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**INTRODUCTION**

As early as 1960, Jack Steele a researcher with the United States

Air Force coined the word “Bionics,” which means taking ideas

from nature (Caidin M, 1984). The process of taking inspiration

from nature for manmade design has been described as “biomimicry

or biomimetics”. Biomimicry (from bios, meaning life, and mimesis,

meaning to imitate) involves studying nature’s most successful

developments and then imitating these designs to create new materials¹ .

Wright brothers pointed to soaring birds as their inspiration for the first

aircraft steering mechanisms².Biomimetic design is a design that, fully

or partially, imitates or evokes some biological phenomenon³.

During the past few decades, a number of men made

materials and devices partially mimicking the natural ones have

been introduced for implantation into humans. The first artificial

heart valve was implanted by Hufnagel in 1952, and the first

artificial hip replacement was performed by Charney in 1954⁴.

The main disadvantage with traditional biomaterials used in

the medical, biotechnological, and pharmaceutical field is that

they lack the ability to integrate with biological systems through

a cellular pathway. This may lead to failure of the material.

Hence the current focus is on developing a biomaterial which

suitably performs the functions of the biological molecule that

needs to be replaced⁵׳⁶.

Biomimetics is gaining popularity in the field of medicine,

especially in skin regeneration. Bioartificial skin is being

produced using patients own cells. Likewise autograft heart

valves and ear cartilage can also be produced⁷.

It is a challenge to design and fabricate new biomimetic materials like enamel, dentin, cementum, pulp, bone and periodontal ligament. Biomimetics provide new strategy that translates our knowledge of biological system and create new synthetic pathways to mimic biological processes. Three approaches are being used for the creation of new tissues by mimicking natural ones which includes the tissue engineering triad; the Cells, Mediators and a biocompatible matrix ⁸.

Marshal Urist and his colleagues in 1972 discovered bone morphogenic protein, or BMP from demineralized bone which controls the regeneration of bone. It also has an important role in regeneration of dentin. Currently research is on in developing gene products associated with enamel formation, such as amelogenin (90%), ameloblastin and enamelin and growth factors which help in the differentiation of odontoblast ⁶. Through guided tissue regeneration advanced periodontal diseases can also be treated. So by using bone morphogenetic proteins and growth factors, the regeneration of hard and soft tissues including dentin, cementum, bone and periodontal ligament is also made possible⁴. Biomimetic restorative materials also play a very important role in the field of endodontics. Focusing on to the future, we should direct our goal to regenerate the diseased and necrotic tissues rather than replacing them with some conventional replacement materials.

The physiological performance of intact teeth is the result of intimate and balanced relationships between biological, mechanical, functional and esthetic parameters. Natural teeth, through the optimal combination of enamel and dentin, constitute the perfect and unmatched compromise between rigidity, strength and resilience⁹. Therefore a biomimetic approach to restorative dentistry would mean aesthetic and functional restorative materials similar to the natural tooth and its individual layers of dentine and enamel¹⁰. This would exclude amalgam and other precious and non precious metal-based materials as they do not mimic the natural tooth in terms of aesthetics or properties.

In 2006 Magne said “The goal of biomimetics in restorative dentistry is to return all of the prepared dental tissues to full function by the creation of a hard tissue bond that allows functional stresses to pass through the tooth, drawing the entire crown into the final functional biologic and esthetic result¹¹. The intact tooth in its ideal hues and shades, and perhaps more importantly in its intracoronal anatomy, mechanics and location in the arch, is the guide to reconstruction that determines success”. According to Magne and Douglas in 1999, teeth have a good equilibrium of strength, flexure and stiffness. They are resistant to fracture and flex to a certain degree. Dental disease, age and restorations weaken these factors. There are certain types of restorations that can restore these factors to a better degree than other types of restorations¹¹ .

Magne states that porcelain bonded to metal and other substances like amalgam which do not follow biomimetic principles and do not attempt to restore the tooths natural properties. He also states that gold is excessively stiff, thereby also not following biomimetic principles. As these materials also are not bonded with the existing tooth structure there is a higher likelihood of cracks, leakage and bacterial invasion causing further deterioration. This is then repaired with the same materials which fail again but with less tooth substance leading to tooth loss. Biomimetics prevents and stops the repair-replace-repair cycle of destruction and deterioration¹¹.

We are aware that there may be some regeneration or stimulation of dentine with certain dental materials. There are also materials that can actually remineralise acid etched dentine. These materials would be classified as being “biomimetic”. Glass Ionomer Cements (GIC) is considered to be useful in deep class I or II cavities to fill up the base as lining material. They are also useful as buccal class V cavities¹². Composite can then be bonded over as a closed sandwhich technique. GIC can also be used to fill any undercuts for preparation of indirect restorations. GIC releases fluoride, is bactericidal, stimulates sclerotic dentine and also has properties similar to dentine. As such would fit the definition of biomimetic. However as their tensile strength is poor they are not advocated in use of high occlusal stress and force .so with advancement many new calcium silicate and calcium aluminate based bioactive and biomimetic materials have introduced that can replace these old restorative materials¹³.

This Library dissertation is an attempt, at providing a compilation of different biomimetic restorative materials and it application in endodontics.

**DEFINITIONS**

**Biomimetics:** *(Merriam Webster online dictionary)* is a term coined by Otto Schmitt in the 1950’s, while studying the nerves in a squid. He attempted to copy and design an artificial device that could replicate the same process of synaptic impulse. It literally means to mimic life. It is considered the study of natural structural processes to try to mimic or replicate it artificially in an attempt to restore the same function or aesthetics. It is synonomous with biomimicry, biomechanics and biomimesis. Age, disease and traditional restorations can cause further problems to the existing tooth structure. As teeth have no natural method of repair, biomimetic principles should be used to artificially repair the tooth to its natural functions and aesthetics. There are two aspects to biomimetics in Dentistry. The lost or missing dental tissue is restored, leading to the full return of function and aesthetics to the tooth. Or the material used can regenerate, replicate or mimic the missing dental tissue closely.

**Bioactive materials** :- *(Merriam Webster online dictionary)*A bioactive material is one that forms a surface layer of an apatite like material in the presence of an inorganic phosphate solultion.The two specific categories calcium silicate and calcium aluminate based cements lie within the broad range of bioactive materials.A wide range of calcium based or calcium containing materials have demonstrated bioactivity,these materials include crystalline calcium phosphate materials including various apatite and hydroapatites, various glasses under the generic terms bioactive glasses or bioglasses ,various glass ceramics such as apatite wollantonite materials. calcium silicate based cements and calcium aluminate based.bioactive cements fall under a well known and long standing group of dental and medical materials:the chemically bonded ceramic cements.theses cements are water based and hence also often termed hydraulic cements.

**Biomaterial** (Hand book of biomaterial and bioengineering, Donald Lee Wise)Any substance of synthetic or natural origin that can be used for a period of time, as whole or as a part of system which treats, augments or replaces any tissue organ, or function of the body.

**Biocompatible material.** (Hand book of biomaterial and bioengineering, Donald Lee Wise)It is defined as one that was capable of been implanted, caused no systemic toxic reactions, has no carcinogenic qualities, and the local tissue response of which neither compromised function nor causes pain, swelling or necrosis.

**NEED FOR BIOACTIVE MATERIALS IN RESTORATIVE DENTISTRY**

Bioactive restorative materials is not a totally new endeavor .for eg Gic have been ascribed bioactive properties because of their dynamic release of fluoride ,as well as their unique mineral based polysalt matrix matrix composition that has been claimed to also contribute to the ability to remineralize calcium-depleted tooth structure. The continuous release of ﬂuoride by GI and RMGIs has also been positioned as a potential mechanism to delay or inhibit secondary caries at the margins of these restorations (GI and RMGI). Yet despite the release of ﬂuoride ions, in some studies, secondary caries has been found to be a reason for clinical failure of glass ionomer cement restorations. GIs are excellent materials in particular restorative situations and clinical indications, but their ability to prevent recurrent caries may be somewhat variable¹⁴.

Likewise, the potential beneﬁts of the use of adhesive monomers both in free-standing dentin-enamel adhesives and now in the self-adhesive cement formulations are still somewhat areas of debate. Current restorative resin/dentin adhesive systems have demonstrated outstanding long-term clinical performance in prospective clinical studies. Many prospective university-based clinical studies conducted in the 1980s, 1990s, and early 2000s executed with protocol-directed procedures and experienced clinical researchers demonstrated quite acceptable performance of enamel-dentin adhesives used in combination with posterior composite resins¹⁵. In a similar time frame, advanced analytical techniques to examine the adhesive resin-dentin interfacial region have revealed a number of potentially deleterious phenomena that could interfere with successful dentin bonding. These mechanisms include adverse eﬀects from delayed hydrolysis within the resin-dentin collagen hybrid zone because of “water-tree” formation and enzymatic degradation of the collagen component within and immediately adjacent to resin-collagen hybrid zone because of reactivation of metalloproteinase enzymes exposed by acidic demineralization of the dentin. Although continual improvement in both adhesives and posterior composites may well address these issues, the potential may exist for radically diﬀerent material chemistries and alternative mechanisms to secure a stable interface between tooth structure and the restoration. For example, it may be possible to secure integration to tooth structure without the use of adhesive monomers¹⁶. So it appears that although the course of dental materials development has produced a number of new technologies to improve dental restoration performance, challenges and issues still remain that encourage the consideration of new chemistries and compositions in restorative dentistry.

**DRAWBACKS OF CONVENTIONAL RESTORATIVE MATERIALS**

Porcelain bonded to metal and other substances like amalgam which do not follow biomimetic principles and do not attempt to restore the tooth’s natural properties. Gold is excessively stiff, thereby also not following biomimetic principles.As these materials also are not bonded with the existing tooth structure there is a higher likelihood of cracks, leakage and bacterial invasion causing further deterioration. This is then repaired with the same materials which fail again but with less tooth substance leading to tooth loss. Biomimetics prevents and stops the repair-replace-repair cycle of destruction and deterioration¹⁷.

Magne and other authors states that the occlusal stresses of the tooth should pass through the whole tooth with a strength bond. Without this bond the restoration will not be successful, Therefore producing high strength bonds from tooth to restoration and /or restoration to restoration is the key. Bonding technology and bond strengths have increased tremendously since it began. Buonocore started in 1955 and since then techniques and materials have developed. There is self etch, total etch, all in one bonding systems and a mixture of the different types. We know that the strongest bonds are in the total etch system with separate etch, prime and bond¹⁸.

There are some disadvantages with total etch technique. It is very technique sensitive. It has been noted that it works well in expert hands but less so in less experienced operators¹⁸.

**CLASSIFICATION OF BIOACTIVE MATERIALS**

Hench introduced some criteria for the evaluation of bioactivity of a material. However, a new classification was proposed in 1994 according to which bioactive materials are divided into 2 groups¹⁹:

**Class A:** Osteoproductive Materials In osteoproductive materials the bioactive surface is colonized by osteogenic stem cells. Class A bioactivity occurs when a material elicits both an intracellular and an extracellular response at its interface.eg: 45S5 Bioglass. These materials are both osteoproductive and osteoconductive.

**Group B:** Osteoconductive Materials The osteoconductive materials simply provide a biocompatible interface along which bone migrates. Osteoconductive bioactivity occurs when a material elicits only an extracellular response at its interface.eg: Synthetic hydroxyapatite (HA).

**COMPOSITIONAL AND MATERIAL ELEMENTS OF BIOMIMETIC/BIOACTIVE DENTAL MATERIALS**

There may be some regeneration or stimulation of dentine with certain dental materials. There are also materials that can actually remineralise dentine. These materials would be classified as being “biomimetic”. Biomimetic materials are materials used to restore the tooth which closely mimic enamel and dentine.Their composition is similar to natural teeth.. Most of these cements used in dentistry are fairly heterogeneous in their composition, and as such contain both silicate and aluminate components in varying proportions. Nevertheless, these materials can be considered in one of two groups: those containing predominantly silicate components versus those who contain predominantly aluminate components.²⁰

**CALCIUM SILICATE CALCIUM ALUMINATE**

MTA DOXADENT

BIODENTINE CERAMIC CROWN AND REPAIR

BIOAGGREGATE

ENDOSEQUENCE

CALCIUM PHOSPHATE SEALERS

IROOT B.P AND I ROOT S.Psealers

**CALCIUM SILICATE MATERIALS BASED ON MINERAL TRIOXIDE AGGREGATE (PORTLAND CEMENT)**



The calcium silicate-based cements were the ﬁrst to appear in dentistry and were focused primarily for use in endodontic therapy as a general root replacement material. The ﬁrst of these calcium silicate materials to appear and develop into a viable material for clinical use was mineral trioxide aggregate (MTA).Abedi and Ingle, Torabinejad et al. Torabinejad and White ﬁrst introduced MTA to dentistry and this material was ultimately demonstrated to be the ﬁrst of the bioactive cements to be adopted for use in endodontics and restorative dentistry.²¹

MTA is a biocompatible material with numerous exciting clinical applications in endodontics. MTA was first described in the dental scientific literature in 1993 by Loma Linda University as a root end filling material and was given approval for endodontic use by the U.S. Food and Drug administration in 1998.²²׳²³

**COMPOSITION**

The first MTA material was described as a fine hydrophilic powder composed predominantly of calcium and phosphorus ions, with added bismuth oxide to provide radiopacity greater than dentin. It appears that a significant change in composition has occurred since it was first proposed as a material for root-end filling and repairs of lateral perforations because newer study shows that calcium is the major component.²²׳²³

MTA materials are a mixture of a refined portland cement and bismuth oxide, and are reported to contain trace amounts of SiO2, CaO, MgO, K2S04, and Na2S04. The major component, Portland cement, is a mixture of tricalcium silicate (55%), dicalcium silicate (20%), tricalcium aluminate (10%), tetracalcium aluminoferrite (10%) and gypsum (5%). The principal components of MTA are Tricalcium oxide, Tricalcium silicate, Tricalcium aluminate, dicalcium silicate, tetracalcium aluminoferrite, bismuth oxide and calcium sulfate dihydrate. Gypsum is an important determinant of setting time, as is tetracalcium aluminoferrate although to a lesser extent.²⁴׳²⁵ It is important to emphasize Portland cement and MTA are not identical materials. MTA products have been reported to have a smaller mean particle size, contain fewer toxic heavy metals, have a longer working time, and appear to have undergone additional processing/purification than regular Portland cement.²⁶

|  |  |  |
| --- | --- | --- |
| **Chemical compositions of GMTA and WMTA (wt %)** | | |
| Chemical | WMTA | GMTA |
| CaO | 44.23 | 40.45 |
| SiO2 | 21.20 | 17.00 |
| Bi2O3 | 16.13 | 15.90 |
| Al2O3 | 1.92 | 4.26 |
| MgO | 1.35 | 3.10 |
| SO3 | 0.53 | 0.51 |
| Cl | 0.43 | 0.43 |
| FeO | 0.40 | 4.39 |
| P2O5 | 0.21 | 0.18 |
| TiO2 | 0.11 | 0.06 |
| H2O+CO2 | 14.49 | 13.72 |

**DIFFERENCE BETWEEN MTA AND PORTLAND CEMENT**

MTA materials have been reported to have a smaller mean particle size, contain less heavy metals, have a longer working time, and appears to have undergone additional processing and puriﬁcation than the Portland cement parent compound Further analysis with respect to major diﬀerences between MTA and Portland cement have indicated a presence of bismuth oxide in MTA, the ﬁneness of MTA powder, and the lower levels of calcium aluminate and calcium sulfate in MTA when compared with Portland cement.

**White MTA**

Earlier MTA was available only as gray coloured powder. In the year 2002 white mineral trioxide aggregate (WMTA) was introduced as ProRoot MTA to address esthetic concerns. Following this, two forms of MTA materials were categorized: the traditional gray MTA (GMTA) and WMTA. Scanning electron microscopy (SEM) and electron probe microanalysis of GMTA and WMTA found that the major difference between GMTA and WMTA is in the concentrations of Al203, MgO, and FeO.²⁵׳²⁷ When compaired to GMTA, WMTA was found to have 54.9% less Al2O3, 56.5% less MgO, and 90.8% less FeO, when compaired to GMTA. WMTA was also reported to possess an overall smaller particle size than GMTA, while it was also suggested that the reduction in magnesium could contribute to the lighter colour of WMTA.²⁸

|  |  |  |  |
| --- | --- | --- | --- |
| **Elemental analysis comparison of Portland cement and ProRoot WMTA (wt %)** | | | |
| Element | Portland Cement | WMTA | Patent |
| O | 48.1 | 38 | 30.5 |
| Ca | 40.3 | 37.1 | 37.2 |
| Si | 6.7 | 6.5 | 7.9 |
| Al | 2.1 | .6 | 1.7 |
| S | 1.5 | .9 | .8 |
| K | .9 | 0 | .3 |
| Mg | .3 | 0 | 1 |
| Fe | 1 | 0 | 2.8 |
| Bi | 0 | 16.9 | 17.9 |



**MANIPULATION**

MTA should be prepared immediately before its use. MTA powder must be kept in containers with tight lids and away from moisture. The MTA product powder is mixed with sterile water in a 3:1 powder/liquid ratio and it is recommended that a moist cotton pellet be temporarily placed in direct contact with the material and left until a follow-up appointment. The mixture can be carried in a plastic or metal carrier to the intended site of operation. Plastic or metal amalgam carriers, messing gun, Donovan carrier, spinal needles can be used to carry the material to the site. It should be condensed gently or can be termed as pressed in the site with moist cotton pellet. If the site is very wet the excess moisture can be removed with gauze. In cases where the mix is very dry, more water can be added to the mix. Because MTA needs water to set, leaving the material in a glass slab will dehydrate the material and a dry sandy mixture will be formed. After the use the material can be easily rinsed from the slab with running water.²⁵׳²⁹׳³⁰

Upon hydration, MTA materials form a colloidal gel that solidifies to a hard structure in approximately 3-4h, with moisture from the surrounding tissues purportedly assisting the setting reaction. Hydrated MTA products have an initial pH of 10.2, which rises to 12.5 three hours after mixing. The setting process is described as a hydration reaction of Tricalcium silicate (3CaO.SiO2) and dicalcium silicate (2CaO.SiO2).²⁹ Although weaker than other materials used for similar purpose, MTA compressive strength has been reported to increase in the presence of moisture for up to 21 days, while MTA product microhardness and hydration behaviour has been reported to be adversely affected with exposure to the pH range of inflammatory environments (pH 5) as compared to physiologic conditions (pH 7).³⁰׳³¹

**SETTING MECHANISM**

MTA is composed of hydrophilic powder, which reacts with water and sets by the process of hydration. MTA materials have been reported to solidify similar to other mineral cements, in which the anhydrous material dissolves, followed by the crystallization of hydrates in an interlocking mass. The basic framework of the hydrated mass is formed by the interlocking of cubic and needle-like crystals in which the needle-like crystals form in sharply delineated thick bundles that fill the inter-grain space between the cubic crystals.³² On hydration the Portland Cement produced calcium silicate hydrate gel and calcium hydroxide. Production of monosulphate phase and ettringite was also evident. The hydration of PC undergoes four stages namely the pre-induction period, the induction (dormant) phase, acceleration and post acceleration phase.

In the ***pre-induction period*** (first few minutes) a rapid dissolution of ionic species occurs. As a result of hydrolysis of the tricalcium silicates a calcium silicate hydrate (C-S-H) phase precipitates at the cement particle surface. Very little dicalcium silicate reacts at the initial stages of the reaction. Tricalcium aluminate dissolves and reacts with the calcium and sulphate ions present in the liquid phase producing ettringite that also precipitates on the cement particle surface.

The preinduction phase is followed by the ***induction (dormant) period*** (first few hours). The hydration of all the clinker minerals progresses very slowly. The silicate hydrate coating on the unreacted cement grains retards further hydration and leads to the 'dormant period' a period of 1-2 h of relative inactivity where the cement is plastic and workable. In this way a barrier is formed between the nonhydrated material and the bulk solution causing a rise in the concentration of dissolved ions in the liquid phase in immediate contact with the nonhydrated material. An initial set is initiated when the calcium silicate hydrate coating breaks up resulting in continuation of the hydration process. Ingrowth of calcium silicate hydrate fibers causes stiffening while increase in the volume of the solids decreases the porosity of the paste. The ettringite decreases the porosity of the paste. The ettringite deposited over the surface of the tricalcium aluminate further reduces the reaction of the tricalcium aluminate.Once the sulphate ions are depleted the ettringite layer is breakdown and is converted to monosulphate.

This is followed by the ***acceleration stage*** (3-12 h after mixing) where the progress of hydration accelerates again and is controlled by the nucleation and growth of the resultant hydration products. The rate of tricalcium silicate hydration increases and more calcium silicate hydrate gel is formed. The hydration of dicalcium silicate also increases at this stage. Crystalline calcium hydroxide (portlandite) precipitates from the liquid phase. The calcium ion concentration thus declines in the liquid phase.

Finally in the ***post-acceleration period*** the hydration rate slows down gradually as the amount of nonreacted material declines and the rate of hydration process becomes diffusion controlled. The silicate hydrate phase continues to be formed due to the continuing hydration of both the tricalcium and the dicalcium silicate. The supply of calcium sulphate becomes exhausted and as a consequence the ettringite phase formed in the early reaction starts being converted to monosulphate.

Mineral trioxide aggregate is composed mainly of Tri and di-calcium silicate. The MTA had a lower level of aluminate phase than is normally reported for white Portland Cement (PC). In the hydrated MTA the main reaction products are calcium silicate hydrate and calcium hydroxide. The low levels of tricalcium aluminate would also explain the low levels of ettringite and monosulphate found in hydrated MTA. Both ettringite and monosulphate are formed on hydration of the tricalcium aluminate in normal PC. The bismuth is present both as unreacted filler in the hydrated MTA and also form a part of the structure of the C-S-H. The microstructure of the paste appears to have been affected by the presence of bismuth: CH and C-S-H appears to be more closely intermixed. The large areas of calcium hydroxide present in the PC was absent in the MTA sample.³³

**Vehicles used for mixing MTA**

When MTA is mixed with different vehicles, there will be a difference in setting time and hardness. Three and five percent calcium chloride solutions, a water-based lubricant, chlorhexidine gluconate, disodium hydrogen orthophosphate and sodium hypochlorite gels decreased setting time; however final compressive strength was significantly lower than that obtained prepared with sterile water. Preparation with saline and 2% lidocaine anaesthetic solution increased setting time; but compressive strength was not significantly affected. Interestingly, a MTA product prepared with chlorhexidine gluconate gel did not set. It seems to reason that the setting reaction of MTA products, like its Portland cement parent compound is a hydration reaction; sufficient water in potential preparation liquids must be present for reaction. Furthermore, it should also be· intuitive that the chosen preparation liquid must also possess water with the necessary diffusion ability to be available for the hydration reaction.³⁴׳³⁵׳³⁶

**Antibacterial property**

WMTA and a ZOE preparation was found to have similar antibacterial properties against Staphylococcus *aureus, Enterococcus* *faecalis,* and *Pseudomonas aeruginosa* in a direct contact test, while substituting 0.12% chlorhexidine gluconate provided more antibacterial activity against *Actinomyces odontolyticus*, *Fusobacterium nucleatum*, *Streptococcus* *sanguis, E*. *faecalis, Escherichia coli, S*. *aureus, P*. *aeruginosa,* and *Candida* albicans than WMTA prepared with sterile water alone. This finding should be tempered with knowledge that MTA materials may not set .when mixed with some chlorhexidinepreparations. Both freshly mixed and set GMTA was reported to be inhibitory to *C. albicans* using an antifungal tube dilution method, while another study reported differences in that GMTA and WMTA at different powder/liquid mixtures were not equally effective at preventing the growth of *C .albicans.* Both WMTA and GMTA in concentrations of 50 and 25 mg/ml were equally inhibitive against *C.* *albicans* for upto 7 days; however, at lower concentrations only GMTA was effective.³⁷׳³⁸׳³⁹

**Compressive strength**

It is an important factor to consider when a filling material is placed in a cavity that bears occlusal pressure. MTA was introduced initially as root end filling material and these materials do not bear direct pressure, the compressive strength of these materials are not as important as those materials used to repair defects in occlusal surfaces. The compressive strength of MTA in 24 hours was found to be 40 MPa, but it gradually improves and increases upto 70 MPa in 21 days.⁴⁰

**Biocompatibility**

One of the greatest advantages of MTA is its biocompatibility. Numerous studies with various test methods and materials have been applied to evaluate biocompatibility. Principal methods are cytotoxicity tests on cell or tissue cultures or implantation into subcutaneous connective tissue or bone in experimental animals.⁴¹ After placement of MTA in root canals and its gradual dissolution, Ca ions are released that contribute to the formation of HA. These Hydroxyapatite crystals nucleate and grow, filling the microscopic space between the MTA and the dentinal wall. Initially, this seal is mechanical. With time, a diffusion controlled reaction between the apatite layer and the dentine leads to their chemical bonding. The result is the creation of a seal at the MTA-dentine interface. This leads to its excellent sealing ability and biocompatibility.²⁴

WMTA was more biocompatible than GMTA after 3 days and that GMTA was more biocompatible than WMTA after 7 days; however’ there-were no significant differences between their biocompatibility after 21 days.⁴² The cytotoxicity of GMTA, amalgam, ZOE, as well as positive and negative controls was measured using a cell viability assay for mitochondrial dehydrogenase activity in human periodontal ligament fibroblasts after 24-h exposure to extracts of varying concentrations of the test materials, in both freshly mixed and 24-h set states. In the freshly mixed state, the sequence of toxicity was amalgam> Super-EBA> MTA. In the 24-h set state, the sequence of toxicity at a low extract concentration was Super-EBA>MTA, amalgam; while at higher extract concentrations was Super- EBA> amalgam> MTA.⁴³

Sarkar et al conclude that MTA is not an inert material in a simulated oral environment; but it is bioactive. In contact with an STF, it dissolves, releasing all of its major cationic components and triggering the precipitation of HA on its surface and in the surrounding fluid. It appears to bond chemically to dentin when placed against it, possibly via diffusion controlled reaction between its apatitic surface and dentin. The clinical success of MTA, in terms of its saleability, biocompatibility, and dentinogenic activity is due to its physicochemical reaction.⁴⁴ Another study suggested that WMTA was more biocompatible than GMTA in supporting human cementoblast and keratinocyte growth.⁴⁵ Bonson et al, found that clinically derived human gingival fibroblasts and periodontal ligament fibroblasts survived and proliferated in the presence of MTA.⁴⁶ Balto found that human periodontal ligament fibroblasts attached to MTA within 4 hours before spreading over the surface over 24 hours.⁴⁷ In a study by sarkar et al on the physicochemical properties of the biological properties of MTA he concluded that, MTA is not an inert material in a simulated oral environment; its bioactive.²⁴

**Biomimetic properties of MTA**

Depending on its use and location MTA has the property of inducing the formation of dentine, cementum or bone. This is one of the prime reasons why MTA has been used extensively in almost every aspect of endodontic treatment. Also MTA has the ability to integrate with biological systems through a cellular pathway, which is the criterion to consider a material to be classified as biomimetic.

1. **Cells**

WMTA effect on dental pulp cell viability and proliferation has been evaluated using mouse MDPC-23 odontoblast like cells and OD-21 undifferentiated pulp cells. After 24-h exposure to WMTA apoptosis was not induced in either cell line, and WMTA was reported to cause DNA synthesis increase, suggesting a positive effect on cellular proliferation.⁴⁸ It has also ability to attract fibroblastic cells and to promote a favourable environment for cementum formation .⁴⁹ Also it has demonstrated that it has osseous and cementum conductivity effect.⁵⁰

Recently investigators compared the cellular response of Portland cement with other materials, including calcium hydroxide cement on cultured human pulp cells. The results suggested that Portland cement is biocompatible and allows the expression of mineralization-genes on cultured human pulp cells. These genes are responsible for inductive process on hard tissues bridge formation with MTA cement.⁵¹

1. **Signaling molecules**

MG-63 cultured human osteoblasts were exposed to GMTA and their cellular response evaluated via alkaline phosphatase activity as well as inflammatory cytokine and osteocalcin production. The MG-63 cells were found to adhere closely to the GMTA surface the cytokines that were responsible for osteoclast recruitment (M-CSF) and activation (IL-la, IL-113, IL-6) were found to be produced, along with observed osteocalcin production and alkaline phosphatase activity. This may be the reason that GMTA causes osteoblast adhesion with release of cytokines from the attached osteoblasts resulting in osteoclast activation via coupled resorption. MTA has the ability to stimulate cytokine release from bone cells has been demonstrated, indicating that it actively promotes hard tissue formation*.*⁵² It also act as a stimulus to the expression of alkaline phosphatase by fibroblasts.⁵³ Gunseli et al in his study concluded that, the production of BMP-2 and TGF beta-1could be two important contributors in the favourable biologic response stimulated by MTA products in human periapical tissues.⁵⁴ Torneck et al pointed out that the presence of large quantities of Ca ions in-vivo could activate ATP which playes a significant role in the mineralization process.⁵⁵ Rashid et al showed that Ca ions specifically elevate BMP-2 levels during pulp calcifications.⁵⁶ The study result of Gallas et al clearly demonstrates the osteoinductive capacities of MTA.⁵⁷ There is increased production of BMP-2 in the presence of MTA, and so the mineralization induction can be measured by BMP-2 expression in the Apexification procedures. He concluded that the exact biologic basis for MTA-induced regeneration of peridontium and healing of dental pulp is still a mater of extensive research.⁵⁸ It is also demonstrated that BMPs induce cementogenisis and periodontal ligament formation.⁵⁹

1. **Extracellular matrix.**

Recently investigation was done on the effect of MTA on the cytotoxicity and on the expression of bone extracellular matrix protein (Type I collagen, osteocalcin, and bone sialoprotein) during hard-tissue formation in osteoblastic MC3T3-E1.⁶⁰

Type I collagen, BSP and OCN take part in forming mineralized matrix.

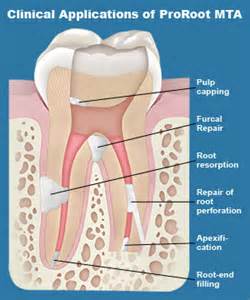
Type I collagen expression is an essential component of the extracellular matrix without which mineralized matrix cannot form (Keiser K et al). MTA down regulated type I collagen expression in rat bone-marrow cells. Type I collagen and alkaline phosphatase expression by cementoblasts at day 3 and 5 appeared on both the MTA and control substrate. In our study, Type I collagen expression by MC3T3-El was increased as compared to controls at 24 and 48 hours. These data suggest that MTA permits odontoblast gene expression.⁴³׳⁶¹ MTA caused an upregulation of OCN messenger RNA expression in MC3T3-E1 cells after 24 hours. The strong presence of OCN gene expression in both MTA and control cells suggests that the mineralization process can proceed under experimental conditions. This study agree with the report of Thomson et al and Koh et al who studied the production of OCN by osteoblastic cells in contact with MTA.⁶¹׳⁸³

BSP is also a major noncollagenous protein in mineralized connective tissues. The expression of BSP is highly specific for mineralizing tissues including bone, mineralizing cartilage, dentin, and cementum. In mineralized bone matrix, the highest BSP concentration is found in areas in which bone is newly synthesized or remodeled.⁶² BSP expression by MC3T3-El cells from 24 to *72* hours was evident· in MTA-treated and control cultures. Therefore, the study concluded that MTA can promote the early stages of bone matrix formation and mineralization.⁶⁰

GMTA has also been reported to be biocompatible with a murine cementoblast model, with the cementoblasts displaying ultrastructural attachment to GMTA surface with normal reverse transcriptase polymerase chain reaction analysis (RT-PCR) indicating osteocalcin production.⁶³

Fibronectin maintain the attachment between cells and the extracellular matrix components in both healthy and affected tissues, acting as a central core in cell adhesion and spreading. The fibronectin is a high molecular weight adhesive protein also involved in the repair process. The adhesive glycoprotein is important for cell migration, adhesion, proliferation and cellular differentiation.⁶⁴ MTA does not contain calcium hydroxide, but after its hardening, it contains calcium oxide that could react with tissue fluid to form calcium hydroxide. These calcite crystals attract fibronectin, which is responsible for cellular adhesion and differentiation.⁶⁵ According to Seux et al, after contact with pulp tissue, MTA presents some structures that are similar to calcite crystals found in calcium hydroxide. They attract fibronectin, which is generally responsible for cellular adhesion and differentiation.⁶⁶

**CLINICAL USES IN DENTISTRY**



MTA has been used as a capping material in mechanically exposed pulps, repair of root perforations, retrograde filling material, pulpotomy and apexification. Attempts have been made to use it as an obturating material also.⁶⁷

1. **Root-end restoration**

The ideal requirement of a root end filling material are, its ability to prevent micro-leakage, radiopacity , biocompatibility, material stability, potential for osseous repair and its ability tore-establishment of apical attachment apparatus.⁶⁸ Histological examination of biopsy specimens following the placement of root-end filling material in the periapical area reveals three types of tissue response: healing with reformation of the periodontal ligament; healing with fibrous tissue (scar); and moderate-to-severe inflammation without scar tissue. Resection of the root end results in an exposed dentinal root face surrounded peripherally by cementum with a root canal in the middle. When MTA is used as a root-end filling material, it directly contacts fibroblast, cementoblast, and osteoblast cells of the periodontal ligament. The deposition of cementum on the cut root face is considered a desired healing response and a prerequisite for the reformation of a functional periodontal attachment. When cementum deposition occurs it is generally seen from the circumference of the root end and proceeds centrally toward the resected root canal. This cementum provides a ‘biological seal,’ in addition to the ‘physical seal’ of the root-end filling, thereby creating a ‘double seal’. Many materials have been used for root-end filling, including amalgam, gutta-percha, zinc oxide–eugenol cements, glass ionomer cement, gold foil pellets, Cavit and composite resin.⁶⁹׳⁷⁰

The stimulatory effect of MTA on the biosynthetic activity of periradicular cells results primarily in stimulation of fibroblasts to lay down a fibrous connective tissue and rapid growth of periodontal ligament due to its high healing capacity. Hard tissue formation seems to be activated progressively from the peripheral root walls to the centre of the MTA. Two mechanisms could be suggested for the process leading to hard tissue formation over the MTA: either the fibrous connective tissue is calcified as the post surgical time interval is increased or cells undergoing differentiation into hard tissue forming cells are progressively migrating between MTA surfaces and fibrous connective tissue, activating mineralization from the periphery of the root walls to the centre of the MTA filling. It is suggested that if activation of cementogenesis occurs after MTA placement at the apex, mineralization of previously formed connective tissue might be excluded as the main mechanism of hard tissue formation.⁷¹

MTA has been reported to have less microleakage than Amalgam, zinc-oxide-eugenol (ZOE) preparation*,* and a conventional glass-ionomer material whenused as a root-end restoration following apical resection.⁷²׳⁷³׳⁷⁴׳⁷⁵ The minimal thickness for MTA to effectively seal the apical area has been investigated with one study reporting a placement thickness of at least 3mm, with another report stating a minimal of 4mm is required for significant microleakage prevention.⁷⁶׳⁷⁷

WMTA and GMTA have been compared for the sealing of simulated canals with open apices using thicknesses of 2 and 5mm followed by gutta percha obturation either immediately after MTA material placement or 24h later. Results found that GMTA had less microleakage than WMTA in samples obturated 24 h after MTA placement; in all groups 5mm of MTA material allowed less leakage.³² Invitro bacterial penetration study found that GMTA resisted S. macescens penetration for up to 49 days after inoculation while the amalgam and ZOE materials displayed trends for more bacterial penetration.⁷⁸ GMTA was also reported to allow significantly less E. coli endotoxin penetration using a modified Limulus Amebocyte Lysate test than amalgam and two ZOE preparations over a 12-week evaluation.⁷⁹ In contrast, GMTA was found to have the same bacterial penetration resistance as a ZOE preparation, amalgam, a bonded resin composite, as well as a bonded amalgam during a 12-week evaluation using Streptococcus salivarius.⁸⁰

When used as a root-end restoration in a canine model, GMTA was reported to be associated with significantly less periapical inflammation than amalgam at both 5 and 18 weeks after placement, with almost all of the GMTA specimens exhibited new cementum tissue growth on the GMTA surface. In another study, GMTA and an epoxy-based, root canal cement both exhibited excellent canine peri-radicular tissue response at 60 days with no statistically significant difference between the materials for new cementum, bone, or periodontal ligament formation. These results were corroborated by a report that evaluated the canine peri-radicular response to GMTA and a ZOE preparation which found the presence of periodontal ligament formation and hard tissue ingrowth on the GMTA surface.⁸¹׳⁸²׳⁸⁴ The result of another investigation comparing amalgam and MTA showed significant differences between the two materials. The use of MTA as root-end filling materials was associated with significantly less inflammation, cementum formation over MTA, and regeneration of the periradicular tissues to almost normal pre-experimental status.⁸⁴

Assessment of histological response associated with GMTA and ZOE as root-end filling material in teeth where the root canals where not filled and the coronal access cavity where not restored. Cementum formation was not found over ZOE specimens in any situations (open or closed). However, cementum was present over MTA in all specimens in both situations. MTA was the only material tested that induced formation of hard tissue, even when used in root-end cavities when the canal system was not filled and the coronal access was not restored.⁸⁵

1. **Repair of perforation**

Root perforation can occur during root canal therapy or post space preparation and also as a result of the extension of an internal resorption into the periradicular tissues. Perforation repair after an accidental procedure or as a consequence of an internal resorption can be achieved intracoronal and/ or by an external surgical approach. Material such as Cavit, ZNO, CH, Amalgam, Gutta-Purcha, Ticalcium Phosphate and HA have been used to repair root perforations.²²

For repair of furcation perforations, ZOE preparation was reported to provide a better seal than GMTA at 24 h, after which no difference in leakage was observed.⁸⁶ However, recently the ability of two mineral trioxide aggregate (MTA) compounds and Intermediate Restorative Material (IRM) to seal large furcation perforations is evaluated using a dye-extraction leakage method. Result showed that ProRoot MTA with and without internal matrix and MTA-Angelus with internal matrix showed the least dye absorbance. IRM without internal matrix showed the highest dye absorbance. IRM with internal matrix and MTA-Angelus without internal matrix had insignificant difference and came at intermediate level between the other groups⁸⁷ but clinical case study with MTA without matrix provides an effective seal of root perforations and clinical healing of the surrounding periodontal tissue.⁸⁸

The furcation perforation repair microleakage of GMTA and WMTA was compared from both an orthograde and retrograde direction. The results found no difference in leakage between the two MTA materials; but findings were that significantly more leakage was found from a microleakage challenge from an orthograde direction. This suggests an impelling need for an adequate coronal barrier material over MTA furcation repairs to adequately protect against coronal microleakage.⁸⁹ Influence of glass-ionomer cement on the setting of MTA using laser Raman spectroscopy (LRS) was also done. The result showed that glass-ionomer cement over MTA after 45 minutes did not affect its setting reaction and calcium salts may be formed in the interface of these two materials.⁹⁰ Another study was to assess the setting time and surface crazing of glass ionomer cement when layered over partially set mineral trioxide aggregate (MTA). The study concluded that the conventional glass ionomer cement might be layered over partially set MTA after 45 minutes and could be used for single visit procedures.⁹¹

When used as perforation repair materials, GMTA did not demonstrate any bacterial leakage during a 45-day evaluation while approximately half of the amalgam-repaired furcation allowed penetration and transmission of F.*nucleatum*.⁹² Furthermore, no significant difference was found between GMTA and WMTA in the resistance to F.*nucleatum* penetration when used for furcation repair.⁹³

For furcation repair, GMTA and amalgam were compared using a canine model using both an immediate- and delayed repair scenario. Endodontically treated teeth with standardized furcation perforations were repaired with both materials either immediately or after 6 weeks of salivary contamination. For the immediate-repair situation at 4 months, the amalgam samples were all associated with inflammation and no repair site cementum formation. The GMTA-repaired specimens were characterized by lack of inflammation with cementum formation noted in five of six specimens. For the delayed-repair group, half of the GMTA-repaired specimens were free from inflammation with cementum formation. The delayed-repair group with amalgam-restored specimens exhibited either moderate or severe inflammation. Although this study did not use statistical analysis, the authors concluded that GMTA had potential when used for furcation repairs.⁹⁴

GMTA was compared to a resin-based, calcium hydroxide root canal sealer repairing lateral root perforations at the junction of the middle and coronal thirds using a canine model. At 30 days, GMTA-treated samples displayed either cementum deposition and/or small areas of ankylosis adjacent to the perforation site. Furthermore, all areas were reported to exhibit little inflammation except for areas with GMTA overfill. However, the root canal sealer largely induced chronic inflammation and ankylosis, with localized periodontal ligament necrosis associated with overfilled areas, At 180 days, GMTA repaired specimens exhibited no ankylosis with most specimens exhibiting healing characterized by cellular cementum formation with PDL formation between the cementum and alveolar bone. In contrast, sealer repaired specimens exhibited some cementum formation but was associated with a chronic inflammatory response consisting of foreign body giant cells and macrophages. Although the authors reported that this study supported the use of GMTA for perforation repair, there was no statistical analysis of the data. The histologic response of canine-periapical tissues was reported comparing GMTA and a glass-ionomer material used as obturation materials. Six months after obturation, all root canals obturated with GMTA exhibited apical closure with new cementum formation, whereas only partial cementum closure was observed in a minority of the glass-ionomer materials. Although both materials were reported to exhibit good biocompatibility, the authors suggested that GMTA exhibited better biologic properties.⁹⁵׳⁹⁶

In one study, they examined the histological response of intentional perforations in the furcation of mandibular premolars of dogs repaired with MTA or amalgam. In the immediately repaired group, all the amalgam specimen where associated with inflammation, where as only one of 6 samples with MTA was inflamed. Furthermore, the 5 non-inflamed MTA specimens have some cementum over the repaired material.⁹⁴

1. **Apexification**

Root end closure, also known as Apexification, is defined as the process of creating an environment within the root canal and the periapical tissues after pulp death that allows a calcific barrier to form across the open apex. This barrier has been characterized as dentin, cementum, bone and osteodentine.  Calcium hydroxide has been used successfully to effect an apical barrier formation i.e. apexification in these teeth. However, the length of time required for this is variable, ranging from 3-18 months. This presents problems with patient compliance, re-infection due to loss of temporary restoration and also predisposes the tooth to fracture. A one step apexification procedure eliminates these problems. It implies the non-surgical compaction of a biocompatible material into the apical end of the root canal, thus, creating an apical stop and enabling immediate filling of the root canal. MTA has been described as a good material for this procedure owing to its good canal sealing property, biocompatibility and ability to promote dental pulp and periradicular tissue regeneration. Studies have reported that MTA root filling placed at the cemental limit showed better results than overfilling.⁹⁷׳⁹⁸׳⁹⁹

MTA was reported to produce both incomplete and complete barrier formation with mild tissue inflammation when used as an apexification medic

ament in a canine model. Specimens that were treated solely with WMTA were found to produce barriers within the root confines where as specimens treated first with calcium hydroxide had mostly incomplete barrier formation that were predominately extracanal, beyond the previous apical area. In a study comparing CH and MTA Omar et al concluded that MTA is superior to CH for the Apexification procedures.¹⁰⁰׳³⁶׳¹⁰¹

When used in the treatment of immature apices, GMTA has been reported to provide resistance to bacterial penetration by E. *faecalis* and s. epidermis but not Enterobacter *aerogenes*.¹⁰² A similar report reinforces GMTA resistance to .E. *faecalis* penetration with no leakage identified by E. *faecalis* 16S rDNA polymerase chain reaction assay after 10 days.¹⁰³ GMTA was also evaluated against Actinomyces viscous microleakage for up to 70 days in simulated immature apices that had received either a 2- or 5-mm apical GMTA restoration, or a series of 2-mm GMTA apical retrograde fillings. Results reported that only the 5-mm thick restoration resisted microleakage for the entire evaluation, and exhibited significantly less leakage compared to the positive control and other GMTA groups.¹⁰⁴ A study by Filippe et al concluded that, when used as an apical plug, MTA favour apexification and periapical healing, regardless of the previous use of CH paste.¹⁰⁰

Regardless of whether the Calcium Hydroxide (CH) was used or not apical repair and barrier formation occurred in 100% of case selected. This result are similar to those obtained by Shavaham et al, who observed apical closure with a calcified barrier in 93% of the roots treated with MTA after using CH pate for 1 week. It was possible to observe deposition of calcified tissue over the MTA. The cellular response to MTA and mechanisms of deposition for barrier formation need further investigation. It is believed that the deposition of hard tissue over the material is related to features such as good sealing ability, biocompatibility, and alkaline pH: the presents of Calcium an phosphate ion in its formulation; the capacity to attract blastic cells and to promote a favourable environment for cementum formation; osseous and cementum conductive effect; the stimulus to adhesion and self proliferation, stimulus to expressions of alkaline phosphatase by fibroblast.

Application of MTA immediately after RCT favoured the establishment of a normal periodontal ligament and formation of a new bone and cementum. The MTA in the presence of inflammation and exudate stimulated the formation of an apical barrier and hard tissue. The histological responses observed in this study indicate that the MTA is a reliable material and should be considered effective in teeth with incomplete root formation. Its application result in predictable apical closure and reduction of the treatment time, number of appointments and radiographs, particularly in young patients. Besides, it seems that treatment of teeth with incomplete root formation using MTA has another advantage compaired with CH treatment. Anderson et al 2002 showed that the fracture strength of immature teeth is markedly decreased following long-term CH treatment. The advantage of a material that promote the immediate formation of an artificial apical plug and that maintains the capability to induce apexification with time means that the definitive root filling can be placed immediately after the material sets.¹⁰⁰

1. **Pulp Capping**

The primary objective of pulp therapy is to maintain the integrity and the health of damaged teeth and its supporting tissues. Direct pulp capping invoves the application of medicament, dressing or dental material to the exposed pulp in an attempt to preserve its vitality. The rationale behind this treatment is to encourage the pulp to initiate reparative dentine formation at the exposure site. The success rate of this treatment is not particularly high in primary teeth. Many materials and drugs have been used as pulp capping agents. Calcium hydroxide has been the standard by which all others have been judged and has been accepted as the material of choice. But the disadvantages include the degradation of material over time, formation of tunnel defects and poor sealing.⁶⁹׳⁷⁰׳⁷¹ A number of new materials have been tested during the last two decades as alternative to CH. One of them is MTA, biocompatible non mutagenic cement and has good sealing ability.⁷⁸׳¹⁰⁵

In animal, canine model study reported that GMTA when used as a pulp-capping medicament induced an osteodentin matrix at 3 weeks that was typically observed with reparative dentin, while WMTA in a different study was reported to exhibit neodentinal bridge formation at 2 weeks with an ultrastructure intimate relationship observed between the pulpal tissues and the WMTA crystals.¹⁰⁶ WMTA and GMTA used as pulp capping agents were both reported to form calcified bridge formation in which all WMTA and a majority of the GMTA specimens exhibited complete calcified bridge formation with mild inflammatory reactions at 2 weeks.¹⁰⁵ In a rodent pulp capping model, GMTA was reported to induce complete hard tissue bridge formation at 2 weeks that stained positive for dentin sialoprotein.¹⁰⁷ A prospective study compared calcium hydroxide and GMTA as permanent dentition pulp-capping medicaments. The calcium hydroxide specimens were hallmarked by tissue inflammation with a 0.15-mm thick dentinal bridge with adjacent pulp tissue necrosis noted at 6 months. These findings were contrasted with GMTA specimens displaying mild tissue reactions with a 0.28~mm dentin bridge noted at 2 months, with 6-month specimens displaying 0.43mm dentin bridge formation, no pulp tissue inflammation, all associated with a near-regular odontoblastic layer.¹⁰⁸

A second prospective study compared WMTA and a calcium hydroxide preparation as direct pulp cap medicaments. Result suggests there is no significant difference was found between the groups in regards to the clinical presentation as well as the histologic status.¹⁰⁹ Tziafas et al also demonstrated the dentinogenic effect of the MTA in short term capping experiments.¹¹⁰Another study evaluated the histomorphological response of human dental pulps capped with MTA and C. It also concluded that MTA heals the pulp faster and form dentin bridge than the CH.¹¹¹Recently a histological, ultrastructural response of the human pulpal cells capped with MTA was investigated.

**One-week observation**

Five of the six samples were characterized by the' presence of a fibrous capsule in contact with the capping material and by the absence of pulpal inflammatory cells as well as of signs of necrosis.

**One-month observation**

Three of the six specimens revealed a complete hard tissue-bridge lining the pulp whilst the other three had a partial bridge. The pulpal cells lining the hard tissue barrier were mostly cuboidal, but also columnar cells were seen in some instances. TEM examination revealed cytoplasmic processes projecting into the bridge. There was no evidence of necrosis or inflammation between the dentinal bridge and the capping material, and the pulps of all the six samples were free from inflammatory cells.

**Three-month observation.**

Four of the five samples revealed complete hard tissue bridge lining the pulp and one specimen a partial bridge. The four specimens with complete bridges were devoid of pulpal inflammation. With respect to pulpal cellular response the MTA performed well in the current study. Superficial local accumulation of inflammatory cells was observed in only one sample out of 17. The pulps of the MTA specimens were dominated in all three observation periods by fibroblasts and almost lacked infiltrating inflammatory cells. Mostly cuboidal cells lined the dentinal bridge. The presence in some specimens of columnar cells with polarized nuclei and cytoplasm rich in rough endoplasmic reticulum projecting into invaginations of the bridge is clearly indicative of the formation of odontoblast like cells and initiation of tubular dentine.¹¹²

1. **Pulpotomy**

Pulpotomy is a therapeutic procedure, which consists of the surgical amputation of coronally inflamed pulp. The wounded surface of the radicular pulp is treated with a medicament or dressing agent to promote healing or to cause fixation of the underlying tissue. The objective is to maintain the vitality of the radicular pulp. Pulpotomy is a common procedure in the treatment of acutely inflamed primary teeth. It is also used in the management of young permanent teeth with open apices. Salako N Joseph studied Bioactive glass (BAG), MTA, ferric sulfate as pulpotomy agents in rat molar. They found that BAG induced severe inflammation in 2 weeks, sometimes irreversible. In 4 weeks there was some attempt to repair the inflammation. If the initial inflammatory response is overwhelming the resultant necrosis eliminated any chances of recovery. But 2 week old MTA showed dentin bridge formation and continues with time. Histologic reaction of vital pulp after the application of formocresol depends on the application time and the concentration used. The usual finding is a zone of necrosis followed by a zone of fixation. Beyond this, there is an inflammatory infiltrate, which gradually leads to normal pulp. Perfect healing without inflammation is not seen with formocresol.⁴²

GMTA and formocresol were compared as pulpotomy dressings in primary molars with carious pulp exposures, with only one reported failure (internal resorption in a formocresol treated specimen) in the 32 teeth available for evaluation ranging 6-30 months. Pulp canal obliteration was noted at a higher frequency in GMTA-treated specimens than that seen with formocresol.¹¹³ Another study compared GMTA, WMTA, and formocresol as pulpotomy dressings in primary teeth demonstrating radiographic caries pulpal involvement. GMTA as found to provide a significantly better outcome than WMTA, with no difference found between WMTA and formocresol.¹¹⁴ These results were contrasted by a different randomized, prospective study that compared formocresol and WMTA as pulpotomy medicaments in primary molars. At 24 months none of the WMTA-treated teeth exhibited clinical or radiographic pathology while the formocresol-treated teeth demonstrated approximately 13% radiographic and 2% clinical failure.¹⁰¹ Another longer (range 4-74, mean 38 months) prospective, randomized study found both formocresol and a MTA material equally successful statistically when used as pulpotomy dressings in primary molars with carious pulp exposures.¹¹⁵

GMTA and WMTA were evaluated as pulpotomy dressings for primary molars in two different short-term studies by the same group of researchers. The first reported that GMTA exhibited clinical success at 6 months with radiographic dentin bridges observed in 50% of the specimens.¹¹⁵ The second study found similar results with WMTA but radiographic analysis was limited only to the mandibular teeth. Result showed that 11.5% of the pulp canals exhibited dentin bridges.¹¹⁷ One clinical study reported GMTA as a pulpotomy medicament in 31 vital, cariously exposed, first molar permanent teeth. At 24 months, sixty-four percent of the specimens had pulpal radiographic hard tissue bridge formation, while seven teeth that initially presented with immature apices displayed radiographic signs of continued root development .¹¹⁸ The histologic pulpal response comparing WMTA to calcium hydroxide as pulpotomy dressings was investigated in premolar teeth extracted for orthodontic purposes, reporting that WMTA induced a more homogenous and continuous dentin bridge with less pulpal inflammation than calcium hydroxide at both 4 and 8 weeks after treatment.¹¹² Mineral trioxide aggregate was more successful than CH and formocresol for pulpotomies in primary molar teeth as none of the MTA-treated teeth showed any clinical or radiographic pathology. Calcium hydroxide shows internal resorption whereas cytotoxicity and mutagenicity where noted in formocresol.¹¹⁹

**SEALING ABILITY OF MTA**

Nakata et al. evaluated the ability of MTA and amalgam to seal furcal perforations in extracted human molars using an anaerobic bacterial leakage model.¹²⁰ Fogel and Peikoff observed that MTA was better than amalgam, IRM, a dentine-bonded resin and super-EBA in preventing microleakage.¹²¹All these studies prove that MTA is equivalent or superior in its sealing ability compared to contemporary root-end filling materials.

**CALCIUM SILICATE CEMENTS CONTAINING PREDOMINANTLY TRICALCIUM SILICATE**



BiodentineTM[[1]](#endnote-1). (Septodont Ltd., Saint Maur des Fausse ´s, France) is a new tricalcium silicate (Ca3SiO5) based inor-ganic restorative commercial cement and advertised as ‘bioactive dentine substitute’. Calcium silicate-based material has been recently developed to overcome some of shortcomings of MTA, which are difficult handling, long setting time, and potential discoloration. Calcium silicate-based material, which called Biodentine, was declared by dental materials manufacturer Septodont in September of 2010, and made available in January of 2011. This material is new biologically active cement which has dentine-like mechanical properties. It also can be used as a dentine replacement in the tooth crown and root region.¹²² The material is claimed to possess better physical and biological properties compared to other tricalcium silicate cements such as mineral trioxide aggregate (MTA) and BioaggregateTM (Bioaggregate).¹²³ As already seen the Portland-type cements designed for medicine and dentistry, also termed hydraulic silicate cements, mainly contain tricalcium silicate (3CaO-SiO2;C 3S), which is responsible for rapid setting, development of early strength, and exhibits higher reactivity than the other calcium silicates.¹²³ But MTA has more limited applications in other major indications in operative dentistry because of its long setting time and low compressive strength compared with other materials.. In order to improve these properties, a fast-setting, calcium silicate-based restorative material designed for expanded indications in restorative dentistry has been brought into the market (Biodentine, Septodont, St Maure des Foss’es, France).

**COMPOSITION OF BIODENTINE**

BiodentineTM is a powder and liquid system where the powder consists of tricalcium silicate, dicalcium silicate, calcium carbonate and oxide filler, zirconium oxide. Liquid contains aqueous solution of a hydrosoluble polymer (water reducing agent) with calcium chloride (decreases the setting time).¹²⁴ Septodont claims to use a new technological platform named ‘Active Biosilicate TechnologyTM’ to control the purity of the raw materials. Manufacturing pure synthetic tricalcium silicate instead of purifying the natural tricalcium silicate is advantageous as the mineral content is not changed by the sintering conditions or variations in the chemical composition of the raw materials.¹²⁴ Moreover, synthetic tricalcium silicate does not contain heavy metals contrary to puriﬁed natural tricalcium silicate.The use of pure synthetic tricalcium silicate instead of speciﬁc clinker has also been shown to result in enhanced material properties of BiodentineTM and BioaggregateTM in comparison to MTA.¹²⁵ Although tricalcium silicate appears to be a common ingredient in both MTA and BiodentineTM, X-ray diffrac tometry of unhydrated cements revealed that BiodentineTM consisted of triclinic form of tricalcium silicate while MTA consisted of the monoclinic form. Another difference would be the ﬁner particle size of tricalcium silicate in BiodentineTM as shown by the greater value of speciﬁc surface area of BiodentineTM (2.811 m2/g) in comparison to that of MTA (1.0335 m2/g).¹²⁵ The tricalcium silicate component is the primary constituent that undergoes the setting reaction. Calcium carbonate is incorporated for both its ability to decrease the setting time, biocompatibility, and its calcium content. The hydrosoluble polymer is based on polycarboxylate and maintains a balance between low water content and consistency of the mixture. This hydrosoluble polymer (water-reducing agent) functions therefore to maintain acceptable ﬂow properties with a low water/solid ratio.¹²⁶

**SETTING REACTION OF BIODENTINE**

The mixing of BiodentineTM powder and liquid results in a gel structure, allowing ionic exchanges and polymerisation over time to form a solid network. The reaction product consists of a cementitious phase containing tri- calcium silicate, a radiopaciﬁer phase comprising of zir- conium oxide, and it is seen that calcium carbonate acts as a nucleation site which allows the formation of reaction rims around it, thereby enhancing the hydration and producing a denser microstructure.¹²⁷ Setting of BiodentineTM is at least partially due to polymerization of the silicate phase to a Q2 chain-like structure, similar to that present in Portland cement but the setting kinetics are faster (12 min) in BiodentineTM.

The rate of the setting time is minimized with the use of calcium chloride and ﬁne particle sizes. The ﬁnal setting time of Bioden tineTM is assessed to be 45 min. An initial volume reduction due to chemical contraction and capillary absorption occurs during the ﬁrst hours followed by a secondary expansion due to continuation of the hydration process. The set BiodentineTM consists of 5ml round particles embedded in a calcium silicate hydrate matrix.¹²⁸ A dense microstructure is seen in set BiodentineTM as the porosity is almost ﬁlled by calcium silicate hydrate and calcium hydroxide. An isothermic calorimetry analysis performed at 37 C to follow the kinetics of hydration of the cement paste revealed the following; BiodentineTM paste displayed a narrow and intense exothermic peak after 30 min, whereas pure tricalcium silicate paste displayed a broad exothermic peak after 210 min. This indicates that BiodentineTM has greater kinetics of hydration than pure tricalcium silicate. The early exothermic peak after 30 min is also an indicator of the rise of mechanical strength of the set BiodentineTM cement.¹²⁹

Energy dispersive X-ray spectroscopy (EDX) analysis of set BiodentineTM conﬁrmed elemental peaks for calcium, silicon, carbon, oxygen, zirconium and chlorine with zirconium concentrated in speciﬁc areas while all other elements were equally distributed. X-ray diffraction (XRD) analysis exhibited deﬁnite peaks for calcium silicate, calcium carbonate, zirconium oxide and calcium hydroxide with a wavy base line indicating the presence of an amorphous compound. Fourier transform infrared spectroscopy (FT-IR) analysis of set BiodentineTM showed peaks at 3,400 (water or calcium hydroxide), 700 and 1,420 cm-1 (calcium carbonate) and an Si–O absorption band at 960 cm-1 referring to calcium silicate hydrate.¹³⁰

**MANIPULATION OF BIODENTINE**

Both parts, powder and liquid, are provided in separate single-dose units. The liquid is provided in a sealed ampule, which after opening is dispensed into a plastic trituration capsule containing the powder. Five drops of liquid are added to the powder in the plastic mixing capsule. The capsule is resealed and titurated for 30 seconds at 4,000 to 4,200 rpm in a conventional titurator. The mixing Biodentine paste is then applied to the tooth without requiring any prior surface treatment. The working time for the material is reported to be 6 minutes and the ﬁnal setting time of approximately 10 to 12 minutes.¹³¹ Thus, it appears that the setting time for Biodentine is signiﬁcantly faster than either MTA or modiﬁed MTA materials such as BA and more in line with setting times displayed by conventional restorative cements such as zinc phosphate and GI.¹³²

Biodentine has been shown to be biocompatible. It is also bioactive and demonstrates the deposition of hydroxyapatite on its cement surface in the presence of simulated body ﬂuid. Its radiopacity was greater than 3-mm aluminum thickness. Biodentine caused the uptake of calcium (Ca) and silicon (Si) in the adjacent root canal dentin in the presence of physiological solution.¹³¹

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**PHYSICAL PROPERTIES**

The compressive strength of BiodentineTM amounts to 10.6 ± 2, 57.1 ± 12 and 72.6 ± 8 MPa after 35 min, 24 h and 28 days, respectively.¹²⁷ The greater strength of BiodentineTM in comparison to other tricalcium silicate cements is attributed to the low water/cement ratio made possible by the water soluble polymer in the liquid. The physical properties of BiodentineTM such as ﬂexural strength (34 MPa), elastic modulus (22,000 MPa) and Vickers hardness (60 HV) are higher than those of MTA but similar to dentine.¹³³BiodentineTM is reported to be more dense and less porous when compared physical properties of Biodentine, BA, and Intermediate Restorative Material (IRM) were evaluated by Grech et al.¹²⁷ Using the testing procedures described in the International Organization for Standardization, International Standard, ISO 9917-1; 2007,88 these investigators found that Biodentine exhibited superior compressive strength values of these three materials tested, with mean compressive strength values, after 28 days immersion in Hanks balanced salt solution, for Biodentine of 67.18 MPa, for BA of 16.34 MPa, and for IRM of 20.38 MPa. Setting time, again using the testing procedure set out in ISO 9917-1; 2007, gave values for the materials as follows: Biodentine, 45 minutes; BA, 1,260 minutes, and IRM, 3 minutes.

**BIOCOMPATIBILITY OF BIODENTINE**

Material biocompatibility was investigated by Ames’ testing and was determined to be nonmutagenic; the material did not interfere with lymphocyte cell function, exhibited a lack of cytotoxicity similar to MTA, and did not alter pulpal ﬁbroblast function with respect to mineralization.¹³²׳¹³⁴

**BIOACTIVITY OF BIODENTINE**

Biodentine considered as bioactive material. Goldberg described the bioactivity of this material, demonstrating the formation of apatite when immersed in phosphate solution. About et al. investigated Biodentine bioactivity by studying its effects on pulp progenitor cells activation, differentiation and dentine regeneration in human tooth cultures. They concluded that Biodentine is stimulating dentine regeneration by inducing odontoblast differentiation from pulp progenitor cells.¹³⁵ Laurent et al. investigated the capacity of Biodentine to induce reparative dentin synthesis by modulating pulp cells to secrete transforming growth factor-beta 1 (TGF-ß1) and stimulate human dental pulp mineralization.¹³⁶

**ANTIBACTERIAL PROPERTIES**

During the setting phase of Biodentine, calcium hydroxide ions are released from the cement. This results in a pH of about 12.5 and a basification of the surroundings. This high pH inhibits the growth of microorganisms and can disinfect the dentine.¹³⁷

**SEALING ABILITY AND SUCCESS**

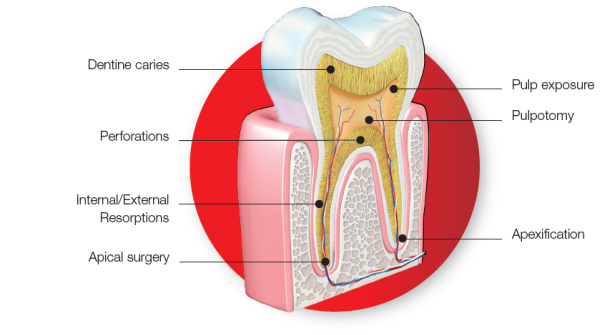
Biodentine is stronger mechanically, less soluble and produces tighter seals. This qualifies it for avoiding three major drawbacks of calcium hydroxide, i.e. material resorption, mechanical instability and the resultant failure of preventing microleakages.

Pradelle Plasse et al. found that Biodentine causes alkaline corrosion on the hard tissue, which leads to a so-called “mineral interaction zone”. Due to remodelling processes, the sealing of the dentine by Biodentine improves in the course of time. They reported that Biodentine can deposit impermeably onto the cavity walls and prevents microleakage.¹³⁸

**CLINICAL APPLICATONS OF BIODENTINE**

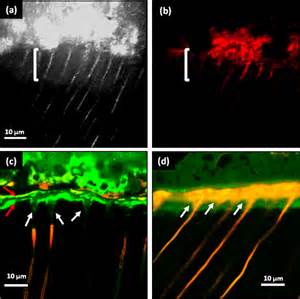
Biodentine was developed as a multipurpose, dentin, and root replacement material. Nevertheless, some of its clinical indications go beyond those of MTA and related Portland cement/calcium silicate products. These new indications include restoration of deep and large coronal carious lesions, restoration of deep cervical and radicular lesions, as well as the well established MTA indications such as pulp capping and pulpotomy, repair of root perforations, furcation perforations, perforating internal resorptions, external resorption, apexiﬁcation, and root-end ﬁlling in endodontic surgery.¹³⁹

1. BiodentineTM could be used as a dentine substitute for permanent dentinal treatment of posterior teeth for up to 6 months. The use of BiodentineTM in treatment modalities (follow-up period indicated in parenthesis) such as deep cari ous lesion (4 months),¹⁴⁰ direct pulp capping after iatrogenic pulp exposure (6 months)¹⁴¹׳¹⁴²and cervical and apical external root resorption (15 months) ¹⁴³ has been reported to show successful healing without any clinical or radiological symptoms... The wide range of documented use in pulp therapy involves direct pulp capping, indirect pulp capping and pulpotomy in both carious as well as traumatized teeth.

   **BIOACTIVITY AND INTERACTIONS WITH DENTIN AND THE PULP**

   The interfacial properties of BiodentineTM and a glass-ionomer cement (GIC Fuji IXGP) with dentin have been studied using confocal laser scanning microscopy (CLSM), scanning electron microscopy (SEM), micro-Raman spectroscopy, and two-photon auto-fluorescence and second harmonic-generation (SHG) imaging by Atmeh et al.¹⁴⁴ Their results indicated the formation of tag-like structures alongside an interfacial layer called the “mineral infiltration zone” where the alkaline caustic effect of the calcium silicate cement’s hydration products degrades the collagenous component of the interfacial dentin. This degradation leads to the formation of a porous structure that facilitates the permeation of high concentrations of Ca2+, OH−, and CO32−ions, leading to increased mineralization in this region. Comparison of the dentin– restorative interfaces shows that there is a dentin- mineral infiltration with the BiodentineTM, whereas polyacrylic and tartaric acids and their salts lead to the diffuse penetration of the GIC; consequently a new type of interfacial interaction, “the mineral infiltration zone”, is suggested for these calcium-silicate-based cements.

   **DIFFERENCE BETWEEN MTA AND BIODENTINE¹⁴⁵**

   |  |  |
   | --- | --- |
   | **MTA** | **BIODENTINE** |
   | Manufactured naturally from raw materials | Manufactured synthetically |
   | Contains gypsum acts as a retarder | Does not contain gypsum |
   | Do not contain calcium chloride | Contains calcium  chloride |
   | Slow setting | Fast setting |
   | Bismuth oxide | Zirconium oxide |
   | Push out bond strength is lower | higher |
   | porous | More dense less porous |
   | Contain heavy metals | Do not contain heavy metals. |
   | Triclinic form of tricalcium silicate | Monoclinic form of tricalcium silicate |
   | Exothermic peaks at 210 minutes | Exothermic peak at 30 |
   | Amount of calcium release as well as depth is less for mta | More for biodentin |
   | Mean thickness of dentin hard tissue for mta is 230.31 | For biodentine is 211.56 |
   | Physical properties are less | Physical properties are more |

   **BIOAGGREGATE**

   BioAggregate is new generation of a root canal repair filling material. The manufacturer claimed that BioAggregate is produced under controlled conditions to form contamination- free ceramic nano-particles. According to manufacturer, BioAggregate is developed as a result of utilizing the advanced science of nano-technology to produce ceramic particles that, upon reaction with water produce biocompatible and aluminum-free ceramic biomaterials. ¹⁴⁶

   BioAggregate has excellent handling characteristics after mixing with water, which aids in a repair process of the affected tooth. BioAggregate’s radiopacity properties, convenient setting and hardening time and easy workability and handling properties make it an ideal root canal filling material. As stated by manufacturer, the working time of BioAggregate is at least 5 minutes. Upon mixing a thick paste-like mixture is formed. If additional working time is required, simply cover the mixture with a moist gauze sponge while unattended.

   **COMPOSITION OF BIOAGGREGATE**

   Bioaggregate is composed of calcium silicate oxides and calcium silicate. Also present are hydroxyapatite, calcium phosphate silicate, calcite, and tantalum oxide as a radiopaciﬁer. In contrast with Portland cement, MTA, and related products, BA is reported to be free of calcium aluminate Furthermore,¹⁴⁷ BA is also reported to contain the addition of higher levels of phosphate in contrast with the minimal phosphate levels found in Portland cement and MTA.Therefore, most of the constituents of BA are the same as that in WMTA except that BA is aluminum-free, uses a diﬀerent metallic oxide as an opaciﬁer, and has added phosphate constituents such as hydroxyapatite.¹⁴⁸

   **SETTING REACTION OF BIOAGGREGATE**

   The BioAggregate powder promotes a complicated set of reactions upon mixing with BioA Liquid (deionized water), which leads to the formation of a nano-composite network of gel- like calcium silicate hydrate intimately mixed with hydroxyapatite bioceramic, and forms a hermetic seal when applied inside the root canal as prescribed by Manufacture. This is also supported by Grech et alwho investigated the composition of materials and leachate of a hydrated prototype cement composed of tricalcium silicate and radiopacifier¹⁴⁷׳¹⁴⁹

   **PROPERTIES OF BIOAGGREGATE.**

   Tuna et al. assessed the long-term fracture resistance of human immature permanent teeth filled with BioAggregate, MTA and calcium hydroxide. They suggested that BioAggregate-filled immature teeth demonstrate higher fracture resistance than other groups at 1year.¹⁵⁰ Considering the long-term risk of cervical root fracture associated with immature teeth, the use of BioAggregate as a root canal filling material appears to be the most advantageous of the materials tested.¹⁵¹

   **Biocompatibility and cytotoxicity**

   BioAggregate is more biocompatible than any other root end filling and repair materials. It does not produce any adverse side effects on microcirculation of the connective tissue. It also has excellent biocompatibility with the vital periradicular tissue.¹⁵²׳¹⁵³

   **Bioactivity**

   Shokouhinejad et al. evaluated the bioactivity of BioAggregate, ERRM, and MTA. They concluded that exposure of MTA, BioAggregate and ERRM to PBS resulted in precipitation of apatite crystalline structures that increased over time. This suggested that the tested materials are bioactive.¹⁵⁴

   **Sealing ability**

   Leal et al compared the ability of Ceramicrete, BioAggregate and MTA to prevent glucose leakage through root-end fillings. They concluded that both endodontic bioceramic repair cements displayed similar leakage results to white MTA when used as root-end fillings materials.¹⁵⁵׳¹⁵⁶

   **CLINICAL APPLICATIONS**

   BioAggregate is a biocompatible pure white powder composed of ceramic particles. Upon mixing, the hydrophilic BioAggregate Powder promotes cementogenesis and forms a hermetic seal inside the root canal. It is effective in clinically blocking the bacterial infection, its ease of manipulation and superior quality makes BioAggregate the most innovative and unique root canal repair material. According to manufacturer, the BioAggregate is indicated for repair of root perforation, repair of root resorption, root end filling, apexification, and pulp capping.¹⁵⁷

   **ENDOSEQUENCE ROOT REPAIR PUTTY MATERIAL**

   Endosequence Root Repair Material Brasseler USA (Savannah, GA) has recently introduced the EndoSequence Root Repair Material (RRM) and EndoSequence Root Repair Putty (RRP), which use bioceramic technology to address some of the inconsistencies associated with conventional MTA. These new materials are produced as a premixed product to provide the clinician with a homogeneous and consistent material.¹⁵⁸

   **CHEMICAL COMPOSITION AND CHARACTERISTICS**

   ERRM is composed of calcium silicates, monobasic calcium phosphate, zirconium oxide, tantalum oxide, proprietary fillers and thickening agents.The material has nanosphere particles with a maximum diameter of 1 x 10³ µm that allow for the material to enter dentinal tubules, be moistened by dentine liquid, and create a mechanical bond upon setting .This material has been manufactured to overcome some of the difficult handling characteristics of MTA.

   Particle size has been shown to affect the early strength of a material. The particle size also affects the ease of handling, which is clinically relevant. ProRoot white MTA and white AMTA particle sizes have been reported anywhere from less than 1 to approximately 30 µm.¹⁵⁹ In comparison, both of the new bioceramic materials from Brasseler report their largest particle size of 0.35 µm, with approximately 50% of the particles being nano (1 X 10-3 µm) in size .The drastic reduction in particle size introduced with the Brasseler products directly addresses one of the chief complaints of MTA users i.e. handling characteristics.

   They have excellent physical and biological properties and are easy to work with. They are hydrophilic, insoluble, radiopaque, aluminum-free, and of high pH – 12.8 .Presence of moisture is required for the materials to set and harden. ¹⁶⁰

   **Bioactivity**

   This material is bioactive due to its ability to form a hydroxyapatite or apatite-like layer on its surface when it comes in contact with phosphate-containing fluids.¹⁵⁴ Hansen et al. compared the diffusion of hydroxyl ions for ERRM and WMTA through root dentine. They found that although both materials showed diffusion of ions through dentine, the effect was less pronounced and of shorter duration for EndoSequence than WMTA.¹⁶¹

   **Biocompatibility and Cytotoxicity**

   As stated the manufacturer, the ERRM is able to bond to adjacent dentine, to have no shrinkage, and to be highly biocompatible. AlAnezi et al. used cultured mouse fibroblast cells to determine the cytotoxicity of ERRM as compared with gray and white MTA and found that both set and fresh samples showed no significant cell viability differences.¹⁶² Damas et al. compared the cytotoxic effect of 2 brands of white MTA (ProRoot MTA and MTA- Angelus), ERRM by using human dermal fibroblasts. They concluded that the ERRM have similar cytotoxicity levels to those of ProRoot MTA and MTA-Angelus.¹⁵⁹ Ciasca et al. concluded that ERRM and MTA showed similar cytotoxicity and cytokine expressions.¹⁶³

   **Sealing Ability**

   Hirschberg et al. compared the sealing ability of MTA to the sealing ability of ERRM using a bacterial leakage model. They concluded that Samples in the ERRM group leaked significantly more than samples in the MTA group.¹⁶⁴

   **Antibacterial Activity**

   Lovato and Sedgley investigated the antibacterial activity of ERRM against Enterococcus faecalis. They found that ERRM and white ProRoot MTA demonstrated similar antibacterial efficacy against clinical strains of E. faecalis. This research again validated earlier studies that found ERRM displayed similar in vitro biocompatiblity to MTA.¹⁶⁵ Additionally, other study found that the ERRM had cell viability similar to Gray and White MTA in both set and fresh conditions .

   **Clinical applications**

   This premixed bioceramic materials recommended for perforation repair, apical surgery, apical plug, and pulp capping.¹⁶⁶

   **RESTORATIVE MATERIALS BASED ON CALCIUM ALUMINATE**

   Similar to the calcium silicate cements (CSCs), the calcium aluminate cements (CAC) are also derived from the class of cements called “hydraulic” or natural cements. Their hydrating solution is water with 30 to 90 ppm lithium to accelerate the hardening process. A typical CAC contains prereacted constituents as follows: Al2O3 =43%; CaO=19%; H2O=15%; ZrO2 =19% (silicon, iron, magnesium, titanium, and alkali oxides less than 10%). The calcium aluminate undergoes very rapid hydration with a setting reaction at a pH of 11.4 to 12.5 and the formation of the reaction products Katoite and Gibbsite.¹⁶⁷The chemical reaction forming the CAC is depicted as follows:

   |  |
   | --- |
   | 3CaO Al₂O₃ + 12H₂O  Calcium Aluminate Water  → Ca[Al(OH)₄]₂(OH)₄ + 4Al(OH)₂  Katoite Gibbsite |

   Mechanically, water dissolves the calcium aluminate powder with the subsequent formation of calcium ions calcium ions (Ca2+), aluminum hydroxyl ions (Al(OH)4-, and hydroxyl ions (OH-). This activity is then ¹followed almost immediately by precipitation of new solid phases (Katoite and Gibbsite) as the solution reaches saturation. These precipitates grow until they meet, and a connected cluster of hydroxide particles is formed continually. Crystallization of the phases proceeds and the hydrates grow in size from nanometers (nm) to microns (μm).¹⁶⁷

   There have been two speciﬁc restorative dental products that have appeared to date based on calcium aluminate chemistry: one as a direct restorative material (Doxadent [DD], Doxa Dental AB, Uppsala, Sweden),2 and one as a luting cement (Ceramir [CM] Crown & Bridge, Doxa Dental AB).

   **USE OF CALCIUM ALUMINATE AS A DIRECT DENTAL RESTORATIVE MATERIAL**

   Clinical use of predominantly CACs appear approximately 8 to 10 years after the ﬁrst documentation of mineral trioxide aggregate (MTA)/calcium silicate/Portland-type cements use in dentistry. DD was a powder-liquid two-component CAC composed of a powder component containing calcium aluminate powder and other components described later, and a liquid component containing water and an accelerator comprising a lithium salt. The material is inorganic and nonmetallic, and the main components are CaO, Al2O3, SiO 2, and water.¹⁶⁸ DD was described in its 510-K approval to market document from the Federal Food and Drug Administration as a “dental ceramic composed of CAC and oxides that is intended to restore carious lesions or structural defectsin teeth.” More speciﬁcally, this restorative cement was described as composed of CAC and oxides, i.e., silica and zirconium oxide (as well as iron oxide as a colorant), as a ﬁller material, and a blend of ﬁne, irregularly shaped particles ranging from 0.5 to 5.0 μm in diameter, and microﬁne particles having a diameter from 0.02 to 0.2 μm. DD was intended for use as a restorative dental material for the permanent restoration of Class I, II, and V cavity preparations.¹⁶⁸

   **DISPENSING**

   The product was presented in a two-component form comprising a tablet that was saturated in a plastic well with a speciﬁc amount of the liquid component. The wet tablet was then condensed into the cavity preparation.¹⁶⁹

   **PHYSICAL PROPERTIES**

   Physical properties of this material have been described by several researchers. The ﬁrst published research report dealt with some important mechanical properties (hardness, dimensional stability, compressive and ﬂexural strength) of an experimental version of a translucent calcium aluminate dental restorative material. All samples investigated have been made from prepressed tablets, with a compaction degree of approximately 60%, hydrated using a 0.15 wt% Li salt solution as an accelerator. The samples were stored in water at 37°C between the measurements. ¹⁶⁹

   As reference materials, one composite, Tetric Ceram, and one glass ionomer, Fuji II, were used with specimens prepared according to the manufacturer’s recommendations. For the reference materials, some of the properties were published data. Vickers hardness for this novel material ranged from 87.1 HV for a coarse ﬁller to 102 HV for a ﬁne ﬁller, and compared with Tetric Ceram (a composite resin) at 71 and 59 HV for Fuji II (a glass ionomer).¹⁷⁰ Compressive strength (CS) using specimen rods 7.5 mm in length and 4 mm in diameter yielded a mean value of 182±12.5 MPa as compared with 300 MPa for Tetric Ceram and 160 MPa for Fuji II (based on technical documentation cited by the authors). Flexural strength was reportedly measured according to ASTM F394 standard for ceramic materials using a circular plate of the material supported on three balls and loaded in the center of the plate by a fourth ball on the opposing side until fracture occurs. Specimens were stored in distilled water at 37°C for 14 days prior to testing.¹⁷¹

   Using this method, mean, Inc.28ﬂexural strength for the calcium aluminate material was 106±28.8 MPa as compared with 142 and 41 MPa for Tetric Ceram and Fuji II, respectively. Expansion values for the material ranged from 0% to 0.1%, to 0.1% to 0.2% for the ﬁne and coarse ﬁller grain materials, respectively. The authors concluded that “the results showed that the calcium aluminate material has suﬃcient mechanical properties to be used as a permanent dental restorative taking as a reference the International Standard Organization (ISO) 9917 and the ISO 4049 as well as the reference materials. In addition the results indicate that the mechanical properties are controlled by the microstructure, which is mainly determined by the grain size of the ﬁller.”¹⁶⁷

   In another research paper describing the physical properties of the calcium aluminate restorative material (now termed a CBC), Lööf et al. report on the diametral tensile strength (DTS). ﬂexural strength, and CS of this calcium aluminate material (believed to a DD) compared directly with dental amalgam (Disperalloy, DeTrey Dentsply, York, PA, USA) and a glass ionomer restorative (Chemﬂex, DeTrey Dentsply).¹⁶⁷ In contrast with the method for CS cited in the study described previously in this review, the CS method in this report was conducted according to ISO 9917; 1991 (cylinder specimen dimensions of 6-mm length by 4-mm diameter). Strength values for were obtained at a variety of time points ranging from 1 hour to 4 weeks. Diametral tensile and ﬂexural strength values, in this study, were in a similar range for both the CBC material (calcium aluminate-based) and the glass ionomer material (Chemﬂex) but lacked a corresponding comparison with Disperalloy, having only data at 1-hour time frame. CS values for the CBC-calcium aluminate were reported as 139.7±20 MPa at 24 hours but increased signiﬁcantly to 197.1±17 MPa at 1 week and 258±12 MPa at 4 weeks.

   Sunnegårdh-Grönberg et al. also evaluated the physical properties of DD in a series of publications. The aim of the ﬁrst study was to compare a new ceramic restorative cement for posterior restorations, DD, with other types of tooth-colored materials for direct use as regards to hardness and in vitro wear.¹⁷² Four hybrid resin composites (RCs)—one polyacid-modiﬁed RC,one resin-modiﬁed glass ionomer (RMGI) cement, one conventional glass ionomer cement (GIC), and one zinc phosphate cement, an experimental version as well as the marketed version of the ceramic restorative cement—were investigated. Hardness of the materials was tested with the Wallace indentation tester, and wear was tested with the Academic Centre for Dentistry Amsterdam wear machine. All tests were carried out on 2-week-old specimens. DD was as hard as the zinc phosphate cement and the hardest RC. The ceramic restorative cement wore signiﬁcantly more than the RCs, the same as the zinc phosphate cement, and less than the GICs. No correlation between hardness and wear was found. It was concluded by the authors that the ceramic restorative cement (DD) is a rather hard material but with a relatively low wear resistance.

   An additional study by this group was conducted to compare this new restorative cement intended for posterior restorations, DD, with other types of tooth-colored materials with regards to ﬂexural strength and ﬂexural modulus. Four hybrid RCs—onepolyacid-modiﬁed RC, one RMGI cement, one conventional GIC, one zinc phosphate cement, and an experimental version as well as the marketed version of DD—were investigated. Flexural strength and ﬂexural modulus were tested according to ISO standard 4049 and determined after 1 day, 1 week, and 2 weeks. Together with the zinc phosphate cement, DD had the lowest ﬂexural strengths (13–22 MPa). The strongest materials were the RCs and the polyacid-modiﬁed RC (83–136 MPa). The highest ﬂexural modulus was found for DD (17–19 GPa). The ﬂexural strength of DD decreased signiﬁcantly from 1 to 2 weeks, whereas ﬂexural modulus remained unchanged. The other materials reacted in diﬀerent ways to prolonged water storage. ¹⁷²

   It can be concluded that the restorative cement DD had signiﬁcantly lower ﬂexural strength and signiﬁcantly higher ﬂexural modulus than today’s materials used for direct posterior restorations.

   Another group also investigated the physical properties of the CAC, DD.¹⁷³ This study compared in vitro the mechanical properties of a directly placed ceramic restorative material (DD) to glass ionomer (Fuji IX), hybrid composite control (Z250), and amalgam control (Tytin). DTS, CS, and Vickers hardness number (VHN) were measured for 10 specimens per group (N=480 total) with time (1 hour, 24 hours, 1 week, 4 weeks). CS and DTS specimens were loaded to failure (Instron, Rate of Strain=0.5 mm/minute). VHN discs were indented. Data were analyzed using analysis of variance (ANOVA) and Tukey’s test (p < 0.05) for pairwise comparisons of group means at each time. The CS of DD, in this in-vitro study, ranged from 44±6 MPa at 1 hour to 63±10 MPa at 24 hours, yet increased signiﬁcantly at 1 week to 118±9, and appeared to level at 4 weeks at a CS of 120±11 MPa. DTS for DD ranged from 7±1 at both 1 and 24 hours, and also increased signiﬁcantly at 1 and 4 weeks to 14±3 MPa and 15±3 MPa, respectively. Vickers hardness values increased progressively from 52±4 at 1 hour to 95±2 at 4 weeks. The investigators concluded from their ﬁndings that for CS and DTS, DD was weakest (p < 0.05) for all testing times except Fuji IX DTS at 1- and 4-week intervals. For VHN, DD was harder than glass ionomer, better than composite except at 1hour and less than amalgam. Except for VHN for Z250, all values improved from 1 to 24 hours. Based on current in vitro results, this novel restorative material does not yet equal composite or amalgam CS or DTS.¹⁷³

   The cytotoxic eﬀects of DD were compared with several currently used direct restorative materials.¹⁷⁴ 11 Specimens of three composites (QuiXﬁl, Tetric Ceram, Filtek Supreme)—one zinc phosphate cement (Harvard Cement), one GIC (Ketac Molar), and the CAC (DD)—were used fresh or after 7-days of pre-incubation in cell culture medium at 37°C, pH 7.2. polyvinyl chloride strips for ISO 10993-5 cytotoxicity test were used as positive control and glass specimens as negative control. L-929 ﬁbroblasts (5-mL aliquots, containing 3×104 cells/mL), cultivated in Dulbecco‵s Modiﬁed Eagle Medium with 10% fetal calf serum, 1% glutamine, and 1% penicillin/streptomycin at 37°C/5% CO2 and trypsinized were exposed to the specimens for 72 hours. The cells were harvested, centrifuged, and resuspended in 500 μL of DMEM and then counted in 500 μL of DMEM for 30 seconds with a ﬂow cytometer at 488 nm. The ANOVA comparing the six materials showed diﬀerent inﬂuences on L-929 ﬁbroblast cytotoxicity (p < 0.0001). The cytotoxicity of all specimens diminished with increasing pre-incubation time (p < 0.0001). Fresh DD exhibited the lowest cytotoxicity, followed by QuiXﬁl. Ketac Molar showed the highest cytotoxicity. After 7 days of pre-incubation, Harvard Cement and Filtek Supreme demonstrated more cytotoxicity than the other materials (p < 0.005).¹⁷⁴

   The clinical performance of DD as a posterior restorative material was also evaluated up to a 3-year recall point.¹⁶⁸ The aim of this study was to evaluate intra-individually the experimental CAC (DD) and an RC in Class II restorations. Each of 57 participants received at least one pair of restorations of the same size, one CAC and one RC (Tetric Ceram). Sixty-one pairs were performed. The restorations were evaluated clinically, according to slightly modiﬁed United States Public Health Service criteria, at baseline, after 6 months, and 1, 2, and 3 years. One hundred and twenty restorations were evaluated at 2 years.12 Postoperative sensitivity was reported for ﬁve restorations (2 RC, 3 CAC). Signiﬁcantly better clinical durability was shown for RC. Five non acceptable CAC restorations (8.2%) were observed at 6 months, 10 CAC (16.7%) and 2 RC (3.3%) at 12 months and 11 CAC (18.3%) at 24 months. This resulted in a cumulative failure frequency, at 24 months, of 43.3% for the CAC material and 3.3% for the RC material. Main reasons for failure for the CAC were partial material fracture (seven restorations) cusp fracture (ﬁve restorations), and proximal chip fracture (six restorations). The CAC showed a non acceptable clinical failure rate for Class II restorations probably caused by its diﬃcult handling and low mechanical properties. This trend continued at the 3-year recall, At 3 years, 62 out of 63 originally placed restorations were evaluated.13 At 6 months, 9.5% non acceptable DD restorations were observed, 17.5% at 12 months, 24.2% at 2 years, and 21% at 3 years, which resulted in a cumulative failure frequency of 72.6% at the end of the 3 years for the new restorative material. Main reasons for failure were material or tooth fracture. The authors of this study concluded that DD showed a non acceptable clinical failure rate as a posterior restorative, especially in Class II cavities. Clearly, based on this study, this calcium aluminate-based material appeared unacceptable as an amalgam replacement for posterior restorations. That said and in view of the observation that the in-vitro physical property performance of the DD material was closer to that of glass ionomer as opposed to composite resin or amalgam, it is interesting to speculate whether this CAC compares more closely in clinical performance with a high-strength glass ionomer restorative in posterior restorations.¹⁶⁸

   A 2-year clinical investigation of a high-strength glass ionomer in Class I and II posterior restorations was reported in 2009.¹⁷⁵ In this controlled, prospective, clinical study, the highly viscous GIC Ketac Molar was clinically assessed in Class I and Class II cavities. Forty-nine subjects (mean age 32.3 years) received 108 restorations placed by six operators in conventional Black Class I and II type cavities with undercuts after excavating primary lesions or after removing defective restorations. At baseline and after 6, 12, and 24 months, restorations were assessed by two independent investigators according to modiﬁed USPHS codes and criteria. Recall rates were 83% after 6 months, 50% after 12 months, and 24% after 24 months. Failure rates after 24 months were 8% for Class I and 40% for Class II ﬁllings mainly because of bulk fracture at occlusally loaded areas. This failure rate for this highly viscous glass ionomer is proportionally similar to failure rates for DD at 2 years recall reported by van Dijken and Sunnegårdh-Grönberg,12 namely 10% for Class I restorations and 43% for Class II restorations.¹⁶⁸׳¹⁷²

   **CALCIUM ALUMINATE—GLASS IONOMER LUTING CEMENT**

   The most recent modiﬁcation in bioactive chemically bonded cements with a predominant use in restorative dentistry has been the introduction of a calcium aluminate–glass ionomer luting cement (CM Crown & Bridge, originally named XeraCem).¹⁷⁶ The luting cement is actually a hybrid composition combining both calcium aluminate and glass ionomer chemistry. The glass ionomer component contains both polyacrylic acid and a reactive glass, which in the presence of the water available in the liquid component, permits a classical glass ionomer reaction. The manufacturer claims that the glass ionomer component contributes to a low initial, short-duration pH, improved ﬂow and setting characteristics, early adhesive properties to tooth structure, and early strength properties. In contrast, the calcium aluminate component in the cement is reported to contribute to: increased strength and retention over time; biocompatibility; sealing of tooth material interface; bioactivity-apatite formation; stable, sustained long-term properties and lack of solubility/degradation; and ultimate development of a stable basic cement pH.¹⁷⁶

   **USES**

   CM is a luting agent intended for permanent cementation of crowns and ﬁxed partial dentures, gold inlays and onlays, prefabricated metal and cast dowel and cores, and high-strength all-zirconia or all-alumina crowns.¹⁷⁷

   **COMPOSITION**

   The cement is a water-based composition comprising calcium aluminate and glass ionomer components, and has been demonstrated to be bioactive. The term “bioactivity” again refers to a property of this new cement to form hydroxyapatite (HA) when immersed in vitro in a physiological phosphate-buﬀered saline (PBS) solution.¹⁷⁷ The laboratory performance of this new cement has been assessed with respect to a number of performance criteria. Assessment of CS, ﬁlm thickness, and setting time all conformed favorability to the ISO standard for water-based luting cements.²⁰

   **MICROLEAKAGE STUDIES**

   Comparative in-vitro microleakage performance of this new bioactive cement has also been assessed by two methodologies. Dye leakage analysis in cemented crowns concluded that CM demonstrated signiﬁcantly less leakage than a conventional GIC, Ketac-Cem (KC). An in-vitro bacterial leakage model comparison of CM with a conventional glass ionomer luting cement, again KC, and an RMGI cement (Rely X Luting Plus, RX) demonstrated that the groups cemented with CM and RX showed no signiﬁcant diﬀerence in microleakage patterns (p > 0.05), whereas both recorded signiﬁcantly lower microleakage scores (p < 0.05) than the group cemented with KC.¹⁷⁹

   **BIOCOMPATIBILITY**

   Biocompatibility ranks as one of the most important properties of a ﬁnal luting cement, and as such, a number of in-vitro and in-vivo tests (as recommended by American National Standards Institute/American Dental Association (ANSI/ADA) Spec. 41 and ISO 10993) were conducted prior to the clinical investigation to evaluate the biocompatibility of CM Crown & Bridge cement. Results for the Ames test for mutagenicity indicated that this new cement formulation did not induce gene mutations.¹⁷⁹ In-vitro cytotoxicity testing indicated cell responses ranging from none to mildly cytotoxic, an acceptable response. The skin sensitization test (in guinea pigs) indicated that this cement is not a skin sensitizer, whereas testing for mucous membrane irritation (hamster pouch test) indicated that it produced no local irritation.. Pulpal testing in Rhesus macaques, according to ANSI/ADA Spec. 41, indicated a virtual absence of pulpal inﬂammation at both 30- and 85-day evaluation periods after CM was used to cement composite resin inlays in a Class V preparation.¹⁷⁹

   **RETENTION**

   Retention is perhaps the most critical factor in the performance of a ﬁnal luting cement. A comparative, in-vitro crown retention study was conducted (also prior to the clinical evaluation) to assess the retentive properties of this new cement with noble metal (gold) crown-copings. Results of this test indicated that it demonstrated retentive values equivalent (no statistically signiﬁcant diﬀerence) to a self-adhesive resin cement, Rely X Unicem, but were signiﬁcantly higher than a conventional glass ionomer, KC, and zinc phosphate cement.¹⁸⁰

   A clinical investigation was initiated approximately 2 years prior to the introduction of CM. The aim of this pilot clinical study (a prospective, consecutive case series clinical study) was to assess the clinical performance of a new bioactive cement as a luting cement for cast high-gold alloy and noble metal porcelain-fused-to-metal restorations.¹⁸¹ This clinical study was conducted to determine the multiyear clinical performance of this new bioactive dental cement (CM Crown & Bridge) for permanent cementation. A total of 38 crowns and bridges were cemented in 17 patients. Thirty-one of the abutment teeth were vital and seven non vital. Six restorations were bridges with a total of 14 abutment teeth (12 vital/2 non vital). One ﬁxed splint comprising two abutment teeth was also included. Preparation parameters were recorded, as well as cement characteristics such as working-time, setting-time, seating characteristics, and ease of cement removal. Baseline data were recorded for the handling of the cement, gingival inﬂammation, and pre-cementation sensitivity. Post-cementation parameters included post-cementation sensitivity, gingival tissue reaction, marginal integrity, and discoloration. All patients were seen for recall examinations at 30 days and 6 months.23 Fifteen of 17 subjects and 13 of 17 patients were also available for subsequent comprehensive 1-24 and 2-year recall examination, 25 and 13 patients were available for a 3-year recall examination.Two-year recall data yielded no loss of retention, no secondary caries, no marginal discolorations, and no subjective sensitivity. All restorations rated “alpha” for marginal integrity at the 2-year recall.¹⁸¹ Restorations available for the 3-year recall examination included 14 single-unit full-coverage crown restorations, four three-unit bridges comprising eight abutments, and one two-unit splint. Three-year recall data yielded no loss of retention, no secondary caries, no marginal discolorations, and no subjective sensitivity. All restorations rated excellent for marginal integrity. Average visual analog scale scores for tooth sensitivity decreased from 7.63 mm at baseline to 0.44 mm at 6-month recall, 0.20 mm at 1-year recall, 0.00 mm at 2- and 3-year recall. Average gingival index scores for gingival inﬂammation decreased from 0.56 at baseline to 0.11 at 6-month recall, 0.16 at 1-year recall, 0.21 at 2-year recall, and 0.07 at 3-year recall. After periodic recalls up to 3 years, CM Crown & Bridge thus far has performed quite favorably as a luting agent for permanent cementation of permanent restorations.

   At the time of reporting the 3-year recall data, additional in-vitro crown-coping retention data were presented using CM and crown-copings utilizing various all-ceramic crown and bridge materials. Mean laboratory retentive forces measured for CM Crown & Bridge were comparable with other currently available luting agents for both metal and additionally all-ceramic indirect restorative materials, specially all-zirconia and lithium disillicate.a lithium disillicate e.Max crown (Ivoclar Vivadent, AG, Bendererstrasse 2, 9494 Schaan, Principality of Liechtenstein) cemented on a mandibular left second premolar with a calcium aluminate/glass ionomer luting cement (CM Crown & Bridge) at 6 months postcementation. An excellent gingival soft-tissue gingival response can be noted in this digital photograph.¹⁸¹

   **BIOACTIVE ROOT CANAL SEALERS**.

   Accomplishment of ideal root canal treatment is attributed to various essential factors such as proper instrumentation, biomechanical preparation, obturation, and ultimately depending upon the case post‑endodontic restoration.¹⁸² The pertinent aim of this treatment is to do away with the microbial entity and any future predilection of re‑infection. In order to achieve this, proper seal is required to denigrate any chance of proliferation of bacteria and future occurrence of any pathology. Sealer along with solid obturating material acts synergistically to create hermetic seal. Bioactive sealers have been introduced in the market in an attempt to provide an obturation method that can be successfully and predictably performed by a majority of practitioners while taking advantage of its biocompatibility and physical properties. Eg. BC Sealer (Brasseler USA); iRoot SP (Innovative BioCreamix Inc).¹⁸²

   **‘Endodontic grafting’**

   Filling of the root canal apical third must be looked upon separately from the filling of the rest of the canal having under consideration the active and constant metabolic processes occurring in the periapical area.¹⁸³ Special attention must be paid to the interface formed between dentinal root canal walls, gutta-percha and sealer on one side and periodontium and body fluids on the other side. Long-term hermetic sealing of apical third achieved in constantly wet environment is an ob- ligatory condition to ensure lack of microbial growth. Another extremely important factor promoting hard tissue closure of the canal is presence of osseocon- ductivity as sealer’s feature. Perfect and lasting in wet environment hermetic seal of apical third combined with osseoconductivity of endodontic sealer .Ceramics-based sealers as new alternative to currently used endodontic sealerscone.conditions for hard tissue closure of root canal apical orifice in time. Filling of the root canal with ceramic sealer, which due to its osseoconductivity action promotes the physiological closure of the canal by cementoid hard tissue, can be called “endodontic grafting.” ¹⁸³Such endodontic grafting can ensure the lasting root’s health while it constantly remains in contact with body fluids. The use of bioceramic-based sealers with their fea- tures — osseoconductivity, hydrophylity, adhesiveness and chemical bonding to root canal dentinal walls — appears to be an effective approach to eliminate on long term, the microspace, otherwise remaining between the root canal walls and the materials filling the root canal. Such microspace is a potential place for possible microbial growth, because of microleakage observed with other kind of sealers. Sealers for ‘endodontic grafting’ Endodontic sealers that set hard and are stable in constantly wet environment are:¹⁸⁴

   a. Recently created calcium silicate phosphate-based bioceramic nano-compositions — Bio- Aggregate, iRoot SP and iRoot BP (IBC, Canada).

   b. MTA-based products — “MTA — Angelus” (AN- GELUS, Brazil), ProRoot (Dentsply, USA), Aureoseal (OGNA, Italy).

   **Mta based sealers**

   This sealer produces calcium hydroxide, which is released in solution and induces formation of hydroxyapatite structures in simulated body fluid. Newer developments of MTA include its use as a root canal sealer. Currently, three MTA sealer formulations are available: ENDO CPM Sealer (EGEO SRL, Buenos Aires,argentina),MTA OBTURA (angelus Londrina PR,brazil) and PROROOT ENDO SEALER(dentsply mallefer,ballaigues,Switzerland).¹⁸⁵

   The composition of CPM sealer after mixing is reported to be 50% MTA (SiO2, K2O, Al2O3, SO3, CaO, and Bi2O3), 7% SiO2, 10% CaCO3, 10% Bi2O3, 10% BaSO4, 1% propylene glycol alginate, 1% propylene glycol, 1% sodium citrate, and 10% calcium chloride.¹⁸⁶

   MTA Obtura is a mixture of white MTA with a proprietary viscous liquid.ProRoot Endo Sealer is calcium silicate– based endodontic sealer.¹⁸⁷

   The major components of the powder of ProRoot Endo Sealer are tricalcium silicate and dicalcium silicate, with inclusion of calcium sulfate as setting retardant, bismuth oxide as radiopacifier, and a small amount of tricalcium aluminate. Tricalcium aluminate is necessary for the initial hydration reaction of the cement. The liquid component consists of viscous aqueous solution of a water‑soluble polymer and to improve The liquid component consists of viscous aqueous solution of a water soluble polymer to improve the workability.¹⁸⁷When placed in the canal, it releases calcium activity and causes cell attachment and proliferation, increases the pH, modulates cytokines like interleukin (IL) 4, IL6, IL8, IL10, and hence causes proliferation, migration, and differentiation of hard tissue producing hydroxyapatite which aids in the formation of physical bond between sealer and MTA.The polymer did not seem to affect the biocompatibility of the materials and the hydration characteristics were similar to those reported for MTA.

   **Biocompatibility of MTA based sealers**

   Sealers based on MTA have been reported to be biocompatible, stimulate mineralization, and encourage apatite‑like crystalline deposits along the apical‑ and middle‑thirds of canal walls.¹⁸⁸ These materials exhibited higher push‑out strengths after storage in simulated body fluid and had similar sealing properties to epoxy resin–based sealer when evaluated using the fluid filtration system.

   Fluoride‑doped MTA demonstrated stable sealing up to 6 months, and was significantly better than conventional MTA sealers and comparable to AH Plus.¹⁸⁹ The study supports the suitability of MTA sealers in association with warm GP for root filling. Loise et al. evaluated the biocompatibility and bioactivity of a new MTA‑based endodontic sealer, MTA Fillapex (MTA‑F; Angelus, Londrina, Brazil), in human cell culture and came to the conclusion that after setting, the cytotoxicity of MTA‑F decreases and the sealer presents suitable bioactivity to stimulate hydroxyapatite crystal nucleation.¹⁸⁹

   Gomes‑Filho et al. evaluated the rat subcutaneous tissue reaction to implanted polyethylene tubes filled with MTA Fillapex and compared it with MTA‑Angelus, and concluded that MTA Fillapex was biocompatible and stimulated mineralization.¹⁹⁰

   Bortolini et al. evaluated in vitro the intratubular penetration and permeability of Endo CPM Sealer in teeth contaminated with Enterococcus faecalis and concluded that Endo CPM sealer showed greater permeability to E. faecalis.¹⁹¹

   Morgental et al.found that MTA Fillapex and Endo CPM Sealer has a good antibacterial effect on E. feacalis before setting, but not after setting despite having high pH.¹⁹²

   Bin et al. studied the cytotoxicity and genotoxicity of MTA canal sealer (Fillapex) compared with white MTA cement and AH Plus, and found that white MTA group was the less cytotoxic material in this study.¹⁹³ Both AH Plus and Fillapex MTA sealer showed the lowest cell viability rates and caused an increased micronucleus formation.

   Vidotto et al.did the comparison of MTA Fillapex radiopacity with five root canal sealers (Endomethasone‑N, AH Plus, Acroseal, Epiphany SE, and RoekoSeal) and concluded that in a decreasing order of radiopacity, AH Plus® (9.4 mm Al) was the most radiopaque sealer, followed by Epiphany SE (7.8 mm Al), MTA Fillapex (6.5 mm Al), RoekoSeal (5.8 mm Al), Endomethasone‑N (4.5 mm Al), and Acroseal (3.5 mm Al). MTA Fillapex™ was the third most radiopaque sealer among all the tested sealers¹⁹⁴. Also, MTA Fillapex has the radiopacity degree in agreement with ADA specification No. 57.

   : (a) Middle third with Endo CPM sealer: low intratubular penetration; (b) cervical third with EndoREZ: good intratubular penetration; and (c) apical third with AH Plus: regular intratubular penetration (1000 magnification)

   **Comparison of physical properties between calcium silicate sealers with AH-PLUS**

   Sagsen et al. assessed the push‑out bond strengths of two new calcium silicate–based endodontic sealers MTA Fillapex and iRoot SP and compared them with AH Plus in the root canals of extracted teeth and found that in the coronal specimens, there was no significant difference between the sealers.¹⁹⁵ In the middle and apical segments, there was no significant difference between IRoot SP and AH Plus groups. However, the IRoot SP and AH Plus had significantly higher bond strength values than the MTA Fillapex. So, they concluded that MTA Fillapex had the lowest push‑out bond values to root dentine compared with other sealers.

   Considering the elastic modulus of dentin which is about 14‑18.6 GPa, the reinforcing effect of MTA may be explained by its similar elastic modulus to dentin. This hypothesis also explains the gradual increase in the fracture resistance of MTA‑filled teeth found by Hatibovic‑Kofman et al. Aalso, fracture resistance of MTA‑filled teeth is time dependant.¹⁹⁶

   The alkalinity of MTA can theoretically weaken root dentin similar to the findings on calcium hydroxide. Another hypothesis is that a combination of little tensile strength of MTA and lack of bonding to dentin can weaken the dentin. Regardless of the excellent biologic properties of MTA, the thin dentinal walls still make these teeth more prone to fracture and a reinforcing technique in these weak roots is necessary.

   The novel sealer based on MTA has efficacious sealing ability. In contact with a simulated body fluid, the MTAs release calcium ions in solution and encourage the deposition of calcium phosphate crystals.¹⁹⁷

   **ADVANTAGES**

   1. Highly biocompatible.\*

   2. Stimulate mineralization.\*

   3. Encourage apatite-like crystalline deposits along the apical and

   middle thirds of canal walls.\* \*

   4. These materials exhibited higher push-out strengths after storage

   5. Fluoride-doped MTA demonstrated stable sealing up to 6 months and

   significantly better than conventional MTA sealers

   6. It has an adequate calcium releasing property

   7. Endo- CPM was also reported to have a similar or better sealing

   ability to resin-based sealers.

   8. ProRoot Endo Sealer demonstrated the superior sealing ability of this

   material comparable to resin-based sealers.

   9. After setting, the cytotoxicity of MTA-F decreases and the sealer

   presents suitable bioactivity to stimulate Hydroxyapatite crystal

   nucleation.

   10. MTA Fillapex yields an impressive, hermetic seal in which the

   MTA particles expand, preventing microinfiltration. And, MTA

   simultaneously releases free calcium ions [Ca2+] to accelerate the

   healing process by stimulating the regeneration of the adjacent

   tissues.

   11. Endo-CPM sealer showed the highest values of bond strength to

   root dentin (8.265 MPa) (P<.05). The values of push-out test were

   similar for MTA Fillapex (2.041 MPa) and AH Plus (3.034 MPa).

   **DISADVANTAAGES**

   1. Do not bind to dentin and core material

   2. MTA Fillapex had the lowest push-out bond values to root dentine

   compared with other sealers.

   3. MTA Fillapex® setting time, which has resin in its composition

   consequently reducing the medium alkalinisation hence less

   mineralisation then other MTA sealers.

   4. The alkalinity of MTA can theoretically weaken root dentin similar to

   the findings on calcium hydroxide.

   5. In cases of MTA-based materials extrusion outside the root canal is

   associated with severe pain felt by the patient

   **ENDOSEQUENCE BIOCERAMIC SEALER**

   EndoSequence BC Sealer and iroot b.p and s.p. (Brasseler, Savannah, GA, USA), (Innovative BioCeramix Inc., Vancouver, BC, Canada), is an example of a calcium phosphate silicate– based cement. Its major inorganic components include tricalcium silicate, dicalcium silicate, calcium phosphates, colloidal silica, and calcium hydroxide. It uses zirconium oxide as the radiopacifier and contains water‑free thickening vehicles to enable the sealer to be delivered in the form of a premixed paste.¹⁹⁸

   Hydroxyapatite is co‑precipitated within the calcium silicate hydrate phase to produce a composite‑like structure, reinforcing the set cement.The introduction of a premixed calcium phosphate silicate–based sealer eliminates the potential of heterogeneous consistency during on‑site mixing. Because the sealer is premixed with non‑aqueous but water‑miscible carriers, the water‑free paste will not set during storage in the syringe and only hardens on exposure to an aqueous environment.

   EndoSequence BC Sealer uses the moisture within the dentinal tubules after canal irrigation to initiate and complete the setting reaction. Moreover, the presence of smear plugs and/or tubular sclerosis can affect the amount of moisture present. The setting time of EndoSequence BC Sealer is 4 h and it may be extended in overly dry canals. The pH of EndoSequence BC Sealer during the setting process is higher than 12 (Material Safety Data Sheet information), which increases its bactericidal properties. The amount of Ca2+ released from EndoSequence BC Sealer was far higher (2.585 mg/l) than that released from AH Plus (0.797 mg/l), mainly after 7 days.¹⁹⁸

   Loushine et al. investigated the setting time and micohardness of a premixed calcium phosphate silicate– based sealer in the presence of different moisture contents (0%‑9 wt%).¹⁹⁹ The moisture content that produced the most optimal setting properties was used to prepare set EndoSequence BC Sealer for cytotoxicity in comparison with AH Plus, and they concluded that cytotoxicity of AH Plus gradually decreased and became noncytotoxic, whereas BC Sealer remained moderately cytotoxic over the 6‑week period. Hence, it shows bioceramic sealer is non‑toxic and biocompatible.

   Zoufan et al. conducted a study which evaluated the cytotoxicity of GuttaFlow and EndoSequence BC sealers and compared them with AH Plus and Tubli‑Seal sealers.²⁰⁰ The GuttaFlow and EndoSequence BC sealers had lower cytotoxicity than the AH Plus and Tubli‑Seal sealers.

   Hess et al. evaluated the efficacy of solvent and rotary instrumentation in the removal of bioceramic sealer (BCS) when used in combination with GP as compared with AH Plus sealer and found that the working length ( WL) was not regained in 70% of samples with BCS/master cone short of the WL.²⁰¹ Patency was not re‑established in 20% of samples with BCS/master cone to the WL or in 70% of samples with BCS/master cone short of the WL. Hence, it was concluded that conventional retreatment techniques are not able to fully remove BCS.

   According to Ghoneim et al., bioceramic‑based sealer (i.e., iRoot SP) is a promising sealer in terms of increasing in vitro resistance to the fracture of endodontically treated roots, particularly when accompanied with ActiV GP cones.²⁰²

   Deyan Kossev and Valeri Stefanov found that when bioceramic‑based sealers BioAggregate or iRoot SP are extruded, the pain is relatively small or totally absent. Such lack of pain may be explained based on the characteristics of these new materials. During hardening, they “produce” hydroxylapatite and after the end of hardening process they exhibit the same features as non‑resorbable hydroxylapatite‑based bioceramics used for bone replacement in oral surgery. Due to the hydroxylapatite formed, they are also osseo‑conductive. During setting, hard ceramic‑based sealers expand. Expansion of BioAggregate and iRoot SP and iRoot BP is significant (0.20%). These new bioceramic sealers also form chemical bond with the canal’s dentin walls. That is why no space is left between the sealer and dentin walls.²⁰²

   Borges et al. compared the changes in the surface structure and elemental distribution, as well as the percentage of ion release, of four calcium silicate containing endodontic materials with a well‑established epoxy resin–based sealer, submitted to a solubility test, and found that AH Plus and MTA‑A were in accordance with ANSI/ADA’s requirements regarding solubility, while iRoot SP, MTA Fillapex, and Sealapex did not fulfil ANSI/ADA’s protocols.²⁰³ High levels of Ca2+ ion release were observed in all materials except AH Plus. Scanning electron microscopy (SEM)/Energy‑dispersive X‑ray spectroscopy (EDX) analysis revealed that all samples had morphological changes in both outer and inner surfaces after the solubility test. High levels of calcium and carbon were also observed at the surface of all materials except AH Plus and MTA‑A

   **Features of ceramic-based endodontic sealers²⁰⁴**

   **1)**.Ceramic-based sealers are highly hydrophilic and have low contact angle. These features allow them to spread easily over the dentin walls of the root canal and to get inside and fill the lateral micro canals, too. Thus necessity to instrument the canals with 06 or higher taper becomes no longer needed. Tooth tissues are preserved, and risk of root fractures is reduced.

   Small micro canal filled with iRoot SP (arrow). Horizontal cut. Polarisation microscopy. Black — root dentin, white — iRoot SP sealer, orange — gutta-percha cone.

   During setting hard ceramic-based sealers expand. Expansion of BioAggregate and iRoot SP and iRoot BP is significant — 0.20 percent. These new bioceramic sealers also form chemical bond with the canal’s dentin walls. That is why no space is left be- tween the sealer and dentin walls. This is well demon- strated by light polimerization microscopy and much better demonstrated by large magnification scanning

   Filling of root canals with iRoot SP. Note excellent radiopacity of this bioceramic sealer.

   Bioceramic-based sealers are capable of achieving fast alleviation of the pain syndrome in cases of acute periapical inflammation. After appropriate instrumentation and cleaning of the root canal, fol- lowed by immediate filling with iRoot SP, pain rapidly diminishes and most often is totally gone within a period of 50 minutes to few hours.

   4).In cases of MTA-based materials extrusion outside the root canal is associated with severe pain felt by the patient. When bioceramic-based sealers BioAggregate or iRoot SP are extruded, the pain is relatively small or totally absent. Such lack of pain may be explained with the characteristics of these new materials. During hardening they “produce” hydroxylapatite and after the end of hardening proc- ess they exhibit the same features as non-resorbable hydroxylapatite-based bioceramics used for bone replacement in oral surgery. Due to the hydroxyla- patite formed, they are also osseoconductive

   5). MTA-based materials and BioAggregate have quite poor radiopacity, different from bioceramic based iRoot SP and iRoot BP sealers. This difference is easily demonstrated by the following experiment. Root canals of extracted teeth have been instru- mented with TF files (SybronEndo) and cleaned. Two of the canals were filled with iRoot SP, and the other two with BioAggregate, respectively (Fig. 19). Note the excellent radiopacity of iRoot SP (left) compared to BioAggregate (right).

   **Advantages**

   1. Biocompatible and do not induce critical cytotoxic effects

   2. Formation of a nano-composite network of gel-like calcium silicate hydrate intimately mixed with hydroxyapatite, bioceramic, and forms a hermetic seal when applied inside the root canal.

   3. Precipitates calcium phosphate on hydration with same strength as human bone

   4. iRoot BP is non-mutagenic, does not cause an allergenic potential

   after multiple uses and has a good tolerance by subcutaneous tissue

   5. High alkalinity increases its mineralisation process also its

   bactericidal properties (pH 12.8)

   6. Hydrophilic, root canal hydration aids in the formation of calcium

   phosphate hence gives strength

   7. Low contact angle hence these features allow them to spread easily

   over the dentin walls of the root canal and to get inside and fill the

   lateral micro canals

   8. These new bioceramic sealers also form chemical bond with the

   canal’s dentin walls. That is why no space is left between the sealer

   and dentin walls.

   9. They are also osseo-conductive

   10. Very good radiopacity (3.8 mm of Al).

   11. Setting time is 3-4 hrs hence it gives ample amount of time for

   placement of root canal.

   12. Bioceramics do not shrink upon setting. In fact, they actually

   expand slightly upon completion of the setting process.

   13. Furthermore (and this is very important in endodontics),

   bioceramics will not result in a significant inflammatory response if

   an overfill occurs during the obturation process..

   14. Remarkable flowability of the BC Sealer. This is a result of its

   particle size and hydrophilicity. (27 mm).

   15. Bioceramic sealer has more fracture resistance then conventional

   sealer

   16. When bioceramic-based sealers BioAggregate or iRoot SP are extruded, the pain is relatively small or totally absent.

   **DISADVANTAGES**

   1. Changes in environmental water content adversely affect the setting time and microhardness of EndoSequence BC Sealer.

   2. Conventional retreatment techniques are not able to fully remove Bioceramic sealer.

   **CALCIUM PHOSPHATE SEALER**

   Bae et al investigated the cellular effects of newly developed calcium phosphate–based sealers (CAPSEAL I and II) using cultured human periodontal ligament cells (HPDLCs), in comparison with epoxy resin sealer (AH26; Dentsply, DeTrey, Konstanz, Germany), ZOE sealer (EWT; Kerr Corporation, Orange, CA, USA), and CPC sealer (Sankin apatite sealer; Sankin‑kogyo, Tokyo, Japan), and found that both CAPSEAL I and II show less cytotoxicity and inflammatory mediators compared with the other sealers and have the potential to promote bone regeneration as root canal sealers.²⁰⁵

   Shon et al. examined the biological effects of new calcium phosphate–based root canal sealers,²⁰⁶ CAPSEAL I and CAPSEAL II (CPS), on human periodontal fibroblast cells by examining the expression levels of inflammatory mediators and compared the effects of CPS on the viability and osteogenic potential of human osteoblast MG63 cells, with those of other commercially available calcium phosphate sealers [Apatite Root Sealer type I (ARS I)] and [Apatite Root Sealer III (ARS III); Sankin Kogyo, Tokyo, Japan] and an ZOE‑based sealer [Pulp Canal Sealer EWT (PCS EWT); Kerr, Detroit, MI, USA) and came to the conclusion that CAPSEAL I and II facilitate the periapical dento-alveolar and alveolar healing by controlling cellular mediators from PDL cells and osteoblast differentiation of precursor cells.

   Khashaba et al. evaluated the histopathologic biocompatibility of two new calcium phosphate–based sealers (CPS‑1 and CPS‑2) with a commercially available calcium hydroxide–based sealer (Acroseal) and found that CPS‑1 sealer was not biocompatible. CPS‑2 sealer and Acroseal had a favorable biocompatibility level based on the histological findings.²⁰⁷

   Accordingly, Yang et al. did field emission‑scanning electron microscopy and found that both CAPSEAL I and II sealers were well adapted to the canal wall and infiltrated into the dentinal tubules.²⁰⁸

   **ADVANTAGES**

   1. CAPSEAL I and II show less cytotoxicity and inflammatory mediators compared with other sealers and have the potential to promote bone regeneration as root canal sealers.

   2. CAPSEAL I and II facilitate the periapical dentoalveolar and alveolar healing by controlling cellular mediators from PDL cells and osteoblast differentiation of precursor cells.

   3. CAPSEAL I and II sealers were well-adapted to the canal wall and infiltrated into the dentinal tubules.

   **DISADVANTAGES**

   1. Fracture resistance is yet to evaluate.

   2. CPS-1 sealer is not biocompatible.

   **CALCIUM‑ENRICHED MIXTURE**

   White et al. showed weakening of dentinal structure in short term and attributed this effect to the structural alteration of proteins caused by the alkalinity of MTA. ²⁰⁹ Recently, a new biomaterial, CEM cement has been introduced. This cement consists mainly of CaO, SO3, P2O5, and SiO2. CEM cement releases calcium hydroxide during and after setting. This cement has antibacterial features similar to calcium hydroxide and better than MTA] On comparison with MTA, this novel cement was found to have similar sealing ability and pH and increased flow, but decreased working time and film thickness. It has shown its capacity in regenerating PDL and induction of cementogenesis.

   Milani et al. evaluated the strengthening effect of MTA and CEM and found it to be the same for MTA and CEM.²¹⁰

   Andreasen et al. have advocated placing calcium hydroxide for a maximum of 4 weeks followed by filling the canal with MTA.²This abbreviates the duration of the high fracture risk phase of calcium hydroxide dressing and allows much earlier placement of strength enhancing restorative materials. In contrast to the aforementioned studies, other investigators believe that the alkalinity of MTA can theoretically weaken root dentin, similar to the findings on calcium hydroxide. Lack of data on modulus elasticity of CEM, the mechanism of reinforcing effect of CEM remains to be elucidated. Lack of data on modulus elasticity of CEM, the mechanism of reinforcing effect of CEM when used as a sealer remains to be elucidated.²¹¹

   An important issue neglected in the studies on fracture strength of MTA‑filled teeth is the role of fatigue. None of these studies applied cyclic loads prior to fracture testing. However, it is recommended to consider this issue in future studies on fracture strength of immature teeth.

   **CONCLUSION**

   Biomimetic is the study of the formation, structure, or function of biologically produced substances and materials and biological mechanisms and processes especially for the purpose of synthesizing similar products by artificial mechanisms which mimic natural ones. And material fabricated by biomimetic technique based on natural process found in biological system is called a biomimetic material. The practice of endodontics has grown by leap and bounce in the past few decades. Replacement of diseased or lost tooth structure with biocompatible restorative materials is currently the order of today. But each of these procedures does have their on limitations and drawbacks. Regeneration of the lost tooth structure rather than replacement during treatment will ensure better prognosis and higher rate of success. Hence the future in endodontics would involve the use of such biomimetic materials which could successfully replace lost dentine, cementum and even the pulp tissue. Efforts are on through tissue engineering to create a biological tooth substitute that could completely replace the lost tooth structure.

   Biomimetic materials and methods will revolutionize the future endodontics with the synergistic confluence of advances in signalling pathways underlying morphogenesis and lineage of stem/progenitor cells.

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