Tricalcium silicate-based cements: properties and modifications

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Declaration of Interests: The authors certify that they have no commercial or associative interest that represents a conflict of interest in connection with the manuscript.

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https://doi.org/10.1590/1807-3107bor-2018.vol32.0070

Submitted: May 08, 2018
Accepted for publication: May 29, 2018
Last revision: June 12, 2018

Abstract: Mineral trioxide aggregate (MTA) has been widely used for different reparative procedures in endodontics. The extensive use of this cement for pulp capping, apexifications, apical surgeries, and revascularization is related to its ability to induce tissue repair and to stimulate mineralization. Several research studies have tested modifications in the composition of MTA-based cements in order to enhance their clinical performance. Novel formulations have been introduced in the market with the aim of increasing flowability. Important properties such as appropriate radiopacity and setting time, color stability, alkaline pH, release of calcium ions, and biocompatibility have to be considered in these new formulations. The latest research studies on the physical, chemical, and biological properties of tricalcium silicate-based cements are discussed in this critical review.

Keywords: Dental Materials; Endodontics; Root Canal Filling Materials; Biocompatible Materials.

Introduction

Reparative procedures are of paramount importance in endodontics,[1] and conservative procedures allow maintaining teeth in good health.[2] Mineral trioxide aggregate (MTA) has been widely used for these purposes since its development in the 1990s.[3,4] MTA has been used for conservative management of root fractures,[2] sealing of perforations,[5] pulp capping,[6] apical plug in apexifications,[7] root-end filling material in apical surgeries,[8] and as a coronal barrier in revascularization.[1] All of these procedures imply contact with living tissues and body fluids, an environment that favors physical modifications and chemical/biological interactions with the material.[9, 10,11]

The physical, chemical, and biological properties of MTA have been studied for decades and novel substances were eventually introduced, but improvements are still required to obtain an ideal composition.[12,13,14] A perfect endodontic restorative material should present physical characteristics such as sealing, dimensional[15] and color stability,[16,17] radiopacity,[18,19] insolubility in contact with fluids,[20,21] flowability, and easy insertion;[22,23] and also chemical and biological properties such as alkaline pH, release of calcium ions,[24] bioactivity,[25] cell attachment,[26] and biocompatibility.[27]

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Several of the ideal properties of a restorative material were present in MTA, but others are lacking.[28] Color and the consistency are some widely discussed and studied properties of MTA that need improvements.[17,22,29] Novel materials have been developed in an attempt to overcome these drawbacks.[30,31, 32] The aim of this critical review is to discuss the physical, chemical, and biological properties of MTA and advancements in novel tricalcium silicate-based cements.

Clinical aspect and properties

The clinical aspect of tricalcium silicate-based cements is the first point to be considered.[9,33,34] The site of placement has a direct influence on the properties of this cement.[35] MTA is a dynamic material and its interaction with tissues and fluids is constant, starting at insertion and persisting for years after its placement.[15,25,36] Calcium hydroxide is leached out of hydrated MTA by the release of calcium ions and the bioactivity of MTA is related to such release.[24,37] MTA can be used mostly in procedures where there is contact with blood.[1, 7]

Contamination of MTA with blood affects the morphology of the set material and reduces the release of calcium ions.[9,38] Furthermore, blood can change the color of the material and interfere in radiopacity over time.[11]

Setting time and solubility are directly affected by moisture. A large amount of water increases both the setting time and solubility of MTA.

MTA is known for its chemical interaction with tissues. The alkalinization of the medium and release of calcium ions are related to the formation of portlandite (calcium hydroxide) by tricalcium silicate and dicalcium silicate during the setting time of MTA.[39] MTA Angelus and ProRoot MTA presented *in vitro* calcium release and alkaline pH when immersed in water[24] and calcium release was identified by Von Kossa staining of rat subcutaneous tissues.[40] These properties favor mineralization on MTA surface when used in pulpotomy,[41,42] the formation of mineralized tissue in the apical tissues of dog's teeth, and the sealing of furcation perforation.[43,44]

Color stability

The first formulation of MTA was gray, which limited its application to anterior teeth.[45] Although white MTA has been introduced in order to eliminate tooth discoloration, several studies have shown changes in tooth color.[46, 47]

White MTA is mainly composed of dicalcium and tricalcium silicate with 20% of bismuth oxide.[37,48] Reductioin of bismuth oxide in bismith and contact with the tooth structure result in a change in the color of the material and, consequently, in the color of the adjacent tooth structure.[16] The loss of stability of bismuth oxide molecules when in contact with a strong oxidizing agent has been pointed out as the cause for color change.[16,49] Replacement of the radiopacifying agent has been suggested to prevent discoloration.[50, 51] Zirconium oxide and calcium tungstate have been tested, but large amounts are required to provide similar radiopacity to that of bismuth oxide, and deterioration of the physical and chemical properties of the material would therefore be expected.[29,50,52]

As previously discussed, the environment exercises some influence over MTA. Contact with blood and color were tested.

The first formulation of MTA was gray, which caused intense discoloration when in contact with the teeth. To overcome this problem, the tooth color formula was introduced in the market. The reduction in the quantity of some components in this material resulted in a white composition. However, this formula also caused tooth discoloration. Thus, studies were carried out to detect the component involved in this interaction and bismuth oxide was found to be associated with tooth discoloration.

To prevent color changes, there are two alternatives. The first one is the replacement of bismuth oxide with calcium tungstate or with zirconium oxide.[16] MTA HP and other new calcium silicate cements such as Biodentine and BC Sealer change the radiopacifying agent into calcium tungstate or zirconium oxide. These substances do not cause color changes.[17] The second alternative is to associate 5% zinc oxide with MTA. Zinc oxide prevents the change in color caused by conversion of bismuth oxide to bismite.[17]

Consistency

The consistency of MTA also comes into question. The powder-to-water ratio is an important factor to consider. However, the increase in the amount of water in the mixture reduces radiopacity.

Particle size is assumed to play a role in this case since new silicate cements have been prepared with calcium silicate nanoparticles. BC sealer and Biosealer contain calcium silicate nanoparticles with the addition of a polymer, which favors the manipulation and consistency of the material. Propylene glycol was associated with MTA and did not interfere in its biological properties.[52,53] The association with propylene glycol using different ratios was evaluated in terms of physical and chemical properties, and 20% propylene glycol mixed with 80% distilled water favored the manipulation of MTA, pH, calcium release, and flowability, causing minor changes in setting time.[53] Another study showed that propylene glycol increased the adhesion of MTA.

New formulations

New formulations that enhance flowability include MTA HP, MTA Flow, and Biodentine, and those which incorporate ceramic compounds are Biodentine and Endosequence.

Biological properties of calcium silicate-based cements and new calcium silicate-based cements

MTA basically consists of calcium silicates. Calcium silicate-based cements with various chemical compositions are, in general, bioactive.[54] New calcium silicate-based restorative cements that offer alternatives to bismuth oxide have been developed, such as Biodentine (Septodont, Saint-Maur-des-Fossés, France), Neo MTA Plus (Avalon Biomed Inc, Bradenton, USA),[55] and MTA Repair HP[31] (Angelus Soluções Odontológicas, Londrina, Brazil).

Calcium silicate-based endodontic cements have also been developed, such as MTA Fillapex (Angelus, Londrina, Brazil), Neo MTA Plus (Avalon Biomed, USA), iRoot SP (Inovate BioCeramix, Inc., Vancouver, Canada), and TotalFill BC sealer (FKG Dentaire, La-Chaux-de-Fronds, Switzerland).[56] MTA Fillapex is a paste-paste endodontic cement, composed of salicylate resin, natural resin, silica nanoparticles, MTA, and calcium tungstate as radiopacifying agent. Neo MTA Plus cement is a dicalcium silicate-based powder-gel system that may be used as restorative or endodontic cement with varying powder-gel ratios. iRoot SP is composed of zirconium oxide, calcium silicates, calcium phosphate, calcium hydroxide, and thickening agents, made available in a ready-for-use formula and used for root canal filling. EndoSequence BC sealer (Brasseler USA, Savannah, USA) and TotalFill BC sealer (FKG, La Chaux-de-Fonds, Switzerland; Brasseler, Savannah, USA) are composed of zirconium oxide, calcium silicates, monobasic calcium phosphate, calcium hydroxide, and thickening agents. This (type of) cement is made available in a ready-to-use formula, sets with dentin moisture, and was developed for root canal filling.

iRoot SP endodontic cement showed no cytotoxicity to rat fibroblasts (L929).[57] The cytocompatibility of iRoot SP endodontic cement was also observed by Zoufan et al.[58] in fresh cement and after the cement had set. The iRoot SP cement could induce greater osteoblast differentiation and a lower level of inflammatory response in periodontal ligament cells than did Sealapex.[59]

Both MTA and iRoot SP could induce cell differentiation in osteoblast cells in the human dental germ.[59] Satisfactory antibacterial action of iRoot SP was observed against *Enterococcus faecalis*.[60] Zhu et al.[61] observed that BioAggregate cement (Innovative Bioceramix, Vancouver, BC, Canada) was capable of promoting cell adhesion, migration, and fixation of human dental pulp cells (HDPCs), indicating its cytocompatibility.

Endosequence BC sealer is a bioceramic endodontic cement that promotes greater cell viability than does AH Plus Jet.[62] EndoSequence BC sealer presented a higher level of biocompatibility than recently manipulated AH Plus and MTA Fillapex, both fresh and after setting. BC sealer has shown adequate adhesion to fibroblasts.[63] When EndoSequence BC sealer cement came into

contact with the physiological solution, there was leaching of calcium and formation of the calcium phosphate phase.[64]

The use of 5% sodium hypochlorite associated with EndoSequence BC sealer promoted greater antibacterial action against biofilm formed on dentin than did the use of irrigant solution only.[65] Wang et al.,[66] in a confocal laser scanning microscopy study, found that in the period of 30 days BC sealer was capable of eliminating 45% of *Enterococcus faecalis* from dentinal tubules, demonstrating that the antimicrobial action of BC sealer persisted even after the material had set.

TotalFill BC sealer is an endodontic cement similar to EndoSequence BC sealer, but it promotes significantly greater cell proliferation than do AH Plus and MTA Fillapex. The morphology of the cells seeded on TotalFill BC Sealer and AH Plus presented similar characteristics, with extracellular matrix production, whereas the fixation of cells on MTA Fillapex discs was limited, with only some cells on the surface of the material.[56]

MTA-Ang (Angelus, Londrina, Brazil), MTA-HP (Angelus, Londrina, Brazil), and Neo MTA-P (Avalon Biomed Inc, Bradenton, USA) showed cell viability and a high degree of cell proliferation and adhesion.[69] When HDPCs were used, MTAP (MTA Plus) had greater cell viability than did MTAF (MTA Fillapex) and FC (Fillcanal). MTAP showed a higher level of alkaline phosphatase activity than did MTAF and FC.[68]

NEO (Neo MTA Plus, Avalon Biomed Inc., Bradenton, USA), MTA (MTA, Angelus, Londrina, Brazil), and TSC/Ta_2O_5 (experimental tricalcium silicate-based cement, with tantalum oxide) had no cytotoxic effect. In an alizarin red assay, the three materials induced mineralized nodule formation; however, NEO produced a larger number of mineralized nodules than did MTA and TSC / Ta_2O_5.[69]

MTA HP (Angelus Indústria de Produtos Odontológicos S/A, Londrina, Brazil) showed greater viability in comparison with White MTA-Ang. Histological analysis after subcutaneous implant in rats demonstrated that MTA HP had biocompatibility and biomineralization potentials similar to those of MTA-Ang.[31]

MTA Plus (MTA P) (Avalon Biomed Inc. Bradenton, USA) and MTA (Angelus, Londrina, Brazil) presented no cytotoxicity and induced mineralized nodule formation. By using PCR, the authors observed that exposure of HDPCs to extracts of the two cements increased the expression of osteogenic markers of these cells.[70]

Petrović et al.[71] observed that calcium silicate-based materials (CS) and hydroxyapatite (HA-CS) presented a higher level of biocompatibility than MTA (MTA Branco, Angelus Soluções Odontológicas, Londrina, Brazil). Furthermore, better results were observed for CS and HA-CS after subcutaneous implant in rats.

In an evaluation of the biocompatibility of three calcium silicate-based endodontic cements, Bioroot BC Sealer (Septodont, Saint-Maur-des-Fosses, France) (BR), Endoseal MTA (EndoSeal, Maruchi, Seoul, Korea) (ES), and Nano-ceramic Sealer (B&L Biotech, Fairfax, USA) (NCS), with human periodontal ligament stem cells (hPDLSCs), BR and NCS presented better cytocompatibility than ES.[72]

In addition to a high level of biocompatibility,[62] BC sealer was capable of inhibiting the release of iCGRP from trigeminal ganglion neurons, reducing the level of symptomatology after extravasation of the cement during root canal filling.[73]

Silva Almeida et al.[74] compared the physicochemical and biological properties of premixed calcium silicate-based endodontic sealers with other conventional root canal filling materials by systematically reviewing laboratory studies. Premixed calcium silicate-based endodontic sealers followed the ISO 6876:2012 standard for most physicochemical properties, except for solubility. The target sealers also presented favorable biological characteristics when compared with conventional sealers. Despite the lack of well-designed long-term clinical trials, the target premixed calcium silicate-based sealers showed good physicochemical and biological properties *in vitro*. In general, the results were similar to or better than those of conventional endodontic sealers, as observed in *in vitro* and *in vivo* animal studies.

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