH)]^{1/2}$. In addition, color change thresholds adopted for perception (PT) and acceptance (AT) were 0.81 and 1.8 units, respectively[23,24].

Whiteness index change analysis. The whiteness index for dentistry (WI_D) was calculated according to the equation: $WI_D = 0.511\ L^* - 2.324\ a^* - 1.100\ b^*$, and the index difference (ΔWI_D) was determined by $T_2 - T_1$. Whiteness index change thresholds adopted for perception (PT) and acceptance (AT) were 0.7 and 2.6 units, respectively[23,24].

Decomposition rate of HP. An automatic titrator (HI902C1-02, Hanna Instruments, Carrolton, TX, USA) evaluated the HP decomposition rate according to the methodology described by Borges et al.[25] (2021). Initially, 0.1 N of $KMnO_4$ solution was normalized using 0.67% (w/v) sodium oxalate ($Na_2C_2O_4$). The experimental bleaching gel was manipulated (as previously described), and the peroxide decomposition rate was determined at 0 and 40 min. An aliquot of the gel (0.01 g) was weighed and diluted in 1 M sulfuric acid (20 mL) with continuous stirring until complete homogenization. Forty minutes after mixing, a new aliquot of the bleaching gel was collected to determine the HP concentration.

pH evaluation overtime. The pH of the combined agents was measured using a pH microelectrode (DG-101SC, Mettler Toledo, Brazil) in triplicate, coupled to a potentiometer (Orion Research Incorporated, Boston, MA) previously calibrated with pH 4 and pH 7 buffer solutions. The bleaching gel was manipulated, and an aliquot of the gel (0.2 g) was added to a test tube containing 2 mL of distilled water and agitated in the vortex until complete homogenization. The analysis was performed at 0, 5, 10, 15, 30, and 40 min.

Statistical analysis. Shapiro-Wilk tested the data for normality. The ΔE_{00} and ΔWI_D data were submitted to logarithmic transformation, and ΔE_{00} and ΔWI_D data was tested by two-way ANOVA and Tukey post hoc test. The HP decomposition rate and pH data were analyzed by Kruskal Wallis test. The SPSS software was used for all analyses (Version 15.0, SPASS, IBM SPSS Inc., Armonk, NY, USA), with a significance level set at 5%.

Results

Color change (ΔE_{00}). Figure 1 shows the color change (ΔE_{00}) 24h after the 3rd bleaching session (T_2) in comparison with baseline values (T_1). No differences among BG/BS-gels and PC (35% HP) were noted, regardless of the BG/BS concentration ($p > 0.05$). The average color differences promoted by bleaching were above the PT ($\Delta E_{00} > 0.8$) and AT ($\Delta E_{00} > 1.8$) thresholds, regardless of the concentration of the experimental BG/BS gels tested.

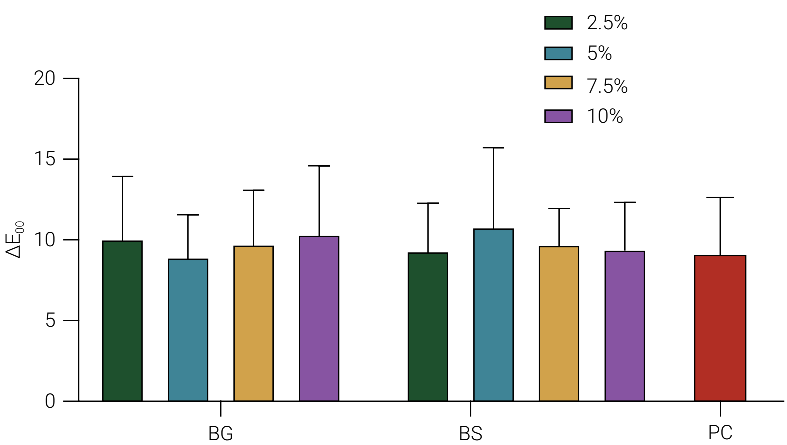

Figure 1. Mean and standard deviation of color change (ΔE_{00}) of experimental BG, BS gels and PC (35% HP) after bleaching (T_2). BG: Bioglass-45S5, BS: Biosilicate®, PC: positive control / 35% HP.

Whiteness index change (ΔWI_D). Figure 2 displays whiteness index change (ΔWI_D) 24 hours after the 3rd bleaching session (T_2) in comparison with baseline values (T_1). No differences among BG/BS-gels and PC (35% HP) were noted, regardless of the BG/BS concentration ($p > 0.05$). The average whiteness index differences promoted by bleaching were above the PT ($\Delta WI_D > 0.7$) and AT ($\Delta WI_D > 2.5$) thresholds, regardless of the concentration of the experimental BG/BS gels tested.

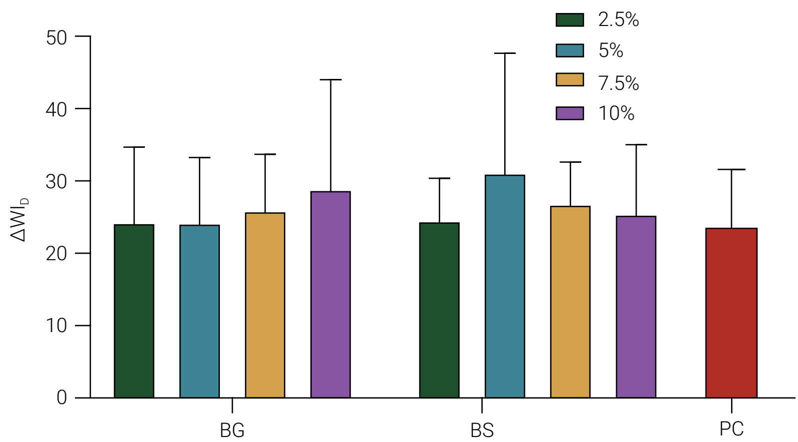

Figure 2. Mean and standard deviation of whiteness index change (ΔWI_D) of experimental BG, BS gels and PC (35% HP) after bleaching (T_2). BG: Bioglass-45S5, BS: Biosilicate®, PC: positive control / 35% HP.

Decomposition rate of HP. Figure 3 depicts the decomposition rate of HP. The PC group (commercial 35% HP) exhibited a concentration close to that described by the manufacturer and significantly higher than that of experimental gels ($p < 0.05$), which exited HP concentrations ranging from 18 to 25%, regardless of the particles used (BG or BS). No significant differences between BG and BS were noted, irrespective of the evaluation time (0 or 40 min, $p > 0.05$). Besides, none of the groups displayed significant variation after 40 min of evaluation ($p > 0.05$).

pH evaluation. The PC group (35% HP) exhibited a pH value close to neutrality (pH 6.75 – 6.86) and statistically lower than the experimental gels with the addition of BG or BS, which displayed alkaline pH (ranging from 9.28 to 9.82, $p < 0.05$) (Figure 4). No significant variation in pH values was noted over time (0, 5, 10, 15, 20, 30, and 40 min), regardless of the gels tested ($p > 0.05$). Although no statistical differences occurred during the 40 min-evaluation, the 10%BS group displayed the highest pH mean values (9.82), followed by the 7.5%BS (9.77) and 10%BG (9.70) groups, respectively.

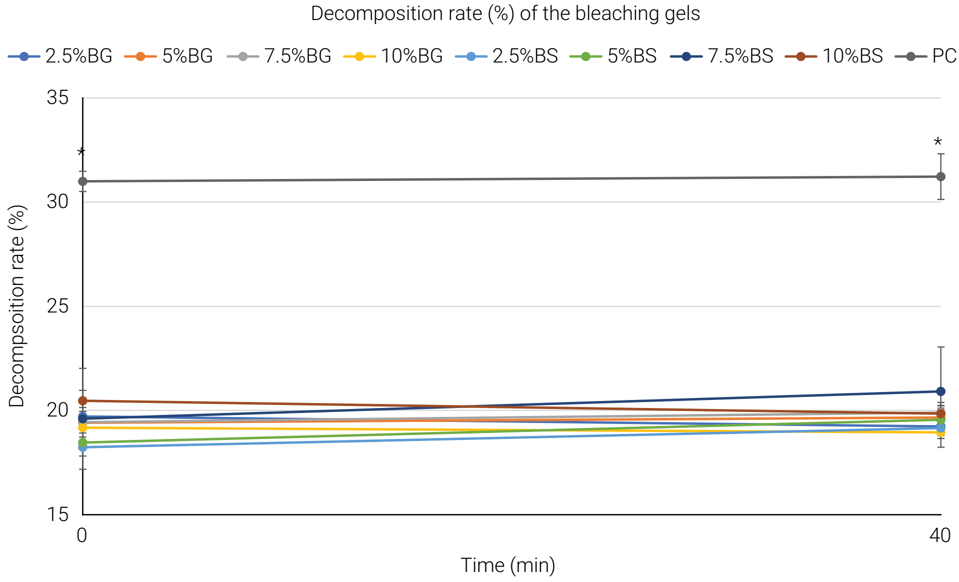

Figure 3. Mean and standard deviation of the decomposition rate (%) of the tested groups. Asterisks (*) indicate statistical differences of PC (positive control, 35% HP) in comparison with BG and BS groups ($p < 0.05$) at 0 and 40 min.

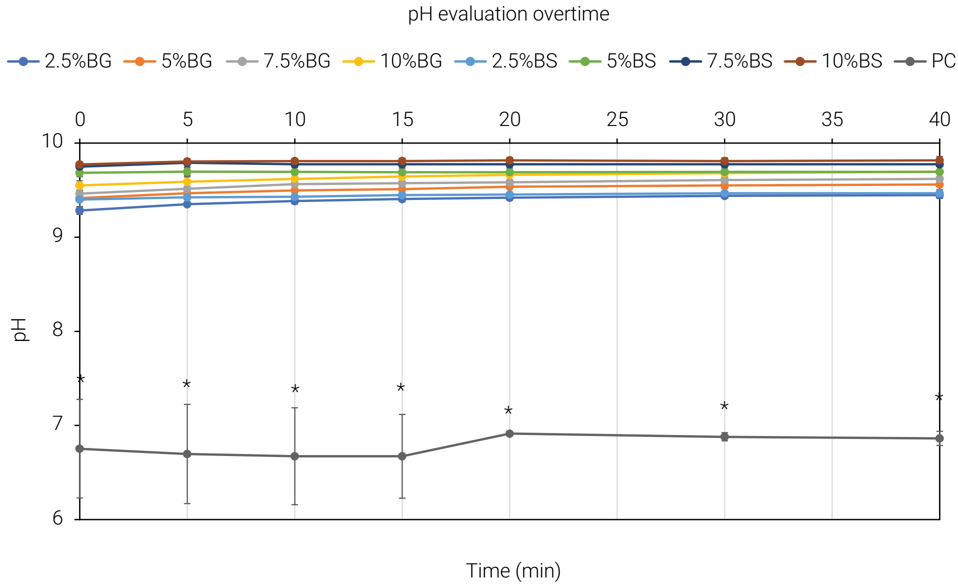

Figure 4. Mean and standard deviation of pH values overtime of the tested groups. Asterisks (*) indicate statistical differences of PC (positive control, 35% HP) in comparison with BG and BS groups ($p<0.05$) at 0, 5, 10, 15, 20, 30 and 40 min.

Discussion

Adding bioactive particles (BG/BS) into bleaching gels aims to minimize the adverse effects of hydrogen peroxide on the enamel surface, without changing HP's bleaching effectiveness. In this study, the addition of 45S5 bioglass (BG) or Biosilicate® (BS) provided similar bleaching efficacy to 35% HP (PC) since ΔE_{00} and ΔWI_D values were comparable among all groups. Hence, the expected bleaching efficacy of 35% HP[25] was not influenced by the combination with experimental BG or BS hydrogels, implying that the bioactive particles would not hamper the bleaching outcome and could be an interesting option to minimize the adverse effects of high concentrations of hydrogen peroxide. Thus, based on this outcome, the first hypothesis was accepted since incorporating BG/BS into 35% HP provides bleaching efficacy similar to the commercial 35% HP agent.

These results agree with earlier findings that combining 45S5-BG with high HP concentrations did not affect HP's bleaching efficacy and kept the enamel surface hardness intact through bleaching[9,10]. In another investigation, we found that the same BG concentrations tested in the current study (2.5, 5, 7.5, and 10 wt%) could decrease enamel surface hardness loss, indicating a positive interaction with the mineral surface[21]. As reported, BG and BS can form an HCA layer[9-11,21,26] on the mineral surface, which could help prevent enamel inorganic loss[9,10,15,17,21]. Hence, this was the fundamental reason for testing the same BG and BS concentrations of that previous evaluation (2.5, 5, 7.5, and 10 wt%)[21] and comprehending the behavior of these experimental gels.

Combining BS and bleaching gels has been perceived to have effects comparable to BG's combinations. Authors reported that BS formulations applied on enamel and dentin exposed to dental bleaching agents effectively maintained bleached enamel microhardness after 16% carbamide peroxide bleaching[17]. In another analysis, hydrogels containing 10% BS and HP promoted a highly beneficial effect, as these hydrogels did not compromise the bleaching efficacy of 35% hydrogen peroxide, and, as a positive gain, significantly favored cell viability, reduced oxidative stress, and decreased cytotoxicity in teeth with early-stage erosion[22].

Bioactive glasses based on Hench's 45S5 can catalyze hydrogen peroxide through a reaction named catalase mimetic activity (CMA)[14]. The CMA, or the ability to catalyze the decomposition reaction, indicates that combining BG or BS with HP could hasten the decomposition rate of HP. From a clinical perspective, this combination could be an extra advantage for using BG and BS-based gels, as higher quantities of ROS would be formed on the enamel surface but, because of ROS's brief half-life, it is believed that lower ROS concentrations would diffuse into the pulp[27].

In this context, the HP decomposition rate was tested to monitor the behavior of the experimental gels in the presence of BG and BS bioactive particles. The bleaching gels exhibited significantly lower HP concentrations than the PC group, even though all the gels were manipulated with 35% HP. Thus, the mere contact of HP with BG/BS drastically decreased hydrogen peroxide concentration to approximately 18-20%, in contrast with the PC group, in which the HP concentration was constant during the evaluation time (34-35%). Hence, these findings corroborate that adding BG or BS to 35% HP increased the decomposition rate of HP, which may be explained by a faster ionic release due to HP catalysis[14]. Therefore, the second hypothesis was accepted because the experimental gels exhibited lower HP than 35%, regardless of the evaluation time points. Also, no significant HP fluctuations were noted through-out the evaluation time (40 min), but it must be noted that 10% BG/BS displayed lower HP concentrations compared to baseline (0 min) values. These results contradict another finding that observed a 15% reduction in the concentration of 35% HP after 40 min of evaluation[28]. We believe that the different results could be explained by the improved stability of the commercial 35% HP tested in this research.

Interestingly, Malavasi and Lusvardi reported that bioglasses containing metal oxides present superior catalytic activity in decomposing HP. The authors observed that adding Co-, Mn-, Cu-, Ce- or Fe in the composition of the bioglass promoted CMA, and a superior decomposition kinetics of HP. Among the metal elements, Ce, a transitional metallic element and the most abundant rare-earth metal, combined with BG, was capable of consuming HP in approximately 40 min, while demonstrating a promising antioxidant property and the ability to decrease the oxidative stress[14]. Thus, incorporating a transition metal oxide into the bioglass structure could enhance the decomposition kinetics of HP and, possibly, decrease ROS diffusion into the pulp chamber.

The experimental bleaching gels containing BG or BS combined with 35% HP exhibited an alkaline pH (9.28 to 9.82), and the values were constant with no significant variations over 40 min, corresponding with the bleaching session time. Thus, the third hypothesis was partially accepted since the pH was kept constant, but alkaline, not close to neutral.

When glasses or bioceramics are diluted in an aqueous medium, the concentration of ions (Na^+, Ca_2^+, and PO_4^{3-}) increases, followed by ion exchange with H^+ in the solution[27]. As these exchanges happen, Ca_2^+ and PO_4^{3-} are released to form a supersaturated ionic reservoir for the enamel apatite[10,27]. Once these ionic exchanges occur, the pH of the solution increases, confirming the pH values found. The increase in local pH leads to the breaking of Si – O – Si bonds of the BG and BS[10], and the "scavenging" of elements from the bioglass may be the reason for the highest pH values of the 10% groups, followed by the 7.5% and 5% groups.

It is important to notice that neutral/alkaline HP gels typically display lower HP diffusion into the pulp chamber than acidic gels[29]. A clinical study confirmed this outcome, as a lower percentage of patients reported tooth sensitivity when submitted to neutral/alkaline pH bleaching gels compared to patients submitted to acidic gels[30]. Thus, the alkaline pH values of the experimental gels are an encouraging outcome to ensure safety for future clinical trials.

The application protocol should also be discussed, as it could influence the pH of the gel. The manufacturer of the commercial 35% HP tested, indicates 3 × 15-minute applications, which is supported by authors that claim that it is preferable to use the 3 x 15 application technique, mainly because the 1 × 45 techniques could result in lower pH, which was not noted in this study. Still, we adopted the 1 × 40 min protocol[4], because a systematic review and meta-analysis showed no significant differences between the single application and the renewal bleaching protocols regarding color change and tooth sensitivity[3].

In this in vitro research, the various concentrations of BG and BS combined with 35% HP did not affect the bleaching efficacy. Besides, the chemical behavior of the experimental gels disclosed lower HP concentration and higher pH values for the BG and BS gels than for the commercial 35% HP. Although these preliminary outcomes lead to the assumption that BG and BS gels could be an interesting alternative to a safer bleaching therapy, further *in vitro* analysis, such as enamel mineral content and surface morphology, must be performed before *in situ* or clinical trials. Though this constitutes a limitation of this study, in another report, it was found that 45S5-BG combined with HP did not change enamel roughness and was effective in controlling enamel surface microhardness[21].

The ability to control enamel inorganic content relates to the bioactivity potential of the bioglass. The particle's shape and size may lead to an improved biological response, as the dissolution process occurs in an aqueous media and on the particle's surface. According to a previous report, the most uniform shape to control ion release is a spherical particle[31]. Besides, others show superior bioactivity and higher mechanical stability of bioglass presenting micro-sized (< 5 μm) and nano-sized (35 nm) particles[32,33]. Since the particles in this study exhibit 5 μm, a high bioactive potential is expected. Yet, the mineral content and surface morphology of enamel submitted to BG/BS gels must be validated before further clinical evaluations.

Within the limitations of this in vitro study, it could be concluded that bleaching gels containing BG or BS did not interfere with the bleaching efficacy of 35% hydrogen peroxide. Furthermore, BG or BS hydrogel exhibited alkaline pH values, and it is suggested that BG or BS affects the decomposition rate of 35% HP.

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Conflict of Interest

The authors have no conflicts of interest to declare.

Data Availability

Datasets related to this article will be available upon request to the corresponding author.

Author Contributions

Camila Siqueira Silva Coelho: conceptualization, methodology, investigation, formal analysis, data curation, writing (original draft, review, and editing). **Izabele Gemeli Rigo:** methodology, investigation, data curation, writing (review and editing). **Rafael Dascanio:** methodology, Investigation, data curation, writing (review and editing). **Marina Trevelin Souza:** conceptualization, writing (review and editing). **Edgar Dutra Zanotto:** conceptualization, writing (review and editing). **Cinthia Pereira Machado**

Tabchoury: conceptualization, writing (review and editing). **Vanessa Cavalli:** conceptualization, resources, supervision, funding acquisition, writing (review and editing). All authors have actively participated in the manuscript's findings, revised and approved the final version of the manuscript.

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