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**Title: CALCIUM SILICATE BASED BIOCERAMICS**

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**CALCIUM SILICATE BASED BIOCERAMICS**

While bioinert materials do not demonstrate osteoconductive or osteoinductive properties, they allow growth of fibrous tissues around the material. Examples of this category are alumina and zirconia. Bioactivate materials, in contrast, have osteoinductive and osteoconductive properties. They are porous and develop an interfacial bond with the hard tissues. Hydroxyapatites, bioactive glasses and glass ceramics are examples of this class of bioceramics. Bioresorbable ceramics enhance the replacement resorption of the material by host tissues when the rate of resorption correlates with the rate of regeneration. Examples of this group of materials are tricalcium silicates and calcium phosphate.3

There has been an increasing trend towards the application of bioceramics in medical and dental fields. In bone tissue engineering, they have been used as bone surrogates, bone implants and as a composition of artificial joints. They are also used in making artificial heart valves. In dentistry, they are widely used as compositions of implants and periodontal surgeries, i.e., for alveolar ridge augmentation. 3 Since 1993, the field of endodontics has seen a huge influx of this category of materials with a wide array of applications. The first endodontic use of this class of materials was in the form of Mineral Trioxide Aggregate (MTA), used for perforation repair and root end filling. From a chemical perspective, most bioactive materials used in endodontics are based on tricalcium and dicalcium silicate. 2,4 When these tri-and dicalcium silicates interact with water, calcium silicate hydrate (CSH) gel is formed, initially as a colloidal gel, which then hardens with time. The bioactivity has also been reported to be due to the release of calcium hydroxide (CH) during the hydration process. 6,7 Thus, this group of materials are also termed “calcium silicate-based cement” or “hydraulic calcium silicate-based cement”. When calcium phosphate monobasic was added to the calcium silicates, a complex reaction ensues, resulting in the formation of CSH gel and CH. In addition, the calcium phosphate monobasic reacts with CH to form hydroxyapatite-like compounds or an apatite-like layer which co-precipitates with the CSH phase, thereby reinforcing the set cement. This property of “biomineralisation” helps improve the tissue attachment of these materials.3

* ProRoot MTA- This is considered a prototype of bioceramics in endodontics. It was developed and first introduced in Loma Linda University, USA in 1993, and was patent registered in 1995. The white ProRoot MTA or tooth-colored ProRoot MTA was later developed in 2002. ProRoot MTA is one of the most widely researched endodontic materials, including short- and long-term treatment outcome studies. ProRoot MTA has been shown to demonstrate the least cytotoxicity and leakage compared with other materials, and has been proven to induce osteogenesis and cementogenesis. 8,9 The compressive strength of MTA was about 40 MPa at 24 hours and 67.3 MPa at three weeks. 19 Clinical applications of ProRoot MTA in endodontics included pulp protection in vital pulp therapy, perforation and resorption repair, apexification, revascularization and root end filling during apicectomy.3



**Figure 1: ProRoot MTA**

* MTA angelus- This commercial formulation of MTA composes of 80% Portland cement and 20% Bismuth oxide. Calcium sulfate was removed from the liquid portion in order to accelerate the setting time, which is reduced down to 14 minutes. MTA Angelus exhibits excellent biocompatibility and sealing ability, and increased bone formation. However, an investigation by Camilleri 30revealed that due to an incomplete sintering process leading to its variability in mineralogy, MTA Angelus contained smaller amount of tricalcium silicate, but more of calcium, aluminum and silicon oxides in the un-hydrated powder compared to Biodentine. The greater amount of CH produced as a by-product of the reaction due to hydration of calcium oxide leads to more porous and less dense microstructure.3



**Figure2 : MTA Angelus**

* MTA Plus & Neo MTA Plus- With an increasing body of evidence demonstrating the biomineralisation properties oftricalcium silicates, the application of MTA logically extended to being used as root canal sealers. ProRoot MTA and MTA Angelus were not intended to be applied as root canal sealers. A newgroup of cost-effective materials (MTA Plus and NeoMTA Plus) were introduced into the market for all conceivable applications of bioactive ceramic materials (vital pulp therapy, apexification, root end filling, perforation repair, resorption management and root canal sealer. While the basic composition of MTA Plus is similar to that of the original MTA, there are two main differences: the powder of MTA Plus is finer and it is recommended that the MTA powder be mixed with a proprietary water-based gel when the material is to be used as a root canal sealer. This gel contains film forming polymers and accelerators but no salts. Currently, three variants of this material are available: Gray MTA Plus, MTA.3



**Figure 3: MTA Plus and Neo MTA**

* Plus and NeoMTA Plus-
* Gray MTA Plus/ MTA Plus is a powder and liquid/ gel system. The powder consists of fine inorganic substance similar to that of ProRoot MTA. Liquid or gel may be used for cavity liner/base, pulp capping, pulpotomy, root apexification, resorption/perforation repair or root-end filling material. The water-based gel (with water soluble thickening agents and polymer) imparts washout resistance and faster setting, which the liquid does not. The manufacturer recommends mixing the powder with gel into a syrupy, stringy consistency when used as a root canal sealer during obturation.
* NeoMTA Plus is a powder-gel system. The powder components are an extremely fine powder primarily tricalcium and dicalcium silicate, quite similar to that of white ProRoot MTA, but contains no bismuth oxide in order to prevent tooth staining. Tantalum oxide is used as the radiopacifier. The manufacturer claims that this material achieves washout resistance in less than three minutes (MTA Plus is about five minutes), thus allowing continuation of the restorative procedure. Also, it has a 20-minute working time and a 50-minute setting time when mixing to a putty consistency. Thus, the setting time of both MTA Plus and NeoMTA Plus are depending on the consistency of the mixed material.3

The setting time of MTA Plus was found retarded when in contact with fluids; about 128 minutes in dry condition and about 1,052 minutes in contact with physiological solution. While the hydration of the core material was not affected by contact with the different solutions but the periphery exhibited microcracking, leaching of calcium hydroxide, partial decalcification of calcium silicate hydrate, and interaction with a physiological solution resulted in inhibition of hydration. The compressive strength was significantly lower when MTA Plus mixed with liquid was exposed to the biological fluid compared with saline. However, the material mixed with gel was not affected in this condition.3

* Endocem - Endocem MTA: this material contains a fine size of pozzolan. Pozzolan is a material that contains silica or silicate (sometimes with aluminium) with little or no cementitious value themselves, but in the presence of water, react chemically with calcium hydroxideto form calcium silicate, with good cementing properties. The major chemical constituents and applications are similar to ProRoot MTA. 36 The manufacturer claims that the pozzolanic reaction blocks the dentinal tubules, thereby preventing discoloration of the tooth. Setting time is about two to four minutes. Endocem Zr: contains zirconium as the most abundant element. The use is similar to that of white MTA but application of direct occlusal force should be avoided because the material exhibits less tensile strength than the conventional MTA. It has also been suggested that this material be used as a liner rather than a base in vital pulp therapy. Setting time is about four minutes.3



**Figure 4: Endocem**

* Endoseal: a root canal sealer without resin as its component, which has MTA as its main ingredient.
* Endodseal MTA: a premixed root canal sealer based on pozzolan in a syringe, which main compositions of calcium silicates, calcium aluminates, calcium aluminoferrite, calcium sulfates, radiopacifier, and thickening agent. The setting time reported by the manufacturer is about 12.31 minutes.
* Calcium ions release from water-immersed set Endocem MTA and Endocem Zr were noted to be significantly less compared with white MTA, and when immersed in phosphate-buffered saline for 14 days, they also produced apatite-like crystalline precipitates like ProRoot MTA, but with less calcium/phosphate ratio. Endocem Zr was also noted to have transient cytotoxicity initially, and the levels of vascular endothelial growth factor and angiogenin were also significantly lower than that of ProRoot MTA. 11 However, a randomized controlled study recently revealed that Endocem exhibited similar success with ProRoot MTA as a direct pulp capping material, evaluated clinically and radiographically over one year after the treatment.3
* Retro MTA & Ortho MTA- The main composition of Ortho MTA is similar to ProRoot MTA, i.e. tricalcium silicate, dicalcium silicate, tricalcium aluminate, tetracalcium aluminoferrite, calcium oxide and bismuth oxide, and is suggested to be used as root-end filling material after apicectomy. Retro MTA is a powder consisting fine hydrophilic particles of calcium carbonate, silicon dioxide, aluminium oxide, and hydraulic calcium zirconium complex as a radiopacifier. Retro MTA is more granular in nature and sets faster than Ortho MTA. This faster setting finds advantage when used as a pulp capping material. 36 Studies of both materials are limited and most data is manufacturer-released information. One investigation compared the cytotoxicity of ProRoot MTA, Ortho MTA and glass ionomer cement and reported that ProRoot MTA and glass ionomer cement had better biocompatibility compared to Ortho MTA, while Retro MTA has similar biocompatibility and angiogenic effects on human pulp cells compared to ProRoot MTA. The setting time of Retro MTA and Ortho MTA are about 1.5-2.5 minutes and three minutes respectively.3



**Figure 6: Ortho MTA and Retro MTA**

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**Figure 7: Commercial and experimental calcium – silicate-based cements45**

* **PORTLAND CEMENT (PC)**

In 1824, Joseph Aspdin patented a product called Portland cement (PC) obtained from the calcination of the mixture of limestones coming from Portland in England and silicon-argillaceous materials. PC is an inexpensive material and except for the absence of bismuth oxide and higher levels of calcium aluminate and calcium sulfate, PC and MTA have a similar main composition. PC like MTA is available as grey and white. Ordinary PC (grey) shows lesser discoloration compared to grey MTA. However, there is an equal lack of discoloration seen by white MTA as well as white PC. Greater solubility is seen with MTA when compared to white PC. It also showed better washout resistance Compared to MTA in different solutions. Maturation of MTA after hydration is more structured than PC hence the former displays better bioactivity. Calcium ion release and formation of hydroxy apatite crystals is seen with both grey and white PC. The particle size of white Pro Root MTA is significantly small white PC both before and after hydration.1 PC shows antibacterial and antifungal properties similar to MTA against Enterococcus faecalis, Micrococcus luteus, Staphylococcus aureus, Staphylococcus epidermidis, Pseudomonas aeruginosa and Candida albicans.13 White and grey MTA had similar sealing ability as a root end filling material when checked by means of dye penetration when compared to white and grey PC.14 However, when checked as a perforation repair material by means of protein leakage, white PC showed better sealing ability compared to white and grey MTA. Cell culture studies have showed variable result as per the cell type. Essentially there was no genotoxicity or cytotoxicity seen associated with PC similar to MTA with respect to fibroblasts. However, with respect to human bone marrow derived mesenchymal stem cells, MTA displayed greater proliferation and migration compared to PC.14 Bio mineralization is greater with MTA compared to PC when observed at 30 and 60 days.13 Pulpotomy performed with PC and MTA was successful both clinically and radio graphically, but the root canals showed greater obliteration with PC.1

Portland cement appeared in dentistry before1878. MTA (mineral trioxide aggregate), a Portland cement-based formulation was developed more than 20 years ago as a root-end filling material but its potential for new clinical applications later became evident thanks to its innovative hydraulic properties and sealing ability. A longlist of new materials based on the original formulation and/or with minor modifications has been introduced in routine clinical practice. A light-curable HCSC is advisable in many clinical cases and at least one material is now on the market. Other experimental materials have been proposed, so many potential new products could soon be available and more very innovative HCSCs can be expected in the future. Despite of the dearth of information from the first *in vitro* experiments and the lack of clinical studies, HCSC gained the trust of many operators who proposed its clinical use for apicogenesis, pulp capping and other procedure. Tayand Pashley introduced the concept of “biomimetic remineralization” of partially demineralized dentin using MTA. This represented a major innovation and opened the way to potential new applications for HCSCs-based materials. At the moment the use of HCSCs-based technology for dentin remineralization is not far from the clinical application. The history of calcium silicate Portland cements dates back to Roman times when a cement able to set in water made by grinding together lime and a volcanic product found at Puteoli (hence called *pozzolana*) around Neapolis (the places described by Pliny the Elder). Pozzolana helped Roman concrete set quickly even when submerged in water, allowing the construction of bridges, harbors, aqueducts, monuments and buildings. During the middle-ages the secret of cement was lost. In the 18th century John Smeaton, an English engineer, rediscovered the correct proportions of cement using clay and limestone. In 1824, Joseph Aspdin, an English brick-layer, patented a process for making what he called Portland cement. The first great bridge built in the USA in the late 19th century was made of Portland–Pozzolanic cements. Modern Portland cement is made by mixing substances containing lime, silica, alumina, and iron oxide and then heating the mixture until it almost fuses. Pozzolana is still the main com-ponent of many Portland cements. Calcium silicate Portland cements set through a hydration reaction after mixing with water or water-containing liquids. Various hydration products form during the reaction, namely different phases of calcium silicate hydrate (CSH) as porous colloidal CSH gel and radial acicular CSH crystals, rhombohedral crystals of portlandite (calcium hydroxide), needle-like crystals of ettringite (hexacalcium alumina tetrisulphate hydrate), and calcium mono sulfo aluminate or calcium mono-carboaluminate. Porous CSH hardens by the formation of a solid network within 1–6 h. The setting reaction requires several days to complete the hydration and hardening phases and includes dissolution and reprecipitation processesof the dehydrated di- and tri-calcium silicate phases (C2S andC3S) and formation of hydration products like calcium di- and tri-silicate hydrates and calcium hydroxide. In this phase, CSH has layer structure, with a layer growing radially from the calcium silicate particles and resulting in a fibrous needle-like complex structure, and cuboidal calcium hydroxide crystals form among the hydrating cement compounds. This phase is difficult to inspect under standard SEM. As demonstrated by Gandolfi et al., environmental SEM (ESEM)analysis can provide more information on the morphology of the early stage of Portland and dental calcium silicate/MTA cements. Original native Pozzolanic cements are very similar to HCSCs under ESEM. Moisture (*i.e.* bio-logical fluids) is essential to allow the setting reaction and to develop/activate the cement’s bioactivity, such as the formation of apatite. The following stages have been proposed by Gandolfi et al. for the nucleation of calcium phosphates on the HCSC surface:1



**Figure 8: Portland Cement**

* A solid–liquid interface forms on the mineral particles, and ion dissolution occurs almost immediately. Ca2+ionsrapidly migrate into the mixing solution and portlandite (Ca(OH)2) forms.15
* Silicates are attacked by OH ion groups in an alkaline environment and a CSH phase forms on mineral particles. CSH is a porous, fine-grained/fibrous and disorganized hydrated silicate gel layer containing Si-OH silanol groups and negative surface charges that may act as nucleation sites for apatite formation.15
* CSH contains an excess of calcium hydroxide/portlandite formed by OH−ions from dissociated water molecules and Ca2+ions from the cement particles, so a strong continuous outflux of calcium hydroxide from CSH occurs during the first hours after mixing causing a marked rise in the pH and an increase in calcium ion concentration in the surrounding environment. Portlandite crystals nucleate inside the hydrating wet paste and are also detectable on the surface by ESEM/EDX. The release of portlandite persists for a long time in immersion/storage conditions, as revealed by the high pH of the soaking medium which remains constant at11.0–12.0, depending on the che++mistry of the material.15
* When exposed to a phosphate-containing fluid – simulated body fluids (SBFs) or body fluids – a sequence of reactions take place on the surface of HCSCs between calcium from the cement and phosphate from the solution, namely the absorption of Ca and P ions on the silanol groups (Si-OH) of the silica-rich CSH surface and the precipitation of calcium phosphates and apatite (as a result of local supersaturation) which matures into a B-type HCA phase at increasing storage times. The calcium phosphate apatite deposits form a layer of spherulites filling the superficial porosities. EDX, FTIR and micro Raman analyses have been used to demonstrate the formation of calcium phosphate and apatite deposits on cements after soaking in different SBFs.15

***Components added to calcium silicate based cements***

In order to improve the intrinsic properties of these materials, certain additional components have been added to the calcium silicate based bioceramic cements that can be depicted as below:16



**Figure 9: Added components to calcium silicate based cements**

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**Figure 10: Hydration process of Portland cement17**

**Properties of Portland cement**

***Compressive strength:*** PC containing bismuth oxide has similar initial and final compressive strength to MTA. Ultimately, it is worth mentioning that physical properties are strongly related to curing conditions.17

***Flexural strength:*** There are limited studies on the flexural strength of PC in comparison with other endodontic cements. Contamination with blood or saliva has no significant effect on the flexural strength of Portland cement. Resin-based pit and fissure sealant containing hydrated PC fillers did not exhibit acceptable flexural strength, and the amount of filler adversely affected this property.18

***Push-out bond strength:*** In 2mm from the root apex, resinous cements showed superior push-out bond strength compared to calcium silicate-based cements, and MTA had similar push-out bond strength to Portland cement containing calcium tungstate or zirconium oxide. Nevertheless, higher values of push-out bond strength have been reported for Portland cement with bismuth oxide. Biomineralization seems to enhance this property and the resistance against displacement of cement. Some modifications such as addition of calcium chloride to PC results in improved push-out strength, while calcium hydroxide affects it adversely.18



**Figure 11: Push out bond strength of calcium based sealers18**

**Bond strength:** Bond strength of Portland cement and MTA to resin cements has been evaluated after immersion in water. According to this study, bond strength of Portland cement was significantly low compared to that of glass ionomer and MTA.17

**Fracture resistance:** Portland cement does not seem to influence the fracture resistance of dentin during 12 weeks, while MTA improved this property. Notwithstanding, due to the limited studies in this regard, the impact of Portland cement on fracture resistance of dentin remains unclear.17

***Sealing ability:*** Preventing micro leakage is an important prerequisite in all endodontic applications. A study, using 1% methylene blue dye after 72 hours, reported no leakage beyond the retro fill area with PC. An orthograde plug of PC was also evaluated with fluid filtration technique, which is a more sensitive and reproducible method. The results suggest that Portland cement has the potential to be developed as a furcation repair material, even though leakage was noted. Compared to the commonly used retro fill materials such as amalgam, micro leakage and variable adaptation gaps on the interface between dentin and root-end filling material were found in all specimens including PC. One possible reason for the sealing ability of PC is its slight expansion upon setting. Mean expansion at 24 hours was noted to be 1.02% for Grey MTA, 0.29% for PC, and 0.08% for White MTA in water immersion. The sealing ability of a material can be enhanced if it has antibacterial properties. One of the proposed antimicrobial mechanisms is the high alkalinity of the cement, comparable to that of calcium hydroxide. The pH of Portland cement rises from that of 7 to 12.3 after mixing and continues rising to a maximum pH of 12.9 after 3 hours. The potassium and sodium ions present come from the minor oxide constituents, which also provide an additional source of hydroxyl ions. The results of studies evaluating the antibacterial effect of PC have been equivocal. While several of the microorganisms such as *Micrococcus luteus* (ATCC9341), *Staphylococcus aureus* (ATCC6538), Staphylococcus epidermidis ATCC 12228, Pseudomonas aeruginosa ATCC 27853, showed inhibition, others such as *Escherichia coli* (ATCC10538) and E. faecalis showed resistance to all the sealers. Other studies have found that despite the highly alkaline pH of both MTA and PC, they showed no antibacterial activity against *S. faecalis, S. aureus* and *B. subtilis* and no effect on any of the strict anaerobic bacteria. The antibacterial effect was not different in either fresh powders or powders from crushed set cements.19

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**Figure 12: Sealing ability of calcium based silicate sealers18**

***Radioopacity:*** While Portland cement in its natural state is slightly radiopaque; it fails to meet the ISO requirement for radiopacity. To overcome this disadvantage, radiopacifier additions have been carried out. Comparing different radiopacifiers, Portland cement/bismuth oxide and Portland cement/lead oxide presented the highest radiopacity values, whereas Portland cement/zinc oxide presented the lowest radiopacity values. However, all presented higher radiopacity than that of dentin and may potentially be added to the Portland cement as radiopacifying agents. The readings of white Portland cement with 15% bismuth oxide did not differ significantly from the reading observed for a thickness of 4 mm of aluminum which is considered ideal for a test specimen by ADA specification #57. Higher concentration of Bismuth oxide failed to improve radiopacity significantly. The compressive strength of Portland cement is not altered with use of 20% bismuth oxide, and the material continues to be biocompatible.53

***Setting time:*** Classically calcium chloride, calcium nitrite/nitrate, and calcium formate have been added as Portland cement accelerators. While it was found that all 3 accelerated the set of PC, statistically significant rise in temperature and pH were found with the use of different accelerators, thus meriting further evaluation including biocompatibility and sealing ability. The setting time of Portland cement can also be reduced by excluding gypsum during the last stage of the manufacturing process without affecting its other properties. An admix of 1% methylcellulose and 2% calcium chloride resulted in a mix of Portland cement, when compared with unmodified MTA,1 handled similarly to a reinforced zinc oxide-eugenol cement, 2 gave an approximately equal compressive strength, and 3 set one third faster (57 +/- 3 minutes).20

***Solubility:*** Portland cement when placed in aqueous environments with prolonged setting times seems to be vulnerable to washout. The cement industry routinely deals with wet conditions (underwater concrete placement) that can potentially affect the properties of the material, not unlike conditions encountered during periapical surgery. The results of a study suggest that the sealing ability of MTA in an aqueous environment might be compromised during the first 72 hours because of the materials excessive solubility may affect particle arrangement in dentinal cavity walls. Portland cement on the other hand behaved differently in that the solubility decreased within the first 24 hours to 1.46%. To address these problems for dental application, an anti-washout mixture (methylcellulose) is added to the cement to facilitate more cohesive cement. The addition of this additive increases the viscosity of the water used in the mixture, therefore, producing a more thixotropic material to resist washout. The behavior of excessive initial solubility followed by a constant decrease over 72 hours is also a feature of routinely used root canal sealers AH 26 or Tubli Seal and does not per se contradict the use of these materials in clinical situations. As the process of cement manufacture requires 15000C temperature and due to the high alkalinity of Portland cement, generally the commercially available samples are found to be sterile. While contaminated samples can be suitably sterilized with no microbial growth seen after dry heat sterilization, gases or by autoclaving**,** the physical properties after sterilization need further evaluation.20,21

***Biocompatibility & Tissue response:*** Freshly-mixed and partially-cured Portland cement (PC) pastes have been shown to exhibit good biological compatibility with a range of cells and tissue-types; particularly those associated with bone formation. Scanning electron microscopy revealed that human pulp cells attached to the Portland cement were flat and had numerous cytoplasmic extensions. These results suggest that Portland cement is biocompatible, allows the expression of mineralization-related genes on cultured human pulp cells, and has the potential to be used as a proper pulp-capping material. The cytotoxicity of MTA and Portland cement on human ECV304 endothelial cells was studied and no statistically significant difference between any of experimental materials was reported. 10 In this respect, using simulated body fluid in vitro, PC has been found to promote the precipitation of a layer of ‘bone-like’ hydroxyapatite which underpins its ability to integrate with living tissue. The dissolution of portlandite and formation of calcite were also observed on contact with SBF.5

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**Figure 13: Biocompatibility of the calcium sealers18**

***Antibacterial effect:*** Complete elimination of microbes from the root canal system is impossible. Thus, the use of root canal sealers with antibacterial effects is essential for the prevention of intracanal infections or bacterial invasion due to microleakage. Enterococcus faecalis is the most frequently isolated microorganism from infected root canals, especially in recurrent infections after root canal treatment. Therefore, most studies have evaluated the antibacterial effect of sealers against E. faecalis. Most calcium silicate sealers showed antibacterial effects against E. faecalis. For iRoot SP, all bacteria were eradicated directly after contact, whereas for AH Plus, the viable bacteria were significantly reduced and eradicated within 5–20 minutes. However, after 7 days, most sealers had lost their antibacterial effect. BioRoot RCS showed stronger antibacterial effects than AH Plus in several studies, and its effects lasted for 30 days. However, EndoSequence BC showed antibacterial effects in 2 articles and no effect in 1 other article that we reviewed. The discrepancy in these results may stem from differences in the testing method. There were only 3 articles about the antibacterial activity of Endosequence BC; therefore, further evaluation is needed. Endoseal MTA showed a stronger antibacterial effect against E. faecalis than EndoSequence BC, due to higher levels of metal oxides, such as Na2O, MgO, Al2O3, SO2, and Fe2O 22. However, only 1 report has dealt with the antibacterial effects of Endoseal MTA; as such, the limitations of our knowledge mean that further studies are required for a definitive assessment.Calcium silicate sealers showed similar or stronger antibacterial effects than AH Plus, particularly BioRoot RCS. The weak antibacterial effect of AH Plus against E. faecalis is ascribed to its lower alkalinity than calcium silicate-containing sealers.18

***Bioactivity:*** Bioactive materials are bone-bonding materials that form bone-like apatite upon immersion in a serum-like solution. Similarly, calcium silicate-based sealers are considered to be bioactive materials because they can induce hard tissue formation in both the periodontal ligament (PDL) and bone. Bioactive properties can be evaluated through osteogenic differentiation and mineralization potential. These properties have been assessed in terms of alkaline phosphatase activity, alizarin red staining, and mineralization-related gene expression. Most research has concluded that calcium silicate sealers show stronger bioactive effects on PDL, osteoblasts, and stem cells than other sealers. Calcium silicate sealers improve the expression of osteoblastic marker genes and induce a higher amount of mineralization matrix than other types of sealers. iRoot SP induces human tooth germ stem cell differentiation into odontoblast-like cells, and further induces osteoblast-like cells to produce more mineralized matrix gene and protein expression]. However, iRoot SP has less inductive potential and hard tissue deposition compared to ProRoot MTA. Apatite Root Sealer, MTA Fillapex, and iRoot SP demonstrated osteogenic potential through osteoblastic differentiation of PDLCs compared with Sealapex. BioRoot RCS had higher bioactivity than ZOE sealers on mouse pulp-derived stem cells and human PDLCs. Human dental pulp stem cells also showed significantly increased mineralization in the presence of BioRoot RCS. The osteogenic potential of calcium silicate sealers seems to be higher than that of AH Plus. Calcium release from calcium silicate sealers is thought to promote osteoblastic differentiation and calcium nodule formation. Studies have also been conducted regarding direct mineral deposition. When the surfaces of sealers immersed in Hank's balanced salt solution were examined with elemental dispersive X-ray microanalysis, BioRoot RCS induced carbonated apatite deposits, with a prolonged ability to release calcium ions and alkalization. In addition, when the root canal was obturated with GP and Endoseal MTA sealer, the biomineralization of the dentinal tubules was confirmed by observations using scanning electron microscopy and energy-dispersive spectroscopy. Therefore, it can be concluded that calcium silicate-based sealers are bioactive and stimulate hard tissue formation.18



**Figure 14: Bioactivity of calcium based silicate18**

***Limitations12***

* Higher amount of lead and arsenic released from PC along with reports of its high solubility compared to MTA has raised questions regarding its safety with respect to the surrounding tissues.
* Higher solubility may jeopardise the long-term seal of the restoration.
* Excessive setting expansion with PC may lead to crack formation with the tooth.
* Biomineralization with PC is not as effective and as long term as with MTA which is critical for bioactive material.

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