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Evaluation of wettability of hesperidin incorporated dentin adhesive -an invitro study

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ABSTRACT

Introduction: Measuring the contact angle of a dental adhesive on dentin can provide valuable information about its wettability and bonding potential. A lower contact angle indicates that the adhesive has better wettability and is more likely to form a strong and durable bond with the dentin. Collagen fibres become gelatinized as a result of acid etching, which inhibits resin diffusion in interfibrillar gaps. As a result collagen fibres that aren't protected can then degrade. This degradation can be avoided by adding substances with collagen crosslinking and MMP inhibitory properties to total etch dentin adhesive.

Materials and methods: The commercially available Adper single bond 2 total etch adhesive was used as a parent material. Control group serves the plain adper single bond 2 and the experimental group was prepared by adding 2% of Hesperidin diluted in Dimethyl sulfoxide to adper single bond 2 . Slices of labial enamel were made using a hard tissue microtome. A micro-syringe was used to apply experimental and control total etch adhesives over a sectioned tooth specimen in order to measure the contact angle of the bonding agent with the tooth specimen using Ossila Goniometer. The results were subjected to SPSS software 23. Student independent t test was done to determine the significant difference between groups.

Results: The mean value of experimental group is 30.80 with a standard deviation of 3.389 and the mean value of control group is 37.02 with a standard deviation of 5.523 with p value 0.242 and 95% confidence interval. The mean values of the experimental group were lower when compared to the control group. This implies that the wettability of test group is better than the control group. However the results are statistically insignificant because of small sample size.

Conclusion: Hesperidin together with Dimethyl sulfoxide synergistically shows improved wettability of total etch adhesive compared to the control group.

Clinical Significance: Total etch dentin adhesive with hesperidin incorporation can reduce the risk of post-operative sensitivity, inhibit MMP activity, and offer a natural substitute for synthetic additives while also enhancing the bond strength between the composite restoration and the tooth.

Keywords: *Hesperidin, Flavonoid, Dentin bonding agent, Micro-organisms, Quality of life*

INTRODUCTION

Adhesion suggests a preliminary condition of physical and chemical interaction between the adherent and adhesive. By measuring the contact angle, it is possible to quantify the extent to which a liquid spreads on a surface, which is a measure of the wettability of surface1. The surface energy of the substrate must be greater than the surface tension of the adhesive in order to achieve high wettability. Microporosities are created on the tooth surface as a result of enamel conditioning with an etchant2. In essence, the surface energy of the enamel surface is increased by the development of microporosities. Thus the penetration of bonding agent into the enamel is made possible by the increase in surface energy of the enamel3. The histological characterisation of dentin demonstrates that it is an inhomogenous tissue since it is made up of two types of dentin, namely the intertubular and peritubular dentins with distinct mineral contents. In dentistry, the contact angle is frequently employed to assess a dental adhesive's capacity to moisten the dentin surface. The bonding agent will adhere better and form a stronger bond if it can spread readily and enter the dentin tubules, which is indicated by a low contact angle. A high contact angle, on the other hand, denotes poor wettability, which could lead to insufficient adhesive penetration and a weaker connection. Achieving high dentin wettability in restorative dentistry is crucial for the successful bonding of restorative materials like composite resins and cements4. The wettability of dentin can be improved, and the bond strength of restorative materials to dentin can be strengthened, using methods including acid-etching and the use of dentin bonding agents. Dentin is typically thought of as being hydrophilic, which means it has a significant affinity for polar solvents like water. This is because the dentin surface contains hydrophilic groups like hydroxyl and carboxyl groups5. Dentin bonding agents can increase the wettability of dentin by forming a micromechanical bond with the dentin surface. However, moisture on the dentin surface might obstruct the bonding procedure by lessening the wettability of bonding agent and preventing its entry into the dentinal tubules6. As a result, the bond between the bonding agent and the dentin may be weaker, which may limit the retention of the restoration and raise the possibility of post-operative discomfort or failure. In addition, total etch adhesives need the dentin surface to be entirely dry before application; any moisture left behind could interfere with the adhesive connection, weaken it, raise the chance that a patient would become more sensitive after procedure, or cause the restoration to fail. Dentin bonding agents frequently have hydrophilic monomers in them, which improve the ability of bonding agent to attract the dentin surface in presence of moisture7. Citrus fruits contain a flavonoid called hesperidin, which has been studied for its possible health advantages, including how it may affect tooth health especially in restorative dentistry8,9. The specific effects of hesperidin on dentin wettability, however, have received little attention in the literature. Hesperidin application to dentin surfaces may boost surface energy and enhance the wettability of dentin10. This is due to the molecule of hesperidin having hydrophilic groups, which may encourage the binding of water molecules to the dentin surface. By acting as a surface modifier, hesperidin may enhance the wettability of dentin11. It has been demonstrated to raise the surface energy of dentin and to encourage the wetting of dentin surfaces by water and other liquids. The hydroxyl groups on the flavonoid molecule, which can form hydrogen bonds with the dentin surface and raise its surface energy, may be the cause of this impact. The solvent DMSO, also known as dimethyl sulfoxide, has been investigated for its potential to increase the wettability of dentin bonding agents4. Due to its high boiling point and low viscosity, it can displace water molecules in the dentin and penetrate there, increasing surface energy and wettability. According to studies, using DMSO as a solvent or co-solvent with different adhesive monomers can increase the wettability of dentin and the bonding efficiency of dentin bonding agents. Additionally, it has been demonstrated that DMSO increases the penetration of adhesive resins into dentinal tubules, enhancing adhesion and bond strength. The purpose of this study is to evaluate the wettability of a total etch dentin adhesive that is incorporated with hesperidin and

DMSO. The findings of this study may open the door for additional investigation into the best strategy to provide and maximise the concentration of hesperidin in dental adhesive formulations in order to enhance quality of life by supplying long-lasting restorations. The null hypothesis is there is no change in wettability of flavonoid free and flavonoid incorporated total etch dentin adhesive. Our team has extensive knowledge and research experience that has translate into high quality publications12–21,22–26

MATERIALS AND METHODS

Preparation of Test adhesive solution

In dentin adhesive 2% of hesperidin (HPN) is incorporated (2 mg powder in 98 ml of bonding agent) . In this study, the total etch adhesive used was Adper single bond 2. Immediate bond strength is provided by 2% HPN by its natural crosslinking ability. Hesperidin was solubilized using dimethyl sulphoxide, a small amount of which was utilised as a solvent. 20 mg of hesperidin (Sigma-Aldrich) powder was directly dissolved in 0.025 ml of pure dimethyl sulfoxide. Adper Single Bond 2, an over-the-counter total etch dentin adhesive (3 M ESPE), served as the parent substance. The final concentration of 2% hesperidin in the total etch adhesive used was obtained by incorporating the Hesperidin/Dimethyl sulfoxide into Adper single bond 2 at the given ratio (20 mg of HPN in 1 ml of bonding agent).

Control group: Flavonoid(HPN)free adhesive

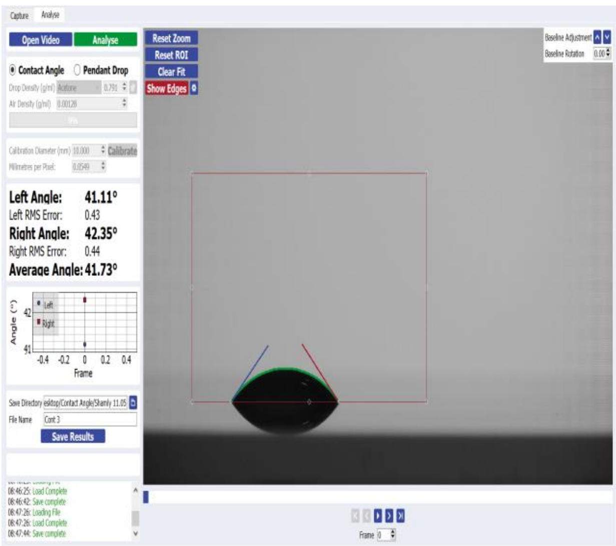
Test group: Flavonoid(HPN) incorporated adhesive (20mg HPN+0.025ml DMSO+ 1ml of Adper single bond 2)

Preparation of sample

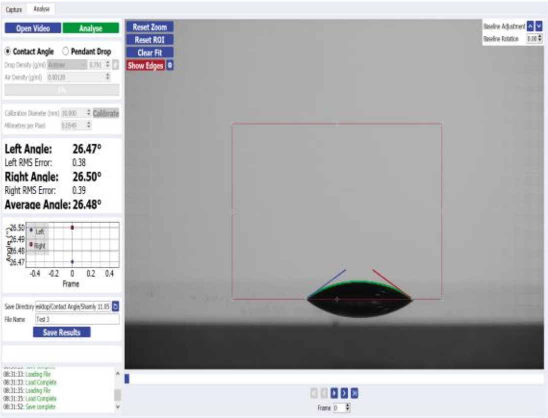
Slices of labial enamel were prepared using a hard tissue microtome (Leica SP1600 saw microtome).The teeth used are extracted teeth without any fillings or cavities that are advised for extraction for orthodontic purposes. To store the teeth until usage, the soft tissue was removed and they were placed in a 0.1% thymol solution at 4°C. The teeth were longitudinally sawed using the hard tissue microtome, to create labial enamel slices that were roughly 2x2mm in size. The enamel sections were cleaned using an ultrasonic cleaner with distilled water for 10 minutes to remove any debris or contaminants. The sections were dried with compressed air.

Contact angle measurement

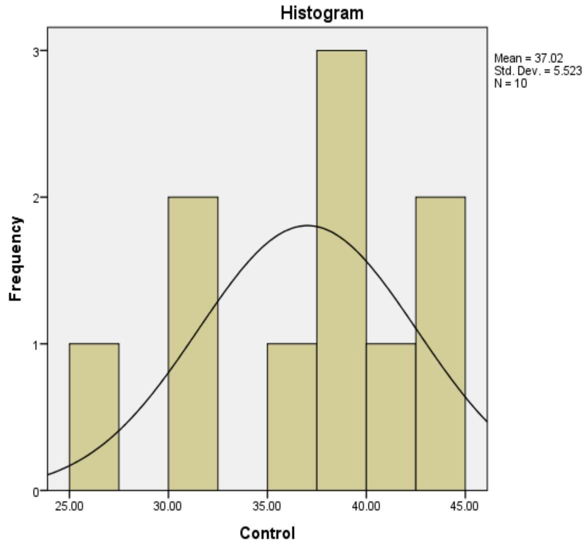
Each bonding agent is applied to the enamel portion with a little drop using a calibrated micro-syringe. Making sure that the enamel part is level and centered, the enamel section is placed onto the Ossila Goniometer stage. To position the camera over the drop of bonding chemical, the angle of the stage was changed. Photos were taken and examined using the built-in software of Ossila goniometer to ascertain contact angles of each drop. The contact angle is the angle created by the surface of the liquid to the tangent to the solid surface (in this case, the enamel section) at the point of contact. For each bonding agent, the process is repeated to guarantee the accuracy and consistency of the outcomes. Better wetting and adhesion are indicated by a lower contact angle. There were twenty readings total from twenty labial enamel slices, and the average mean of those readings provides the final value. The measured readings were analysed using statistical software SPSS 23. Mean and standard deviation data were calculated, and an independent t-test was carried out, to enable comparison between research groups.



Control group



Test group



Histogram chart representing the mean value of Control group

RESULTS

The mean value of experimental group is 30.80 with a standard deviation of 3.389 and the mean value of control group is 37.02 with a standard deviation of 5.523 with p value 0.242 and 95% confidence interval.

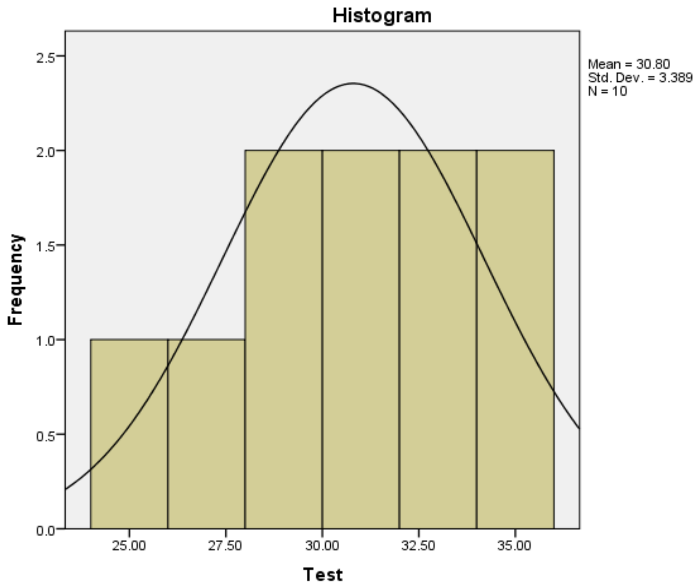
The mean values of the experimental group, are lower when compared to the control group. This implies that the wettability of test group is better than the control group. However the results are statistically insignificant.

Statistics

Control

N	Valid	10
	Missing	0
Mean		37.0240

Mean value of Control group



Histogram chart representing the mean value of Test group

Statistics

Test

N	Valid	10
	Missing	0
Mean		30.8010

Mean value of Test group

Group Statistics

	group	N	Mean	Std. Deviation	Std. Error Mean
value	1	10	37.0240	5.52278	1.74646
	2	10	30.8010	3.38907	1.07172

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
value	Equal variances assumed	1.467	.242	3.037	18	.007	6.22300	2.04907	1.91806	10.52794
	Equal variances not assumed			3.037	14.936	.008	6.22300	2.04907	1.85389	10.59211

Independent sample t test shows that there is difference between contact angle values of test and control groups which are statistically insignificant with 95% Confidence interval

DISCUSSION

In restorative dentistry, total etch dentin adhesives are frequently used for bonding composite resin to dentin. However, the wettability of the adhesive on dentin can impact the strength of the bond4,27. A lack of wettability might cause the adhesive to only partially penetrate the dentin, reducing bond strength and raising the possibility of marginal leakage. Known for their anti-inflammatory and antioxidant capabilities, flavonoids are a class of plant-based chemicals28. They have the ability to enhance the characteristics of dental materials, such as adhesives used in restorative dentistry. It has been demonstrated that adding flavonoids to total etch dentin adhesives enhances their wettability on dentin. This is due to the fact that flavonoids can interact with the hydroxyapatite in dentin to produce a more hydrophilic surface that enhances the adhesive's ability to wet29. Stronger and longer-lasting interactions may arise from this increased adhesive penetration into the dentin due to the greater wettability30.

Flavonoids have been demonstrated to have a number of advantageous impacts on the characteristics of dental adhesives, including enhanced bond strength and lower cytotoxicity, in addition to enhancing wettability31. To fully comprehend the potential of flavonoids in restorative dentistry and to maximise their absorption into dental materials, more research is nonetheless required. Matrix metalloproteinases (MMPs) like MMP-2, -3, -8, and -9 are present in mineralized dentin. The activation of salivary MMPs and/or collagen-bound MMPs by the use of etch-and-rinse adhesive components has also been linked to the degradation of resin-sparse collagen fibrils in aged bonded dentin in vivo32. The water "wet bonding" method, which was developed in the early 1990s to address the issue of collagen collapse following acid etching, enhanced resin infiltration into dentin that had undergone acid etching3,4. This bonding method maintains complete hydration of the acid-etched dentin during the bonding process.In order to make dentin adhesives more suitable for bonding to naturally moist, acid-etched dentin, manufacturers have included increasing amounts of hydrophilic and ionic monomers. Many dentin adhesives contain two-hydroxyethyl methacrylate (HEMA) to act as a solvent for non-water-compatible resin monomers, reduce phase separation of those monomers after evaporation of the volatile solvents, and improve the adhesives' wetting properties on acid-etched dentin33–35. Newer hydrophilic adhesives that form dentin bonds are vulnerable to pulpal pressure-induced fluid permeability, which accelerates dentin hydrolysis and reduces bond stability. By controlling non-catalytic domains allosterically, the application of cross-linking agents may help to silence MMP. In vitro tests showed that cross-linking agents increased the stability of the resin-dentin interface, decreased the susceptibility of additionally cross-linked dentin collagen to enzymatic degradation by collagenases, and improved the short-term mechanical properties of dentin collagen36.

The potential of several flavonoids to enhance the wettability of dentin bonding agents has been investigated. The following are some flavonoids that have demonstrated potential in this regard: Green tea contains a flavonoid called epigallocatechin-3-gallate (EGCG), which has been demonstrated to increase the wettability and binding strength of dentin bonding agents37. Research has revealed that the flavonoid quercetin, which is present in many fruits and vegetables, increases the wettability of dentin bonding agents31,38. The flavonoid kaempferol, which is present in tea, broccoli, and other plants, may increase the wettability and binding strength of dentin bonding agents39. Studies have demonstrated that the flavonoid fisetin, which is present in strawberries, apples, and other fruits, increases the wettability of dentin bonding agents. Overall, these flavonoids have demonstrated potential for enhancing the wettability and bond strength of dentin bonding agents, and they may have application in restorative dentistry3138. To fully realise their potential and maximise their inclusion into dental materials, more research is necessary.

Oranges, lemons, and grapefruits are among the citrus fruits that contain the most hesperidin, a flavonoid40. Hesperidin's potential to enhance the wettability of dentin bonding agents has not received much research, although some studies have suggested that it may possess special qualities that make it a suitable choice for usage in dental materials. Hesperidin is employed in this investigation to assess the bonding agent's wettability. Hesperidin's capacity to increase the bonding agent's wettability may have been aided by its special chemical structure, which includes a methoxy group and a rhamnose sugar moiety11,41. Hesperidin may play a dual role in enhancing the wettability of dentin bonding agents and suppressing MMP activity to increase their longevity42. Hesperidin may have special qualities that make it a good choice for enhancing the wettability and durability of dentin bonding agents, while more research is required to fully grasp its potential in dental materials. In this present study, Hesperidin incorporated total etch dentin adhesive shows improved wettability compared to control group. This is because , Hesperidin has the capacity to interact with the mineral hydroxyapatite, which makes up a portion of dentin, and this interaction may help bonding agents become more wettable. The methoxy group and rhamnose sugar moiety in hesperidin interact with the hydroxyapatite surface to provide a more hydrophilic surface, which improves the bonding agent's ability to wet surfaces. Stronger and longer-lasting bonding may arise from the adhesive penetrating the dentin more effectively as a result of the greater wettability. Hesperidin has also been demonstrated to block the activity of matrix metalloproteinases (MMPs), which can break down the collagen in dentin and weaken the bonds between dentin bonding agents. Hesperidin can assist maintain the integrity of the dentin-collagen matrix by decreasing MMP activity, which can strengthen and lengthen the bonding agent's durability. Overall, hesperidin may have the potential to enhance the wettability and durability of dentin bonding agents due to its capacity to interact with hydroxyapatite and decrease MMP activity43. Ghorab et al. (2018) examined the antimicrobial effectiveness and adhesive characteristics of a total-etch adhesive system containing varying concentrations of hesperidin (HPN), coming to the conclusion that doing so significantly increased the immediate Tensile Bond Strength (P 0.05). Thermocycling significantly reduced the TBS of dental adhesives with 0.5 wt % HPN incorporated, and the adhesive properties remained unaffected while the antibacterial impact was promising. In this study, 2% HPN is used as it has ability to improve immediate bond strength without causing marginal staining. Hesperidin also has many properties like Antiinflammatory, analgesic, antimicrobial, antioxidant, bone loss prevention, prevents demineralization and promotes remineralization apart from anticaries effect like preventing caries progression because of its collagen cross linking property, MMP inhibition and collagen cross linking property. In the present study there is no significant difference in wettability between control and test groups. This may be because of small sample size. However wettability of test group is better compared to the control group. The wettability of the bonding agent has also been increased by the dimethyl sulfoxide utilised as a solvent in this investigation.Thus Hesperidin together with Dimethyl sulfoxide synergistically shows improved wettability of total etch adhesive. To completely comprehend the mechanisms by which hesperidin regulates the wettability of bonding agents and to optimise its incorporation into dental materials, more study is nonetheless required.

CONCLUSION

In conclusion, the incorporation of hesperidin into dentin adhesive has been shown to improve its wettability. This is likely due to hesperidin's unique chemical properties, which enable it to interact with hydroxyapatite and create a more hydrophilic surface. These findings suggest that hesperidin has potential as a natural additive to enhance the performance of dentin adhesive, and further research is warranted to explore its full potential in dental applications.

REFERENCES

1. Law K-Y, Zhao H. Surface Wetting: Characterization, Contact Angle, and Fundamentals. Springer, 2015.
2. Lopes GC, Perdigão J, Baptista D, et al. Does a Self-etching Ceramic Primer Improve Bonding to Lithium Disilicate Ceramics? Bond Strengths and FESEM Analyses. Oper Dent 2019; 44: 210–218.
3. Katyal D, Subramanian AK, Venugopal A, et al. Assessment of Wettability and Contact Angle of Bonding Agent with Enamel Surface Etched by Five Commercially Available Etchants: An In Vitro Study. Int J Dent 2021; 2021: 9457553.
4. Stape THS, Uctasli M, Cibelik HS, et al. Dry bonding to dentin: Broadening the moisture spectrum and increasing wettability of etch-and-rinse adhesives. Dent Mater 2021; 37: 1676–1687.
5. Patil DRD. DENTIN BONDING AGENTS. Blue Rose Publishers, 2022.
6. Garg N, Garg A. Textbook of Operative Dentistry. Boydell & Brewer Ltd, 2010.
7. Ponnaappa KCD, Rao RN. Shear bond strength of 4th & 5th generation dentin bonding agents in the presence and absence of moisture. An in vitro study. Indian J Dent Res 2002; 13: 147–157.
8. Leal I de C, Rabelo CS, Viana ÍEL, et al. Hesperidin reduces dentin wear after erosion and erosion/abrasion cycling in vitro. Arch Oral Biol 2021; 129: 105208.
9. Islam SM, Hiraishi N, Nassar M, et al. In vitro effect of hesperidin on root dentin collagen and de/re-mineralization. Dent Mater J 2012; 31: 362–367.
10. Al-Gerny Y-A, Ghorab S-M, Soliman T-A. Bond strength and elemental analysis of oxidized dentin bonded to resin modified glass ionomer based restorative material. J Clin Exp Dent 2019; 11: e250–e256.
11. Xia H-Q, Gu T, Fan R, et al. Comparative investigation of bioflavonoid electrocatalysis in 1D, 2D, and 3D carbon nanomaterials for simultaneous detection of naringin and hesperidin in fruits. RSC Adv 2022; 12: 6409–6415.
12. Malli Sureshbabu N, Selvarasu K, V JK, et al. Concentrated Growth Factors as an Ingenious Biomaterial in Regeneration of Bony Defects after Periapical Surgery: A Report of Two Cases. Case Rep Dent 2019; 2019: 7046203.
13. Ahad M, Gheena S. Awareness, attitude and knowledge about evidence based dentistry among the dental practitioner in Chennai city. J Adv Pharm Technol Res 2016; 9: 1863.
14. PradeepKumar AR, Shemesh H, Jothilatha S, et al. Diagnosis of Vertical Root Fractures in Restored Endodontically Treated Teeth: A Time-dependent Retrospective Cohort Study. J Endod 2016; 42: 1175–1180.
15. Jangid K, Alexander AJ, Jayakumar ND, et al. Ankyloglossia with cleft lip: A rare case report. J Indian Soc Periodontol 2015; 19: 690–693.
16. Kumar A, Sherlin HJ, Ramani P, et al. Expression of CD 68, CD 45 and human leukocyte antigen-DR in central and peripheral giant cell granuloma, giant cell tumor of long bones, and tuberculous granuloma: An immunohistochemical study. Indian J Dent Res 2015; 26: 295–303.
17. Manohar J, Abilasha R. A Study on the Knowledge of Causes and Prevalance of Pigmentation of Gingiva among Dental Students. Indian Journal of Public Health Research & Development 2019; 10: 95.
18. Sekar D, Mani P, Biruntha M, et al. Dissecting the functional role of microRNA 21 in osteosarcoma. Cancer Gene Ther 2019; 26: 179–182.
19. Girija SA, Jayaseelan VP, Arumugam P. Prevalence of VIM- and GIM-producing Acinetobacter baumannii from patients with severe urinary tract infection. Acta Microbiol Immunol Hung 2018; 65: 539–550.
20. Maheswari TNU, Venugopal A, Sureshbabu NM, et al. Salivary micro RNA as a potential biomarker in oral potentially malignant disorders: A systematic review. Ci Ji Yi Xue Za Zhi 2018; 30: 55–60.
21. Subashri A, Maheshwari TNU. Knowledge and attitude of oral hygiene practice among dental

students. J Adv Pharm Technol Res 2016; 9: 1840.
22. Sridharan G, Ramani P, Patankar S, et al. Evaluation of salivary metabolomics in oral leukoplakia and oral squamous cell carcinoma. J Oral Pathol Med 2019; 48: 299–306.
23. Ezhilarasan D, Apoorva VS, Ashok Vardhan N. Syzygium cumini extract induced reactive oxygen species-mediated apoptosis in human oral squamous carcinoma cells. J Oral Pathol Med 2019; 48: 115–121.
24. Mathew MG, Samuel SR, Soni AJ, et al. Evaluation of adhesion of Streptococcus mutans, plaque accumulation on zirconia and stainless steel crowns, and surrounding gingival inflammation in primary molars: randomized controlled trial. Clin Oral Investig 2020; 24: 3275–3280.
25. Vijayashree Priyadharsini J. In silico validation of the non-antibiotic drugs acetaminophen and ibuprofen as antibacterial agents against red complex pathogens. J Periodontol 2019; 90: 1441–1448.
26. Chandrasekar R, Chandrasekhar S, Sundari KKS, et al. Development and validation of a formula for objective assessment of cervical vertebral bone age. Prog Orthod 2020; 21: 38.
27. Mirzaei K, Ahmadi E, Rafeie N, et al. The effect of dentin surface pretreatment using dimethyl sulfoxide on the bond strength of a universal bonding agent to dentin. BMC Oral Health 2023; 23: 250.
28. Andersen OM, Markham KR. Flavonoids: Chemistry, Biochemistry and Applications. CRC Press, 2005.
29. Montone AMI, Papaianni M, Malvano F, et al. Lactoferrin, Quercetin, and Hydroxyapatite Act Synergistically against. Int J Mol Sci; 22. Epub ahead of print 26 August 2021. DOI: 10.3390/ijms22179247.
30. Rudawska A. Adhesives: Applications and Properties. BoD – Books on Demand, 2016.
31. Epasinghe DJ. Applications of Proanthocyanidin in Dentistry. Open Dissertation Press, 2017.
32. Wang H, Guo Z, Liu P, et al. Luteolin ameliorates cornea stromal collagen degradation and inflammatory damage in rats with corneal alkali burn. Exp Eye Res 2023; 231: 109466.
33. Balkaya H, Demirbuğa S. Evaluation of six different one-step universal adhesive systems in terms of dentin bond strength, adhesive interface characterization, surface tension, contact angle, degree of conversion and solvent evaporation after immediate and delayed use. J Esthet Restor Dent 2023; 35: 479–492.
34. Botelho MPJ, Isolan CP, Schwantz JK, et al. Rubbing time and bonding performance of one-step adhesives to primary enamel and dentin. J Appl Oral Sci 2017; 25: 523–532.
35. Ahmed MH, Yoshihara K, Yao C, et al. Multiparameter evaluation of acrylamide HEMA alternative monomers in 2-step adhesives. Dent Mater 2021; 37: 30–47.
36. Mazzoni A, Angeloni V, Comba A, et al. Cross-linking effect on dentin bond strength and MMPs activity. Dent Mater 2018; 34: 288–295.
37. Hardan L, Daood U, Bourgi R, et al. Effect of Collagen Crosslinkers on Dentin Bond Strength of Adhesive Systems: A Systematic Review and Meta-Analysis. Cells; 11. Epub ahead of print 4 August 2022. DOI: 10.3390/cells11152417.
38. Dávila-Sánchez A, Gutierrez MF, Bermudez JP, et al. Influence of flavonoids on long-term bonding stability on caries-affected dentin. Dent Mater 2020; 36: 1151–1160.
39. Yamazaki S. Inhibitory Effect of Kaempferol on Skin Fibrosis in Systemic Sclerosis by the Suppression of Oxidative Stress. 2017.
40. Gupta A, Al-Aubaidy HA, Narkowicz CK, et al. Analysis of Citrus Bioflavonoid Content and Dipeptidyl Peptidase-4 Inhibitory Potential of Commercially Available Supplements. Molecules; 27. Epub ahead of print 25 July 2022. DOI: 10.3390/molecules27154741.
41. Jaiswal AK. Nutritional Composition and Antioxidant Properties of Fruits and Vegetables. Academic Press, 2020.
42. Kim KM, Im A-R, Lee JY, et al. Hesperidin Inhibits UVB-Induced VEGF Production and Angiogenesis via the Inhibition of PI3K/Akt Pathway in HR-1 Hairless Mice. Biol Pharm Bull 2021; 44: 1492–1498.
43. Beck F, Ilie N. Antioxidants and Collagen-Crosslinking: Benefit on Bond Strength and Clinical Applicability. Materials ; 13. Epub ahead of print 1 December 2020. DOI: 10.3390/ma13235483.