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REVIEW ARTICLE

BIOACTIVE MATERIALS USED FOR ROOT END FILLING-A REVIEW

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ABSTRACT

The periradicular pathosis develops when there is exposure to bacteria, due to inadequate apical seal, complex anatomic variations in the roots such as non negotiable dilacerated roots, extensive canal calcifications, non negotiable parallel canals, internal or external root perforations, immature apex development, accessory canals wherein apical seal of the root canal cannot be obturated. So there is a need to treat the apical end of the root in such cases. An ideal material to seal the root-end cavities should hermetically seal the apex & prevent leakage of microorganisms and their by-products into the periradicular tissues. It should also be non-toxic, non-carcinogenic, be biocompatible with the tissue fluids, non resorbable, impervious to dissolution by tissue fluids, closely adapt to the dentinal walls of root end preparation, be radiopaque and dimensionally stable.

The bioactive materials were introduced as root end filling material due to its superior sealing ability, promotion of cementogenesis, & biocompatibility forming a hermetic seal inside the root canal. This article focuses on physical properties of root end filling materials.

INTRODUCTION

Most endodontic failures occur as a result of leakage of irritants from pathologically involved root canals[4]. The periradicular pathosis develops when there is exposure to bacteria, due to inadequate apical seal[1], complex anatomic variations in the roots such as non negotiable dilacerated roots, extensive canal calcifications, non negotiable parallel canals, internal or external root perforations, immature apex development, accessory canals wherein apical seal of the root canal cannot be obturated[2]. According to Gartner and Dorn[5] an ideal material to seal the root-end cavities should hermetically seal the apex & prevent leakage of microorganisms and their by-products into the periradicular tissues. It should also be non-toxic, non-carcinogenic, be biocompatible with the tissue fluids, non resorbable, impervious to dissolution by tissue fluids, closely adapt to the dentinal walls of root end preparation, be radiopaque and dimensionally stable. The presence of moisture should not affect its sealing ability.

Various materials have been used for root repair, including amalgam, cavit, zinc oxide-eugenol, intermediate restorative material (IRM), composite resins, carboxylate cements, zinc phosphate cements and glass ionomers. However, none of them fulfilled the ideal requirements of root filling materials.

These materials had certain limitations like, poor sealing ability to the root surface therefore presence of more microleakage, biocompatibility was not desirable.

In an order to overcome the limitations of these materials, newer root end filling materials known to be bioactive materials were introduced in 1969. Hench[6,7] gave the concept of bioactivity as, "A bioactive material is one that elicits a specific biological response at the interface of the material which results in the formation of a bond between the tissues and the material".

One of the characteristics of a bioactive material is its ability to form an apatite-like layer on its surface when it comes in contact with physiologic fluids. Apatite formation is a common characteristic of calcium silicate–containing biomaterials.

Various bioactive materials are as follows

Mineral trioxide aggregate, Endosequence, Biodentine, Endobinder, Bio-aggregate & Ceramicrete have better physical properties as compared to the root end filling materials used previously[8]

Mineral Trioxide Aggregate (MTA)

Mineral trioxide aggregate (MTA) was developed for use as a dental root repair material by Dr. Mahmoud Torabinejad, Professor in Endodontics at Loma Linda University School of Dentistry and was formulated from commercial Portland cement combined with bismuth oxide powder for radiopacity[9]

Composition of MTA

It consists of Tricalcium silicate, Dicalcium silicate, Tricalcium aluminate, Tetracalcium aluminoferrite, Gypsum,

& Bismuth oxide, added to enhance the radio-opacity of MTA. MTA consisted of particles ranging between <1 μm to approximately 30 μm in size.

Camilleri *et al*. (2008) showed through x-ray diffraction analysis, the components of MTA to be tricalcium silicates and aluminates with bismuth oxide. They also showed that the material was crystalline in structure. It was found that blood contamination affected the retention characteristics of MTA. It was seen that unreacted MTA was composed of impure tri-calcium and di-calcium silicate and bismuth oxide and traces of aluminate. Angela *et al* (2006) investigated the bacterial leakage of MTA when used as a root end filling material in the presence & absence of contamination with blood, saline & saliva & they concluded that MTA contaminated with saliva demonstrated maximum microleakage as compared to uncontaminated MTA.

Mechanism of Action

When MTA comes in contact with physiologic fluids or body fluids it undergoes hydration reaction. During this process there is a slow release of calcium ions which promotes alkaline pH of set MTA. These calcium ions diffuse in the dentinal tubules of the root canals & their concentration increases with time. Also MTA shows the production of hydroxyapatite crystals as follows;

When calcium ions released by MTA comes in contact with tissue fluids an amorphous calcium phosphate phase is formed initially which later gets transformed to apatite phase.(Camelleri *et al* 2008)

Apatite formation is a common characteristic of calcium silicate–containing biomaterials. Hydroxyapatite releases calcium and phosphorus continuously, a process required for bone metabolism. In addition, this phenomenon increases the sealing ability of MTA and promotes the regeneration and remineralization of hard tissues. Based on this mechanism it can be suggested that the biocompatibility, sealing ability, and dentinogenic activity of MTA is due to physiochemical reactions between MTA and tissue fluids.

Properties

Strength

The compressive strength of set MTA is about 70 MPa, MTA's compressive strength is not significantly affected by condensation pressure. MTA has a prolonged maturation process, with increased compressive strength, push-out strength, and retention strength of the material with time (up to 21 days) in the presence of moisture. The initial compressive strength following 24 hours is 40 MPa, which increases to 67.3 MPa after 21 days. A similar increase in flexure and push-out strength was also observed under moist conditions with the passage of time. This is because the dicalcium silicate hydration rate is slower than that of tri-calcium silicate.

Microhardness

An exposure to acidic pH-5, as observed in inflammatory environment, has an adverse effect on the microhardness of both GMTA and WMTA. It is attributed to the absence and growth of needle-like crystals between the cubic crystals during the hydration phase. A 5-mm thickness of MTA is significantly harder than a 2-mm thickness.

pH

Hydrated MTA has an initial pH of 10.2, which rises to 12.5 (similar to calcium hydroxide) 3 hours after mixing and following setting. The high pH is responsible for the antimicrobial action and biological activity of the material. Which is due to the constant release of calcium from MTA and also the formation of calcium hydroxide. The usual pH (11 to 12) of MTA materials decreases slightly with time.[11]

Marco[140] *et al* (2003) conducted study to evaluate the pH and calcium ion release of ProRoot and MTA-Angelus at the duration of 3, 24, 72, and 168 hours, the water in which each had been immersed was tested to determine the pH changes and released calcium. The values for pH and calcium ion release were slightly higher for MTA-Angelus than ProRoot. They concluded that both materials released calcium and had an alkaline pH.

Saghiri[141] *et al* (2008) conducted a study to evaluate the effect of pH on microleakage of MTA. Rootend fillings were exposed to acidic environments with pH values of 4.4, 5.4, 6.4, or 7.4 for 3 days & Microleakage was evaluated by using protein leakage method. It was concluded that MTA is more resistant to an acidic environment & a significantly longer time is needed for leakage to occur in samples stored in higher pH values.

Carvalho[142] *et al*(2009) conducted a study to evaluate the pH and calcium ion release of Grey ProRoot MTA, gray MTA-Angelus, white MTA-Angelus, and CPM compared to Portland cement with a modified mixing liquid, and MBPc, an epoxy-resin based cement containing calcium hydroxide for a duration of 3, 24, 72, and 168 hours. The water in which each sample had been immersed was tested to determine the pH and calcium ion release. The results suggest that all materials investigated presented alkaline pH and had ability to release calcium.

Sealing Ability (Microleakage)

Results[12] obtained from dye leakage, fluid filtration, protein leakage, and bacterial leakage and endotoxin leakage studies (*S. epidermis, S. salivaris, S. marcescens, E. coli, F. nucleatum*) indicate that MTA showed less microleakage and better sealing ability. The better sealing ability can be due to expansion of MTA during setting. MTA has also been shown to leak significantly less compared to amalgam, IRM, and super EBA. Torabinejad *et al* (1994) conducted a study to evaluate sealing ability of amalgam, Super EBA, IRM, & MTA using dye leakage in-vitro with or without blood present in root end preparation to simulate the clinical condition. Moisture is an important factor as it affects the physical property & sealing ability of the material. However they concluded that presence or absence of blood had no significant effect on amount of dye leakage & MTA showed least microleakage as compared to other materials. Wu *et al* (1998) used a fluid transport device for determination of microleakage of amalgam, super EBA, GIC & MTA. The leakage of materials was measured at duration of 24hrs, or 3, 6 or 12 months. It was found that MTA showed significantly less microleakage as compared to other materials. Aqrabawi *et al* (2000) compared the apical microleakage of amalgam, EBA & MTA using dye penetration method & they concluded that MTA provides better seal than amalgam & EBA when used as a root end filling material. Tang *et al* (2002) evaluated the sealing ability of MTA when tested with modified limulus

amebocyte lysate test for the presence of endotoxin as a tracer & compared the sealing ability of Super EBA, IRM, amalgam, & MTA. The results showed that MTA permitted less endotoxin leakage than IRM & amalgam at 1,2,6 & 12 weeks & leaked less than Super EBA at 2 & 12 weeks. De Bruyne *et al* (2006) conducted a comparative study using capillary flow porometry (as it gives more accurate & reproducible data) to assess the seal provided at 48hrs duration by MTA, IRM, gutta percha used with a sealer, glass ionomer cements with & without dentin conditioners, & reinforced zinc oxide eugenol cements with & without dentin conditioners. It was concluded that MTA, IRM, Gutta percha with sealer showed better results & glass ionomers leaked the most.

Biocompatibility

Both GMTA and WMTA are biocompatible. They produce no genetic damage, genetic mutation, chromosomal breakage, altered DNA repair capacity, or cellular transformation.[13] Neither freshly mixed nor set MTA displayed neurotoxicity. It was less cytotoxic than amalgam, super EBA, and IRM. Animal and human studies[14] have shown minimal or no inflammation to bone and connective tissue following implantation of MTA. MTA stimulates cytokine release and interleukin production, which may actively promote hard-tissue formation. Torabinejad *et al* at 1995

Kim *et al* (2016) conducted a Randomized Controlled Study of Long-term Outcomes of Mineral Trioxide Aggregate and Super Ethoxybenzoic Acid as Root-end Filling Materials in Endodontic Microsurgery. Additionally, this study aimed to compare the clinical outcome of endodontic microsurgery at the 1-year follow-up with that at the 4-year follow-up. They concluded that no significant difference in the 4-year success rates of MTA and Super EBA as root-end filling materials in endodontic microsurgery. Also, compared with short-term outcomes, long-term follow-up outcomes were not significantly different.

Antimicrobial Properties

In vitro studies have shown antibacterial activity of MTA against M. luteus, S. aureus, E. coli, P. aeruginosa, E. faecalis, and S. sangui*s*. MTA was found to have an antibacterial effect on facultative bacteria, & fungi[15]

Regenerative Potential and Biological Activity

MTA has an osteoconductive, osteoinductive, and cementogenic property. It has the capacity to induce bone, dentin, and cementum formation and regeneration of periapical tissues[16]. MTA provides a good biological seal and can act as a scaffold for the formation and regeneration of hard tissue periapically. Baek[17] *et al* studied Periapical Bone Regeneration after Endodontic Microsurgery with three Different Root-end Filling Materials: Amalgam, SuperEBA, and Mineral Trioxide Aggregate in dogs. They determined the bone regeneration potential of these materials by evaluating the distance between the materials and newly regenerated bone after root-end surgery. They concluded that MTA showed the most favorable periapical tissue response. The distance from MTA to the regenerated bone was similar to the normal average periodontal ligament thickness in dogs.

Radiopacity

MTA has a mean radiopacity of 7.17 mm of equivalent mm thickness of aluminum. It has a similar radiodensity to zinc oxide eugenol and slightly greater radiopacity than dentin.

Biodentine

Biodentine is a fine hydrophilic powder composed of modified powder composition of MTA by addition of setting accelators and softners and a new pre dosed capsule formulation to be used in a mixing device.[18]

Composition

Powder consists of core materials like, Tricalcium silicate & Dicalcium silicate, calcium carbonates & oxides are the fillers, zirconium oxide is the radiopacifier and Iron oxide

Liquid consists of Calcium chloride as an accelerator, Hydrosoluble polymer as a water reducing agent

Mechanism of Action

Biodentine induces mineralization after its application. Mineralization occurs in the form of osteodentine. Biodentine induces apposition of reactionary dentine by odontoblast stimulation and reparative dentin by cell differentiation; Because of its high alkality it has inhibitory effects on micro organism.[18]

Properties

Tissue Regeneration & Early Mineralization

Biodentine induces early mineralization by increasing the secretion of TGF-61 from pulpal cells after its application. It also acts by odontoblasts stimulation and cell differentiation, there by facilitating reactionary and tertiary dentin formation.

Setting time

Biodentine sets within 12 minutes, intraorally without material deterioration.

Biodentine has a high wash out, low fluid uptake, resorption values, low setting time and superior mechanical properties.

Anti bacterial properties

Due to high alkaline pH Biodentine has inhibitory effect on the micro organisms.

Bio compatibility

Biodentine preserves pulp vitality and promotes its healing process. The material was not found to affect the specific functions of the target cells and thus could safely be used. About *et al*. (2010) investigated Biodentine™ bioactivity by studying its effects on pulp progenitor cells activation, differentiation and dentine regeneration in human tooth cultures. The study concluded that Biodentine™ is stimulating dentine regeneration by inducing odontoblast differentiation from pulp progenitor cells. Han & Okiji (2011) compared calcium and silicon uptake by adjacent root canal dentine in the presence of phosphate buffered saline using Biodentin and ProRoot MTA. The results showed that both materials formed a tag-like structure composed of the material itself or calcium- or phosphate rich crystalline deposits. The thickness of the Ca- and Si-rich layers increased over time, and the thickness of the Ca- and Si-rich layer was significantly larger in Biodentin compared to MTA after 30 and 90 days, concluding that the

dentine element uptake was greater for Biodentin than for MTA.

Simsek *et al* (2015) conducted assessment of the biocompatibility of mineral trioxide aggregate, bioaggregate, and biodentine in the subcutaneous tissue of rats to evaluate the tissue inflammation caused by these materials. While MTA and BioAggregate showed a similar biocompatibility, Biodentine was more biocompatible as compared to other materials in the 1st week of the experiment. However, there was no difference between the materials at the end of the 45th day. Therefore Biodentine can be considered suitable endodontic repair materials.

Push out Bond Strength Of Biodentine

Biodentine has significantly higher push-out bond strength than MTA amalgam≥IRM≥Biodentine>MTA.

Good material handling

Ease of manipulation, better consistency, and safety handling with favorable setting kinetics – about 12minutes.[19] Gupta PK *et al* (2015) evaluated the sealing ability of Biodentine as retrograde filling materials using two different manipulation methods such as manual & machine triturated. Least microleakage was seen when Biodentine was machine triturated. This can be attributed to the fact that mechanical trituration produces more homogenous mix whereas the water powder ratio gets altered in manual mixing resulting in non homogenous mix

Specific properties of Biodentine as Dentin Substitute

Elastic modulus, at 22.0 Gpa, is very similar to that of dentine at 18.5; Compressive strength of about 220 MPa is equal to average for dentine of 290 MPa. Microhardness of Biodentin at 60 HVN is same as that of natural dentin.

Mariginal Adaptation and Sealing Ability- The micromechanical adhesion of Biodentine is caused by the alkaline effect during the setting reaction. Srivastava *et al*. (2016) evaluated the sealing ability of Glass Ionomer Cement(GIC), Biodentine, Mineral Trioxide Aggregate (MTA) and Bone Cement when used as a retrograde filling material. The mean microleakage was significantly higher in GIC followed by MTA, Bone cement and least with Biodentine. Therefore they concluded that Biodentine has better sealing ability as root end filling material in comparison to MTA, Bone Cement and GIC. Biodentine adapts well to cavity surface due to smaller particle size, and also set Biodentine has less porosity and pore volume when compared to MTA.

Mathew *et al* (2016) evaluated and compared the microleakage of blood‐contaminated mineral trioxide aggregate (MTA) and Biodentine as root end filling materials using a glucose filtration model. The sealing ability of Biodentine showed comparable results with that of MTA in dry and blood‐contaminated environments and hence Biodentine can be used as an alternative to MTA for root‐end filling procedures in a blood contaminated environment as it is a calcium silicate cement like MTA

Radiopacity of Biodentine - Tanalp *et al* (2013) conducted a comparative evaluation of Biodentine, MM-MTA, and MTA Angelus. The radiographic densities of the specimens were determined, and the values were converted into millimetres of Aluminium. All materials had significantly higher radiopacities compared to dentine. They concluded that the relatively lower radiopacity of Biodentine can be improved to achieve more reliable results in procedures such as retrograde fillings.

Endodsequence

EndoSequence is a bioceramic material & it was introduced to endodontics, in 2007 to overcome the short comings of MTA.

1. As MTA is a modified Portland cement, it is not available in premixed form & thus manual mixing is indicated which is difficult to use as a root end filling material.
2. It has a large particle size which cannot be extruded through a small syringe

Therefore these endodontic pre-mixed bioceramic products with a fine particle size of less than 2microns were formulated in two different forms such as

1. EndoSequence BC RRM (Root Repair Material, a syringable paste), and
2. EndoSe-quence BC RRM-Fast Set Putty

The bioceramic materials have shown considerable clinical success over time.

Composition

They include alumina, zirconia, bioactive glass, glass ceramics, hydroxyapatite and resorbable calcium phosphates. It has the ability to form hydroxyapatite during setting process creating a bond between dentin and the filling material. It is hydrophilic in nature so its adaptation with the dentinal tubules is excellent in the presence of moisture.

Due to its property of bioactivity it does not cause inflammatory response if an over fill occurs during the root repair procedure. It is a highly biocompatible material Alanezi *et al* (2009) evaluated the cytotoxicity of EndoSequence Root Repair Material and compared it with gray and white MTA. They concluded that ERRM may have cell viability similar to Grey MTA and White MTA in both set and fresh conditions. Shinbori *et al* (2015) did a retrospective study to determine the clinical and radiographic outcome of root-end surgery when EndoSequence BC Root Repair was used as the root-end filling material and to identify any possible prognostic factors that may have affected the healing outcome. They concluded that EndoSequence BC Root Repair is a suitable root-end filling material to be used in endodontic surgery. Chen *et al* evalauated healing after Root-end Microsurgery by Using Mineral Trioxide Aggregate and EndoSequence Root Repair Material in Dogs. A comparative study for healing after root-end surgery by using grey mineral trioxide aggregate and EndoSequence Root Repair Material as root-end filling material in an animal model was done. They concluded that endosequence root repair material exhibited superior healing tendency and could be detected by CBCT and micro CT.

It is available in pre mixed form which can overcome the poor handling properties of MTA and therefore reduces manipulation time, is convenient to use and a homogenous mix can be obtained.

Advantages

1. It has high pH -12.8 during the initial 24 hours of the setting process due to which it is strongly antibacterial.
2. High resistance to washout,

3. No shrinkage during setting,
4. Excellent biocompatibility
5. Excellent physical properties
6. Excellent sealing ability;
7. Setting time of 3-4 hours
8. They are easy to dispense as the particle size is so small it can be extruded through a syringe.
9. It has a compressive strength of 50-70 MPa, which is similar to MTA

Properties and setting mechanism of all bioceramic materials are similar to each other.[7]

Other calcium aluminosilicate cements are

Generex A

Generex A is a calcium-silicate-based material that has some similarities to ProRoot MTA but is mixed with unique gels instead of water used for MTA. Generex A mixes to a dough-like consistency, making it easy to roll into a rope-like mass similar to intermediate restorative material.[20]

Capasio

Capasio is composed primarily of bismuth oxide, dental glass, and calcium alumino-silicate with a silica and polyvinyl acetatebased gel. Capasio and MTA promote apatite deposition when exposed to synthetictissue fluid thus had the mineralization capacity. Capasio is more likely to penetrate dentinal tubules.[21]

Quick-Set

Recently, Capasio powder has been refined and renamed as Quick-Set, and the cationic surfactant was removed from the liquid gel component, which was thought to interfere with cytocompatibility. They possess less in vitro toxicity after evaluation of toxic components.[22] Quick-Set is a calcium aluminosilicate cement that is a potential alternative to mineral trioxide aggregate (MTA) with greater acid resistance and faster setting. Kohout *et al* (2015) did a comparative study for the regeneration of apical tissues after root-end surgery when the apical tissues were exposed to Quick-Set and White ProRoot MTA by root end resection. They concluded that Quick-Set and White MTA had a similar effect on bone quality, cementum formation, and periodontal ligament formation after root end surgery in dogs. Quick-Set was associated with greater inflammation.

CONCLUSION

Many different materials have been advocated for use as root end filling materials.[3] Sealing ability is an important factor, that has an ability to fight infection, tolerance of surgery and rate of healing that may influence the outcome of periradicular surgery. However, from the biologic perspective of regeneration of the periradicular tissues, bioactive materials appear to have a clear advantage over the other available materials.[7] Various studies, of all the recent root end filling materials, conclude that MTA has more favourable properties as it is non-toxic, non-carcinogenic, biocompatible, dimensionally stable, has high radioopacity, good tissue tolerance and possible induction of mineral tissue and is considered the gold standard for all the future root end filling materials. The most commonly cited disadvantage of MTA is its handling properties. Even when properly prepared, MTA is more difficult to place in the root end cavity than most other materials.[10] There are various new materials under research as there is no sufficient literature to support these recent root end filling materials they cannot be used in clinical practice.[26] Studies have revealed that MTA, Super EBA, & IRM are also used successfully over 30 years & are found superior to other retro-grade filling materials.[27]

The root end filling materials should be biologically and clinically evaluated and should have evidence of long term success.[28,3] An ideal root-end filling material is still elusive because each of these above discussed materials have their own advantages and disadvantages.[29] Apical seal with the root end filling material is an absolute pre-requisite for surgical endodontic management of the root end to have successful outcome of periradicular surgery.[30]

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