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Current strategies for biomimetic remineralization of human dentin: a scoping review

Estratégias atuais para remineralização biomimética da dentina humana: uma revisão de escopo

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RESUMO

O objetivo desta revisão de escopo foi apresentar as técnicas e estratégias de sucesso já publicadas para a remineralização biomimética da dentina humana. Foram incluídos estudos cujo objetivo principal era apresentar alguma estratégia bem-sucedida da remineralização biomimética da dentina. Não houve restrição de tempo, idioma ou idade dos participantes. Os estudos foram recuperados via CENTRAL (Cochrane), LILACS, PubMed/MEDLINE, SciELO, SCOPUS e Web of Science. Pesquisas de literatura cinzenta no Google Scholar e OpenGrey também foram realizadas para encontrar referências adicionais. Com base nos objetivos principais da pesquisa, os artigos foram classificados por técnica de acordo com a metodologia utilizada para a pesquisa. Cento e quarenta e cinco artigos, publicados entre 2003 e 2019, foram incluídos na scoping review final. Protocolos que imitam a mineralização natural da dentina buscam repor os minerais perdidos nos tecidos dentários. A remineralização biomimética propõe diferentes formas de substituir o colágeno desmineralizado na dentina utilizando materiais inorgânicos como minerais naturais, com o objetivo principal de otimizar a longevidade clínica das restaurações e melhorar o tratamento odontológico.

Palavras-chave: Materiais Biomiméticos; Materiais Dentários; Odontologia; Remineralização Dentária; Biomineralização.

ABSTRACT

The purpose of this scoping review was to present the published successful techniques and strategies for biomimetic remineralization of human dentin. Studies whose primary objective was to present the strategy of successful dentin biomimetic remineralization were included. No language, participant age, or time restrictions were set. Stud-ies were retrieved via CENTRAL, LILACS, PubMed/MEDLINE, SciELO, SCOPUS and Web of Science. Gray literature searches on Google Scholar and OpenGrey were also conducted to find additional references. Based on the main research objectives, articles were classified by technique according to the methodology used for the research. One hundred forty-five articles, published be-tween 2003 and 2019, were included in the final scoping review. Protocols that imitate dentin's natural mineralization seek to restore lost minerals in dental tissues. Biomimetic remineralization proposes different ways to replace demineralized collagen in dentin by using inorganic materials like natural minerals, with the primary purpose of optimizing the clinical longevity of restorations and improving dental treatment.

Keywords: Biomimetic Materials, Dental Materials, Dentistry, Dentin, Tooth Remineralization, Biomineralization.

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INTRODUCTION

Consistent with current health science trends to seek regenerative therapies which mimic the body's innate biological processes, several strategies have been developed to recover lost dental tissue. The mineral replacement in type I collagen is critical for stabilizing the mechanical properties of calcified tissues such as dentin. In dentin, nearly 90% of the organic content is composed of type I collagen, whereas non-collagenous proteins account for 10% of its content (ZURICK et al., 2013). These non-collagenous proteins play a key role in the mineralization process, as their components are highly anionic, phosphorylated and multifunctional (VEIS & DORVEE, 2013).

However, the remineralization of dentin appears more challenging than of enamel because of the greater scarcity of apatite particles in dentin (BERTASSONI et al., 2009). Different strategies have been applied to the remineralization of dentin, and a recent systematic review has presented some techniques used (CAO et al., 2015). Biomineralization is a biological process based on a matrix particle-mediated, non-classical and organic crystallization (CAO et al., 2014). Extracellular matrix proteins execute an essential function in apatite nucleation growth and control for the process of dentin remineralization (NUDELMAN et al., 2013). Some materials have been proposed for restoring demineralized dentin by inducing remineralization.

A common classification used for remineralization techniques on biomaterials is called “top-down” or “bottom-up” strategies. The top-down approach involves free particles of biomaterials responsible for incorporating minerals over crystallites in collagen, at a nanoscale level (BRAGA & FRONZA, 2020). In this group, the ions involving calcium, phosphate, and sodium are incorporated into gels or in recently developed materials. However, for these techniques, there is a need to deposit the non-collagenous protein analogs (NCPs) already mentioned for growth using already existing primers, since there will be no spontaneous nucleation.

The bottom-up approach uses matrix protein biomimetic analogs to stabilize nanoprecursors, starting from organized materials forming a template or scaffold (BRAGA & FRONZA, 2020; CAO et al., 2015). It is considered a “non-classical” pathway technique and is based on the importance of the dentin's intrafibrillary mineral zones (CAO et al., 2015). The term "biomimetic" usually refers to the use of analogues to guide mineral deposition, therefore, mimicking the biological process. "Top-down"

approaches, for instance, are usually not considered biomimetic. The bottom-up approach plays a fundamental role in biomechanics by making use of the partially or totally dissolved minerals in these areas to create large gaps. In these situations, in the presence of NCP analogs, the free calcium and phosphate ions assemble in the groups considered pre-enucleation and are added to the amorphous calcium phosphate (ACPs) nanoprecursors recruited by the NCPs. They then fill the intrafibrillary gaps, stimulating the growth of regular apatites in the mineralization process. this strategy includes biomimetic analogs and results in the primordial formation of amorphous ACP nanoprecursors.

Partial caries removal in procedures with minimal intervention are used clinically to save the tooth structure and prevent damage to the pulp. The infected dentin is removed and the partially demineralized dentin is sealed with materials that enhance remineralization. The glass ionomer cement has been known to be used for this purpose. Furthermore, studies have demonstrated potential bioactive cements and adhesives which promote dentin repair through other strategies including ion release Ca-P, biomimetic remineralization tissue-guided, and others (HERNÁNDEZ; COBB; SWIFT, 2014).

Protocols that imitate the natural mineralization of dentin seek to restore minerals in dental tissues that are lost mainly because of caries. Biomimetic remineralization proposes different ways to replace demineralized collagen in dentin by using inorganic materials similar to natural minerals (CAO et al., 2015; NIU et al., 2014).

Thus, preventive and operative dentistry researchers have sought to discover methods to induce there mineralization of hypomineralized human dental tissues, especially dentin (BRAGA & FRONZA, 2020). Therefore, the purpose of this scoping review was to present all the published successful techniques and strategies for biomimetic remineralization of human dentin.

MATERIAL AND METHODS

Protocol and registration

The reporting of this scoping review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist (TRICCO et al., 2018).

The scoping review protocol was registered at the International Prospective Register of Systematic Reviews in association with the systematic review of registration number CRD42016049821. The scoping review final protocol was registered prospectively with the Open Science Framework on 21 December 2020 (https://osf.io/5c3vm/).

Eligibility criteria

Studies in which the primary objective was to present any successful biomimetic remineralization strategy for dentin were included. No language or time restrictions were set.

Articles were excluded for the following reasons: (1) articles that did not address a remineralizing technique based on processes that mimic natural biomineralization; (2) articles that were not research studies, including letters, conference abstracts, personal opinions, book chapters, theses, congress proceedings, case reports or case series.

The “PCC” mnemonic (population, concept and context) was used as a guide to construct a clear and meaningful title and strategy search for this review.

Information sources

Electronic searching in databases, namely, CENTRAL, LILACS, PubMed/MEDLINE, SciELO, SCOPUS and Web of Science, identified relevant studies. Non peer-reviewed literature searches with Google Scholar and OpenGrey were also conducted to find additional references. No language, time or other restrictions were set.

After obtaining all references, duplicates were excluded by using softwares programs EndNote Web®, Thomson Reuters, USA and Rayyan®, QCRI, Qatar. All the electronic database searches were conducted for the last time on January 1st, 2020.

Search

Studies were identified by using a search strategy adapted for each electronic database with the aid of a health sciences librarian: Cochrane Central Register of

Controlled Trials (CENTRAL), LILACS, PubMed (MEDLINE), SciELO, SCOPUS and Web of Science.

A non peer-reviewed literature search was performed using Google Scholar and OpenGrey by screening the title and abstracts for the first 150 hits (filtered by "relevance"). In addition, a hand search was performed on the reference lists of the selected articles for any additional references that might have been omitted in the electronic search.

Selection of sources evidence

The study selection was conducted in three phases. In phase 1, two investigators (S. J. L. S. and P. F. A.) independently screened the titles of potentially relevant studies and selected articles that appeared to meet the inclusion criteria. In phase 2, the same reviewers independently read the abstracts of all previously selected articles. In phase 3, the two investigators independently read the full text of all selected articles and excluded studies that did not meet the inclusion criteria.

Any disagreements in any of the three phases were resolved by discussion and agreement between the two reviewers. If a consensus could not be reached, a third author (F. S. N.) was involved in making a final decision.

Data charting process and data items

The first investigator (S. J. L. S.) collected the following data from the selected articles: study characteristics (author(s), year, country, and type of study), design (approach or protocol tested) and results characteristics (objectives, main results and conclusions). The second author (P. F. A.) checked all retrieved information for analysis. If the required data were not complete, attempts were made to contact the authors to retrieve any pertinent missing information.

Synthesis of results

Based on the main research objectives, articles were classified by their strategies according to the methodology used for research. Authors and year of publication were

used to categorize the included studies. The methodological characteristics were analyzed and grouped according to similarity. All findings in this review are based on published research, as listed in the references.

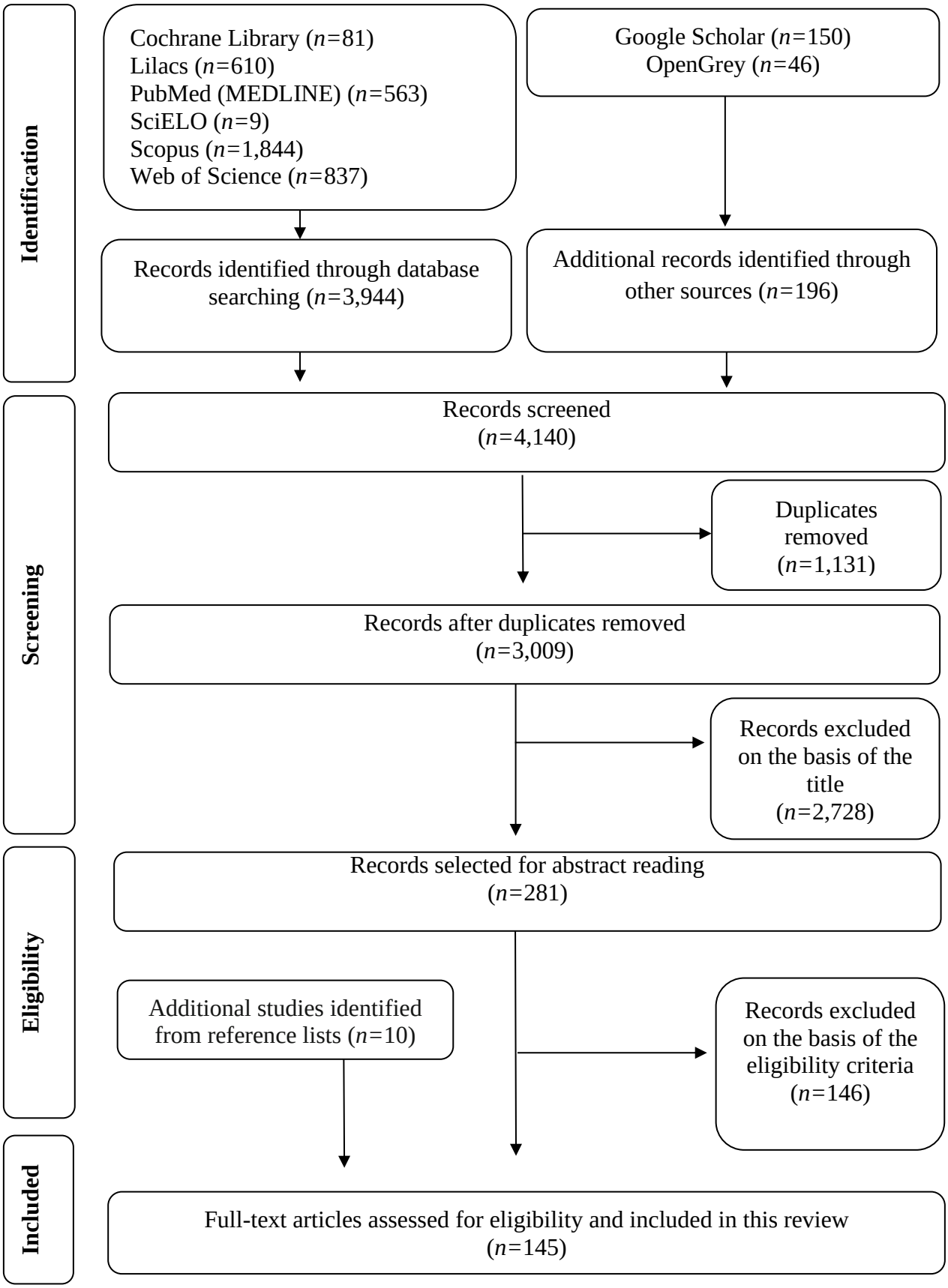
RESULTS

Selection of sources of evidence

In phase 1 of the study selection, 3,944 citations were identified across six electronic databases. The non peer-reviewed literature results added 196 references; 44,700 citations were identified with Google Scholar, but only 150 citations were considered for analysis (filtered by "relevance") with 46 results identified by OpenGrey. After the duplicated articles were removed, 3,009 citations remained. In the first phase, 2,728 articles were excluded by title. A thorough screening of 281 abstracts was conducted, and 146 references were excluded in phase 2. The hand search from the reference lists of the identified studies yielded 10 additional studies. Finally, 145 studies satisfied the inclusion criteria and remained in phase 3 after full-text reading and were selected for this review.

Seven authors were contacted to send some relevant information about their study. Two authors responded with some information after contact by email and Re-searchGate. Another five authors did not respond. Figure 1 details the process of iden-tification, inclusion and exclusion of studies.

Figure 1 – Flow diagram of literature search and selection criteria.



Source: Authors according to PRISMA Statement

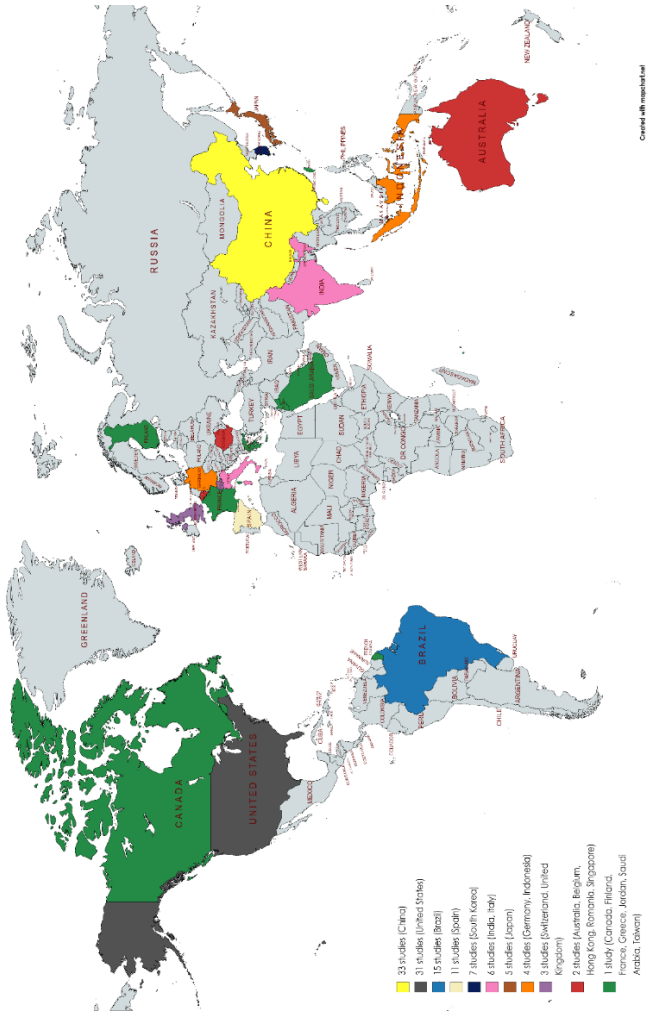
A qualitative analysis was performed in a descriptive manner. A meta-analysis and the risk of bias analysis were not foreseen, as it is a scoping review. The types of

studies included were diverse, including In-vitro, Ex-vivo, and In-vivo studies. Due to the heterogeneity of the included studies, studies were grouped by material similarity.

Characteristics of sources of evidence

Searches identified studies from 2003 to 2020. Figure 2 shows the global overview of the countries included in this scoping review. Table 1 summarizes the characteristics of the strategies of the included studies. The data were grouped into products using chemical elements from dentin remineralization, products derived from acids, and other diverse compounds.

Figure 2 – Publications included originating from countries



Source: Authors created by *MapChart.net*

Table 1 – Strategic characteristics of all the included studies, grouped by chemical elements, acids and other compounds.

Product	References	N=Total
Chemical elements		
Calcium	1, 5, 7, 9, 17, 18, 19, 33, 35, 36, 39, 41, 44, 48, 49, 50, 52, 53, 59, 61, 68, 69, 70, 71, 74, 76, 77, 81, 82, 86, 90, 91, 92, 93, 95, 97, 98, 100, 101, 102, 103, 107, 110, 111, 115, 116, 118, 119, 123, 130, 131, 139, 141	53
Silica	5, 9, 17, 18, 29, 35, 39, 41, 65, 68, 69, 74, 76, 77, 81, 82, 92, 93, 97, 98, 100, 101, 102, 103, 107, 110, 111, 115, 116, 118, 119, 139, 141	33
Phosphate	1, 14, 17, 18, 19, 26, 33, 36, 44, 46, 47, 48, 49, 50, 52, 53, 59, 61, 70, 71, 81, 86, 90, 92, 93, 95, 98, 100, 107, 109, 122, 123, 130, 132, 139, 142	36
Sodium	1, 12, 13, 16, 26, 44, 46, 47, 48, 49, 81, 90, 92, 93, 98, 107, 142	17
Hydroxide	7	1
Chloride	2, 16, 26, 57	4
Tin	16	1
Zinc	80, 90, 91, 92, 93, 121, 122, 123	8
Zirconium	74, 115	2
Aluminum	41	1
Fluoride	10, 12, 13, 16, 22, 36, 37, 44, 55, 84, 85, 108	12
Carbonate	2, 29, 50	3
Niobium	14	1
Copper	64	1
Amina/Ammonia	2, 10, 16, 22, 50, 84, 85	7
Potassium	22	1
Iodide	22	1
Silver	22, 84, 85	3

Nitride	32	1
Boron	32	1
Lithium	57	1
Tantalum	43	1
Acids		
PAA (PolyAcrylic Acid)	1, 41, 48, 49, 50, 68, 76, 77, 81, 82, 83, 98, 109, 114, 118, 119, 126, 128	18
PVPA (Polyvinylphosphonic Acid)	50, 68, 69, 76, 82, 83, 118, 119	8
pAsp (Polyaspartic Acid)	11, 21, 87, 90, 105, 107, 109, 120, 131	9
L-Glu (Glutamic Acid)	114	1
EDTA (Ethylenediaminetetraacetic Acid)	40, 124	2
Citric Acid	40	1
Other compounds		
Hydroxyapatite (calcium/phosphate)	17, 18, 44, 52, 71, 123	6
Glass Ionomer	7, 9, 11, 56, 88, 110	6
Bioactive glass	14, 15, 30, 31, 34, 38, 52, 60, 64, 110, 125, 129, 133, 143, 145	15
PILP (polymer-induced liquid-precursor)	21, 87, 105, 108, 109, 120	6
Chitosan	8, 16, 54, 106, 137, 138, 140	7
Biomimetic analogs and/or synthetic peptides	2, 10, 12, 13, 25, 51, 59, 68, 76, 80, 94, 112, 127	13
EMD/DMP (Enamel Matrix Derivates or Dentin Matrix Protein)	10, 25, 80, 94, 127	5
CPP/ACP	3, 4, 8, 12, 13, 23, 26, 36, 55, 63, 70, 72, 75, 96, 99, 106, 126, 130, 131, 132	20
Chlorhexidine	23, 58, 66, 67, 70, 122	6

Natural extract	2, 6, 19, 20, 22, 27, 36, 37, 58, 63, 77, 78, 79, 104, 113, 117, 136	17
PAMAM (Polyamidoamine dendrimer)	42, 45, 62, 73, 75, 128, 132, 134, 135, 144, 145	11
Agarose	24, 53, 86, 140	4
Methacrylate	32, 41, 45, 59, 72	5
Glutaraldehyde	28	1

Source: Authors

Results of individual sources of evidence

Each strategy used with different products and the strategic sources used are described in Table 2.

Table 2 – Strategic characteristic of all the included studies described by authors

Code	Author	Year	Strategy
1	Abuna *et al.*	2016	Experimental calcium phosphate-based adhesive, PAA, STMP.
2	Abunawareg *et al.*	2017	Natural extract (riboflavin), UV, EDC-HCl
3	Ackermann *et al.*	2019	aCa-polyP-MP-dentifrice
4	Adebayo, Burrow & Tyas	2010	CPP-ACP
5	Aggarwal & Bhasin	2018	Calcium silicate materials (CSM) after acid etching
6	Aguiar *et al.*	2014	PAC, Natural extract
7	Al-Abdi, Paris & Schwendicke	2017	Glass Hybrid
8	Annisa *et al.*	2019	p-Chi, CMC/ACP
9	Atmeh *et al.*	2015	Calcium-silicate cement, cement Biodentine(TM) and Glass Ionomer
10	Bachli *et al.*	2019	DMP/EMD, AMF

Code	Author	Year	Strategy
11	Bacino *et al.*	2019	PILP, pAsp, RMGI
12	Barbosa-Martins *et al.*	2018a	NaF, MP™ e CR™
13	Barbosa-Martins *et al.*	2018b	NaF, CPP-ACP, New peptide
14	Bauer *et al.*	2016	NPG
15	Bauer *et al.*	2019	Bioactive glass
16	Beltrame *et al.*	2018	PBS, AMF/NaF/SnCl2, Chi, p-Chi
17	Besinis, Van Noort & Martin	2014	Silica and hydroxyapatite nanoparticles
18	Besinis, Van Noort & Martin	2012	Silica and hydroxyapatite nanoparticles
19	Bortolotto *et al.*	2017	Riboflavin, Calcium-phosphate based product
20	Boteon *et al.*	2017	PAC, Natural extract
21	Burwell *et al.*	2012	PILP, pAsp
22	Cai *et al.*	2019	PAC, Natural extract, Fluoride based treatment, Silver diamine fluoride
23	Cai *et al.*	2017	Chlorhexidine, ACP
24	Cao & Li	2016	Agarose
25	Cao *et al.*	2014b	DMP1-derived peptides
26	Cao *et al.*	2013	CPP-ACP, STMP
27	Castellan *et al.*	2011	PAC, Natural extract
28	Chen *et al.*	2016	Glutaraldehyde
29	Chiang *et al.*	2014	CCMS-HP
30	De Caluwé *et al.*	2017	Bioactive glass
31	De Morais *et al.*	2018	Bioactive glass
32	Degrazia *et al.*	2018	Methacrylate-based adhesive containing boron nitride nanotubes
33	Dickens, Flaim & Takagi	2003	Calcium-phosphate cement

Code	Author	Year	Strategy
34	D'Onofrio *et al.*	2016	Bioactive glass
35	Dreger *et al.*	2012	MTA, Portland cement
36	Epasinghe, Yiu & Burrow	2016	PAC, Natural extract, Fluoride, CPP-ACP
37	Epasinghe *et al.*	2017	PAC, Natural extract, Fluoride
38	Forsback, Areva & Salonen	2004	Bioactive glass, SBF
39	Gandolfi *et al.*	2009	Calcium-silicate cements
40	Gandolfi *et al.*	2019	EDTA, Citric Acid, SBF
41	Gandolfi *et al.*	2011	Calcium-silicate cement, Portland cement
42	Gao *et al.*	2017	PAMAM
43	Garcia *et al.*	2018	Tantalum oxide
44	Gavrila *et al.*	2016	Artificial saliva, Fluoride, Hydroxiapatite particles
45	Ge *et al.*	2017	PAMAM, DMADDM
46	Gonçalves *et al.*	2018a	STMP
47	Gonçalves *et al.*	2018b	STMP
48	Gu *et al.*	2011a	Portland cement, PAA, STMP
49	Gu *et al.*	2010	Portland cement, PAA, STMP
50	Gu *et al.*	2011b	Portland cement, PVPA, PAA
51	Guentsch *et al.*	2019	Experimental biomimetic mineralization kit (BIMIN)
52	Gupta *et al.*	2017	Bioactive glass, Hydroxyapatite nanoparticles
53	Han *et al.*	2017	Agarose gel
54	Huang *et al.*	2019	p-Chi
55	Iafisco *et al.*	2018	Fluoride, ACP
56	Iijima *et al.*	2019	S-PRG

Code	Author	Year	Strategy
57	Ishimoto *et al.*	2015	Lithium chloride
Islam *et al.*	2012	Hesperidin, Chlorhexidine, Natural extract	
59	Ito *et al.*	2012	Phosvitin and CEMET (4-METCa salt)
60	Jang *et al.*	2018	Bioactive glass
61	Jayasree *et al.*	2017	Tetracalcium phosphate cement
62	Jia *et al.*	2014	PAMAM
63	Jose, Sanjeev & Sekar	2016	CPP-ACP, Natural extract
64	Jun *et al.*	2018	Bioactive glass, Copper
65	Jung *et al.*	2019	Bioactive glass, Silica nanoparticles
66	Kim *et al.*	2011	Chlorhexidine
67	Kim *et al.*	2012	Chlorhexidine
68	Kim *et al.*	2010a	Portland cement, PAA, PVPA
69	Kim *et al.*	2010b	Portland cement, PVPA
70	Kovtun *et al.*	2012	ACP, Chlorhexidine
71	Kutsch, Chaiyabutr & Milicich	2013	Hydroxyapatite nanoparticles
72	Li *et al.*	2014	DMADDM, ACP
73	Li *et al.*	2013	PAMAM
74	Li *et al.*	2017	Tricalcium silicate, zirconium oxide
75	Liang *et al.*	2019	ACP, PAMAM
76	Lin *et al.*	2016	Portland cement, PVPA, PAA
77	Liu *et al.*	2014	PAC, Natural extract
78	Liu *et al.*	2012	PAC, Natural ext[90][90]ract
79	Liu *et al.*	2011a	PAC, Natural extract
80	Liu *et al.*	2013	DMP1-derived peptides

Code	Author	Year	Strategy
81	Liu *et al.*	2011b	PAA, Portland cement, STMP
82	Liu *et al.*	2011c	Portland cement, PAA, PVPA
83	Mai *et al.*	2009	PVPA, PAA
84	Mei *et al.*	2017	SDF
85	Mei *et al.*	2014	SDF
86	Ning *et al.*	2012	Agarose gel, Calcium, Phosphate
87	Nurrohman *et al.*	2016	PILP, pAsp
88	Okuyama *et al.*	2016	S-PRG
89	Osorio *et al.*	2014a	Zinc
90	Osorio *et al.*	2016a	Zinc, Portland cement, pAsp, STMP
91	Osorio *et al.*	2016b	Zinc-loaded nanoparticles, Calcium-loaded nanoparticles
92	Osorio *et al.*	2018	Zinc, Silica, Calcium, Sodium, Phosphate
93	Osorio *et al.*	2014b	Zinc, Calcium-silicate cement
94	Padovano *et al.*	2015	DMP1-derived peptides
95	Peters *et al.*	2010	Calcium-phosphate cement
96	Poggio *et al.*	2013	CPP-ACP
97	Pratiwi, Meidyawati & Djauharie	2017	MTA
98	Qi *et al.*	2012	MTA, PAA, STPP
99	Rahiotis & Vougiouklakis	2007	CPP-ACP
100	Revankar *et al.*	2017	MTA, Calcium phosphate cement
101	Reyes-Carmona, Felippe & Felippe	2009	MTA, Portland cement
102	Reyes-Carmona, Felippe & Felippe	2010	MTA, Portland cement

Code	Author	Year	Strategy
103	Reyes-Carmona *et al.*	2010	MTA
104	Rubel *et al.*	2016	PAC, Natural extract
105	Saeki *et al.*	2017	PILP, p-Asp
106	Santoso *et al.*	2019	ACP, p-Chi
107	Sauro *et al.*	2015	STMP, pAsp, Calcium-silicate cement
108	Saxena *et al.*	2018	Fluoride-dopped PILP
109	Saxena *et al.*	2019	PAA, pAsp, TPP, PILP
110	Schwendicke *et al.*	2019	Bioactive glass, Fluoride, Glass ionomer, MTA, Calcium-silicate cement
111	Seo *et al.*	2013	MTA
112	Sfeir *et al.*	2014	DPP-inspired peptides
113	Shi, Li & Wang	2015	Natural extract
114	Sun *et al.*	2014	PAA, L-Glu
115	Suprastiwi, Putranto & Maharti	2019	Biodentine™, Calcium-silicate cement, Zirconium
116	Taddei, Prati & Gandolfi	2017	Calcium-silicate cement
117	Tang *et al.*	2013	PAC, Natural extract
118	Tay & Pashley	2009	Portland cement, PVPA, PAA
119	Tay & Pashley	2008	Portland cement, PVPA, PAA
120	Thula-Mata *et al.*	2011	PILP, pAsp
121	Toledano *et al.*	2015	Zinc
122	Toledano *et al.*	2020	Chlorhexidine, Phosphate, Zinc
123	Toledano *et al.*	2018	EDTA
124	Toledano *et al.*	2014	Hydroxyapatite, Zinc
125	Vollenweider *et al.*	2007	Bioactive glass
126	Wang *et al.*	2013	CPP-ACP, PAA

Code	Author	Year	Strategy
127	Wang *et al.*	2011a	DMP1-derived peptides, synthetic peptides
128	Wang *et al.*	2015	PAMAM, PAA
129	Wang *et al.*	2011b	Bioactive glass
130	Weir *et al.*	2017	ACP, TTCP
131	Wu *et al.*	2017	ACP, pAsp
132	Xiao *et al.*	2017	BMC, PAMAM, ACP
133	Xie *et al.*	2008	Bioactive glass
134	Xie *et al.*	2015	PAMAM
135	Xie *et al.*	2016	PAMAM
136	Xie, Bedran-Russo & Wu	2008	PAC, Natural extract
137	Xu *et al.*	2011	p-Chi
138	Xun *et al.*	2014	p-Chi
139	Yoo *et al.*	2016	MTA
140	Zaharia *et al.*	2017	Agarose, p-Chi
141	Zanini *et al.*	2012	Biodentine™, Calcium silicate cement
142	Zhang *et al.*	2012	STMP
143	Zhang *et al.*	2019	Bioactive glass, Aminoacids
144	Zhou *et al.*	2014	PAMAM
145	Zhou *et al.*	2012	Polydopamine

Abbreviations: 4-METCa: Salt calcium salt of 4-methacryloxyethyl trimellitate, aCa-polyP-MP: Amorphous Ca-polyP microparticles, ACP: Amorphous calcium phosphate, AMF: Amine fluoride, BMC: Bioactive multifunctional composite, CCMS-HP: Silica mesoporous with phosphoric acid, CMC/ACP: Carboxymethyl chitosan/amorphous calcium phosphate, CPP-ACP: Casein phospho-peptide-amorphous calcium phosphate, CR: Curodont Repair™, DMADDM: Dimethylamino-dodecyl methacrylate, DMP: Dentin matrix protein, DPP: Dentin phosphophoryn, EDC-HCl: car-bodiimide hydrochloride, EDTA: Ethylenediaminetetraacetic acid, EMD: enamel matrix deriva-tives; L-Glu: L-Glutamic acid, MP: Mi Paste™, MTA: Mineral trioxide aggregate, NaF: Sodium flu-oride, NCPs: Non-collagenous proteins, NPG: Niobium–phosphate bioactive glass, PA: Phosphoric acid,PAA: Polyacrylic acid, PAC: Proanthocyanidin, PAMAM: Poly(amidoamine) dendrimer, pAsp: Poly-aspartic acid, PBS: Phosphate-buffered

saline, P-chi: Phosphorylated chitosan, PILP: Polymer-Induced Liquid-Precursor, PVPA: Polyvinylphosphonic acid, RMGI: Resin modified glass ionomer, SBF: Simulated body fluid, SDF: Silver diamine fluoride, S-PRG: Surface reaction-type pre-reacted glass-ionomer, STMP: sodium trimetaphosphate, STPP: sodium tripolyphosphate, TCS: Tricalcium silicate, TPP: Tripolyphosphate, TTCP: Tetracalcium phosphate, ZrO2: Zirconium oxide.

Synthesis of results

All 145 studies were analyzed, and the data extracted. In-vitro, In-vivo, and Ex-vivo studies were included. Materials can be classified according to method, activity, or composition, according to Supplemetary Table S4. Several studies are currently looking at strategies to turn restorative materials into remineralizing antimicrobial and antifouling without compromising mechanical and adhesive properties. Sometimes these strategies even increase the adhesive properties.

DISCUSSION

Current techniques for dentin remineralization involve chemical processes based on the original tissue formation (CAO et al., 2020). Therefore, we found that the literature pointed to the development of biomaterials that seek to achieve this objective of mineral replacement through different strategies, and so this review listed the chemical elements involved in each of these biomaterials.

About 90% of the organic matrix of dentin is formed by type I collagen, and caries, acid challenges or other factors can expose this collagen in the oral environment. The action of enzymes, such as endometalloproteinases, can degrade it, after being exposed (CAO et al., 2020). This type of collagen is important for biomineralization, as it attracts amorphous calcium phosphate (ACP) nanoprecursors. This review identified several recent studies that used type I collagen as a framework for attracting ACPS mediated by NCPs. This strategy has been exhaustively studied and is explained by the interfibrillar and intrafibrillar remineralization of dentin from the attraction of ACP nanoprecursors and the apatite nucleation of collagen fibrils (NIU et al., 2014). Likewise, casein phosphopeptide - amorphous calcium phosphate (CPP / ACP) has been used and reported as a potential remineralization inducer from the same chemical perspective.

The collagen matrix serves as a deposition of minerals. However, it does not provide clustering mechanisms for hydroxyapatite. There are non-collagenous proteins (NCPs) for this mediation, which correspond to only 10% of the dentin organic composition. NCPs, such as dentin matrix protein (DMP1) and dentin phosphoryn (DPP, DMP2), have an affinity for calcium and collagen and regulate the nucleation and growth of minerals (NUDELMAN et al., 2013) Different proteins can act as nucleating or mineral inhibitors. Therefore, other strategies involve the study of this part of dentin for the dentin remineralization process. Much research is currently focused on the development of biomimetic analogs of these NCPs, since the purification process of these natural NCPs is difficult and unfeasible on a large scale. Acids such as polyacrylic acid (PAA) and polyvinylphosphonic acid (PVPA) can be used as analogs of these proteins in the biomimetic dentin mineralization process (CAO et al., 2020). Other acids, such as citric acid, polyaspartic acid (pAsp), polycarboxylic acid, glutamic acid (L-Glu), and even ethylenediaminetetraacetic acid (EDTA) have been proposed as analogs for this same clinical situation in the studies identified in this review.

Using EDTA, dentin's biomimetic remineralization occurs in the preservation of dentin collagen and the maintenance of an exposed layer, free of minerals in dentin. This mechanism has also been proposed in the use of NCP analogs for remineralization. In this same method, strategies using 37% phosphoric acid (PA) using the same methodology have been identified, mainly to mimic the demineralization/remineralization processes of natural physiological imbalance processes, as with dental caries. Phosphoric acid mimics dentin etching for bonding procedures. Dental caries can be mimicked by acids such as lactic acid in pH cycling models.

The combination of acids with a function analogous to NCPs and other materials containing elements also present in the dentinal matrix, such as phosphorus, calcium, and sodium, has also been investigated. The current strategies recommend using materials with known remineralizing potential, such as MTA or Portland cement, and other hydraulic cements with different trade names, but based on the same chemical structure containing phosphate, calcium, and sodium. These cements also include silica, resulting in the formation of a more stable aggregated polymer for the remineralization process (BERTASSONI et al. 2009). Therefore, together with materials such as cements containing this composition, these acids more easily stabilize the rescued ACP nanoprecursors. These are small enough to penetrate the intermineralized and damaged

collagen interfibrillary and intrafibrillary spaces, imitating the formation of a regularly ordered apatite. However, each acidic chemical attack increases the surface energy and subsequent chemical bonding of ACP nanoprecursors, and some of them are still being elucidated and evaluated in these studies.

The phosphorylated collagenous matrix will serve as a model or niche for attracting the ACP nanoprecursors responsible for the regular apatite nucleation of the remineralization process. This dentin collagen is important because it is phosphorylated so that it can promote remineralization. In addition to the acids already mentioned and the cements that act together, other materials such as chitosan (Chi), peptides and oligopeptides with a phosphate group, PAMAM dendrimer, phosphate solutions and protein analogs have also demonstrated effective results with this same mechanism. Studies included in this review indicated strategies using bioactive glasses, agarose, zinc, chlorhexidine, methacrylate, glutaraldehyde, synthetic peptides, and natural extracts (obtained from grapes, green tea and others).

Strategies involving fluoride with the potential to aid in dentin remineralization have also been extensively studied, and this review identified methods using its free form, ions, gels, varnishes, or materials such as glass ionomer. More recent studies also point to new strategies using several chemical precursors such as tin, aluminum, carbonate, niobium, copper, amine or ammonia, potassium and iodide, silver, nitride, boron, lithium and tantalum, grouped in this review according to their composition by chemical elements of commercially available materials, in Table 1. However, these studies are sparse, and their action mechanisms are still not completely elucidated, despite the positive results obtained for dentin remineralization.

The included articles document the growth of studies in this promising area for the development of new dental materials. However, some limitations are the impossibility of grouping the studies due to the heterogeneity of the articles included, and the impossibility of performing statistical analysis with quantitative synthesis. Even though the biomimetic approaches have demonstrated a potential for promoting dentin remineralization, more studies are required to confirm other desirable properties of remineralizing action, such as materials with antifouling, antibacterial, biocompatibility characteristics for better performance, clinical applicability, and increased dentin-resin bond strength.

For future studies, clinical trials with more extended observation periods and a high degree of scientific evidence would be advisable to confirm the data collected in this scoping review. More research is suggested, mainly with clinical application methodology and In-vivo monitoring since most of the included studies have been In-vitro. Understanding the dentin remineralization process in vivo allows considering other parameters such as oral hygiene conditions and control of the patient's biofilm habits, diet, age, and oral microbiota, which may influence the success of restorative treatment depending on strategy. Therefore, despite the scientific challenges in these studies, the main results showed the importance of the biomimetic dentin remineralization in improving the bonding performance of adhesive restorations.

Biomimetic remineralization of dentin is a promising area for the development of new dental materials. The remineralizing action can be enhanced in materials with anti-fouling, antibacterial, and biocompatible characteristics, without compromising mechanical and adhesive properties.

REFERÊNCIAS

ABUNA, G.; FEITOSA, V.P.; CORRER, A.B.; CAMA, G.; GIANNINI, M.; SINHORETI, M.A.; et al. Bonding performance of experimental bioactive/biomimetic self-etch adhesives doped with calcium-phosphate fillers and biomimetic analogs of phosphoproteins. **J. Dent**. v. 52, n. 1, p.79-86, 2016.

ABUNAWAREG, M.; ABUELENAIN, D.A.; ELKASSAS, D.; HAIMED, T.A.; AL-DHARRAB, A.; ZIDAN, A.; et al. Role of dentin cross-linking agents in optimizing dentin bond durability. **Int. J. Adhes.** v. 78, n. 1, p. 83-88, 2017.

ACKERMANN, M.; TOLBA, E.; NEUFURTH, M.; WANG, S.; SCHRÖDER, H.C.; WANG, X.; et al. Biomimetic transformation of polyphosphate microparticles during restoration of damaged teeth. **Dent. Mater**. v. 35, n. 2, p. 244-256, 2019.

ADEBAYO, O.A.; BURROW, M.F.; TYAS, M.J. Resin–dentine interfacial morphology following CPP–ACP treatment. **J. Dent.** v. 38, n. 2, p. 96-105, 2010.

AGGARWAL, V.; BHASIN, S. Application of Calcium Silicate Materials After Acid Etching May Preserve Resin-Dentin Bonds. **Oper. Dent.** v. 43, n. 5, p. E243-E252, 2018.

AGUIAR, T.R.; VIDAL, C.M.P.; PHANSALKAR, R.S.; TODOROVA, I.; NAPOLITANO, J.G.; MCALPINE, J.B.; et al. Dentin Biomodification Potential Depends on Polyphenol Source. **J. Dent**. Res. v. 93, n. 4, p. 417-422, 2014.

AL-ABDI, A,; PARIS, S.; SCHWENDICKE, F. Glass hybrid, but not calcium hydroxide, remineralized artificial residual caries lesions in vitro. Clin. **Oral Investig**. v. 21, n. 1 , p. 389-396, 2016.

ANNISA, R.N.; DJAUHARIE, N.; SUPRASTIWI, E.; AVANTI, N. The effect of carboxymethyl chitosan/amorphous calcium phosphate to guide tissue remineralization of dentin collagen. I. J. Appl. **Pharm**. v. 11, n . 1 , p. 181-183, 2019.

ATMEH, A.R.; CHONG, E.Z.; RICHARD, G.; BOYDE, A.; FESTY, F.; WATSON, T.F. Calcium silicate cement-induced remineralisation of totally demineralised dentine in comparison with glass ionomer cement: tetracycline labelling and two-photon fluorescence microscopy. **J. Microsc**. v. 257, n. 2, p. 151-160, 2014.

BÄCHLI, K.; SCHMIDLIN, P.R.; WEGEHAUPT, F.; PAQUÉ, F.; RAMENZONI, L.; BOTTER, S. Remineralization of Artificial Dentin Caries Using Dentin and Enamel Matrix Proteins. **Materials (Basel).**v. 12, n. 13, p. 2116, 2019.

BACINO, M.; GIRN, V.; NURROHMAN, H.; SAEKI, K.; MARSHALL, S.J.; GOWER, L.; et al. Integrating the PILP-mineralization process into a restorative dental treatment. **Dent. Mater**. v. 35, n. 1, p. 53-63, 2019.

BARBOSA-MARTINS, L.; SOUSA, J.; ALVES, L.; DAVIES, R.; PUPPIN-RONTANTI, R. Biomimetic Mineralizing Agents Recover the Micro Tensile Bond Strength of Demineralized Dent. **Mat. (Basel).** v. 11, n. 9, p. 173, 2018.

BARBOSA-MARTINS, L.F.; DE SOUSA, J.P.; DE CASTILHO, A.R.F.; PUPPIN-RONTANI, J.; DAVIES, R.P.W.; PUPPIN-RONTANI, R.M. Enhancing bond strength on demineralized dentin by pre-treatment with selective remineralising agents. **J. Mech. Behav. Biomed. Mater**. v. 81, n. 1, p. 214-221, 2018.

Bauer, J.; Carvalho, E.M.; Carvalho, C.N.; Meier, M.M.; de Souza, J.P.; Carvalho, R.M.; et al. Development of a simplified etch-and-rinse adhesive containing niobiophosphate bioactive glass. **Int. J. Adhes. Adhes**.v. 69, n. 1, p. 110-114, 2016.

Bauer, J.; Silva e Silva, A.; Carvalho, E.M.; Ferreira, P.V.C.; Carvalho, C.N.; Manso, A.P.; et al. Dentin pretreatment with 45S5 and niobophosphate bioactive glass: Effects on pH, antibacterial, mechanical properties of the interface and microtensile bond strength. **J. Mech. Behav. Biomed. Mater**. v. 90, n. 1, p. 374-380, 2019.

Beltrame, A.P.C.A.; Suchyta, D.; Abd Alraheam, I.; Mohammed, A.; Schoenfisch, M.; Walter, R.; et al. Effect of Phosphorylated Chitosan on Dentin Erosion: An in vitro Study. **Caries Res.** v. 52, n. 5, p. 378-386, 2018.

Bertassoni, L. E.; Habelitz, S.; Kinney, J. H.; Marshall, S. J.; Marshall, G. W. Biomechanical perspective on the remineralization of dentin, **Caries Res**. v. 43, n. 1, p. 70-77, 2009.

Bertassoni, L.E.; Habelitz, S.; Kinney, J.H.; Marshall, S.J.; Marshall, G.W.Jr. Biomechanical perspective on the remineralization of dentin. **Caries Res**. v. 43, n. 1, p. 70-77, 2009.

Besinis, A.; van Noort, R.; Martin, N. Infiltration of demineralized dentin with silica and hydroxyapatite nanoparticles. **Dent. Mater**. v. 28, n. 9, p. 1012-1023, 2012.

Besinis, A.; van Noort, R.; Martin, N. Remineralization potential of fully demineralized dentin infiltrated with silica and hydroxyapatite nanoparticles. **Dent. Mater**. v. 30, n. 3, p. 249-262, 2014.

Bortolotto, T.; Ryabova, A.; Nerushay, I.; Kling, S.; Hafezi, F.; Garcia-Godoy, F.; Krejci, I. Effects of riboflavin, calcium-phosphate layer & adhesive system on stress-strain behavior of demineralized dentin. **Am. J. Dent**. v. 30, n. 4, p. 179-184, 2017.

Boteon, A.P.; Prakki, A.; Rabelo Buzalaf, M.A.; Rios, D.; Honorio, H.M. Effect of different concentrations and application times of proanthocyanidin gels on dentin erosion. Am. J. **Dent**. v. 30, n. 2, p. 96-100, 2017.

Braga, R.R.; Fronza, B.M. The use of bioactive particles and biomimetic analogues for increasing the longevity of resin-dentin interfaces: A literature review. **Dent. Mater. J.** v. 39, n. 1, p. 62-68, 2020.

Burwell, A.K.; Thula-Mata, T.; Gower, L.B.; Habeliz, S.; Kurylo, M.; Ho, S.P.; et al. Functional Remineralization of Dentin Lesions Using Polymer-Induced Liquid-Precursor Process. **PLoS ONE.** v. 7, n. 6, p. e38852, 2012.

Cai, J.; Burrow, M.F.; Manton, D.J.; Tsuda, Y.; Sobh, E.G.; Palamara, J.E.A. Effects of silver diamine fluoride/potassium iodide on artificial root caries lesions with adjunctive application of proanthocyanidin. **Acta Biomater.** v. 88, n. 1, p. 491-502, 2019.

Cai, X.; Han, B.; Liu, Y.; Tian, F.; Liang, F.; Wang. X. Chlorhexidine-Loaded Amorphous Calcium Phosphate Nanoparticles for Inhibiting Degradation and Inducing Mineralization of Type I Collagen. **ACS. App. Mater. Interfaces.** v. 9, n. 9, p. 12949-12958, 2017.

Cao, C.; Mei, M.; Li, Q-L.; Lo, E.; Chu, C. Methods for Biomimetic Remineralization of Human Dentine: A Systematic Review. **Int. J. Mol. Sc.** v. 16, n. 3, p. 4615-4627, 2015.

Cao, C.Y.; Li, Q-L. Scanning electron microscopic analysis of using agarose hydrogel microenvironment to create enamel prism-like tissue on dentine surface. **J. Dent.** v. 55, n. 1, p. 54-60, 2016.

Cao, C.Y.; Mei, M.L.; Li, Q.L.; Lo, E.C.; Chu, C.H. Methods for biomimetic remineralization of human dentine: a systematic review**. Int. J. Mol. Sci.** v. 16,n. 1, p. 4615- 4627, 2015.

Cao, Y.; Liu, W.; Ning, T.; Mei, M.L.; Li, Q-L.; Lo, E.C.M.; et al. A novel oligopeptide simulating dentine matrix protein 1 for biomimetic mineralization of dentine. **Clin. Oral. Investig.** v. 18, n. 3, p. 873-881, 2013.

Cao, Y.; Mei, M.L.; Li, Q-L.; Lo, E.C.M.; Chu, C.H. Agarose Hydrogel Biomimetic Mineralization Model for the Regeneration of Enamel Prismlike Tissue. **ACS Appl. Mater. Interfaces.** v. 6, n. 1, p. 410-420, 2013.

Cao, Y.; Mei, M.L.; Xu, J.; Lo, E.C.M.; Li, Q.; Chu, C.H. Biomimetic mineralisation of phosphorylated dentine by CPP-ACP. **J. Dent.** v. 41, n.9, p. 818-825, 2013.

Castellan, C.S.; Bedran-Russo, A.K.; Karol, S.; Pereira, P.N.R. Long-term stability of dentin matrix following treatment with various natural collagen cross-linkers**. J. Mech. Behav. Biomed. Mater.** v. 4, n. 7 , p. 1343-1350, 2011.

Chen, C.; Mao, C.; Sun, J.; Chen, Y.; Wang, W.; Pan, H.; et al. Glutaraldehyde-induced remineralization improves the mechanical properties and biostability of dentin collagen. **Mater Sci. Eng. C. Mater. Biol. Appl.** v. 67, n. 1, p. 657-665, 2016.

Chen, K.; Tang, X.; Yue, Y.; Zhao, H.; Guo, L. Strong and Tough Layered Nanocomposites with Buried Interfaces. **ACS Nano.** v. 10, n. 4, p. 4816-4827, 2016.

Chiang, Y-C.; Lin, H-P.; Chang, H-H.; Cheng, Y-W.; Tang, H-Y.; Yen, W-C.; et al. A Mesoporous Silica Biomaterial for Dental Biomimetic Crystallization. **ACS. Nano.** v. 8, n. 12, p. 12502-12513, 2014.

D'Onofrio, A.; Kent, N.W.; Shahdad, S.A.; Hill, R.G. Development of novel strontium containing bioactive glass based calcium phosphate cement. **Dent. Mater.** v. 32, n. 6, p. 703-712, 2016.

De Caluwé, T.; Vercruysse, C.W.J.; Ladik, I.; Convents, R.; Declercq, H.; Martens, L.C.; et al. Addition of bioactive glass to glass ionomer cements: Effect on the physico-chemical properties and biocompatibility. **Dent. Mater.** v. 33, n. 4, p. e186-e203, 2017.

De Morais, R.C.; Silveira, R.E.; Chinelatti, M.; Geraldeli, S.; de Carvalho Panzeri Pires-de-Souza, F. Bond strength of adhesive systems to sound and demineralized dentin treated with bioactive glass ceramic suspension. **Clin. Oral. Investig.** v. 22, n. 5, p. 1923-1931, 2017.

Degrazia, F.W.; Genari, B.; Leitune, V.; Arthur, R. A.; Luxan, S.A.; Samuel, S.; Collares, F.M.; Sauro, S. Polymerisation, antibacterial and bioactivity properties of experimental orthodontic adhesives containing triclosan-loaded halloysite nanotubes**. J. Dent.** v. 69,n. 1, p. 77-82, 2018.

Degrazia, F.W.; Leitune, V.C.B.; Visioli, F.; Samuel, S.M.W.; Collares, F.M. Long-term stability of dental adhesive incorporated by boron nitride nanotubes. **Dent. Mater.** v. 34, n. 3, p. 427-433, 2018.

Dickens, S.H.; Flaim, G.M.; Takagi, S. Mechanical properties and biochemical activity of remineralizing resin-based Ca–PO4 cements. **Dent. Mater.** v. 19, n. 6, p. 558-566, 2003.

Dreger, L.A.S.; Felippe, W.T.; Reyes-Carmona, J.F.; Felippe, G.S.; Bortoluzzi, E.A.; Felippe, M.C.S. Mineral Trioxide Aggregate and Portland Cement Promote Biomineralization In Vivo. **J. Endod.** v. 38, n. 3, p. 324-329, 2012.

Epasinghe, D.; Yiu, C.; Burrow, M. Synergistic effect of proanthocyanidin and CPP-ACFP on remineralization of artificial root caries. **Aust. Dent. J.** v. 60, n. 4, p. 463-470, 2015.

Epasinghe, D.J.; Kwan, S.; Chu, D.; Lei, M.M.; Burrow, M.F.; Yiu, C.K.Y. Synergistic effects of proanthocyanidin, tri-calcium phosphate and fluoride on artificial root caries and dentine collagen. **Mater. Sci. Eng. C-Materials Biol. Appl**. v. 73, n.1, p. 29-299, 2017.

Forsback, A.; Areva, S.; Salonen, J. Mineralization of dentin induced by treatment with bioactive glass S53P4 in vitro. **Acta Odontol. Scand**. v. 62,n. 1, p. 14-20, 2004.

Gandolfi, M.G.; Ciapetti, G.; Perut, F.; Taddei, P.; Modena, E.; Rossi, P.L.; Prati, C. Biomimetic calcium-silicate cements aged in simulated body solutions. Osteoblast response and analyses of apatite coating. **J. Appl. Biomater. Biomech.** v. 7, n.3, p. 160-170, 2009.

Gandolfi, M.G.; Taddei, P.; Pondrelli, A.; Zamparini, F.; Prati, C.; Spagnuolo, G. Demineralization, Collagen Modification and Remineralization Degree of Human Dentin after EDTA and Citric Acid Treatments. **Materials (Basel).** v. 12, n. 1, p. 25, 2018.

Gandolfi, M.G.; Taddei, P.; Siboni, F.; Modena, E.; De Stefano, E.D.; Prati, C. Biomimetic remineralization of human dentin using promising innovative calcium-silicate hybrid "smart" materials. **Dent. Mater.** v. 27, n. 11, p. 1055-1069, 2011.

Gao, Y.; Liang, K.; Li, J.; Yuan, H.; Liu, H.; Duan, X.; Li, J. Effect and Stability of Poly(Amido Amine)-Induced Biomineralization on Dentinal Tubule Occlusion. **Materials (Basel).** v. 10, n. 4,p. 383, 2017.

Garcia, I.M.; Leitune, V.C.B.; Ferreira, C.J.; Collares, F.M. Tantalum oxide as filler for dental adhesive resin. **Dent. Mater. J.** v. 37, n. 6, p. 897-903, 2018.

Gavrila, L.; Balan, A.; Murariu, A.; Sandu, A.V.; Savin, C. In vitro study regarding the effect of various commercial remineralizing products on primary and permanent teeth dentine caries lesions. **Rev. Chim.** v. 67, n. 11, p. 2228-2230, 2016.

Ge, Y.; Ren, B.; Zhou, X.; Xu, H.; Wang, S.; Li, M.: Weir, M.D.: Feng, M.; Cheng, L. Novel Dental Adhesive with Biofilm-Regulating and Remineralization Capabilities. **Materials (Basel).** v. 10, n. 1, p. 26, 2017.

Ge, Y.; Ren, B.; Zhou, X.; Xu, H.; Wang, S.; Li, M.; et al. Novel Dental Adhesive with Biofilm-Regulating and Remineralization Capabilities. M**aterials.** v. 10, n. 1, p. 26, 2017.

Gonçalves, R.S.; Scaffa, P.M.C.; Giacomini, M.C.; Rabelo Buzalaf, M.A.; Honório, H.M.; Wang, L. Use of sodium trimetaphosphate in the inhibition of dentin matrix metalloproteinases and as a remineralizing agent**. J. Dent**. v. 68,n. 1, p. 34-40, 2018.

Gonçalves, R.S.; Scaffa, P.M.C.; Giacomini, M.C.; Vidal, C.M.P.; Honório, H.M.; Wang, L. Sodium Trimetaphosphate as a Novel Strategy for Matrix Metalloproteinase Inhibition and Dentin Remineralization. **Caries Res.** v. 52,n. 3, p. 189-198, 2018.

Gu, L.; Kim, J.; Kim, Y.K.; Liu, Y.; Dickens, S.H.; Pashley, D.H.; et al. A chemical phosphorylation-inspired design for Type I collagen biomimetic remineralization. **Dent. Mat.** v. 26,n. 11, p. 1077-1089, 2010.

Gu, L.; Kim, Y.K.; Liu, Y.; Ryou, H.; Wimmer, C.E.; Dai, L.; et al. Biomimetic Analogs for Collagen Biomineralization. **J. Dent.** Res. v. 90, n. 1, p. 82-87, 2011.

Gu, L.; Kim, Y.K.; Liu, Y.; Takahashi, K.; Arun, S.; Wimmer, C.E.; et al. Immobilization of a phosphonated analog of matrix phosphoproteins within cross-linked collagen as a templating mechanism for biomimetic mineralization. **Acta Biomater.** v. 7, n. 1, p. 268-277, 2011.

Guentsch, A.; Fahmy, M.D.; Wehrle, C.; Nietzsche, S.; Popp, J.; Watts, D.C.; et al. Effect of biomimetic mineralization on enamel and dentin: A Raman and EDX analysis. **Dent. Mater.** v. 35, n. 9, p. 1300-1307, 2019.

Gupta, T.; Nagaraja, S.; Mathew, S.; Narayana, I.H.; Madhu, K.S.; Dinesh, K. Effect of Desensitization Using Bioactive Glass, Hydroxyapatite, and Diode Laser on the Shear Bond Strength of Resin Composites Measured at Different Time Intervals: An In vitro Study. **Contemp. Clin. Dent.** v. 8, n. 2, p. 244-247, 2017.

Han, M.; Li, Q.L.; Cao, Y.; Fang, H.; Xia, R.; Zhang, Z.H.; In vivo remineralization of dentin using an agarose hydrogel biomimetic mineralization system. **Sci. Rep.** v. 7, n. 1, p. 41955, 2017.

Hernández, M.; Cobb, D.; Swift, E.J. Current Strategies in Dentin Remineralization. **J. Esthet. Restor. Dent.** v. 26, n. 2 , p. 139-145, 2014.

Huang, W.; Restrepo, D.; Jung, J.Y.; Su, F.Y.; Liu, Z.; Ritchie, R.O.; McKittrick, J.; Zavattieri, P.; Kisailus, D. Multiscale Toughening Mechanisms in Biological Materials and Bioinspired Designs. **Adv. Mater.** v. 31, n. 43, p. 1901561, 2019.

Huang, Z.; Qi, Y.; Zhang, K.; Gu, L.; Guo, J.; Wang, R.; Mai, S. Use of experimental-resin-based materials doped with carboxymethyl chitosan and calcium phosphate microfillers to induce biomimetic remineralization of caries-affected dentin. **J. Mech. Behav. Biomed.** Mater.v.89, n. 1, p. 81-88, 2019.

Iafisco, M.; Esposti, L.D.;, Ramírez-Rodríguez, G.B.;, Carella, F.; Gómez-Morales J.; Ionescu, A.C.; Brambilla, E.; Tampieri, A.; Delgado-López, J.M. Fluoride-doped amorphous calcium phosphate nanoparticles as a promising biomimetic material for dental remineralization. **Sci. Rep.** v. 8, n. 1, p. 17016, 2018.

Iijima, M.; Ishikawa, R.; Kawaguchi, K.; Ito, S.; Saito, T.; Mizoguchi, I. Effects of pastes containing ion-releasing particles on dentin remineralization. **Dent. Mater**. J. v. 38,n. 2, p. 271-277, 2019.

Ishimoto, K.; Hayano, S.; Yanagita, T.; Kurosaka, H.; Kawanabe, N.; Itoh, S.; Ono, M.; Kuboki, T.; Kamioka, H.; Yamashiro, T. Topical application of lithium chloride on the pulp induces dentin regeneration. **PloS one.** v. 10, n. 3, p. e0121938, 2015.

Islam, S.M.; Hiraishi, N.; Nassar, M.; Sono, R.; Otsuki, M.; Takatsura, T.; Yiu, C.; Tagami, J. In vitro effect of hesperidin on root dentin collagen and de/re-mineralization. **Dent. Mater. J.** v. 31, n.3, p. 362-367, 2012.

Ito, S.; Iijima, M.; Motai, F.; Mizoguchi, I.; Saito, T. Effects of calcium salts of acidic monomers on mineral induction of phosphoprotein immobilized to agarose beads. **J. Biomed. Mater. Res. A.** v. 100, n. 10, p. 2760-2765, 2012.

Jang, J.H.; Lee, M.G.; Ferracane, J.L.; Davis, H.; Bae, H.E.; Choi, D.; Kim, D.S. Effect of bioactive glass-containing resin composite on dentin remineralization. **J. Dent.** v. 75, n. 1, p. 58-64, 2018.

Jayasree, R.; Kumar, T.S.S.; Mahalaxmi, S.; Abburi, S.; Rubaiya, Y.; Doble, M. Dentin remineralizing ability and enhanced antibacterial activity of strontium and hydroxyl ion co-releasing radiopaque hydroxyapatite cement. **J. Mater. Sci. Mater. Med.** v. 28, n. 6, p.95, 2017.

Jia, R.; Lu, Y.; Yang, C.W.; Luo, X.; Han, Y. Effect of generation 4.0 polyamidoamine dendrimer on the mineralization of demineralized dentinal tubules in vitro. **Arch. Oral. Biol.** v. 59, n. 10 , p. 1085-1093, 2014.

Jose, P.; Sanjeev, K.; Sekar, M. Effect of Green and White Tea Pretreatment on Remineralization of Demineralized Dentin by CPP-ACFP-An Invitro Microhardness Analysis. **J. Clin. Diagn. Res.** v. 10 , n. 4, ZC85-ZC89, 2016.

Jun, S.K.; Kim, H.W.; Lee, H.H.; Lee, J.H. Zirconia-incorporated zinc oxide eugenol has improved mechanical properties and cytocompatibility with human dental pulp stem cells. **Dent. Mater.** v. 34, n. 1 , p. 132-142, 2018.

Jun, S.K.; Yang, S.A.; Kim, Y.J.; El-Fiqi, A.; Mandakhbayar, N.; Kim, D.S.; Roh, J.; Sauro, S.; Kim, H.W.; Lee, J.H.; Lee, H.H. Multi-functional nano-adhesive releasing therapeutic ions for MMP-deactivation and remineralization. **Sci. Rep.** v. 8, n. 1, p. 5663, 2018.

Jung, J.H.; Park, S.B.; Yoo, K.H.; Yoon, S.Y.; Bae, M.K.; Lee, D.J.; Ko, C.C.; Kwon, Y.H.; Kim, Y.I. Effect of different sizes of bioactive glass-coated mesoporous silica nanoparticles on dentinal tubule occlusion and mineralization. **Clin. Oral. Investig.** v. 23, n. 5, p. 2129-2141, 2019.

Kim, D.S.; Kim, J.; Choi, K.K.; Kim, S.Y. The influence of chlorhexidine on the remineralization of demineralized dentine. **J. Dent.** v. 39, n. 12, p. 855-862, 2011.

Kim, D.S.; Kwon, J.M.; Park, S.H.; Choi, S.C.; Kim, S.Y. Mechanical and micromorphological evaluation of chlorhexidine-mediated dentin remineralization. **Scanning.** v. 34, n. 3, p. 151-158, 2012.

Kim, J.; Arola, D.D.; Gu, L.; Kim, Y.K.; Mai, S.; Liu, Y.; Pashley, D.H.; Tay, F.R. Functional biomimetic analogs help remineralize apatite-depleted demineralized resin-infiltrated dentin via a bottom-up approach. **Acta. Biomater.** v. 6, n. 7 , p. 2740 -2750, 2010.

Kim, J.; Vaughn, R.M.; Gu, L.; Rockman, R.A.; Arola, D.D.; Schafer, T.E.; Choi, K.K.; Pashley, D.H.; Tay, F.R. Imperfect hybrid layers created by an aggressive one-step self-etch adhesive in primary dentin are amendable to biomimetic remineralization in vitro. **J. Biomed. Mater. Res. A.** v. 93, n. 4, p. 1225-1234, 2010.

Kovtun, A.; Kozlova, D.; Ganesan, K.; Biewald, C.; Seipold, N.; Gaengler, P.; et al. Chlorhexidine-loaded calcium phosphatenanoparticles for dental maintenance treatment: combination of mineralising and antibacterial effects. **RSC. Adv.** v. 2, n. 3 , p. 870-875, 2012.

Kutsch, V. K.; Chaiyabutr, Y.; Milicich, G. Reconsidering remineralization strategies to include nanoparticle hydroxyapatite. **Compend. Contin. Educ. Dent**. v. 34, n. 3, p. 170-176, 2013.

Li, F.; Wang, P.; Weir, M.D.; Fouad, A.F.; Xu, H.H. Evaluation of antibacterial and remineralizing nanocomposite and adhesive in rat tooth cavity model. Evaluation of antibacterial and remineralizing nanocomposite and adhesive in rat tooth cavity model. **Acta Biomater.** v. 10, n. 6, p. 2804–2813, 2014.

Li, J.; Yang, J.; Li, J.; Chen, L.; Liang, K.; Wu, W.; Chen, X.; Li, J. Bioinspired intrafibrillar mineralization of human dentine by PAMAM dendrimer. **Biomaterials.** v. 34, n. 28, p. 6738–6747, 2013.

Li, X.; De Munck, J.; Yoshihara, K.; Pedano, M.; Van Landuyt, K.; Chen, Z.; Van Meerbeek, B. Re-mineralizing dentin using an experimental tricalcium silicate cement with biomimetic analogs. **Dent. Mater.** v. 33, n. 5, p. 505-513, 2017.

Liang, K., Gao, Y., Xiao, S., Tay, F. R., Weir, M. D., Zhou, X., Oates, T. W., Zhou, C., Li, J., & Xu, H. Poly(amido amine) and rechargeable adhesive containing calcium

phosphate nanoparticles for long-term dentin remineralization**. J. Dent.** v. 85, n. 1 , p. 47-56, 2019.

Lin, H.P.; Lin, J.; Li, J.; Xu, J.H.; Mehl, C. In vitro remineralization of hybrid layers using biomimetic analogs**. J. Zhejiang. Univ. Sci.** B. v. 17, n. 11, p. 864-873, 2016.

Liu, R. R., Fang, M., Zhao, S. J., Li, F., Shen, L. J., & Chen, J. H. The potential effect of proanthocyanidins on the stability of resin-dentin bonds against thermal cycling. **Chi. J. of Stomatol.** v. 47, n. 5, p. 268-272, 2012.

Liu, R.; Fang, M.; Xiao, Y.; Li, F.; Yu, L.; Zhao, S.; Shen, L.; Chen, J. The effect of transient proanthocyanidins preconditioning on the cross-linking and mechanical properties of demineralized dentin. **J. Mater. Sci. Mater. Med.** v. 22, n. 11, p. 2403-2411, 2011.

Liu, R.R.; Fang, M.; Zhang, L.; Tang, C.F.; Dou, Q.; Chen, J.H; Anti-proteolytic capacity and bonding durability of proanthocyanidin-biomodified demineralized dentin matrix. **Int. J. Oral Sci.** v. 6, n. 3, p. 168-174, 2014.

Liu, W., Cao, Y., Shen, J., Xu, Q., Zhu, Z., & Li, Q. Design and evaluation of a kind of biomimetic peptides of dentin matrix protein-1. **Chi. J. of Stomatol.** v. 31, n. 4, p. 341-344, 2013.

Liu, Y.; Li, N.; Qi, Y.; Niu, L.N.; Elshafiy, S.; Mao, J.; Breschi, L.; Pashley, D.H.; Tay, F.R. The use of sodium trimetaphosphate as a biomimetic analog of matrix phosphoproteins for remineralization of artificial caries-like dentin. **Dent. Mater.** v. 27, n.5, p. 465-477, 2011.

Liu, Y.; Mai, S.; Li, N.; Yiu, C.K.; Mao, J.; Pashley, D.H.; Tay, F.R. Differences between top-down and bottom-up approaches in mineralizing thick, partially demineralized collagen scaffolds. **Acta Biomater.** v. 7, n. 4, p. 1742-1751, 2011.

Mai, S.; Kim, Y. K.; Toledano, M.; Breschi, L.; Ling, J.Q.; Pashley, D.H.; Tay, F.R. Phosphoric acid esters cannot replace polyvinylphosphonic acid as phosphoprotein analogs in biomimetic remineralization of resin-bonded dentin. **Dent. Mater.** v. 25, n. 10, p. 1230-1239, 2009.

Mei, M.L.; Ito, L.; Cao, Y.; Lo, E.C.; Li, Q.L.; Chu, C.H. An ex vivo study of arrested primary teeth caries with silver diamine fluoride therapy. **J. Dent.** v. 42, n. 4, p. 395-402, 2014.

Mei, M.L.; Nudelman, F.; Marzec, B.; Walker, J.M.; Lo, E.; Walls, A.W.; Chu, C.H. Formation of Fluorohydroxyapatite with Silver Diamine Fluoride. **J. Dent. Res.** v. 6, n. 10, p. 1122-1128, 2017.

Ning, T.Y.; Xu, X.H.; Zhu, L.F.; Zhu, X.P.; Chu, C.H.; Liu, L.K.; Li, Q.L. Biomimetic mineralization of dentin induced by agarose gel loaded with calcium phosphate. **J. Biomed. Mater. Res. B. Appl. Biomate.** v. 100, n.1 , p. 138-144,2012.

Niu, L.; Zhang, W.; Pashley, D.H.; Breschi, L.; Mao, J.; Chen, J.; et al. Biomimetic remineralization of dentin. **Dent. Mater.** v. 30, n. 1, p. 77-96, 2014.

Nudelman, F.; Lausch, A.J.; Sommerdijk, N. A.; Sone, E.D. In vitro models of collagen biomineralization. **J. Struct. Biol.** v. 183, n. 2, p. 258-259, 2013.

Nurrohman, H.; Saeki, K.; Carneiro, K.; Chien, Y.C.; Djomehri, S.; Ho, S.P.; Qin, C.; Marshall, S.J.; Gower, L.B.; Marshall, G.W.; Habelitz, S. Repair of dentin defects from DSPP knockout mice by PILP mineralization. **J. Mater. Res.** v. 31, n. 3, p. 321-327, 2016.

Okuyama, K.; Kadowaki, Y.; Matsuda, Y.; Hashimoto, N.; Oki, S.; Yamamoto, H.; Tamaki, Y.; Sano, H. Efficacy of a new filler-containing root coating material for dentin remineralization. **Am. J. Dent**. v. 29, n. 4 , p. 213-218, 2016.

Osorio, R.; Cabello, I.; Medina-Castillo, A.L.; Osorio, E.; Toledano, M. Zinc-modified nanopolymers improve the quality of resin-dentin bonded interfaces. **Clin. Oral Investig.** v. 20, n. 9 , p. 2411-2420, 2016.

Osorio, R.; Osorio, E.; Cabello, I.; Toledano, M. Zinc induces apatite and scholzite formation during dentin remineralization. **Caries. Res.** v. 48, n. 4, p. 276-290, 2014.

Osorio, R.; Sauro, S.; Watson, T.F.; Toledano, M. Polyaspartic acid enhances dentine remineralization bonded with a zinc-doped Portland-based resin cement. **Int. Endod. J.** v. 49,n. 9 , p. 874-883, 2016.

Osorio, R.; Toledano-Osorio, M.; Osorio, E.; Aguilera, F.S.; Padilla-Mondéjar, S.; Toledano, M. Zinc and silica are active components to efficiently treat in vitro simulated eroded dentin. **Clin. Oral Investig.** v. 22, n. 8, p. 2859-2870, 2018.

Osorio, R.; Yamauti, M.; Sauro, S.; Watson, T.F.; Toledano, M. Zinc incorporation improves biological activity of beta-tricalcium silicate resin-based cement. **J. Endod.** v. 40, n. 11, p. 1840-1845, 2014.

Padovano, J. D.; Ravindran, S.; Snee, P. T.; Ramachandran, A.; Bedran-Russo, A.K.; George, A. DMP1-derived peptides promote remineralization of human dentin. **J. Dent. Res.** v. 94, n. 4, p. 608-614, 2015.

Peters, M.C.; Bresciani, E.; Barata, T.J.; Fagundes, T.C.; Navarro, R.L.; Navarro, M.F.; Dickens, S. H. In vivo Dentin Remineralization by Calcium-phosphate Cement. **J. Dent. Res**, v. 89, n. 3, p. 286-291, 2010.

Poggio, C.; Lombardini, M.; Vigorelli, P.; Ceci, M. Analysis of Dentin/Enamel Remineralization by a CPP-ACP Paste: AFM and SEM Study. **Scanning.** v. 35, n. 6, n. 366-374, 2013.

Qi, Y.P.; Li, N.; Niu, L.N.; Primus, C.M.; Ling, J.Q.; Pashley, D.H.; Tay, F.R. Remineralization of artificial dentinal caries lesions by biomimetically modified mineral trioxide aggregate. **Acta Biomate.** v. 8, n. 2, p. 836-842, 2012.

Rahiotis, C.; Vougiouklakis, G. Effect of a CPP-ACP agent on the demineralization and remineralization of dentine in vitro. **J. Dent.** v. 35, n. 8, p. 695-698, 2007.

Revankar, V.D.; Prathap, M.S.; Shetty, K.; Shahul, A.; Sahana, K. Effect of Biomineralization Ability on Push-out Strength of Proroot Mineral Trioxide Aggregate,

Mineral Trioxide Aggregate Branco, and Calcium Phosphate Cement on Dentin: An In vitro Evaluation**. J. Pharm. Bioallied. Sci.** v. 9. n. 1, p. S121-S126, 2017.

Reyes-Carmona J.F.; Felippe M.S.; Felippe W.T. The Biomineralization Ability of Mineral Trioxide Aggregate and Portland Cement on Dentin Enhances the Push-out Strength. **J. Endod.** v. 36, n. 2, p. 286-291, 2010.

Reyes-Carmona, J.F.; Felippe, M.S.; Felippe, W.T. A phosphate-buffered saline intracanal dressing improves the biomineralization ability of mineral trioxide aggregate apical plugs. **J. Endod**. v. 36, n. 10 , p. 1648-1652, 2010.

Reyes-Carmona, J.F.; Felippe, M.S.; Felippe, W.T. Biomineralization Ability and Interaction of Mineral Trioxide Aggregate and White Portland Cement With Dentin in a Phosphate-containing Fluid. **J. Endod.** v. 35, n. 5 ,p. 731-736, 2009.

Reyes-Carmona, J.F.; Santos, A.S.; Figueiredo, C.P.; Baggio, C. H.; Felippe, M.C.; Felippe, W.T.; Cordeiro, M.M. Host–Mineral Trioxide Aggregate Inflammatory Molecular Signaling and Biomineralization Ability. **J. Endod.** v. 36, n. 8 , p. 1347-1353,2010.

Roubel, M.; Prashant G.M.; Kumar P.G.N.; Sushanth, V.H.; Imranulla M.; Potlia, I.; Mallick, S. Effect of grape seed extract on remineralization of artificial caries: An in-vitro study. **Asian J. Pharm. Clin. Res.** v. 9, n. 5, p. 174, 2016.

Saeki, K.; Chien, Y.C.; Nonomura, G.; Chin, A.F.; Habelitz, S.; Gower, L.B.; Marshall, S.J.; Marshall, G.W. Recovery after PILP remineralization of dentin lesions created with two cariogenic acids. **Arch. Oral. Biol.** v. 82, n. 1, p. 194-202, 2017.

Santoso, T.; Djauharie, N.K.; Kamizar, Ahdi, W.; Latief, F.D.E.; Suprastiwi, E. Carboxymethyl chitosan/amorphous calcium phosphate and dentin remineralization. **J. Int. Dent. Med. Res,** v. 12, n. 1 , p. 84-87, 2019.

Sauro, S., Osorio, R., Watson, T. F., & Toledano, M. Influence of phosphoproteins' biomimetic analogs on remineralization of mineral-depleted resin-dentin interfaces created with ion-releasing resin-based systems**. Dent. Mater**. v. 31, n. 7 , p. 759-777, 2015.

Saxena, N.; Cremer, M.A.; Dolling, E.S.; Nurrohman, H.; Habelitz, S.; Marshall, G.W.; Gower, L.B. Influence of fluoride on the mineralization of collagen via the polymer-induced liquid-precursor (PILP) process. **Dent. Mater.** v. 34, n. 9, p. 1378-1390, 2018.

Saxena, N.; Habelitz, S.; Marshall, G.W.; Gower, L.B. Remineralization of demineralized dentin using a dual analog system. **Orthod. Craniofac. Res.** v. 1, n. 1 , p. 76-81, 2019.

Schwendicke, F.; Al-Abdi, A.; Moscardó, A.P.; Cascales, A.F.; Sauro, S. Remineralization effects of conventional and experimental ion-releasing materials in chemically or bacterially-induced dentin caries lesions. **Dent. Mater.** v. 35, n. 5, p. 772-779, 2019.

Seo, M.S.; Hwang, K.G.; Lee, J.; Kim, H.; Baek, S.H. The Effect of Mineral Trioxide Aggregate on Odontogenic Differentiation in Dental Pulp Stem Cells. **J. Endod.** v. 39, n. 2 ,p. 242-248, 2013.

Sfeir, C.; Fang, P.A.; Jayaraman, T.; Raman, A.; Xiaoyuan, Z.; Beniash, E. Synthesis of bone-like nanocomposites using multiphosphorylated peptides. **Acta Biomater.** v. 10 , n. 5, p. 2241-2249, 2014.

Shi, J.H.; Li, H.; Wang, Y.N. In vitro remineralization effect of grape seed extract on artificial dentin caries. **Shanghai Kou Qiang Yi Xue**. v. 24, n. 1 , p. 18-22, 2015.

Sun, J.; Chen, C.; Pan, H.; Chen, Y.; Mao, C.; Wang, W.; Tang, R.; Gu, X. Biomimetic promotion of dentin remineralization using L-glutamic acid: inspiration from biomineralization proteins. **J. Mater. Chem.** v. 2, n. 28, p. 4544-4553,2014.

Suprastiwi, E.; Putranto, A.W.; Maharti, I.D. The ability of biodentineTM of guided tissue remineralization (GTR): Analysis using SEM, EDX and TEM. **Pesqui. Bras. Odontopediatria Clin. Integr.** v. 19, n. 1 , p. 1-8, 2019.

Taddei, P.; Prati, C.; Gandolfi, M.G. A poly(2-hydroxyethyl methacrylate)-based resin improves the dentin remineralizing ability of calcium silicates. **Mater. Sci. Eng. C.** v. 77, n. 1, p. 755-764, 2017.

Tang, C.F.; Fang, M.; Liu, R.R.; Dou, Q.; Chai, Z.G.; Xiao, Y.H.; Chen, J.H. The role of grape seed extract in the remineralization of demineralized dentine: Micromorphological and physical analyses. **Arch. Oral Biol.** v. 58, n. 12, p. 1769-1776, 2013.

Tay, F. R., & Pashley, D. H. Biomimetic remineralization of resin-bonded acid-etched dentin. **J. Dent. Res.** v. 88, n. 8, p. 719-724, 2009.

Tay, F. R., & Pashley, D. H. Guided tissue remineralisation of partially demineralised human dentine. **Biomaterials.** v. 29, n. 8, p. 1127-1137, 2008.

Thula-Mata, T.; Burwell, A.; Gower, L.B.; Habeliz, S.; Marshall, G.W. Remineralization of Artificial Dentin Lesions via the Polymer-Induced Liquid-Precursor (PILP) Process. **MRS Proc.** v. 1355, n. 1, p. 1114, 2011.

Toledano, M.; Aguilera, F.S.; Osorio, E.; Cabello, I.; Toledano-Osorio, M.; Osorio, R. Self-etching zinc-doped adhesives improve the potential of caries-affected dentin to be functionally remineralized. **Biointerphases.** v. 10, n. 3, p. 031002, 2015.

Toledano, M.; Muñoz-Soto, E.; Aguilera, F.S.; Osorio, E.; Pérez-Álvarez, M.C.; García-Menocal, J.A.; Toledano-Osorio, M.; Osorio, R. The mineralizing effect of zinc oxide-modified hydroxyapatite-based sealer on radicular dentin. **Clin. Oral Investig.** v. 24, n. 1, p. 285-299, 2019.

Toledano, M.; Osorio, E.; Cabello, I.; Osorio, R. Early dentine remineralisation: Morpho-mechanical assessment. **J. Dent.** v. 42, n. 4, p. 384-394, 2014.

Toledano-Osorio, M.; Cabello, I.; Lynch, C.D.; Aguilera, F.S. Mild acids facilitate functional dentin remineralization under thermo-mechanical stimuli. **Am. J. Dent.** v. 31, n. 3, p. 155-165, 2018.

Tricco, A.C.; Lillie, E.; Zarin, W.; O'Brien, K.K.; Colquhoun, H.; Levac, D.; et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation**. Ann. Intern. Med.** v. 169, n. 7, p. 467, 2018.

Veis, A.; Dorvee, J. R. Biomineralization mechanisms: A new paradigm for crystal nucleation in organic matrices. **Calcif. Tissue Int.** v. 93, n. 1, p. 307-315, 2013.

Vollenweider, M.; Brunner, T.J.; Knecht, S.; Grass, R.N.; Zehnder, M.; Imfeld, T.; Stark, W.J. Remineralization of human dentin using ultrafine bioactive glass particles. **Acta Biomater.** v. 3, n. 6, p. 936-943, 2017.

Wang, J.; Chen, Y.; Li, L.; Sun, J.; Gu. X.; Xu, X.; et al. Remineralization of dentin collagen by meta-stabilized amorphous calcium phosphate. **CrystEngComm.** v. 15, n. 31, p. 6151, 2013.

Wang, Q.; Wang, X.M.; Tian, L.L.; Cheng, Z.J.; Cui, F.Z. In situ remineralizaiton of partially demineralized human dentine mediated by a biomimetic non-collagen peptide. **Soft. Matter.** v. 7, n. 20 , p. 9673, 2011.

Wang, T.; Yang, S.; Wang, L.; Feng, H. Use of multifunctional phosphorylated PAMAM dendrimers for dentin biomimetic remineralization and dentinal tubule occlusion. **Rsc. Adv.** v. 5, n. 15, p. 11136–11144. 2015.

Wang, Z.; Jiang, T.; Sauro, S.; Wang, Y.; Thompson, I.; Watson, T.F.; Sa, Y.; Xing, W.; Shen, Y.; Haapasalo, M. Dentine remineralization induced by two bioactive glasses developed for air abrasion purposes. **J. Dent.** v. 39, n. 11, p. 746-756, 2011.

Weir, M.D.; Ruan, J.; Zhang, N.; Chow, L.C.; Zhang, K.; Chang, X.; Bai, Y.; Xu, H. Effect of calcium phosphate nanocomposite on in vitro remineralization of human dentin lesions. **Dent. Mater.** v. 33, n. 9, p. 1033-1044, 2017.

Wu, Z., Wang, X., Wang, Z., Shao, C., Jin, X., Zhang, L., Pan, H., Tang, R., & Fu, B. Self-Etch Adhesive as a Carrier for ACP Nanoprecursors to Deliver Biomimetic Remineralization. **ACS Appl. Mater. Interfaces.** v.9, n. 21, p. 17710-17717, 2017.

Xiao, S.; Liang, K.; Weir, M.D.; Cheng, L.; Liu, H.; Zhou, X.; Ding, Y.; Xu, H. Combining Bioactive Multifunctional Dental Composite with PAMAM for Root Dentin Remineralization. **Materials (Basel).** v. 10, n. 1 , p. 89 ,2017.

Xie, D.; Zhao, J.; Weng, Y.; Park, J.G.; Jiang, H.; Platt, J.A. Bioactive glass-ionomer cement with potential therapeutic function to dentin capping mineralization. **Eur. J. Oral. Sci.** v. 116, n. 5 , p. 479-487, 2008.

Xie, F.; Li, Q.; Wei, X.; Zhou, T. Effect of Ca(OH)2 pre-treated on remineralization of the demineralized dentin induced by polyamidoamine dendrime**. Zhonghua Kou Qiang Yi Xue Za Zhi**, v. 50, n. 4, p. 244-247, 2015.

Xie, F.; Wei, X.; Li, Q.; Zhou, T. In vivo analyses of the effects of polyamidoamine dendrimer on dentin biomineralization and dentinal tubules occlusion. **Dent. Mater. J**. v. 35, n. 1, p. 104-111, 2016.

Xie, Q.; Bedran-Russo, A.K.; Wu, C.D. In vitro remineralization effects of grape seed extract on artificial root caries. **J. Dent.** v. 36, n. 11, p. 900-906, 2008.

Xu, Z.; Neoh, K.G.; Lin, C.C.; Kishen, A. Biomimetic deposition of calcium phosphate minerals on the surface of partially demineralized dentine modified with phosphorylated chitosan. **J. Biomed. Mater. Res. B. Appl. Biomater.** v. 98, n. 1 , p. 150-159, 2011.

Xun, R.; Jing, Y.; Qin, D.; Chuhang, L.; Kun, T. Chitosan-collagen polymer induced remineralization of tooth hard tissue through self-growing methods. **Hua Xi Kou Qiang Yi Xue Za Zhi.** v. 2 , n. 5 , p. 519-524, 2014.

Yoo, Y.J.; Baek, S.H.; Kum, K.Y.; Shon, W.J.; Woo, K. M.; Lee, W. Dynamic intratubular biomineralization following root canal obturation with pozzolan-based mineral trioxide aggregate sealer cement. **Scanning.** v. 38, n. 1 , p. 50-56, 2016.

Zaharia, A.; Plescan, V.G.; Anghel, E.M.; Musat, V. Human dentine remineralization under non-colagen materials action. **Rev. Chim.** v. 68, n. 5 , p. 928-932, 2017.

Zanini, M.; Sautier, J.M.; Berdal, A.; Simon, S. Biodentine Induces Immortalized Murine Pulp Cell Differentiation into Odontoblast-like Cells and Stimulates Biomineralization. **J. Endod.** v. 38, n. 9 ,p. 1220-1226, 2012.

Zhang, X.; Neoh, K.G.; Lin, C.C.; Kishen, A. Remineralization of partially demineralized dentine substrate based on a biomimetic strategy. **J. Mater. Sci. Mater. Med.** v. 23, n. 3, 733- 742, 2012.

Zhang, Y.; Wang, Z.; Jiang, T.:, Wang, Y. Biomimetic regulation of dentine remineralization by amino acid in vitro. **Dent. Mater.** v. 35, n. 2, p. 298-309, 2019.

Zhou, Y.; Yang, J.; Lin, Z.; Li, J.; Liang, K.; Yuan, H.; Li, S.; Li, J. Triclosan-loaded poly(amido amine) dendrimer for simultaneous treatment and remineralization of human dentine. **Colloids Surfa. B. Biointerfaces.** v. 115, n. 1 , p. 115-237, 2014.

Zhou, Y.Z.; Cao, Y.; Liu, W.; Chu, C.H.; Li, Q.L. Polydopamine-Induced Tooth Remineralization. **ACS Appl. Mater. Interfaces,** v. 4, n. 12 , p. 6901-6910, 2012.

Zurick, K. M.; Qin, C.; Bernards, M. T. Mineralization induction effects of osteopontin, bone sialoprotein, and dentin phosphoprotein on a biomimetic collagen substrate, **J. Biomed. Mater. Res. A**. v. 101, n. 1 , p. 1571-1581, 2013.

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