Mineral trioxide aggregate: present and future developments

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Portland cement is used in the building industry to make concrete. It is hydraulic and thus it develops its properties well in the presence of moisture. The oral environment is inherently wet, however, all dental materials need a dry field for optimal performance. A mixture of Portland cement and bismuth oxide was developed and marketed as mineral trioxide aggregate (MTA). The first formulation was gray in color followed by a white version and eventually by various similar materials, which are all composed of a tricalcium silicate-based cement and radiopacifier. The MTA was originally suggested for particular clinical uses, such as root-end filling and perforation repair, where maintenance of a dry field is difficult. The suggested uses were extended to apexification and dressing over pulpotomies, pulp capping and also as a sealer cement. The multipurpose use of MTA necessitated the development of improved formulations where material additives were included to the original cement/radiopacifier formulation. These additives supposedly enhance the material’s properties and improve its function. Furthermore, the original Portland cement formulation was replaced with tricalcium silicate to avoid the inclusion of an aluminum phase and eliminate the inclusion of trace elements. The bismuth oxide was also replaced with alternative radiopacifiers. The multifaceted use of MTA allows the material to come into contact with different oral environmental conditions, including blood, saliva, tissue fluids, dental restorative materials, tooth structure and even air. These different conditions affect the properties and setting of the material. Future developments should further investigate the material’s interactions and strive to create materials which are suited to a specific use.

Received 6 March 2015; accepted 22 March 2015.

Introduction

Mineral trioxide aggregate is a mixture of Portland cement and bismuth oxide. The physical properties of most dental materials deteriorate when in contact with moisture. Portland cement, used in the construction industry, has hydraulic properties and was therefore introduced as a dental material in order to counteract this problem. The bismuth oxide was added to Portland cement to enhance the material’s radiopacity (1).

Portland cement is manufactured from limestone and shale. These raw materials are burnt in a kiln to produce tricalcium silicate, dicalcium silicate, and tricalcium aluminate. Other trace oxides, namely magnesium oxide and phosphorous pentoxide, are commonly found with calcium carbonate mineral deposits. Other accessory oxides in Portland cement are sodium oxide, potassium oxide, titanium oxide, manganese oxide, nickel oxide, barium oxide, chromium oxide and fluoride. These are usually in quantities lower than 0.5%, and many lower than 100 ppm. The sodium oxide, potassium oxide, sulfates (from the raw materials or fuel) and fluoride act as fluxing agents, reducing the firing temperature for Portland cement and therefore reducing the cost of the cement production. Traces of arsenic, lead and chromium are also present in the material (2). The clinker is interground with calcium sulfate thus forming Portland cement.

The first reported use of Portland cement in dental literature dates to 1878, when Dr. Witte in
Germany published a case report on using Portland cement to fill root canals (3). Portland cement was invented in 1824 by Joseph Aspdin in England. Over a century later Dr. Mahmoud Torabinejad at Loma Linda University and his co-inventor Dean White obtained two US patents (4,5) for a Portland cement-based endodontic material, which became known as Mineral Trioxide Aggregate (MTA).

The original MTA was dark gray in color and was commercialized as ProRoot® MTA (Dentsply, Tulsa Dental, Johnson City, TN, USA) in 1998. In 2002, the “tooth-colored ProRoot MTA” was introduced and later patented (6). The gray and white versions of ProRoot MTA have similar compositions, but the tooth-colored ProRoot MTA uses white Portland cement, which contains less iron. Iron is part of the calcium alumino-ferrite phase in Portland cement. During manufacture the ferrite phase functions as a fluxing material, thus keeping the temperatures during clinkering low, and results in a more efficient manufacturing process. Clinkering of white cement requires the addition of a fluxing agent. Usually alumino-silicate is added to the raw feed and allows material clinkering at low temperatures. Regardless of the presence of alumino-silicate in the white cement, the biocompatibility of the gray and white versions has not been altered (7). However, in contrast other researchers have reported that white MTA exhibited less biocompatibility when tested using osteosarcoma cells than the gray version (8).

Composition of the unhydrated material

The original MTA patents were registered in 1993 and 1995 (4,5) and stated, ‘MTA consists of 50-75% (wt) calcium oxide and 15-25% silicon dioxide. These two components together comprise 70-95% of the cement. When these raw materials are blended, they produce tricalcium silicate, dicalcium silicate, tricalcium aluminate, and tetracalcium aluminoferrite’. They also stated, ‘MTA is Type I Portland cement (American Society for Testing Materials), with a fineness (Blaine number) in the range of 4500-4600 cm²/g. A radiopacifier (bismuth oxide) is added to the cement for dental radiological diagnosis’.

Scanning electron microscopy (SEM) of polished sections of unhydrated MTA embedded in resin shows distinctive cement grains and bismuth oxide particles, which are separated from one another. This feature indicates that the material is composed of a simple mixture of the two components (Fig. 1). The elemental composition of MTA as shown by energy dispersive spectroscopy (EDS) indicates the presence of calcium, silicon and oxygen with minor peaks for aluminum, potassium, magnesium and bismuth.

The phases present in MTA are determined by X-ray diffraction analysis. Using this method of analysis, unhydrated MTA exhibits peaks for tricalcium silicate, dicalcium silicate and bismuth oxide. Using a copper Kα tube, each phase has a particular pattern, as shown in Figure 2, which can be subsequently searched and matched with data derived from the International Centre of Diffraction. MTA contains other phases such as dicalcium silicate and tricalcium aluminate in minimal quantities. X-ray diffraction analysis of MTA eliminates the myth that MTA is composed mainly of oxides. Thus, the term “trioxide aggregate” is essentially a misnomer. In the first publication on MTA composition, calcium phosphate was stated to be the main constituent of MTA (9). In the publication, MTA was purportedly reported to be composed of “calcium oxide and calcium phosphate. Further analysis demonstrated that the former appeared as discrete crystals and the latter as an amorphous structure with no apparent crystal growth but a granular appearance. The mean value of the prisms was 87% calcium and 2.47% silica, the remainder being oxygen. In areas of amorphous structure, there seemed to be 33% calcium, 49%
phosphate, 2% carbon, 3% chloride, and 6% silica”. This was discredited in a later publication where it was shown that the phosphate phase was due to material contamination from processing for SEM evaluation (10).

**Setting reaction**

Mineral trioxide aggregate hydrates when it comes into contact with water and undergoes two main reactions. The tricalcium silicate and dicalcium silicate react with water to form calcium silicate hydrate and calcium hydroxide. The tricalcium aluminate reacts with water, and in the presence of calcium sulfate initially produces ettringite. When the sulfate containing phases are depleted, a monosulfate phase is formed (11, 12).

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\begin{align*}
2(3\text{CaO}.\text{SiO}_2) + 6\text{H}_2\text{O} & \rightarrow \text{tricalcium silicate} + \text{water} & 3\text{CaO}.2\text{SiO}_2.3\text{H}_2\text{O} + 3\text{Ca}(\text{OH})_2 \\
2(2\text{CaO}.\text{SiO}_2) + 4\text{H}_2\text{O} & \rightarrow \text{dicalcium silicate} + \text{water} & 3\text{CaO}.2\text{SiO}_2.3\text{H}_2\text{O} + \text{Ca}(\text{OH})_2 \\
3\text{CaO}.\text{Al}_2\text{O}_3 + \text{CaSO}_4 + \text{H}_2\text{O} & \rightarrow \text{tricalcium aluminate} + \text{gypsum} + \text{water} & 3\text{CaO}.\text{Al}_2\text{O}_3.3\text{CaSO}_4.31\text{H}_2\text{O} \text{ (ettringite)}
\end{align*}
\]

The reactions that occur in MTA after hydration are the same reactions which are seen in Portland cement. During the initial stages of the reaction, calcium silicate hydrate is formed, coating the cement particles and preventing further reactions. Tricalcium aluminate dissolves and reacts with the calcium and sulfate ions present in the liquid phase to produce ettringite, which also precipitates on the cement particle surface. The initial phase is followed by a dormant period, wherein the hydrate coating on the cement grains prevents further hydration. The dormant period lasts for 1-2 hours, which is a period of relative inactivity and the cement is plastic and workable. Following the completion of the dormant period, setting of the cement proceeds to the acceleration stage, where the hydration process accelerates again. The rate of tricalcium silicate hydration increases and more calcium silicate hydrate gel is formed. Hydration of dicalcium silicate also increases at this stage. Sulfate ions are depleted and monosulfate forms from ettringite. Crystalline calcium hydroxide also precipitates from the liquid phase (11).
Reaction by-products produced upon hydration of the cement are deposited around the periphery of the unhydrated cement particles. As hydration proceeds, there is evidence of more reaction by-products (11,13). The hydration reaction takes several years to complete, although the cement mass would have achieved the final hardening and maximum physical and mechanical properties by 28 days. Hydrating MTA can be observed on back-scatter scanning electron micrographs of polished cement specimens (Fig. 3a). The formation of cement by-products can be monitored by scanning electron microscopy. Calcium silicate hydrate exhibits a typical honeycomb appearance, while calcium hydroxide is deposited in the form of hexagonal plates (Fig. 3b).

Material hydration can be monitored using X-ray diffraction analysis, since most of the hydration by-products are crystalline. As hydration progresses, a rise in calcium hydroxide peak (ICDD: 44-1481) is seen at 18 and 34°2θ using a copper Kα X-ray radiation. The unhydrated tricalcium silicate phase (ICDD: 86-0402) at 29.4, 32.1, 32.5, 32.6, 34.3 and 41.2°2θ usually reduces in intensity (Fig. 4). Quantitative measurements of the different phases of MTA may be performed using Rietveld refinement of X-ray diffraction plots (Table 1). This quantitative assessment verifies the reduction in tricalcium silicate and dicalcium silicate levels of the unhydrated cement as hydration proceeds with the formation of calcium silicate hydrate. Calcium hydroxide and low levels of ettringite are also produced (13).

If MTA is left exposed to the environment, the calcium hydroxide reacts with the atmospheric carbon dioxide resulting in the deposition of calcium carbonate on the cement surface (Fig. 5a). These deposits are commonly mistaken as being an integral part of the cement microstructure (7). When in contact with tissue fluids and synthetic tissue fluids, which contain phosphate ions, the calcium hydroxide produced, as a by-product of cement hydration, reacts to form calcium phosphate and is deposited on the cement surface. Calcium phosphate is crystal-

![Fig. 3a. Back scatter scanning electron micrograph of hydrated MTA after immersion for 28 days in water showing unhydrated cement particle enclosed by a reaction rim. Shiny particles are bismuth oxide (X 500 mag.).](image)

![Fig. 3b. Secondary electron scanning electron micrograph of MTA surface showing calcium silicate hydrate (honeycomb appearance) and calcium hydroxide (hexagonal plates) deposited on its surface (X 2500 mag.).](image)

![Table 1: Quantitative analysis using Rietveld X-ray diffraction of the phases present in unhydrated and hydrated ProRoot MTA. Reproduced from Camilleri (13).](table)
line and its presence can be demonstrated by X-ray diffraction analysis (Fig. 5b). The formation of calcium phosphate on the material surface has been reported to be the reason for the bioactivity shown by MTA (Fig. 6). This phenomenon is well researched (14–18).

Limitations of the original formulation

The original formulation of MTA is composed of Portland cement and bismuth oxide in a 4:1 proportion, as specified by the MTA patent (4–6), and marketed by Dentsply as ProRoot MTA, originally as gray MTA and later as white. Some concerns have been raised with the original formulation for a number of reasons and these are listed below.

Trace element inclusion

Since the main constituent of MTA is Portland cement, some concerns have been raised about the inclusion of trace elements. Portland cement is manufactured from naturally occurring raw materials in a kiln. Sometimes, waste materials are used as the raw materials in the manufacturing of Portland cement for the construction industry. Additionally, waste materials are also used as a replacement for primary fuels in order to keep the manufacturing costs low. This potentially leads to the inclusion of trace elements in the final product. Traces of arsenic, lead and chromium have been reported in both gray and white MTA (19–25). Although the levels of acid-extractable trace elements are high, the amounts leached in the solution are negligible. The inclusion of heavy metals in Portland cement has raised concerns regarding its use as a base material for MTA because when it is applied, the MTA is in contact with both hard and soft human tissues.

Presence of aluminum

Aluminum is part of the calcium aluminate phase of the Portland cement. This phase is an integral part of the cement and cannot be removed as it is produced during the cement manufacture. Aluminum is not indorsed in dental and biomaterials due to risk of Alzheimer’s from excessive exposure to aluminum in close contact with the human tissues (26).

Stability and leaching of bismuth

Bismuth oxide is added to MTA to act as a radiopacifying agent since Portland cement is not sufficiently radiopaque. Quantitative X-ray diffraction analysis

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Fig. 4. X-ray diffractogram of unhydrated and hydrated MTA after 1 and 28 days showing the main phases present. BO: bismuth oxide, P: Portlandite/calcium hydroxide, TCS: tricalcium silicate.
(Table 1) identifies a reduction of bismuth oxide after cement hydration, with 8.4% present in the hydrated cement as opposed to the 21.6% in the unhydrated material (13). Atomic ratio plots of Bi/Ca versus Si/Ca demonstrate a linear relationship between bismuth and silicon; the result infers that bismuth is replacing silicon in the calcium silicate hydrate structure (13).

Bismuth oxide has also been implicated in tooth discoloration. Tooth discoloration has been reported with the use of both gray and white MTA. Most of the reports were incidental findings while investigating the efficacy for multifactorial use of MTA (27–32). Gray MTA led to clinically perceptible crown discoloration after 1 month, while the total color change caused by white MTA exceeded the perceptible threshold for the human eye after 3 months. This suggests that the application of gray MTA in the aesthetic zone should be avoided, while white MTA should be used with caution when filling pulp chambers with the materials (33). The causative factors implicated in the change in color of bismuth oxide from yellow to dark brown (Fig. 7) include reaction with sodium hypochlorite (34), formaldehyde (35) and also contact with collagen thus tooth structure (36). Light and the presence of oxygen have also been shown to be precipitating factors leading to material discoloration (37,38).

Material manipulation and other physical properties

Another main concern with the original MTA formulation is the consistency of the freshly mixed material, which is usually termed as grainy or sandy. The original formulation is also hand spatulated and
delivery to the operative site is difficult. MTA presents longer setting time (2 hours and 45 minutes) in comparison to other retrograde filling materials such as amalgam, Super-EBA and IRM (9). The long setting time makes MTA unsuitable for most of the clinical applications. Different powder-to-water ratios, which tend to be a frequent occurrence in clinical practice since the gram supplied is usually not used in one application, also exerts influence on MTA’s properties and promoting a longer setting time (39,40).

Developments
More MTA formulations were introduced after the ProRoot by Dentsply. The first was introduced by Angelus, which had both gray and white formulations. The MTA Angelus is also composed of Portland cement and bismuth oxide. However the quantities of tricalcium and dicalcium silicate in MTA Angelus are different to ProRoot and other Portland cements (13,41). The difference is due to variations in the manufacturing of Portland cement, used as a raw material for preparing MTA. Quantitative phase analysis also showed a percentage of calcium oxide which is responsible for the initial high heat flux exhibited on calorimetry (41). This calcium oxide is a result of a raw mix with poor combustibility and with an unstable thermal profile. Furthermore MTA Angelus was found to contain tricalcium aluminate but no sulfate-containing phase (Table 2). The manufacturer claims that the absence of gypsum reduces the setting time of the material. In fact, MTA Angelus has been shown to set in less than 50 minutes (42), as opposed to ProRoot MTA which was reported to have a setting time of over 2 hours (9,43,44). MTA Angelus also exhibits a lower level of bismuth oxide when compared to ProRoot MTA (Table 2) which accounts for the lower radiopacity of MTA Angelus (18).

More recently, MTA Plus was introduced by an American company, Avalon Biomed. Both ProRoot MTA and MTA Angelus were found to have a similar fineness (1 m²/g) when tested using the Brunauer–Emmett–Teller (BET) gas adsorption method (12,41). MTA Plus has a specific surface area of 1.537 m²/g, which is higher than the values obtained for the other MTAs (12). The higher specific surface area allows more surface availability for the cement reaction and consequently results in a more rapid reaction rate.

Replacement of Portland cement
The associated risks to lead, arsenic and chromium exposure, coupled by the presence of aluminum led
Fig. 6. Characterization of precipitates formed by MTA BIO after 2 months of immersion in phosphate-buffered saline. A. SEM image showing the acicular nature of spherules (original magnification, 8000x). B. Energy dispersive X-ray (EDAX) spectrum for precipitates in (A) and semi-quantitative chemical composition showing their Ca/P
to the development of materials based on pure tricalcium silicate. Tricalcium silicate cement is manufactured with laboratory-grade materials using the sol-gel method. The lack of natural minerals, and wastes used to fire the kiln, reduces the risk of trace element contamination.

Materials that use tricalcium silicate as their main cementitious phase include Biodentine and BioAggregate. Tricalcium silicate cement hydrates in a similar way to Portland cement and produces calcium hydroxide on hydration (45). The tricalcium silicate-based materials are collectively known as bioceramics, which distinguishes them from the Portland cement-based materials and thus signifying a purer product. In fact, this is incorrect, since the term ceramics encompasses a wider variety of materials with a different chemistry.

Replacement of bismuth oxide

The newer MTA variants do not use the bismuth oxide as radiopacifier. Several alternative radiopacifiers have been investigated and most do not impart the necessary radiopacity to the final material formulation. Addition of gold powder, silver/tin alloy (46), barium sulfate (46–48), iodoform (47), zirconium oxide (39,47), zinc oxide (46,48), lead oxide, bismuth subnitrate, bismuth carbonate and calcium tungstate (48) results in a radiopacity value of more than 3 mm of the aluminum scale. The commercial materials use zirconium oxide and tantalum oxide. The latter is found in BioAggregate. Zirconium oxide is found in Biodentine, BioRoot RCS and EndoSequence BC Sealer and has been shown to be inert (49). It does not leach and zirconium does not take part in the material hydration to form zirconium-based complexes. Other alternative radiopacifiers such as barium sulfate and metallic components, like silver–tin alloys, leach into the solution and are therefore not ideal replacements (50). Although gold is inert and imparts adequate radiopacity, its cost and color limits its use. Leaching of barium has been demonstrated from barium zirconate and even when used in conjunction with tricalcium silicate cement with a resin matrix (51).
Improvement in the physical properties, material manipulation and suitability for specific use

One of the main clinical concerns with the original MTA formulation is the mixing and delivery system. Classically, MTA is mixed by manipulating the powder and liquid components on a mixing pad. Alternative mixing techniques, such as the use of an amalgamator, have been investigated (52–54). MM-MTA, manufactured by Micro-Mega (Besançon Cedex, France), uses MTA capsules that enable the MTA to be mixed using an amalgamator. Biodentine also uses capsules. The advantage of the MM-MTA delivery system is that the capsule incorporates a delivery system similar to what is available with glass ionomer cements. The effectiveness of mechanical mixing is not clear, although the compressive strength of the set material was shown to be enhanced (52). In addition to enhanced material microhardness (53), other research has shown that the various mixing methods have no significant effects on the resultant MTA mixtures (54).

Another clinical concern with the use of the original MTA formulation is the setting time, which was reported to be more than 3 hours (9). A long setting time is not an issue if the material is being used for root-end filling and perforation repair. However when used as a pulp capping material and as dressing over pulpotomies a shorter setting time is necessary. There have been a large number of reports regarding the addition of various chemicals to the mixing liquid or the substitution of the water for other liquids. The most popular chemicals are calcium chloride (44,55–57), calcium nitrite/nitrate and calcium formate (57). These additions are also used in the construction industry to accelerate the setting of Portland cement. Setting accelerators affect the setting reaction of both tricalcium silicate and tricalcium aluminate (58). Biodentine and MM-MTA have a reduced setting time and both use calcium chloride accelerator in their systems (59,60).

The development of resin modified tricalcium silicate-based materials result in a command cure material which is useful for pulp capping. Resins also result in increased material flow consequently making the material suitable as a root canal sealer. The mixing liquid, which is usually water, has been replaced by various resins. These modifications have resulted in the development of light-activated MTA and resin-modified MTA for use in root canal sealer cements. A number of resin systems have been investigated. The main ones being light-curing systems, containing Bisphenol A-glycidyl methacrylate (Bis-GMA), and a biocompatible resin (61,62) consisting of 2-hydroxyethyl methacrylate (HEMA),

<table>
<thead>
<tr>
<th>Phases identified</th>
<th>Material type in mass %</th>
<th>Portland cement</th>
<th>ProRoot MTA* (∞)</th>
<th>MTA Angelus*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tricalcium silicate</td>
<td>74.7</td>
<td>53.1 (51.9)</td>
<td>66.1</td>
<td></td>
</tr>
<tr>
<td>Dicalcium silicate</td>
<td>7.4</td>
<td>22.5 (23.2)</td>
<td>8.4</td>
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<tr>
<td>Tricalcium aluminate</td>
<td>3.6</td>
<td>0.0 (3.8)</td>
<td>2.0</td>
<td></td>
</tr>
<tr>
<td>Gypsum</td>
<td>1.1</td>
<td>0.0</td>
<td>0.0</td>
<td></td>
</tr>
<tr>
<td>Hemihydrate</td>
<td>1.1</td>
<td>0.0</td>
<td>0.0</td>
<td></td>
</tr>
<tr>
<td>Anhydrite</td>
<td>2.7</td>
<td>1.5 (1.3)</td>
<td>0.0</td>
<td></td>
</tr>
<tr>
<td>Calcium oxide</td>
<td>0.0</td>
<td>0.0</td>
<td>8.0</td>
<td></td>
</tr>
<tr>
<td>Bismuth oxide</td>
<td>0.0</td>
<td>21.6 (19.8)</td>
<td>14.0</td>
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</tr>
</tbody>
</table>

* Camilleri (13).
~ Camilleri et al. (41).
triethylene glycol dimethacrylate (TEGDMA), camphorquinone and ethyl-4-(dimethylamino)benzoate (EDMAB), with or without polyacrylic co-maleic acid (63,64), Bis-GMA, TEGDMA (65) and Bis-GMA, pyromellitic acid diethylmethacrylate (PMDM) and HEMA (66). Chemically-cured resins have also been employed (65,67) and investigated in vitro. The addition of different resin systems has shown to alter the hydration mechanism of the resultant material. Resins are mostly hydrophobic and limit ion exchange with the surrounding environment. This restricts the absorption of fluids and reduces cement hydration, therefore the calcium ions, even if formed, would find it difficult to move along the resin matrix. This modification of hydration and restricted ion movement has been reported (51). Thus if hydration is incomplete the use of resin modified tricalcium silicate is useless as no calcium hydroxide is released to interact with the pulp.

One light curable tricalcium silicate-based material marketed for pulp capping is Theracal (Bisco, Schaumburg, IL, USA). Theracal hydration is affected by the environmental conditions and fluid availability. In fact when used as a pulp capping material the low fluid availability reduces material hydration (68). The calcium releasing ability of Theracal is debatable, in one study it was shown to be comparable to calcium hydroxide (69), while in later investigations no calcium was formed and calcium ion leaching was shown to be very low compared to Biodentine (70). Theracal extracts were shown to be cytotoxic when in contact with pulp cells (71). A modified MTA-based resin is marketed by Angelus (Angelus, Londrina, Brazil) as MTA Fillapex. This is composed of MTA, a salicylate resin (methyl salicylate, butylene glycol and colophony) and other additives. Other proprietary brands such as MTA Obtura and Endo CPM sealer exist and contain other additives to the MTA formula which enhances material flow. In MTA Fillapex, the hydration reaction does not occur and therefore no calcium hydroxide is leached to the surrounding tissues (72).

Material flow can be enhanced by the addition of water-soluble polymers (73–76) as shown in prototype materials. ProRoot Endo Sealer is a commercial formulation using cement particles dispersed in a water-soluble polymer (77,78). The water-soluble polymer creates a charge on the cement particles, resulting in the repulsion of these charged particles, with reduced flocculation and increased material flow at low water/cement ratios (58). Biodentine and BioRoot RCS are both manufactured by Septodont and have a water soluble polymer which improves the material handling. Propylene glycol, another soluble polymer, has also been used to improve MTA flow (79).

Other polymers have been included to reduce the washout of the unset cement. Anti-washout liquid is included in the MTA Plus formulation (Avalon Biomed Inc., Bradenton, FL, USA). Washout refers to the tendency of a freshly prepared cement paste to “disintegrate upon early contact with blood or other fluids” (80) and is one of the disadvantages of MTA after it is placed in situ. The addition of an anti-washout liquid to MTA Plus reduces washout considerably when compared to MTA Angelus (81). Intermediate Restorative Material (IRM) and dental amalgam exhibit no washout (82).

Most of the newer formulations contain additives which enhance material properties. Both Biodentine and MM-MTA include calcium carbonate and is a component of Portland cement when used in the building industry. The addition of calcium carbonate reduces the material costs and acts as a nucleating agent, thus enhancing hydration. This has been demonstrated for Biodentine, where the hydration product was shown to deposit around the calcium carbonate particles (83,84). In MM-MTA the calcium carbonate changes the hydration reaction. Since MM-MTA is Portland cement-based it contains an aluminate phase. The calcium carbonate affects the formation of ettringite, which is a by-product of the hydration of tricalcium aluminate, calcium sulfate and water during hydration, consequently modifying the hydration process. During the formation of ettringite, the sulfate ions are replaced by carbonate ions producing calcium carbosilicate and calcium carboaluminate (60). Calcium carbonate has been also shown to impede crystallization of calcium hydroxide. In fact no formation of calcium hydroxide was demonstrated for MM-MTA (60).

BioAggregate, EndoSequence BC Sealer and the material range from Brasseler contains calcium phosphate monobasic (84,85). There is no literature on the effect of adding phosphate containing materials to tricalcium silicate-based materials, however a reduction in the formation of calcium hydroxide over a period of 28 days was demonstrated for Bio-
aggregate (84). MTA Fillapex contains microsilica, which affects the hydration of Portland cement. It reacts with the calcium hydroxide produced during hydration and forms more calcium silicate hydrate in the long term and improves the material properties at the expense of calcium hydroxide formation. However, MTA Fillapex does not produce calcium hydroxide as shown by X-ray diffraction analysis (72). The different additives may potentially affect the cytocompatibility of the materials since different calcium silicate-based materials exhibited different cytotoxicity to human gingival fibroblasts (85).

Material use and effect of environmental conditions

Although MTA is a hydraulic material, when used in clinical dentistry it never comes in contact with water. The material has been suggested for use as a root-end filling material, for perforation repair, apexification and pulpotomy procedures and also as a pulp capping material (87). More recently MTA has also been developed as a root canal sealer. All the beneficial properties of MTA are related to its hydraulic nature and the formation of calcium hydroxide, as a by-product of material hydration. Each material application brings MTA in contact with different environments. Blood comes into contact with MTA when it is used for perforation repair, as a root-end filling material and to a minor extent in cases of direct pulp capping. Blood interferes with material hydration and reduces the MTA microhardness (88–90). Tissue fluids and serum also affect material properties (91) and failure of material setting (92). The phosphates present in tissue fluids have been implicated in material bioactivity, as reaction of calcium hydroxide with phosphates results in the formation of hydroxyapatite on the material surface (14–16). However phosphates have also been shown to interfere with material setting (12).

The interaction with pulp and dentin also provides an interesting and beneficial phenomena. MTA induces pulp healing and regeneration (93). However MTA does have several drawbacks. The flexural strength of the tooth when in contact with MTA was reduced (94) and MTA’s interaction with collagen also caused tooth discoloration (36). Furthermore the long setting time of MTA makes unset MTA come in contact with other dental materials affecting the material hydration and setting (95,96). The development of tricalcium silicate root canal sealers is based on the hypothesis of the interaction of dentin with the tricalcium silicate and bio-mineralization, consequently forming dentin tags. This is postulated for the hydrated material. MTA Fillapex does not produce calcium hydroxide after it sets. EndoSequence, and materials which are hybrids of tricalcium silicate and calcium phosphate, may not produce calcium hydroxide in the long term. Thus the hypothesis of bio-mineralization may be erroneous. MTA and related materials are affected by various irrigants used during root canal treatment (97), particularly EDTA which is a calcium chelator (98). Material and tooth discoloration will result from the interaction of sodium hypochlorite with bismuth oxide in MTA (34).

Conclusions

For the past two decades MTA and tricalcium silicate cement-based materials have become a mainstay in clinical dentistry and are used for a variety of clinical applications. The original formulation and modified cements are still used in these applications. The materials are reactive and additives tend to affect the hydration process, which can be deleterious to the material chemistry and resultant properties of the set material. Furthermore the materials interact with the oral environment during use, which changes material microstructure and even demonstrates setting failure. Future developments in MTA and related materials should outline first the particular material use and then tailor-make the material according to the desired properties.

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