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Bioactive Materials for Direct and Indirect Restorations: Concepts and Applications

Mutlu Özcan[1]*, *Lucas da Fonseca Roberti Garcia*[2] and *Claudia Angela Maziero Volpato*[2]

[1] Division of Dental Materials, Center for Dental and Oral Medicine, Clinic for Reconstructive Dentistry, University of Zürich, Zurich, Switzerland, [2] Department of Dentistry, Health Sciences Center, Federal University of Santa Catarina, Florianópolis, Brazil

Currently, minimally invasive restorations could be made in dentistry applying adhesive materials and adhesion principles to the dental structures. Following this philosophy, endodontic interventions have been avoided largely, preserving hard tissues, and maintaining dental vitality. Advances in biologically favorable bioactive materials enabled clinicans to induce repair and regeneration of dental tissues. Such materials are primarily used for pulp protection and cementation of indirect restorations. This review highlights current bioactive materials available, principles of bioactivity and their mechanisms of action.

Keywords: bioactive materials, biomaterials, resin-based luting cements, adhesion, pulp capping agents

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****Correspondence:***
Mutlu Özcan
mutluozcan@hotmail.com

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INTRODUCTION

Minimally invasive approaches aim to restore the shape, function and aesthetics of teeth, preserving hard tissues and preventing damage, especially in relation to the dentin-pulp complex (1, 2). The main objective of these strategies is to extend the functional life of the restored teeth, with the least possible restorative intervention (3). These approaches that are frequently increasing in dentistry, are governed by a therapeutic philosophy in which traditional restorations are replaced by direct or indirect adhesive restorations, performed on conservative dental preparations (4, 5).

Direct adhesive restorations may be inserted in cavity preparations resulting, basically, from the removal of dental caries and/or old restorative materials (6). In the past, sound dental structure was sacrificed to compensate for the limitations of tecnhiques and restorative materials (3). Currently, based on the minimally invasive philosophy, the preparation of a cavity takes the preservation of the sound dental tissue into account, giving a chance for the tissues for potential remineralization (7). Therefore, this philosophy integrates concepts of prevention, control and dental treatment (2), using restorative materials of low cost and easy repair (8).

In indirect restorations, classic approaches are based on subtractive techniques, where the tooth must be prepared to create enough space for the restorative material (9). In order to avoid undesirable prosthetic overcontours, often a greater amount of tooth preparation is performed by the clinician, which may result in loss of pulp vitality. In addition, devitalized abutment teeth associated with these prostheses generally have intraradicular posts, which require more removal of dental tissue, impacting negatively the clinical survival of these restorations (10, 11).

Crowns, onlays, veneers and small fixed dental prostheses, made with ceramic materials may react to acid etching techniques (12), as well as CAD-CAM polymers and hybrid materials (13, 14), are considered as alternatives to traditional metal-ceramic crowns with high success rates (15–17). Due to the bonding agents and the adhesive cements currently available on the market,

thinner restorations may be performed, which results in conservative dental preparations and the maintenance of dental vitality (18, 19). Therefore, due to the advancement of esthetic materials and the introduction of adhesive techniques, dental vitality has been preserved after restorative procedures, decreasing the cycle of invasive dental interventions (9). Supported by the minimally invasive philosophy, direct and indirect restorations are increasingly applied in vitalized teeth. Hence, it is important to keep in mind that vital dental tissues must be carefully handled and protected, as the survival of the tooth is prolonged due to the maintenance of pulp vitality and preservation of sound hard tissues (4, 9).

Based on this philosophy, biomaterials and bioactive materials have been suggested in the literature to be used as pulp protection materials, or for the cementation of indirect restorations, due to their ability in inducing the dental tissue repair and regeneration (20, 21). Biomaterials and bioactive protective materials applied on pulp may be effectively and be permanently used in cases of indirect and direct pulp capping or pulpotomy (22, 23). Cements, such as traditional glass ionomer cements (GICs), GICs modified by resin (RMGICs), or more recently, GICs associated with calcium aluminate, have been used to lute indirect restorations, especially in vital dental preparations and/or preparations with sub-gingival cervical margins (21, 24, 25).

PULP RESPONSE TO EXTERNAL INJURIES

The pulp is a loose, highly differentiated, innervated and vascularized connective tissue, which is responsible for the vitality of the tooth (26). In addition to its nutritive, sensitive and defensive potential, the pulp tissue is mainly composed by odontoblasts, and their odontoblastic extensions inside the dentinal tubules account for the dentin deposition (26, 27).

The pulp is protected from external irritating agents by the enamel and dentin walls, although these tissues limit its expansion and vasodilation in injury episodes. In its central region, it is formed by blood vessels, nerve fibers and cells distributed in a matrix composed of collagen fibers and a fundamental substance (27). A layer of primary odontoblasts is present in the peripheral pulp region. When the pulp is subjected to mechanical, thermal, chemical or bacterial injuries, an effective defense reaction is triggered (28). This response depends on the factors such as the intensity and duration of the irritating stimulus and the previous condition of the pulp tissue (29, 30).

Tertiary dentin formed after an aggressive stimulus, may be reactive or reparative (31). The primary odontoblasts secreted dentin matrix of the reactive-type, while the reparative dentin is secreted by odontoblast-like cells originated from differentiate pulp cells originated after the primary odontoblast destruction (29). The dentin-pulp complex also has biologically active molecules, such as transforming growth factors-ß1 (TGF-ß1) and bone morphogenetic proteins-7 (BMP-7), which act by stimulating and/or inhibiting specific events, as the modulation of embryogenic development, cell differentiation, immunoregulation, repair process and tissue regeneration (32, 33).

BIOACTIVITY

Biocompatibility is the ability of a material in interacting with a living tissue without causing damage or adverse effects to it (34). All materials capable of presenting a certain degree of biological compatibility with the tissues are called "biomaterials." However, when a biomaterial comes into contact with a living tissue, and despite its biocompatibility, it chemically interacts with the tissue, this phenomenon is called bioactivity (35, 36). Therefore, bioactive materials may be described as those that promote a specific biological response in organisms or cells, inducing chemical bonding or tissue formation, as occurs in the pulp, enamel, dentin and bone (37). A good example of a bioactive material widely used in dentistry is the GICs (38). These cements release fluoride ions that are replaced by hydroxyl ions of hydroxyapatite present in dental tissue, forming the fluorohydroxyapatite crystal (FHA). FHA is more resistant to acid demineralization caused by the oral microbiota and may release fluoride ions whenever the pH of the oral environment becomes acidic (38). In addition, GICs are capable to bond to the dental tissues, due to the chemical bonds of carboxylic radicals to calcium ions present in the dentin and enamel (38).

Several types of bioactive materials have been used in dentistry, some of which are based on calcium hydroxide and mineral aggregate-based materials (39, 40). Calcium hydroxide is able to induce the organism in forming mineralized tissue, assisting the repair of an injured area. The same phenomenon may be observed in mineral aggregate-based cements, which release calcium hydroxide during their hydration process (39, 40). These materials may be used in different clinical situations such as the repair of root and furcation perforations, apical surgery (retrofilling), apexification, treatment of root resorption and dentin hypersensitivity, and indirect or direct pulp capping (41).

BIOACTIVE MATERIALS FOR PULP PROTECTION

The pulp capping procedure, whether indirect or direct, consists of applying a specific biomaterial on a thin dentinal remnant (indirect), or on the pulp tissue exposed accidentally (direct) (42). Such protective material is characterized by its ability in stimulating the pulp tissue to produce specific and intentional mineral bonds with the dentinal substrate, maintaining its function and vitality (7). Ideally, these materials should be radiopaque (43), non-resorbable, non-toxic, resistant to bacterial infiltration and insoluble in tissue fluids (40, 44). In addition, they must enable an efficient marginal sealing to minimize infiltrations and secondary caries (45).

Calcium Hydroxide Cements

Several studies have already proved the effectiveness of calcium hydroxide as a material for pulp protection in its different forms of presentation (cement, powder, and paste) (46–48). When in direct contact with the pulp, calcium hydroxide causes necrosis on the surface of this tissue, inducing the organism to promote the deposition of mineralized tissue in the affected area, leading

to its repair (47, 48). Despite the widespread use for decades, and still being one of the most used materials in this type of procedure, doubts regarding the clinical performance of calcium hydroxide, mainly due to its low mechanical resistance and poor sealing ability, still persist (49).

Mineral Aggregate-Based Cements

The need for a more appropriate material for pulp therapy stimulated the development of the Mineral Trioxide Aggregate (MTA) (50). This cement was initially conceived as a material for apical surgery (retrograde filling) and for the treatment of perforations located at the root and furcation (39, 40, 51, 52). However, the remarkable clinical performance of this cement has led to its use in several other clinical situations, such as apexification (53), treatment of root resorption (54, 55), in pulpotomies (56–58) and pulp protection (59–62).

MTA is a calcium silicate-based cement, being composed mainly (% by weight) by Portland cement (75.0), widely used in civil engineering in the construction area, in addition to Bi_2O_3 (20.0), its radiopacifying agent and dehydrated $CaSO_4$ (5.0), for the setting-time control (44, 63). In turn, the main components of Portland cement are SiO_2 (21.2), CaO (68.1), Al_2O_3 (4.7), MgO (0.48), and Fe_2O_3 (1.89) (64).

As it is a hydraulic cement, water is added to the MTA powder for manipulation, starting its hydration process (44, 65). During the hydration process of MTA, calcium disilicate and trisilicate react, leading to the formation of calcium hydroxide and hydrated calcium silicate gel (44, 66). The calcium ions released during the setting process of MTA diffuse within the dentinal tubules and increase their concentration over the course of time. This phenomenon raises the pH of the medium, making it alkaline, ensuring the bioactivity of the cement (66, 67).

In comparison with the calcium hydroxide, MTA is more capable in maintaining the pulp tissue integrity after conservative treatments (68). Studies have shown that the pulp tissue submitted to capping with MTA presented the formation of a thick-mineralized barrier (58, 69, 70). In addition, the underlying pulp tissue had a mild inflammatory response, significantly less intense than observed in pulps treated with calcium hydroxide (62, 68, 71). Other studies have reported that MTA stimulates pulp cells to synthesize and deposit mineralized dentin matrix faster than calcium hydroxide (62, 72). During the hydration of MTA, a by-product of calcium hydroxide, the hydrated calcium silicate is formed (73). The hydrated calcium silicate reaction results in the hydrogenation of CaO and $Ca(OH)_2$. Then, a large concentration of Ca^{++} ions is released into the medium (66). These Ca^{++} ions are produced from the $Ca(OH)_2$ formed during the MTA setting reaction, and from the decomposition of hydrated calcium silicate, which is deposited at a slower rate than observed in pulps treated with hydroxide calcium cement (73). However, the mechanism of action of MTA on the pulp tissue has not been fully explained yet. It is speculated that the MTA action is similar to calcium hydroxide, with an initial inflammatory response, followed by a necrosis limited to the area below the connective tissue submitted to protection (74, 75).

In addition to the superior mechanical resistance and greater sealing ability (76) of MTA, when compared to calcium hydroxide, it also stands out for its lower solubility and better marginal adaptation (77, 78). However, some negative characteristics of MTA must be considered as well, such as its poor handling, which results in the formation of several pores in the cement microstructure and makes it highly unstable (79); high cost (80); staining of dental tissues (55, 81); arsenic release (82–84) above the safety limits proposed by the ISO 9917-1 (2001) (85); low adhesion to the dentin substrate (86, 87) and long setting-time (88).

During the last two decades, it was the clinical success of MTA, combined with its undesirable properties that led to the development of several other mineral aggregate-based cements containing calcium silicate as main component, (89). Among these cements, Biodentine (Septodont, France) stands out. This cement is known as "dentin substitute" due to its mechanical resistance similar to that of the human dentin (89, 90) and is basically composed of tricalcium silicate, calcium carbonate and zirconium oxide, as a radiopacifying agent (91, 92). The liquid to be mixed with the cement powder contains calcium chloride significantly reduces its setting-time in comparison to MTA, and a water-soluble polymer in the composition acts as a water-reducing agent, in addition to sodium and magnesium (91, 92). According to Stefaneli Marques et al. (93), Biodentine has physicochemical properties similar to Portland cement. Moreover, the biocompatibility and bioactivity promoted by this cement are similar to that of MTA, making both cements, the main choice for several conservative therapies involving the dentin-pulp complex (94, 95).

In the same way as calcium silicate-based cements, calcium aluminate cement (CAC), also coming from civil engineering, where it is used for manufacturing refractory castables (96), started to be used in dentistry, mainly in areas involving pulp therapy. The main difference between Portland cement, the basic component of MTA, and CAC, is the nature of the active phase responsible for the setting process of both cements (96). The main oxides of Portland cement are CaO and SiO_2, which are presented in the forms of tricalcium ($3CaO\ SiO_2$) and dicalcium silicates ($2CaO\ SiO_2$). The main hydrates formed from the manipulation of the cement with water are amorphous hydrated calcium silicate (C-S-H) and crystalline calcium hydroxide (CH) (96). In CAC, the main oxides are CaO and Al_2O_3, which are combined in order to form calcium monoaluminate (CA). After manipulation with water, calcium aluminate hydrates and aluminum hydroxide are formed (97), making up the main active phase of the cement during its setting process (96).

CAC is composed of (% by weight) Al_2O_3 ($\geq$68.0), CaO ($\leq$31), SiO_2 (0.3–0.8), MgO (0.4–0.5), and Fe_2O_3 (<0.3), and the cement consists of three main phases, responsible for its hydraulic setting process, namely, anhydrous CA phase ($CaO.Al_2O_3$), comprising about 40–70% of the cement; phase CA_2 ($CaO.2Al_2O_3$), which is the second in proportion (>25%), and phase $C_{12}A_7$ ($12CaO.7Al_2O_3$), with about 10% of the cement (98).

Three different phenomena occur during the CAC hydration process: ion dissolution, nucleation and precipitation of the hydrated phases (98). When the particles of the cement powder come into contact with the water during manipulation,

anhydrous calcium aluminate phases are formed and dissociate, releasing Ca^{++} and HO^{-} ions (99). As the ion concentration reaches saturation, the dissolution phase ends, initiating the precipitation of calcium aluminate hydrates by nucleation and growth mechanism (98). The precipitation of these particles decreases the concentration of Ca^{++} ions and hydroxyl at levels below of the saturation, leading to the formation of anhydrous phases, resulting in a continuous dissolution/precipitation process (98). This process prolongs the release of Ca^{++} ions into the medium (100), and significantly increases the bioactivity of the cement (98, 101).

More recently, the use of materials for pulp protection containing active molecules aims to simulate the behavior of the dentin-pulp complex, allowing events, as repair, regeneration, control of the inflammatory process and deposition of mineralized tissue. Among these materials, the Activa BioActive-Base/Liner, combine the release and recharge of calcium, phosphate and fluoride ions (102) with the physical properties of the resin-based materials (103). These properties are due to its hydrophilicity and different composition (glass particles and a hydrophilic ionic resin matrix) and, according to the manufacturer, the material induces mineralization at the tooth restoration interface with resilient ionic resin matrix. Moreover, Activa showed potential to stimulate biomineralization at the same level as MTA and Biodentine, based on the release of the same amount of Ca^{++} and OH^{-} ions (supplemented ionic conditions) (104). This hybrid cement may be both chemically or photo-polymerized, resulting in a favorable setting time of about 3 min.

BIOACTIVE MATERIALS FOR CEMENTATION OF INDIRECT RESTORATIONS

Historically, zinc phosphate-based cements are used for fixing dental prostheses. Its powder consists of a basic reagent (zinc oxide, 90%) and a retarding agent (magnesium oxide, 10%), while the liquid contains orthophosphoric acid, water and metal salts (105). An ionic reaction occurs between orthophosphoric acid and zinc oxide after manipulation, forming an amorphous mass with a low pH (106). However, due to its high solubility, an effective link between zinc phosphate cement and dentin is not achieved, leading to the chemical dissolution of the cement, followed by microleakage and an increased risk of recurrent caries (107, 108).

The advent of the adhesive technology allowed partial restorations, as inlays, onlays and veneers, to be bonded to prepared or non-prepared dental tissues using resin-based composite cements (109). After dentin substrate etching, these cements are able to infiltrate within the dentinal tubules and the demineralized collagen fibril network, bonding to the dentin by micro-mechanical retention (109, 110). When adhesive cements containing functional monomers such as 10-methacryloyloxidecyl dihydrogen phosphate (10-MDP) are used, chemical bonding is also achieved due to the strong ionic bonds established between the adhesive and the calcium ions of the hydroxyapatite crystals (110, 111).

Due to the favorable survival rates of partial indirect restorations (112), adhesive cementation techniques have also been used for the fixation of single crowns and fixed dental prostheses (109). However, these techniques are sensitive to moisture, requiring that cementation protocols be performed in an operative field free of saliva and moisture, in order to guarantee the durability of the adhesive interface (113). Thus, adhesive cementation of crowns and fixed dental prostheses in preparations with subgingival margins is a major clinical challenge. The difficulty to control the local moisture and in performing an adequate isolation of the area often leads the clinician to choose a non-adhesive cement (114, 115). Bioactive cements, as GICs, resin-modified glass ionomers cements (RMGICs) and glass ionomers associated with calcium aluminate are interesting alternatives to lute fixed dental protheses in moisture conditions.

Glass Ionomer Cements (GICs)

Glass ionomer cements are cements composed of a powder of fluoroaluminosilacate glass and aqueous solution containing polyalkenoic acids (24). The powder is responsible for the resistance, stiffness and fluoride release, while the liquid modulates the setting time of the cement (116). The setting takes place due to the crosslinking of the polyacrylic acid polymer chains with the calcium and aluminum ions present in the powder (24). Despite being sensitive to moisture when newly placed in the oral cavity, GICs have good mechanical properties after long-term storage in water (117, 118).

These cements have the ability to chemically adhere to dental structures by chelating the carboxyl group of acidic polymer chains and calcium ions (Ca_2^+), with the apatite of the enamel and dentin (116). In addition, they release fluoride ions when they come into contact with the dental tissue (119, 120). Hydroxyl ions are replaced by fluorine ions, leading to the formation of fluorohydroxyapatite crystal (FHA). FHA is quite resistant to acid demineralization promoted by bacteria associated with caries, in addition to being chemically more stable than other forms of hydroxyapatite (121). Even after the final setting of the cement, the GIC matrix remains porous, allowing free and constant movement of fluoride ions within the material. Thus, the release of fluoride occurs during the entire useful life of the restoration, direct or indirect, helping it to maintain the marginal seal (122, 123).

Despite their chemical bonding capacity and active fluoride release, the adhesive potential and wear resistance of GICs are lower than the resin composites and resinous cements (124, 125). Pulp reactions and post-operative sensitivity have been reported after the use of GICs (126), although the marginal infiltration rate of these materials is low (127–129). According to several studies, these clinical findings may be related to the pH ($\geq$3) of the initial period of the cement in contact with the dental tissue, resulting in an acidity responsible for pulp sensitivity (107, 126).

Due to their antimicrobial and anticariogenic properties, GICs are indicated mainly for patients with high cariogenic activity (130), and may also be used to seal fissures; temporary

sealing of cavities; primary tooth restorations; repairing defective margins for restorations; conservative class I and II restorations without involvement of the marginal ridge; cervical restorations; lining material in deep cavities; filling cores; cementation of intraradicular posts; crowns and fixed dental prostheses, and bonding of orthodontic brackets (130–134).

Resin-Modified Glass Ionomer Cements (RMGICs)

In order to minimize the mechanical limitations of GICs, resinous components such as HEMA and/or bis-GMA, and photosensitive components were added to the GIC (135), resulting in a product with greater wear resistance, better surface finishing and less solubility (136–138). RMGICs are hybrid materials that contain a basic ionizable leachable glass, a water-soluble polymeric acid, organic monomers and an initiator system (38). They aim to combine the mechanical properties of a composite resin with the anticariogenic potential of GICs (139).

The polymerization of RMGICs occurs by the acid-base reaction of conventional GICs and by the photoactivation of resin monomers (135, 136). Photoactivation allows for the formation of additional cross-links, while the acid-base reaction that occurs after about 15–20 min, enabling the maturation process and final strength of the cement. The flexural strength of RMGICs after final setting is higher (about 70 MPa) than the flexural strength of conventional GICs (11 MPa) (140). However, despite its adequate flexural strength, disadvantages, such as greater polymerization contraction and cytotoxicity have been reported (141).

RMGICs have a daily fluoride ion release of 8–15 ppm for the first 24 h, decreasing after 1 week (1–2 ppm) and stabilizing in 10 days to 3 weeks (142–144). The level of fluoride ions released by RMGICs is similar to the conventional GIC (145), and the process of fluoride release by these cements is very complex, being affected by different variables, such as cement composition; powder/liquid ratio; manipulation method; amount of fluoride available for release, type and amount of resin used, and pH of the environment (146–149).

Nanostructurally Integrating Bioceramics Materials

More recently, bioactive cements based on calcium aluminate have been introduced into the market for the cementation of indirect restorations, mainly on vital dental preparations (21, 115, 150). These cements combine the favorable properties of GICs, with the advantages of CAC. The glass ionomer allows adhesion to the tooth structure and low initial pH, while calcium aluminate contributes to the bioactivity-apatite formation, reduced solubility/degradation and stable pH over time (21, 151). Some cements available on the market have up to 50% calcium aluminate in their composition (e.g., Calibra Bio Cement, Dentsply Sirona, USA).

The setting mechanism of these hybrid cements is a combination of the reaction of the glass ionomer and an acid-base reaction that occurs in hydraulic cements. The cement is easy to handle, and a creamy and smooth mixture is obtained right after its manipulation (150, 152). Working and setting times [2–2.5 and 4–5 min, respectively] are comparable to the GICs values (150). A basic pH (∼8.5) is reached after 3–4 h after mixing (150, 151) and an oxygen-inhibiting layer is not formed after using this cement, making removal of the cement easier and faster (152).

These cements, which have been called nanostructurally integrating bioceramics (NIB) cements (115), aim to combine principles of adhesion, integration and dentin sealing by the association of different materials (21). Such principles are based on the potential for chemical adhesion, remineralization of the dental structure and formation of hydroxyapatite (HAp), helping to reduce the incidence of secondary caries and post-operative sensitivity, and improving the marginal sealing of the restoration (150, 153). In addition, the introduction of nano-sized glass particles allows the reduction of the setting time and enhance the compressive strength and elastic modulus of the GICs (154, 155).

Hydroxyapatite (HAp) was formed after immersing samples of a calcium aluminate/glass ionomer luting cement in physiological phosphate-buffered saline (PBS) solution. The formation of HAp was observed after 7 days, demonstrating that the cement has dynamic self-sealing properties (156). In this way, areas of marginal degradation that emerge over time could be treated by means of bioactive resealing via hydroxyapatite deposition (21, 156). However, one study noted that HAp, or another phase of calcium phosphate, developed on the surfaces of samples of a calcium aluminate/glass ionomer luting cement did not last for 30 days (115). According to the authors, this finding may be related to the content of phosphorus, 10 times lower compared to PBS, suggesting the need for further follow-up studies.

The microleakage of crowns cemented with calcium aluminate/glass ionomer luting cements was also evaluated *in vitro*, where the scores were significantly lower than the scores found for conventional GICs (157). Local irritation and induction of genetic mutations were not observed after using this cement (21), and physical properties (compressive strength, film thickness, setting time) and *in vitro*/*in vitro* biocompatibility (21) showed favorable results.

A clinical evaluation of indirect restorations cemented with a calcium aluminate/glass ionomer luting cement was performed at different periods of observation [pilot study (158), 1 year (152), 2 years (150), and 3 years (151)]. Thirty-eight crowns and fixed dental prostheses were fabricated and cemented on 31 vital and 7 non-vital abutment teeth. The authors observed the working time and setting time of the cement, the laying characteristics and the ease of removing excess cement. Parameters, such as gingival tissue reaction, post-cementation sensitivity, marginal integration and discoloration were also observed. After 2 years, no secondary caries, marginal discoloration and dentin sensitivity were observed (150). After 3 years, the restorations were still adequate, without gingival inflammation or discoloration, and were classified as excellent in relation to marginal integrity (151), confirming the clinical performance of this cement as a luting agent for crowns and fixed prostheses. Patients

also did not report any pain or discomfort in relation to cemented restorations.

Future Trends

The therapeutic approaches involving bioactive materials are able to promote the repair and/or regeneration of the injured tissues through an intimate interaction between these materials and dental substrates. However, such materials still have a number of limitations, which must be overcome through new basic and clinical research over time. It is consolidated in the scientific literature that bioactive proteins present in the dentin substrate interact with several types of cells through their surface receptors. Therefore, the development process of a novel bioactive material must consider the presence of such proteins in the composition of materials in order to activate potential bioactivity. The effect of these proteins may range according to their dosage, activation state, differentiation stage of the cells or interaction with other bioactive molecules and extracellular matrix. Conversely, the development of bioactive materials containing dentinal matrix proteins requires a high-cost production, and further studies envolving the extraction of dentin proteins at low-cost is imperative to produce feasible alternatives in the future.

CONCLUSIONS

Due to their ability in inducing repair and regeneration of the dental tissue, biocompatible and bioactive materials, such as MTA-like cements, CAC, GICs, RMGICs, and other bioceramics materials have been routinely indicated for the protection of the dentin-pulp complex. According to their rheological properties, these materials may be used for pulp protection in direct restorations, or for the cementation of indirect restorations. Their bioactivity is one of the most favorable characteristics for the maintenance and preservation of pulp vitality, reinforcing the application of these materials in vital dental preparations.

AUTHOR CONTRIBUTIONS

MÖ conceived and designed, critically revised, and wrote the paper. LG analyzed the data and drafted the paper. CV analyzed the data and wrote the paper. All authors contributed to the article and approved the submitted version.

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