DOI: 10.7860/JCDR/2023/66278.18811

Review Article

Dentistry Section

Scope of Bioaggregate in Paediatric Dentistry: A Narrative Review

YATIKA SARASWAT[1], ESWARI RAMASSAMY[2], PRATHIMA GAJULA SHIVASHANKARAPPA[3]

ABSTRACT

Paediatric Dentistry has witnessed significant changes in the materials used in pulp therapy in recent years. Bioceramic materials have been considered as the dawn of a new era in dentistry. The introduction of these materials into pulp therapy as mineralising materials has brought about enormous productive changes. Bioaggregate (BA) is a newly introduced nanoparticle-sized bioceramic material produced as an alternative to Mineral Trioxide Aggregate (MTA), aiming to overcome the disadvantages of the material. In-vitro studies and a few clinical studies have demonstrated its biocompatibility and other properties, establishing it as an alternative to MTA and expanding its clinical applications. The aim of the present narrative review is to provide insight into the properties of BA, considering its scope in Paediatric dentistry.

Keywords: Bioaggregate, Bioceramic material, Mineral trioxide aggregate, Properties

INTRODUCTION

Bioceramics are one of the oldest synthetic materials based on natural resources whose properties have been considered very attractive in the fields of both medicine and dentistry. Bioceramics are considered exceedingly biocompatible, non toxic materials that are chemically stable within the biological environment. Another advantage of the material is its ability to form hydroxyapatite during its setting reaction, thereby creating a chemical bond with dentin [1].

Various bioactive glasses and glass ceramics are available and used in dentistry under different trade names. Several calcium silicate materials, such as MTA, Biodentine and BA, are also used in dentistry as root repair materials and for apical retrofills [1,2]. MTA, a bioceramic material, has a few limitations such as long setting time, manipulation difficulty, high cost and tooth discolouration. BA was introduced as an alternative to MTA to overcome its limitations. It contains additives similar to MTA, such as silicon dioxide and calcium phosphate, but does not contain bismuth oxide or aluminum oxide [3]. Although the properties of BA have been proven to be comparable and superior to MTA in many in-vitro studies [1,4,5], there are still only a handful of in-vivo reports.

Bioaggregate (BA)

The BA, a new generation bioceramic material, is the first nanoparticulate material that has properties similar to MTA [6]. It is produced as a pure and fine white hydraulic cement-like powder containing contamination-free ceramic nanoparticles [4]. The material was first manufactured by Innovative Bioceramics in Vancouver, Canada [1] and is also manufactured by Diadent under the brand name Diaroot. The composition of BA is given in [Table/Fig-1] [5,7].

Energy Dispersive Analysis (EDS) of the material shows homogeneous aggregates of small, round particles made up of calcium, silicon, and tantalum. BA does not contain bismuth as a radiopacifier [8].

Setting Reaction

The material should be mixed according to the instructions given by the manufacturer. The powder-liquid ratio is one vial of liquid, which is the exact volume needed to dissolve 1 gram of powder (0.38 mL). Adding excessive liquid to the powder may alter the setting time and properties of the material [7]. To begin the mixing process, dispense one pouch of powder into the mixing cup, and then dispense one vial of liquid into the powder. Gradually incorporate the liquid into the powder using a spatula for approximately two minutes or until all the particles are hydrated and the mixture resembles a thick paste.

Composition		Properties
Powder	Tricalcium silicate	It serves as a key structural element; and offers hardness, strength, and sealing properties of set cement.
	Dicalcium silicate	
	Calcium hydroxide {$Ca(OH)_2$} (Less than MTA)	It acts as a hydration product of calcium silicates and is structurally weak.
	Amorphous silicone dioxide	It actively eliminates some of the $Ca(OH)_2$ that was being used to hydrate and set calcium silicates.
	Hydroxyapatite	Reacts by removing some of the $Ca(OH)_2$ that was added to calcium silicates to set them. The calcium silicate hydrogen is strengthened by highly distributed in-situ precipitation.
	Calcium phosphate monobasic	Adjusts its hydrate setting [5].
	Tantalum oxide	Provides radiopacity.
Liquid	Deionised water	

[Table/Fig-1]: Composition of Bioaggregate (BA) [5,7].

The mixing time of the material is two minutes, the working time is five minutes, and the setting time of the material is four hours [7]. If needed, the mixture can be covered with a moist gauze sponge while unattended in order to increase the working time and retard the dehydration process [7]. After the addition of liquid to the powder, calcium silicate hydrate and calcium hydroxide are produced from the tricalcium silicate. Calcium silicate hydrate forms around the cement grains as a result of the reaction between calcium hydroxide and silicon dioxide. Consequently, the amount of calcium hydroxide in the aged cement decreases [9]. The final product formed in the reaction will be the nano-composite network of gel-like calcium silicate hydrate mixed intimately with the hydroxyapatite bioceramic [10]. Tantalum oxide is an inert material and does not leach out in solution. BA exhibits early high calcium ion release, which is maintained over a 28-day period but decreases as the material ages [9].

PROPERTIES OF BIOAGGREGATE (BA)

The properties of Bioaggregate (BA) are discussed below:

Colour Stability

Tooth discolouration has been a concern in cases involving Mineral Trioxide Aggregate (MTA) due to its metal oxide content. In contrast,

BA contains tantalum oxide as a radiopacifier. In a clinical pilot study conducted by Tuloglu N and Bayrak S it was found that approximately 15.39% of teeth treated with MTA showed coronal discolouration, while none of the teeth treated with BA exhibited discolouration [11]. The absence of bismuth oxide in BA explains the significant difference in colour stability compared to MTA [12]. Furthermore, a study by Caliskan S et al., reported no coronal discolouration when using BA as a partial pulpotomy material for fractured teeth with incomplete apex formation [1].

Antibacterial Activity

The BA is known to exhibit antibacterial activity. Zhang H et al., demonstrated in their in-vitro study that BA has antibacterial activity comparable to that of MTA. They observed a significant decrease in bacterial viability within six minutes. The antibacterial activity is attributed to the increase in pH resulting from the dissociation of calcium hydroxide [5].

Biocompatibility

The BA has demonstrated biocompatibility similar to that of MTA, as shown by various in-vitro studies. In an in-vitro study conducted by Yan P et al., BA was found to be biocompatible and promoted the development of human Periodontal Ligament (PDL) fibroblasts by promoting the expression of the genes for alkaline phosphatase (ALP) and type I collagen [13]. Another study by Jang YE et al., compared the cytotoxicity of MTA, BA and biodentine. The results indicated that both BA and MTA did not exhibit any cytotoxic effects on human periodontal ligament fibroblasts, whereas Biodentine showed higher cytotoxicity [14]. Zhu L et al., in their in-vitro study, stated that Bioaggregate exhibited excellent cytocompatibility and facilitated cellular adhesion, migration, and attachment of Human Dental Pulp Cell (HDPC). Therefore, BA can be considered a suitable alternative to MTA [4].

Bioactivity

A small controversy exists regarding the bioactivity of BA. Camilleri J et al., conducted a study comparing the properties of MTA angelus and BA. Their findings demonstrated that BA exhibited early high calcium ion release, but after 28 days of hydration, the absence of calcium hydroxide was observed. As a result, they concluded that the absence of calcium ions negatively influences the bioactivity of the material [15]. However, other in-vitro studies on the bioactivity of BA provide positive reviews of the material.

Yuan Z et al., concluded in their study that BA showed non toxicity to osteoblast cells and promoted the production of genes related to mineralisation in osteoblast cells when used as a biomaterial for root-end filling. The exact mechanism by which BA influences mineralisation-related gene expression is not well known, but it has been suggested that this effect may be due to the presence of hydroxyapatite in BA [16]. Lee BN et al., also supported these findings in their in-vitro study and concluded that the messenger Ribonucleic Acid (RNA) level of osteogenic genes significantly increased in both the MTA and BA groups [17].

Jung JY et al., demonstrated in their study that BA stimulated odontoblastic differentiation and mineralisation nodule formation by activating the Mitogen-activated Protein Kinases (MAPK) pathway, similar to MTA and Biodentine [18]. Chang SW et al., confirmed these findings in their study as well [19]. MAPKs are essential components for numerous physiological processes, including cell development, proliferation, differentiation, and death. Therefore, Jung JY et al., recommended the use of BA as a pulp capping agent, as it stimulates reparative odontogenesis from injured dental pulp tissue [18]. Shokouhinejad N et al., studied the bioactivity of MTA, Endosequence Root Repair Material (ERRM), and BA by exposing them to simulated tissue fluid, which resulted in the precipitation of apatite crystals. While all the materials exhibited crystallisation of apatite after two months on their surface and at the dentin-material interface, Scanning Electron Microscopy (SEM) analysis showed that BA and ERRM formed uniform and homogeneous mature apatite-like spherical aggregates, in contrast to MTA, which had agglomerates of large and small particles [20].

Fracture Resistance

Tuna EB et al., conducted an investigation and found that when BA was used for root filling in immature teeth, it resulted in superior fracture resistance compared to ProRoot MTA [21]. However, Bayram E et al., observed in their study that there was no significant difference in the fracture resistance among MTA, BA and Biodentine materials [22]. Therefore, BA can be considered for reinforcing the root of immature teeth.

Bond Strength

Majeed A and AlShwaimi E conducted a comparison of the push-out bond strength among calcium silicate-based cements, including BA, ProRoot MTA, and Biodentine. Their conclusion was that BA exhibited significantly lower bond strength compared to ProRoot MTA and Biodentine [23]. Amin SA and Gawdat SI conducted a study comparing the retention of BA and MTA when used as coronal plugs after the application of different intracanal medicaments in regenerative endodontics. The conclusion was that the retention of MTA was better than BA, regardless of the type of intracanal medicament used, and the failure mode of BA was more likely to be cohesive [24]. Shokouhinejad N et al., compared the push-out bond strength of BA and ERRM. The conclusion was that the bond strength of ERRM was significantly higher than that of BA and MTA. Additionally, it was noted that the failure mode of BA was both cohesive and adhesive [25].

Porosity

Camilleri J et al., conducted a study to evaluate the porosity and root dentin to material interface of Biodentine, BA, Intermediate Restorative Material (IRM) and a prototype radiopacified tricalcium silicate cement under dry and moist conditions. The results showed that Biodentine exhibited the least porosity (13%), while BA had 36% porosity. The pore diameters in all the materials were less than 0.05 µm. The study also concluded that although BA had high porosity, it was less susceptible to the negative effects of various environmental factors [26]. According to Chang SW, the root dentin to material interface in BA showed the highest porosity, but there were relatively few macroscopic and microscopic alterations observed [8].

Leakage Resistance

Memis Özgül B et al., conducted a study to compare the resistance to leakage of different thicknesses of 4 mm-thick White MTA (WMTA) and BA using the fluid filtration method. The study demonstrated that root filling with a 12 mm thick BA provided superior sealing ability compared to 2 mm and 4 mm BA and 4 mm WMTA apical plugs. The results also indicated similar sealing properties between 2 mm and 4 mm BA and 4 mm WMTA. BA may be considered a viable material for use in trauma-induced endodontic treatment of teeth with immature apices due to its demonstrated superior biocompatibility compared to MTA, good biomineralisation, and sealing capacity [27].

Leal F et al., conducted a study to compare the root canal sealing properties of Ceramicrete, BA, and white ProRoot MTA by assessing glucose leakage through the aforementioned fillings. The study concluded that Ceramicrete exhibited better leakage resistance compared to BA, while both MTA and BA displayed similar leakage. The presence of hydroxyapatite in BA is attributed to its sealing ability [28].

Acid Resistance

Akinci L et al., conducted an in-vitro study to investigate the influence of low pH on MTA, BA, and Biodentine, with the purpose

of evaluating their potential usage as perforation repair or root repair materials. The study found that all the materials experienced high volume loss when exposed to an acidic environment, with Biodentine showing the highest volume loss among them. The change in volume and porosity of BA, when exposed to an acidic environment, was comparable to that of MTA [29].

Hashem AAR and Amin SAW conducted an in-vitro study to compare the dislodgement resistance of BA and MTA when used as perforation repair materials in an acidic environment. The study concluded that calcium hydroxide, being the weakest link, is more susceptible to chemical attack when exposed to an acidic environment. Compared to MTA, BA exhibited greater resistance to acid attack due to the lower content of calcium hydroxide. However, despite the negative effects of an acidic environment on MTA, MTA still outperformed BA in terms of retention [30]. The authors recommended caution when restoring an endodontically treated tooth with furcation perforations repaired using BA and MTA in contact with acidic chemicals or inflamed tissues in the pulp chamber [30].

CLINICAL STUDIES

Caliskan S et al., compiled eight case reports in which BA was used for various procedures such as pulpotomy, partial pulpotomy, root resorption repair, artificial apical barrier construction in permanent teeth, root canal treatment in permanent teeth, treatment of dens in dente, and pulpectomy in primary teeth with congenitally missing succedaneous teeth. All treated teeth were observed for 24 months, and no clinical symptoms or radiographic pathologies were observed in any of the cases [1].

Tuloglu N and Bayrak S compiled three case reports of complicated crown fractures in immature permanent teeth where BA was used for partial pulpotomy. All three cases were observed for 24 months, and no clinical symptoms or radiographic pathologies were observed. Ongoing root development was observed radiographically, and no crown discolouration was seen. Therefore, BA can be considered a suitable alternative to MTA [31]. Tuloglu N and Bayrak S conducted a pilot study to compare and evaluate the use of MTA and BA as apical barrier materials in children with traumatised non vital, immature permanent maxillary incisors, in terms of their clinical and radiological success. Over the 24-month follow-up period, all teeth treated with MTA and BA showed clinical and radiographic success. It was concluded that BA could be used as a potential substitute for MTA [11].

A comparison between the properties of MTA and BA is provided in [Table/Fig-2] [1,5,11-14,20,21,23,24,27].

Properties	MTA	Bioaggregate (BA)
Colour stability [1,11,12]	Tooth discolouration evident in several studies	No tooth discolouration
Antibacterial activity [5]	Antibacterial activity with decrease in bacterial viability is seen	Antibacterial activity comparable to MTA
Biocompatibility [13,14]	No cytotoxic effect	Bioaggregate (BA) shows no cytotoxic effect compared to MTA and Biodentine
Bioactivity [20]	Agglomerates of large and small particles	Uniform and homogenous mature apatite-like spherical aggregates
Fracture resistance [21]	ProRoot MTA fractured easily when used for root filling	Bioaggregate (BA) showed superior fracture resistance
Bond strength [23,24]	Higher bond strength	Least bond strength compared to Biodentine and MTA
	Superior retention when used as a coronal plug	Poor retention
Leakage resistance [27]	Inferior sealing ability with 4 mm thick apical plug	Root filling with 12 mm thick Bioaggregate (BA) provides superior sealing ability

[Table/Fig-2]: Comparison between the properties of MTA and Bioaggregate (BA) [1,5,11-14,20,21,23,24,27].

CONCLUSION(S)

In conclusion, based on several in-vitro studies, a few clinical studies and case reports on BA, it could be considered a suitable alternative to other calcium silicate-based materials for the management of deep carious lesions and endodontic procedures. However, further clinical studies and research is needed, especially in the field of Paediatric dentistry, to establish the efficacy of this material compared to other bioceramic materials.

REFERENCES

[1] Caliskan S, Tuloglu N, Bayrak S. Clinical applications of BioAggregate in pediatric dentistry: Case reports. Srp Arh Celok Lek. 2019;147(11-12):746-50. Doi: 10.2298/sarh190509124c.
[2] Utneja S, Nawal RR, Talwar S, Verma M. Current perspectives of bio-ceramic technology in endodontics: Calcium enriched mixture cement-review of its composition, properties and applications. Restor Dent Endod. 2015;40(1):01-13. Doi: 10.5395/rde.2015.40.1.1.
[3] Eram A, Zuber M, Keni LG, Kalburgi S, Naik R, Bhandary S, et al. Finite element analysis of immature teeth filled with MTA, Biodentine and Bioaggregate. Comput Methods Programs Biomed. 2020:190:105356. Doi: 10.1016/j.cmpb.2020.105356.
[4] Zhu L, Yang J, Zhang J, Peng B. A comparative study of bioaggregate and ProRoot MTA on adhesion, migration, and attachment of human dental pulp cells. J Endod. 2014;40(8):1118-23. Doi: 10.1016/j.joen.2013.12.028.
[5] Zhang H, Pappen F, Haapasalo M. Dentin enhances the antibacterial effect of mineral trioxide aggregate and bioaggregate. J Endod. 2009;35(2):221-24. Doi: 10.1016/j.joen.2008.11.001.
[6] Jitaru S, Hodisan I, Timis L, Lucian A, Bud M. The use of bioceramics in endodontics-literature review. Med Pharm Rep. 2016;89(4):470-73. Doi: 10.15386/cjmed-612.
[7] http://endo.bg/image/data/files/DiaRoot_Booklet.pdf.
[8] Chang SW. Chemical composition and porosity characteristics of various calcium silicate-based endodontic cements. Bioinorg Chem Appl. 2018;2018:2784632. Doi: 10.1155/2018/2784632.
[9] Raghavendra S, Jadhav GR, Gathani KM, Kotadia P. Bioceramics in endodontics-a review. J Istanb Univ Fac Dent. 2017;51(3 Suppl 1):S128-S137. Doi: 10.17096/jiufd.63659.
[10] http://ibioceramix.com/bioaggregate.html.
[11] Tuloglu N, Bayrak S. Comparative evaluation of mineral trioxide aggregate and bioaggregate as apical barrier material in traumatised nonvital, immature teeth: A clinical pilot study. Niger J Clin Pract. Niger J Clin Pract. 2016;19(1):52-57. Doi: 10.17096/jiufd.63659.
[12] Keskin C, Demiryurek EO, Ozyurek T. Colour stabilities of calcium silicate-based materials in contact with different irrigation solutions. J Endod. 2015;41(3):409-11. Doi: 10.1016/j.joen.2014.11.013.
[13] Yan P, Yuan Z, Jiang H, Peng B, Bian Z. Effect of bioaggregate on differentiation of human periodontal ligament fibroblasts: Effect of BA on differentiation of PDL. Int Endod J. 2010;43(12):1116-21. Doi: 10.1111/j.1365-2591.
[14] Jang YE, Lee BN, Koh JT, Park YJ, Joo NE, Chang HS, et al. Cytotoxicity and physical properties of tricalcium silicate-based endodontic materials. Restor Dent Endod. 2014;39(2):89-94. Doi: 10.5395/rde.2014.39.2.89.
[15] Camilleri J, Sorrentino F, Damidot D. Characterization of un-hydrated and hydrated BioAggregateTM and MTA AngelusTM. Clin Oral Investig. 2015;19(3):689-98. Doi: 10.1007/s00784-014-1292-4.
[16] Yuan Z, Peng B, Jiang H, Bian Z, Yan P. Effect of bioaggregate on mineral-associated gene expression in osteoblast cells. J Endod. 2010;36(7):1145-48. Doi: 10.1016/j.joen.2010.03.025.
[17] Lee BN, Lee KN, Koh JT, Min KS, Chang HS, Hwang IN, et al. Effects of 3 endodontic bioactive cements on osteogenic differentiation in mesenchymal stem cells. J Endod. 2014;40(8):1217-22. Doi: 10.1016/j.joen.2014.01.036.
[18] Jung JY, Woo SM, Lee BN, Koh JT, Nör JE, Hwang YC. Effect of Biodentine and Bioaggregate on odontoblastic differentiation via mitogen-activated protein kinase pathway in human dental pulp cells. Int Endod J. 2015;48(2):177-84. Doi: 10.1111/iej.12298.
[19] Chang SW, Lee SY, Kum KY, Kim EC. Effects of ProRoot MTA, Bioaggregate, and micromega mta on odontoblastic differentiation in human dental pulp cells. J Endod. 2014;40(1):113-18. Doi: 10.1016/j.joen.2013.09.036.
[20] Shokouhinejad N, Nekoofar MH, Razmi H, Sajadi S, Davies TE. Bioactivity of endosequence root repair material and bioaggregate. Int Endod J. 2012;45(12):1127-34. Doi: 10.1111/j.1365-2591.
[21] Tuna EB, Dinçol ME, Gençay K, Aktören O. Fracture resistance of immature teeth filled with BioAggregate, mineral trioxide aggregate and calcium hydroxide: Fracture resistance of immature teeth. Dent Traumatol. 2011;27(3):174-78. Doi: 10.1111/j.1600-9657.2011. 00995.x.
[22] Bayram HM, Saklar F, Bayram E, Orucoglu H, Bozkurt A. Determination of the apical sealing abilities of mineral trioxide aggregate, portland cement, and bioaggregate after irrigation with different solutions. J Int Oral Health. 2015;7(6):13-17. PMCID: PMC4479766.
[23] Majeed A, AlShwaimi E. Push-out bond strength and surface microhardness of calcium silicate-based biomaterials: An in-vitro study. Med Princ Pract. 2017;26(2):139-45. Doi: 10.1159/000453455.
[24] Amin SA, Gawdat SI. Retention of BioAggregate and MTA as coronal plugs after intracanal medication for regenerative endodontic procedures: An ex vivo study. Restor Dent Endod. 2018;43(3):e18. Doi: 10.5395/rde.2018.43.e18.

[25] Shokouhinejad N, Razmi H, Nekoofar MH, Sajadi, Dummer P, Khoshkhounejad M. Push-out bond strength of bioceramic materials in a synthetic tissue fluid. J Dent (Tehran). 2013;10(6):540-47. PMCID: PMC4025432.
[26] Camilleri J, Grech L, Galea K, Keir D, Fenech M, Formosa L, et al. Porosity and root dentine to material interface assessment of calcium silicate-based root-end filling materials. Clin Oral Investig. 2014;18(5):1437-46. Doi: 10.1007/s00784-013-1124-y.
[27] Memiş Özgül B, Bezgin T, Şahin C, Sarı Ş. Resistance to leakage of various thicknesses of apical plugs of Bioaggregate using liquid filtration model. Dent Traumatol. 2015;31(3):250-54. Doi: 10.1111/edt.12150.
[28] Leal F, De-Deus G, Branda C, Luna AS, Fidel SR, Souza EM. Comparison of the root-end seal provided by bioceramic repair cements and White MTA. Int Endod J. 2011;44(7):662-68. Doi: 10.1111/j.1365-2591.2011.01871.x.
[29] Akinci L, Simsek N, Aydinbelge HA. Physical properties of MTA, BioAggregate and Biodentine in simulated conditions: A micro-CT analysis. Dent Mater J. 2020;39(4):601-07. Doi: 10.4012/dmj.2018-429.
[30] Hashem AAR, Amin SAW. The effect of acidity on dislodgment resistance of mineral trioxide aggregate and bioaggregate in furcation perforations: An in-vitro comparative study. JOE. 2012;38(2)245-49. Doi: 10.1016/j.joen.2011.09.013.
[31] Tuloglu N, Bayrak S. Partial pulpotomy with bioaggregate in complicated crown fractures: Three case reports. J Clin Pediatr Dent. 2016;40(1):31-35. Doi: 10.17796/1053-4628-40.1.31.

PARTICULARS OF CONTRIBUTORS:
1. Postgraduate, Department of Paediatric and Preventive Dentistry, Indira Gandhi Institute of Dental Sciences, Sri Balaji Vidyapeeth, Deemed to be University, Puducherry, India.
2. Senior Lecturer, Department of Paediatric and Preventive Dentistry, Indira Gandhi Institute of Dental Sciences, Sri Balaji Vidyapeeth, Deemed to be University, Puducherry, India.
3. Professor and Head, Department of Paediatric and Preventive Dentistry, Indira Gandhi Institute of Dental Sciences, Sri Balaji Vidyapeeth, Deemed to be University, Puducherry, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Eswari Ramassamy,
No. 9, Vaigai Street, Ashok Nagar, Lawspet, Puducherry-605008, India.
E-mail: eswari80ashok@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Jul 08, 2023
- Manual Googling: Sep 20, 2023
- iThenticate Software: Oct 21, 2023 (10%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? NA
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Jul 05, 2023**
Date of Peer Review: **Aug 30, 2023**
Date of Acceptance: **Oct 28, 2023**
Date of Publishing: **Dec 01, 2023**