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Evaluation of Bond Systems Associated or not to Grape seed Proanthocyanidin in Cervical Dentinary Hypersensitivity Control

Avaliação do Emprego de Sistemas Adesivos Associados ou não à Proantocianidina da Semente da Uva no Controle da Hipersensibilidade Dentinária Cervical

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Abstract

The purpose of this study was to clinically evaluate the bond systems Adper Single Bond 2 (3M ESPE) and Ambar (FGM) associated or not with previous dentin treatment with grape seed extract (*Vitis vinifera*) for cervical dentin hypersensitivity (HD) treatment. To evaluate dental sensitivity degree tactile and evaporative stimuli were used. After stimuli exposure patients were asked to associate sensitivity experienced to a verbal pain scale, ranging from zero to three. Twenty patients were pre-selected, among which 10 were invited to participate in the study according to inclusion criteria, from those patients were evaluated an amount of 20 teeth with HD, which were classified according to the degree of sensitivity presented, following: Grade 1 = 8 (40%), Grade 2 = 6 (30%) and Grade 3 = 6 (30%). Teeth were randomly distributed among the 4 material groups evaluated, so that each group had n = 5. After bond application, the sample was reexposed to stimuli for up to 3 weeks. Significant reduction in pain sensitivity was observed in all four groups, all materials showed immediate and up to 3 weeks efficacy in HD control. It is possible to conclude that the products tested were able to satisfactorily control cervical dentin hypersensitivity.

Keywords: Dentin Sensitivity. Adhesives. Grape Seed Extract.

Resumo

O objetivo do presente estudo foi avaliar clinicamente os sistemas adesivos convencionais Adper Single Bond 2 (3M ESPE) e Ambar (FGM) associados ou não ao tratamento prévio da dentina com extrato de semente de uva (Vitis vinifera) rico em proantocianidinas no controle da hipersensibilidade dentinária (HD) cervical. Para avaliar os graus de sensibilidade dentinária foram utilizados estímulos mecânico e evaporativo. Em seguida à exposição aos estímulos os pacientes associavam a sensibilidade experienciada a um dos graus de uma escala verbal de dor, variando de zero a três. Foram triados 20 pacientes, dentre os quais 10 tornaram-se elegíveis para participação na pesquisa de acordo com critérios de inclusão pré-estabelecidos, destes pacientes foram avaliados na pesquisa 20 dentes com HD, estes foram classificados de acordo com o grau de sensibilidade apresentado, resultando na seguinte distribuição: Grau 1 = 8 (40%), Grau 2 = 6 (30%) e Grau 3 = 6 (30%). Os dentes foram distribuídos de forma aleatória entre os 4 grupos de materiais avaliados, de modo que cada grupo tivesse n=5. Após a aplicação dos materiais foi feito o controle com reexposição aos estímulos por até 3 semanas. Foi observada diminuição significativa da sensibilidade dolorosa em todos os quatro grupos, todos os materiais mostraram eficácia imediata e até 3 semanas no controle de HD. Podemos concluir que os produtos testados foram capazes de controlar satisfatoriamente a hipersensibilidade dentinária cervical.

Palavras-chave: *Sensibilidade da Dentina. Adesivos. Extrato de Sementes de Uva.*

1 Introduction

Dental hypersensitivity (HD) is a common clinical dental condition in permanent teeth caused by dental exposure to the oral environment as a result of loss of enamel and/or cement. This sensitivity is characterized by short and acute pain, in a way that it can be physically and psychologically uncomfortable to the patient. Pain is triggered by dental tubules exposed in response to thermal, tactile, osmotic, chemical or evaporative stimuli [1,2] . The diagnosis of this condition is given by exclusion, and it is the duty of the surgeon-dentist to perform a careful differential diagnosis [3] .

HD tends to become a growing clinical problem as a result of reducing dental losses during aging. Thus, dentists will have to be able to promote the appropriate diagnosis and intervention to each case. For this purpose, routine screening of all dental patients is recommended. In this regard, under-diagnosis of the condition will be avoided and preventive management can be initiated early [4] .

Active management of HD generally starts with supervised home therapy, in which brushing with desensitizing dental creams is the most important. Complete management usually involves a combination of home-made and in-office therapies[3,4] .

Treatment of dental hypersensitivity can be challenging and studies generally use the words “control”, “relief” or “improvement” of the clinical picture, since many of the treatments proposed cannot eliminate the painful sensation of HD and prevent recurrence[5,6] .

Within this context, the research has been trying to improve

the materials in order to find one that is effective in the short term, that does not allow recurrence of hypersensitivity and that effectively eliminates the painful sensation, besides presenting biocompatibility, not causing pain, being quick and easy to apply, fast action and not staining the teeth, as suggested by Grossman since 1935[7] .

Currently, many natural products are being considered as promising sources of new therapeutic agents, among them the proanthocyanidin (PA) that has received increasing attention due to its biocompatibility and many beneficial biological properties, including anticancer, anti-inflammatory, anti-bacterial and immuno-stimulant effects[8-10]. After successful applications in medical science, BP was also introduced in the field of dental research[11].

Studies indicate that there is a reduction in the proteolytic activity of dentin after application of proanthocyanidin[12,13]. There are indications that the application of PA in demineralized dentin has significant results both in the mechanical properties and in the bonding strength of the adhesive interface[13-16]. It is possible that these characteristics can improve the performance of adhesive systems used not only in restorative procedures but also in the HD control.

In this context, the objective of this study was to clinically evaluate different materials associated or not to the use of PA from grape seed extract in the HD control.

2 Material and Methods

This research was approved by the Research Ethics of the Federal University of Pernambuco - UFPE (30684214.2.0000.5208). An initial screening of patients enrolled for treatment at the clinics of the Odontology course of UFPE was performed, under which the following inclusion criteria were applied: To present at least one tooth with sensitivity to the air jet; to present absence of occlusal trauma on the teeth to be evaluated; To enjoy good systemic health; to present good oral hygiene; patients should reside in the Metropolitan Region of Recife, preferably with residence and fixed employment in the city. Patients who : present cervical lesions with a depth greater than 1 mm; present carious lesions or prosthetic crowns; were submitted to orthodontic treatment; present with painful symptoms associated with irreversible endodontic involvement; present with gastric reflux or regurgitation were excluded from the study.

A total of 22 patients expressed an interest in participating in the study, after the initial phase of guidance and data collection of each of these patients, detailed clinical examinations were performed in order to verify the presence or absence of interproximal caries, periapical lesions and evaluation of periodontal condition. When necessary, interproximal and periapical X-rays were performed in the areas involved, in order to confirm clinical diagnoses.

After screening and application of pre-established inclusion and exclusion criteria, only 10 patients became eligible for participation in the research, all of them females aged between 18 and 25 years. Patients were clearly and objectively informed of the nature of this study, highlighting its importance and certifying the integrity and safety of the procedures to be performed. The patients signed the Free and informed consent form, authorizing their participation.

Before proceeding to the experimental phase, all patients were instructed and guided in terms of the Bass brushing technique and in terms of eating habits, eliminating the consumption of citrus fruits, acid and alcoholic beverages and preserved foods, In view of the fact that every therapeutic proposal for HD should include guidelines on relevant eating habits and self-care in order to intervene in the probable causes[3] of the condition.

Sensitivity degrees were measured before materials were applied (baseline) and weekly for up to 3 weeks after treatment was started. For this purpose, the mechanical stimulus was used by means of an exploratory probe number 5 and the evaporative stimulus applied by the application of the air jet for 2 seconds at a distance of 2mm and perpendicular to the vestibular surface of the tooth that was evaluated. The stimuli lasted 1 second with a 1-minute interval between their applications. The neighboring teeth, anterior and posterior to the tooth, were also submitted to mechanical and thermal stimuli with the objective of clarifying the responses provided by the patients.

The sensitivity severity was referred to by the patients according to the degrees and type of sensitivity proposed by Uchida et al.[17], as it can be seen in Table 1.

Table 1 - Degrees and characteristic of induced sensitivity

Degrees	Characteristic
0 (Zero)	No significant discomfort (absence of pain after stimulation).
1 (one)	Mild discomfort (mild pain after stimulation).
2 (two)	Severe discomfort (acute pain during stimulus application).
3 (three)	Severe discomfort (acute pain during and after stimulus application for more than ten seconds).

Source: Research data.

Among the patients, a total of 36 teeth presented HD, of which 20 were randomly selected, which were randomly subdivided into four groups of 5 teeth each, according to Chart 2.

Table 2 - Division of groups, abbreviation and method of use of the material

Groups	Abbreviation	Forms of use
Group 1 Adper Single Bond 2 (3M ESPE)	SB2	Prophylaxis with pumice stone and water followed by washing and drying with light jets of air; acid conditioning for 15 seconds in dentin and 30s in enamel; washing and drying with light jets of air; Application of two layers of adper Single bond 2 adhesive with the aid of a micro applicator (Cavibrich-FGM), drying with a light jet of air for 5s; photopolymer for 10s
Group 2 Adper Single Bond 2 + grape seed extract (*Vitis vinífera)*	SB2 + ESU	Prophylaxis with pumice stone and water followed by washing and drying with light jets of air; acid conditioning for 15 seconds in dentin and 30s in enamel; washing and drying with light jets of air; Application ESU on the demineralized dentin for 30 seconds, washing and drying with light jets of air, application of two layers of adper Single bond 2 adhesive with the aid of a micro applicator (Cavibrich- FGM), drying with a light jet of air for 5s; photopolymer for 10s
Group 3 Ambar (FGM)	**AB**	Prophylaxis with pumice stone and water followed by washing and drying with light jets of air; acid conditioning for 15 seconds in dentin and 30s in enamel; washing and drying with light jets of air; With the aid of a micro applicator (Cavibrush - FGM), the adhesive is then applied to a wet surface, rubbing the first drop of the product vigorously for 10 seconds. Then, new adhesive layer is applied to the same surface for more 10 seconds. It is then applied air jet for 10 seconds, photopolymerization for 10 seconds
Group 4 Ambar + grape seed extract (*Vitis vinífera)*	**AB + ESU**	Prophylaxis with pumice stone and water followed by washing and drying with light jets of air; acid conditioning for 15 seconds in dentin and 30s in enamel; washing and drying with light jets of air; application of ESU on the demineralized dentin for 30 seconds, washing and drying with light jets of air ;With the aid of a micro applicator (Cavibrush - FGM), the adhesive is then applied to a wet surface, rubbing the first drop of the product vigorously for 10 seconds. Then, new adhesive layer is applied to the same surface for more 10 seconds + grape seed extract. It is then applied air jet for 10 seconds, photopolymerization for 10 seconds

Source: Research data.

The data were presented in a descriptive manner through absolute and percentage frequencies and mean and standard deviation measurements. In order to verify whether there is a significant difference among the groups in each evaluation, the Kruskal-Wallis test was used and for the comparison between the evaluation times in each group, the Friedman test was used with multiple comparison of the test mentioned herein. The choice of the tests mentioned was due to the size of the samples per group. The margin of error used for statistical tests was 5.0%.

The data were entered in the excel spreadsheet and the programs used to obtain statistical calculations were SPSS (Statistical Package for the Social Sciences), version 23 and MEDCALC 14.8.1.

3 Results and Discussion

In Table 3, the frequencies of the sensitivity degree according to the evaluation and the group can be observed. In the initial evaluation, the degrees varied from 1 to 3, and the highest frequency in grade 3 was equal to 2 in SB+ ESU and AB groups; in the 1st week, the degrees varied from 0 to 2, and the frequencies in the 0 degree varied from two to 4; In the 2nd week with the exception of one tooth in grade 1 in SB2 and AB ESU groups, the others were equal to zero; in the 3rd week all measurements were classified in grade 0; Among the groups, the greatest frequency difference occurred among the groups SB+ ESU and SB2 groups in Grade 1, which had respectively degrees 3 and zero.

Table 3 - Sensitivity data by evaluation and group

Assessment	Degree of sensitivity	Group			
		I	II	III	IV
		(SB2)	(SB + ESU)	(AB)	(AB + ESU)
		n (5)	n (5)	n (5)	n (5)
Initial	0	-	-	-	-
	1	3	1	2	2
	2	1	2	1	2
	3	1	2	2	1
1st Week	0	3	2	4	4
	1	-	3	1	1
	2	2	-	-	-
	3	-	-	-	
2nd Week	0	4	5	5	4
	1	1	-	-	1
	2	-	-	-	-
	3	-	-	-	-
3rd Week	0	5	5	5	5
	1	-	-	-	-
	2	-	-	-	-
	3	-	-	-	-

Source: Research data.

In Table 4, the statistics: average and standard deviation of the sensitivity degrees according to the evaluation and the group can be observed. The averages ranged from 1.60 (SB2 group) to 2.20 (SB group ESU) in the initial evaluation, in

the 1st week the averages varied from 0.20 (AB and AB ESU groups) to 0.80 (SB2); In week 2nd the means were null in the SB+ ESU and AB groups and were 0.20 in the other two groups; in the 3rd week the averages were all null, however for the fixed error margin (5%) no significant differences were recorded among the groups for any of the evaluations. The averages reduced in all groups of the initial assessment to the 1st week. From the 1st week, they reduced or remained the same in the 2nd and 3rd weeks, and significant differences were observed among the evaluations in all the groups and through the multiple comparisons tests significant differences were observed among: In the SB2 group between the initial evaluation with all other evaluations and between 1st week and 3rd week; in the group SB+ESU, with the exception of 2nd and 3rd weeks significant differences between the other evaluation pairs were observed; in the AB and AB + ESU groups significant differences were found between the initial evaluation and each of the other evaluations.

Table 4 - Means and standard deviation of the sensitivity degrees according to the evaluation and the group

		Group				
		I	**II**	**III**	**IV**	**Value of p**
Variable	**Assessment**	**(SB2)**	**(SB+ESU)**	**(AB)**	**(AB + ESU)**	
		n (5)	**n (5)**	**n (5)**	**n (5)**	
Mean	Initial	1.60 (A)	2.20 (A)	2.00 (A)	1.80 (A)	p (1) = 0.732
	1st Week	0.80 (B)	0.60 (B)	0.20 (B)	0.20 (B)	p (1) = 0.539
	2nd Week	0.20 (BC)	0.00 (C)	0.00 (B)	0.20 (B)	p (1) = 1.000
	3rd Week	0.00 (C)	0.00 (C)	0.00 (B)	0.00 (B)	p (1) = 1.000
Value of p		**p (2) = 0.006***	**p (2) = 0.003***	**p (2) = 0.003***	**p (2) = 0.003***	
Initial	Standard	0.89	0.84	1.00	0.84	
Standard	1st Week	1.09	0.55	0.45	0.45	
	2nd Week	0.45	0.00	0.00	0.45	
	3rd Week	0.00	0.00	0.00	0.00	

(*) significant difference at 5%; (1) through the Kruskal-Wallis test; (2) through the Friedman's test with comparisons of the aforementioned test. Notes: If the letters in brackets are all distinct, significant differences between the corresponding groups are demonstrated.
Source: Research data.

Due to the differences between the habits and diets of the populations evaluated, and, mainly, the disconformities of the investigative methods, there is a disagreement among the authors regarding the prevalence of HD[18]. However, there is a consensus to point to dental hypersensitivity as one of the most common clinical complaints among dental patients[19]. In this way, the search for better materials and therapeutic approaches to this condition becomes important. Although the use of adhesive systems in the treatment of HD is already recommended[3,20], this study brings the difference of the evaluation of the combination of adhesives with an extract of plant origin, encouraging the search for improvements in therapeutic capacities.

The application of adhesive systems stands out within the therapeutic alternatives for the control of dental hypersensitivity because it is an inherent low-cost material that is easy and quick to apply[20] . As a negative point, its inefficiency in preventing recurrence is highlighted[6]. It is likely that the return of painful sensitivity is due to the process of degradation of the adhesive interface, unblocking the dental tubules that had been obliterated.

In this degradation process of the adhesive interface, there are the metalloproteinases of the matrix (MMPs), which are released and activated when the mineral content of the dentin is removed, either by a decay process or by conditioning with phosphoric acid, it can degrade the exposed collagen fibrils at the base of the hybrid layer[13,21]. Studies indicate that PA can inhibit the action of these enzymes[13,22], in addition to favoring the formation of collagen cross-links [23,24] increasing the stability of the collagen matrix and its resistance to enzymatic degradation[25].

This relationship observed between PA and the collagen matrix of dentin is time-dependent, that is, the longer the contact period between PA and demineralized collagen, the greater the amount of MMPs interacting with the solution and, consequently, the greater the inhibition of MMPs. The study by Al-Ammar et al.[14] indicated significant results in both the mechanical properties and the joint resistance of the adhesive interface after 10 and 60 minutes of treatment, despite the inherent benefit the required time is not clinically feasible. However, another study demonstrated that PA was able to inactivate MMPs even in extremely short periods of time, such as 5 seconds, but with better results when longer periods, 15 or 30 seconds, are used [22] . In the present study, the application of PA occurred for 30 seconds in order to obtain, virtually, better control of the dentin proteolytic activity.

Increasing collagen resistance to hydrolysis through its biomodification can be an effective alternative to improving the stability of the adhesive interface [26] . Natural and synthetic substances capable of increasing the number of intra and intermolecular peptide bonds, and collagen microfibrillar may be used for this purpose [23,27] . Thus, the use of PA can increase the stability of the adhesive interface, extending the period that the material remains obliterating the dental tubules, thus

increasing the duration of the effectiveness of the adhesive systems in controlling the HD.

However, despite the results of the laboratory studies indicate the viability of this relationship, it is still not possible to affirm that clinically significant alterations can be observed in the control of HD by the adhesive systems on surfaces previously treated by PA, other studies are still necessary to further clarify this process, increase the follow-up time of patients and work with a larger sample is interesting in this sense.

All the materials evaluated in the present study were clinically successful in controlling dental hypersensitivity, even in cases where the patient reported a more severe degree of pain, as it can be seen in Table 3. The relief obtained lasted during the 3 weeks of control after the materials were applied (Tables 3 and 4). However, Ferrari et al.[28] stated that even after 3 months of follow-up of patients who received the application of an adhesive system with a therapeutic purpose for HD, there was no recurrence. To identify whether proanthocyanidin was capable of increasing the stability of the adhesive interface a longer follow-up is necessary.

Since all the materials evaluated in this study presented a similar profile of effectiveness, it was not possible to confirm whether or not the presence of grape seed extract was determinant in the performance of the tested adhesive systems. However, no negative effect was due to the association of ESU with adhesive systems. The application of this extract to the adhesive systems proved to be effective and safe, thus providing support for future investigations that could better clarify the PA role of grape seed extract in the control of dental hypersensitivity.

4 Conclusion

It can be concluded that all the tested products were effective in immediate relief and within 3 weeks of dental hypersensitivity. Thus, grape seed extract can be associated with adhesives without compromising the efficacy of adhesion agents in the control of hypersensitivity.

References

1. Shiau HJ. Dentin hypersensitivity. J Evidence-Based Dental Practice 2012;12(3):220-8 doi: 10.1016/S1532-3382(12)70043-X
2. Bahsi E, Dalli M, Uzgur R, Turkal M, Hamidi MM, Colak H. An analysis of the aetiology, prevalence and clinical features of dentine hypersensitivity in a general dental population. Eur Rev Med Pharmacol Sci 2012;16(8):1107-16.
3. Hypersensitivity CABoD. Consensus-based recommendations for the diagnosis and management of dentin hypersensitivity. J Can Dent Assoc 2003;69(4):221-6.
4. Martens LC. A decision tree for the management of exposed cervical dentin (ECD) and dentin hypersensitivity (DHS). Clin Oral Investig 2013;17 Suppl 1:S77-83.
5. Pamir T, Dalgar H, Onal B. Clinical evaluation of three desensitizing agents in relieving dentin hypersensitivity. Oper Dent 2007;32(6):544-8 doi: 10.2341/07-5.
6. Samuel SR, Khatri SG, Acharya S. Clinical Evaluation of self and professionally applied desensitizing agents in relieving dentin hypersensitivity after a single topical application: a randomized controlled trial. J Clin Exp Dent 2014;6(4):e339-43 doi: 10.4317/jced.51439
7. LE G. The treatment of hypersensitive dentine. J Am Dental Assoc 1935;592-602.
8. Furiga A, Lonvaud-Funel A, Badet C. In vitro study of antioxidant capacity and antibacterial activity on oral anaerobes of a grape seed extract. Food Chem 2009;113(4):1037-40 doi: 10.1016/j.foodchem.2008.08.059
9. Maier T, Schieber A, Kammerer DR, Carle R. Residues of grape (Vitis vinifera L.) seed oil production as a valuable source of phenolic antioxidants. Food Chem 2009;112(3):551-9 doi: 10.1016/j.foodchem.2008.06.005
10. Toker H, Balci Yuce H, Lektemur Alpan A, Gevrek F, Elmastas M. Morphometric and histopathological evaluation of the effect of grape seed proanthocyanidin on alveolar bone loss in experimental diabetes and periodontitis. J Periodontal Res 2018;53(3):478-86.
11. Tang CF, Fang M, Liu RR, Dou Q, Chai ZG, Xiao YH, et al. The role of grape seed extract in the remineralization of demineralized dentine: micromorphological and physical analyses. Arch Oral Biol 2013;58(12):1769-76 doi: 10.1016/j.archoralbio.2013.09.007
12. Green B, Yao X, Ganguly A, Xu C, Dusevich V, Walker MP, et al. Grape seed proanthocyanidins increase collagen biodegradation resistance in the dentin/adhesive interface when included in an adhesive. J Dent 2010;38(11):908-15 doi: 10.1016/j.jdent.2010.08.004.
13. Sanon K, Sanchavanakit N, Srisawasdi S. Grape Seed Extract Reduces Active Gelatinases Using an Etch-and-Rinse Mode Universal Adhesive. J Adhes Dent 2019;21(2):159-65 doi: 10.3290/j.jad.a42306
14. Al-Ammar A, Drummond JL, Bedran-Russo AK. The use of collagen cross-linking agents to enhance dentin bond strength. J Biomed Mater Res B Appl Biomater 2009;91(1):419-24 doi: 10.1002/jbm.b.31417
15. Nagi SM, Hassan SN, Abd El-Alim SH, Elmissiry MM. Remineralization potential of grape seed extract hydrogels on bleached enamel compared to fluoride gel: an in vitro study. J Clin Exp Dent 2019;11(5):e401-e7 doi: 10.4317/jced.55556
16. Coelho MC, Sanchez PKV, Fernandes RR, Souza FPP, Siessere S, Bombonato-Prado KF. Effect of grape seed extract (GSE) on functional activity and mineralization of OD-21 and MDPC-23 cell lines. Braz Oral Res 2019;33:e013 doi: 10.1590/1807-3107bor-2019
17. Uchida A, Wakano Y, Fukuyama O, Miki T, Iwayama Y, Okada H. Controlled clinical evaluation of a 10% strontium chloride dentifrice in treatment of dentin hypersensitivity following periodontal surgery. J Periodontol 1980;51(10):578-81.
18. Davari A, Ataei E, Assarzadeh H. Dentin hypersensitivity: etiology, diagnosis and treatment; a literature review. J Dent (Shiraz) 2013;14(3):136-45.
19. Terry DA. Cervical dentin hypersensitivity: etiology, diagnosis, and management. Dent Today 2011;30(4):61-2.
20. Al-Sabbagh M, Brown A, Thomas MV. In-office treatment of dentinal hypersensitivity. Dent Clin North Am 2009;53(1):47-60. doi: 10.1016/j.cden.2008.11.003

21. Hebling J, Pashley DH, Tjäderhane L, Tay FR. Chlorhexidine arrests subclinical degradation of dentin hybrid layers in vivo. J Dent Res 2005;84(8):741-6 doi: 10.1177/154405910508400811

22. Delgado CC, Scheffel DLS. Scheffel RH, et al. Redução da atividade proteolítica da dentina após curtos períodos de aplicação de proantocianidina. Rev Odontol UNESP 2015;44(6):355-9 doi: 10.1590/1807-2577.02115

23. Castellan CS, Bedran-Russo AK, Karol S, Pereira PN. Long-term stability of dentin matrix following treatment with various natural collagen cross-linkers. J Mech Behav Biomed Mater 2011;4(7):1343-50 doi: 10.1016/j.jmbbm.2011.05.003

24. Silva AC, Melo P, Ferreira J, Oliveira S, Gutknecht N. Influence of grape seed extract in adhesion on dentin surfaces conditioned with Er,Cr:YSGG laser. Lasers Med Sci 2019 doi: 10.1007/s10103-019-02749-w.

25. Liu Y, Wang Y. Proanthocyanidins' efficacy in stabilizing dentin collagen against enzymatic degradation: MALDI-TOF and FTIR analyses. J Dent 2013;41(6):535-42 doi: 10.1016/j.jdent.2013.03.007

26. Bedran-Russo AK, Pashley DH, Agee K, Drummond JL, Miescke KJ. Changes in stiffness of demineralized dentin following application of collagen crosslinkers. J Biomed Mater Res B Appl Biomater 2008;86(2):330-4 doi: 10.1002/jbm.b.31022

27. Bedran-Russo AK, Pauli GF, Chen SN, McAlpine J, Castellan CS, Phansalkar RS, et al. Dentin biomodification: strategies, renewable resources and clinical applications. Dent Mater 2014;30(1):62-76 doi: 10.1016/j.dental.2013.10.012.

28. Ferrari M, Cagidiaco MC, Kugel G, Davidson CL. Clinical evaluation of a one-bottle bonding system for desensitizing exposed roots. Am J Dent 1999;12(5):243-9