Revolutionizing Pediatric Dentistry: Bioactive Materials for Lasting Smiles

RICHA WADHAWAN¹, POULOMI DE ², NAYANLATA SAXENA³, SHUBHI KHARE⁴, SUNANDINI RAJPUT⁵, SWAGATALAXMI MAHATO⁶, PRIYA RAJ⁷

1. PROFESSOR, ORAL MEDICINE, DIAGNOSIS & RADIOLOGY, PDM DENTAL COLLEGE & RESEARCH INSTITUTE, BAHADURGARH, HARYANA 2. PROJECT JUNIOR MEDICAL OFFICER, INDIAN COUNCIL OF MEDICAL RESEARCH-NATIONAL INSTITUTE OF NUTRITION, AGARTALA, TRIPURA 3. MEDICAL OFFICER. DATIA DISTRICT HOSPITAL DATIA. MADHYA PRADESH 4. DENTAL SURGEON. S R MEMORIAL HOSPITAL, GWALIOR, MADHYA PRADESH DENTAL SURGEON, CHANDNA'S DENTAL AND IMPLANT CENTRE, GURUGRAM HARAYANA 6. DENTAL SURGEON, DEBEN MAHATA GOVERNMENT MEDICAL COLLEGE & HOSPITAL, PURULIA, WEST BENGAL 7. DENTAL SURGEON, DR. KASHI'S ASHWATHI SUPER SPECIALITY DENTAL CLINIC, THIRUVANANTHAPURAM, KERALA

Corresponding author: wadhawanricha1@gmail.com

Abstract: In recent years, advancements in dental materials have paved the way for a paradigm shift in pediatric dentistry. This article explores the emergence and potential of bioactive materials in improving dental treatments for children. Bioactive materials offer unique advantages over traditional materials by promoting re mineralization and enhancing tissue integration. These materials not only restore but actively contribute to the health and longevity of dental structures, crucial for the growing dentition of pediatric patients. Moreover, their antimicrobial properties mitigate the risk of secondary caries, addressing a common concern in pediatric dental care. This review examines the scientific basis, clinical applications, and future directions of bioactive materials in pediatric dentistry, highlighting their transformative impact on oral healthcare practices and patient outcomes.

Keywords: Re mineralization, Bio active materials, Pediatric dentistry, Antimicrobial, Pulp vitality

Date of Submission: 01-07-2024Date of Acceptance: 11-07-2024

I. Introduction:

In dentistry, "biomimetic materials" can be used synonymously with "bioactive materials." These substances are engineered to mimic natural biological processes or promote specific biological responses, such as facilitating the re-mineralization and regeneration of tooth tissues.¹ They aim to interact actively with the body's natural processes rather than merely being inert or biocompatible. Bioactivity in dentistry refers to a material's capacity to provoke a response from living tissues. Bioactive materials induce reactions in tissues, organisms, or cells, such as encouraging hydroxyapatite formation. These materials are valued for properties like their bactericidal or bacteriostatic effects, sterility, ability to stimulate reparative dentine, and capacity to maintain pulp vitality.² Clinically, they are used in restorative dentistry to prevent pulp necrosis and initiate dentinal bridge formation during both direct and indirect pulp capping procedures. Their alkalinity plays a crucial role in their effectiveness by significantly contributing to their bioactivity. Bioactive materials assist in pulpal repair by stimulating proteins such as bone morphogenic protein and transforming growth factor-beta from surrounding dentin. Furthermore, they form an antibacterial seal over pulp exposures, thereby enhancing their therapeutic efficacy.³ The material should be non-toxic and well-tolerated by oral tissues, ensuring it does not cause any adverse reactions or sensitivities in children. Materials should have ability to interact positively with biological tissues, promoting beneficial responses such as remineralization of tooth structure or inhibiting bacterial growth. Given the susceptibility of children to dental caries, bioactive materials should ideally have antibacterial effects to help prevent or minimize the risk of new cavities forming. The material should effectively seal and protect exposed dental tissues, preventing micro leakage and reducing the likelihood of recurrent decay. Bioactive materials should have suitable mechanical strength and durability to withstand the forces within the

5.

oral cavity, especially in children who may have habits like teeth grinding or chewing on hard objects.⁴ Pediatric dental materials should be easy for dentists to manipulate and apply, allowing for efficient procedures, especially considering the challenges posed by treating young, potentially uncooperative patients. While not always essential, it can be beneficial for bioactive materials to have acceptable esthetic qualities, especially for visible areas of the oral cavity, to ensure a natural appearance after treatment. Some bioactive materials release ions like calcium, phosphate, or fluoride, which can aid in remineralization and strengthening of tooth structure, making them desirable for pediatric use.⁵ Radiopacity is important for dental materials used in restorations, as it allows for easy identification on dental X-rays, aiding in diagnosis and assessment of treatment effectiveness. While not a property per se, bioactive materials should ideally be cost-effective and offer good value for money, considering the volume of pediatric dental treatments performed and the financial considerations of families. By possessing these ideal properties, bioactive materials can contribute significantly to the successful treatment and long-term oral health of pediatric patients.⁶In modern dentistry, biomimetic or bioactive materials are highly valued for their ability to actively interact with biological processes, promoting healing and regeneration of dental tissues. The term "bioactive" varies in meaning depending on its context: in restorative dentistry, it typically denotes a material's capacity to promote the formation of hydroxyapatite crystals on its surface. In implantology, bioactivity pertains to materials like calcium phosphate ceramics and glasses, which can form a direct chemical bond with recipient bone, enhancing implant stability. Additionally, in preventive dentistry, bioactive toothpastes are utilized to remineralize the outer enamel surface.⁷ Bioactive materials represent an advanced alternative to conventional dental materials, offering several distinct advantages. They possess remineralizing properties that strengthen hard dental tissues and protect them from acid erosion due to their elevated pH levels from mineral saturation.⁸

These materials can chemically bond to tooth structure, reducing sensitivity caused by bonding defects. Additionally, bioactive materials release calcium and phosphorus ions, facilitating the formation of a mineral similar to natural hydroxyapatite.⁹ This capability supports durable restorations and aids in repairing damaged dental structures, thereby reducing the risk of recurrent decay around existing restorations. In modern dentistry, bioactive materials are highly valued for their restorative, regenerative, and preventive benefits. They actively interact with biological tissues to promote dental health.¹⁰ According to Hench's 1994 classification, Class A bioactive materials are osteoinductive, attracting osteogenic stem cells to their interface and triggering both intracellular and extracellular responses. An example of a Class A material is Bio glass. Class B bioactive materials, classified as osteoconductive; stimulate an extracellular response by providing a biocompatible surface that supports bone migration. Synthetic hydroxyapatite is an example of a Class B material.¹¹ Widely regarded as the "gold standard" for direct pulp capping, calcium hydroxide's antibacterial properties help prevent bacterial penetration into pulpal tissue, reducing irritation. Various bioactive materials in pediatric dentistry, including Mineral Trioxide Aggregate (MTA), Bio Dentine, Bio Glass, Bio-Ionomer, Calcium Enriched Mixture (CEM), Amorphous Calcium Phosphate (ACP), Bio Aggregate, TheraCal LC, and EndoSequence Root Repair Material (ERRM), play crucial roles in diverse dental procedures. Bioactive materials used in pediatric dentistry should possess several ideal properties to ensure they are safe, effective, and suitable for the unique needs of children.12

II. Discussion:

Calcium hydroxide (Ca(OH)2), introduced to clinical dentistry by Hermann in 1990, is widely regarded as the standard material for protecting pulp during direct and indirect pulp capping procedures, as well as for use as a liner or sub-base.

It is a white, odorless powder with a molecular weight of 74.08 g/mol, known for its high alkalinity (pH 12.5–12.8) and low water solubility (approximately 1.2 g/L at 25°C). Initially recognized for promoting hard tissue formation and healing in vital pulpal and periapical tissues, its clinical applications have expanded over time.¹³ Despite its solubility in water and limited thermal insulation in thin layers, calcium hydroxide is not recommended as a sole base or luting cement due to these factors. Therefore, additional thermal protection should be provided with a separate high-strength base material. It promotes reparative dentin formation through its high alkalinity and antibacterial properties. Its hydroxyl group creates an alkaline environment that supports healing, active calcification, and acts as both bactericidal and bacteriostatic. Its elevated pH also stimulates fibroblasts, neutralizes acids' low pH, and prevents internal resorption. It is cost-effective and easy to apply but does not exclusively promote dentinogenesis or reparative dentin formation. Its use carries risks such as primary tooth resorption.¹⁴ Alkaline phosphatase, a hydrolytic enzyme, releases inorganic phosphate from phosphate esters, which reacts with calcium ions in the bloodstream to form calcium phosphate In pediatric dentistry, calcium hydroxide is used as a pulp capping agent, pulpotomy agent, and for apexification procedures.

However, it has limitations. It typically requires 2–3 months to induce coronal hard tissue barriers during pulp capping and 6–18 months for apexification.¹⁵ These barriers may remain incomplete due to vascular inclusions, potentially allowing bacterial invasion. Changes in dentin's structure, caused by the loss of inorganic and organic components, can increase the risk of cervical root fractures. It may also initially induce zones of sterile pulp necrosis at the contact area with vital pulp tissue, which could later become infected via micro leakage under restorations, leading to pulpitis and eventual pulp necrosis.¹⁶ It has been widely utilized in pediatric dentistry for various applications due to its unique properties and beneficial effects on dental tissues.

It is commonly used for direct pulp capping in primary teeth when the pulp is minimally exposed due to caries removal. It helps stimulate the formation of reparative dentin and promotes pulp vitality by creating a favourable environment for healing. Its high pH (approximately 12) is antibacterial, which aids in preventing bacterial penetration into the pulp tissue.¹⁷ In cases where pulpotomy is indicated in primary teeth, calcium hydroxide can be applied to the remaining pulp tissue to encourage healing and maintain pulp vitality. It has been traditionally used in the pulpotomy procedure known as the "pulpotomy with calcium hydroxide" technique. It supports apexogenesis in immature permanent teeth with open apices. By encouraging continued root development and thickening of dentinal walls, it helps preserve the vitality of the pulp and promotes natural root maturation. It is also used in the treatment of inflammatory root resorption in primary teeth. Its antibacterial and biocompatible properties aid in disinfection and promote healing of the affected root structure.¹⁸

Calcium Enriched Mixture (CEM): A modified form of calcium hydroxide, known as CEM cement, has been developed and is used in various endodontic procedures in both primary and permanent teeth. It exhibits improved sealing ability and biocompatibility compared to traditional calcium hydroxide. It was introduced in 2006 for endodontic use, features favourable physical properties such as flow, film thickness, and setting time.¹⁹ Biologically, CEM cement promotes hydroxyapatite formation in saline, potentially aiding stem cell differentiation and hard tissue formation. It sets rapidly in aqueous environments, with a shorter setting time than MTA, while offering sealing abilities akin to MTA. In pediatric dentistry, CEM cement serves well as a root-end filling material due to its comparable micro-leakage performance with MTA and Portland cement.²⁰

Its biocompatibility, flow ability, good clinical handling, antibacterial properties, and low cytotoxicity further recommend it for this application. Regenerative endodontic treatment using CEM cement promotes revascularization in immature necrotic teeth, supporting ongoing root development.²¹ Studies demonstrate successful revascularization in necrotic immature molars with CEM cement, using a modified approach.²² In pulpotomy procedures, CEM cement exhibits superior outcomes compared to Ca(OH)2 and MTA, including reduced inflammation, improved quality or thickness of calcified bridges, enhanced pulp vitality, and preservation of odontoblast cell morphology in permanent teeth.²³ A randomized clinical trial confirmed that CEM cement is an effective treatment option for pulpotomy in deciduous molars, demonstrating success rates comparable to those of MTA during a two-year follow-up period.²⁴ In a study involving permanent molars with open apices and extensive decay, reversible/irreversible pulpitis was observed.²⁵ A subsequent one-year trial demonstrated successful complete pulpotomy using both MTA and CEM. Another study by Zarrabi MH et al. indicated that CEM resulted in a thicker dentinal bridge and lower pulp inflammation compared to MTA in direct pulp capping, although these differences did not reach statistical significance.²⁶ Recent randomized trials have shown that CEM and MTA provide comparable and satisfactory outcomes for direct pulp capping in deciduous molars, addressing ongoing debates among pediatric dentists.²⁷ Regarding indirect pulp capping with CEM cement, an interesting case report detailed treatment of a mature symptomatic first mandibular molar with irreversible pulpitis associated with apical periodontitis. The clinical and radiographic outcomes were favourable, with complete resolution of symptoms and healing of the apical lesion observed within a 15-month follow-up period.²⁸ Despite its benefits, calcium hydroxide has limitations, such as its high solubility in oral fluids and the potential for inducing tooth discoloration over time.

Nonetheless, its longstanding use in pediatric dentistry continues to demonstrate its effectiveness in promoting dental tissue healing, preserving pulp vitality, and supporting the overall success of vital pulp therapies in children.²⁹

Glass ionomers (GICs) are dental materials renowned for their ability to release ions like calcium and aluminium, which aid in tooth remineralization and swiftly neutralize lactic acid, shifting from active caries pH to arrested caries pH within seconds.³⁰ This property helps reduce erosion and potentially prevents secondary caries around restorations. Bioactive glass, exemplified by 45S5 Bio glass developed by Larry Hench in 1969, has been incorporated into GIC formulations to boost bioactivity and facilitate tooth regeneration.³¹ Bio-Ionomers, which consist of aluminosilicate glass particles reacted with polymeric acids, are widely used in dentistry as both filling materials and luting cements. They exhibit natural adhesion to tooth structure and release fluoride. These materials have been extensively researched and modified to enhance their bioactivity, bio

mineralization capabilities, and physical properties. Conventional GICs are activated chemically through an acid-base reaction involving glass powder and polymeric acids like polyacrylic acid, releasing ions such as Ca2+ and Al3+ into the surrounding medium. Recent studies have highlighted the beneficial properties of Bio-Ionomers.³² Research has focused on enhancing the mineralization potential of GIC by incorporating additives such as bioactive glasses, beta-tricalcium phosphate, wollastonite, or MTA.³³ These modifications have demonstrated the ability to form mineralized surface layers in simulated body fluid without compromising compressive strength or setting properties. Notably, the addition of MTA has been shown to improve Compressive Strength as the modified GIC matures compared to conventional controls. Incorporating bioactive glass, CPP-ACP, or chitosan into GIC powders significantly enhances compressive strength and flexural strength. ³⁴

Bioactive glass-modified GICs release higher levels of fluoride and exhibit reduced bacterial adhesion compared to conventional GIC. Adding 15% nano- beta-tricalcium phosphate to GIC improves protection against acid demineralization and promotes enamel remineralization. GIC demonstrates good adhesion in moist environments, lower cytotoxicity, and hydrophilicity enabling bonding in the presence of residual fluids. Bio-Ionomers are widely used in pediatric restorations for their ease of placement and superior marginal adaptation.³⁵ GIC is suitable for restoring permanent teeth in low-stress areas like class III and class V lesions, preferred for high-caries-risk patients due to its fluoride-releasing capabilities. It acts as a pulp protector under metallic and composite restorations, and serves as a luting agent for indirect restorations including crowns, posts, core placements, and orthodontic appliances. These applications highlight the versatility and clinical effectiveness of Bio-Ionomers in contemporary dental practice.³⁶

Mineral Trioxide Aggregate (MTA), introduced by Mahmoud Torabinejad at Loma Linda University in California, United States of America, and documented in dental literature in 1993, is highly valued for its superior sealing ability, long-term efficacy, ease of handling, and strong biocompatibility.³⁷ Widely used in endodontics, MTA is prized for being non-toxic, non-carcinogenic, and biocompatible. It releases calcium ions, akin to Ca(OH)2, which promote tissue regeneration, cell attachment, and proliferation. Its alkaline pH creates an antibacterial environment, regulates cytokine production, and supports the formation of hard tissue, including hydroxyapatite, for effective sealing.³⁸ It finds extensive application in pediatric dentistry due to its outstanding properties and versatility. It is frequently employed for direct pulp capping and pulpotomy in primary teeth, facilitating dentin bridge formation, preserving pulp vitality, and fostering a conducive environment for healing.

It plays a crucial role in apexification procedures; promoting apical closure in immature permanent teeth with open apices, thereby aiding subsequent root canal treatment.³⁹ In cases of exposed pulp with ongoing root development, MTA supports apexogenesis by encouraging continued root growth and thickening of dentinal walls. Furthermore, MTA effectively seals root perforations during root canal procedures, preventing the spread of infection and maintaining the structural integrity of the tooth. It is preferred for root-end surgeries (apicoectomies) in primary teeth, ensuring reliable sealing and promoting healing around the apex. Despite its longer setting time, MTA's biocompatibility, antimicrobial properties, and ability to stimulate dentinogenesis justify its widespread use and favourable clinical outcomes in various vital pulp therapies and endodontic treatments for children.⁴⁰

Biodentine serves as a versatile dentin substitute in pediatric dentistry, applicable for various procedures such as indirect and direct pulp capping, as well as a base/liner in restorative work. Its notable advantage over MTA lies in its quicker setting time, allowing for immediate crown restoration or functional use intraorally without compromising material integrity. During its setting process, Biodentine releases calcium hydroxide, creating a highly alkaline environment that induces a zone of coagulation necrosis. This environment is beneficial as it stimulates precursor cell proliferation and migration to the surface, where they differentiate into odontoblast-like cells. This process promotes the formation of reactionary dentin through odontoblast stimulation and reparative dentin through cell differentiation.⁴¹ Additionally, Biodentine's high alkalinity inhibits microorganisms, enhancing its biological properties in dental applications. Compared to MTA, which also offers advantages like being non mutagenic, non neurotoxic, and exerting anti-inflammatory effects on pulp tissue, Biodentine promotes odontoblast activity and dentin formation through calcium hydroxide production, making it promising in pediatric dentistry.

Its flexural strength is approximately 14.27 ± 1.96 MPa. MTA creates an alkaline environment (pH 10.2, rising to 12.5) conducive to dental applications.⁴² It releases calcium ions, supports cell attachment and proliferation, and encourages differentiation of hard tissue-producing cells. However, MTA has drawbacks including longer setting times, challenging handling, higher cost, and potential tooth discoloration. Removal after placement is difficult due to the absence of a solvent. Biodentine is a bioactive dentin replacement material with properties similar to dentin, promoting the formation of tertiary dentin in vital pulp cells. It consists of a

powder component, housed in a capsule, composed of tricalcium silicate, zirconium oxide, calcium carbonate, and minor additives like iron oxide for coloration.⁴³ The liquid component, contained in an ampoule, includes water, calcium chloride, and a water-soluble polymer. This design ensures optimal clinical performance. To prepare Biodentine, 5 drops of liquid are mixed with 0.7 grams of powder using an amalgamator at 4000-4200 revolutions per minute for 30 seconds. Its short setting time of around 12 minutes allows its use in restorative procedures, unlike MTAs which set in 3-4 hours initially.⁴⁴ Biodentine, as highlighted by Allazzam et al. (2015), possesses several advantageous properties essential for clinical applications. These include a rapid setting time, high biocompatibility, robust compressive strength, exceptional sealing capabilities, and ease of handling, making it versatile for both endodontic repair and restorative procedures without causing tooth staining. Additionally, its highly alkaline pH (pH=12) contributes to excellent antimicrobial properties.⁴⁵Moreover, it is cost-effective compared to similar materials. In pediatric dentistry, as outlined by Raju et al. (2021), Biodentine serves various roles: it functions as a dentine substitute beneath composite restorations, is effective in pulp capping procedures, serves as a material for pulpotomy, and supports apexification processes.⁴⁶

Biodentine's effectiveness as a pulp capping agent lies in its ability to promote dentine bridge formation and tissue reaction, facilitated by its capability to initiate early mineralization from pulpal cells through the release of transforming growth factor–beta. Similarly, in pulpotomy procedures, Biodentine offers the advantage of reducing treatment time while acting as both a filling and a dressing material. Studies have demonstrated its capacity to maintain pulp vitality, as evidenced by findings from Nasrallah et al. (2018).⁴⁷ Biodentine is also used in apexification. It was found that immature necrotic teeth after proper regenerative endodontic procedure with biodentine can still produce continued root development. It is highly recommended due to its property to induce new cementum and periodontal ligament formation.⁴⁸

In pediatric dentistry, amorphous calcium phosphate (ACP) acts as a substitute for dentin and is employed in procedures such as pulp capping and apexification. It stimulates alkaline phosphatase activity, cell proliferation, and adhesion. ACP undergoes transformation into crystalline phases like octacalcium phosphate or apatite, essential for tissue repair, and represents a promising agent for remineralization in dental care. Dentin matrix protein 1 (DMP1) facilitates ACP's conversion into hydroxyapatite.⁴⁹ ACP-filled polymeric composites release calcium and phosphate ions, aiding tooth repair similarly to natural hydroxyapatite deposition. Casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) stabilizes ACP clusters, supporting nucleation and phase transformation. Incorporating CPP-ACP into Fuji IX enhances bond strength, compressive strength, and ion release in acidic oral environments. CPP-ACP also improves the protection of enamel and dentin around restorations compared to Fuji IX alone.⁵⁰ In mouth rinses, CPP-ACP increases calcium and phosphate ions in plaque, competing with calcium for binding sites, thereby reducing calcium bridging and limiting mineral loss during cariogenic episodes. CPP-ACP acts as a calcium source to inhibit demineralization and promote remineralization over three days.

In food products, CPP-ACP effectively prevents demineralization without altering taste; combating cariogenic properties in beverages, confections, and dairy.⁵¹Toothpastes combining CPP-ACP with fluoride significantly reduce caries by localizing ACFP on tooth surfaces. This co-localization of calcium, phosphate, and fluoride in a slow-release amorphous form enhances clinical efficacy. GC Tooth Mousse is a sugar-free topical crème used for remineralizing dentin and enamel to prevent caries. Studies from 2013 have indicated that CPP-ACP is more effective than sodium fluoride mouthwash and fluoridated toothpaste for enamel caries remineralization, supported by both in-vivo and in-vitro research.⁵²

Bioactive glass is made of synthetic mineral containing sodium, calcium, phosphorous and silica (sodium calcium phospho silicate) which are naturally found in the body. When these particles come in contact with saliva or water, they rapidly release sodium, calcium and phosphorous ions into the saliva which are available for re-mineralization of the tooth surface. Unlike other calcium phosphate technologies, the ions that bioactive glass release form hydroxycarbonate apatite (HCA) directly, without the intermediate amorphous calcium phosphate phase. These particles also attach to the tooth surface and continue to release ions and remineralize the tooth surface after the initial application. These particles have been shown, in in-vitro studies, to release ions and transform into HCA for up to two weeks. Ultimately these particles will completely transform into HCA which is the mineral of our teeth. In a clinical trial on tooth hypersensitivity a bioactive glass containing toothpaste was shown to decrease sensitivity significantly greater than strontium chloride toothpaste. They have also been shown to have significant anti microbial properties and can kill up to 99.99% of oral pathogens associated with periodontal disease and caries.⁵³

Bio Aggregate is an advanced bio ceramic material in pediatric dentistry that leverages nanotechnology to produce aluminium-free ceramic particles upon hydration. It consists of tricalcium silicate, dicalcium silicate, tantalum pent oxide, and calcium phosphate monobasic. Known for its superior biocompatibility, it forms a

thick paste-like mixture with a working time of approximately 5 minutes, extendable with a moist gauze sponge. The material demonstrates excellent handling and high sealing ability, surpassing other root-end filling materials. It releases calcium ions and maintains a high pH, supporting mineralization crucial for tissue healing. Clinical applications include root perforations, repairs of root resorption, root-end fillings, apexification, pulpotomy, and pulp capping. Bio Aggregate's radiopacity, convenient setting time, and ease of manipulation make it an ideal choice for root canal procedures, effectively blocking bacterial infection and promoting cementogenesis. Overall, it represents a new generation of bio ceramic materials developed through advanced nanotechnology, noted for its innovative qualities and clinical versatility in pediatric dental care.⁵⁴

TheraCal LC, also known as a light-cured, resin-modified calcium silicate-filled base/liner material, is synonymous with a fourth-generation calcium silicate material. It is primarily used for pulp capping and as a protective liner beneath restorative materials. It sets through hydration, a process initiated by absorbing water from the surrounding environment. According to manufacturer instructions, it is applied on moist dentin. Biologically, TheraCal LC releases calcium ions that stimulate dental pulp cell growth and differentiation, promoting the formation of mineralized tissue. It also releases hydroxyl ions, which can increase local pH levels. This may initially cause irritation to pulp tissue and superficial necrosis but ultimately aids in mineralization and dentin repair by forming hydroxyapatite-like crystals, thereby creating a biological seal.

It is highly regarded in pediatric dentistry for direct pulp capping, promoting superior hard tissue bridge formation and enhancing dentinal bridge quality compared to alternatives.⁵⁵ Studies show it induces comparable reparative dentin and manages inflammation effectively when compared with Septocal LC and Dycal.⁵⁶ In indirect pulp capping, TheraCal LC and MTA have shown successful outcomes in primary teeth, including pain relief, absence of sinus tracts, and positive radiographic results.⁵⁷ Research indicates no significant difference in success rates between TheraCal LC, ProRoot MTA, and Dycal for both primary and permanent teeth (p > 0.05, modified USPHS criteria).⁵⁸ It contains tricalcium silicate particles in a hydrophilic monomer matrix, promoting substantial calcium release essential for dentin-pulp complex healing and regeneration. Its user-friendly syringe application eliminates the need for hand mixing or trituration. It is recommended for optimal aesthetics when applied thinly due to its opaque white colour, which can influence final shade when covered with translucent composite, each layer cured for 20 seconds.⁵⁹ TheraCal LC provides advantages in pediatric dentistry such as accelerated setting times enabling immediate restoration, straightforward and accurate application, and excellent flow characteristics. It supports pH alkalization, acts as a scaffold for reparative dentin, and reduces micro leakage for effective sealing.⁶⁰ However, compared to Bio dentine, TheraCal LC releases calcium ions more slowly and lacks post-setting calcium hydroxide formation, potentially leading to risks like internal root resorption and pulpal irritation due to elevated pH. Concerns also include cytotoxicity from unpolymerized resin monomers, which may diminish its bioactive potential compared to Bio dentine. In clinical use, TheraCal LC is applied directly over exposed sites and layered for sealing in pulpotomy procedures for primary teeth.⁶⁰ Two studies evaluated TheraCal LC's efficacy in pediatric dentistry: Wassel, Amin, and Badran found it to be relatively biocompatible in primary teeth, showing clinical and radiographic success comparable to Formocresol over six months in pulpotomy treatments.⁶¹ In contrast, Bakhtiar et al. observed that Bio dentine and ProRoot MTA outperformed TheraCal LC in partial pulpotomy treatments, demonstrating superior clinical outcomes.62

EndoSequence Root Repair Material (ERRM) is a biocompatible dental material used in root repair composed of tricalcium silicate, zirconium oxide, tantalum pent oxide, di calcium silicate, calcium sulfate, calcium phosphate monobasic, and filler agent. It sets and hardens in a minimum of 2 hours, requiring water for the setting reaction, which may be prolonged in dry application sites. Moisture from dentinal tubules suffices, eliminating the need for additional moisture. ERRM is insoluble, produces calcium hydroxide upon contact with water, maintains a pH above 12, exhibits antimicrobial properties, is radiopaque, and offers excellent sealing as a root-end filling material. Importantly, it is free from aluminium. Human studies comparing ERRM and MTA showed similar outcomes in dentinal bridge formation and pulp inflammation appearance. However, MTAtreated patients reported less cold sensitivity than those treated with ERRM.⁶³ Anujalkhur et al. observed chronic mild inflammation in the dentinal bridge of two out of five sample specimens treated with ERRM during direct pulp capping.⁶⁴ In another study by Sultana N et al., ERRM showed double the odds of treatment failure compared to MTA in vital pulp therapies with a 730-day follow-up. Further clinical research is needed to fully assess ERRM's long-term efficacy as a pulp-capping agent in primary and permanent teeth.⁶⁵Activa[™] BioActive Restorative, developed by Pulpdent Corp., combines the strength and aesthetics of composite materials with the benefits of glass ionomers to mimic natural teeth. It features a patented bioactive ionic resin, a durable rubberized resin, and bioactive ionomer glass. This material supports the diffusion of calcium, phosphate, and fluoride ions, which aids in remineralization and strengthens bonds. With minimal polymerization shrinkage (1.7%) and a deep light cure capability (4 mm), Activa[™] allows for efficient and quick restorations with larger increments. It effectively manages class I and class II caries in primary molars,

particularly in challenging isolation conditions or high caries index scenarios, thanks to its fluoride-releasing properties.⁶⁶

III. Conclusion:

In today's era focused on regeneration, the re-mineralization of demineralized dental hard tissue is a critical necessity. Continuous advancements in technology drive an ongoing search for biomimetic materials that can safeguard and preserve the health of both hard and soft tissues. It is crucial to comprehend the properties of current bioactive materials thoroughly to harness their beneficial effects optimally. Furthermore, there is a pressing need for increased research to develop new materials based on existing concepts, capable of mimicking and replacing natural hard and soft tooth structures, as well as surrounding bone. Novel approaches for adhesion and integration of these materials are being actively pursued, promising to revolutionize the treatment of teeth and shape the future of dentistry.

Financial support and sponsorship Nil

Conflicts of interest There are no conflicts of interest

References

- [1]. Deeksha Grotra, Subbarao CV et al. Bio active materials used in endodontics. Recent Research in Science and Technology. 2012; 4(6):25-27.
- [2]. Mqazzaoui et al. Incorporation of CPP-ACP into GIC. J Dent Res. 2003; 82(11):914-8.
- [3]. Eda S. Histochemical analysis on the mechanism of dentin formation in dog's pulp. Bull Tokyo Dent Coll. 1961; 2:59-88.
- [4]. Rose RK. Effects of an anticariogenic casein phosphopeptide on calcium diffusion in streptococcal model dental plaques. Arch Oral
- Biol. 2000; 45:569-575.
 [5]. Nongonierma AB, FitzGerald RJ. Biofunctional Properties of Caseino phosphopeptides in the Oral Cavity. Caries Res.2012; 46:234-267.
- [6]. Shen Cai et al. Acid resistance of enamel subsurface lesions remineralized by a sugar-free chewing gum containing casein phosphopeptide-amorphous calcium phosphate. Caries Res. 2004; 38(6):551-6.
- [7]. Dutta A, Saunders W. Calcium silicate materials in endodontics, Dental Updates. 2014; 41(8):708-722.
- [8]. Asgary S, Shahabi S, Jafarzadeh T, Amini S, Kheirieh S. The properties of a new endodontic material. J Endod. 2008; 34:990-993.
- [9]. Glickman GN, Koch KA. 21st-century endodontics. JAm Dent Assoc. 2000; 131:39S-46.
- [10]. Asgary S, Eghbal MJ, Parirokh M, Ghoddusi J. Effect of two storage solutions on surface topography of two rootend fillings. Aust Endod J. 2009; 35:147-152.
- [11]. Gopika GJ, Ramarao S, Usha C, et al. Histological evaluation of human pulp capped with light-cured calcium based cements: a randomized controlled clinical trial. International Journal of Scientific Reports. 2017; 3(5):120-127.
- [12]. Olszta MJ, Cheng X, Jee XX. Bone structure and formation: A new perspective. Mat Sci Eng. 2007; 58:77-116.
- [13]. Poggio C, Lombardini M, Colombo M, Beltrami R, Rindi S. Solubility and pH of direct pulp capping materials: a comparative study. Journal of Applied Biomaterials & Functional Materials. 2015; 13(2):73-193.
- [14]. Yamamoto S, Han L, Noiri Y, Okiji T. Evaluation of the Ca ion release, pH and surface apatite formation of prototype tricalcium silicate cement. International Endodontic Journal. 2017; 50:1-10.
- [15]. Gandolfi MG, Siboni F, Botero T, Bossu M, Riccitiello F, Prati C. Calcium silicate and calcium hydroxide materials for pulp capping: biointeractivity, porosity, solubility and bioactivity of current formulations. Journal of Applied Biomaterials and Fundamental Materials. 2014; 13(1):43-60.
- [16]. Estrela C, Sydney GB, Bammann LL, Felippe O Jr. Mechanism of action of calcium and hydroxyl ions of calcium hydroxide on tissue and bacteria. Brazilian. Dental Journal 1995; 6:85-90.
- [17]. Mohammed Mustafa, Saujanya KP. Role of Calcium Hydroxide in Endodontics: A Review. GJMEDPH.2012; 1(1):66-70.
- [18]. Mohammadi Z, Dummer PMH, et al. Properties and applications of calcium hydroxide in endodontics and dental traumatology. International Endodontic Journal. 2011; 44(8):697-730.
- [19]. Fallahinejad Ghajari M, Asgharian Jeddi T, Iri S, Asgary S. Direct pulp-capping with calcium enriched mixture in primary molar teeth: A randomized clinical trial. Iran Endod J.2010; 1:1-4.
- [20]. Estrela C, Bammann LL, Estrela CR, Silva RS, Pécora JD. Antimicrobial and chemical study of MTA, Portland cement, calcium hydroxide paste, Sealapex and Dycal. Braz Dent J. 2000; 11:3–9.
- [21]. Nosrat A, Seifi A, Asgary S. Pulpotomy in caries exposed immature permanent molars using calciumenriched mixture cement or mineral trioxide aggregate: A randomized clinical trial. Int J Paediatr Dent. 2013; 23:56-63.
- [22]. Kangarlou A, Sofiabadi S, Yadegari Z, Asgary S. Antifungal effect of calcium enriched mixture cement against Candida albicans. Iran Endod J. 2009; 4:101–105.
- [23]. Razmi H, Aminsobhani M, Bolhari B, Shamshirgar F, Shahsavan S, Shamshiri AR. Calcium enriched mixture and mineral trioxide aggregate activities against Enterococcus Faecalis in presence of dentin. Iran Endod J.2013; 8:191–196.
- [24]. Murray PE, García Godoy C, García Godoy F. How is the biocompatibility of dental biomaterials evaluated? Med Oral Patol Oral Cir Bucal. 2007; 12:e258–e266.
- [25]. Torabzadeh H, Asgary S. Indirect pulp therapy in symptomatic mature molar using calcium enriched mixture cement. J Conserv Dent. 2013; 16:83-86.
- [26]. Zarrabi MH, Javidi M, Jafarian AH, Joushan B. Immunohistochemical expression of fibronectin and tenascin in human tooth pulp capped with mineral trioxide aggregate and a novel endodontic cement. J Endod. 2011; 37:1613-8.
- [27]. Mozayeni MA, Milani AS, Marvasti LA, Asgary S. Cytotoxicity of calcium enriched mixture cement compared with mineral trioxide aggregate and intermediate restorative material. Aust Endod J. 2012; 38:70–75.
- [28]. Asgary S, Eghbal MJ. The effect of pulpotomy using calcium-enriched mixture cement versus one-visit root canal therapy on postoperative pain relief in irreversible pulpitis: A randomized clinical trial. Odontology. 2010; 98:126-33.
- [29]. Tabarsi B, Pourghasem M, Moghaddamnia A, Shokravi M, Ehsani M, Ahmadyar M, Asgary S. Comparison of skin test reactivity of two endodontic biomaterials in rabbits. Pak J Biol Sci.2012; 15:250–254.
- [30]. Matsuya S, Matsuya Y, Yamamoto Y. Erosion process of glass ionomer cement in organic acids. Dent Mater J. 1984; 3:210-219.

- [31]. Nicholson JW, Aggarwal A, Czarnecka B, LimanowskaShaw H. The rate of change of pH of lactic acid exposed to glass ionomer dental cements. Biomaterials. 2000; 20:1989-1993.
- [32]. Yli-Urpo H, Lassila LV, Närhi T, Vallittu PK. Compressive strength and surface characterization of glass ionomer cements modified by particles of bioactive glass. Dent Mater. 2005; 21:201-9.
- [33]. Xie D, Brantley WA, Culbertson BM, Wang G. Mechanical properties and microstructures of glassionomer cements. Dent Mater. 2000; 16:129-38.
- [34]. Yli-Urpo H, Närhi M, Närhi T. Compound changes and tooth mineralization effects of glass ionomer cements containing bioactive glass (S53P4), an in vivo study. Biomaterials. 2005; 26:5934-41.
- [35]. Xie D, Zhao J, Weng Y, Park JG, Jiang H, Platt JA. Bioactive glass-ionomer cement with potential therapeutic function to dentin capping mineralization. Eur J Oral Sci. 2008;116:479-87.
- [36]. 29. Ngo H, Mount GJ, Peters MCRB. A study of glass ionomer cement and its interface with enamel and dentin using a low-temperature, high resolution scanning electron microscopic technique. Quintessence Int. 1997; 28:63-69.
- [37]. Lee SJ, Monsef M, Torabinejad M. Sealing ability of a mineral trioxide aggregate for repair of lateral root perforations. J Endod 1993; 19:541-544.
- [38]. Zarrabi MH, Javidi M, Jafarian AH, Joushan B. Histologic assessment of human pulp response to capping with mineral trioxide aggregate and novel endodontic cement. J Endod. 2010; 36:1778-81.
- [39]. Menon NP, Varma BR, Janardhanan S, Kumaran P, Xavier AM, Govinda BS. Clinical and radiographic comparison of indirect pulp treatment using light-cured calcium silicate and mineral trioxide aggregate in primary molars: a randomized clinical trial. Contemporary Clinical Dentistry. 2016; 7(4):475-480.
- [40]. Reyes-Carmona JF, Felippe MS, Felippe WT. Biomineralization Ability and Interaction of Mineral Trioxide Aggregate and White Portland Cement With Dentin in a Phosphate-containing Fluid. J Endod. 2009; 35(5):731-6.
- [41]. Malekafzali B, Shekarchi F, Asgary S. Treatment outcomes of pulpotomy in primary molars using two endodontic biomaterials. A 2-year randomised clinical trial. Eur J Paediatr Dent. 2011; 12:189-93.
- [42]. Nicholson JW, Czarnecka B, Limanowska-Shaw H. The long-term interaction of dental cements with lactic acid solutions. J Mater Sci Mater Med. 1999; 10:449-452.
- [43]. Dr. Vipin Arora et al. Bioactive dentin replacement. Journal of Dental and Medical Sciences. 2013; 12(4):51-57.
- [44]. Priyalakshmi S, Manish Ranjan, et al. Review on Biodentine-A Bioactive Dentin Substitute. IOSR Journalof Dental and Medical Sciences.2014; 13(1):13-17.
- [45]. Allazzam SM, Alamoudi NM and El Meligy O.A.E.S. Clinical applications of biodentine in pediatric dentistry: a review of literature. Journal of Oral Hygiene & Health.2015; 3(3): 1-6.
- [46]. Raju SS, Srujana MP, Kiranmayi M, Reddy ER and Sai S. Bio active materials in pediatric dentistry: A review. Int J Appl Dent Sci.2021; 7(1):345-51.
- [47]. Nasrallah H, El Noueiri B, Pilipili C and Ayoub F. Clinical and radiographic evaluations of Biodentine[™] pulpotomies in mature primary molars (Stage 2). International journal of clinical pediatric dentistry.2018; 11(6):496=504.
- [48]. Ahmed Madfa A, Fadhel Al-Sanabani A, et al. Endodontic Repair Filling Materials: A Review Article. British Journal of Medicine & Medical Research. 2014; 4(16):3059-3079.
- [49]. Butler WT. Dentin Matrix Proteins and Dentinogenesis.Connect Tissue Res. 1995; 33(13):59-65.
- [50]. Krithikadatta J, Fredrick C, Abarajithan M, Kandaswamy D. Remineralization of occlusal white spot lesion with a combination of 10% CPP-ACP and 0.2% sodium fluoride evaluated using diagnodent: a pilot study. Oral Health Prev Dent. 2013; 11:191-196.
- [51]. Somasundaram P, Vimala N, Mandke LG. Protective potential of casein phosphopeptide amorphous calcium phosphate containing paste on enamel surfaces. J Conserv Dent. 2013; 16:152-156.
- [52]. Asgary S, Eghbal MJ, Parirokh M. Sealing ability of novel endodontic cement as a root-end filling material. J Biomed Mater Res A. 2008; 87:706-709.
- [53]. Kazem M, Mahjour F, Dianat O, Fallahi S, Jahankhah M. Root-end filling with cement-based materials: An in vitro analysis of bacterial and dye microleakage. Dent Res J. 2013; 10:46-51.
- [54]. Tabarsi B, Parirokh M, Eghbal MJ, Haghdoost AA, Torabzadeh H, Asgary S. A comparative study of dental pulp response to several pulpotomy agents. Int Endod J. 2010; 43:565-71.
- [55]. Cannon M, Gerodias N, Viera A, Percinoto C, Jurado JR. Primate pulpal healing after exposure and TheraCal application. Journal of Clinical Pediatric Dentistry. 2014; 38(4):333-337.
- [56]. Gurcan AT, Seymen F. Clinical and radiographic evaluation of indirect pulp capping with three different materials: a 2-year followup study. European Journal of paediatric dentistry. 2019; 20(2):105-110.
- [57]. Gandolfi MG, Siboni F, Prati C. Chemical-physical properties of TheraCal, a novel light-curable MTA-like material for pulp capping. International Endodontic Journal.2012; 45(6):571-579.
- [58]. Cannon M, Gerodias N, Viera A, Percinoto C, Jurado JR. Primate pulpal healing after exposure and TheraCal application. Journal of Clinical Pediatric Dentistry. 2014; 38(4):333-337.
- [59]. Martínez-Cortés M, Tinajero-Morales C, Rosales C, UribeQuerol E. Cytotoxicity assessment of three endodontic sealing cements used in periapical surgery. In vitro study. Revista Odontol Mexicana. 2017; 21:40-8.
- [60]. Mariem O, Wassel, Dina H, Amin, Amira Badran S. Clinical, Radiographic, and Histological Evaluation of TheraCal Pulpotomy in Human Primary Teeth. Egypt dental journal 2017; 63(3):365-375.
- [61]. Hengameh Bakhtiar, Mohammad Hossein Nekoofar, Pouyan Aminishakib. Human Pulp Responses to Partial Pulpotomy Treatment with TheraCal as Compared With Biodentine and ProRoot MTA: A Clinical Trial. J Endod. 2017; 43(11):1786-1791.
- [62]. Nosrat A, Seifi A, Asgary S. Regenerative endodontic treatment (revascularization) for necrotic immature permanent molars: a review and report of two cases with a new biomaterial. J Endod. 2011; 37:562-567.
- [63]. Anujalkhur. Comparative evaluation of response of human dental pulp on direct pulp capping with MTA. ERRM. IOSR-JDMS 2016; 15(6):52-57.
- [64]. Sultana N, Singh M, Nawal RR, Chaudhry S, Yadav S, Mohanty S et al. Evaluation of biocompatibility and osteogenic potential of tricalcium silicate–based cements using human bone marrow–derived mesenchymal stem cells. J Endodontics. 2018; 44:446-451.
- [65]. Ana ID, Matsuya S, Ohta M, Ishikawa K. Effects of added bioactive glass on the setting and mechanical properties of resin modified glass ionomer cement. Biomaterials. 2003; 24:3061-7.