Mineral Trioxide Aggregate: A Comprehensive Literature Review—Part I: Chemical, Physical, and Antibacterial Properties

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Abstract

Introduction: An ideal orthograde or retrograde filling material should seal the pathways of communication between the root canal system and its surrounding tissues. It should also be nontoxic, noncarcinogenic, nongenotoxic, biocompatible with the host tissues, insoluble in tissue fluids, and dimensionally stable. Mineral trioxide aggregate (MTA) was developed and recommended initially because existing root-end filling materials did not have these “ideal” characteristics. MTA has also been recommended for pulp capping, pulpotomy, apical barrier formation in teeth with open apexes, repair of root perforations, and root canal filling. Since MTA’s introduction in 1993, numerous studies have been published regarding various aspects of this material. The aim of Part I of this literature review is to present investigations regarding the chemical, physical, and antibacterial properties of MTA. Methods: A review of the literature was performed by using electronic and hand-searching methods for the chemical and physical properties and antibacterial activity of MTA from November 1993–September 2009. Results: There are many published reports regarding the chemical, physical, and antibacterial properties of MTA. Our search showed that MTA is composed of calcium, silica, and bismuth. It has a long setting time, high pH, and low compressive strength. It possesses some antibacterial and antifungal properties, depending on its powder-to-liquid ratio. Conclusions: MTA is a bioactive material that influences its surrounding environment. (J Endod 2010;36:16–27)

Key Words
Antibacterial effect, chemical and physical properties, mineral trioxide aggregate, MTA

Most endodontic failures occur as a result of leakage of irritants into the periapical tissues (1–3). An ideal orthograde or retrograde filling material should seal the pathways of communication between the root canal system and its surrounding tissues. It should also be nontoxic, noncarcinogenic, nongenotoxic, biocompatible with the host tissues, insoluble in tissue fluids, and dimensionally stable (4, 5). Furthermore, the presence of moisture should not affect its sealing ability; it should be easy to use and be radiopaque for recognition on radiographs (4). Because existing restorative materials used in endodontics did not possess these “ideal” characteristics (4), mineral trioxide aggregate (MTA) was developed and recommended initially as a root-end filling material and subsequently has been used for pulp capping, pulpotomy, apexogenesis, apical barrier formation in teeth with open apexes, repair of root perforations, and as a root canal filling material. MTA has been recognized as a bioactive material (6) that is hard tissue conductive (7), hard tissue inductive, and biocompatible. Several reviews have been published about MTA’s chemical properties, biocompatibility, and clinical applications (8–10). Only one article has extensively studied MTA and addresses numerous articles regarding the material’s physical and chemical properties, leakage studies, biocompatibility, and clinical applications (10). The authors found 245 articles with their selected key words since the introduction of MTA in 1993 to August 2006. Of these, 156 articles met their criteria for citation. Since then, additional articles have been published regarding the various properties and clinical uses of MTA. The purpose of this literature review is to update previously published information (10) and present a comprehensive list of articles from November 1993–September 2009 regarding the chemical and physical properties and antibacterial activity of MTA.

Inclusion and Exclusion Criteria

MTA publications from peer-reviewed journals published in English from November 1993–September 2009 are included in this review. Studies that do not meet the above criteria are excluded.

Search Methodology

An electronic search was conducted in the PubMed and Cochrane databases with appropriate MeSH headings and key words related to the physical, chemical, and antibacterial properties of MTA. To enrich the results, a hand-search was conducted of the last 2 years’ worth of issues of the following major endodontic journals: International Endodontic Journal; Journal of Endodontics; Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontology. The process of cross-referencing continued until no new articles were identified.
**Chemical Properties**

MTA powder contains fine hydrophilic particles that set in the presence of moisture. Several liquids have been used to hydrate MTA powder. Various methods have been used to examine MTA composition including energy dispersive analysis with x-ray (EDAX), inductively coupled plasma optical emission spectroscopy (ICP-OES), x-ray diffraction analyses (XRD), x-ray fluorescence spectrometry (XRF), energy x-ray spectrometry, and energy dispersive spectroscopy (11–20).

The MTA patent (21) shows that it contains calcium oxide (CaO) and silicon (SiO). Several investigations have reported that the main elemental components of MTA are calcium and silica, as well as bismuth oxide (13, 16, 22, 23).

MTA is currently marketed in 2 forms: gray (GMTA) and white (WMTA). MTA was introduced in gray, but because of the discoloration of potassium and the presence of bismuth oxide (17). An investigation evaluated the dry powder of GMTA and WMTA, as well as ordinary and white Portland cement (PC), finding that all tested materials have similar major constituents: tricalcium silicate, tricalcium aluminate, calcium silicate, and tetracalcium aluminoferite (18).

GMA basically consists of dicalcium and tricalcium silicate and bismuth oxide, whereas WMTA is primarily composed of tricalcium silicate and bismuth oxide (16). When MTA powder is mixed with water, calcium hydroxide (CH) and calcium silicate hydrate are initially formed and eventually transform into a poorly crystallized and porous solid gel (19). The ratio of calcium silicate drops because of the formation of a calcium precipitate. The precipitated calcium produces CH, which is the cause of MTA’s high alkalinity after hydration (26). The production source for CH is a matter of controversy. Camilleri (26) believed that CH is formed from dicalcium and tricalcium silicate after mixing MTA powder with water, whereas Dammashcke et al (14) reported that CH is a product of tricalcium aluminete hydrogenation.

Bismuth affects CH precipitation after MTA hydration (19). Because bismuth oxide dissolves in an acidic environment, it has been suggested that placing MTA in an acidic environment such as inflammatory tissues might result in the release of bismuth oxide (19). This might decrease MTA’s biocompatibility because bismuth oxide does not encourage cell proliferation in cell culture (27).

In 2005 Dammashcke et al (14) reported that the amount of sulfur at the surface of set MTA is 3 times higher than the powder forms of MTA, and that this layer protects the cement from further hydration and increases the cement’s setting time. MTA is known as an active biomaterial with the potential to interact with the natural fluids present in tissues (28). Recently published articles have used phosphate-buffered saline (PBS) or other media that are more similar to an in vivo medium (29–32).

A qualitative surface analysis of WMTA and GMTA showed that the crystal size of GMTA is approximately 8 times larger than that of WMTA (22). Map images show that oxygen is distributed throughout both crystalline and amorphous phases of GMTA and WMTA, and therefore all of the elements are present in their oxide form (22).

Two investigations analyzed the set condition and powder form of GMTA, WMTA, and PC (16, 17). One reported that crystals were only observed when the set material was placed in a phosphate solution (16). They concluded that set MTA contains CH in a silicate matrix and attributed the high pH of MTA to the presence of CH (16). The other investigation reported differences in the presence and percentage of the content of the powder and the set condition of PC, WMTA, and GMTA (17).

Bismuth oxide in MTA provides its radiopacity. Bismuth is present in both hydrated and nonhydrated MTA and is also a part of calcium silicate hydrate (19).

On the basis of the results of various studies regarding the chemical composition of MTA, these differences are related to the various liquids used to mix with MTA powder (11–13, 16, 17, 22, 33–35) and various equipments to test its composition (11–20).

**Physical Properties**

Hydration of MTA powder results in a colloidal gel that solidifies into a hard structure. Characteristics of the mixture can be influenced by the powder/liquid ratio, method of mixing (ie, the amount of entrapped air), pressure used for condensation, humidity of the environment, the type of MTA, the type of storage media, the pH value of the environment, the type of vehicle, the length of time between mixing and evaluation, thickness of the material, and temperature (14, 16, 27–35). Fridland and Rosado (42) believed that some of these factors cannot be controlled easily; therefore, different results might be obtained during a study on physical properties of MTA. Several investigators have examined MTA’s setting time and expansion, solubility, compressive and flexural strength, push-out strength, bond strength to other materials, retentive strength, displacement, pH, radiopacity, particle size, porosity, microhardness, and fracture resistance. Others have studied the effect of environment and methods of placement of MTA on its physical properties. Furthermore, physical and chemical properties of other types of MTA as well as its new compositions have been studied and compared with each other and with PC.

**Setting Time**

MTA is prepared by mixing its powder with sterile water in a 3:1 powder-to-liquid ratio (39). The mean setting time of MTA is 165 ± 5 minutes, which is longer than amalgam, Super EBA, and intermediate restorative material (IRM) (11). GMTA exhibits significantly higher initial and final setting times than WMTA (45, 46). The longer setting time of WMTA in comparison with PC is attributed to the lower levels of sulfur and tricalcium aluminete in WMTA (14).

In an attempt to use MTA for 1-visit perforation repair, a study placed glass ionomer cement (GIC) over WMTA. The authors reported that placing GIC 45 minutes after WMTA placement did not affect the formation of calcium salts in the interface of the 2 materials. In addition, placement of GIC over WMTA did not affect setting of this material (56). A separate study by the same authors confirmed that the GIC setting was not disrupted by the presence of WMTA (57).

To improve its handling, a recent study used MTA in its powder form as a root canal filling material (58). The authors reported that the majority of samples set after storage in normal saline, albeit during a longer period of time (72 hours). MTA setting time and bacterial leakage are adversely influenced when the samples are kept in dry conditions (50). Because 2-sided hydration of MTA results in more flexural strength than 1-sided hydration (47), placing MTA in 1 visit without external moisture is not recommended.

MTA’s long setting time is one of the major drawbacks of the material. Many investigations have been performed to overcome this clinical disadvantage (38, 59–62).

**Setting Expansion**

There are conflicting results regarding the setting expansion of various types of MTA (37, 45, 46). Two investigations showed that
WMTA expands slightly more than GMTA (45, 46). Another investigation compared the expansion of GMTA with WMTA after covering the material’s surface with Hank’s balanced salt solution (HBSS) or sterile water. In this study, GMTA expanded significantly more than WMTA with either sterile water or HBSS (37). GMTA expanded less in HBSS than in sterile water. In contrast, WMTA expansion was higher in HBSS than in sterile water. The different expansion behavior of GMTA and WMTA stored in HBSS might be due to the composition of the immersion liquid (H$_2$O$_2$P) or the difference in chemical composition between the 2 formulations of MTA (13, 16, 22). This information indicates that storing MTA in different environments affects its setting expansion (37).

Solubility

The degree of solubility of MTA is a matter of debate among investigators (11, 46, 49, 63–65). Most investigations reported low or no solubility for MTA (11, 49, 64, 65). However, increased solubility is reported in a long-term study (65).

When comparing the physical properties of WMTA with those of GMTA, the former material demonstrates significantly more solubility (46). Varying results are reported when comparing PC with WMTA (46, 49). One study reported that both ordinary and white PC (WPC) exhibited significantly less solubility than WMTA (46). These findings are in contrast with another study that shows GMTA is less soluble than 2 different types of PC (49). The differences are attributed to the type of PC used in these investigations. In addition, the powder-to-water ratio might influence the amount of solubility. In fact, higher water-to-powder ratios increased MTA porosity and solubility (42). The authors reported that using more water would increase calcium release from MTA. The addition of bismuth oxide to MTA, which is insoluble in water, is another cause for MTA insolubility. In an experiment on the hydration of MTA, Camilleri (19) confirmed the reaction of bismuth oxide with both calcium and silicate contents of MTA.

A recent investigation has reported that WMTA decreases its weight 7 days after immersion in physiologic solutions with different pH values, whereas the material increases in weight 30 days after immersion. The investigators have attributed the weight loss to the release of CH and the increase in WMTA weight to the formation of apatite crystals over the material surface (65).

The release of calcium ions from MTA is reported by several investigations (33, 34, 42, 66, 67). Antunes Bortoluzzi et al (34) added CaCl$_2$ to WMTA, revealing a significant increase in calcium release from WMTA during the first 24 hours. It has been confirmed that high amounts of calcium in a cell culture environment might down-regulate cell proliferation (68).

Releasing calcium from MTA might be influenced by clinical conditions. A recent study placed MTA inside the canals with simulated resorbed roots, reporting significantly more calcium ion release than in teeth without MTA root filling (35). It should be emphasized that the method of solubility assessment in most studies (11, 42, 49, 63) is based on the difference between weight before and after placing the cement into the water. Although it is a standard method for assessing material solubility, the test, in fact, measures the elution of water-soluble material, not the solubility. Solubility of a solid material is defined as the amount of a substance that can be dissolved in a given amount of solvent. However, measuring weight difference before and after storage of the material in water might not result in solubility, because particles of the material might detach from the cement during storage, or the cement might absorb water. These interactions might prevent the evaluation of actual solubility in spite of releasing some of the cement contents into the storage media (69, 70). Because various investigators used different methods to evaluate this property of MTA, it is very difficult to compare the results of these investigations with one another. In fact, recent investigations raised a question regarding clinical relevancy of the method of assessing solubility for bioactive materials such as MTA (65–67, 71).

Other reasons for difference in MTA solubility include the time of immersion of the material, the type of MTA, and the powder-to-liquid ratio (42, 46, 71, 72).

Compressive Strength

The compressive strength of MTA is significantly less than that of amalgam, IRM, and Super EBA after 24 hours. However, after 3 weeks, there is no significant difference between Super EBA, IRM, and MTA in terms of compressive strength (11). MTA is composed primarily of tricalcium and dicalcium silicate (16) with the addition of bismuth oxide. Because the dicalcium silicate hydration rate is slower than that of tricalcium silicate (14), the compressive strength (11) and push-out strength of MTA reach their maximum several days after mixing (40, 48).

There are conflicting results regarding the compressive strength of WMTA and GMTA (29, 46, 52). One study reported that compressive strength of WMTA at 3 and 28 days after mixing is significantly less than that of GMTA (46). In contrast, 2 other investigations comparing the compressive strength of GMTA and WMTA reported more compressive strength for WMTA (29, 52). In general, MTA’s compressive strength is not significantly affected by condensation pressure (51).

Another recent experiment revealed that keeping WMTA in dry conditions decreases its compressive strength (50). Even the samples kept moist after mixing show variations in compressive strength, depending on the amount of time elapsed between mixing and examination. The samples that were kept for 2–7 days in moisture exhibited greater compressive strength than the 4-hour samples.

A recent investigation reported significantly lower compressive strength for WMTA when the material was etched by phosphoric acid (37%). The investigators suggested that restoration with acid-etch composite after MTA placement should be postponed for at least 96 hours (73).

Several factors might influence MTA’s compressive strength, including the type of MTA, the liquid that is mixed with the material, the condensation pressure on the material, the pH value of the mixing liquid, and the condition of MTA storage (29, 46, 50–52).

Flexural Strength

Torabinejad and Chivian (8) recommended placing a wet cotton pellet over GMTA when it is used for perforation repair, pulp capping, or an apical plug. An investigation compared the effects of setting condition on flexural strength of WMTA. The material was mixed and received moisture from 1 or 2 sides (47). Two-sided moisture, as has been recommended (8), showed significantly more flexural strength after 24 hours (47). The authors suggested that cotton pellets should be removed after 24 hours because the flexural strength decreases 72 hours after WMTA receives moisture from both sides (47).

On the basis of limited literature, it appears that placing a moist cotton pellet over MTA for the first 24 hours increases its flexural strength.

Push-out Strength

The push-out strength of perforation repair materials is an important factor because shortly after perforation repair, tooth function might dislodge the material. MTA has lower push-out strength in comparison with IRM or Super EBA after immersion in walking bleach materials (sodium perborate mixed with saline, Superoxol, sodium perborate
mixed with Superoxol) (74). The importance of moisture on the push-out strength of MTA has been confirmed (48). MTA is reported to be composed basically of dicalcium and tricalcium silicate in addition to bismuth oxide (16). Because the dicalcium silicate hydration rate is slower than the tricalcium silicate rate, storing MTA in a wet environment gives it more strength with the passage of time (14).

On the basis of available data, it appears that MTA gains optimal physical properties such as flexural strength, compressive strength, and push-out strength when it receives enough moisture after being placed in an operation site.

**Bond Strength with Other Dental Materials**

An in vitro study investigated dentin-bond strength of MTA after immersion in 5.25% NaOCl and 2% chlorhexidine (CHX) and Glyde file preparation for 2 hours. Results of the study showed that Glyde file preparation significantly decreased bond strength between dentin and MTA; however, the result has no clinical relevance because none of the above materials is left in the tooth for 2 hours during a clinical procedure (75). Another investigation (76) compared composite and compomer shear bond strength with WMTA. Results determined that placing total-etch 1-bottle adhesive with a composite or compomer over MTA produces significantly higher bond strength compared with a 1-step self-etch system. Limited information shows that the presence of a chelating agent and the type of etch system affect MTA bond strength.

**Retentive Strength**

An in vitro study (77) investigated MTA’s retentive strength as a luting agent for prefabricated posts and compared it with zinc phosphate and glass ionomer cements. The results revealed that the retentive strength of glass ionomer or zinc phosphate cement is significantly superior to that of MTA. The results of this study indicated that MTA is not a suitable luting agent.

**Displacement**

A research article investigated displacement of MTA as an apical barrier material in teeth with open apexes (41), showing that 4-mm thickness of the apical barrier offers significantly more resistance to displacement than 1-mm thickness. This suggests that the thickness of MTA directly affects its displacement when used as an apical barrier.

**pH**

The pH value of MTA is 10.2 after mixing. This value rises to 12.5 at 3 hours (11). Comparing pH values of GMTA with WMTA, the latter material displays a significantly higher pH value 60 minutes after mixing (45, 46). MTA kept its high pH value throughout the course of a long-term study (63); the authors attributed the high pH value to the constant release of calcium from MTA and the formation of CH.

Comparing pH values at different periods of time, both WMTA and GMTA exhibit significantly higher pH values than 2 types of PC immediately after mixing (46). However, 30 minutes after mixing, no statistical difference can be found among the tested materials. At 60 minutes, GMTA has a significantly lower pH value than WMTA and both types of PC (46). Available data show that mixing MTA with water results in the formation of CH and a high pH environment.

**Radiopacity**

The mean radiopacity for MTA has been reported at 7.17 mm of an equivalent thickness of aluminum (11). This value is higher than that reported for Super EBA or IRM in a separate investigation (78). Another study compared the same materials and reported more radiopacity for Super EBA and IRM than MTA (79). The difference can be due to the use of different methods to evaluate the radiopacity of test materials. Comparing the radiopacity of WMTA with that of GMTA, 2 separate studies reported more radiopacity for WMTA (45, 46). Because a similar amount of bismuth oxide is used to produce radiopacity in both materials, the presence of other substances in WMTA might be the reason for this difference between the two.

**Particle Size**

On the basis of the manufacturer data sheet and MTA patent, a large portion of MTA’s components are similar to PC (21, 80). The handling characteristic of PC is dependent on its particle size and shape. Many investigations evaluated particle size and shape of MTA (14, 16, 19, 22, 36, 81). WMTA has finer particles than 2 types of PC (14). Dammaschke et al (14) attributed the mechanical and biocompatibility characteristics of WMTA to the homogeneity of its particles and the material’s surface morphology.

Many investigations compared the particle size and shape of WMTA, GMTA, and PC (16, 22, 81). The results showed that WMTA’s particle size is finer than GMTA’s (16, 22, 81), whereas PC has many similarities to GMTA (81). In addition, WMTA particles are more homogeneous than GMTA particles.

The particle size of MTA is reported in many articles. Lee et al (36) reported particle sizes ranging from 1–10 μm for GMTA powder, whereas Camilleri (19) reported that the WMTA powder has particles less than 1 to approximately 30 μm before hydration.

The physical properties of cement might be influenced by crystal size. Smaller particles increase surface contact with the mixing liquid and lead to greater early strength as well as ease of handling. A recent study reported that some particles of MTA are as small as 1.5 μm, which is smaller than the diameter of some dentinal tubules (81). The authors hypothesized that this might play an important role in the sealing ability of MTA after hydration and production of a hydraulic seal. This hypothesis might not be clinically relevant, because the dentinal tubules after root canal instrumentation or root-end cavity preparation are not open unless the operator removes the smear layer by acid-etching these surfaces.

A recent study showed adverse effects of ethylenediaminetraacetic acid (EDTA) on MTA hydration, microhardness, and cell adhesion (82). Successful treatment with MTA after placement of the material as a root-end filling has been reported in several animal and human studies without acid etching (83–93). Available information shows that WMTA has finer particles in comparison to GMTA. Particle sizes might affect the handling characteristics of these materials.

**Porosity**

Many studies have evaluated MTA porosity (54, 55). The amount of porosity in mixed cement is related to the amount of water added to make a cement paste, entrapment of air bubbles during the mixing procedure, or the environmental acidic pH value (35, 39, 42, 54, 55).

**Microhardness**

The microhardness of MTA can be influenced by several factors such as the pH value of the environment, the thickness of the material, the condensation pressure, the amount of entrapped air in the mixture, humidity, acid etching of the material, and temperature (14, 36, 39, 44, 49, 51, 54, 73, 82). An acidic environment has an adverse effect on the microhardness of both GMTA and WMTA (36, 54). An investigation evaluating the effect of environment on the hydration behavior of MTA determined that MTA in the hydration phase consists of needle-like and dominant cubic crystals (36). The needle-like crystals growing
between the cubic crystals were absent in the acidic environment. Decreased microhardness has been attributed to the absence of these needle-like crystals.

The microhardness of 2-mm and 5-mm thicknesses of GMTA and WMTA was investigated when the materials were used as an apical barrier. Regardless of the formulation of MTA or placement technique used, a 5-mm thickness is significantly harder than a 2-mm thickness (44).

An investigation compared the microhardness of WMTA with 2 types of PC. WMTA showed significantly more microhardness than both types of PC (49), which can be attributed to the different chemical and physical properties of the tested materials (14, 17, 81).

A recent study confirmed a trend of less microhardness after using more pressure during MTA condensation (51). Two separate investigations reported that EDTA and acid-etch procedure significantly reduce MTA microhardness (73, 82).

Present data show that less humidity, low pH values, the presence of a chelating agent, and more condensation pressure might adversely affect MTA microhardness.

Fracture Resistance

The fracture resistance of the tooth structure has been investigated in teeth with open apexes after using MTA as an apical barrier (94–98). One investigation disclosed that 5 weeks of exposure to MTA, CH, and sodium hypochlorite significantly decreases the resistance of bovine dentin to fracture (94). Investigations with WMTA or GMTA as an apical barrier and filling the rest of the canal with various materials showed that composite resins significantly increase resistance to fracture in comparison to roots that are filled with other materials (95, 98).

Another investigation examined the fracture resistance of immature sheep roots that were premedicated with CH for 30 days and demonstrated no significant effect on the fracture resistance of teeth after MTA placement (96). Another experiment on immature sheep roots used various time intervals from 2 weeks to 1 year for evaluating fracture resistance (97); results showed that after 1 year, the teeth filled with MTA had significantly more resistance to fracture compared with those filled with CH or the controls. With immunofluorescence imaging, investigators observed the presence of tissue inhibitor of metalloprotei- nase-2 (TIMP-2) only in the MTA samples. They attributed the resistance to fracture of MTA-filled teeth to the TIMP-2 effect in inhibiting collagen destruction (97). However, because the method of the study has been questioned, an increased TIMP-2 expression ratio in MTA-treated teeth is not yet confirmed (99).

Effect of Environment on the Physical Properties of MTA

Some clinicians used EDTA for smear layer removal before root canal obturation. This procedure has also been recommended before placing a root-end filling material during periradicular surgery (100). In one study, MTA samples were placed in normal saline, distilled water, or EDTA (82). The authors examined the samples under scanning electron microscopy (SEM) and energy-dispersive x-ray spectroscopy and evaluated cell adhesion to the MTA surface in a cell culture environment. The samples that were kept in EDTA showed poor cell adhesion; the authors concluded that poor cell adhesion to MTA’s surface in their investigation might be due to poor hydration of the material, which leads to a higher concentration of toxic ions such as aluminum, iron, and sulfur on the surface of EDTA-stored MTA.

Another study examined the effects of BioPure MTAD (a mixture of tetracycline, an acid, and a detergent) and EDTA on dissolution as well as the surface and ultrastructural characteristics of WMTA. Although the depth of etching of the EDTA and BioPure MTAD effect was not high, the latter material produced greater surface roughness and more calcium extraction from WMTA compared with EDTA (53).

There are some disagreements regarding the effects of the environment and pH on MTA’s physical properties (36, 54). In an investigation in which MTA was stored in distilled water at pH 7, both needle-like and cubic structures were seen (36). MTA stored in normal saline at pH 7 showed the same structure with larger-sized crystals and additional laminate formation on the outer surface of the cubic crystals. The microstructure of the specimens that were stored in pH 5 for 7 days demonstrated fewer cubic crystals and no needle-like crystals (36).

Another investigation showed no specific internal microstructure difference between the samples that were kept in acidic and normal pH values, except a trend for more porosity in the former environment (54). A recent investigation reported WMTA surface changes after an acid-etch procedure by phosphoric acid (73). Another recent investigation on the effect of an alkaline environment on the microhardness of WMTA has shown significantly lower microhardness in normal (7.4) and high (10.4) pH values in comparison to 8.4 and 9.4 pH values (101).

Previous investigations regarding the effect of acids on PC showed that various types of acids produce either retarding or accelerating effects on setting of the cement. Moreover, different concentrations of an acid might also have an accelerating or retarding effect on PC hydration and setting time. It should be noted that various types of PC (low-heated PC or normal PC) might react differently with various acids (102–104).

To produce a more clinically relevant environment, one investigation used fetal bovine serum as a storage medium for WMTA and GMTA after mixing (31). They examined MTA’s surface structure by SEM and reported differences in surface morphology and chemical composition distribution on the MTA surface when the material set in the presence of water or fetal bovine serum (31).

The surface morphology of dental materials that come in contact with tissues is important, at least for in vitro cell culture attachment, differentiation, and proliferation (105, 106). Unfortunately, most in vitro studies, such as the investigations on physical properties or leakage, do not allow MTA to set in synthetic tissue fluids such as PBS. On the basis of the available information, it appears that the presence of different solutions affects MTA’s physical properties.

Effect of the Method of Placement on MTA Physical Properties

The handling of MTA has been viewed as one of its shortcomings (45, 58). Various carriers have been used to enhance the ease of handling, including Teflon sleeves and pluggers specially designed for placement of MTA, specially designed carriers for dispersing MTA, and scooping out MTA from grooves in a plastic block (107) and a MesiJet gun-type syringe (108).

One investigation compared hand and ultrasonic placement of different thicknesses of MTA in polyethylene tubes (43). The authors used an endodontic plugger for hand placement, whereas ultrasonic placement was performed by activating an ultrasonic tip inside the tube. Radiographic and microscopic evaluation showed that the hand method resulted in better adaptation with fewer voids than the ultrasonic method for all thicknesses. In contrast, an investigation with the bacterial penetration model reported more resistance to bacterial penetration after using ultrasonic MTA placement (95). In corroborations with that study, a heavier sample was reported after filling the canals inside resin blocks by using hand condensation with indirect ultrasonic activation in comparison with hand condensation alone (109). Obtaining heavier
samples does not necessarily translate to better physical properties (51). The differences between the results of these studies can be attributed to the type of model (polyethylene tubes or human teeth), the method of evaluation, and the method of ultrasonic activation (direct or indirect).

An investigation compared the effect of condensation pressure on the compressive strength and microstructure of WMTA (51). Results revealed that surface hardness decreases when more pressure is applied during WMTA condensation. Greater condensation pressure results in fewer voids and microchannels. The authors hypothesized that with the application of greater condensation pressure, the material becomes more compact with fewer microchannels. They attributed reduced compressive strength and surface hardness to reduced water uptake that hinders complete MTA setting.

Current data show that the method of MTA insertion has great impact on its physical properties. In addition, using more condensation pressure does not necessarily improve MTA physical properties.

Chemical and Physical Properties of Other Types of MTA

Several modifications of MTA are marketed. The original formulation developed at Loma Linda University is manufactured by Dentsply International (ProRoot MTA and Tooth Colored MTA; Dentsply-Tulsa Dental, Tulsa-USA; Dentsply-Johnson City-USA).

Other types of MTA are Angelus (AMTA) from Brazil (white and gray: AGMTA, AWMTA; Angelus, Londrina, PR, Brazil), and Egeo (CPM) in white from Argentina (Egeo, Buenos Aires, Argentina) (110). Many other brands of experimental MTA have been developed and investigated, including MTA Bio, light-cured MTA, and an MTA root canal sealer named CPM sealer (Egeo) and MTA-Obtura (Angelus) (110–112). Unfortunately, most articles do not mention the type of MTA used; therefore, they are referred to as AMTA in this review.

The actual composition of GMTA is 75% PC, 5% calcium, and 20% bismuth oxide. AMTA is composed of 80% PC and 20% bismuth oxide (20, 113). One investigation compared the powder composition form of GMTA and AGMTA by using x-ray diffraction analysis and reported that GMTA contains a greater amount of bismuth oxide and magnesium phosphate (17). In contrast, the amount of calcium carbonate, calcium silicate, and barium zinc phosphate in AGMTA is greater than that in GMTA. The investigators also reported that more than 50% of the crystalline structures of GMTA are composed of bismuth oxide, in comparison with 40% for AGMTA.

Another investigation used energy dispersive spectroscopy to compare GMTA and AMTA, showing that the amount of calcium in AMTA is higher than in GMTA, whereas the amounts of carbon, oxygen, bismuth, and silica are higher in GMTA (20). AMTA showed the presence of aluminum and the absence of iron; conversely, GMTA exhibited the presence of iron and an absence of aluminum.

An investigation assessed pH value and calcium release for both types of GMTA and AMTA at 3–168 hours after mixing; results showed that AMTA produced a slightly higher pH value and calcium release than GMTA (113). In this study, the pH value found was lower than in other investigations (11, 45, 46). The authors attributed the lower pH to the presence of tricalcium silicate, tricalcium phosphate, and tricalcium aluminate, and other oxides.

Endo CPM sealer is also an Argentine form of MTA root canal sealer. The composition of this sealer is similar to MTA, except for the presence of calcium carbonate for reducing the pH of the material. Subcutaneous implantation of Endo CPM sealer and AMTA resulted initially in mild to moderate tissue reaction, followed by a similar response to control samples 30 days after implantation. Both Endo CPM sealer and AMTA produce mineralization in subcutaneous tissues.

Chemical and Physical Properties of New Compositions of MTA

Several investigations have been carried out to enhance the physical properties of MTA, its antimicrobial effects, and ease of handling (34, 38, 48, 52, 59, 60, 124). However, none of those compositions has been extensively investigated to fulfill all biocompatibility tests, chemical and physical properties, antibacterial activity and clinical investigations. It is important to note that changes in the physical
and/or chemical components of MTA can adversely affect other properties such as setting time or compressive strength of the material (38, 52).

Mixing anesthetic solution with MTA powder increases its setting time (38). In an investigation with MTA powder mixed with an anesthetic solution (2% Xylocaine with 1:100,000 epinephrine) as a perforation repair material (40), investigators placed wet or dry cotton pellets over MTA for 24–72 hours. The samples showed significantly higher push-out strength at 72 hours than at 24 hours. The authors reported no significant difference in MTA retention in the presence of dry or moist cotton pellets placed over the material after its insertion in perforation sites. The investigators in this study placed saline-moistened Gelfoam at the perforation site to simulate a clinical condition that would provide moisture to MTA in the samples that received dry cotton pellets. In contrast, another experiment showed significantly higher push-out strength with the application of moisture after placement of the MTA mixture (48).

An investigation compared the effect of blood contamination on WMTA mixed with sterile water, lidocaine, or saline when the material is used for repairing furcation perforations. Results revealed that none of the mixtures increased WMTA retention characteristics. Uncontaminated samples showed significantly more resistance to displacement (125).

One investigation added calcium chloride (CC) to WMTA to lower its setting time, which resulted in significantly higher pH values immediately after mixing (34). Furthermore, the authors reported more calcium ion release from WMTA and CC in comparison with unmodified WMTA in the first 24-hour period. It should be mentioned that although the calcium ion plays an important role in cell viability and the production of hard tissue, the amount of ion should be at a specific concentration because it might inhibit cell growth (68, 126). A recent investigation evaluated AWMTA setting time, solubility, disintegration, and pH when the material is mixed with CaCl₂. AWMTA showed an increase in weight, a higher pH value, and significantly lower setting time (127). A dye leakage investigation showed that the addition of CC to WMTA increases its sealing ability when used as a root-end filling material (128). Another investigation used sterile water, saline, 2% lidocaine, 3% NaOCl gel, GH gluconate gel, K-Y Jelly (Johnsson & Johnsson, New Brunswick, NJ), and 3% and 5% CC in combination with MTA powder (38). The NaOCl gel, K-Y Jelly, and 5% CC decreased the setting time to 20–25 minutes. However, set MTA mixed with sterile water showed significantly higher compressive strength than the rest of the tested materials, except for 2% lidocaine.

An investigation mixed WMTA and GMTA with anesthetic solution and evaluated their compressive strength (29). Results showed that the compressive strength of both tested materials decreased significantly when the materials were stored in PBS with an acidic pH value. WMTA had significantly stronger compressive strength in comparison with GMTA. Placing the samples in PBS resulted in significantly lower compressive strength at 28 days in comparison with the samples that were placed in PBS for 7 days.

Another research study used well-known PC accelerators such as CC, calcium nitrate (CN), and calcium formate (CF) to investigate their effects on the physical properties of GMTA and WMTA and PC (59). All 3 mixtures significantly accelerated the setting time of GMTA; however, only CC and CF showed the same effect on WMTA. Mixing MTA powder with CC had no significant effect on the pH values of both types of MTA, whereas CN significantly decreased the pH value of GMTA and PC. In contrast, using CF as an accelerator significantly increased the pH value of WMTA.

Ber et al (60) mixed MTA with 2% CC and methylcellose and showed similar compressive strength while setting time improved.

Three investigations have used 15% di-sodium hydrogen orthophosphate (Na₂HPO₄) as a liquid to decrease WMTA setting time. The results of these studies showed that addition of this accelerator has no significant adverse effect on diametral tension strength and phase composition, microstructure, solubility, or strength of WMTA in either normal or different acidic pH value environments (61, 62, 65).

Various studies showed that changing MTA’s composition might have an adverse effect on its physical and possibly its bioactive properties (10, 38, 52). Comprehensive investigations should be performed before introducing a new composition for clinical application.

**Portland Cement**

PC is an inexpensive material. Because of its chemical similarity to MTA (12, 18, 20, 129), some investigations suggested PC as a substitute material for MTA (16, 35, 37, 59, 60, 130–149). A number of investigations showed that both PC and MTA can have a similar composition, except for the bismuth oxide (12, 17, 18, 20, 120, 129). Camilleri et al (27) demonstrated that both PC and MTA are composed of tricalcium and dicalcium silicate, which on hydration produce calcium silicate hydrate gel and CH. At the same time, a recent investigation reported a lower content of calcium diaminate and calcium sulfate unhydrated in MTA than type 1 PC (23).

However, many differences are reported between the materials in terms of setting expansion, chemical composition, surface chemical composition, porosity, compressive strength, radiopacity, cation releases, and particle sizes (12, 14, 17, 19, 22, 26, 46, 48, 81). A recent study investigated the effect of adding bismuth oxide on PC physical properties (35), reporting that the porosity and compressive strength could be influenced by the addition of various weight percentages of bismuth oxide. It also reported an increase in porosity, solubility, and degradation of the material with increasing amounts of bismuth oxide. Moreover, because of the presence of more flaws in the composition of the above mixture, the amount of cracks in the set material also increased. An investigation confirmed the similarity of PC and MTA, except for the presence of potassium and lack of bismuth oxide (17). Another study showed lower amounts of aluminum and sulfur in WMTA compared with WPC (19).

A recent investigation reported that some types of MTA and WPC with or without CC show presence of precipitation and formation of an interfacial layer between the material and dentin, which could potentially affect the sealing ability of these materials (71).

The biocompatibility of some types of PCs is evaluated in several studies (15, 135, 136, 140, 144, 148). Three separate studies using endothelial, I929 fibroblast, and human osteosarcoma cell cultures compared PC and MTA (15,136, 140). These studies revealed no significant differences between the tested materials. MTA, unmodified PC, and modified PC samples with added 10% and 15% CC for acceleration of setting time showed the same effect on SaSO₂ osteosarcoma cell morphology, characteristics, and attachment to these cells (135). However, a study comparing MTA and PC containing varying ratios of bismuth oxide on immortalized human periodontal ligament cells showed that PC without the addition of bismuth oxide has the same level of cell viability as MTA at 12 and 24 hours. The addition of bismuth oxide to PC powder at all ratios in this study significantly lowered cell viability during early evaluation time (148). Asgary et al (12) determined that the crystalline particles in WMTA were smaller than those present in WPC. A study comparing WPC and WMTA revealed lower amounts of the aluminate phase in the latter material (19). These investigators proposed that WMTA is manufactured in the laboratory instead of clinkering, which is the method of PC production. SEM image evaluation showed a large area of CH in WPC that is not observed in WMTA (12). The efficacy of PC for pulp capping is comparable to
that of MTA (134). A recent review concluded that both MTA and PC exhibit no genotoxicity (5).

There are several reasons that PC cannot be used in clinical applications as a substitute for MTA:

1. PC is manufactured widely all around the world, and it is impossible to control the quality, composition, and biocompatibility of these materials (150).

2. WMTA contains fewer heavy metals such as copper, manganese, and strontium, which are known to be toxic (14). One of the major concerns about using PC is that the amount of lead and arsenic in its composition. Duarte et al (115) showed that the amount of arsenic release is not very high in WMTA, GMTA, and 1 type of PC. However, a recent study compared the amount of arsenic in GMTA, ordinary PC (OPC), and WPC showed that OPC contains more than 6 times the amount of arsenic compared with GMTA (110). It is impractical to evaluate the amount of these elements in all types of PC. Because of the high solubility of some types of PC and the release of toxic elements into the surrounding tissues (49), its long-term safety is questioned (150).

3. The higher solubility of some types of PC is also a matter of concern. It is possible that PC might degrade after clinical application and jeopardize the seal of the material (49).

4. The compressive strength of some types of OPC and WPC is significantly lower than GMTA and GM 25 days after hydration (46). Attaining adequate compressive strength is important for some of the clinical applications of MTA such as repairing perforations and pulp capping. These procedures require materials with adequate compressive strength to be stable against occlusal pressure.

5. Excessive expansion that might result in a cracked root is an undesirable property when a material is used as a root-end filling substance (46). The setting expansion of PC is a matter of controversy in the literature. One investigation reported that both types of WPC and OPC show greater expansion than GMTA and WMTA (46). In contrast, another experiment showed that the setting expansion of PC is less than GMTA and more than WMTA (37). This might be attributed to the differences of chemical composition among various types of PC (150).

6. Carbonation results in a drop in tensile strength and resiliency of PC. This process occurs when the amount of carbon dioxide increases in inflamed tissues. The carbon dioxide readily reacts with any available water to form carbonic acid, which reacts with the cement, converting it into calcium hydrogen carbonate (151). Low tensile strength and resiliency of the material might cause it to crack and buckle under high stress, instead of deforming. This process is important in some clinical applications of MTA such as perforation repair or pulp capping.

7. The amount of calcium release in WMTA is reported to be much more than that released by WPC, and the mechanism of hydration is different in these materials (26). It is important to note that complete healing occurs only when the proper amounts of elements and signal molecules are present in tissues after injury. A lack of an element or an imbalance between elements might prevent complete regeneration.

8. MTA is manufactured in laboratories as a medical material under close supervision in terms of its composition and prevention of contamination (150). It is approved by the U.S. Food and Drug Administration for use in human beings (17).

In a recent review article Steffen and van Waes (152) highlighted the need for more investigations on PC as a medical material. The authors explained their concern regarding the exact type of PC, which is not mentioned in some investigations. They believe that if PC is intended for use in clinical applications, the material needs to be sterile, the amount of toxic heavy metal ions of the material should be detected, and the material particle size should be similar and more unique.

Despite some similarities between PC and MTA, it is not safe to use PC, which has not been formulated for human use, in place of a bioactive medical material such as MTA.

### Antibacterial Effects of MTA

Several studies examined the antibacterial effects of MTA, its variants, and its new composition on various organisms.

### Antibacterial and Antifungal Properties of MTA

The antibacterial and antifungal properties of MTA have been extensively evaluated, with conflicting reports (52, 124, 133, 153–164). Several investigations reported that MTA has limited antimicrobial effect against some microorganisms (133, 153, 155, 161). An investigation (153) on facultative and strict anaerobic bacteria showed that MTA has an antibacterial effect on some facultative bacteria and no effect on any species of strict anaerobes. In contrast, Super EBA and ZOE pastes exhibit some antibacterial effect on both types of tested bacteria (153). An antimicrobial study on PC and GMTA against Staphylococcus aureus, Enterococcus faecalis, Pseudomonas aeruginosa, Bacillus subtilis, Candida albicans, a wild fungus, and a mixture of these bacterial and fungal species, both materials exhibited diffusion in agar without inhibition of microbial growth (153). Some investigations showed that GMTA (154, 159, 162) and WMTA (159) have an antibacterial effect. In contrast, others showed that GMTA has limited or no antifungal effect (133, 155, 161). One experiment showed that freshly mixed and 24-hour set GMTA have an antifungal effect on C. albicans (154). The antifungal effect of MTA might be due to its high pH or to substances that are released from MTA into the media. In contrast, a study comparing the effect of MTA and PC on C. albicans, S. aureus, and Escherichia coli showed no antimicrobial effect for either of the tested materials (156). Another investigation reported antimicrobial activity of GMTA, WPC, and OPC on Micrococcus luteus, S. aureus, E. coli, P. aeruginosa, C. albicans, and Enterococcus faecalis (162).

Al-Hezaimi et al (156) evaluated the antifungal effect of WMTA on C. albicans and revealed that the concentration of MTA is a significant factor in the antifungal effect of this material. Plates containing a WMTA concentration of less than 25 mg/mL showed no antifungal effect. In contrast, plates containing a concentration of 25 mg/mL showed antifungal activity at 1 and 24 hours, whereas a concentration of 50 mg/mL of WMTA was effective against C. albicans during the whole study time. Another investigation compared the antifungal effect of GMTA and WMTA in different concentrations on C. albicans (157). Results confirmed a previous study by the same authors for WMTA (156). However, GMTA in concentrations lower than 25 mg/mL was significantly more effective against C. albicans than WMTA (157). The results for WMTA and GMTA in concentrations of 25 mg/mL and 50 mg/mL were similar.

Comparing the antibacterial effects of different concentrations of GMTA and WMTA against E. faecalis and S. sanguis shows the former material requiring lower concentrations to produce the same antibacterial effects against each of the bacteria tested (158). Comparing both species of bacteria, E. faecalis requires a higher MTA concentration for growth inhibition. However, a recent investigation reported similar antibacterial properties for both types of WMTA and GMTA (163).

An investigation on the antibacterial effect of several freshly mixed and set root-end filling materials (IRM, GMTA, amalgam, Super-Bond C&B, Geristore, Dytract, Clearfil APX composite with SE Bond and
Antibacterial Properties of Other Types of MTA

An experiment compared the antimicrobial properties of Sealapex, Fill Canal, AMTA, PC, and EndoRez on E. faecalis, E. coli, M. luteus, S. aureus, Staphylococcus epidermidis, P. aeruginosa, and C. albicans (141). Results indicated that except for E. coli, AMTA and PC were effective against microorganisms. Another study comparing GMTA, AGMTA, AWMTA, WPC, and GPC showed that all of the tested materials had antimicrobial activity against the following microorganisms: M. luteus, S. aureus, E. coli, P. aeruginosa, c. albicans, and E. faecalis (162). These studies showed that other types of MTA have some antibacterial and antifungal properties. Recent investigations have reported similar suitable antibacterial activity in WMTA, AWMTA (168), Endo CPM sealer, and WAMAT (169).

Antibacterial Properties of New Compositions of MTA

Some investigations replaced distilled water with other liquids to mix with MTA powder. An investigation evaluated the antibacterial and antifungal activities of mixtures of WMTA with 0.12% CHX and sterile water against Actinomyces odontolyticus, Fusobacterium nucleatum, Streptococcus sanguis, E. faecalis, E. coli, S. aureus, P. aeruginosa, and C. albicans (124). Regardless of the type of mixing agent, all WMTA samples inhibited microbial growth. A mixture of WMTA and CHX showed significantly more antimicrobial activity than WMTA and water, with the exception of its effect on F. nucleatum and S. sanguis. Another study mixed 2% CHX with MTA powders and reported a significant increase in the antibacterial effect of WMTA and GMTA against E. faecalis (52). It should be noted that adding CHX to WMTA can cause cell apoptosis (170) and a decrease in the compressive strength of MTA (52), although biocompatibility of MTA mixed with CHX was reported in a subcutaneous investigation (171). The liquid or gel type of CHX has different effects on MTA setting. Kogan et al (38) mixed MTA powder with CHX gel to measure the compressive strength of this mixture. Because this mixture had not set 7 days after mixing, they could not measure its compressive strength. Holt et al (52) used the liquid form of CHX and mixed it with MTA powder, reporting that most of the samples were set adequately after 72 hours and were ready to be examined for their compressive strength.

On the basis of these results, it appears that enhancing selective properties of MTA, such as its antibacterial property, by adding various liquids might adversely affect other properties of the material. Comprehensive investigations for all properties of the new compositions of MTA (physical properties, sealing ability, biocompatibility, and cytotoxic production) are needed before recommending them for clinical applications.

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