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Effect of CPP-ACP Application on Flexural Strength of Bleached Enamel and Dentin Complex

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Clinical Relevance

In the absence of saliva, flexural strength of the bovine enamel-dentin complex decreases after *in vitro* simulation of both at-home and in-office bleaching procedures. Application of Casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) subsequent to both bleaching regimens could compensate for this decrease.

SUMMARY

Introduction: Controversy continues over the effects of bleaching treatments on tooth structures in the literature. In addition to tooth sensitivity, a number of studies have reported adverse effects of bleaching procedures on dental hard tissues, including decreased hardness, fracture toughness, flexural strength, and other changes in the mechanical properties. The purpose of this *in vitro* study was to investigate the effect of casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) application on the flexural strength (FS) of bleached teeth.

Methods and Materials: One hundred twenty blocks (2×3×8 mm) were prepared from the middle portion of the facial surfaces of 120 sound bovine teeth. Specimens were randomly divided into six groups (n=20). Group 1 consisted of the control group, stored in distilled water at 37°C. The experimental groups (2 to 6) were immersed in CPP-ACP (0.5 h/d for 14 days, twice daily), 9.5% hydrogen peroxide (HP) (0.5 h/d, twice daily for 14 days), 9.5%

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HP+CPP-ACP, 38% HP (1 h/d, twice weekly for 2 weeks), and 38% HP+CPP-ACP, respectively. Flexural strength test was performed 24 hours after the last treatment session using a universal testing machine with a crosshead speed of 0.5 mm/min. Results were analyzed by two-way analysis of variance (ANOVA) and a post hoc Tukey's test (á=0.05).

Results: **Mean ± SD values for FS were 179.50 ± 24.16, 194.00 ± 21.31, 155.25 ± 32.7, 177.50 ± 30.15, 158.50 ± 27.49, and 177.50 ± 28.09 MPa, respectively. Statistically significant differences were observed in FS values between groups (*p*<0.05). Tukey analysis showed that using CPP-ACP subsequent to both bleaching techniques has a significant effect on tooth flexural strength.**

Conclusion: **Simulated in-office or at-home bleaching regimens performed in the absence of saliva decrease the FS of tooth structure. Application of CPP-ACP subsequent to both bleaching regimens could compensate for the decreased FS of the bovine enamel-dentin complex in this environment.**

INTRODUCTION

Bleaching agents, including carbamide and hydrogen peroxide, act as oxidizing agents through the formation of free radicals, reactive oxygen molecules, and hydrogen peroxide anions. These reactive molecules attack and split apart chromophores on teeth to exert a whitening effect.[1] Although bleaching procedures are intended to be applied topically to the enamel surface, the effects of such procedures are not necessarily restricted to enamel only. Previous studies have reported that peroxides penetrate from the enamel surface into the pulp.[2]

A general concern in bleaching procedures relates to the possible weakening of tooth structure subsequent to such procedures.[3] It has been demonstrated that abrasion resistance of bleached enamel decreases by up to 30%.[4] Furthermore, changes in enamel surface characteristics such as porosity, pitting, erosion, demineralization of enamel, and quantitative mineral loss have been reported subsequent to bleaching procedures.[5-10] In addition, alterations in the mechanical properties of dental tissues after bleaching have been reported in several studies.[11-19] Previous studies have also reported that bleaching can significantly reduce the tensile strength of enamel[17,18] and tooth resistance to fracture.[19] According to Tam and others, bleaching procedures have a significant influence on the flexural strength and elastic modulus of intact dentin.[13] In cases of root exposure and occlusal attrition, the bleaching agent is directly applied to the dentin surface.[13] Changes in mechanical properties indicate that structural alterations are likely to occur in the enamel-dentin complex exposed to bleaching agents.[15]

Vital tooth bleaching can be associated with some complications, including tooth hypersensitivity, which has been reported in 15% to 78% of patients undergoing such procedures.[18,20] Various treatments have been undertaken to manage tooth hypersensitivity, including the use of oxalates and nitrates of potassium or a combination of potassium nitrate and fluoride, as well as the use of amorphous calcium phosphates (ACPs).[21] Topical application of ACP has been demonstrated to reduce root surface hypersensitivity.[22]

Casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) is ACP complexed with the milk protein, casein phosphopeptide. [23] Casein phosphopeptide stabilizes ACP[22] and localizes ACP in dental plaque, thereby concentrating calcium and phosphate on the tooth surface.[22,23] By maintaining a high-concentration gradient of calcium and phosphate ions, CPP-ACP helps suppress demineralization and promote remineralization of enamel by the deposition of apatite.[23] CPP-ACP has been shown in laboratory and *in situ* studies to remineralize human enamel subsurface lesions.[24-26] The remineralized enamel has also been shown to be more resistant to subsequent acid attack.[27] Therefore, CPP-ACP has been incorporated into oral health products, such as chewing gums and mouthwashes.[27,28]

Recently, CPP-ACP has been used as a paste, in conjunction with or following treatments such as bleaching, to decrease tooth sensitivity. The effect of applying CPP-ACP to enamel surfaces, subsequent to bleaching procedures, on bond strength has been investigated in numerous studies.[29,30] One study reported that the application of CPP-ACP does not affect bond strength to enamel for the total etch (Single Bond) or the self-etching primer (Clearfil SE Bond) adhesives.[29] According to another study, CPP-ACP application does not decrease bond strength for two-step self-etching adhesives, but it significantly reduces bond strength for all-in-one adhesives when the smear layer is removed before paste treatment.[31] Acid preconditioning has no effect on dentin bond strength with or without CPP-ACP.[31] Furthermore, it has been reported that treatment with CPP-ACP does not inhibit phosphoric acid etching of enamel; however, enamel etching/conditioning improves the bonding efficacy of self-etching primer adhesives after CPP-ACP application.[32]

Although some studies have evaluated the structural and ultrastructural effects of CPP-ACP,[29-31] no study to date has been carried out on the probable physicomechanical effects of the agent on tooth structures. Therefore, the aim of this study was to investigate the effects of CPP-ACP application between at-home and in-office bleaching sessions on the FS values of the enamel-dentin complex.

Three hypotheses were evaluated: (1) There are no differences in FS values of the enamel-dentin complex subsequent to bleaching; (2) there are no differences in FS values of the enamel-dentin complex after application of CPP-ACP; and (3) there are no differences in FS values of the enamel-dentin complex when CPP-ACP is applied during bleaching treatments.

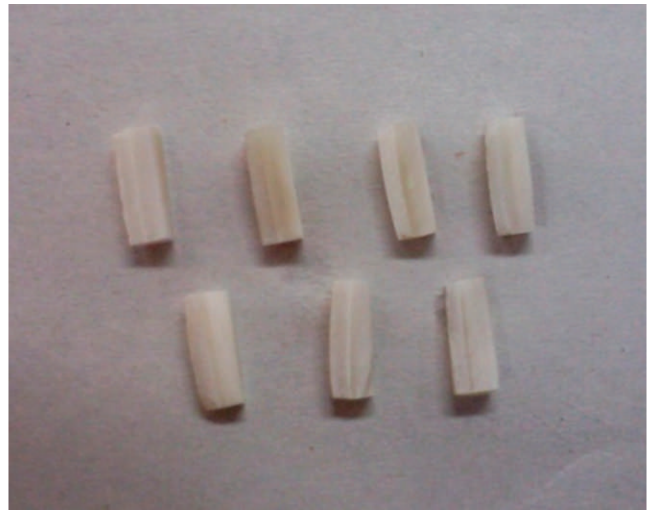

Figure 1. *Prepared enamel dentin specimens before receiving different treatments.*

METHODS AND MATERIALS

One hundred forty bovine incisors were extracted from cows 2 to 3 years of age. The teeth were stored in distilled water at 4°C until the study was initiated.

Rectangular blocks measuring 8 mm in length, 2 mm in width, and 3 mm in height were prepared from the middle part of the facial surfaces of the freshly extracted incisors. Mean height and width of the specimens were measured using digital calipers to an accuracy of 0.01 mm at three locations along the specimen length. A total of 120 of the most accurate and intact specimens were chosen. The specimens were randomly divided into six groups (n=20):

- Group 1 comprised the control group, which received no bleaching treatment and was kept in distilled water at 37°C.
- Specimens in group 2 were immersed in CPP-ACP (Tooth Mousse, GC Inc, Tokyo, Japan) 0.5 h/d for 14 days twice daily.
- Group 3 specimens were immersed in 9.5% hydrogen peroxide gel (HP) (Day White, Discus Dental, Culver City, CA USA) for 0.5 h/d, twice daily for 14 consecutive days; then the specimens were thoroughly rinsed with distilled water for 30 seconds and stored in relative humidity at 37°C.
- The specimens in group 4 were bleached as group 3 specimens, except for the fact that between bleaching sessions they were immersed in CPP-ACP, similar to the regimen in group 2.
- Group 5 specimens were immersed in 38% HP (Opalescence Xtra Boost, Ultra Dent Products Inc, South Jordan, UT, USA) for 1 h/d twice weekly for 2 consecutive weeks. After each bleaching session, the specimens were thoroughly rinsed with distilled water for 30 seconds and stored in relative humidity at 37°C.
- The specimens in group 6 were bleached as group 5, except for the fact that between bleaching sessions they were immersed in CPP-ACP, similar to the regimen in group 2.

After the end of bleaching intervals in each group, the specimens were rinsed and incubated in distilled water for 24 hours at 37°C before being tested.

The specimens were subjected to a three-point bending test (TPBT) on a Universal Testing Machine (Dartec, HC10, Dartec Ltd, Stourbridge, UK) that applied force to the center of the enamel side of the specimens at a crosshead speed of 0.5 mm/min. The mounting apparatus consisted of two rods (2 mm in diameter), mounted parallel, with 6 mm between the centers (Figure 1). The maximum load supported by the specimen prior to failure was used to calculate the flexural strength (FS) value. FS was determined using the following formula:

$$FS = 3P_fL/2WH^2$$

P_f is the measured maximum load at the time of specimen fracture; L is the distance between supports on the tension surface (6 mm); W is the mean specimen width; and H is the mean height of the specimen between the tension and compression surfaces.

Table 1: *Flexural Strength of the Specimens in Study Groups in MPa (n=20)*

Groups	Group Definitions	Minimum	Maximum	Mean	SD	CI (95%)	
						LB	UB
1	Negative control	135	225	179.5	24.16	168.19	190.81
2	CPP-ACP	145	240	194	21.31	184.03	203.97
3	At-home bleaching	115	225	155.25	32.7	139.94	170.56
4	At-home bleaching+CPP-ACP	125	230	177.5	30.15	163.39	191.61
5	In-office bleaching	95	220	158.5	27.49	145.64	171.36
6	In-office bleaching+CPP-ACP	140	225	173.71	28.09	164.30	190.70

Abbreviations: CPP-ACP, casein phosphopeptide-amorphous calcium phosphate; CI, Confidence Interval; LB, Lower Bond; UB, Upper Bond.

Results were subjected to statistical analyses using two-way analysis of variance (ANOVA) and a post hoc Tukey test (α=0.05).

RESULTS

Flexural strength values in MPa (mean±SD), minimum/maximum values, and confidence intervals (CIs) of 95% for the groups are summarized in Table 1. Analysis of variance revealed significant differences in FS values among the six groups ($p<0.05$). Bleached specimens showed lower FS values compared with group 1 ($p<0.05$). Group 2 specimens immersed in CPP-ACP demonstrated FS values similar to those in group 1, but significantly higher FS values compared with the bleached groups (groups 3 and 5). No significant differences were observed between groups 3 and 5 or between groups 4 and 6 ($p>0.05$) (Figure 2).

Two-way ANOVA revealed that FS values were influenced by "bleaching" (f=6.736; p=0.002) and "bleaching/CPP-ACP application" (f=13.606; $p<0.001$); however, they were not influenced by "CPP-ACP application" (f=0.199; p=0.82) (Figure 3).

Multiple comparisons by Tukey test demonstrated significantly higher FS values in groups 2, 4, and 6 compared with their corresponding groups ($p<0.05$).

DISCUSSION

The most frequent side effect of vital bleaching procedures is tooth sensitivity.[22] In addition, according to several reports, some concerns have been raised about the possibility of demineralization of tooth hard tissues subsequent to tooth bleaching.[2,12,13] Therefore, in recent years, not only have desensitizing agents been added to bleaching compounds, but substances that are believed to have remineralization and hardening effects on dental tissues have been emphasized. Some products such as GC Tooth Mousse (containing CPP-ACP and marketed as MI Paste in some areas) have been demonstrated to have desensitizing and/or rehardening effects.[22,23,28,33-36] Therefore, in the present study, the effect of Tooth Mousse, as a multipotential substance after bleaching, on the FS of the enamel-dentin complex was investigated for the first time.

Natural enamel, as a hard and brittle tissue, has a low flexural strength (high elastic modulus); however, enamel supported by dentin is naturally protected by a tissue with lower elastic modulus. Therefore, because dentin provides a supporting base for both enamel and cementum, it is largely responsible for the structural integrity of the entire tooth. It has been reported that bleaching agents diffuse through enamel in 15 to 25 minutes. However, some factors such as enamel thickness, the existence of enamel fractures and cracks, permeability, and the direction of dentinal tubules influence the diffusion of bleaching agents through dentin.[11,14] In addition, bleaching agents influence enamel features by the influencing enamel organic matrix with the action of free radicals. It has been claimed that porosities created by the bleaching agent along the exposed area of enamel might act as stress raisers during bending tests, resulting in their early fracture during fracture resistance investigations.[10,17] Hy-

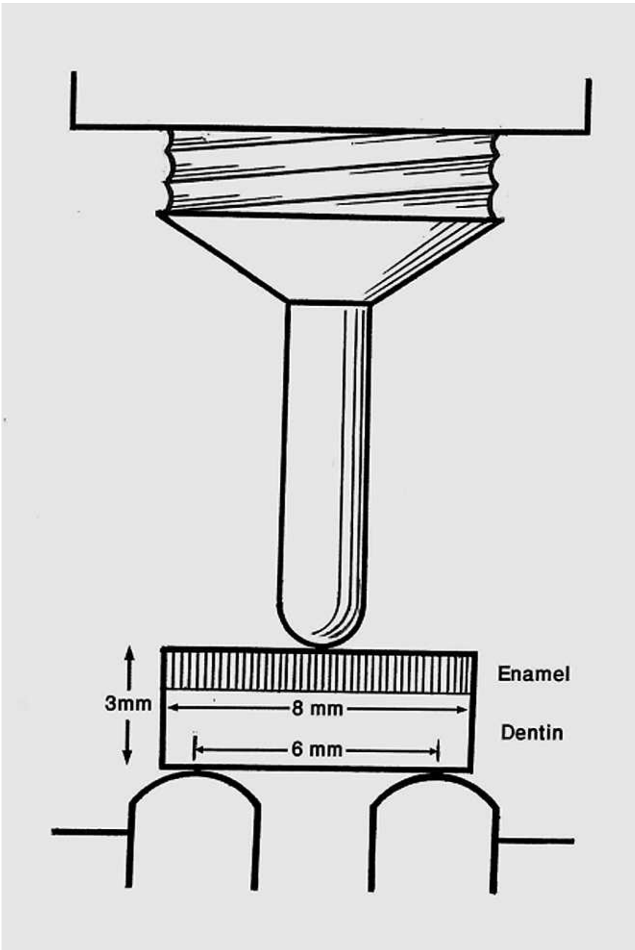

Figure 2. *Schematic view of three-point bending force on the prepared specimen.*

drogen peroxide has been reported to change the internal structure of enamel, producing scratches on the enamel surface.[2]

In the present study, FS was investigated as a factor involved in tooth strength. Material strength is a measure of a material's resistance to fracture, which is represented by FS parameters.[13] Furthermore, in this study, the crosshead speed of 0.5 mm/min was selected for the test. Because the three-point bending test is a static test, the authors speculated that lower speeds better mimic the flexure of tooth structure. In addition, prepared blocks for performing the test included the enamel and dentin complex. It seems that in this condition, the results are more similar to clinical conditions.

Results of the present study show a significant decrease in flexural strength of the enamel-dentin complex after both in-office and at-home bleaching procedures compared with the control group. Struc-

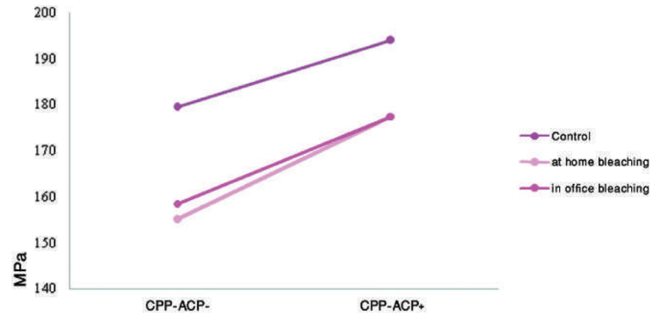

Figure 3. *Flexural strength variations in the study groups in MPa according to the two variables: "kind of bleaching" and "CPP-ACP application."*

tural changes reported previously, including increased roughness of enamel and dentin, increased porosity, increased cracks, enamel and/or dentin morphologic changes, and decreased microhardness following bleaching treatments, are consistent with the results of the present study.[2,12,15] Subsequent to repeated bleaching procedures with longer periods and higher concentrations, the weakening of tooth structure is more probable.[2] When enamel and dentin structures are weakened, fracture resistance is reduced.[14,19] Some of the structural alterations in bleached dentin have been attributed to alterations in the water, mineral, and collagen content of dentin and to noncollagenous protein changes.[11] Furthermore, it has been reported that tooth whitening reduces the organic contents of dentin, and this is followed by a relative increase in nonorganic contents of dentin and cementum.[12] Hydrogen peroxide and carbamide peroxide target the organic parts of dentin by denaturing collagen and oxidizing dentin proteins. Bleaching agents find improved access to intratubular minerals by dispersing collagen fibrils. Loss of minerals results in loss of the binding matrix. Therefore, the destruction of organic and mineral parts of dentin occurs continuously.[11]

In the present study, two types of bleaching agents, including 38% and 9.5% hydrogen peroxide, were used, and flexural strength was clearly decreased. The results are consistent with the results of a study carried out by Ghavamnasiri and others.[15] However, another study[14] has reported no significant effects on flexural strength with a range of hydrogen peroxide concentrations. This discrepancy in results can be attributed to the type and concentration of the bleaching agents evaluated, the substrate under study (dentin in that study, whereas the dentin-enamel complex in this study), and different bleaching protocols.

In the present study, comparison of in-office and at-home bleaching techniques revealed no significant differences in flexural strength values. This seems logical given that the concentration of the two substances used (9.5% vs 38%) and their application periods (14 hours vs 4 hours) with both techniques reduced tooth flexural strength; however, the effect of the at-home bleaching technique on flexural strength was slightly more noticeable than that of the in-office bleaching technique, which might be attributable to the slightly higher acidic pH of Daywhite (pH=6.2) in comparison with the neutral pH of Xtra Boost (pH=7). It has previously been emphasized that long exposure times to bleaching agents with lower pH can increase enamel and dentin demineralization and can change the mechanical properties of the teeth involved.[12]

Previous studies, which have examined the effects of CPP-ACP–containing products subsequent to bleaching, have reported decreases in postbleaching tooth sensitivity, a demineralization effect of the bleaching agent, and increases in tooth glittering by increasing tooth translucency and value.[22,33,37] Consistent with the results of these studies, CPP-ACP significantly increased the flexural strength of bleached groups in the present study. Tooth Mousse composition in detail includes CPP-ACP 10%, Ca content 13 mg/g, P content 5.6 mg/g, and a pH of 7.8.[36] It has been emphasized that this substance can work as a nonorganic source of calcium and phosphate, both of which are released on the enamel surface, giving rise to increased enamel mineralization.[30] In addition, when CPP-ACP is applied to the tooth surface, it binds to biofilms, plaque, bacteria, hydroxyapatite, and surrounding soft tissues, localizing bioavailable calcium and phosphate; saliva will also enhance the efficacy of CPP-ACP. In addition, the flavor of Tooth Mousse will help to stimulate saliva flow.[36] From this viewpoint, the clinical effects of this substance are probably greater than the effects shown in this study and in similar experimental studies.

On the other hand, it should be pointed out that in this study, prepared tooth samples were immersed in bleaching gels and/or GC Tooth Mousse, and thus were permeable from six dimensions. Regarding the results of bleached specimens in groups 3 and 5, and bleached/CPP-ACP specimens in groups 4 and 6, it seems that demineralization and remineralization phenomena are the reasons for the results obtained. It has been shown that CPP-ACP is a potent remineralizing paste, and that its action on enamel can reverse the structural damage caused by bleaching agents or demineralizing solutions.[22–26,33] This finding is consistent with a recent study, which showed that application of CPP-ACP subsequent to a bleaching procedure significantly enhances tooth microhardness and remineralization.[33] Moreover, it has been reported that teeth treated with CPP-ACP are more resistant to acid attacks and decalcification; treatment increases tooth remineralization as well.[23,29,38] It seems that application of CPP-ACP after each bleaching session enhances tooth resistance to the demineralization effects of bleaching agents and probable acid attack with low-pH products and subsequent remineralization; it also preserves the organic parts of the tooth by preserving the mineral content of enamel and dentin. However, it must be pointed out that although CPP-ACP seems to increase the calcium and phosphate content of dental tissues after bleaching, it cannot reverse the effects if the organic matrices of dental tissues are denatured by bleaching gels. Probably, this is the reason for lower flexural strengths of bleached/CPP-ACP–applied specimens in groups 4 and 6 compared with groups 1 and 2.

In the present study, the treatments for groups 4 and 6 were instituted to address the question of whether the tooth could be remineralized on the assumption that some demineralization occurs during exposure to bleaching agents, and whether any decrease in tooth flexural strength as a result of in-office or at-home bleaching procedures could be reversed.

According to the results of the present study, the flexural strength of unbleached samples on which Tooth Mousse was applied (group 2) increased but not significantly, which might be attributed to the strengthening and hardening effects of the product on enamel and dentin.[22] In addition, it seems that the application period and the existence of factors such as saliva, biofilms, and plaque in the mouth might lead to different results.

Although the present study clearly shows the effect of each variable, it had some limitations, which need to be mentioned, including the fact that after each bleaching treatment, the samples were stored in distilled water. It has been reported that bleaching agents have dehydration effects on dental tissues, and keeping them in distilled water can provide some rehydration for the specimens. At the same time, there is the potential for some demineralization of enamel and dentin in distilled water because it lacks calcium and phosphate.[13] Human saliva not only has buffering properties and prevents demineralization, it is also rich in calcium and phosphate and acts as a source of remineralization after bleaching procedures.[39] Therefore, it is recommended that similar studies with storage in saliva and replenishing saliva between sessions be carried out.

Another consideration is that the effects of bleaching agents on tooth structure might be clinically less than what was shown in this study because of factors such as buffering properties and the outward flow of intratubular fluids, which prevents the diffusion of bleaching agents through dentin and the presence of saliva, which contains required substances for remineralization of enamel and dentin.[12,40]

CONCLUSION

In the absence of saliva, application of 9.5% HP or 38% HP for 2 weeks simulating at-home and in-office bleaching agents, respectively, caused a statistically significant decrease in the FS of the enamel-dentin complex. Application of CPP-ACP after each bleaching session for 0.5 hours could reverse the negative effects of bleaching on FS in this environment.

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