Material Modifications and Related Materials

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7.1 Introduction

During the past decades, the introduction of biocompatible sealing materials has facilitated performing an effective and efficient endodontic procedure. Although this revolutionary phase has not necessarily made endodontic treatment easy, better materials and improved technology have enabled the clinician to provide a better treatment in a wide range of complicated cases.

Since 1993, the basic principles of endodontic therapy have been strictly followed, and introduction of *mineral trioxide aggregate* (MTA) [110] maximizes the predictability of optimal treatment outcomes in compromised cases such as sealing the open apex or perforated area, retrograde filling, and also covering the vital pulp tissue during the endodontic procedure [72].

However, it should be noted that MTA has some drawbacks that have made it difficult to use in some cases. A questionnaire-based study [64] on postgraduate students in operative dentistry in the UK revealed that factors preventing the use of MTA in permanent and primary dentition are related to the material cost and the lack of evidence, respectively.

Another survey conducted in Turkey among the senior members of the endodontic departments of fourteen dental schools revealed that they used MTA in their clinical practice, apexification, perforations, retrograde fillings, and root resorption as the most common treatment procedure. Financial limitation was the main reason for negative responses, followed by other factors such as the difficult handling properties and low radiopacity of the material [158].

MTA has been used for several applications such as root perforation repair, root-end filling, and vital pulp therapy and as an apical plug; therefore, its essential properties for each treatment are expected to be different. For example, serving as a suitable retrograde filling material, apical plug, and perforation repair materials requires intimate sealing capacity, insolubility, biocompatibility, and promotion of tissue regeneration without provoking inflammation and mechanical strength; the latter however will not be an important factor for capping materials in vital pulp therapies.

To improve the undesirable properties of MTA (i.e., setting time, handling, antibacterial effect, discoloration), researchers have attempted to add some materials to its formulation. As some of the essential properties of MTA have been negatively changed, it is important to note that for gaining a suitable modification, all essential properties of the new material should be taken into consideration.

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7.2 Modifications

7.2.1 Improving the Setting Time

The materials used in oral cavity should ideally have a rather short setting time to avoid being washed away by saliva and to reduce the possibility of the unset materials present in the mouth which may cause oral tissue irritation [2]. Being very grainy and having a poor consistency make it difficult to use MTA in some of the clinical applications. Unfortunately, MTA is assumed as a difficult material to handle because of its granular consistency [106], slow setting time [44], and low compressive strength [67, 106] compared to other materials and being loose early after mixing [162]. To improve its application in endodontics, the development of a new formulation(s) of MTA is necessary to optimize both the strength and the setting time without compromising its other advantages [31].

Kao et al. [100] used reagent grade SiO_2, CaO, and Al_2O_3 powders as matrix materials and MgO, ZnO, and Fe_2O_3 powders as additives to produce an MTA-like cement. These cements exhibited a significantly faster setting time (14 min) than MTA when mixed with water, although there was a significant decrease in diametric tensile strength, ranging from 0.9 to 3.1 MPa in comparison with MTA (4.4 MPa). The addition of ZnO, MgO, and Fe_2O_3 to the MTA-like cement led to significantly higher strength compared to the original MTA. The pH values of the MTA-like cements were changed from 11 to 13, similar to the results obtained with MTA.

7.2.1.1 Excluding the Gypsum

In industry, the setting time of the *Portland cement* is modified at the end stage of the manufacturing process by grinding the cement with calcium sulfate (gypsum). All dental materials using Portland cement as the main cementitious phase will thus include some gypsum in the formulation. This inadvertently retards the material set. Removal of the gypsum results in a flash set, which may be controlled by the application of a superplasticizing admixture to increase the effectiveness of the material.

A novel cement *Proto A* was produced by inter-grinding the cement clinker without gypsum and mixing it with water and superplasticizer. It has been shown that both Proto A and MTA were made from similar constituent elements and phases, namely, tricalcium and dicalcium silicate. The setting time of a Portland cement may be reduced by excluding the gypsum during the final stage of the manufacturing process without affecting its other properties. The new prototype cement has improved workability and a reduced setting time. This could reduce a chairside time and the number of visits [32]. A new technique for biocompatibility evaluation was employed for testing of these new prototypes [44]. The biocompatibility of the test materials was assessed by a direct test method using Alamar Blue dye, which quantitatively evaluated the cell viability. Indirect test method was also used for evaluation of cells grown on material elution. The results showed the presence of no toxic leachable substances from the experimental materials. Cell growth was poor when seeded in direct contact with cements. Both cements were shown to have similar biocompatibility.

7.2.1.2 Addition of Calcium Aluminate

Mixtures of calcium aluminate cement and Portland cement result in a fast setting material with an associated reduction in compressive strength of the resultant material [43]. The compressive strength and setting time can be improved by adding calcium sulfate in the anhydrous form to the mixture of Portland cement and calcium aluminate cement thus creating a calcium sulfoaluminate. The physical properties and handling properties can be improved further by a reduction in the water to cement ratio. This is achieved through an application of the superplasticizing admixture. The physical and mechanical properties of two experimental types of Portland cement (calcium sulfoaluminate and calcium flouro-aluminate cement) when mixed with the superplasticizer were compared [31]. They showed satisfactory setting times and compressive strength values in comparison with glass ionomer cement.

7.2.1.3 Hydration Accelerators

Many studies have been conducted on $CaCl_2$ as a hydration accelerator mixed with MTA. A dental Portland cement accelerated with calcium chloride was initially introduced by Aquilina in 1999 at Guy's Hospital, London. This was followed by an investigation to evaluate the biocompatibility of the accelerated Portland cement [2]. An addition of 10 or 15 % $CaCl_2$ to the Portland cement as an accelerant has no adverse effect on the biocompatibility of MTA mixture. This study indicated that acceleration of Portland cement by adding the $CaCl_2$ stimulates the proliferation of SaOS-2 cells in vitro and actively supports a biological response in these cells through the production of cytokines like IL-1β, IL-6, IL-18, and osteocalcin. Many researchers have shown that modified ProRoot MTA has lower setting time [6, 18, 109, 173] and better handling, but lower compressive strength [106, 109] in comparison with unmodified MTA. Improvement in the sealing ability of the MTA and Portland cement mixed with calcium chloride has also been demonstrated [25, 90].

Some researchers used calcium nitrate and calcium formate as an accelerator mixed with the MTA and gained similar findings [173]. One of the most important criteria for using materials in contact with human tissues is biocompatibility. The biocompatibility of the MTA mixed with calcium chloride, calcium nitrate, or calcium formate was assessed, and these accelerators may be a biocompatible alternative when a rapid set is indicated [118]. The addition of calcium chloride to the MTA did not change the biological properties in the formation of mineralized barrier after pulpotomy [24]. Conversely, other researchers demonstrated that the addition of $CaCl_2$ to MTA as a pulp capping biomaterial has a deteriorating effect on calcific bridge formation, inflammation, and necrosis in dogs' teeth [134].

The early application of the endodontic irrigants may weaken the bond strength in the interface between accelerated MTA and dentin [91]. Therefore, after using MTA mixed with $CaCl_2$ for perforation repair, its exposure to the NaOCl irrigation during early setting phase caused an improvement in the push-out strength of the accelerated MTA and an increase in formation of calcium hydroxide crystals on the surface of accelerated MTA.

Calcium lactate gluconate (CLG) has also been mixed with MTA in order to improve the setting time and handling properties. A reduced setting time, inferior compressive strength, and lower pH in MTA mixed with CLG [109] were reported, although its sealing ability was improved [92] and adequate biocompatibility [98] was observed. The biocompatibility of MTA mixed with different hydration accelerators such as calcium chloride, calcium lactate gluconate, and citric acid was assessed [99]. The most favorable biocompatibility was observed in 0.1 wt% citric acid group. In addition, 10 wt% $CaCl_2$ showed poor cell viability and indicated less cell attachment in SEM evaluation.

In other studies, disodium hydrogen orthophosphate (Na_2HPO_4) was used instead of water to be mixed with MTA [56, 93]. A significant reduction in the setting time (26 min) was shown when 15 % Na_2HPO_4 was added to the MTA without adverse effects on the diametric tensile strength. Ding et al. [56] observed biocompatibility of Na_2HPO_4 solution mixed MTA on L929 cells.

For increasing the working time of MTA, some researchers added an alternative delivery vehicle, KY Jelly (Johnson and Johnson, New Brunswick, NJ) [106]. Its cellular toxicity appears to be acceptable [102]; however, the most important issue that needs to be ruled out is whether this composition offers suitable biological activity for routine clinical use. To date, no documents have supported other important properties of this material.

7.2.1.4 Finer Particle Size Modification

A novel mineral trioxide aggregate (MTA Plus; Avalon Biomed Inc., Bradenton, FL, USA) has been introduced which has a similar composition to MTA but is ground finer; thus, the material has a higher specific surface area [39]. MTA Plus is provided with either a hydrosoluble gel or water ampoules for mixing. When used with anti-washout gel, its washout was reduced [65]. The high specific surface area increases the rate of reaction but does not necessarily reduce the setting time. The high rate of reaction was

demonstrated by an increased release of calcium hydroxide in solution [39].

A new version of MTA has been patented in the USA and claimed to set faster with acceptable resistance to acidic environmental conditions by adding a small amount of strontium and reducing the particle size (US Patent application No. 13/211.880). Based on previous investigations [145–147], the nano-modification of the MTA with nanoparticles of strontium has resulted in reduction in the setting time and the surface porosity and increase in acid resistance, microhardness, and compressive strength.

7.2.2 Handling Improvement

The hardened MTA mixture is influenced by several factors: quantity of water during mixing, the procedure for mixing, pressure used for compaction, environment humidity, and temperature [162]. Many clinicians subjectively have reported that the handling properties of MTA are not ideal thus creating an apical plug, or perforation repair and obturation of the tooth in a single visit were not possible [5].

MTA is difficult to manipulate due to its dry consistency [30]. To improve this consistency, propylene glycol has been proposed and added to MTA Angelus [57]. The mixture of MTA with the ratio of 80 % distilled water and 20 % propylene glycol is favorable, but increasing the PG proportion interfered with setting time. The effect(s) of using the volume of 100 % on setting time has yet to be observed.

7.2.3 Enhancement of the Antibacterial Properties

The antibacterial and antifungal properties of the MTA have been extensively evaluated and conflicting results have been reported [62, 89, 121, 155, 163, 176, 180]. Several investigations reported that MTA has limited antimicrobial effect against some microorganisms [62, 121, 176]. MTA has an antibacterial effect on some facultative bacteria and no effect on any species of strict anaerobes [163]. To enhance the antimicrobial properties of MTA, some investigators replaced distilled water with some antimicrobial reagents such as chlorhexidine [86, 89, 106, 120, 152, 155, 156, 174], iodoform [52, 144], sodium hypochlorite [97, 106, 174], and silver zeolite [129].

Although many studies showed that substituting 0.12 % chlorhexidine gluconate with water enhanced the antimicrobial properties of MTA [120, 155], it should be noted that this mixture may cause cell apoptosis [86] and a decrease in the compressive strength of MTA [89]. Conversely, the implantation of a mixture of MTA and chlorhexidine subcutaneously resulted in no adverse effect on the tissue response [156]. In addition, MTA mixed with chlorhexidine leads to antibacterial effects against *E. faecalis* for at least 48 h [120].

The use of 3 % NaOCl gel mixed MTA resulted in freshly mixed MTA having a lower cell viability than the set one [97]. Iodoform in combination with MTA has been used for enhancing the antibacterial effect and showed no improvement in antimicrobial properties of MTA [144]. No significant difference in inflammatory tissue responses between MTA and Portland cement when mixed with iodoform was observed [52].

According to the results of the aforementioned investigations, it seems that improving selective properties of MTA such as setting time and antibacterial properties, by adding some liquids, may adversely affect other advantages of the material. New compositions of MTA should be evaluated comprehensively before their recommendation for clinical application.

7.2.4 Reducing the Discoloration

Although white MTA was developed to solve the problem of tooth discoloration produced by gray MTA, several studies have reported tooth discoloration after using both kinds of MTA [27, 96, 101, 135, 166]. This effect limits the application of MTA in aesthetically sensitive areas for treatment of perforations, pulp capping, and pulpotomy and as an apical barrier recommended to seal the dentinal tubules by dentin bonding agents before using both types of MTA is recommended to

prevent further tooth discoloration [4]. Removing the discolored dentin and internal bleaching has also been recommended to improve the aesthetic following the use of MTAs [17].

7.2.5 Elimination of the Heavy Metals

A major concern regarding the use of cements like MTA which are made from naturally occurring minerals is the amount of leachable arsenic and lead present in material components. According to the ISO 9917, the leachable lead and arsenic must be less than 100 and 2 ppm, respectively [140]. Many researchers [54, 58, 117] reported that MTA and Portland cement displayed very low amount of arsenic release; hence, no contraindication was demonstrated for its use in clinical practice regarding the presence of this chemical element. It has been recommended to use in a very small amount, e.g., less than 1 g, in clinical endodontic procedure [123]. Thus, the recorded amount of 34.27 mg arsenic per kilogram of material for gray Portland cement leads to 34.27 μg of arsenic per gram of MTA cement which is less than the toxic dose (140–210 mg for an individual weighing 70 kg).

A water-based cement labeled as MTA Bio (Angelus, Londrina, PR, Brazil) has been marketed with the aim of avoiding the presence of arsenic and lead. MTA Bio have been claimed to be fully synthesized in a laboratory under controlled, clean, and segregated conditions to ensure that the final product is free of contamination. According to the manufacturer, as a consequence of high-quality control of the cement production, the final cement is free of undesirable contaminant substances, in particular, arsenic. Compared to the original MTA, its similar sealing ability [55], shorter setting time [169], and low cytotoxic effects [113] on cultures of odontoblast-like cells have been demonstrated.

Novel formulations of root-end filling materials are based mostly on tricalcium silicate. Tricalcium silicate cement exhibited a similar microstructure and hydration characteristics to Portland cement [36]. Tricalcium silicate cement and materials based on this latter cement, namely, Biodentine and Bioaggregate, exhibited a low-level release of acid-extractable trace elements [42]. Thus, tricalcium silicate can be a suitable substitution to the Portland component in MTA.

7.2.6 Light-Curable MTA-Like Materials

The use of a number of resin systems has been reported with the main ones being light-curing systems Bis-GMA and a biocompatible resin [73, 74]; 2-hydroxyethyl methacrylate (HEMA), tetraethylene glycol dimethacrylate (TEGDMA), camphorquinone, and ethyl-4-(dimethylamino) benzoate (EDMAB) and with and without polyacrylic co-maleic acid [69, 70]; Bis-GMA and TEGDMA [66]; and Bis-GMA, pyromellitic acid diethylmethacrylate (PMDM), and HEMA [141]. The light-curing systems proposed so far have exhibited alkalinizing pH, calcium ion release, formation of apatite [66, 69], and functional groups able to chelate calcium ions [69]. Furthermore, therapeutic remineralization of dentin was observed [69, 70, 141, 150]. The light-cure MTA was well accepted by the alveolar tissue of rats, with the formation of mineralized tissue close to the materials [74]. It presented a moderate chronic inflammatory response at 30 days that decreased at 60 days but was more intense than with MTA Angelus and without dystrophic calcifications. It was possible to conclude that light-cure MTA was similar to MTA at 60 days, but it did not stimulate mineralization [73]. Regardless the calcium-releasing ability and the bioactivity, little or no hydration was exhibited by resin-modified MTA. Reaction rims around the cement particles were absent, and the formation and leaching of calcium hydroxide was shown to be negligible [66].

7.2.7 Replacement the Radiopacifiers

Bismuth oxide was added in 1:4 proportions as radiopacifier to the MTA so the material could easily be distinguished from the surrounding

anatomical structures on a radiograph. Bismuth oxide in MTA does not act as inert material. The bismuth replaces the silicon in the calcium silicate structure [33]. Furthermore, only 8 % of bismuth in the oxide form was present in the set material, while the un-hydrated MTA presented 21.6 % bismuth oxide. Leaching in increasing amounts was also shown for bismuth in ProRoot MTA [33]. Studies reported that the cytotoxicity of Portland cement containing bismuth oxide (BPC) was higher than that of PC after a short-term culture period of 1 day, whereas this cytotoxic effect was recovered during the long-term culturing [119]. Bismuth oxide induces cell death [45]. On the contrary, other researchers showed that BPC exhibited greater radiopacity and similar biocompatibility to PC in human periodontal ligament cells [105]. Bismuth oxide is used in a number of dental materials particularly root canal sealers. It has always been associated with tooth discoloration. Reports of discoloration of MTA with resultant tooth discoloration are found in the literature. The discoloration of MTA has been associated with a lack of oxygen in the root canal [166, 167] and also as a result of reaction with sodium hypochlorite used for root canal irrigation [38].

The bismuth oxide in MTA can be replaced by other radiopacifying materials. Ideally, an alternative radiopacifier should only impart the necessary radiopacity to the cement and should be inert, free from any contaminants, colorless, and nontoxic and be added in minimal amounts. Addition of gold powder, silver/tin alloy [40], barium sulfate [26, 40, 95], iodoform [26], zirconium oxide [26, 49], zinc oxide [40, 95], lead oxide, bismuth subnitrate, bismuth carbonate, and calcium tungstate [95] results in a radiopacity value of more than 3 mm of the aluminum scale. The gold powder was completely inert and was not leached out in solution [35]. The main disadvantages with using gold to replace the bismuth oxide in MTA include the cost of the gold and also the resultant color of the cement imparted by the gold. A filler loading of 30 % zirconium oxide to Portland cement mixed at a water to cement proportion of 0.3 resulted in a material with comparable properties to mineral trioxide aggregate. Addition of zirconium oxide powder as radiopacifying material did not seem to affect the compressive strength of the resultant material [49].

7.3 Related Materials

Root-end filling material is placed in contact with the periradicular tissue and thus requires biocompatibility as its main property. Therefore, an ideal root-end filling material should be nontoxic, noncarcinogenic, biocompatible with the host tissue, dimensionally stable, insoluble in tissue fluids, antibacterial, radiopaque, easy to manipulate, have adequate working time with fast setting time, and adhere to the tooth structure.

Some examples of the endodontic materials are gutta-percha, zinc oxide eugenol-based cements, composite resin, glass ionomer cements, gold foil, polycarboxylate cements, polyvinyl cements, and amalgam. Unfortunately, most of them have shown different levels of weakness in biocompatibility, leakage, solubility, handling properties, moisture incompatibility, and cost.

Although nowadays MTA has been thoroughly examined and revealed promising results, the ideal root-end filling material has yet to be found. New materials have claimed to have all the advantages of MTA without any of its drawbacks. More evidence is required to support these materials as an improved MTA or as its new alternatives. In this section, new products with new formulation, with similar application to MTA, are discussed (summarized in Table 7.1). According to the findings from Owadally and Pitt Ford's investigation [132], newly formulated products should be evaluated to determine whether they have compatible properties even when the majority of its constituents are similar to those of MTA.

7.3.1 Tricalcium Silicate-Based Endodontic Repair Cements

7.3.1.1 Bioaggregate

Bioaggregate (Innovative BioCeramic, Vancouver, Canada) is a relatively new product containing calcium silicate hydrate, calcium hydroxide,

Table 7.1 Characteristics of some related materials

Base materials	Derivatives	Composition	Properties
Tricalcium silicate-based endodontic materials	Bioaggregate	Calcium silicate hydrate + calcium hydroxide + hydroxyapatite + tantalum oxide + amorphous silicon oxide	Nontoxic [53, 175, 177, 182], nontoxic [104], antibacterial effect [180], sealing ability [59, 108], fracture resistant [164]
	EndoSequence root repair material	Calcium silicate + monobasic calcium phosphate + zirconium oxide + tantatum oxide + filler agent	Bioactive [5, 88, 115, 153], not bioactive [122], sealing ability [127], not sealing ability [87], antibacterial [114]
	Biodentine	Tricalcium silicate + calcium carbonate + zirconium oxide + calcium chloride	Remineralization induction [81], odontoblast differentiation [107], adverse effect on the dentin toughness [111, 151], not sealing ability [37], low porosity [41]
	Calcium-enriched mixture (CEM)	Calcium hydroxide + calcium oxide + calcium phosphate + calcium sulfate + calcium silicate + calcium carbonate	Hydroxyapatite formation [13], sealing ability [11, 84, 103], antimicrobial [14, 83], acceptable cytotoxicity [15, 125], suitable biocompatibility [1, 136], induce hard tissue formation [142], suitable for vital pulp therapy [8–10, 12, 63, 116, 128, 157]
	Generex A	Calcium silicate + unique gels + hydroxyapatite	Suitable compressive strength, washout resistant and setting time [139]
	Capasio	Calcium aluminosilicate + dental glass + bismuth oxide	Adequate physical and chemical properties [139], promote apatite deposition [138], osteoblast growth and nodule formation [171]
	Theracal	CaO + calcium silicate particles + strontium glass + fumed silica + barium sulfate + barium zirconate + resin containing Bis-GMA and PEGDMA	Calcium ion release and hydroxyapatite formation [68], decreasing cell metabolism [85]
Endodontic cements not based on tricalcium silicate	Calcium aluminate cement	Calcium aluminate + calcium dialuminate	Rapid setting, good flow, improved handling properties, high mechanical strength, reduced porosity [131]
	EndoBinder	Calcium aluminate based	Adequate physical and chemical properties [130], biocompatible [3, 48]
	Castor oil	Polymer derived from the castor oil plant (triglyceride of ricinoleic acid)	Antibacterial [165], biocompatible [22, 112], acceptable cytotoxicity and genotoxicity [28, 29], sealing ability [51]
	Ceramicrete D	Phosphosilicate ceramic + hydroxyapatite + cerium oxide + deionized water	Sealing ability [108], clinical handling and washout resistant [139]

hydroxyapatite, tantalum oxide, and amorphous silicon oxide, which is intended to be used for perforation repair and as a retrograde filling material. In a study using X-ray diffraction analysis [137], the absence of aluminum-based compounds was demonstrated. Furthermore, tantalum oxide has been included as a radiopacifier. The hydrated material released less calcium in solution than Biodentine [79]. In vitro studies [53, 175, 177, 182] revealed that Bioaggregate is nontoxic to human fibroblasts and osteoblasts. In addition, it may induce fibroblast differentiation and expression of the mineralization-association gene in osteoblasts.

On evaluation of the systemic toxic effect of MTA and Bioaggregate on the kidney and liver, some adverse effects on liver and kidney cells in

rats were demonstrated. The effect of MTA was significantly more severe than the Bioaggregate [104]. Evaluation of an antibacterial activity of this cement against *E. faecalis* revealed comparable results with MTA which was even enhanced after addition of the dentin powder [180]. Its sealing ability has been assessed by dye [59] and glucose [108] leakage, and results indicated similar ability to MTA as a root-end filling material. In one study [164], fracture resistance of immature teeth filled with Bioaggregate was higher than MTA, suggesting this cement can be used in immature teeth, as a root canal filling material.

7.3.1.2 EndoSequence Root Repair Material

Recently, a new root repair material has been introduced to the market: *EndoSequence Root Repair Material* (ERRM; Brasseler, Savannah, GA). According to the manufacturer, it is composed of calcium silicate, monobasic calcium phosphate, zirconium oxide, tantatum oxide, and filler agents and is available as paste in preloaded syringes and also in a moldable putty form. The preloaded syringe also has intracanal tips that can be bent to facilitate its placement in clinical situations. According to the manufacturer instruction, it has a working time of 30 min and a setting reaction initiated by moisture with a final set achieved approximately 4 h thereafter.

Although in one study, elutes of ERRM significantly reduced the bioactivity and alkaline phosphatase activity of human osteoblast-like cells [122], the results of other studies conducted on its bioactivity revealed that it may have cell viability similar to MTA in both set and fresh conditions [5, 88, 115, 153]. Sealing ability of this novel material was compared with MTA, and the results showed no significant difference in bacterial leakage between either of them [127]. In contrast, by using a bacterial leakage model [87], it was concluded that samples in ERRM group leaked significantly more than those in MTA group.

Antibacterial activity of ERRM was compared with MTA, and results demonstrated similar antimicrobial properties during their setting reaction against ten clinical strains of *E. faecalis* [114]. In an in vitro study [82], simulated root resorption defects were prepared, and after filling the root canal with either ERRM or MTA, the pH at the root surface of the teeth was measured. In the ERRM group, pH values declined during the first 24 h, and its 1-week evaluation was comparable with MTA during the 1st and 2nd weeks [82].

7.3.1.3 Biodentine

Biodentine is manufactured by Septodont (Septodont, Saint-Maur-Fosses Codex, France) and is composed of tricalcium silicate, calcium carbonate, and zirconium oxide as the radiopacifier, while its liquid form contains calcium chloride as the setting accelerator and water-reducing agent. This composition has been verified in a recent publication [46]. The calcium chloride accelerates the setting time of Biodentine, while the other additives enhance the physical properties [80]. According to the manufacturer, Biodentine is produced using a novel technological platform called Active Biosilicate Technology, which guarantees the purity of the material. An investigation of the presence of leachable arsenic, lead, and chromium from Biodentine exhibited the low levels of toxic heavy elements in this material [42]. The fine particle size [46] accompanied by the presence of calcium carbonate which enhances the material hydration results in the release of calcium hydroxide in solution [79]. A study demonstrated the formation of a silicate- and calcium-rich layer in dentin in contact with Biodentine and MTA. Silicon is known to enhance the rate of new bone growth and also induce remineralization of demineralized dentin when released from bioactive materials [81].

When Biodentine is applied directly onto the pulp, it induces an early odontoblast differentiation and the initiation of mineralization, probably due to a modulation of TGF-β1 secretion from the dental pulp cell [107]. Prolonged contact of mineralized dentin with calcium silicate-based materials, such as Biodentine, has an adverse effect on the dentin toughness and integrity of the dentin collagen matrix; therefore, caution is recommended when these materials are applied to the thin dentinal walls [111, 151].

When Biodentine was used as a dentin replacement material in the sandwich technique overlaying with composite, significant leakage occurred at the dentin-material interface [37]. Drying of Biodentine results in cracking and micro-leakage. Biodentine exhibits very low porosity when compared to MTA Bioaggregate and intermediate restorative material (IRM) (Dentsply Caulk, Milford, Delaware) [41].

7.3.1.4 Calcium-Enriched Mixture

Asgary et al. [16] introduced a new endodontic cement in 2008 to combine the superior biocompatibility of MTA with appropriate setting time (less than 1 h), handling characteristics, chemical properties, and reasonable price. This newly formulated biomaterial, named *calcium-enriched mixture* (CEM) cement (BioniqueDent, Tehran, Iran), was made using different calcium compounds; the patent is granted from US Patent and Trademark Office (USPTO) (endodontic filling material; USA, 7,942,961, 2011 May 17).

The manufacturer claimed that the mixed paste of CEM is not sticky; it does not tend to adhere to the applicator and can be easily condensed by the operator. In addition, some calcium compounds in CEM such as calcium sulfate and calcium silicate may cause a slight expansion of the material through continuous hydration after initial setting of the material and further crystalline maturation.

The results of recent investigations revealed that CEM comprises water-soluble calcium and phosphate ions and forms hydroxyapatite after setting [13]. Its sealing ability as a root-end filling material has been also evaluated and comparable results with MTA have been shown [11, 84, 103]. In presence of saliva contaminations, CEM showed superior sealing ability compared to MTA [84].

Antimicrobial properties of CEM against gram-negative, gram-positive, and cocci/bacilli bacteria were compared with MTA and calcium hydroxide (CH) using *agar diffusion test*. Results showed comparable antibacterial effects with CH and significantly better results than MTA [14, 83]. In addition, recent studies in cell culture revealed its cytotoxicity to be within acceptable range [15, 125], suitable biocompatibility [1, 136], and ability to induce hard tissue formation [142]. The results of in vivo studies on dogs showed that as pulp capping materials, MTA and CEM showed similar favorable biological outcomes, and both better than CH especially in terms of inducing the formation of the dentinal bridge [12, 157]. In several clinical trials in primary and permanent teeth [8–10, 63, 116, 128], CEM was used as a vital pulp therapy agent, and results indicated that the performance of new biomaterials may trend toward more biological treatments.

7.3.1.5 Generex A

Generex A (Dentsply Tulsa Dental Specialties, Tulsa, OK) is a calcium silicate-based material with similarities to ProRoot MTA. However, Generex A is mixed with unique gels instead of water and, together with a powder consistency, results in improved material handling and shorter setting time. Generex A powders contain hydroxyapatite to nucleate the production of hydroxyapatite in vivo which might be responsible for acceleration of osteoblastic activity in rats [170]. In addition, in an in vitro study, its compressive strength, washout resistance, and setting time were found to be better than MTA [139].

7.3.1.6 Capasio

Capasio (Primus Consulting, Bradenton, FL) is the new calcium aluminosilicate-based material which has been introduced in an effort to improve the weaknesses of previous materials. It is composed primarily of bismuth oxide, dental glass, and calcium aluminosilicate with a water-based gel. Upon the final setting (e.g., 9 min), this material is slightly more acidic (pH = 10.9) than WMTA (pH = 11.6). Moreover, it has demonstrated similar or improved physical characteristics such as setting time, radiopacity, compressive strength, pH, and washout resistance [139].

When used as a root-end filling material, Capasio is more likely to penetrate dentinal tubules, and similar to MTA, it promotes apatite deposition when exposed to synthetic tissue fluid [138]. In a comparative study, Capasio has not been shown to support the primary osteoblast growth and facilitate nodule formation in comparison with MTA and Generex A [21]. Recently,

Capasio powder has been refined and renamed as *Quick-Set* (Primus Consulting), and the cationic surfactant was removed from the liquid gel component, which was proposed to interfere with cell cytocompatibility. In a study, Quick-Set demonstrated similar cytotoxicity profile to MTA [171].

7.3.1.7 TheraCal

TheraCal (Bisco Inc., Schaumburg, IL, USA) is a new light-cured resin-modified paste containing CaO, calcium silicate particles (type III Portland cement), strontium glass, fumed silica, barium sulfate, barium zirconate, and resin containing Bis-GMA and poly(ethylene glycol) dimethacrylate (PEGDMA) (International Patent A61K33/42), which has been introduced as a pulp capping material. It has the ability to release calcium ions and create an environmental pH close to physiological pH after 7 days. The latter characteristic favors the formation of apatite and induces the differentiation of new odontoblasts, thus resulting in the formation of new dentin. Its ability to polymerize to a depth of 1.7 mm may eliminate the risk of untimely dissolution [68]. Although bioactive and calcium-releasing properties have been demonstrated for TheraCal, decreased cell metabolism when compared to the control has been demonstrated [85].

7.3.2 Endodontic Cements Not Based on Tricalcium Silicate

7.3.2.1 Calcium Aluminate Cement

A novel *calcium aluminate endodontic cement* was developed at the Federal University of São Carlos, Brazil, by Pandolfelli et al. [133] (Patent registration INPI 0704502–6). This cement aims to preserve the positive properties and clinical applications of MTA while increasing the possibility of extended applications without the disadvantages of the original material. The calcium aluminate cement is comprised of calcium aluminate ($CaO{\cdot}Al_2O_3$) and calcium dialuminate ($CaO.2Al_2O_3$) phases, which are responsible for the hydraulic setting process [138]. In one study, the chemical, physical, and mechanical properties of the cement were assessed, and results showed more rapid setting, better flow, improved handling properties, rather high mechanical strength, and reduced porosity with lower pore size compared to MTA Angelus [131]. On the other hand, on the surface of this cement in combination with accelerator, stoichiometric hydroxyapatite was detected after immersion in simulated body fluid solution [130].

7.3.2.2 EndoBinder

A new calcium aluminate-based endodontic cement (Patent Number PI0704502-6-2007) called EndoBinder (Binderware, São Carlos, SP, Brazil) has been developed, with the aim of preserving the properties and clinical applications of MTA without its negative characteristics. The cement is produced by the process of aluminum oxide and calcium carbonate calcination at temperatures between 1,315 and 1,425 °C. The formed calcium aluminate is cooled and then triturated until an adequate particle size is obtained. Free magnesium oxide and calcium oxide, which are responsible for the undesired expansion, and ferric oxide which leads to tooth darkening have been eliminated. This material has been shown to present adequate physical and chemical properties [130] and induce a higher rate of osteogenic cells differentiation compared to those exposed to MTA [48]. In addition, when tested on rat subcutaneous tissues, it proved to be biocompatible [3]. In a 1-year in vitro study, GMTA, WMTA, and EndoBinder with and without radiopacifying agent displayed color alteration after 360 days [71].

7.3.2.3 Castor Oil Cement

Recently, a material-based polymer derived from the *castor oil plant* (*Ricinus communis*) was introduced to endodontics, also known as *castor bean polyurethane cement* (COB, Poliliquil, Araraquara, SP, Brazil), is composed of 81–96 % triglyceride of ricinoleic acid, and is considered as a natural polyol containing three hydroxyl radicals.

This cement has been reported to have antibacterial activity against *E. coli* [165] and is progressively integrated into the alveolar bone in the wound-healing process [47]. Aiming at

Table 7.2 Properties of MTA-based sealers

Sealers	Composition	Biocompatibility	Antibacterial	Sealing ability	Calcium ion release
Endo-CPM-Sealer	MTA + calcium chloride + calcium carbonate	(+) [76, 77]	(+) [159] (–)[124]	(+)[50]	(+) [160]
iRoot SP Sealer	Calcium silicate based (unknown)	(+) [181]	(+) [179]	(+) [61, 178]	(+) [23]
MTA Fillapex	MTA + salicylate resin + natural resin + silica nanoparticles + bismuth oxide + dehydrated calcium sulfate	(+) [78, 149] (–) [20]	(+) [124]	(+) [75] (–) [154]	(+) [23]
MTA Obtura	White MTA + viscous fluid	N/Y/E[a]	N/Y/E[a]	(–) [168]	N/Y/E[a]
ProRoot Endo Sealer	Tricalcium silicate + dicalcium silicate + calcium sulfate + calcium aluminate + bismuth oxide	N/Y/E[a]	N/Y/E[a]	(+) [172]	N/Y/E[a]

[a]Not yet evaluated

evaluation of its cytotoxicity and genotoxicity, this material proved to be biocompatible when used in maxillary sinus floor augmentation [22] and is well osseo-integrated [112], without any negative influence on the cell survival [28, 29]. The sealing ability of this cement has been evaluated by the dye leakage method, and results have shown an efficient sealing ability [51].

7.3.2.4 Ceramicrete

Ceramicrete is a self-setting phosphate ceramic developed at the Argonne National Laboratory that sets in an ambient condition formed by acid-base reaction between an acid phosphate (KH_2PO_4) and a negligible soluble basic metal oxide (calcined MgO). More recently, a biocompatible, radiopaque Ceramicrete-based dental/bone material has been created by incorporating hydroxyapatite powder and cerium oxide radiopaque filler into the phosphosilicate ceramic. The Ceramicrete-based material has an initial setting time of 6 min and a final setting time of 12 min, it can also be rolled into a sausage-like formation for easier manipulation with dental instruments and sets under water with minimal washout [143]. A modified version of the material (Ceramicrete D) was introduced by mixing the powder with deionized water. The sealing ability of Ceramicrete D was reported to be favorable [161].

In another study by Leal et al. [108], two endodontic bioceramic repair cements (Bioaggregate and Ceramicrete D) displayed similar leakage results to white MTA when used as root-end fillings materials. Ceramicrete D had significantly lower glucose penetration. Physical and chemical analyses showed that the clinical handling and washout resistant of the Ceramicrete D were superior to those of MTA; however, it was weaker, less radiopaque, and initially more acidic than Generex A and Capasio [139].

7.3.3 MTA-Based Sealers

Despite favorable characteristics, MTA presented some physical properties that hinder its application for root canal filling. An appropriate material for using as a root canal filling should be biocompatible, induce mineralized tissue formation, has suitable flow rate and manipulation. Recently, in an effort to incorporate the desirable biological properties of MTA into an easy to manipulate and insert material, some manufacturers have added specific components to MTA-based cements. Materials resulting from this attempt are listed in Table 7.2.

7.3.3.1 Endo-CPM-Sealer

The *Endo-CPM-Sealer* (Egeo S.R.L., Buenos Aires, Argentina) was introduced in an attempt to combine the physicochemical properties of a root canal sealer with the biological properties of MTA. According to the manufacturer, CPM Sealer is composed of MTA, SiO_2, $CaCO_3$, Bi_2O_3, $BaSO_4$, propylene glycol alginate, propylene glycol, sodium citrate, and calcium chloride after mixing. Calcium carbonate, as a component that reduces the pH of the mixture, restricts the surface necrosis of cells in contact with the material and thus allows the action of the alkaline phosphatase and, consequently, the deposition of mineralized tissue [76]. Hydroxyl and calcium ions have also been shown to release from this cement similar to MTA, and therefore, they may act as an alternative root-end filling material [160]. Researchers demonstrated that Endo-CPM-Sealer has a good antimicrobial activity [159]. In addition, fibroblast cultures revealed that Endo-CPM-Sealer is not cytotoxic [77]. According to the manufacturer and study results [50], Endo-CPM-Sealer can be considered as an alternative sealing material in the treatment of root perforations. When used as an apical plug, the CPM and MTA had similar adaptation to the dentin walls.

7.3.3.2 iRoot SP Sealer

A new bioceramic-based sealer *iRoot SP* (Innovative Bioceramix, Vancouver, Canada) is described by the manufacturer as a convenient, premixed, ready-to-use, injectable, white hydraulic cement paste. This material uses the natural moisture of the dentinal tubules to initiate and complete its setting reaction. According to the manufacturer, iRoot SP is an aluminum-free, hydrophilic, calcium silicate-based material that requires the water to set and harden. In addition to its antibacterial activity and biocompatibility [179, 181], it showed good sealing ability [61, 178] and bonding to root canal dentin even under different degrees of dentin moisture [60, 126]. Intracanal placement of calcium hydroxide seems to improve the dislodgment resistance of the iRoot SP [7].

7.3.3.3 MTA Fillapex

MTA Fillapex (Angelus, Londrina PR, Brazil) is a new double paste MTA-based root canal sealer. Its composition after mixing is basically mineral trioxide aggregate, salicylate resin, natural resin, bismuth oxide, and dehydrated calcium sulfate. This material has excellent radiopacity, easy handling, and good working time. MTA Fillapex showed antibacterial activity against *E. faecalis* before setting [124]. According to the manufacturer, this is the only root canal sealer that promotes cementum regeneration. However, one study showed lower cell viability rates when compared with the control group [20]. On the contrary, other investigations on human osteoblast-like cells and rat tissues showed the sealer presents suitable bioactivity [78, 149]. In some studies, MTA Fillapex presented lower sealing ability than MTA [154] and lower push-out bond values to root dentin compared with other sealers [148].

7.3.3.4 MTA Obtura

MTA Obtura (Angelus, Solucoes Odontologicas, Londrina, PR, Brazil) is a mixture of white MTA with a proprietary viscous liquid. In an in vitro study, MTA Obtura showed progressive increased leakage during extended experimental periods [168]. On the other hand, another study concluded that MTA Obtura presented greater flow than the minimum recommended level in the ADA_{57} specification [19].

7.3.3.5 ProRoot Endo Sealer

ProRoot Endo Sealer (Dentsply Maillefer, Ballaigues, Switzerland) is reported to be calcium silicate based with liquid-to-powder ratio of 1:2. The liquid is composed of water and a viscous water-soluble polymer. The addition of a polymer to improve the workability had been reported previously [44]. The polymer addition does not seem to affect the biocompatibility of the material [34, 44]. Sealing property of ProRoot Endo Sealer is comparable to other tested sealers [172], and also the presence of spherical amorphous calcium phosphate-like and apatite-like phases after immersion in simulated body fluid is demonstrated [94].

Conclusion

The introduction of *mineral trioxide aggregate* (MTA) in 1993 started a new revolutionary phase in endodontic practice. However, despite solving many problems in the treatment of complicated cases, some difficulties have been reported with MTA. The loose and sandy nature and also lack of uniformity in MTA mixture have caused some difficulties for application of MTA paste into the desired space.

While some modifications have been proposed for easier application of MTA in order to overcome its disadvantages, these modifications have had a negative influence on some properties of the material.

A new generation of materials with at least similar properties to those of original ProRoot MTA have also been introduced as its suitable alternatives in complicated cases. More evidence is required to support these materials as an improved MTA or as its new alternatives.

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