Potential Combination of Acemannan Sponge and Calcium Phosphate Cement-Calcium Sulfate Hemihydrate (CPC-CSH) as Direct Pulp Capping Alternative Materials for Reparative Dentin Formation

Anis Irmawati[1] Annisa Indah Pratiwi[2] Muh Rizki Aqsanu Azizi[2] Nurul Annisa Apriliyanti[2] Ayu Annafi[2] Yassir Ahmad Azzaim[3] Ala'a Saif Alqhtani[4]

[1] Department of Oral Biology, Faculty of Dental Medicine, Universitas Airlangga, Surabaya, Indonesia
[2] Faculty of Dental Medicine, Universitas Airlangga, Surabaya, Indonesia
[3] Magister Program, Dental Health Sciences, Faculty of Dental Medicine, Universitas Airlangga, Surabaya, Indonesia
[4] Depertment of Dental Medicine, Faculty of Medicine, Ibb University, Ibb, Yemen

Address for correspondence Anis Irmawati, DDS, MDS, Department of Oral Biology, Faculty of Dental Medicine, Universitas Airlangga, Jln. Prof. Dr. Moestopo 47, Surabaya 60132, Indonesia (e-mail: anis-m@fkg.unair.ac.id).

J Health Allied Sci[NU] 2024;14:47–53.

Abstract

Background Health problem that affects hard tissues of the teeth is dental caries, which is experienced by around 2.3 billion people in the world, with prevalence in Indonesia reaching 88.8. Direct pulp capping (DPC) is a vital pulp therapy used to maintain pulp vitality. Calcium hydroxide ($Ca(OH)_2$) is the gold standard pulp capping material, but has poor adhesion to dentin and mechanical properties, bacterial infiltration, formation of tunnel defects in the pulp resorption, and dentin bridge. Therefore, it is necessary to develop alternative therapy, namely, a combination of acemannan sponge and calcium phosphate cement (CPC)-calcium sulfate hemihydrate (CSH) for reparative dentin formation.

Purpose This article describes the potential combination of acemannan sponge and CPC-CSH as DPC alternative materials for reparative dentin formation.

Reviews Acemannan extracted from aloe vera exhibits anti-inflammatory, antimicrobial, and cytocompatibility properties. As DPC material, acemannan induces pulp proliferation and differentiation to osteoblast-like, growth factor synthesis, and promotes reparative dentin formation. However, acemannan sponge is radiolucent, allowing misinterpretation between pulp and acemannan sponge. CPC can be combined with CSH to shorten the setting time. CPC-CSH is radiopaque, has good compressive strength, and biocompatibility. CPC-CSH is a calcium-based material with neutral pH that can induce the dentin bridge formation. CPC-CSH showed good bioactivity because it induces the formation of apatite which plays a significant part in dentin and pulp regeneration.

Conclusion The combination of acemannan sponge and CPC-CSH has the potential as DPC alternative materials for reparative dentin formation.

Keywords
- acemannan sponge
- calcium phosphate cement-calcium sulfate hemihydrate
- direct pulp capping
- dental caries
- reparative dentine
- human and health

article published online
May 16, 2023

DOI https://doi.org/10.1055/s-0043-1768594.
ISSN 2582-4287.

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

Introduction

One of the main dental and oral health problems in many developing countries, such as Indonesia, is dental caries. The incidence of caries worldwide is 2.3 billion people with permanent teeth caries and 530 million children with primary teeth caries.[1] Caries prevalence in Indonesia is 88.8%.[2] Dental caries is a disease characterized by damage to the hard tissues of the teeth due to dissolution of organic components and demineralization of inorganic components caused by bacteria.[3] Severe caries causes exposure of the dental pulp thereby affecting the vitality of the pulp. Vital pulp therapy has a purpose to maintain tooth vitality that is indicated for primary teeth with apical foramina that are still wide open.[4,5]

A dental treatment known as vital pulp therapy which removes infected pulp tissue and cleans the root canals,[6] based on case studies the success rate of this treatment is 73 to 99%.[7] Direct pulp capping (DPC) is a noninvasive vital pulp therapy that involves the application of drugs, dressings, or dental materials, used to support the formation of reparative dentin, maintain vitality, and seal exposed pulp.[8]

For decades, the gold standard for pulp capping materials has been calcium hydroxide [$Ca(OH)_2$]. This material still has weaknesses such as adhesion to dentin restorations, bacterial infiltration, poor mechanical properties, formation of tunnel defects in the dentinal pulp resorption and bridge, and dissolution over time.[9] This material still cannot prevent microleakage in the long term because it has poor adhesive qualities. Mineral trioxide aggregate (MTA) is a dental material that is also frequently used for pulp capping, but this material has the disadvantage of being easily broken during treatment and long setting time.[6]

Therefore, it is necessary to develop alternative therapies to stimulate the reparative dentin formation to maintain the teeth vitality with exposed pulp. Currently, alternative pulp capping materials are being developed using natural ingredients, for example, acemannan. Acemannan is an active compound derived from aloe vera in the form of natural polysaccharides, which stimulates cell proliferation, osteogenic, immunomodulating, antimicrobial, synthesis of extracellular matrix, and increases growth factor expression. Acemannan material still has a weakness in the form of radiolucent properties, so it is necessary to combine it with radiopaque inorganic materials to prevent misinterpretation of radiographic images as empty cavities or secondary caries.[4] Calcium phosphate cement (CPC) is a radiopaque material that is commonly used for hard tissue repair in the dental and medical fields because it is biocompatible, non-exothermic, and has a paste-like consistency so that it can enter various cavities or defects.[10] The addition of calcium sulfate hemihydrate (CSH) material can shorten the setting time and is not toxic or inhibits cell proliferation, so it has the potential to be an alternative material of DPC therapy.[6]

Methods and Materials

The search for literature reviews was conducted using the databases ScienceDirect, PubMed, and Google Scholar. The search was limited to articles focusing on acemannan and CPC-CSH in DPC for reparative dentine formation. The selected literature was published between 2016 and 2022 in English and Indonesian. The selected literature was accessed in full text by selecting the article type in the research and review form. Articles were selected and reviewed according to the inclusion criteria. Then, the selected articles were reviewed and summarized by the author from the relevant previous research results, so the author can make an article based on the study results.

Reviews

Dental Caries

Dental caries is a pathological process that causes damage to the hard tissues of the teeth, as well as local and general complications.[11] Caries is a multifactorial disease that is influenced by time, bacteria, and fermentable carbohydrates. Colonies of bacteria on teeth form biofilms through autoaggregation and coaggregation so that they have different morphological structures. The biofilm formed is supported by changes of microenvironment from aerobic to facultative anaerobic. In addition, the main cause of dental caries is a sticky substance that adheres to the tooth surface as a complex biofilm called dental plaque.[12] The microorganism involved in caries initiation is *Streptococcus mutans*.[13]

Caries is caused by the byproducts or acids of the fermentation of carbohydrates by bacteria in the mouth.[4] *S. mutans* acts as enamel caries initiation through producing lactic acid as a result of fermentation, which then causes demineralization of the enamel.[12] *S. mutans* initiates and sustains microbial growth, produces acid at low pH, metabolizes sugars into lactic acid, and also produces other organic acids that cause demineralization quickly than other plaque bacteria. *S. mutans* changes the environment into conditions rich in extracellular polysaccharides and low pH which creates a favorable acidogenic and aciduric environment bacteria so that it can assist other bacteria to establish dental caries.[14]

Direct Pulp Capping

Maintaining pulp vitality and supporting the formation of dentinal bridges is the goal of vital pulp therapy.[15] One of the alternative therapies to avoid root canal treatment by covering the exposed pulp with a dressing is DPC.[16] DPC is a mechanical treatment using biomaterials that aims to maintain the exposed dental pulp to form reparative dentin.[17] Indications for DPC treatment are: (1) pulp is still vital, (2) absence of clinical signs or symptoms indicating nonvital teeth such as abscess, spontaneous pain, and periodontal tissue swelling, (3) a deep carious lesion, (4) adequate structure of teeth for restoration, and (5) radiolucency absence in the periapical and furcation region, and root resorption.[18] In addition, pulp capping material must be able to stimulate the formation of reparative dentin,

maintain pulp vitality, has antibacterial properties agent, be adhesive between restorative materials and dentin, be sterile, be radiopaque, and be resistant to pressure during restoration placement and throughout the restoration period.[19]

$Ca(OH)_2$ has been the gold standard for pulp capping materials for decades.[20] Widely, $Ca(OH)_2$ is used as an endodontic treatment because it has the ability to heal tissue. $Ca(OH)_2$ has the advantage of having excellent pH and antibacterial properties.[21] The alkaline pH of $Ca(OH)_2$ is the reason for good antibacterial properties and plays a significant part in the initiation of tooth remineralization. High hydroxyl ions released from $Ca(OH)_2$ can kill microorganisms that cause inflammation by denaturing proteins and hydrolyzing lipopolysaccharides (LPS) so that bacterial cell walls are damaged and the bacteria die. The OH- ions in $Ca(OH)_2$ cause a low probability of bacteria survival, while Ca^{2+} ions can stimulate the formation of dentine bridges and maintain pulp vitality. $Ca(OH)_2$ has several disadvantages, including weaknesses, formation of tunnel defects in the dentine bridge, having high solubility, the pulp surface becomes inflamed and necrotic after application, being degraded over time, and low mechanical resistance, which can lead to failed treatment and microfiltration.[15]

MTA is a material that is often used in endodontic treatment. MTA is a powder containing trioxide and hydrophilic particles. MTA has a composition of 75% Portland cement, and 20% bismuth oxide, which provides radiopacity. MTA has conductive activity in calcified tissue and helps the mineralization process in dental pulp cells. That means MTA has potential as a material for pulp capping. MTA is proven to be biocompatible and has excellent potential when used in endodontic treatment. The advantages of MTA are that it has biocompatibility, bioactivity, and can promote the formation of mineralized tissue. MTA has many advantages over $Ca(OH)_2$, among others, it can facilitate pulp cell proliferation, limited tissue necrosis, and stimulate the formation of a dentine bridge quickly.[5]

Reparative Dentin

Dentin is the hard tissue structure of the teeth that lies beneath the enamel, is slightly yellowish in color, and makes up the bulk of the tooth. Odontoblasts can produce dentin after going through the differentiation process of dental papillary cells. Meanwhile, the pulp is a tooth structure that includes soft connective tissue in the blood vessels and nerves in the dental cavity which is located under the dentin.[22] Dentin chemically has a protein matrix composition and pathways that regulate the differentiation of odontoblasts and osteoblasts. Dentine morphologically does not have the ability to undergo remodeling, whereas dental pulp can differentiate into odontoblasts and osteoblasts, consisting of fibroblasts, endothelial cells, and progenitor cells. Damaged dentin and pulp due to injury induces an odontoblast and pulp response through the process of differentiating odontoblasts from progenitor cells in the dental pulp, and then secreting osteodentin reparative dentin matrix.[23]

Reparative dentin is a tertiary dentin matrix secreted by odontoblast-like cells to response a strong stimuli following the death of postmitotic odontoblasts responsible for primary or secondary dentin secretion due to trauma or caries.[23] The incidence of caries has passed through the enamel layer and caused the exposed dentin to respond to the formation of reparative dentin on the pulp surface just below the exposed dentin. The reparative dentin formation aims to prevent the pulp from being exposed to harmful injury.[24] The reparative dentin response occurs on the exposed side of the pulp due to missing odontoblasts, in this area the formation of dentin bridges also occurs. Formation of reparative dentin, which covers the pulp exposure, results in a bone-like structure made of collagen and noncollagenous proteins (osteocalcin and osteopontin). The composite structure of reparative dentine is called osteodentin.[5]

Acemannan

Aloe vera is a herbal medicinal ingredient for the treatment or prevention of metabolic, skin, cancer, and cardiovascular diseases.[25] Acemannan is a polymannose acetate molecule B-(1–4) produced from aloe vera gel extract.[26] The main components of the acemannan molecule are mannose (57–77%), glucose (15–22%), and galactose (5–7%), forming a chain of repeating tetrasaccharide units o-(acetyl mannose)-o-(acetyl mannose)-o -(glucose)-o-(acetyl mannose) of four mannose residues in single-branched galactose on the second or fourth.[25]

Acemannan material has been widely used for pharmacology from biology to medicine and industry, such as for the treatment of oral, metabolic, cardiovascular, and tumor diseases. Recent research on acemannan focused on dentistry, especially in wound healing in oral infections.[27] Acemannan has good immunomodulating and antimicrobial properties as well as cytocompatibility and biocompatibility with various cell types.[28] In vivo tests have shown that acemannan accelerates the formation of reparative dentin and oral wound healing. In addition, in vivo tests showed acemannan as a wound healing agent caused increased bone mineral density and faster wound healing compared with wounds that were not treated with acemannan. In vitro test showed acemannan caused bone marrow-derived mesenchymal stem/stromal cell (BMSC) proliferation, sialoprotein, vascular endothelial growth factor, alkaline phosphatase activity, BMP-2 and osteopontin expression, and increased mineralization.[29] It is shown that acemannan stimulates the formation of dentin bridges and stimulates the formation of dental pulp tissue when DPC treatment was applied on rat molars.[30] Based on these studies, the acemannan molecule functions as a bioactive molecule that stimulates differentiation into osteoblasts, extracellular matrix synthesis, and BMSC proliferation thereby inducing bone formation.[29]

Calcium Phosphate Cement-Calcium Sulfate Hemihydrate

CPC is a bioactive material used in the medical and dental fields for hard tissue engineering because it has a chemical structure similar to bone and teeth.[31] The main components

of this material are dicalcium phosphate anhydrous (DCPA) and tetracalcium phosphate (TTCP).[9] CPC material is biocompatible, non-exothermic, and has a paste-like consistency. The combination of calcium phosphate powder with water or solution will undergo a setting reaction through a hydrolysis process between components, followed by dissolution and re-precipitation at room temperature or body temperature.[10,31,32] This process may benefit from CPC's molding ability, or it can enter cavities or defects with a fit. [33] Hydroxyapatite is the CPC application's final product, which is the main mineral in dentin that helps form the dentinal bridge barrier.[9]

CSH is an inorganic component that is widely used in dentistry for repair of root perforations, treatment of periradicular lesions, repair of periodontal defects, and as a membrane barrier. This material is nontoxic, inexpensive, and biocompatible with bone and gingival tissue. This material is able to release calcium ions which can increase the activity of osteoblasts. Based on the research of Ulusoy et al, CSH as a material for DPC showed a fairly high success rate such as $Ca(OH)_2$ material.[34,35] The combination of CPC-CSH can shorten setting time, maintain compressive strength, and has good handling properties.[6]

Discussion

One of the treatments for exposed pulp due to caries, mechanical and chemical trauma, or mechanical excavation is root canal treatment or vital pulp therapy. However, for teeth condition with a wide-open apical foramen (immature permanent teeth) due to the incomplete root formation process, it is not appropriate to treat them using root canal treatment. Root formation does not occur without vital pulp because tooth eruption stops, the roots are thin and not strong enough to withstand masticatory forces, so the tooth will break easily. Therefore, one of the treatments to maintain pulp vitality as a substitute for root canal treatment is DPC.[4]

Invasive complex treatments such as endodontics or extractions can be prevented if DPC is successful.[36] DPC is indicated for teeth with vital pulp tissue without residual pain due to pulp exposure or trauma with a width of less than 1.5 mm, deep dental caries lesion, carious lesions located near the pulp to the lamina dura, and the furcation and periphery areas with no radiolucency, pulp obliteration chamber and root canals, or the occurrence of internal or external root resorption.[17,18]

The ideal material for DPC should have bactericidal properties, be nonhazardous to the pulp and its structure, stimulate formation of reparative dentine, and does not interfere with the physiological process of root resorption by osteoclasts.[5] The process by which dental pulp stem cells (DPSCs) differentiate into odontoblast-like cells will be the beginning of the formation of reparative dentin structures when the pulp is exposed and the existing odontoblast layer is damaged. DPSCs migrate and proliferate in the materio-pulpal complex, this event undergoes a process of reparative dentin formation resulting from odontogenic differentiation.[37]

In recent decades, the popular material for pulp capping treatment in dental restoration is $Ca(OH)_2$. Despite being the gold standard, $Ca(OH)_2$ has several disadvantages especially the formation of tunnel defects in the dentinal bridge. This can lead to failure of microfiltration and restoration treatment. MTA is a widely used pulp capping material and provides excellent result in in vitro and clinical tests.[15] In a systematic review, MTA had higher efficacy than $Ca(OH)_2$, showed more predictable dentine bridge formation than $Ca(OH)_2$, and less pulp inflammation.[38] In a previous studies, MTA as dentin regeneration material for dentin regeneration as a treatment material for primary and permanent teeth whose pulp chambers have not been completely closed. However, this material still has some drawbacks that need to be considered, such as being expensive, there is a discoloration of the teeth after treatment, and a long setting time of approximately 2 to 3 hours[6] (►**Fig. 1**).

Because of its anti-inflammatory and antibacterial qualities, acemannan is recommended as an efficient and effective DPC agent. Acemannan exhibits good biocompatibility and induces reparative dentin formation. In a study by Elhag et al, acemannan as a material for direct pup capping the success rate on mandibular permanent first molars with carious lesions was 77.8%, while in human primary teeth it was 72.73% after 6 months of observation. When applied as a DPC agent, acemannan material will induce the growth of dental pulp cells to stimulate dental pulp cells differentiation into growth factor synthesis and osteoblast-like cells of the extracellular matrix, as well as the formation of new dentin and mineral deposition, according to Elhag et al[28] in vitro studies.[28] Gonna et al evaluated the histological impacts of acemannan and formocresol as a material for pulp-dressing treatment in primary teeth undergoing pulpotomy treatment. The acemannan and formocresol groups had effectiveness of 75 and 25%.[39] In vivo investigation showed acemannan induces pulp repair and reparative dentin formation in caries-exposed canines with LPS-induced reversible pulpitis, as well as reversible pulpitis in human primary teeth. Acemannan application, like MTA application, produced a dentine bridge with normal supporting pulp tissue and no pulp inflammation or necrosis[4] (►**Fig. 2**).

As a result, acemannan has the potential to be a useful capping material to stimulate the formation of economical and efficient reparative dentin. On the other hand, acemannan sponges are radiolucent due to their monosaccharide composition. According to cone beam computed tomography pictures, the dentine bridge covering the dental pulp was found in the radiolucent zone between the acemannan sponge material and the dental pulp. To avoid any misunderstanding as empty cavities or secondary caries, acemannan must be combined with other materials, namely calcium phosphate in an acemannan sponge, to create a radiopaque hybrid organic-inorganic picture that cannot be misinterpreted.[4]

CPC is an inorganic material that is radiopaque and biocompatible because its chemical structure is similar to that of teeth.[10] The addition of CSH aims to shorten cement

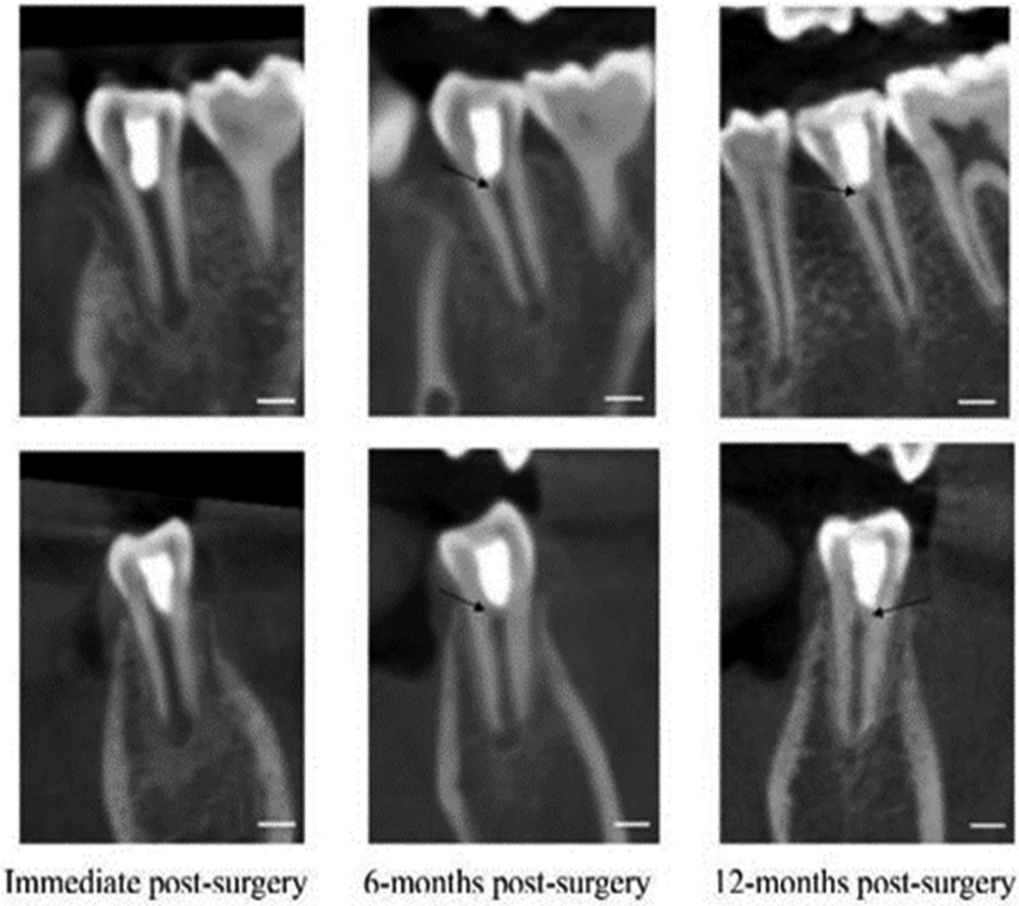

Fig. 1 Radiographic features before and after direct pulp capping with mineral trioxide aggregate (MTA).[4]

setting time. Initial setting time of cement consisting of CPC-CSH is short, approximately 15 to 20 minutes, sufficient time for the doctor to apply the material over the exposed pulp without applying pressure.[6] CPC-CSH biphasic cement had a pH of 6.5 to 6.9, which was near to neutral. Several investigations have shown that significant alkaline nature of a material is not necessary to promote dentine bridge formation, and that neutral calcium-based materials can induce dentine bridge formation in non-necrotic locations.[9]

In addition to a pH that supports CPC-CSH as a pulp capping material, CPC-CSH also shows satisfactory bioactivity in simulated body fluid (SBF). The CPC-CSH cement releases calcium ions into the SBF, which causes the concentration of calcium ions to become saturated. Calcium ions react with phosphate ions at higher concentrations, causing apatite to develop on the cement surface. After 28 days of hydration, morphology of the cement submerged in SBF revealed that CPC-CSH formed a significant amount of hydroxyapatite. Hydroxyapatite plays a vital function in dentin production and pulp regeneration due to the formation of a bioactive surface. Hydroxyapatite supports the differentiation and growth of odontoblastic process in human dental pulp cells (HDPCs).[9] Based on previous studies, CPC-CSH cement showed minimal toxicity to HDPC.[6,9]

Acemannan was isolated from a homogenized, centrifuged, and alcohol-precipitated aloe vera gel. To remove protein and monosaccharide molecules, acemannan was inserted into a 10,000 MWCO (Thermo Scientific-Pierce Biotechnology) semi-permeable dialysis tube for 24 hours and then lyophilized. Gas chromatography–mass spectrometry and 13C nuclear magnetic resonance were used to examine monosaccharide composition and polysaccharide structure, with acemannan being the polysaccharide isolated from aloe vera gel. The extraction yield of acemannan is approximately 0.2%, then the acemannan is dissolved and sterilized by autoclaving. Thereafter, an acemannan sponge was made by freezing and lyophilizing the acemannan solution aseptically.[29]

DCPA and TTCP are the components of CPC. TTCP powder [$Ca_4(PO_4)_2O$] is made by heating 2 moles of calcium carbonate ($CaCO_3$) and 1 mol of calcium pyrophosphate ($Ca_2P_2O_7$) to 1400°C for 3 hours in a solid-state process. The product was allowed to cool to room temperature before being pulverized in a mortar and sieved to obtain TTCP powder, which was then combined with DCPA powder ($CaHPO_4$) to form CPC. CPC has a low viscosity and handling properties increase when CSH is added. Mixing between CPC-CSH is done by adding deionized water with a liquid-to-powder (L/P) ratio of 0.35 mL/g to form a paste-shaped mixture.[9] The combination of CPC and CSH was made with a ratio of 70% CPC and 30% CSH. The addition of CSH can shorten setting time and improve handling properties, but reduce compressive strength. This comparison is used to get the right setting

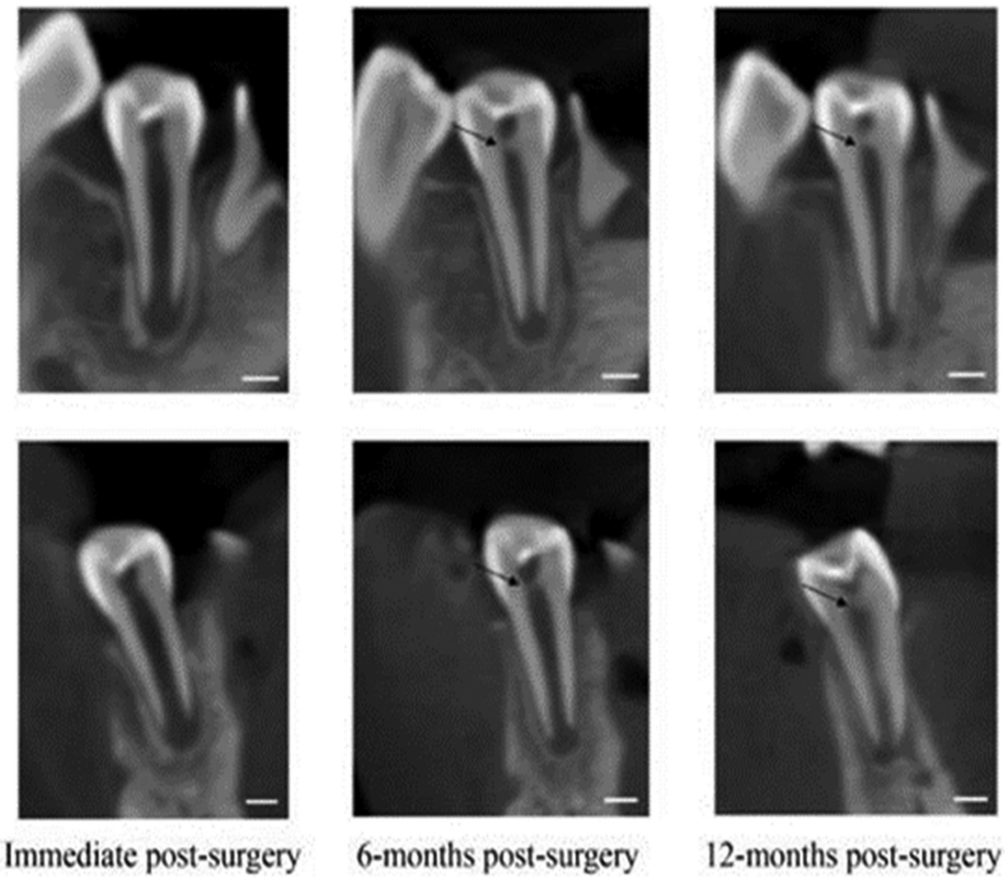

Fig. 2 Radiographic appearance of dentine bridge formation and continued root formation after application of acemannan to teeth.[4]

time and optimal compressive strength for clinical use.[6] Therefore, CPC-CSH has the potential to have a synergistic effect with the addition of acemannan sponge as a DPC material in the production of reparative dentin and the preservation of pulp vitality.

Conclusion

The combination of acemannan sponge and CPC-CSH has the potential as DPC alternative materials for reparative dentin formation.

Clinical Relevance

The use of alternative material on direct pulp capping treatment is recommended to improve the performance of dentin reparative formation. The use of combination between acemannan sponge and calcium phosphate cement-calcium sulfate hemihydrate (CPC-CSH) is effective for dentine reparative formation to maintain pulp vitality.

Authors' Contributions

A.I.: research concept and design, data analysis and interpretation, writing the article, critical revision of the article, final approval of article. A.I.P.: research concept and design, collection and/or assembly of data, data analysis and interpretation, writing the article, critical revision of the article, final approval of article. M.R.A.A.: collection and/or assembly of data, writing the article, critical revision of the article, final approval of article. N. A.A.: research concept and design, collection and/or assembly of data, data analysis and interpretation, writing the article. A.A.: research concept and design, collection and/or assembly of data, data analysis and interpretation, writing the article. Y.A.A.: writing the article, critical revision of the article, final approval of article. A.S.A.: critical revision of the article, final approval of article.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of Interest

None declared.

References

1 World Health Organization. World Health Assembly Resolution paves the way for better oral health care. World Health Organization. 2020. Accessed April 7, 2023, at: http://www.who.int/mediacentre/factsheets/fs396/en/

2 Kementerian Kesehatan Republik Indonesia. Laporan Nasional Riskesdas 2018. Lembaga Penerbit: Badan Penelitian dan Pengembangan Kesehatan 2019. 2019. p, 204

3 Teshome A, Muche A, Girma B. Prevalence of dental caries and associated factors in East Africa, 2000-2020: systematic review and meta-analysis. Front Public Health 2021;9:645091
4 Vu TT, Nguyen MT, Sangvanich P, Nguyen QN, Thunyakitpisal P. Acemannan used as an implantable biomaterial for vital pulp therapy of immature permanent teeth induced continued root formation. Pharmaceutics 2020;12(07):1–16, 644
5 Goldberg M. Indirect and direct pulp capping: reactionary vs reparative dentins. JSM Dentist 2020;8(01):1119
6 Chang HH, Chang YJ, Yeh CL, Lin TA, Lin CP. Development of calcium phosphate/calcium sulfate biphasic biomedical material with hyaluronic acid containing collagenase and simvastatin for vital pulp therapy. Dent Mater 2020;36(06):755–764
7 Aguilar P, Linsuwanont P. Vital pulp therapy in vital permanent teeth with cariously exposed pulp: a systematic review. J Endod 2011;37(05):581–587
8 Songsiripradubboon S, Banlunara W, Sangvanich P, Trairatvorakul C, Thunyakitpisal P. Clinical, radiographic, and histologic analysis of the effects of acemannan used in direct pulp capping of human primary teeth: short-term outcomes. Odontology 2016;104(03): 329–337
9 Chang KC, Chang CC, Chen WT, Hsu CK, Lin FH, Lin CP. Development of calcium phosphate/sulfate biphasic cement for vital pulp therapy. Dent Mater 2014;30(12):e362–e370
10 Shieh TM, Hsu SM, Chang KC, Chen WC, Lin DJ. Calcium phosphate cement with antimicrobial properties and radiopacity as an endodontic material. Materials (Basel) 2017;10(11):1256
11 Sicca C, Bobbio E, Quartuccio N, Nicolò G, Cistaro A. Prevention of dental caries: a review of effective treatments. J Clin Exp Dent 2016;8(05):e604–e610
12 Tahir L, Nazir R. Dental caries, etiology, and remedy through natural resources [Internet]. Dental Caries - Diagnosis, Prevention and Management. InTech; 2018. Available at: http://dx.doi.org/10.5772/intechopen.75937
13 Conrads G. About I. Pathophysiology of dental caries. Monogr Oral Sci 2018;(27):1–10
14 Sachidananda MP, Mallya S. Microbiology and clinical implications of dental caries–a review. J Evol Med Dent Sci 2020;9(48): 3670–3676
15 Brizuela C, Ormeño A, Cabrera C, et al. Direct pulp capping with calcium hydroxide, mineral trioxide aggregate, and biodentine in permanent young teeth with caries: a randomized clinical trial. J Endod 2017;43(11):1776–1780
16 Schwendicke F, Brouwer F, Schwendicke A, Paris S. Different materials for direct pulp capping: systematic review and meta-analysis and trial sequential analysis. Clin Oral Investig 2016;20 (06):1121–1132
17 Mali RS, Mangala TM. Histological analysis of reparative dentin formation using bio dentine and MTA as pulp capping agent: an in vivo study. J Crit Rev 2020;7(07):653–657
18 Ahmed ME, Ali A, El-Bayoumy SY, Al-Azhar AAE. Clinical and radiographic evaluation of acemannan as direct pulp capping material in young permanent teeth. J Dent Sci 2020;23(04):415–421
19 Qureshi A, E Soujanya, Nandakumar, Pratapkumar, Sambashivarao. Recent advances in pulp capping materials: an overview. J Clin Diagn Res 2014 Jan;8(01):316–321
20 Dubey A. Calcium hydroxide in dentistry: a review. Chetinad Health City Medical Journal. 2016;5:30–33
21 Chandrasekhar H, Sharma S. Efficient agents for pulp protection: a review. J Pharmaceut Sci Res 2016;8(11):1308–1311
22 Ariesdyanata C, Lunardhi CGJ, Subiwahjudi A. Perbedaan Angiogenesis Pada Pulpa Setelah Aplikasi Ekstrak Propolis Dan Kalsium Hidroksida. Conserv Dentist J 2019;9(01):48
23 Jung JK, Gwon GJ, Neupane S, et al. Bortezomib facilitates reparative dentin formation after pulp access cavity preparation in mouse molar. J Endod 2017;43(12):2041–2047
24 Kurniasari A. Efektivitas Pasta Biji Kopi Robusta (coffea robusta) Sebagai Bahan Direct Pulp Capping Terhadap Jumlah Sel Makrofag Dan Sel Limfosit Pulpa Gigi. Fakultas Kedokteran Gigi, Universitas Jember; 2017
25 Liu C, Cui Y, Pi F, Cheng Y, Guo Y, Qian H. Extraction, purification, structural characteristics, biological activities and pharmacological applications of acemannan, a polysaccharide from aloe vera: a review. Molecules 2019;24(08):1554
26 Le Van C, Thi Thu HP, Sangvanich P, Chuenchompoonut V, Thunyakitpisal P. Acemannan induces rapid early osseous defect healing after apical surgery: a 12-month follow-up of a randomized controlled trial. J Dent Sci 2020;15(03):302–309
27 Taschieri S, Corbella S, Tsesis I, Bortolin M, Del Fabbro M. Effect of guided tissue regeneration on the outcome of surgical endodontic treatment of through-and-through lesions: a retrospective study at 4-year follow-up. Oral Maxillofac Surg 2011;15(03): 153–159
28 Elhag A, El-Bayoumy S, Eisa AE. Clinical and radiographic evaluation of acemannan as direct pulp capping material in young permanent teeth. Al-Azhar J Dental Sci 2020;23(04): 415–421
29 Boonyagul S, Banlunara W, Sangvanich P, Thunyakitpisal P. Effect of acemannan, an extracted polysaccharide from aloe vera, on BMSCs proliferation, differentiation, extracellular matrix synthesis, mineralization, and bone formation in a tooth extraction model. Odontology 2014;102(02):310–317
30 Songsiripradubboon S, Kladkaew S, Trairatvorakul C, et al. Stimulation of dentin regeneration by using acemannan in teeth with lipopolysaccharide-induced pulp inflammation. J Endod 2017;43 (07):1097–1103
31 Al-Sanabani JS, Madfa AA, Al-Sanabani FA. Application of calcium phosphate materials in dentistry. Int J Biomater 2013;2013; 876132
32 Gu Y, Zhuang R, Xie X, Bai Y. Osteogenic stimulation of human dental pulp stem cells with self-setting biphasic calcium phosphate cement. J Biomed Mater Res B Appl Biomater 2020;108(04): 1669–1678
33 Xu HH, Wang P, Wang L, et al. Calcium phosphate cements for bone engineering and their biological properties. Bone Res 2017;5 (01):17056
34 Ulusoy AT, Bayrak S, Bodrumlu EH. Clinical and radiological evaluation of calcium sulfate as direct pulp capping material in primary teeth. Eur J Paediatr Dent 2014;15(02):127–131
35 Sinjab YH, Sinjab KH, Navarrete-Bedoya C, Gutmann JL. Calcium sulfate applications in dentistry: a literature review. Endodontology 2020;32(04):167
36 Li Z, Cao L, Fan M, Xu Q. Direct pulp capping with calcium hydroxide or mineral trioxide aggregate: a meta-analysis. J Endod 2015;41(09):1412–1417
37 Song M, Yu B, Kim S, et al. Clinical and molecular perspectives of reparative dentin formation: lessons learned from pulp-capping materials and the emerging roles of calcium. Dent Clin North Am 2017;61(01):93–110
38 Vallés M, Mercadé M, Duran-Sindreu F, Bourdelande JL, Roig M. Color stability of white mineral trioxide aggregate. Clin Oral Investig 2013;17(04):1155–1159
39 Gonna S, Deraz E, Ghoname N, Kabbash A, Yagi A. Acemannan and formocresol pulpotomies in primary teeth: a comparative histopathological study. Gastroenterol Hepatol Res 2017;6(04): 2386–2391