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Time Frame Analysis of Potassium Nitrate and Hydrogen Peroxide Diffusion into the Pulp Chamber

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Clinical Relevance

Patient safety and satisfaction are crucial to dental practitioners. Tooth sensitivity is frequently reported as one of the most bothersome side effects of tooth-whitening. While many tooth desensitizing agents are available, there is no in-market technique that provides a desirable, time-efficient outcome.

SUMMARY

Objectives: The primary objective of this study was to evaluate the effect of an innovative double-layer, single-application desensitizing/whitening technique of potassium nitrate (PN) and hydrogen peroxide (HP) diffusion at different time points. Methods and Materials: Specimens were prepared from extracted caries-free human molars (n=90). Teeth were randomly assigned into four groups: Group A (HP CTRL) treated with 25% HP for 45 minutes, group B (PN CTRL) received a single-layer treatment of 5% PN for 45 minutes, group C received the double-layer treatment of 5% PN and 25% HP for 45 minutes, and group D received a 3% PN incorporated in a 40% HP gel for 45 minutes. PN and HP concentrations were measured at 5, 15, 30, and 45 minutes using standard chemical kits. Group comparisons were made using a repeated measures analysis of variance (ANOVA) test. Pairwise tests for differences in diffusion were done, using the Tukey adjustment of p values for multiple comparisons. A significance level of 5% was used.

Results: Group A showed no significant difference in HP diffusion rates between the 5- and 15-

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minute, 15- and 30-minute, or 30- and 45-minute time points; group D showed a similar trend; however, group C differed significantly at the 5- and 15-minute time points (p=0.0004), at the 15- and 30-minute time points (p=0.0026), and the 30- and 45-minute time points (p=0.0014). For PN diffusion, groups B and C had significantly different levels at the 15-, 30-, and 45-minute time points (p=0.0005, p=0.0002, and p<0.0001, respectively); and at the 15-, 30-, and 45-minute time points, groups D and C had significantly different PN diffusion (p=0.0327, p=0.0004, and p< 0.0001, respectively). Group C had significantly different PN diffusion at the 5- and 15-minute time points (p=0.0004), the 15- and 30-minute time points (p=0.0026), and at the 30- and 45-minute time points (p=0.0014).

Conclusion: The double-layer technique showed superior diffusion of PN into the pulp chamber and did not affect the diffusion of HP when compared to other techniques. The double-layer technique may be suggested as an alternative tooth-whitening treatment to minimize tooth sensitivity.

INTRODUCTION

Even though tooth whitening is effective, side effects still adversely affect patient compliance and satisfaction. Tooth sensitivity is the most commonly reported side effect, with an incidence rate as high as 75%.[1] The degree of sensitivity can vary from mild to intolerable, leading some patients to discontinue treatment.

A study showed that, of the subjects who underwent tooth-whitening treatment with 30% hydrogen peroxide (HP), 63% reported tooth sensitivity[2]; even higher sensitivity rates of 70% or 80% have been reported.[3,4]

Although exposed dentin, root caries, or exposed root surfaces could induce sensitivity, tooth-whitening-induced tooth sensitivity is believed to be related to the passage of HP molecules through intact dentin, dentinal tubules, and eventually the coronal part of the pulp.[5] The sensation commonly presents itself as generalized sensitivity to cold stimuli, but can also manifest as spontaneous sharp, shooting pain in a few teeth, indicating a direct effect on the nerve of the tooth.[5] HP causes cell damage or directly activates the neuronal receptor of the dental pulp complex. Recent research has shown that peroxides and other oxidizing agents oxidize cysteine residues in the TRPA1 neuron channel in the pulp complex, resulting in activation and perception of pain.[6]

Decreasing nerve excitations and blocking the transmission of pain to the central nervous system provides a potential treatment modality for tooth sensitivity. Potassium nitrate (PN) acts as a desensitizing agent, which reduces the nerve excitations by diffusing the potassium salts through enamel and dentin. These salts can reach nerve termination and affect nerve impulses. When K^+ concentration is increased above the normal physiologic level around the cell, it causes imbalance between K^+ and Na^+, and the cell depolarizes, creating a period of inactivation resulting in pain reduction or elimination.[7]

Several techniques for the delivery of PN as a desensitizing agent are available.[8] While the application of PN in a tray for 30 minutes prior to the whitening treatment[9] succeeded in reducing tooth sensitivity, this two-step technique was time consuming and inconvenient for the patient and clinician. Incorporating PN in the whitening gel[10] was introduced, eliminating the two-step application protocol, but similar diffusion times into the pulp chamber for both PN and HP were reported. Studies have shown that PN could be detected as early as five minutes[11] and HP as early as five to 10 minutes.[12] We believe this mixed approach is not effective due to the similar diffusion time of both PN and HP and, because of the lower molecular weight of HP, we assume that hydrogen will diffuse faster through the tooth and activate neuronal receptors in the pulp complex; by that time, reducing transmission of nerve impulses by PN is no longer possible.

To overcome these drawbacks, an innovative new technique, "the double-layer technique,"[13] utilizes a layer of PN covered by a layer of HP. This technique combines efficiency and efficacy, and will result in a better diffusion of PN. Since the PN layer will act as a physical barrier to the HP layer, we believe that PN will have a head start on diffusion. Hence, the purpose of this study is to establish a timeframe in which PN and HP diffusion are detected within the pulp chamber and to also evaluate the effect of PN on HP diffusion.

Our hypotheses were: 1) There is no difference in HP and PN diffusion times into the pulp chamber when used in different tooth-whitening techniques, and 2) HP and PN are not detected within the pulp chamber at, and at time points after, five minutes.

METHODS AND MATERIALS

Sample Preparation

Recently extracted human molars without any identifiers were obtained from the Iowa Institute for Oral Health Research at the University of Iowa. Teeth were thoroughly cleaned using non-fluoridated pumice

(Pumice Preppies, Whip Mix, Louisville, KY, USA) and prophy cups (Young Dental, Earth City, MO, USA) to remove debris from the tooth surface that was treated. Teeth were examined for caries, restorations, fractures. and cracks; teeth with these conditions were excluded. Teeth were sectioned 3 mm apical to cementoenamel junction (CEJ): 1) to achieve an open pulp chamber, and 2) to enlarge the pulp chamber vertically to be able to retain the 100-μL buffer solution that acted as a reservoir for the nitrate/HP residue. Diamond burs were used to enlarge the pulp chamber circumferentially to allow for the retention of assay solutions.

Following chamber enlargement, the remaining tooth thickness was measured using a boley gauge (HuFriedy Group, Chicago, IL) to ensure that a 2-mm wall thickness remained in all specimens. The average thickness is 2 mm, and for standardization purposes, all samples were reduced to a thickness of 2 mm.

A standardized circular treatment area 6 mm in diameter was established on the buccal surface. This aided in standardizing the treatment application along with treatment gel thickness.

Treatment and Group Distribution

Treatment application time and gel concentration followed the manufacturers' guidelines to resemble a clinical setting. Group A (HP control) was treated with 25% HP for 45 minutes (Philips Zoom WhiteSpeed, Philips Oral Healthcare, Stamford, CT, USA); group B (PN control) received a single-layer treatment of 5% PN (Relief ACP, Philips Oral Healthcare, Stamford, CT, USA) to act as a baseline for the amount of PN diffusion for 45 minutes; group C received the double-layer treatment (Figure 1) of 5% PN and 25% HP for 45 minutes; and group D received 3% PN incorporated in a 40% HP gel (Opalescence Boost PF, Ultradent, South Jordan, UT, USA) for 45 minutes. The amount of PN and HP in the pulp chamber was measured using standard chemical assays.

A sealed tooth-whitening technique was used for the groups using HP; HP was covered with a linear, low-density polyethylene wrap (Professional Plastic Food Wrap Film, Bakers & Chefs, Bentonville, AR, USA) to avoid evaporation. Since HP needs to be replenished every 15 minutes, this technique eliminated the need to replenish the gel during the tooth-whitening procedure for 45 minutes.[14] Groups treated with Zoom HP were continuously exposed to a light-emitting diode (LED: Zoom WhiteSpeed, Philips Oral Healthcare, peak wavelength: 466 nm) set at high intensity (190 mW/cm^2) throughout treatment time.

Gel quantity was measured using the formula $V=\pi r^2 h$. For PN, measurements were as follows: r=3 mm, h=1 mm, V=28.27 mm^3=28.27 μL. Values for HP were: r=3 mm, h=2 mm, and V=56.54 mm^3=56.54 μL.

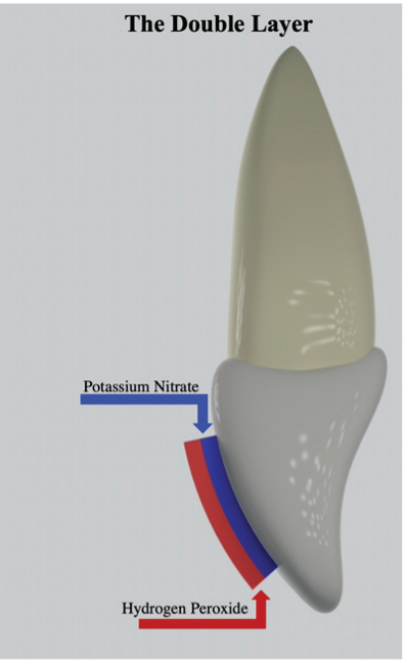

Figure 1. *Illustration of the application of the double layer technique*

Time Point Measurements

For quantifying the concentration of HP and PN within the pulp chamber at different time points, HP and/or PN residue within the pulp chamber was measured at 5, 15, 30, and 45 minutes in all groups. Choosing these time points was based on the amount of time PN and HP had been applied clinically. At these time points, a sample was withdrawn from the tooth's enlarged pulp chamber, and the amount of HP or PN residue within the pulp chamber was measured.

Hydrogen Peroxide Calculation

Acetate buffer solution was placed in the pulp chamber to calculate the amount of HP residue. Using a Fluorimetric HP assay kit and following the manufacturer's instructions (Sigma-Aldrich Co LLC, St Louis, MO, USA). A master mix was formulated by combining 50 μL Red Peroxidase Substrate Stock, 200 μL Horseradish Peroxidase, and 4.75 mL Assay Buffer. To calculate HP concentration within the sample, 50 μL of the Master Mix was added to each of the sample wells (50 μL sample volume), and the plate was incubated at room temperature for 15 to 30 minutes. The intensity of the color was proportional to the HP concentration and was measured in a UV/visible spectrophotometer at a wavelength of 596 nm

against a reference prepared in the same manner but without HP using a microplate reader.

Potassium Nitrate Calculation

One hundred microliters of phosphate buffer solution were placed in the pulp chamber. This buffer solution acts as a reservoir for the PN that possibly diffuses through the tooth into the pulp chamber after treatment. A colorimetric nitrate/nitrite assay kit (Sigma-Aldrich Co LLC) composed of nitrate and nitrite standard solutions, buffer solution, nitrate reductase, enzyme co-factors, and Griess dyes were used for the colorimetric determination of nitrate in the samples. The nitrate and nitrite concentration in the sample solution was calculated. Further, the final nitrate concentration in the sample solution was obtained by the following equation[15]: [Nitrate]=[Nitrate/Nitrite]-[Nitrite].

Statistical Analysis

Based on pilot data available to help guide the sample size determination, 15 samples/group were deemed sufficient to detect the desirable difference between groups. Diffusion of HP and PN was repeatedly measured at 5, 15, 30, and 45 minutes using donated extracted teeth, n = 15 in each group (n=90 total). The concentration was measured separately for four preparation combinations of HP and PN, resulting in six groups to compare in total. The groups were defined as the following:

- Group A: 25% Hydrogen Peroxide-A-HP (n=15)
- Group B: 5% Potassium Nitrate-B-PN (n=15)
- Group C: 5% PN, 25% HP-C-PN (n=15) & C-HP (n=15)
- Group D: 3% PN, 40% HP-D-PN (n=15) & D-HP(n=15)

Two repeated measures of analysis of variance (ANOVA) were done; both analyses assumed a compound symmetric correlation matrix. Tests of overall significance were conducted to determine if there is an overall effect of time, group, and the interaction of group and time. Following this, pairwise tests for difference in diffusion were done, using the Tukey adjustment of p values for multiple comparisons.

RESULTS

Hydrogen Peroxide

Summary statistics for the HP groups are found in Table 1 and Figure 2.

For group A-HP there was not a significant increase in concentration between consecutive time points; although the A-HP concentration did increase between the beginning and later time points (5 to 45 minutes, $p<0.0001$). Similarly, for group D, there was no significant difference between any consecutive time points. However, there was a significant difference between time points 5 and 45 minutes ($p=0.0025$). Group C showed a different trend compared to groups A-HP and D-HP. HP concentration for group C was significantly different at time points 5 and 15 minutes ($p=0.0004$), at time points 15 and 30 minutes ($p=0.0026$), and time points 30 and 45 minutes ($p=0.0014$). See Table 2.

The differences between groups at each time point can also be considered. At time points 5, 15, and 30 minutes,

Table 1: *Summary Statistics for the Concentration of Hydrogen Peroxide by each Time Interval*

Group	Time (Min)	Mean (μM)	SD (μM)	Median (μM)
A-HP	5	57.66	47.91	25.05
C-HP	5	33.96	21.35	28.5
D-HP	5	60.6	44.26	33.57
A-HP	15	103.13	55.5	82.88
C-HP	15	144.18	99.98	145.87
D-HP	15	107.82	59.13	111.73
A-HP	30	170.77	76.36	175.41
C-HP	30	243.46	166.43	254.52
D-HP	30	135.37	79.06	125.68
A-HP	45	236.96	88.51	234.66
C-HP	45	346.84	225.68	370.8
D-HP	45	160.08	96.67	130.45

Abbreviations: A-HP, 25% HP; C-HP, 5% PN, 25% HP; D-HP, 3% PN, 40% HP; HP, hydrogen peroxide; PN, potassium nitrate.

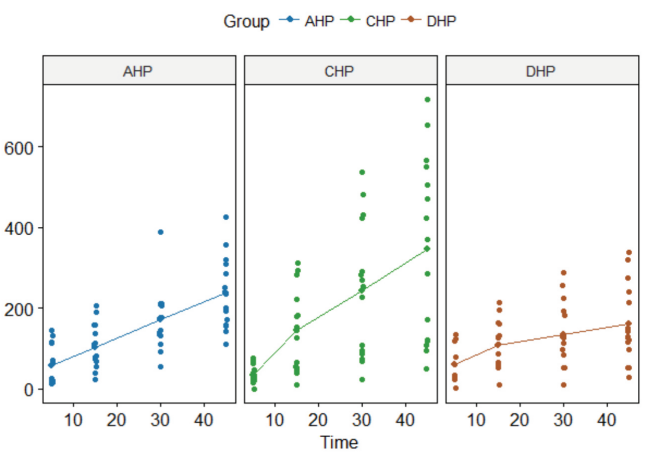

Figure 2. *Plot of hydrogen peroxide concentration (μm) with time (minutes), by group with means*

Table 2: *Repeated Measures ANOVA Results for Hydrogen Peroxide* (p-*value*) *per Group*

Group 1	Time 1 (Min)	Group 2	Time 2 (Min.)	Adj *p*-value
A-HP	5	A-HP	15	>0.05
A-HP	15	A-HP	30	>0.05
A-HP	30	A-HP	45	>0.05
C-HP	5	C-HP	15	0.0004
C-HP	15	C-HP	30	0.0026
C-HP	30	C-HP	45	0.0012
D-HP	5	D-HP	15	>0.05
D-HP	15	D-HP	30	>0.05
D-HP	30	D-HP	45	>0.05
A-HP	5	C-HP	5	>0.05
C-HP	5	D-HP	5	>0.05
A-HP	15	C-HP	15	>0.05
C-HP	15	D-HP	15	>0.05
A-HP	30	C-HP	30	>0.05
C-HP	30	D-HP	30	>0.05
A-HP	45	C-HP	45	>0.05
C-HP	45	D-HP	45	0.0002

Abbreviations: A-HP, 25% HP; C-HP, 5% PN, 25% HP; D-HP, 3% PN, 40% HP; HP, hydrogen peroxide; PN, potassium nitrate.

there were no significant differences in concentration among the three HP groups. At the 45-minute time point, C-HP and D-HP were significantly different (p=0.0002).

Potassium Nitrate

Summary statistics for the PN groups are found in Table 3 and Figure 3.

For group B-PN, there were no significant differences between the 5- and 15-minute time points or between the 30- and 45-minute time point; however, there was a significant difference between the 15- and 30-minute time points (p=0.0137). For group D, there were no differences between any consecutive time points; however, there were differences between the early and later time points (Table 4). For group C, there was a difference between every consecutive time point (5- vs 15-minutes, p=0.0003; 15- vs 30-minutes, p=0.0034; and 30- vs 45-minutes, p=0.0002). So, groups B and D had little diffusion of PN over time, but group C showed a consistent increase.

At the 5-minute time point, there were no differences among any of the groups. At the 15-, 30-, and 45-minute time points, groups B and C had significantly different PN concentrations (p=0.0005, p=0.0002, and p<0.0001, respectively). Also, at the 15-, 30-, and 45-minute time points, groups C and D had significantly different PN concentrations (p=0.0327, p=0.0004, and p<0.0001, respectively). However, groups B and D did not show significantly different concentrations of PN at any time point (Table 4).

Table 3: Summary Statistics for the Diffusion of Potassium Nitrate by Time

Time (Min)	Group	Mean (µM)	SD (µM)	Median (µM)
5	B-PN	0.83	3	0
5	C-PN	8.66	7	11.49
5	D-PN	3.07	7.84	0
15	B-PN	1.52	5.49	0
15	C-PN	22.82	4.97	22.18
15	D-PN	7.29	11.22	0
30	B-PN	13.04	14.86	10.99
30	C-PN	35.12	7.08	35.35
30	D-PN	14.02	14.46	13.24
45	B-PN	20	21.51	16.09
45	C-PN	49.42	16.16	47.57
45	D-PN	18.84	13.42	17.84

Abbreviations: B-PN, 5% potassium nitrate; C-PN, 5% PN, 25% HP; D-PN, 3% PN, 40% HP; PN, potassium nitrate.

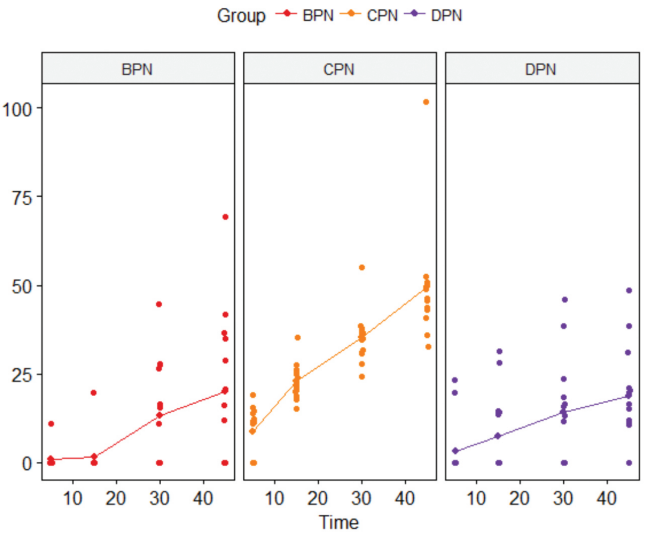

Figure 3. *Plot of potassium nitrate concentration (µm) with time (minutes), by group with means*

Table 4: *Repeated Measures ANOVA Results for Potassium Nitrate (*p*-value) by Group*

Group 1	Time 1 (Min)	Group 2	Time 2 (Min)	Adj *p*-value
B-PN	5	B-PN	15	>0.05
B-PN	15	B-PN	30	<0.013
B-PN	30	B-PN	45	>0.05
C-PN	5	C-PN	15	<0.0003
C-PN	15	C-PN	30	<0.003
C-PN	30	C-PN	45	<0.0002
D-PN	5	D-PN	15	>0.05
D-PN	15	D-PN	30	>0.05
D-PN	30	D-PN	45	>0.05
B-PN	5	C-PN	5	>0.05
C-PN	5	D-PN	5	>0.05
B-PN	15	C-PN	15	0.0005
C-PN	15	D-PN	15	0.0327
B-PN	30	C-PN	30	0.0002
C-PN	30	D-PN	30	0.0004
B-PN	45	C-PN	45	<0.0001
C-PN	45	D-PN	45	<0.0001

Abbreviations: B-PN, 5% PN; C-PN, 5% PN, 25% HP; D-PN, 3% PN, 40% HP; PN, potassium nitrate.

DISCUSSION

Tooth whitening is the first approach when considering enhancing tooth color. The at-home approach is the most popular due to its low cost and minimal chair time. However, people feel safe under a dentist's supervision, thus the in-office approach is emerging as the most desirable with less time to reach results. Using high concentration HP presents issues such as high prevalence of tooth sensitivity.[16] The use of desensitizing agents has proved to be beneficial to overcome this unwanted side effect.[8] However, using the desensitizing agent in a tray prior to tooth whitening is time consuming, and studies have shown lower efficacy in combining the desensitizing agent with the tooth whitening agent.[17] The double-layer technique reduced the desensitizing/tooth whitening protocol and presents an approach that favors the diffusion of the desensitizing agent.

The purpose of this study was to establish a time frame at which PN and HP concentrations are detected within the pulp chamber and also evaluate the effect of PN and HP diffusion. It is crucial for PN to be detected at early stages in the tooth-whitening treatment to be effective. In this study, different modalities of the application of PN were evaluated to understand its mechanism of diffusion.

Diffusion is the movement or spreading of molecules from a high concentration to a low concentration area. The molecular weight of a compound is crucial, with the lower molecular weight compounds generally diffusing faster. The molecular weight of PN is 101.1 g/mol compared to HP, which is 34.01 g/mol. Diffusion is influenced by factors such as pressure and temperature, in which more pressure or higher temperature increases the rate of diffusion.[18,19] In dentistry, the concentration of the agent, thickness of the tooth, and diameter of the dentinal tubules are additional factors to be considered.[11,20]

In this study, we evaluated different hypotheses regarding the diffusion of HP and PN. Our hypothesis was that HP diffusion is similar regardless of the method used. Our results support the rejection of the first null hypothesis. When considering the different time points (5, 15, 30, and 45 minutes), group A-HP and D-HP showed no significant difference between time points. However, group C-HP showed a different trend. The HP diffusion for group C-HP was significantly different at consecutive time points. So, while A-HP and D-HP showed modest increases in diffusion over time, C-HP showed a consistent increase in diffusion. The increase of HP diffusion over time in this study is in agreement with other studies that found that the diffusion of HP is time dependent.[21,22]

For diffusion, there was no statistically significant difference between group C-HP at 30 minutes and group A-HP or D-HP at 45 minutes (p>0.05 for both comparisons). Our innovative tooth-whitening technique showed equivalent diffusion of HP with less treatment time. Studies have reported that HP diffusion is directly correlated with tooth color change,[20,23] and we believe that with our technique, treatment time could be reduced and tooth color change could be reached more efficiently when compared to other techniques.

Concentration of HP is another factor that influences diffusion, since higher concentration creates a larger driving force for diffusion[11,24]; in this study, we compared concentrations of 25% and 40% HP. At the end of treatment, data showed a significant increase in diffusion with 25% when compared to 40% HP (p=0.0002). In this study, diffusion was not concentration-dependent, thus we believe that other factors such as temperature could have substantial impact on diffusion.[20,25] LED light was used with 25% HP so that, through thermocatalysis, light energy was converted to heat to increase efficiency of the tooth-whitening agent.[26]

Our hypothesis stated that HP is not detected in the pulp chamber at 5, 15, 30, and 45 minutes, and our data support the rejection of the hypothesis as concentrations of HP were found at all time points. Our results are in agreement with other studies that showed HP could be detected in the pulp chamber as early as 5 minutes.[22,27] Tooth-whitening sensitivity is believed to be related to the diffusion of HP. Fast diffusion of HP posed a dilemma for what is the best approach to overcome this issue; PN regimens were effective but did not fully eliminate tooth sensitivity. PN needs to be detected in pulp chamber early to mask the side effect of HP.

Considering PN diffusion, our hypothesis stated that there is no difference in PN diffusion into the pulp chamber when used in different tooth-whitening techniques. In this study PN was used alone, mixed into the tooth-whitening agent, or placed as a first layer in the double-layer technique. Our results support the rejection of the hypothesis: at the 15-, 30-, and 45-minute time points, groups B-PN and C-PN had significantly different PN diffusion (p=0.0005, p=0.0002, and p<0.0001, respectively), and at the 15-, 30-, and 45-minute time points, groups D-PN and C-PN had significantly different PN diffusion (p=0.0327, p=0.0004, and p<0.0001, respectively). Although PN diffusion increased at each time point, groups B-PN and D-PN showed no significant difference between any consecutive time points. However, group C-PN showed a different trend compared to groups B-PN and D-PN: PN was significantly different at the 5- and 10-minute time points (p=0.0004), the 15- and 30-minute time points (p=0.0026), and the 30- and 45-minute time points (p=0.0014). Our data are in agreement with studies that proved that PN is time dependent.[14]

The double-layer technique showed superior diffusion when compared to other techniques. At 5 minutes, the mean PN residue in the pulp chamber was 0.83 μM, 8.66 μM, and 3.07 μM for groups B-PN, C-PN, and D-PN, respectively; having higher PN diffusion is indicative of surplus potassium salts that interact with the nerve endings and could cause a prolonged desensitizing effect (Table 3). In this study, a number above 10 μM is of interest, as a study by Hodgkin and others[28] looked at the amount of PN diffusion when effective desensitization happens. In that study, they concluded that an increase of K^+ in the vicinity of the interdental nerve endings by 10 μM inhibits nerve impulses. When we look at our results reported, and with the limitation of this being an *in vitro* study, we can say an effective desensitization happens in group B-PN and D-PN around 30 minutes, while desensitization will happen earlier in group C-PN, between 10 to 15 minutes.

Faster diffusion was observed when HP was included, regardless of the technique; the viscosity of the compound might have contributed to the reported results as studies have concluded that viscosity is correlated with diffusion.[14,29] The use of light as a supplement to the tooth-whitening procedure was investigated in many studies. Light produces heat and whenever heat is exerted on the tooth-whitening agent, the temperature of the agent increases and increases its efficiency in releasing hydroxyl free radicals.[26,30] Superior diffusion of PN was observed in the double-layer technique when compared to PN control and the mixed technique as LED light was used in this technique, which could have an influence on the PN diffusion. However, there are no studies on the effect of light on a desensitizing agent's diffusion.

This *in vitro* study is one of few studies that evaluated the diffusion of PN into the pulp chamber and added to the literature regarding HP diffusion. The results of our study are somewhat challenging to compare to an *in vivo* setting. *In vivo* studies have two added variables-positive pulpal pressure and osmotic pressure of the gels[31]-that significantly affect diffusion.

Tooth preparation to encompass the 100 μL of buffer was another limitation since it is not a representation of a clinical situation. However, the tooth preparation protocol in our study took into consideration the safe amount of buccal thickness to be left, closely mirroring *in vivo* settings. The diffusion of PN into the pulp chamber has been investigated only recently. The limited literature on this topic showed that diffusion of PN into the pulp is controlled by different factors, such as concentration, viscosity, and other internal factors. It is crucial for the management of tooth-whitening-induced sensitivity that future studies should be directed toward innovative techniques that are effective and easy to implement.

A double layer, PN covered by HP, was evaluated to assess whether this technique will have an adverse effect on the diffusion of HP. Findings from our study showed promise in the advancement of managing tooth sensitivity. A model could be suggested in which a double layer of PN and HP could be formulated with the addition of a sealing varnish that provides isolation from the outer environment.

An *in vivo* study should be conducted to evaluate this technique, assess its effectiveness in managing tooth sensitivity, and analyze its effect on tooth color change, with a consideration of the clinical variables that might influence the outcome of such a technique.

CONCLUSIONS

This study evaluated whether the application of PN as a desensitizing agent prior to in-office tooth whitening

impairs HP diffusion. It also evaluated whether an in-office whitening agent impairs the diffusion of PN.

The findings of this study showed that the application of PN as a layer prior to an in-office tooth-whitening agent does not impair HP diffusion. Additionally, the application of the in-office whitening agent did not impair the diffusion of PN into the pulp chamber.

Within the limitations of this study, the double-layer technique showed superior diffusion of PN into the pulp chamber when compared to other techniques. The double-layer technique increased the efficiency of PN diffusion. The double-layer technique may be suggested as an alternative tooth-whitening treatment to minimize tooth sensitivity.

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Regulatory Statement

This study was conducted in accordance with all the provisions of the human subjects oversight committee guidelines and policies of the University of Iowa. The approval code issued for this study is 201710755.

Conflict of Interest

The authors of this article certify that they have no proprietary, financial, or other personal interest of any nature or kind in any product, service, and/or company that is presented in this article.

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