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## Mineral trioxide aggregate: A review

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**Abstract**--The purpose of this two-part series is to review the composition, properties, products, and clinical aspects of mineral trioxide aggregate (MTA) materials. search engines to include relevant scientific citations from the peer-reviewed journals published in English. MTA is a refined form of the parent compound, Portland cement (PC). It demonstrates a strong biocompatible nature owing to the high pH and its ability to form hydroxyapatite. MTA materials provide a better seal than traditional endodontic materials as observed in dye leakage, fluid filtration, protein leakage, and bacterial penetration leakage studies, and it has been recognized as a bioactive material. Currently a variety of MTA commercial products are available, including Proroot® Gray MTA and White MTA both from DENTSPLY Tulsa Dental Specialties, and MTA Angelus. Although these materials are indicated for various dental uses. This first of this series highlights and discusses the composition, physical, and/or chemical properties of MTA. A subsequent article will offer an overview of the material aspect (commercial products) and clinical considerations for MTA materials.

**Keywords**--biocompatible dental material, mineral trioxide aggregate, MTA.

## **Introduction**

Endodontic failures may occur as a result of leakage of irritants into the periapical tissues.<sup>1</sup> Therefore, an ideal orthograde and/or retrograde filling material should seal the pathways of communication between the root canal system and its surrounding tissues; thus, this material should be biocompatible and dimensionally stable. This led to the development of mineral trioxide aggregate (MTA) materials possessing these ideal characteristics. The initial literature regarding the material was published in 1993 by Lee et al. Following this, the material received Food and Drug Administration (FDA) approval in 1998. Initially recommended as a root-end filling material, it is currently being used for pulp capping, pulpotomy, apexogenesis and apexification, apical barrier formation, repair of root perforations and resorptive defects, and as a root canal and root-end filling material. It is mainly composed of tricalcium silicate, tricalcium aluminate, and bismuth oxide, and consists of fine hydrophilic particles that harden in the presence of dampness or blood. It has a better sealing capacity and biocompatibility compared to other classic materials such as amalgam, cements, super ethoxy benzoic acid (EBA), and interim restorative material (IRM). This review highlights the compositional characteristics and featured properties of MTA materials.<sup>2</sup>

## **Composition**

MTA is an ash-colored powder made up of fine hydrophilic particles. Available as Gray MTA (GMTA) and White MTA (WMTA), both formulae basically are 75% Portland cement, 20% bismuth oxide, and 5% gypsum (Ca) by weight. Thus, MTA is a mixture of a refined Portland cement and bismuth oxide (17% to 18%) with trace amounts of SiO<sub>2</sub>, CaO MgO, K<sub>2</sub>SO<sub>4</sub>, and Na<sub>2</sub>SO<sub>4</sub>. Bismuth oxide is added to make the material radiopaque. Bismuth affects calcium hydroxide precipitation after MTA hydration; and under acidic conditions (inflammation), bismuth oxide can be released in the environment decreasing MTA's biocompatibility as it inhibits cell proliferation. Gray MTA (GMTA) principally consists of tricalcium silicate, dicalcium silicate, tricalcium oxide, tricalcium aluminate, tetracalcium aluminoferrite, calcium sulphate, silicate oxide, and bismuth oxide, with a predominance of calcium and phosphorus ions (as per earlier reports).<sup>3</sup> However, recent investigations using electron probe microanalysis suggested that phosphorus levels in MTA products are very low. White MTA (WMTA) basically lacks the tetracalcium aluminoferrite component with a lesser quantity/content of iron, aluminium, and magnesium oxides. Another commercially available MTA material is MTA-Angelus, which is 80% Portland cement and 20% bismuth oxide, and is more radiopaque than GMTA.<sup>3</sup>

## **Properties**

Due to its sealing properties, biocompatibility, and hydrophilic nature, MTA is considered the best choice for a retrofilling material. Its handling characteristics are considered to be excellent. In particular, the material can be used in the presence of blood. Biocompatibility studies in general considered both GMTA and WMTA as biocompatible. No genetic damage, genetic mutation, chromosomal breakage, altered DNA repair capacity, or cellular transformation was observed

with MTA. MTA has shown to possess neither mutagenic (Ames mutagenicity assay, *Salmonella typhimurium*) nor genotoxic effects (single cell gel/comet assay).<sup>8</sup> Neither freshly mixed nor set MTA displayed neurotoxicity. It was found to be less cytotoxic than amalgam, super EBA, and IRM, with set MTA being less cytotoxic than fresh MTA.<sup>9</sup> Enhanced attachment and proliferation of periodontal ligament and gingival fibroblasts were observed on the set-surfaces of MTA. Similarly, cell cultures studies (animal and human) using human alveolar bone cells, mouse preosteoblasts, osteoblasts, dentinoblasts, and mouse cementoblasts have shown good survival, proliferation, and attachment, with a faster and better growth of cells on the MTA surface. MTA has also shown to have a better stimulating effect on human dental pulp cells than a commercial calcium hydroxide preparation. It was proposed that cellular proliferation is via intra- and extracellular  $Ca^{2+}$  and Erk-dependent pathways, and cell survival is via the PI3K/Akt signaling pathway. Animal cells (rat bone marrow cells, mouse preosteoblasts) and human cells (gingival fibroblasts, periodontal ligament fibroblasts, alveolar bone cells) exposed to MTA have been shown to express alkaline phosphatase, bone sialoprotein, periostin, and osteocalcin, along with the formation of extensive collagenous matrix. Addition of enamel matrix derivative to MTA has been shown to improve human dental pulp cell differentiation, alkaline phosphatase activity, and mineralization. Although addition of chlorhexidine improved the antibacterial properties of MTA, it adversely affected the biocompatibility of the material.<sup>4</sup>

Animal and human studies have shown minimal or no inflammation to bone and connective tissue following implantation of MTA. When used (in a canine model) for root-end restoration or for the repair of lateral/furcation perforation, MTA has shown favorable healing characteristics, such as lack of inflammation, no ankylosis, cellular cementum formation (overgrowth), and PDL regeneration between the cementum and alveolar bone. MTA stimulates cytokine release and interleukin production, which may actively promote hard-tissue formation.<sup>9</sup> Shabahang et al observed that MTA induced hard-tissue formation more often than osteogenic protein-1 and  $Ca(OH)_2$ .<sup>5</sup> Intra-osseous implantation of MTA showed a relatively mild-to-minor inflammatory response, which is more favorable compared to amalgam, super EBA, and IRM.

Some studies considered that the biocompatibility of MTA is attributable to the release of hydroxyl ions and formation of calcium hydroxide during the hydration process. Other reports had observed the formation of a white interfacial material (precipitates) between GMTA and tooth structure within 1 to 2 hours when exposed to physiologic fluids (phosphate-buffered physiologic solution) in vivo or with simulated body fluids in vitro. SEM and x-ray diffraction (XRD) analysis of these precipitates revealed the presence of chemically and structurally similar hydroxyapatite (HA)-like structure with a chemical composition of oxygen, calcium, and phosphorus, along with trace amounts of bismuth, silicon, and aluminum. However, the calcium-to-phosphorus ratios reportedly differed from that of natural hydroxyapatite. This HA-like structure can release calcium and phosphorus continuously, promoting the regeneration and remineralization of hard tissues and increasing the sealing ability of MTA. The HA-layer also creates a chemical bond between MTA and the dentinal walls.<sup>6</sup> The particle size and dimensional shape of MTA can also occlude dentinal tubules, which might harbor

microorganisms. GMTA has a greater amount of HA-crystal formation than WMTA with the presence of lower levels of silica and phosphorus in GMTA crystals and more calcium ions in WMTA crystals. Thus, release of hydroxyl ions, a sustained high pH for extended periods, modulation of cytokine production, formation of calcium hydroxide, and a mineralized interstitial layer (HA) may be responsible for the excellent biocompatibility and biological activity of the material.<sup>7</sup>

### **Antimicrobial Properties**

In vitro studies have shown antibacterial activity of MTA against *M. luteus*, *S. aureus*, *E. coli*, *P. aeruginosa*, *E. faecalis*, and *S. sanguis*. A study evaluated the antimicrobial property of MTA, amalgam, and super EBA against nine strict anaerobes. MTA was found to have an antibacterial effect on five of the nine facultative bacteria, but no effect on any of the strict anaerobes. Thus, the use of MTA as an antibacterial agent may not be very beneficial in endodontic cases. The use of 2% CHX and 0.12% CHX in combination with MTA has been reported to significantly increase the antibacterial effect of both types of MTA.

Al-Nahazan and Al-Judai evaluated the antifungal activity of both freshly mixed and 24-hour-set MTA using a tube dilution test. It was observed that both types were effective against *Candida albicans*. The antifungal effect of MTA might be due to its high pH or to substances that are released from MTA and is dependent on the concentration of MTA; a concentration of 25 mg/mL to 50 mg/mL is required to show an antifungal effect<sup>8</sup>

### **Regenerative Potential and Biological Activity**

MTA has the capacity to induce bone, dentin, and cementum formation and regeneration of periapical tissues (periodontal ligament and cementum). MTA provides a good biological seal and can act as a scaffold for the formation and/or regeneration of hard tissue (periapical). It is an osteoconductive, osteoinductive, and cementogenic (cementoconductive and cementoinductive) agent.<sup>9</sup> MTA stimulates immune cells to release lymphokines and bone coupling factors required for the repair and regeneration of cementum and healing of osseous periapical defects.<sup>64,73</sup> MTA can also stimulate periodontal ligament fibroblasts to display osteogenic phenotype and produce osteonectin, osteopontin, and osteonidogen.<sup>14</sup> Cell culture studies have shown an up-regulation of various cytokines, biological markers, and interleukines, like IL-1 $\alpha$ , IL-1 $\beta$ , IL-4, IL-6, osteocalcin, alkaline phosphatase, bone sialoprotein, osteopontin, BMP-2, PGE2, and cyclooxygenase-2, by MTA.<sup>9</sup> Shabahang et al concluded that MTA can induce the formation of apical hard tissue with significantly greater consistency than osteogenic protein-1 and calcium hydroxide.<sup>65</sup> The biologic activity of MTA is attributed to the high pH level associated with formation of calcium hydroxide. Current studies indicated that the biological activity of MTA is attributed to the formation of hydroxyapatite-like precipitate on its surface. GMTA was observed to produce twice as much hydroxyapatite crystals as WMTA, suggesting different levels of bioactivity of the two materials.<sup>9</sup>

### **Pulp Capping With MTA**

Among the materials available today for direct pulp capping, MTA is the material of choice. Pulp capping is indicated for teeth with immature apices when the dental pulp is exposed and there are no signs of irreversible pulpitis. In such cases, the maintenance of pulp vitality is extremely important, and MTA is preferred to calcium hydroxide. Recent studies have shown that MTA stimulates dentin bridge formation adjacent to the dental pulp; dentinogenesis of MTA can be due to its sealing ability, biocompatibility, and alkalinity. Faraco and Holland<sup>16</sup> demonstrated that in teeth treated with MTA, all bridges were morphologically tubular, and in some specimens the presence of a slight layer of necrotic pulp tissue was observed in the superficial portion of these bridges. This suggested that the material, similarly to calcium hydroxide, initially causes necrosis by coagulation in contact with pulp connective tissue. This reaction may occur because of the product's high alkalinity, as the pH is 10.2 during manipulation and 12.5 after 3 hours. Holland et al<sup>6</sup> demonstrated the presence of calcite crystals in contact with MTA implanted in rat subcutaneous tissue. Those calcite crystals attract fibronectin, which is responsible for cellular adhesion and differentiation. Therefore, it is believed that the MTA mechanism of action is similar to that of calcium hydroxide, but in addition, MTA provides a superior seal against bacteria<sup>10</sup>.

For those reasons, MTA is preferred to calcium hydroxide. Nevertheless, MTA has only recently been introduced, and no long-term studies on its efficacy have been published. Therefore, it is necessary to recall treated patients on a regular basis to determine if treatment has been successful or if root canal therapy is needed.<sup>10</sup>

### **Perforation Repair with MTA**

Recently, the prognosis of teeth with a perforation has improved with the use of the operating microscope and the introduction of MTA. When clinicians want to predictably repair a perforation, they face two challenges:<sup>14</sup> (1) to establish hemostasis, and (2) to select a restorative material that is easy to use, seals well, does not resorb, and is biocompatible, supporting new tissue formation. Generally, a barrier is created to achieve a dry field and prevent the extrusion of the restorative material. On the other hand, all of the restorative materials currently used (amalgam, Super EBA, IRM, composite resins) require a dry field and do not promote new tissue formation. Operative Sequence for Treatment of a Perforation The operative sequence to treat a perforation of the root or of the floor of the pulp chamber is as follows: <sup>11</sup>

- First visit
  - (1) isolation of the operative field with a rubber dam
  - (2) cleansing of the perforation site
  - (3) in case of bacterial contamination, application of calcium hydroxide for 1 week. If this step is performed, the patient goes home, then returns to resume steps 4 through 7 at the second visit.
  - (4) application of 2 to 3 mm of MTA
  - (5) radiograph to check the correct positioning of the material

- (6) application of a small, wet cotton pellet in contact with MTA
- (7) temporary cement

- Second visit

- (1) after 24 hours, removal of temporary cement to check if MTA is set
- (2) completion of therapy.<sup>11</sup>

### **Immature Pulpless Teeth**

Despite the demonstrated clinical success of calcium hydroxide apexification, there are some disadvantages of this technique. The apical closure is unpredictable. The time necessary to achieve the final result is variable, and for adults, an acceptable result may never be achieved. The treatment time necessary for induced apical closure in pulpless teeth in humans has not been established. This therapy requires multiple appointments for either reapplication of calcium hydroxide or to check its presence inside the root canal, and the time interval between visits is at least 3 months. This may lead to loss of the coronal seal with consequent recontamination and exposure of the healing tissues to bacteria. In these cases, an acute exacerbation and delayed healing response may occur.<sup>12</sup>

For these reasons, many clinicians advocated obturation of teeth with open apices without inducing a natural apical barrier. In fact, the concept of obturating teeth with immature apices without first inducing a natural apical barrier is not new; several investigators have likewise indicated that success is attainable with this approach, which does not require repeated applications of calcium hydroxide.<sup>13</sup>

### **Root End Filling**

Due to its sealing properties, biocompatibility, and hydrophilic nature, MTA is considered the best choice for a retrofilling material. Its handling characteristics are considered to be excellent. In particular, the material can be used in the presence of blood.<sup>14</sup>

### **Operative Sequence for Root End Filling**

After the preparation of the root end has been completed with ultrasonic instruments, the MTA is placed with a carrier and gently compacted with a small plugger. The best instruments for this purpose include the use of amalgam carriers like the Messing gun (R. Chige, Inc), or the new Dovgan MTA carriers, which are straight, bendable, or prebent (Quality Aspirators). The material should be kept relatively dry so it does not readily flow, yet moist enough to allow manipulation and a workable consistency. If the assistant touches the plugger with an ultrasonic tip during the placement process, voids are eliminated, the density of the fill is better, and radiopacity is increased.<sup>15</sup>

The working time of MTA is approximately 2 hours, and this eliminates problems related to rapid setting that accompanies other materials. Finishing of MTA is accomplished by simply carving away excess material with a spoon excavator to

the level of the resected root end. The moisture necessary to achieve the final set is from the blood, which fills the crypt after surgery<sup>16</sup> The mineral trioxide aggregate (MTA) is a hydrophilic and biocompatible endodontic cement, capable of stimulating healing and osteogenesis.<sup>16</sup> It consists of a powder of fine trioxides (tricalcium oxide, silicon oxide, bismuth oxide) and other hydrophilic particles (tricalcium silicate, tricalcium aluminate, responsible for the chemical and physical properties of this aggregate), which hardens in the presence of humidity. The hydration of the powder results in the formation of a colloidal gel with pH 12.5, which solidifies in a structure in about 3 to 4 hours.<sup>17</sup>

In the past 10 years, the MTA found its application in the field of dentistry with specific fit within the conservative and endodontic treatments. A dental trauma is an event that cannot be predicted and usually it is not easy for the clinicians to manage it. The dentist should therefore be prepared to intervene in patient who has suffered a dental trauma. Early intervention is often crucial to improve the prognosis of the trauma itself. In the presence of a coronal fracture with dentine exposure, the primary objective should be to seal dentinal tubules. Especially in a young patient, the size and number of dentinal tubules are large: even a small amount of exposed dentin therefore allows a large number of plaque bacteria and their metabolites to move to the underlying pulp and cause inflammation. An occurrence of this type could, sometimes in short time, lead to necrosis. When the dental trauma has caused a pulp exposure, the emergency intervention consists with the management of the exposed pulp. One of the treatments, besides the endodontic treatment, is direct capping or partial pulpotomy. Partial pulpotomy could be performed using MTA. The MTA could be applied as cement for its high compatibility, which has a mechanism similar to calcium hydroxide ( $\text{Ca(OH)}_2$ ) (extremely basic) and therefore a powerful antibacterial.<sup>18</sup>

Unlike  $\text{Ca(OH)}_2$ , however, the MTA hardens, reaching a good consistency; it is, therefore, extremely suitable for any restoration. Fast hardening therefore allows partial pulpotomies performed with MTA to be restored in a definitive manner.<sup>19</sup> Pulp consisting of a cellular component, vessels and nerves; this tissue is called mature mucosal connective tissue. Endodontic therapy is used if a tooth carious or traumatic injury has caused an irreversible alteration of the pulp tissue and its necrosis. It is also possible to use this method if the dental element is to be involved in prosthetic rehabilitations, which due to the considerable reduction of the dental tissue, it would determine, with high probability, an irreversible pulp alteration<sup>19</sup>. During endodontic treatment, blood contamination should be absolutely avoided, and the roots canal system needs to be dry, to obtain a successful root canal filling. During direct pulp capping or perforation sealing, it is fundamental to control the bleeding and obtain a dry field too. The mechanism of action of the MTA is related with the clinical features of the human oral cavity. MTA, when placed in direct contact with human tissues, is able to release calcium ions for cell proliferation. Moreover, it creates an antibacterial environment by its alkaline pH, regulating the cytokine production. Therefore, it favors the migration and differentiation of hard tissue producing cells forming hydroxyapatite on MTA surface and providing a biological seal Finally, during a surgical endodontic procedure, the retrograde cavity should be completely dry. This cement differs from all other materials currently in existence, thanks to its biocompatibility, its antibacterial properties, its marginal adaptation, and its sealing capacities, and

finally, thanks to its hydrophilic nature. It is important to understand the functioning of this biomaterial, its behavior with contact with other materials used in dentistry, and above all, over time or from a clinical and radiographic point of view. Investigating these topics requires a research into the international literature, which also includes the use of cutting-edge technologies for examination.<sup>20</sup>

## Conclusion

Mineral Trioxide Aggregate (MTA) is a relatively new material that has become the material of choice for certain endodontic applications. This article has described those applications, including the operative sequence for specific procedures.

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