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EVALUATION OF *PSIDIUM GUAJAVA* LEAF EXTRACT AS MATRIX METALLOPROTEINASE-9 INHIBITOR FOR ENHANCED DENTIN PRESERVATION IN COMPOSITE RESTORATIONS: AN IN-VITRO STUDY

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ABSTRACT: The bond strength at the dentin-adhesive interface diminishes over time due to hydrolytic degradation of dentin collagen, which weakens the interface stability. Inhibiting collagen-degrading enzymes, such as matrix metalloproteinases (MMPs), particularly MMP-9, can enhance bond durability by protecting collagen fibers within the adhesive layer, thus prolonging the lifespan of the restoration. Psidium guajava extract has anti-inflammatory properties, but its role as an MMP-9 inhibitor is yet to be explored. This study examines the inhibitory effect of *Psidium guajava* extract on MMP-9 activity to enhance the longevity of composite restorations. Dried Psidium guajava leaves were used to prepare an ethanol extract. Fifteen freshly extracted teeth were collected and stored at 4 °C. Human dentin samples were demineralized with 10% phosphoric acid and treated with 2% chlorhexidine (positive control),*Psidium guajava extract at* 100 µg *and Psidium guajava extract at* 200µg. The enzymatic activity was measured using ELISA, with absorbance values recorded, and statistical analysis was conducted via ANOVA and post hoc tests.Sample size was determined based on previous in-vitro studies evaluating dentin MMP activity. The control group showed MMP-9 activity at 106.5 pg/mL. Psidium guajava extract at 100 µg reduced MMP-9 activity by 16.61% to 87.4 pg/mL. The 200 µg dose further reduced MMP-9 activity by 36.2% to 68.2 pg/mL. The p-value was $p < 0.05$, indicating statistical significance. This reflects the differences in MMP activity due to the treatments applied. The study demonstrates that Psidium guajava is an effective MMP-9 inhibitor in human dentin, exhibiting a dose-dependent reduction in MMP-9 activity. These findings suggest that Psidium guajava extract could be a natural therapeutic agent in dental restorations to prevent collagen degradation.

Keywords: chlorhexidine, ELISA, human dentin, MMP-9, Psidium guajava.

1. INTRODUCTION:Matrix metalloproteinases (MMPs) are a family of zinc-dependent endopeptidases responsible for degrading extracellular matrix components, including collagen, elastin, and gelatin[1,2].These enzymatic activities are thought to play a crucial role in maintaining the structural integrity of dentin and in the tissue's response to external stimuli[2].When exposed to variations in pH, the altered microenvironment may influence the activity of matrix metalloproteinases (MMPs) and other enzymes within the dentin matrix[3].This could lead to the modulation of collagen breakdown and the remodeling processes, which are important in physiological and pathological conditions, such as during caries progression or following restorative procedures[4,5]. Furthermore, the breakdown of the hybrid layer due to MMP activation is not an immediate process but occurs gradually over time. This degradation can lead to restoration failures. Factors such as bacterial infiltration, changes in oral pH, and enzymatic activity in the oral environment can exacerbate this degradation[6].

In recent years, there has been increasing interest in identifying inhibitors of MMPs that could be used to preserve the integrity of the dentin collagen matrix and enhance the success of dental restorations[7]. Studies have shown promising results, with certain MMP inhibitors, such as chlorhexidine, tetracyclines, and synthetic peptides, effectively reducing collagen breakdown and thereby enhancing the durability and performance of adhesive restorations[8(1)]. Integrating MMP inhibitors into dental treatments represents a promising advancement in adhesive dentistry, aiming to counteract the enzymatic degradation of the dentin matrix. By effectively inhibiting collagenolytic activity, these inhibitors protect the hybrid layer from deterioration, thereby maintaining bond strength and reducing the risk of restoration failure over time[9]. In addition to extending the longevity of restorations, MMP inhibitors may also help in minimizing postoperative sensitivity and microleakage, which are often linked to compromised bonding[10].

Chlorhexidine is the most studied MMP inhibitor and has demonstrated the most efficient effectiveness in preserving the collagen structure within the hybrid layer. Still, its long-term stability remains a concern due to its large, water-soluble nature[11].Over time, chlorhexidine may leach out of the hybrid layer, reducing its protective effects[8(2)]. Studies have shown that while collagen activity can be preserved for up to six months, the hybrid layer's integrity degrades after one year[12]. Additionally, studies have indicated that chlorhexidine exhibits cytotoxic effects on odontoblast-like cells and stem cells derived from human exfoliated deciduous teeth, emphasizing the need to consider chlorhexidine's use in dentistry[13]. This highlights the need to develop more stable, long-lasting inhibitors or alternative approaches that protect against enzymatic degradation, ensuring longer-lasting dental restorations.

In recent years, plant extracts and traditional treatments have gained widespread popularity. Research has shown that Grape seed extract, green tea extract, cranberry extract have been utilized as natural inhibitors of matrix metalloproteinases (MMPs), targeting enzymatic activity responsible for collagen degradation and contributing to the preservation of tissue integrity in dental and medical applications[3,14-16].*Psidium guajava*, commonly known as guava, is a tropical fruit extensively used in traditional medicine across various cultures[17(3)]. *Psidium guajava leaves* are rich in bioactive compounds such as flavonoids, tannins, and terpenoids, which are known for their anti-inflammatory, antimicrobial, and antioxidant properties[18,19].Previous studies have demonstrated that the bioactive compounds in *Psidium guajava* can inhibit various enzymatic activities[17,18,20].This study explores the potential of *Psidium guajava* leaf extract as an MMP inhibitor, specifically in human dentin. By evaluating its efficacy in vitro, we aim to determine whether Psidium guajava can be developed as a natural adjunct in dental treatments to protect the collagen matrix and improve the longevity of restorations.

2. MATERIALS AND METHODS :

2.1 Preparation of *Psidium guajava* Extract: Fresh leaves from mature guava plants were collected to ensure the highest concentration of bioactive compounds. They were thoroughly washed with sterile water to remove dirt and contaminants, and then air-dried for 10 days under sunlight to preserve the integrity of the phytochemicals. The dried leaves were then finely ground into a powder using a mechanical grinder. This powder was subjected to ethanol extraction, effectively isolating the active components, particularly flavonoids and tannins, known for their potential MMP inhibitory properties. The ethanol extraction process involved mixing the powdered leaves with ethanol in a specific ratio, followed by continuous stirring for 48 hours at room temperature to maximize the extraction efficiency. The mixture was then filtered to remove any solid residues, and the filtrate was concentrated using a rotary evaporator at reduced pressure to remove the ethanol, yielding a concentrated guava extract. This concentrated extract was stored at -20°C to preserve its bioactivity until further use in the experiments.

2.2 Collection and Preparation of Human Dentin Samples: Human dentin samples were meticulously prepared to provide a reliable substrate for the in vitro analysis. Fifteen freshly extracted premolars, collected for orthodontic purposes, were stored at 4°C until use. Informed consent was obtained from the patients, ensuring compliance with ethical standards in research. Once collected, the teeth were cleaned to remove any remaining soft tissue and then sectioned using a diamond saw. The dentin was separated from the enamel and pulp, and subsequently ground into a fine powder using a mechanical mill (Retsch ZM200) operating at 6000 rpm for 5 minutes. This process ensured uniformity in the dentin samples, providing a consistent surface area for the subsequent experimental treatments. Sample size was determined based on previous in-vitro studies evaluating dentin MMP activity.

2.3 Demineralization of Dentin Powder: The powdered dentin was demineralized to expose the collagen matrix, the substrate for matrix metalloproteinase (MMP) activity. This was achieved by mixing the dentin powder with 10% phosphoric acid, a common demineralizing agent in dental research. Phosphoric acid effectively dissolves the mineral components of dentin, primarily hydroxyapatite. The demineralization process was carefully monitored to ensure the complete removal of the mineral content while preserving the organic matrix. After demineralization, the acidic environment was neutralized by adding 1 M sodium hydroxide (NaOH). This step was crucial in restoring the pH to neutral (approximately 7.0), creating an environment similar to physiological conditions, which is necessary for accurately assessing MMP activity. The neutralized dentin powder was then thoroughly rinsed with distilled water to remove residual acid or base and dried under sterile conditions.

2.4 Experimental Group Design: The study was designed to evaluate the inhibitory effects of Psidium guajava extract on MMP activity in human dentin, with three distinct groups established for comparison. The first group, the positive control group, was treated with chlorhexidine, a well-known synthetic MMP inhibitor commonly used in dental research to validate the experimental model. The other two groups, designated as test groups, were treated with different concentrations of Psidium guajava extract (100 µg and 200 µg, respectively). These concentrations were selected based on preliminary studies that indicated their potential effectiveness in inhibiting MMP activity. Each group of dentin powders was incubated in phosphate-buffered saline (PBS) at 37°C for 24 hours, a temperature that simulates the human body's conditions. This incubation period allowed the extract or control solutions to interact with the exposed collagen matrix, facilitating the evaluation of their effects on MMP activity

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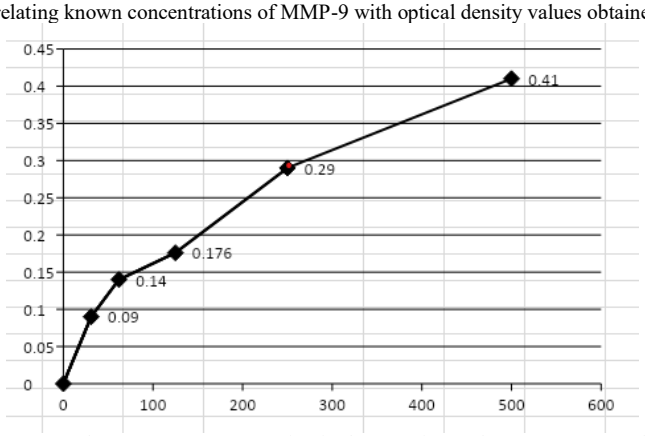
2.5 Measurement of MMP Activity: To quantitatively assess MMP-9 activity in the treated dentin samples, commercially available enzyme-linked immunosorbent assay (ELISA) kits specific to MMP-9 were utilized. ELISA is a sensitive and specific method for detecting and quantifying proteins, making it ideal for measuring MMP activity in this context. After the 24-hour incubation, the supernatants from each sample group were collected and subjected to the ELISA procedure. The assay involved binding MMP-9 present in the samples to specific antibodies coated on the microplate wells, followed by a series of reactions that produce a color change proportional to the amount of MMP-9. The intensity of the color was measured as absorbance using a microplate reader at a specific wavelength. The absorbance values were recorded, allowing for the quantification of MMP-9 activity in each sample group.

2.6 Data Analysis: The absorbance data obtained from the ELISA were statistically analyzed to determine the significance of the differences in MMP activity between the control and test groups. The data were expressed as mean ± standard deviation (SD) to account for variability within each group. Statistical comparisons were made using one-way analysis of variance (ANOVA), a robust statistical method for comparing means across multiple groups. Post hoc tests, such as Tukey's, were employed to identify specific group differences. The level of statistical significance was set at $p < 0.05$, meaning that any differences observed with a p-value below this threshold were considered statistically significant. This rigorous statistical approach ensured that the conclusions drawn from the study were reliable and reflective of actual differences in MMP activity due to the treatments applied.

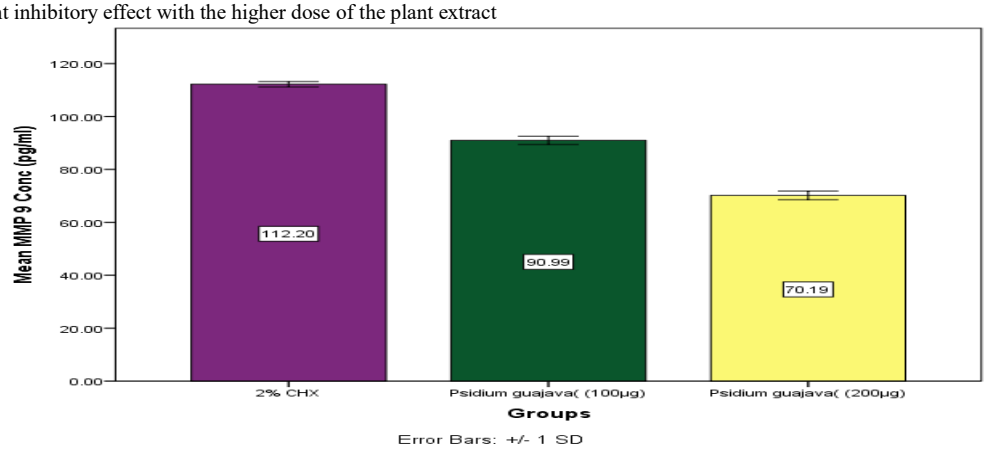
3. RESULTS: This study clearly demonstrated dose-dependent inhibition of MMP-9, indicating that higher concentrations of Psidium guajava lead to more significant inhibition of MMP-9 activity in the dentin samples. The standard curve was generated by correlating known concentrations of MMP-9 (expressed in pg/mL) with the optical density (OD) values obtained through ELISA (Enzyme-Linked Immunosorbent Assay). Graph 1 illustrates this curve, which determines MMP-9 levels in treated samples by comparing their OD values to the curve. The graph demonstrates a linear relationship between MMP-9 concentration and OD values, showing that absorbance increases proportionally with MMP-9 concentration.

3.1 Graph 1 - ELISA Standard Curve

The standard curve was established by correlating known concentrations of MMP-9 with optical density values obtained from ELISA.



3.2 Graph 2 - Bar Graph Of MMP-9 Levels: It values MMP-9 concentration in the experimental groups. Group 2 demonstrated a 16.65% reduction compared to the control, suggesting that even at lower concentrations, the plant extract exhibits significant MMP-9 inhibiting properties. Group 3 showed a 36.2% reduction, indicating a more potent inhibitory effect with the higher dose of the plant extract



Graph 2- The bar chart illustrates the MMP-9 concentrations (in pg/mL) across different treatment groups, including the control (chlorhexidine) group and the two test groups treated with 100 µg and 200 µg of Psidium guajava extract.

The data presented in Table 1 indicate that Psidium guajava demonstrates a dose-dependent inhibitory effect on MMP-9 concentrations, with higher dosages correlating with progressively lower MMP-9 levels. The standard error of the mean (SEM) values provides a quantitative assessment of the precision of the mean estimates, with relatively low SEMs signifying robust statistical reliability and confidence in the reported data.

Groups	Mean±SD	Oneway- ANOVA
2% CHX	112.20±1.018	0.000
Psidium guajava((100µg)	90.99±1.580	
Psidium guajava((200µg)	70.18±1.642	

Table 1: Mean and standard deviation and One way ANOVA with percent inhibition of MMP-9 for three groups

(I) Groups	(J) Groups	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
2% CHX	Psidium guajava(100µg)	21.20800*	.64458	.000	19.6098	22.8062
	Psidium guajava(200µg)	42.01300*	.64458	.000	40.4148	43.6112
Psidium guajava(100µg)	2% CHX	-21.20800*	.64458	.000	-22.8062	-19.6098
	Psidium guajava(200µg)	20.80500*	.64458	.000	19.2068	22.4032
Psidium guajava(200µg)	2% CHX	-42.01300*	.64458	.000	-43.6112	-40.4148
	Psidium guajava(100µg)	-20.80500*	.64458	.000	-22.4032	-19.2068
*. The mean difference is significant at the 0.05 level.						

Table 2: one way ANOVA analysis for 3 groups.

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These findings confirm that both concentrations of Psidium guajava extract significantly reduced MMP-9 activity compared with the positive control group, and the higher concentration exhibited significantly greater inhibition than the lower concentration.

4. DISCUSSION

A successful outcome in adhesive dentistry signifies achieving durable and aesthetically pleasing restorations that maintain their integrity over time. It relies on strong bonding between the restorative material and tooth structure. However, evidence suggests that achieving long-term durability in resin-dentin bonding remains a challenge[21].The stability of the adhesive interface is compromised over time primarily due to the hydrolytic degradation of adhesive monomers within the hybrid layer. As a result, the exposed, unprotected demineralized collagen fibrils become vulnerable to enzymatic breakdown by host-derived matrix metalloproteinases (MMPs) and cathepsins. This proteolytic activity weakens the hybrid layer's structural integrity, undermining the durability and success of adhesive restorations[21,22].

Matrix metalloproteinases (MMPs) are a family of enzymes that play a significant role in the remodeling and degradation of the extracellular matrix (ECM), including in the dentin organic matrix. MMP-2, MMP-8, MMP-9, MMP-13, and MMP-20 are commonly found in dentin, with MMP-2 and MMP-9 being the most abundant forms[23].MMP-9 plays a key role in the degradation of the extracellular matrix, including collagen, during dental caries and after restorative procedures[22]. Several studies showed that the inhibition of MMP-9 enhanced the bond strength and longevity of dental restorations[24,25,26].

Currently, chlorhexidine is the most explored MMPs inhibitor. It functions as a non-specific inhibitor, altering their three-dimensional structure and chelating the metal ions (Ca^{2+}, Zn^{2+}) required to activate their enzymatic activity. Even at low concentrations, such as 0.02%, chlorhexidine effectively inactivates all MMPs in dentin[27]. The binding mechanism of chlorhexidine to dentin is mainly electrostatic, raising concerns that cations from dentinal fluid or saliva may displace chlorhexidine, thereby reducing its anti-proteolytic action. This could explain the findings of Breschi et al, where it was observed that chlorhexidine preserves the stability of the resin-dentin bond for only up to 6 months, but after1 year, it starts degrading.

Tjäderhane et al. explained that chlorhexidine is water soluble and has a large molecule that may leach out of the hybrid layer[1]. Recent in vitro studies have also shown its cytotoxicity effect in deciduous teeth[13]. Benzalkonium chloride is another popular synthetic MMP inhibitor. It also inhibits enzyme activity immediately and over extended periods, but eventually, it showed increased gelatinolytic activity and a decline in bond strength[27]. Barcellos et al. used Zinc salts as MMP inhibitors and observed a 6- month lasting bond strength[28]. In another study, Almeida et al observed the high solubility of zinc salts, which may undergo high solubility in the oral cavity over time[29]. Additionally, synthetic inhibitors are as effective as MMP inhibitors, but their drawbacks, such as cytotoxicity and interference with resin bonding, necessitate alternative solutions.

The results of the present study suggest that *Psidium guajava* extract has a significant inhibitory effect on MMP-9 activity in human dentin, supporting its potential as a natural agent for preventing dentin degradation during restorative dental procedures. These findings align with previous studies that have explored the bioactive properties of guava extracts, particularly their antimicrobial, anti-inflammatory, and antioxidant effects, which are vital for maintaining the structural integrity of dentin[30,31].In literature, the use of green tea extract, which shares some biochemical properties with *Psidium guajava*, was found to significantly reduce MMP activity[32,33]. In addition to green tea, propolis extract, a resinous substance produced by bees, has been studied for its ability to inhibit MMPs. Propolis has shown promise due to its rich composition of flavonoids and phenolic compounds, which are also present in *Psidium guajava.* Oliveira et al investigated the effect of Brazilian green propolis. They found that it significantly reduced MMP activity, especially MMP-2 and MMP-9, suggesting that its effects are comparable to those of *Psidium guajava.*[34]

The results from this study demonstrate a clear dose-dependent reduction in MMP-9 activity with increasing concentrations of *Psidium guajava*, likely due to the presence of bioactive compounds such as flavonoids, tannins, and phenolic acids in the guava extract. These compounds have been documented in several studies to possess inhibitory effects on enzymes like MMP-9 by modulating inflammatory pathways and directly binding to active sites of the enzyme, thereby reducing its activity[17,35].

Its natural origin and demonstrated inhibitory effects on MMP-9 position it as a promising candidate for developing biocompatible adhesive systems. Psidium guajava extract could offer a more patient-friendly option with fewer side effects and better biocompatibility. Furthermore, the presence of antioxidant properties in guava could provide additional benefits by neutralizing free radicals, which also contribute to the degradation of the adhesive interface

5. Conclusion

The study demonstrates that Psidium guajava is an effective MMP-9 inhibitor in human dentin, exhibiting a dose-dependent reduction in MMP-9 activity. These findings suggest that Psidium guajava extract could be a natural therapeutic agent in dental restorations to prevent collagen degradation. Further research, particularly clinical trials, is needed to validate these findings and explore broader applications in dental care.

AUTHORS CONTRIBUTIONS

K. Esha Gayathri : Literature search, data collection, analysis, manuscript drafting.
Aparna ME: Aided in conception of the topic, has participated in the study design, statistical analysis and has supervised in preparation and final correction of the manuscript.

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CONFLICT OF INTEREST

The author declares that there were no conflicts of interest in the present study.

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6. References

1. Tjäderhane L. Dentin bonding: can we make it last? Oper Dent. 2015;40:4–18.
2. Sorsa T, Tjäderhane L, Salo T. Matrix metalloproteina ses (MMPs) in oral diseases. Oral Dis. 2004;10:311–8.
3. Anumula L, Ramesh S, Kolaparthi VSK, Kirubakaran R, Karobari MI, Arora S, et al. Role of Natural Cross Linkers in Resin-Dentin Bond Durability: A Systematic Review and Meta-Analysis. Mater Basel Switz. 2022;15:5650.
4. Jain A, Bahuguna R. Role of matrix metalloproteinases in dental caries, pulp and periapical inflammation: An overview. J Oral Biol Craniofacial Res. 2015;5:212–8.

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Vol. 36 Issue 2, 2026, Pages 1366-1369

5. Anumula L, Ramesh S, Kolaparthi VSK. Matrix metalloproteinases in dentin: Assessing their presence, activity, and inhibitors - a review of current trends. Dent Mater Off PublAcad Dent Mater. 2024 ;40:2051–73.
6. Perarivalan I, Karunakaran J, Anbalagan N, Harishma S, Prasad V. Matrix metalloproteinase inhibitors in restorative dentistry. J Conserv Dent Endod. 2024;27:566–71.
7. Kumar GB, Nair BG, Perry JJP, Martin DBC. Recent insights into natural product inhibitors of matrix metalloproteinases. MedChemComm. 2019 ;10:2024–37.
8. Breschi L, Mazzoni A, Nato F, Carrilho M, Visintini E, Tjäderhane L, et al. Chlorhexidine stabilizes the adhesive interface: a 2-year in vitro study. Dent Mater Off PublAcad Dent Mater. 2010;26:320–5.
9. Yaghmoor RB, Jamal H, Abed H, Allan E, Ashley P, Young A. Incorporation of MMP inhibitors into dental adhesive systems and bond strength of coronal composite restorations: A systematic review and meta-analysis of in vitro studies. Jpn Dent Sci Rev. 2022;58:298–315.
10. Salama F, Balto H, Al-Yahya F, Al-Mofareh S. The effect of cavity disinfectants on microleakage of composite restorations in primary teeth. Eur J Paediatr Dent. 2015;16:295–300.
11. Nagpal M, Taneja S, Kumar M, Dudeja C. Evaluation of the effect of natural versus synthetic matrix metalloproteinase silencers in preservation of dentin collagen and long-term bond strength of total etch adhesive. J Conserv Dent JCD. 2020;23:221–6.
12. Francisconi-dos-Rios LF, Casas-Apayco LC, Calabria MP, Francisconi PAS, Borges AFS, Wang L. Role of chlorhexidine in bond strength to artificially eroded dentin over time. J Adhes Dent. 2015;17:133–9.
13. Tu YY, Yang CY, Chen RS, Chen MH. Effects of chlorhexidine on stem cells from exfoliated deciduous teeth. J Formos Med Assoc Taiwan Yi Zhi. 2015;114:17–22.
14. Wang Y, Green A, Yao X, Liu H, Nisar S, Gorski JP, et al. Cranberry Juice Extract Rapidly Protects Demineralized Dentin against Digestion and Inhibits Its Gelatinolytic Activity. Mater Basel Switz. 2021;14:3637.
15. A L, Ramesh S, Kolaparthi VSK, Ch Nv M, Kvl SR, Mandava D. Natural Polyphenols From Moringa and Centella Extracts as Collagen Cross-Linkers and Matrix Metalloproteinase (MMP) Inhibitors in Dentin Preservation: An In Vitro Study. Cureus. 2023;15:e48530.
16. Nandakumar M, Nasim I. Comparative evaluation of grape seed and cranberry extracts in preventing enamel erosion: An optical emission spectrometric analysis. J Conserv Dent JCD. 2018;21:516–20.
17. Ravi K, Divyashree P. Psidium guajava: A review on its potential as an adjunct in treating periodontal disease. Pharmacogn Rev. 2014 ;8:96–100.
18. Lok B, Babu D, Tabana Y, Dahham SS, Adam MAA, Barakat K, et al. The Anticancer Potential of Psidium guajava (Guava) Extracts. Life Basel Switz. 2023;13:346.
19. Kumar NK, Geervani VS, Kumar RSM, Singh S, Abhishek M, Manimozhi M. Data-driven dentistry: Computational revelations redefining pulp capping. J Conserv Dent Endod. 2024;27:649–53.
20. Nayak N, Varghese J, Shetty S, Bhat V, Durgekar T, Lobo R, et al. Evaluation of a mouthrinse containing guava leaf extract as part of comprehensive oral care regimen- a randomized placebo-controlled clinical trial. BMC Complement Altern Med. 2019;19:327.
21. BrunieraAnchieta R, Silveira Machado L, Herman Sundfeld R, Figueiredo Reis A, Giannini M, Luersen MA, et al. Effect of partially demineralized dentin beneath the hybrid layer on dentin-adhesive interface micromechanics. J Biomech. 2015;48:701–7.
22. de Moraes IQS, do Nascimento TG, da Silva AT, de Lira LMSS, Parolia A, Porto ICC de M. Inhibition of matrix metalloproteinases: a troubleshooting for dentin adhesion. Restor Dent Endod. 2020;45:e31.
23. Tezvergil-Mutluay A, Mutluay M, Seseogullari-Dirihan R, Agee KA, Key WO, Scheffel DLS, et al. Effect of phosphoric acid on the degradation of human dentin matrix. J Dent Res. 2013;92:87–91.
24. Tezvergil-Mutluay A, Agee KA, Hoshika T, Uchiyama T, Tjäderhane L, Breschi L, et al. Inhibition of MMPs by alcohols. Dent Mater Off PublAcad Dent Mater. 2011;27:926–33.
25. Daood D, Yiu CKY, Burrow MF, Niu LN, Tay FR. Effect of a novel quaternary ammonium silane cavity disinfectant on durability of resin-dentine bond. J Dent. 2017;60:77–86.
26. Kiuru O, Sinervo J, Vähänikkilä H, Anttonen V, Tjäderhane L. MMP Inhibitors and Dentin Bonding: Systematic Review and Meta-Analysis. Int J Dent. 2021
27. Carrilho MR, Tay FR, Donnelly AM, Agee KA, Tjäderhane L, Mazzoni A, et al. Host-derived loss of dentin matrix stiffness associated with solubilization of collagen. J Biomed Mater Res B Appl Biomater. 2009;90: 373–80.
28. 28.Barcellos DC, Fonseca BM, Pucci CR, Cavalcanti BD, Persici Ede S, Gonçalves SE. Zn-doped etch-and-rinse model dentin adhesives: Dentin bond integrity, biocompatibility, and properties. Dent Mater 2016;32:940-50.
29. Almeida GS, da Silva EM, Guimarães JGA, da Silva RNL, Dos Santos GB, Poskus LT. ZnCl2 Incorporated into Experimental Adhesives: Selected Physicochemical Properties and Resin-Dentin Bonding Stability. BioMed Res Int. 2017
30. Joshi DM, Pathak SS, Banmare S, Bhaisare SS. Review of Phytochemicals Present in Psidium guajava Plant and Its Mechanism of Action on Medicinal Activities. Cureus. 2023;15:e46364.
31. M V, Sga S, S G, Vp J. Computational Evaluation on the Interactions of an Opaque-Phase ABC Transporter Associated with Fluconazole Resistance in Candida albicans, by the Psidium guajava Bio-Active Compounds. J Pharmacopuncture. 2024;27:91-100.
32. Carvalho C, Fernandes FP, Freitas V da P, França FMG, Basting RT, Turssi CP, et al. Effect of green tea extract on bonding durability of an etch-and-rinse adhesive system to caries-affected dentin. J Appl Oral Sci Rev FOB. 2016;24: 211–7.
33. B A, Mp L, N BG, M P, D G, R B. Green tea polyphenol (-)-epigallocatechin 3-gallate inhibits MMP-2 secretion and MT1-MMP-driven migration in glioblastoma cells. BiochimBiophys Acta 2002; 1542:1–3.
34. de Oliveira AB, Ferrisse TM, França GG, de Annunzio SR, Kopp W, Fontana CR, et al. Potential Use of Brazilian Green Propolis Extracts as New Photosensitizers for Antimicrobial Photodynamic Therapy against Cariogenic Microorganisms. Pathog Basel Switz. 2023; 12:155.
35. Kd C, K K, V S, S M. Antibacterial evaluation of guava leaves extract and its effect on reactive oxygen species formed by calcium hydroxide and chlorhexidine mixture. J ConservDent JCD2021;24:389-392.
36. Khan, Hooriyah & Bhandari, Sarita & Uddin, Dr. (2026). Relationship between Matrix metalloproteinase inhibitors for dentin pre treatment and secondary caries inhibition at the tooth restoration interface - Systematic Review. International Journal of Drug Delivery Technology. 16. 10.25258/ijddt.16.3s.94.
37. Anumula L, Ramesh S, Kumar Kolaparthi VS, Govula K. Knowledge, Attitude, and Practices on the Use of Cross-Linkers During Dentin Bonding among Practitioners Specialised in Conservative Dentistry. Journal of Clinical & Diagnostic Research. 2023 Aug 1;17(8).
38. Website [Internet]. Available from: https://doi.org/10.7860/JCDR/2023/64287.18304
39. Katariya C, Rajasekar A. Extracellular matrix metalloproteinase inducer as a biomarker for oral cancer. Bioinformation. 2023 Apr 30;19(4):433–5.
40. Murthykumar K, Veerappan P, Ganapathy D, Jayaraman S. Comparative Analysis of Matrix Metalloproteinase-1 in Completely Edentulous Diabetic and Nondiabetic Individuals and Its Correlation with Glycemic Control Markers. World Journal of Dentistry. 2026 Feb 5;16(12):1124-31.