SYSTEMATIC REVIEW OPEN ACCESS

Effect of Incorporation of Bioactive Agents in Dentin Bonding Agent on Bond Strength: A Systematic Review

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ABSTRACT

Background: This study analyzed how incorporating bioactive agents in dentin bonding agents affects bond strength.

Methods: Full-text English articles were retrieved from PubMed, ScienceDirect, and Web of Science using MeSH terms and Boolean operators until July 2024. Studies from the last ten years were included and analyzed for bond strength changes. A total of 36 studies were reviewed, with 32 showing improved or stable bond strength, while four reported decreased strength. The modified CONSORT checklist for in vitro studies of dental materials was used to document the risk of bias.

Results: Bioactive glass was the most common additive, used in ten studies. Micro-tensile bond strength was measured in 24 studies, while 12 assessed shear bond strength. Bioactive agents positively impacted bond strength, forming a stable resin-dentin interface.

Discussion: Future research should focus on optimizing these products for improved clinical outcomes. The limited lifespan and marginal staining of dental composite restorations remain concerns for patients and clinicians. This systematic review seeks to provide an in-depth analysis of the impact of incorporating various bioactive agents into dentin bonding agents on the bond strength to dentin.

Keywords: Dentin Bonding Agent, Dental adhesive, Shear Bond Strength, Micro Tensile Bond Strength, Bioactive Glasses, Bioactive Agents, Human Dentin, Bovine Dentin, Dentine.

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INTRODUCTION

Dental caries is a common oral health problem that has affected around 2.3 billion people of the world and is labelled as a non-communicable and most prevalent disease in the world population [1]. This is usually removed physically with rotary devices, and various restorative materials like Dental Amalgam, Glass Ionomer Cements, and Dental Composites are used to repair the tooth structure [2]. Dental Composites is considered the best option for tooth restoration, due to their minimal invasiveness and excellent esthetics but the average span is around 5 years [3].

Dental Composites form a micro-mechanical bond with tooth structure and therefore require the use of adhesive resin to bond the restorative composite to the tooth structure [4]. The hybrid layer is resin-reinforced in the collagen fibril of tooth structure that forms a three-dimensional interface responsible for bonding of dental composite. The mechanical stability of this resin-dentin bond is dependent on the stability of the resin component and collagen network [5]. In case of failure to establish a stable bond, marginal leakage takes place [6]. This micro-leakage will lead to demineralization of the tooth at the restoration interface, eventually secondary caries, and failure of the restoration [7, 8]. Various modifications are being done to prevent Secondary caries and increase the lifespan of the restoration [9, 10].

According to the literature, various bioactive agents are added in the dentin bonding agent to establish a stable resin-dentin interface [11]. These bioactive agents will induce remineralization potential in the dentin bonding agent that will form an apatite layer in the marginal gaps at the interface, increasing the bond strength and preventing secondary caries [12].
The objective of this systematic review was to critically analyze and appraise the current scientific literature to determine the efficacy of different studies that have attempted to increase the stability of the bond by incorporating bioactive agents in dentin bonding agents. This systematic review was carried out by working according to the updated guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and the research question was formulated using the PICO framework: "What bioactive agents have been incorporated in adhesive resin, used for composite restorations, and how do they affect bond strength to dentin?"

METHODS

Inclusion Criteria

Studies included for the systematic review were as follows:
Original research studies, regardless of the type of study design. Human Dentin and Bovine Dentin were used as substrates. Intervention was the incorporation of bioactive agents in a dentin bonding agent. Dental Composite was bonded using dentin bonding agent as a restorative material. The outcome was measurement of bond strength using standards already established evaluating shear bond strength or micro tensile bond strength at specific forces over unit area at different time points.

Exclusion Criteria

Studies excluded from the systematic review were as follows:
Full text not retrieved or text language other than English. Literature reviews, systematic reviews, case reports, case studies, and conference abstracts. Conditioning or Pretreatment of dentin before application of dentin bonding agent. Bioactive agents used in resin-based composite and Glass ionomer cement restoration. Bioactive agents incorporated in bonding agents are used in other applications like pulp capping, luting, endodontics, and treatment of dentin hypersensitivity. Bioactive agents incorporated in adhesives; bone cements used in tissue engineering applications. Bonding to the enamel surface and radicular dentin.

Literature Search and Study Selection:

MeSH (Medical Subject Headings) terms connected with Bolean operators were used to search and retrieve articles in **PubMed, ScienceDirect**, and **Cochrane Library**. The literature search for this review was conducted using three major scientific databases: PubMed, ScienceDirect, and the Cochrane Library. The following search terms and Boolean operators were used to identify relevant studies: ("Dentin bonding agent" OR "dental adhesive") AND ("Shear Bond Strength" OR "Micro Tensile Bond Strength") AND ("Bioactive Glasses" OR "Bioactive Agents") AND ("Human Dentin" OR "Bovine Dentin" OR "Dentine"). Only articles published in the past 10 years until July 10th, 2024, were included. The articles were added to EndNote (Clarivate Analytics, EndNote 20, 2022). After removing duplicate studies, initial article screening was done according to titles and abstracts. The full text of articles retrieved was screened according to PRISMA guidelines. A manual search of studies was conducted of the retrieved full-text to include the eligible studies.

Data Acquisition Process and Data Items

The titles and abstracts of the studies were assessed and screened by two reviewers separately for the inclusion criteria. Complete texts of the studies to be included in the review process were retrieved and studied to confirm their eligibility by two reviewers independently. Apart from the variables of the study listed above, there were no other variables on which the data were sought. However, the additional filters applied were in vitro studies, randomized controlled trials, and full-text availability. Alternative terms such as "dentin bonding system" for dentin bonding agent and "micro tensile" for micro tensile were considered to ensure a comprehensive literature search. The intervention was the incorporation of bioactive agents in the dentin bonding agent. The measured outcome of the included studies was bond strength. This study was conducted without any financial support from external sources.

Risk of Bias Assessment of Included Studies

The extracted data from selected studies was noted in a personalized Excel sheet. The excluded studies [13, 14] are listed in **Table 2**. Both assessors used a modified CONSORT checklist for in vitro studies of dental materials to report the risk of bias and level of evidence of the included studies.

Table 2: Excluded Studies (Met the Inclusion Criteria, But Were Excluded)

Author and Year	Country	Study Objectives	Reason for Exclusion
Li et al., 2015[13]	China and USA	To investigate the inhibition qualities of new antibacterial monomer (dimethylaminododecyl methacrylate, DMADDM) on matrix metalloproteinases (MMPs), and determine its effects on both soluble recombinant human MMPs (rhMMPs) and dentin matrix-bound endogenous MMPs.	No Bond Strength Test was performed in the study.
Yu et al., 2016[14]	China	This study investigated shear adhesive strength and the potential of resin bonding agents to prevent demineralization, containing different amounts of bioactive glass (BG).	Full Text in the Chinese Language. Only the abstract is in English

RESULTS

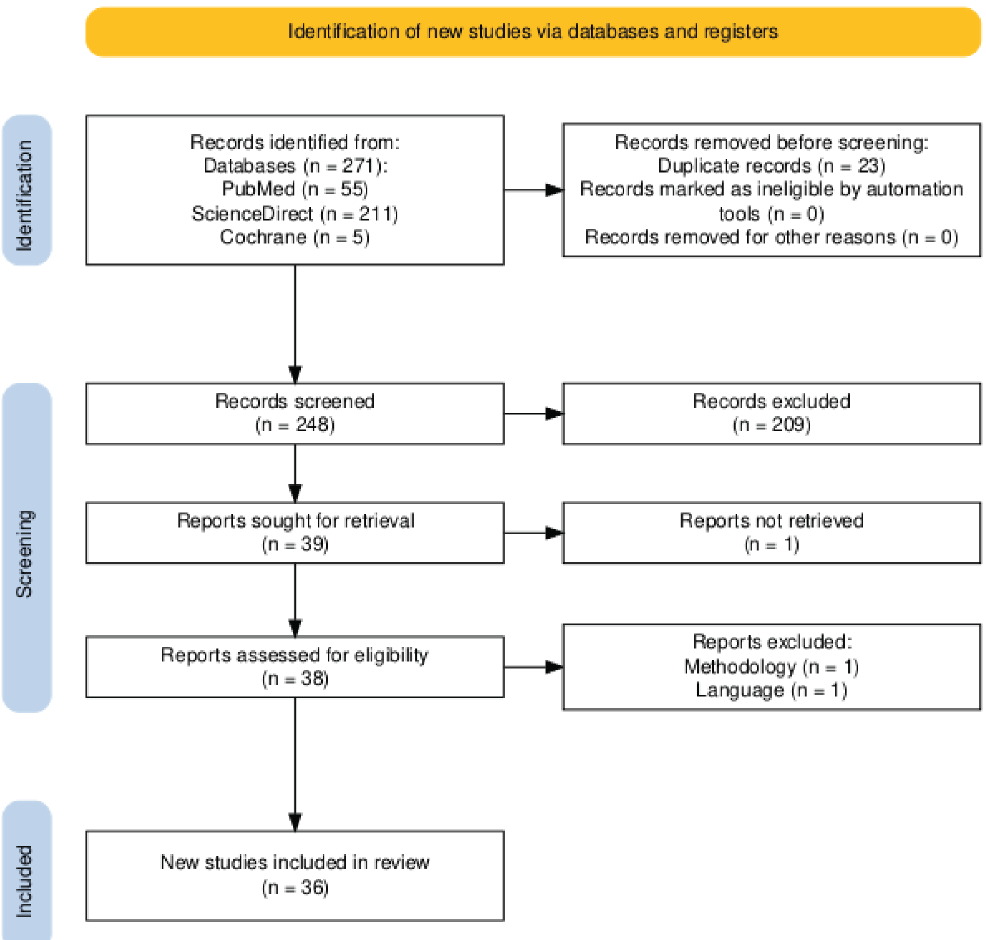

Figure 1: Flow Chart according to PRISMA guidelines

The initial search revealed 271 studies. After the removal of Duplicate Studies (23) using EndNote 20, 248 papers were left for screening. After screening as per the inclusion/exclusion criteria and PRISMA guidelines, a total of 36 studies[16-51] were included for further analysis. **Table 3** summarizes the general characteristics of the included studies. **Table 4** comprehensively describes the data extracted and the major findings of these studies.

Table 3: General Characteristics of Included Studies

Author and Year	Country	Type of Bond Strength Test	Time Points	Bioactive Agents
Mi et al., 2022[44]	China	Shear Bond Strength	Immediate	Cecropin and Fe3O4-coated Nanoparticles
Alania et al., 2022[18]	USA	Micro-Tensile Bond Strength	24 hr, 1 year, and 2 years of SBF immersed at 37°C	Proanthocyanidin (PAC) incorporated Poly-lactide (PLA) capsules.
Alkatheeri et al., 2015[19]	USA and Thailand	Shear bond strength (SBS)	24 h	Halloysite® aluminosilicate clay nanotube (HNT)
Cascales et al., 2022[34]	UK and Spain	Micro-Tensile Bond Strength	Baseline (T0) and 1 year (T1)	Phospho-proteins and Fluoride-doped bioglass
Ashtijoo et al., 2022[20]	Iran	Shear bond strength	24 h	Amorphous calcium phosphate (ACP) and calcium silicate (CS) nanoparticles (NPs)
Ezz El-Din et al., 2023[38]	Egypt	Micro Tensile Bond Strength	Immediately and thermo-cycled for 24 h	Chitosan and Nano Chitosan
Abuna et al., 2016[52]	Brazil, Belgium, USA, and Spain	Micro-Tensile Bond Strength	24h and 6 months	Dentin phospho-proteins like Polyacrylic acid (PAA) and Sodium trimetaphosphate (TMP)
Carneiro et al., 2016[22]	Brazil	Micro-Tensile Bond Strength	24h and 6 months	Niobium Phosphate Bioactive Glass (NbG)
Daood and Fawzy, 2023[37]	Malaysia and Australia	Micro-Tensile Bond Strength	24 hours, 6 months, and 12 months	Magnesium-doped Hydroxyapatite crystals (HAp)
Bauer et al., 2016[32]	Brazil and Canada	Micro-Tensile Bond Strength	24 h and 6 months	Niobium–phosphate bioactive glass (NPG)
Yezdani et al., 2023[51]	India	Shear Bond Strength	24h	Chicken eggshell-derived HAp (CES-HAp), NovaMin (NM), Casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) and Pro Argin (PA)-based commercial dentifrices
Rolim et al., 2022[47]	Brazil and the USA	Micro-Tensile Bond Strength	24h and 12 months	Epigallocatechin-3-gallate (EGCG) or Proanthocyanidin (PA)
Ashraf et al., 2022[30]	China, Pakistan, and Saudi Arabia	Micro-Tensile Bond Strength	24h, 30 days, 6, and 12 months	Dimethacrylate monomers with fluorine (FUDMA)
Mousavinasab et al., 2023[29]	Iran and Malaysia	Shear Bond Strength	24h	Bioactive glasses (BAGs
Chiari et al., 2021[36]	Brazil and the USA	Micro-Tensile Bond Strength	24h and 2 months	Mineral trioxide Aggregate (MTA) or Di-calcium phosphate dihydrate (DCPD).
Ñaupari-Villasante et al., 2022[45]	Brazil and Chile	Micro-Tensile Bond Strength	Immediately and 4 years	Copper nanoparticles (CuNp)
Rifane et al., 2023[27]	Brazil and Spain	Micro-Tensile Bond Strength	24h and 6 months	Pure Bioglass 45S5 or Strontium containing Bioglass Sr-45S5

Sauro et al., 2015[48]	Spain and the UK	Micro-Tensile Bond Strength	24h and 90 days	Ca-Silicate micro-fillers with Poly-aspartic acid (PAA) and Sodium trimetaphosphate (TMP)
Kalagi et al., 2020[41]	USA, KSA, and Brazil	Micro-Tensile Bond Strength	24h and 6 months	Halloysite nanotubes (HNTs) encapsulated with chlorhexidine(CHX)
Kazem et al., 2024[23]	Egypt	Micro-tensile bond strength	1 day and 6 months	Bioactive Glass (BAG)
Kim et al., 2021[24]	Korea and the USA	Micro-Tensile Bond Strength	24h and aged with 10% naocl	Bioactive glass (85% SiO2, 15% CaO)
Li et al., 2018[42]	China and the USA	Shear Bond Strength	24h	Amorphous calcium phosphate nanoparticles (NACP), Di-methylaminohexadecyl methacrylate (DMAHDM), and Magnetic nano-particles (MNP)
Cavaleiro-de-Macedo et al., 2024[35]	Brazil and Canada	Micro-Tensile Bond Strength	24h and 1 year	45S5 Bioactive Glass
Rizk et al., 2020[46]	Germany and Switzerland	Shear Bond Strength	24h	Polyhedral oligomeric silsesquioxanes (POSS-8, Multifunctional Methacryl)
Balbinot et al., 2020[53]	Brazil	Micro-Shear Bond Strength	24h	Niobium Silicate particles
Xie et al., 2017[50]	China and the USA	Shear Bond Strength	24h	Nanoparticles of amorphous calcium phosphate (NACP)
Oltramare et al., 2021[25]	Switzerland and Croatia	Micro-Tensile Bond Strength	24h and 6 months	Nano-sized bioactive glass 45S5 (BAG)
Profeta, 2014[26]	UK	Micro-Tensile Bond Strength	24h and 10 months	MTA and Bioglass
Al-Qarni et al., 2018[54]	USA, Saudi Arabia, and China	Shear Bond Strength	24h	Nanoparticles of Amorphous Calcium Phosphate (NACP) and 2-methacryloyloxyethyl phosphorylcholine (MPC)
Ilie et al., 2022[40]	Germany and Romania	Shear Bond Strength	24h and thermocycled (TC) (10000 Cycles)	Graphene and hydroxyapatite
Liang et al., 2018[43]	China and USA	Micro-Tensile Bond Strength	24h	Quaternary ammonium monomer (QAM), triethylamine dodecyl acrylate (TEADDA)
Stürmer et al., 2021[49]	Brazil	Micro-Tensile Bond Strength	24h and 1 year	Titanium dioxide nano-tubes (TiO2nt) or Titanium dioxide nano-tubes containing Triazine-methacrylate monomer (TiO2:TATnt)
Stürmer et al., 2021[49]	Brazil	Micro-Tensile Bond Strength	24h and 1 year	Titanium dioxide nano-tubes (TiO2nt) or Titanium dioxide nano-tubes containing Triazine-methacrylate monomer (TiO2:TATnt)
Bendary et al., 2020[33]	Brazil	Micro-Tensile Bond Strength	24h and 1 year	Wollastonite
Zhang et al., 2018[28]	China and USA	Shear Bond Strength	1,30, 90 and 180 days	Meth-acryloyloxyethyl phosphorylcholine (MPC) and Di-methylaminohexadecyl methacrylate (DMAHDM)
Garcia et al., 2020[39]	Brazil	Micro-Tensile Bond Strength	24h and 6 months	Simonkolleite (SKT)- Zn based
Barcellos et al., 2016[31]	Brazil and the USA	Micro-Tensile Bond Strength	24h and 6 months	Zinc Oxide nanoparticles (ZnOn) and Zinc methacrylate (Zn-Mt).

Table 4: Data Extracted from Included Studies, Measured Outcomes, and Their Major Findings

Author and Year	Sample Type	Specimen Dimensions	Sample Size and Grouping	Storage Medium	Dentin Demineralizing Agent	Bonding System	Measured Outcomes	Reported Findings
Mi et al., 2022[44]	Human sound third molars	Composite block (4mm). No further details of the specimen are mentioned.	Total=40 4 groups (n=10) 1. Scotch Bond universal adhesive. 2. Fe3O4-coated Scotch bond adhesive. 3. Cecropin-coated scotch-bond adhesive. 4. Cecropin and Fe3O4-coated scotch-bond adhesive.	N-A	Tris-HCl Buffer Solution (pH=7.4)	Etch & Rinse	Shear Bond Strength with Universal Testing Machine (UTM)	Increase in the bonding strength due to the remineralization potential of cecropin and $Fe3O_4$- coated adhesives.
Alania et al., 2022[18]	Human sound third molar	Resin dentin beams having a transverse area of 0.8 ± 0.05 mm^2.	3 groups (n = 8), 1. Control 2. 1.5wt% of submicron 3. 1.5 wt % of Micron.	SBF	Glycolic acid 35 wt% (pH = 1.30)	Etch & Rinse	Bond Strength using UTM, a Ciucchi jig under tensile forces at a cross-head velocity of 1 mm/min.	No negative effects of PLA capsules on dentin-PAC-resin bonding strength. The bond strength of group 2 decreases by 25% after 2 years. Group 3 bond strength reduced after 1 year, yet recovered in the second year.
Alkatheeri et al., 2015[19]	Non-carious human molars	Composite button (2.38mm diameter* 2mm thickness)	Total= 120 10 groups of study (n=12) 1. Commercial control-ER 2. Experimental control-ER 3. 5 % HNT-ER 4. 10 % HNT-ER	Deionized Water at 37 °C	Phosphoric acid 32%	Etch-and-rinse (ER)- two step and Self-etch (SE) - one step.	Custom notched fixture under a UTM at a cross-head velocity of 1 mm/min.	20% HNT-ER and 10% HNT-SE had higher SBS to dentin than experimental control.

			HNT-ER 5. 20 % HNT-ER 6. Commercial control-SE 7. Experimental control-SE 8. 5 % HNT-SE 9. 10 % HNT-SE 10. 20 % HNT-SE					
Cascales et al., 2022[34]	Natural Cavitated Human molars with deep carious lesion	Tooth sectioned into matchstick-shaped specimens with cross-sectional area of $0.9mm^2$	Total= 50 5 experimental groups (n= 10/group) EXP-SE 1. ER-SE 2. ER-EXP 3. Resin-modified Glass ionomer cement (RMGIC) 4. Three-step Adhesive system 5. SE-Universal adhesive (SE-SUA).	DPBS (Dulbecco's Phosphate Buffered Saline)	36% Phosphoric Acid, Self-Etch Primer containing Polyacrylic Acid	Self-etch and Etch and Rinse both	Microtensile bond strength evaluation device (Stroke length- 50 mm, Peak force- 500 N and Displacement resolution- 0.5 mm).	1. At T0, no significant difference in bond strength between groups. 2. At T1, Group 1 and Group 2 had a significant reduction in bonded strength.
Ashtijoo et al., 2022[20]	Human third molars	Thickness of dentin slices 1±0.1 mm	Three Groups, 1. Control 2. Calcium Silicate 2.5 % 3. ACP 2.5%.	Distilled Water (DW) at Room Temperature (RT)	Phosphoric Acid	Etch & Rinse	UTM at a velocity of 1 mm/min.	Group 2 and group 3 showed bioactivity and remineralization potential without a reduction in bond strength.
Ezz El-Din et al., 2023[38]	Sound human premolars	Four composite-dentin sticks (1 mm × 1 mm)	Total =50 2 Groups; Immediate n=25, Thermocycling n=25, each group had subgroups (n=5) 1. Control 2. 0.5% bulk chitosan	DW at RT	N/A	Single Bottle System	UTM with tensile load at a cross head velocity of 1 mm/min until debonded	Subgroups 4 and 5 containing 0.5% and 1% nano-chitosan) improved the microtensile bond strength and bond durability.

Abuna et al., 2016[52]	Extracted non-carious human molars	Resin dentin sticks (0.9 mm*0.9 mm)	Total = 50 Five groups (n=5) 1. CTR- P + CTR-R 2. CTR-P + IR-R 3. PAA-P+ IR-R 4. TMP-P + IR-R 5. PAA-P/TMP + IR-R	De-ionized water and SBF	Self-etch primer	Self-Etch Primer followed by adhesive	The sticks were fixed to jig with cyanoacrylate cement and subjected to tensile failure in a UT with a 50N load cell (cross head velocity: 1 mm/min)	TMP and PAA had most stable μTBS for 6 months
Carneiro et al., 2016[22]	Freshly extracted human third molars	Perpendicular and longitudinal sequences cut in cross sections to obtain specimens of 0.8 mm^2.	Total = 48 (n=8) 1. OS 2. OsNbg 3. OsNbgs 4. PB 5. PbNbg 6. PbNbgs	N/A	H_3PO_4 (37%)	One Step and Prime and Bond	Samples were subjected to a UTM using Geraldeli jig with crosshead velocity of 1.0 mm/min.	NBg micro-fillers had no significant effect on bonding strength of the adhesives.
Daood and Fawzy, 2023[37]	Extracted sound human molars	Resin-dentine beams (1 mm^2)	Total = 160 (n=40) 1. Control 2. 0.5% Ad 3. 1% Ad 4. 2% Ad	Artificial saliva	Self-etch	One Bottle System	Beams were fractured at cross head velocity of 1 mm/min in UTM.	Adhesive specimens containing 0.5% Mg-hap showed the highest micro tensile bond strength.
Bauer et al., 2016[32]	Extracted sound human third molars	The cross-sectional area of resin-dentin bonded stick was measured using a digital caliper (nearest 0.01 mm)	Total = 16 (n=8) 1. Adh-Control 2. Adh-NPG	DW at 37 °C	H_3PO_4 (37%)	Two Step, Etch & Rinse	The individual sticks were glued on a Geraldeli device with cyanoacrylate. Each stick then kept under stress till failure in UTM at a cross head velocity of 1 mm/ min.	Adh-NPG prevented decreases in bond strength.
Yezdani et al., 2023[51]	Non-Carious Intact Human Molars	Tygon tube (d=2 mm and h= mm) was adjusted in the center of the bonded surface.	Total=218, 5 groups (n = 43), 1. Control - No desensitizing treatment, 2. Novamin (NM) 3. Casein phospho-peptide-Amorphous calcium	DW	17 % EDTA	Self-Etch Adhesive	A semicircular notched blade shape jig descended with cross head velocity of 1 mm/ min in a UTM equipped with a load cell of 3 KN.	No significant SBS values difference between control and experimental desensitized groups. The highest SBS was recorded with nHAp, which is significantly higher in comparison to CPP-ACP alone.

			phosphate (CPP-ACP), 4. Pro Argin (PA), 5. CES-nHAp.					
Rolim et al., 2022[47]	Human molars	Resin–dentin sticks (1 mm^2)	Total=96, 6 Groups (n=16). 1. Ambar Universal (AUSE Control), 2. AUSE + PA, 3. AUSE + EGCG, 4. Clearfil SE Bond (CSE Control), 5. CSE + PA, 6. 6. CSE + EGCG.	DW	Self-Etch	Two Step CSE and One Step AUSE	The bonded stick under tensile forces in a UTM with cross head velocity of 0.5 mm/ min and a load cell of 500 N.	No significant difference at multiple time points (24hr and 12m) in the results.
Ashraf et al., 2022[30]	Sound human molars extracted for orthodontic purposes or periodontal issue	Resin-dentin beams of 1.0 mm^2	Total=120, 10 groups (n=12): SPP 1. T0= no fiilers 2. T2= 2wt.% BAG 3. T5= 5wt.% BAG 4. T10= 10wt.% BAG 5. ASBM (control). Non-SPP 6. T0= no fillers 7. T2= 2wt.% BAG 8. T5= 5wt.% BAG 9. T10= 10 wt.% BAG 10. ASBM (control	DW	32% phosphoric acid etchant gel	Two Step, Etch & Rinse	Tensile forces in UTM at a crosshead velocity of 1 mm /min.	5 wt% BAG fillers incorporated in FUDMA/ TEGDMA have more stable adhesion to dentine than being incorporated in Bis-GMA/ HEMA resin.

Mousavi nasab et al., 2023[29]	Healthy third molars	Not mentioned clearly	Total= 80, 5 main groups (n= 4) 1. BAG (0%), 2. BAG (0.2%), 3. BAG (0.5%), 4. BAG (2%), 5. Adper Single Bond (Control) Each group is divided into Sound and Demineralized teeth, which are further subdivided into thermocycled and non-thermocycled subgroups.	DW at RT	Phosphoric acid 37%	Two-step, Etch & Rinse	Knife-like mandrel jig Shear bond strength was measured using a UTM with a cross-head velocity of 0.5 mm /min.	μ-SBS to sound dentin groups were higher than demineralized groups for group A 0% and group D 2%. μ-SBS in non-thermocycled samples were higher than those in thermocycled samples for the control group. BAG filler incorporation in the adhesive from 0 to 2 wt% produced no significant effects on the shear bonding strength of the modified samples.
Chiari et al., 2021[36]	Human sound third molars	Beams (0.8 × 0.8 mm^2)	Total=56, Four groups (n=14); 1. Control , 2. DCPD-DEGDMA, 3. DCPD-CA , 4. MTA .	SBF	37% Phosphoric acid	Two-step, Etch & Rinse	Microtensile testing machine was subjected to a tensile force at 1 mm/min.	μTBS found among adhesives in the order, control = MTA > DCPD-CA > DCPD-DEGDMA, but no difference between storage times.
Naupari-Villasante et al., 2022[45]	Extracted healthy human third molars	Resin dentin beam shaped specimens having transverse area of 0.8 mm^2	Total= 35, Seven Groups (n= 5) containing CuNp concentration in 1. 0wt% [control] , 2. 0.0075 wt%, 3. 0.015wt%, 4. 0.06wt%, 5. 0.1wt%, 6. 0.5wt% 7. 1wt%	DW at 37 ◦C	37% phosphoric acid	Etch and rinse (ER)	Each resin dentin beam under tensile force in UTM with	The micro tensile bond strength of 0.5% CuNp significantly increased in comparison to control group when

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Rifane et al., 2023[27]	Extracted human third molars	Resin dentin sticks of approximately 1 mm^2	Total=30, 5 Groups 1. No Bioglass - Ambar Universal (Control), 2. Bioglass (45S5)+ Ambar Universal Adhesive, 3. Bioglass - Strontium(Sr-45S5) + Ambar Universal Adhesive , 4. Silanized Bioglass (Sil-45S5)+ Ambar	DW at 37 ◦C	Phosphoric Acid	Etch and Rinse	Sticks were tested in a UTM, having a load cell of 500-N and cross head speed of 1 mm /min.	After 6 months, μTBS redacted for Control and Sil-Sr-45S5. Bioglass and Strontium-doped Bioglass presented stable and higher values. Silanized groups showed an increase in μTBS due to mineral deposition after 6-months.
Sauro et al., 2015[48]	Sound human third molars	Bonded-sticks of 0.9mm^2	Total=6, 6 Groups (n=1) 1. CTR. Res 2. PLA. Res 3. TMP. + PLA. Res 4. IR. Res 5. IR/PLA. Res 6. IR/TMP + PLA. Res	Artificial saliva	37% H_3PO_4	4th Gen, Etch and Rinse	Microtensile bond strengths with a linear actuator having a specialized micro tensile jig.	Groups 2 and 3 have stable microtensile bonding strength after 90 days of AS storage.
Kalagi et al., 2020[41]	Sound human molars	Beams (1 × 1 mm^2)	Total=105, 7 Groups (n=15) 1. SBMP-Control ; 2. 0.2% CHX prior to SBMP; 3. CHX-Primers (10%) + SBMP-Adhesive; 4. CHX-Primer (20%) + SBMP-Adhesive;	DW at 37C	35% phosphoric acid	3-step Etch and Rinse adhesive (Multipurpose [SBMP]).	UTM at a cross head velocity of 1 mm/ min.	At 24 h, all groups showed similar results At 6-months, 0.2% CHX solution treatment and CHX-modified primers resulted in bond strength greater than control

			5. SBMP-Primer + CHX-Adhesives(10%); 6. SBMP-Primer + CHX-Adhesives(20%); 7. SBMP-Primer + CHX-free-HNT Adhesive.					
Kazem et al., 2024[23]	Freshly extracted human third permanent molars	Beam of thickness 0.9 × 0.9mm^2 and height 8 mm	Total= 24, Four Groups (n=6) 1. ER Control, 2. ER 5% BAG, 3. SE Control, 4. SE 5% BAG.	DW containing 0.5% thymol	Phosphoric acid 37%	Etch & Rinse and Self- Etch	Tensile forces in UTM at a cross head speed of 1 mm /min.	The MTBS mean values of ER and SE statistically decreased with time in the control group. 5 wt% BAG had stable results in ER and SE modes for different time points, respectively.
Kim et al., 2021[24]	Caries-free human permanent third molars (10 for MTBS)	Composite-Dentin beams with 1.0 × 1.0 mm^2	Total=36, Four Groups (n=9) 1. SCA Immediate, 2. SCA Aged, 3. BAG Immediate 4. BAG Aged	DW at 37 ◦C	37% phosphoric acid gel	Etch and Rinse	μTBS was calculated using UTM with a cross-head velocity of 1.0 mm/ min.	The immediate and aging had no difference in the μTBS for SCA and BAG groups. After aging, μTBS significantly decreased for each adhesive.
Li et al., 2018[42]	Extracted caries-free human third-molars	N/A, Composite (d=4mm*t=1.5mm)	Total=50, 5 Groups (n=10) 1. SBMP Control, 2. SBMP+ MNP, 3. SBMP+ MNP+ Magnetic Force, 4. SBMP+ MNP+DMAHDM+ Magnetic Force, 5. SBMP+ MNP+DMAHD	DW at 37 ◦C	37% phosphoric acid gel	Etch and Rinse	A chisel aligned parallel to the composite-dentin interface on UTM applied load at cross head velocity of 0.5 mm/ min.	Under Magnetic forces, Magnetic nanoparticles with DMAHDM and NACP yielded greater dentin bond strength in comparison to the control.

			M+ NACP+ Magnetic Force					
Cavaleiro-de-Macedo et al., 2024[35]	Extracted human molars	"Toothpick" shape with Rectangular Sections- 0.8 ± 0.1 mm^2.	Total=21, 6 Groups (n=not clear), 1. Sound Dentin Control, 2. Sound Dentin 5% 45S5, 3. Sound Dentin 20% 45S5, 4. Caries-Affected Dentin Control 5. Caries-Affected Dentin 5% 45S5, 6. Caries-Affected Dentin 20% 45S5.	Teeth were stored in SBF solution at 37◦C	Self-Etch Primer	Self-Etch Adhesive	UTM	Bio-active adhesives containing 5 % and 20 % concentration were not affected by dentin type. In Caries-affected dentin, Bio-active glasses had therapeutic action maintaining bonding strength values.
Rizk et al., 2020[46]	Bovine incisors	Rectangular dentin specimens (6 * 6 mm^2)	Total= not mentioned, 10 Groups. 1. Adhese Universal, 2. Adhese Universal+ POSS-8, 3. CLEARFIL Universal Bond, 4. CLEARFIL Universal Bond+ POSS-8, 5. Futurabond U, 6. Futurabond U+ POSS-8, 7. ibond Universal, 8. ibond Universal+ POSS-8, 9. Scotchbond Universal,	Water at 8C	Self-etch	Self-etch universal Adhesives	Loading device with chisel shape applied shear force on interface in UTM at velocity of 1 mm/ min.	POSS-8 filled and control had no significant changes in Shear-Bond Strength(SBS) values.

			10.! Scotch bond Universal + POSS-8.					
Balbinot et al., 2020[53]	Anterior bovine teeth	h= 1 mm x d=1 mm cylinders (Adhesive).	Total=36, Three Groups (n=12), 1.! Sinb0%, 2.! Sinb1%, 3.! Sinb2%.	DW at 37 ◦C	37% phosphoric acid gel	Etch and Rinse	The load cell of 500 N applies a force with a cross-head velocity of 1 mm/ min in UTM	Sinb2% showed higher values than Sinb0% and Sinb1%.
Xie et al., 2017[50]	Extracted human third molars	N/A	Total= not mentioned, Six groups 1. Commercial control 2. Experimental control 3. DMAHDM+MPC 4. DMAHDM+MPC+20-NACP 5. DMAHDM+MPC+30-NACP 6. DMAHDM+MPC+40-NACP.	DW at 37 ◦C	37% phosphoric acid gel	Etch and Rinse	Chisel shaped jig, UTM at a cross-head speed of 0.5mm/min	NACP 20–30% containing adhesive had dentin bond strengths equal to control while NACP 40% containing adhesive had significantly lower.
Oltramare et al., 2021[25]	Extracted noncarious human molars	Interface area of sticks (0.907 ±0.221 mm^2)	Total=120, Four groups(n=30) 1. BAG 0% (Control) 2. BAG 5% 3. BAG 10% 4. BAG 20%.	SBF	35% phosphoric acid and Acrylic Acid in Primer	Self-Etch and Etch and Rinse	UTM, with a load cell of 500 N and tensile force velocity of 1 mm/ min.	10 wt% for ASB and 5 wt% for SB, after 24 hr and 6 months, had similar MTBS as their controls. 20 wt% BAG of all three adhesives decreased the MTBS in comparison to their controls.
Profeta, 2014[26]	Intact, caries-free sound molars	Beams cross-sectional area (0.9 mm^2).	Total=30, Three Groups (n=10) 1. BG/3-E&RA, 2. MTA/3-E&RA, 3. Control /3-E&RA.	DPBS solutions at 37 C	N/A	3-step, etch and rinse adhesive	Notched Geraldeli's jig made of stainless steel UTM at 1.0 mm/ min cross-head speed.	After 24 hr storage in DPBS, MTBS values were higher in all groups. BG/3-E&RA and MTA/3-E&RA specimens showed no significant reduction in MTBS after 10 months.

Al-Qarni et al., 2018[54]	Human third molars (0.01% thymol solution at 4 °C).	N/A, Composite (d=4mm*t=1.5mm)	Total= not mentioned, 6 Groups, 1. Scotch bond (SBMP); 2. PEHB (Pyromellitic glycerol dimethacrylate and ethoxylated bisphenol-A dimethacrylate), 3. 20%NACP+ PEHB; 4. 30%NACP+ PEHB; 5. 20%NACP+ 3%MPC + PEHB; 6. 30%NACP+ 3%MPC + PEHB.	DW at 37 ◦C	37% phosphoric acid	Etch and Rinse	A chisel on a UTM at cross head velocity= 0.5 mm/ min till failure of bond.	MPC containing adhesive had bond strength close to SBMP control. The 0-30% NACP fillers produced no significant changes.
Ilie et al., 2022[40]	Freshly Extracted-Human third molars (0.4 % sodium azide solution at 4 ° C)	N/A	Total=40, 4 Groups (n=10). 1. Silver-silica-graphene (Ag-SiO2--Gr); 2. Silver-doped hydroxyapatite (Ag-HA); 3. Silver and Graphene doped Hydroxyapatite (Ag-Gr-HA); 4. Silica (SiO2).	DW at 37 ◦C in dark environment	35% phosphoric acid	Two Step Etch and Rinse	UTM with cross head velocity of 0.5 mm /min till fracture.	After 24hr and TC, no significant differences in all groups. After TC, significant decrease in SBS in all experimental groups except the control.
Liang et al., 2018[43]	Human third molars	Sticks (1mm width)	Total= not mentioned, 8 Groups (n=6). 1. Control, 2. 2.5% TEADDA, 3. 2.5% DMADDM, 4. 5% TEADDA,	De-ionized Water for 24h	Self-etch Primer	Self-etch	Microtensile bond strength test performed using computer-controlled UTM at 1mm /min	Group 7 and 8 showed significant drop in TBS with other groups

			A, 5. 5% DMADDM, 6. 10% TEADDA, 7. 10% DMADDM, 8. 20% TEADDA.					
Stürmer et al., 2021[49]	Bovine mandibular incisors	4-6 sticks with 0.7 mm* 0.7 mm bonded area	Total=100, Five groups (n=20) 1. Control, 2. 2.5% nt-TiO_2, 3. 5% nt-TiO_2, 4. 2.5% nt-TiO_2: TAT, 5. 5% nt-TiO_2:TAT.	DW at 37 °C	37% Phosphoric Acid	Etch and Rinse	Tensile strength in a UTM at 1 mm/min until failure	The immediate MTBS decreased slightly for 2.5 wt.%. Initially, other groups had no difference compared to control but after 1 yr MTBS decreased significantly.
Bendary et al., 2020[33]	Extracted sound bovine teeth	Beams (Size not specified)	Total=160, Four groups (n=40), 1. G 0% W (control), 2. G 0.5% W, 3. G 1% W, 4. G 2% W.	SBF changes every month	37% Phosphoric Acid	Etch and Rinse	UTM with a constant velocity of 1 mm /min.	G 0% had the highest value after 24 h of storage in comparison to G2% but no differences in comparison to G0.5 % and G1%. After 1 year, no significant differences between the groups. Wollastonite had no significant effects between 24 hr and 1 year on MTBS.
Zhang et al., 2018[28]	Extracted healthy human molars	N/A	Total=not mentioned, Four groups 1. Control SBMP, 2. MPC+SBMP, 3. DMAHDM+SBMP, 4. MPC +DMAHDM+SBMP.	Water at 37C	Acid-etched (Acid name and percentage not mentioned)	4th Gen, Etch and Rinse	Chisel-shaped jig, UTM at the velocity of 0.5 mm/ min.	During 180 days in water, the bond strength of the control group dropped significantly Experimental groups yielded better results than the control.

Garcia et al., 2020[39]	Bovine teeth	Sticks (0.7 x 0.7 mm bonded area)	Total not mentioned, Four groups, 1. SKT Control, 2. SKT 1%, 3. SKT 2.5%, 4. SKT 5%.	DW at 37 ◦C	37% Phosphoric Acid	Etch and Rinse	Microtensile bond strength test at the standard speed of 1 mm/ min until fracture	After 6 months of storage in DW, the μ-TBS decreased for all groups, except SKT 5% which had a significant difference.
Barcellos et al., 2016[31]	Extracted healthy human molars	Sticks of $1mm^2$	Total=60, Three groups (n=20) 1. Control, 2. Zn-Mt 1 wt%, 3. ZnOn 1wt%.	DW at 37 ◦C	37% Phosphoric Acid	Etch & Rinse	UTM, with a load cell of 10kg with cross head velocity of 0.5mm/ min following ISO Standard 11405.	After 24 hrs, all groups showed similar values After 6 months, Bond strength values remained stable for the ZnOn containing adhesive.

Risk of Bias-Assessment of Included Studies

The quality of in-vitro studies and risk of bias are categorized as high, medium, and low risk using the Modified CONSORT Checklist. The modified consort statement consists of 14 14-item checklists. It helps in the standardization of research studies that are shown in **Table 5**. Twenty-one studies[18, 19, 23-25, 27, 29, 33,34,35,36,37, 39, 40, 42, 44, 45, 48, 51,52,53] had low risk (58.33%), nine studies[20, 32, 38, 41, 43, 46, 47, 50, 54] had medium risk (25%) while six studies [22, 26, 28, 30, 31, 49] with high risk (16.67%) on bias assessment.

Table 5: Risk Bias Assessment using Modified CONSORT Checklist

Author and Year	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Risk of Bias
Mi et al., 2022[44]	-	+	+	+	?	-	?	?	-	+	+	+	+	+	Low
Alania et al., 2022[18]	+	+	+	+	-	-	-	-	-	+	+	+	+	-	Low
Alkatheeri et al., 2015[19]	+	+	+	+	-	-	-	-	-	+	+	+	+	+	Low
Cascales et al., 2022[34]	+	+	+	+	-	-	-	-	-	+	+	+	+	?	Low
Ashtijoo et al., 2022[20]	+	+	+	+	-	-	?	-	-	+	+	?	-	-	Medium
Ezz El-Din et al., 2023[38]	+	+	+	+	-	-	-	-	-	+	+	+	-	-	Medium
Abuna et al., 2016[52]	+	+	+	+	-	-	-	-	-	+	+	+	+	-	Low
Carneiro et al., 2016[22]	-	+	+	+	-	-	-	-	-	+	+	-	+	-	High
Daood and Fawzy, 2023[37]	-	+	+	+	-	-	-	-	-	+	+	+	+	?	Low
Bauer et al., 2016[32]	+	+	+	+	-	-	-	-	-	+	+	-	+	-	Medium
Yezdani et al., 2023[51]	+	+	+	+	-	-	-	-	-	+	+	+	-	?	Low
Rolim et al., 2022[47]	-	+	+	+	-	-	-	-	-	+	+	+	+	-	Medium
Ashraf et al., 2022[30]	-	-	+	+	-	-	-	-	-	+	+	+	+	-	High
Mousavinasab et al., 2023[29]	+	+	+	+	+	-	?	-	?	+	+	?	+	-	Low
Chiari et al., 2021[36]	+	+	+	+	-	-	-	-	-	+	+	+	+	-	Low
Ñaupari-Villasante et al., 2022[45]	+	+	+	+	+	-	-	-	-	+	+	+	+	?	Low
Rifane et al., 2023[27]	?	+	+	+	-	-	-	-	-	+	+	+	+	-	Low

Sauro et al., 2015[48]	+	+	+	+	-	-	-	-	-	+	+	+	+	-	Low
Kalagi et al., 2020[41]	+	+	+	+	-	-	-	-	-	+	+	+	-	-	Medium
Kazem et al., 2024[23]	+	+	+	+	+	?	-	-	-	+	+	+	+	+	Low
Kim et al., 2021[24]	-	+	+	+	-	-	-	-	-	+	+	+	+	+	Low
Li et al., 2018[42]	+	+	+	+	-	-	-	-	-	+	+	+	+	-	Low
Cavaleiro-de-Macedo et al., 2024[35]	+	+	+	+	-	-	-	-	-	+	+	-	+	?	Low
Rizk et al., 2020[46]	+	+	+	+	-	-	-	-	-	+	+	-	+	-	Medium
Balbinot et al., 2020[53]	+	+	+	+	-	-	-	-	-	+	+	-	+	+	Low
Xie et al., 2017[50]	+	+	+	+	-	-	-	-	-	+	+	-	+	-	Medium
Oltramare et al., 2021[25]	-	+	+	+	?	-	-	-	-	+	+	+	+	+	Low
Profeta, 2014[26]	+	+	+	+	-	-	-	-	-	+	+	?	-	-	High
al-Qarni et al., 2018[54]	+	+	+	+	-	-	-	-	-	+	+	-	+	-	Medium
Ilie et al., 2022[40]	-	+	+	+	-	?	-	-	?	+	+	+	-	?	Low
Liang et al., 2018[43]	+	+	+	+	-	-	-	-	-	+	+	-	+	-	Medium
Stürmer et al., 2021[49]	+	+	+	+	-	-	-	-	-	+	+	-	?	-	High
Bendary et al., 2020[33]	+	+	+	+	-	-	-	-	-	+	+	?	+	-	Low
Zhang et al., 2018[28]	-	+	+	+	-	-	-	-	-	+	+	-	-	-	High
Garcia et al., 2020[39]	+	+	+	+	-	-	-	-	-	+	+	?	+	-	Low
Barcellos et al., 2016[31]	+	+	+	+	-	-	-	-	-	+	+	-	-	-	High

Note: Key: (Low Risk of Bias = +, High Risk of Bias = -, and unclear?)

Analysis of Findings

1. Type of Bioactive Agents used to Improve Bond Strength

Among the evaluated studies, various types of bioactive agents have been added to dentin bonding agents to improve bond strength. Most Common is Bioactive Glass in ten studies (27.78%)[22-27, 29, 32, 34, 35], amorphous calcium phosphate in three (8.33%)[17, 20, 50], hydroxyapatite in three (8.33%), one alone37 and in two with amorphous calcium phosphate and graphene[40, 51] respectively, halloysite in two (5.56%)[19, 41], DMAHM in two studies (5.56%)[28, 42] with NACP and MPC respectively. In the remaining studies (44.44%), various bioactive agents were incorporated into the dentin bonding agent as listed in **Table 3**.

2. Evaluation of Bond Strength

Twenty-four studies[16, 18, 22-27, 30-39, 41, 43, 45, 47-49] measured Micro-Tensile Bond Strength (66.67%) whereas the rest twelve Studies[17, 19-21, 28, 29, 40, 42, 44, 46, 50, 51] measured Shear Bond Strength (33.33%) to dentin.

The Universal Testing Machine is a common device used for the evaluation of bond strength in 33 studies (91.67%), whereas the remaining 3 studies (8.33%)[34, 36, 48] used a micro-tensile tester, a micro-tensile evaluation device, and linear actuator respectively as mentioned in **Table 3**.

3. Bond Strength at Different Time Points

10 Studies (27.78%)[17, 19-21, 29, 42, 43, 46, 50, 51] measured bond strengths at 24 hours. In 16 studies (44.44%), [16, 22, 23, 25,26,27, 31,32,33,34,35, 36, 39, 41, 47,48,49,] extended time measurement of bond strength was done. 10 studies (27.78%)[18, 24, 28, 30, 34, 37, 38, 40, 44, 45] reported bond strengths at varied time points.

The majority of studies stated that bond strength decreased with time/age after 6 months or 1 year [22, 23, 32, 34, 37].

4. Type of Tooth and Substrate

The data showed that Thirty Studies used extracted human molars for evaluation of bond strength, in which, seventeen studies clearly mentioned use of third molars. A single study38 reported using human pre-molars. Five studies[21, 33, 39, 46, 49] used Bovine teeth, three mentioned bovine incisors or anterior while other two did not specify the teeth used.

5. Storage Media Used
Distilled/de-ionized water was used as a storage medium in twenty-four studies. SBF in five studies[18, 25, 33, 35, 36,] DPBS in two studies[26, 34]. Artificial Saliva in two studies[37, 48] and two studies[22, 44] did not mention any storage medium.

6. Thermo-Cycling
Two studies (5.55%)[29, 38] used thermo-cycling for the aging process, one performing a thermo-cycling process for 24h and the other for 10000 cycles **(Table 4).**

7. Types of Bonding Systems
Twenty-seven studies reported using the etch and rinse system, out of which twenty-three reported using Phosphoric acid as a demineralizing agent rest of the four[18, 26, 28, 44], used various other demineralizing agents. Nine Studies used the Self-Etch System or the One-Bottle System. Self-etch primer was used as a demineralizing agent in six studies[16, 35, 37, 43, 46], [47] whereas a single study used phosphoric acid and EDTA[34, 51] respectively.

DISCUSSION
Several studies showed that bioactive agents have a positive impact on the bond strength either in maintenance or in increasing the bond strength at different time intervals. The improvement in the studies was due to the remineralization potential of bioactive agents. The agents lead to the formation apatite layer at the adhesive interface, thus strengthening the bond and restoring life. However, there are 4 studies [23, 25, 39, 48] in which a decrease in the bond strength is observed.

The study has identified and critically appraised 36 articles that evaluated the bond strength after incorporation of various bioactive agents. In 32 studies (88.89%), the results observed were positive as the bond strength improved to some extent [16, 19, 21, 26, 27, 29, 30, 36-38, 41-45] or bond strength value remained same for longer time as compared to control[17, 18, 20, 22, 24, 28, 31-35, 40, 46, 47, 49-51]. Aging is another important factor that affects bond strength, as the bond strength value has decreased after 6 months or more.

Various bioactive agents were used in these studies. The most common bioactive agent used was bioactive glass, either in pure form, commonly used silicate-based, phosphate-based, or ion-doped. The second common bioactive agents were Amorphous calcium phosphate and Hydroxyapatite, used in various forms and sizes. These agents, being closest to the tooth structure, had positive effects on bond strength. Other agents were halloysite, DMAHM, Cecropin and Iron oxide nanoparticles, PLA capsules, Chitosan, Phosphoproteins, Cross linkers PA/EGCG, FUDMA, Dicalcium Phosphate and MTA, Copper Nanoparticles, Calcium Silicate particles, POSS, Niobium Silicate, QAM-TEADDA, Titanium Oxide, Wollastonite, Simonkolleite, Zinc methacrylate and Zinc oxide nanoparticles that were incorporated in dentin bonding agent to observe changes in bond strength.

The majority of the thirty-two studies (88.89%) had improved or stable bond strength for a longer time as compared to only four studies, [23, 25, 39, 48], which showed a decline in the bond strength. Most of the studies have evaluated micro-tensile bond strength via different techniques with specific specimen dimensions, mostly using rods and beams of around $1mm^2$. Remaining studies evaluated shear bond strength, which has no specific requirements for specimen preparation. Besides this time has an important role in bond strength, which usually decreases with aging. Bond strength is evaluated at 24 hours in all studies, in which few researchers have compared it with extended time intervals and different time points to evaluate time/aging effects on bond strength, which has decreased.

The in-vitro studies were carried out using human molars, especially third molars extraction in most of the studies, with only a few studies carried out on bovine teeth. Distilled water was used as storage media in the majority of studies for evaluation of bond strength at different time points. SBF, DPBS, and Artificial Saliva were also used as storage medium in this test in other included studies. The two main bonding systems are etch and rinse and self-etch. The etch and rinse system shows better results than the self-etch system in terms of failure rates according to evidence[55]. These are important in the formation of the hybrid layer, which is responsible for the stable micro-mechanical bond at the resin-dentin interface. This is a key to increased restoration life.

Thus, the increase in bond strength observed in 32 studies out of the included studies shows that the bioactive agents show better results than the control. Further studies and experiments to select and optimize a bioactive agent to be incorporated in dentin bonding agents for the enhancement of restoration life are required to produce a new modified dentin bonding agent that shows excellent results in characterization procedures.

LIST OF ABBREVIATIONS
UTM- Universal Testing Machine
SBS-Shear Bond Strength
MTBS-Micro Tensile Bond Strength
PRISMA-Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PICO - Patient/Population, Intervention,

Comparison, and Outcome
PLA- Polylactide
PAC- Proanthocyanidin
HNT- Halloysite Aluminosilicate Nanotube
ACP- Amorphous Calcium Phosphate
CS- Calcium Silicates
NP- Nanoparticles
NBG- Niobium Phosphate Bioactive Glass
PAA- Polyacrylic acid
TMP- Trimetaphosphate
HAp- Hydroxyapatite crystals
CPP-ACP- Casein Phosphopeptide-Amorphous Calcium Phosphate
NM- NovaMin
CES-nHAp- Chicken eggshell-derived nHAp
EGCG- Epigallocatechin-3-gallate
BAG- Bioactive Glass
DCPD- Dicalcium phosphate dihydrate
CuNp- Copper nanoparticles
PAA- Polyaspartic acid
CHX- Chlorhexidine
DMAHDM- Dimethylaminohexadecyl methacrylate
POSS-8- Polyhedral Oligomeric Silsesquioxanes
MPC-Methacryloyloxyethyl Phosphorylcholine
QAM- Quaternary ammonium monomer
TEADDA- Triethylamine Dodecyl Acrylate
SKT- Simonkolleite
ZN-Mt- Zinc methacrylate
ZnOn- Zinc oxide nanoparticles
SBF- Simulated Body Fluid
DPBS- Dulbecco's Phosphate Buffered Saline
DW- Distilled Water
RT- Room Temperature

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AUTHORS' CONTRIBUTIONS
UWU Methodology, data curation, formal analysis, and original draft preparation, **ZB** Conceptualization, Data extraction, Validation, and Writing, Review & Editing, **MON** Data visualization, Literature search, review & editing, **MAB** Validation, risk of bias assessment, and review.

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