Ref: Ro J Stomatol. 2023;69(4) DOI: 10.37897/RJS.2023.4.11

# Materials used in pulpotomy: an overview

Mahir Mirah

Department of Restorative Dental Science, College of Dentistry, Taibah University, Madinah Munawara, Saudi Arabia

## ABSTRACT

A pulpotomy is a dental method that can be used on both children and adults. Tooth decay can lead to an infection wherein the pulp inside the tooth gets affected. In such cases, a pulpotomy is performed, wherein the pulp present in the crown (the visible part of the tooth) is extracted while the pulp in the root canal is retained. Devitalization, preservation, and regeneration have been the three main directions that pulpotomy therapy for primary teeth has taken. Formocresol and electrocautery are examples of devitalization (mummification, cauterization), which is when vital tissue is intended to be destroyed. Treatment with glutaraldehyde and ferric sulphate is an example of preservation (minimum devitalization, noninductive), which is the retention of the most vital tissue without inducing reparative dentin. Calcium hydroxide has long been linked to regeneration (inductive, reparative), the activation of a dent in bridge. In the upcoming years, regeneration is anticipated to grow the fastest of the three categories.

Keywords: MTA, pulpotomy, formocresol, devitalization, preservation

#### Abbreviations:

ABS - Ankaferd Blood Stopper Ca(OH) – Calcium hydroxide FDA - Food and drug administration II. Interleukin

MSDS - Material safety data sheet MTA

- Mineral trioxide aggregate

Nigella sativa

NS

## INTRODUCTION

When a permanent tooth has large caries but no sign of radicular infection, a procedure known as a pulpotomy is used to remove the caries and part of the coronal pulp tissue. The pulpotomy procedure removes the coronal pulp and puts a pulp-capping biocompatible substance material to promote healing or an agent and restores the remaining pulp tissue [1]. The medication widely used for pulpotomy was formocresol, according to the literature [2]. Despite the success rate, there are still many unknowns around the usage of formocresol, including its potential for mutagenic, carcinogenic, and allergic effects [3]. Between the ages of 2 and 11, 42% of children develop cavities in their baby teeth. Severe decay can cause inflammation of the pulp, known as pulpitis. A pulpotomy may be performed on primary or permanent teeth if it has already reached the critical stage and the decay has reached the pulp. It has been stated that there are limited signs for both reversible and irreversible pulpitis. Reversible pulpitis hurts when handled, but the soreness goes away and is treated with over-the-counter painkillers. Unexplained tooth pain, abnormal tooth mobility, and soft tissue irritation unrelated to gum disease are examples of irreversible conditions. Pulpotomy is typically utilized on primary teeth in young children because it preserves the tooth's roots, leaving them open to development. Primary teeth must be left intact because they maintain the space between developing permanent teeth. Empirical evidence has demonstrated that endodontic therapy can be efficaciously administered to both adult and pediatric patients, provided that an adequate amount of healthy pulp tissue is present within the tooth to ensure its vitality and operational capacity.

The pulpotomy procedure is suggested when caries removal exposes the pulp of a primary tooth with a normal pulp or reversible pulpitis. It is also recommended when the pulp becomes uncomfortable or exposed to pulp, even if there is no pathologic resorption or radiographic evidence of inflammation [4]. After removing the coronal tissue, it's important to ensure that the remaining radicular tissue is healthy and free of pus, necrosis, or continuous bleeding that cannot be controlled with a cotton pellet after several minutes [1].

In the absence of any negative health indicators or symptoms like sensitivity, irritation or edema, the root pulp should remain asymptomatic. After surgery, there may be no radiographic evidence of external root resorption. Internal root resorption is likely to be stable and self-limiting [5-8].

### DISCUSSION

#### Formocresol

For 80 years, dental professionals have utilized formocresol for the deciduous pulpotomy of teeth. The formocresol pulpotomy devitalization strategy is the molecular, reparative method for primary pulp treatment. In 1904, Buckley introduced formocresol for primary teeth treatment in the USA. In the primary dentition, formocresol was a popular pulpotomy medication [2]. Because of formocresol's toxicity and potential for cancer, there are now questions about its usage in humans [2]. Despite these problems, pulpotomy using formocresol has become a widely accepted treatment. In the UK, a study found that 66.5% of pediatric dentists use formocresol for pulpectomy. However, 54.2% of those dentists are concerned about their choice of drug and are considering changing their technique. In the US, a survey found that most dentists use formocresol as a pulpotomy drug, and they are not worried about any adverse effects. The pulpotomy protocol was first developed by Europeans [9]. Sweet created the formocresol pulpotomy system in 1930. As a result, formocresol is now a widely used pulpotomy medication for primary teeth. The operation was initially included in five trips. Sweet has lowered the number of appointments over time due to concerns with behavior change and the economy [10]. Doyle et al. compared the effects of formocresol and calcium hydroxide Ca(OH) using a two-visit procedure [11]. Spedding and Redig advocated a single pulpotomy visit lasting 5 minutes with a partial devitalization as the end result [12]. The five-minute formocresol therapy has been the benchmark for evaluating all new treatment methods, ever since Redig's successful single visit pulpotomy in humans. However, the original purpose of complete mummification, sterilization, and metabolic suppression has been overlooked. Instead, the fast treatment only weakly devitalizes the pulp. The pulp typically remains chronically inflammatory, half-dead, and half-vital [12]. Garcia Godoy proposed the one-minute pulpotomy visit in 1991 [13]. In 2011, Zahra et al. used the diluted or full-strength solutions for five minutes and observed that a one-minute formocresol pulpotomy resulted in performance rates comparable to those reported in the literature [14]. The clinical outcomes of this approach vary between 55% and 98% [5,15]. Although formocresol has shown high success rates, its toxicity has been subject to scrutiny. Formocresol is thought to be carcinogenic, mutagenic, and poisonous to cells [16]. Eugenia has discovered dentigerous cysts connected to formocresol pulpotomies deciduous molars, [17]. IARC (June 2004) classified formocresol as a carcinogen with the potential to lead to leukemia and nasopharyngeal cancer. However, Ranly assessed the level of formocresol after pulpotomy and calculated that the same organism would need to have 3000 pulpotomies in order to reach hazardous levels [18]. The entire coronal and radicular pulp tissue is repaired throughout the course of two phases of pulpotomy devitalization. It is utilized when shorter sessions are necessary and to improve patient outcomes. Miyamato advised a pulpotomy visit for the effective handling of uncooperative children [19].

Formocresol is a solution that is used to prevent the breakdown of tissues by attaching to the peptide group of an amino acid side chain. It is a reversible process and doesn't alter the basic structure of protein molecules [2]. Due to the controversies surrounding the use of formocresol, several alternatives have been researched. This narrative analysis aims to provide a summary of these alternatives.

#### Calcium hydroxide

The first material that was used in pulpotomy and was capable of dentine regeneration was Ca(OH). This material triggers a stimulation that is delicately balanced between resorption and repair. The main disadvantage of this alternate method is internal resorption.

Zander reported a 70% success rate using a thick Ca(OH) paste and water [20]. The creation of dentine bridges and full healing of pulp stumps was noted by Doyle et al., while some patients experienced treatment failure, which was manifested as internal resorption [21]. Cvek pulpotomy outcomes with Ca(OH) were less noteworthy [22].

#### Ferric sulphate

A 15.5% acidic solution of ferric sulphate, a hemostatic chemical, developed without the use of aldehyde [23]. Ferric sulphate can be easily adjusted and produces the same effect as formocresol when administered for 15 seconds without having any hazardous side effects [24].

The mechanism of action in which ferric sulphate works is not yet fully understood. It was previously believed that the reaction of blood to ferric sulphate ions caused blood proteins to cluster together and form a metal protein complex that might block capillaries and lead to hemostasis. As a result, there will be less concern about uncontrolled bleeding, which will lower the dangers of infection and internal resorption. Reduced working and manipulation times are the main advantages of ferric sulphate over formocresol [24]. Ferric sulphate, in contrast, is less strong and easily accessible, making it simple for children to use. Ferric sulphate has antibacterial properties as well [23]. Ferric sulphate performed similarly to formocresol in certain trials while outperforming it in others [23].

#### Nigella sativa oil

An indigenous herbaceous plant called Nigella sativa (NS) is widely utilized in herbal therapy throughout the world. NS, also known as black cumin and black seed, has been shown to have numerous medicinal benefits. It acts as a bronchodilator, hypotensive, analgesic, antibacterial, anti-inflammatory, and immune-potentiating agent, among other things [25]. NS has the ability to speed up the healing of burn wounds since it contains proteins that can cause human keratocytes to release fibronectin into the dermal fibroblast [25]. NS can be also used as a preventative addition to conventional chemotherapy to treat oral mucositis in rats [26].

The NS extracts demonstrated analgesic, anti-inflammatory, and antibacterial action has led to its usage as a pulpotomy agent. In order to categorize the pulpal response to sodium hypochlorite and formocresol, the histopathology of the pulp tissues of dogs was examined [27].

According to their claims, NS has anti-inflammatory properties, and when used to treat pulp, the pulp's potency is maintained. Then it was suggested to use the chemical as a pulpotomy drug for primary teeth [27]. Additionally, NS is used in dentistry to prevent dental caries and treat oral ulcers, oral mucositis, gum, and periodontal infections [25,28,29].

#### Aloe Vera

Aloe vera, an African native that is frequently referred to as a "medicinal herb", has a number of properties, including antifungal, antibacterial, immunomodulatory, anti-inflammatory, antiviral, and defensive against a variety of pathogens [30]. It is used as a therapeutic agent in the treatment of lichen planus, chronic oral conditions, extraction sockets, and aphthous ulcers in dentistry [31]. Steroids' ability to reduce inflammation is well-developed in A. Vera gel, which causes low amounts of prostaglandin to grow [32]. They concluded that freshly extracted gel can be used as a pulpotomy agent successfully [33].

Aloe vera, when applied directly to exposed rat pulpal tissue, demonstrates good biocompatibility and promotes the formation of tertiary dentin bridges [34]. This result was caused by various bioactive components, such as beta-sitosterol, glycoproteins, and polysaccharides. These components promote cell proliferation, angiogenesis, and wound healing [34].

#### Honey

Honey has a solid reputation among natural goods in the literature due to its medicinal properties. It is antibacterial and promotes the healing of wounds [35]. Polyphenols found in honey have protective effects against periodontal disease, oral cancer, and dental caries [36]. It can be used to create dental caries prevention products like toothpaste and mouthwash [37].

This natural product was chosen by Kumari et al. as a pulpotomy agent, with similar results on both the clinical and radiological fronts [38]. Another important aspect of honey's effectiveness as a pulpotomy agent is the higher rate of anti-inflammatory and healing qualities brought on by its acidic existence.

As honey acidity lowers the pH of the wound and increases the amount of oxygen accessible in the blood from hemoglobin, it tries to supply oxygen to healing tissue. Honey has been shown to significantly increase the release of certain cytokines from monocytes, including tumor necrosis factor-alpha, interleukin (IL)-1, and IL-6, which have been found to be crucial for tissue repair and healing. Ankaferd Blood Stopper (ABS) is an herbal extract that was created from five different plants: Thymus vulgaris, Glycyrrhiza glabra, Vitis vinifera, Alpinia officinarum, and Urtica dioica [39]. These plants have various effects on the endothelium, blood cells, angiogenesis, cell proliferation, vascular dynamics, and act as cell mediators. In a study conducted by Goker et al., the possible mechanisms of ABS are described in detail [39].

As soon as ABS is applied, a protein network that is enclosed forms, providing focal areas for crucial erythrocyte aggregation. The primary and secondary hemostatic systems are covered by the ABS-induced blood cell protein network growth, specifically in erythrocytes, without any disruption of the specific coagulation components [40].

ABS pulpotomy tests have shown a progress rate between 89 and 100 percent [41]. But in this case, further research is required.

#### Mineral trioxide aggregate

Mineral trioxide aggregate (MTA) introduced by Mohammed Taorabinejad in 1993 at Loma Linda University in California, USA. At 1998 this material gets the approval by U.S food and drug administration (FDA). ProRoot MTA, the first commercially available MTA product, was introduced by Dentsply Tulsa Dental Specialties in 1999. Since that there were different companies introduced multiple MTA products in the market. This product was used in There are a number of dental procedures which involve the treatment of pulp. These procedures include pulp capping, pulpotomy, apexogenesis, apexification, regeneration, repair of perforations, and root end filling [42-47]. According to the material safety data sheet (MSDS), Pro Root MTA (White) is composed of powder made up of tricalcium silicate, dicalcium silicate, tricalcium aluminate, calcium oxide, calcium sulfate dihydrate, bismuth oxide, aluminum oxide, and sulfur oxide. Mixing of powder and water is essential to apply MTA, however, there is a definite water to powder ratio specified by each manufacture. After mixing of MTA powder with liquid and application of the material for the specific purpose, final setting time of three hours need to be go before placing a root filling material or final restorative material [48]. When compared to other restorative materials, MTA showed the least cytotoxicity to human gingival fibroblasts and L-929. It also resulted in complete dentinal bridge formation with minimal or no pulp response and minimal or no inflammation [49,50]. Addition of dentin powder to MTA helps to accelerate the process of killing bacteria [51].

In comparison of MTA with zinc oxide eugenol cements, MTA has generally shown better sealing ability as a root-end filling material and discovered to promote the formation of thicker dentin bridge [52,53].

Clinical reports have also shown highly successful outcomes such as preservation of pulp vitality and continued root formation using MTA [54].

Pulpotomy procedures have seen a rise in the usage of MTA as a common material in recent years of permanent teeth showing symptoms of curable and non-curable pulpitis and in complex coronal fractures of immature and mature teeth [55].

By contrast, the high solubility, high price, and color-changing effect of both the gray and white forms are among the drawbacks of MTA as a pulpotomy agent [56].

MTA contains of calcium sulphate dehydrate, tetracalcium alumina, bismuth oxide, ferrite, and tricalcium silicate. After mixing, MTA has a pH of 10.2. After three hours of setting, the pH rises to 12.5. When MTA comes into touch with pulp tissue, dentin bridge development is promoted. Most trials had the drawback of having a short follow-up duration and follow-up absences. Recent meta-analyses and reviews by Simancas-Pallares et al. [21], Po-Yen Lin et al. [57], Shirvani and Agasy [58], and others have found that pulpotomy with MTA has a high success rate. On the other hand, Anthonappa et al. found no proof that MTA was more effective than modern tools and materials as a pulpotomy medication [59].

#### **Biodentine**

Biodentine is a calcium silicate-based material designed to replace the dentine and be dentine substitute. This material became commercially available in 2009-2010 [60,61]. According to MSDS, Biodentine is a dental material that consists of a combination of powder and liquid components. The powder is composed of calcium carbonate, zirconium dioxide, and calcium oxide, while the liquid contains calcium chloride dihydrate. Together, these components create a material that has various dental applications, such as in pulp therapy and root canal treatment. To start using the Biodentine in any procedure five drops of the liquid need to be placed inside the capsule which contains the powder before placing it in the mixing device for 30 seconds with 4200 vibration per minute. When biocompatibility was assessed, no mutagenic effect nor DNA damage or break was observed in vitro [62]. Furthermore, when the material was directly applied to the pulp tissue can help in the healing process by improving the migration and proliferation of stem cells and induce the mineralization process [63,64].

It is popular to use for multiple procedure such as perforation repair, apexification, retrograde filling and more even though that it can cause death of the pulpal cells under the material [65]. In 2013 Biodentine was used for the first time in pulpotomy of permanent teeth by Villat, Grosgogeat [66] which was successful with 6 months follow-up.

#### **BMP (Bone Morhogenic Protein)**

BMP is a substance that promotes the growth of reparative dentin by using recombinant dentin proteins similar to the body's natural proteins. The most extensively researched proteins in pulp tissue are BMP-2, BMP-4, and BMP-7 (OP-1).

Fibroblast-like cells from the lower pulp migrate to the amputation area, which is free of contamination. They then proliferate and transport the tissues. Either the inactive matrix is formed, or the same scaffolds are used to adhere the age-undifferentiated stem and mesenchymal cells [67].

#### Glutaraldehyde Pulpotomy

Gravenmade proposed using glutaraldehyde for pulpotomy. Recently, it has been suggested as an al-

ternative to formocresol due to its superior fixative properties. Glutaraldehyde has the advantage of eliminating cresol, being less toxic, having a low antidote and self-limiting penetration. In comparison, formocresol has weaker crosslinking properties than glutaraldehyde [67].

## CONCLUSION

The success of pulpotomy procedures depends on various critical variables, including case evaluation, clinical and diagnosis, and the material used for the procedure. The two most commonly used pulpotomy agents are formocresol and MTA. While formocresol still has good clinical and radiological

#### REFERENCES

- Fuks AB. Pulp therapy for the primary and young permanent dentitions. *Dent Clin North Am.* 2000;44(3):571-96. doi: 10.1016/S0011-8532(22)01746-3
- Fuks AB. Vital pulp therapy with new materials for primary teeth: new directions and treatment perspectives. J Endod. 2008;34(7 Suppl):S18-24. doi: 10.1016/j.joen.2008.02.031
- Al-Dlaigan YH. Pulpotomy medicaments used in deciduous dentition: an update. J Contemp Dent Pract. 2015;16(6):486-503. doi: 10.5005/ jp-journals-10024-1711
- Camp JH. Diagnosis dilemmas in vital pulp therapy: treatment for the toothache is changing, especially in young, immature teeth. J Endod. 2008;34(7 Suppl):S6-12. doi: 10.1016/j.joen.2008.03.020
- Huth KC, Paschos E, Hajek-Al-Khatar N, Hollweck R, Crispin A, Hickel R et al. Effectiveness of 4 pulpotomy techniques-randomized controlled trial. J Dent Res. 2005;84(12):1144-8. doi: 10.1177/154405910508401210
- Thompson AG, Davis BR. Technical note: Force control in electrohydraulic active suspensions revisited. Veh Syst Dyn. 2001;35(3):217-22. doi: 10.1076/vesd.35.3.217.2048
- Chavdarov AV. Morphological and anatomical features of the genus Gagea Salisb., growing in the East Kazakhstan region. J Mech Continua Math Sci. 2020;(Spl10):1. doi: 10.26782/jmcms.spl.10/2020.06.00041
- Siqueira JF Jr, Rôças IN, Paiva SS, Guimarães-Pinto T, Magalhães KM, Lima KC. Bacteriologic investigation of the effects of sodium hypochlorite and chlorhexidine during the endodontic treatment of teeth with apical periodontitis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2007;104(1):122-30. doi: 10.1016/j.tripleo.2007.01.027
- Shah S. Paediatric dentistry- novel evolvement. Ann Med Surg (Lond). 2017;25:21-9. doi: 10.1016/j.amsu.2017.12.005
- 10. Yildiz E, Tosun G. Evaluation of formocresol, calcium hydroxide, ferric sulfate, and MTA primary molar pulpotomies. *Eur J Dent*. 2014;8(2):234-40. doi: 10.4103/1305-7456.130616
- Aminabadi NA, Farahani RM, Oskouei SG. Formocresol versus calcium hydroxide direct pulp capping of human primary molars: two-year follow-up. J Clin Pediatr Dent. 2010;34(4):317-21. doi: 10.17796/ jcpd.34.4.pntq604021604234
- Srinivasan D, Jayanthi M. Comparative evaluation of formocresol and mineral trioxide aggregate as pulpotomy agents in deciduous teeth. *Indian J Dent Res.* 2011;22(3):385. doi: 10.4103/0970-9290.87058
- Ranly DM, Garcia-Godoy F. Reviewing pulp treatment for primary teeth. J Am Dent Assoc. 1991;122(9):83-5. doi: 10.14219/jada. archive.1991.0263
- 14. Nazeri R, Nourbakhsh N, Talebi A, Akhlaghi N, Manshaei M. Comparison of the clinical, radiographic, and histological outcomes of pulpotomy of deciduous teeth in dogs with formocresol, Gutta-percha, and mineral trioxide aggregate. *J Pediatr Dent.* 2016;4(1):1. doi: 10.4103/2321-6646.174924

success rates and remains a popular choice, MTA has gained popularity due to its biocompatibility, excellent sealing ability, and promotion of dentine bridge formation. However, there is still not enough evidence to determine conclusively which pulpotomy treatment is superior. Ultimately, the choice of pulpotomy agent should be based on individual case assessment and the clinician's expertise.

Acknowledgments: all authors contributed equally to the manuscript Conflict of interest: the authors declare no conflicts of interest Financial support: none declared

- 15. Carrotte P. An investigation of primary molar vital pulp therapy. *Br Dent J.* 2000;188(1):25. doi: 10.1038/sj.bdj.4800377a
- Lewis BB, Chestner SB. Formaldehyde in dentistry: A review of mutagenic and carcinogenic potential. J Am Dent Assoc. 1981;103(3):429-34. doi: 10.14219/jada.archive.1981.0341
- Asián-González E, Pereira-Maestre M, Conde-Fernández D, Vilchez I, Segura-Egea JJ, Gutiérrez-Pérez JL. Dentigerous cyst associated with a formocresol pulpotomized deciduous molar. *J Endod*. 2007;33(4):488-92. doi: 10.1016/j.joen.2006.10.011
- 18. Coates A. Current status of chemotherapy of breast cancer. *Drugs*. 1984;28(2):93-8. doi: 10.2165/00003495-198428020-00001
- Shumayrikh NY, Adenubi JO. Clinical evaluation of glutaraldehyde with calcium hydroxide and glutaraldehyde with zinc oxide eugenol in pulpotomy of primary molars. *Dent Traumatol.* 1999;15(6):259-64. doi: 10.1111/j.1600-9657.1999.tb00784.x
- Dominguez M, Witherspoon D, Gutmann J, Opperman L. Histological and scanning electron microscopy assessment of various vital pulp-therapy materials. *J Endod*. 2003;29(5):324-33. doi: 10.1097/00004770-200305000-00003
- Godhi B, Sood PB, Sharma A. Effects of mineral trioxide aggregate and formocresol on vital pulp after pulpotomy of primary molars: an in vivo study. *Contemp Clin Dent.* 2011;2(4):296-301. doi: 10.4103/0976-237X.91792
- Magnusson B. Attempts to predict prognosis of pulpotomy in primary molars bacteriologic and histologic examination. *Eur J Oral Sci.* 1970;78(1-4):232-40. doi: 10.1111/j.1600-0722.1970.tb02069.x
- Caicedo R, Abbott PV, Alongi DJ, Alarcon MY. Clinical, radiographic and histological analysis of the effects of mineral trioxide aggregate used in direct pulp capping and pulpotomies of primary teeth. *Aust Dent J.* 2006;51(4):297-305. doi: 10.1111/j.1834-7819.2006.tb00447.x
- Ibricevic H, Al-Jame Q. Ferric sulfate as pulpotomy agent in primary teeth: twenty month clinical follow-up. J Clin Pediatr Dent. 2000;24(4):269-72. doi: 10.17796/jcpd.24.4.d7u6405nw1132705
- Al-Attass SA, Zahran FhM, Turkistany SA. Nigella sativa and its active constituent thymoquinone in oral health. *Saudi Med J.* 2016;37(3):235-44. doi: 10.15537/smj.2016.3.13006
- Aras MH, Sezer U, Erkilic S, Demir T, Dagli SN. Effect of dietary boron on 5-fluorouracil induced oral mucositis in rats. *Eur J Dent.* 2013;7(3):310-4. doi: 10.4103/1305-7456.115415
- Omar OM, Khattab NM, Khater DS. Nigella Sativa oil as a pulp medicament for pulpotomized teeth: a histopathological evaluation. J Clin Pediatr Dent. 2012;36(4):335-41. doi: 10.17796/jcpd.36.4.n6674435856q86w8
- 28. Al-Bayaty FH, Kamaruddin AA, Ismail MA, Abdulla MA. Formulation and evaluation of a new biodegradable periodontal chip containing thymoquinone in a chitosan base for the management of chronic periodontitis. J Nanomater. 2013;2013:1-5. doi: 10.1155/2013/397308

- 29. Kavaz T, Özdemir H. Effect of Streptococcus mitis and Streptococcus mutans on the adhesion of Streptococcus salivarius to lithium disilicate glass-ceramics of varying roughnesses. *Int Dent Res.* 2023;13(1):27-34. doi: 10.5577/idr.2023.vol13.no1.5
- Sujatha G, Kumar GS, Muruganandan J, Prasad TS. Aloe vera in dentistry. J Clin Diagn Res. 2014;8(10):ZI01-Z2. doi: 10.7860/ JCDR/2014/8382.4983
- Poor MR, Hall JE, Poor AS. Reduction in the incidence of alveolar osteitis in patients treated with the SaliCept Patch, containing Acemannan Hydrogel. J Oral Maxillofac Surg. 2002;60(4):374-9. doi: 10.1053/joms.2002.31222
- 32. Shelton RM. Aloe Vera. *Int J Dermatol*. 1991;30(10):679-83. doi: 10.1111/j.1365-4362.1991.tb02607.x
- Gupta N, Bhat M, Devi P, Girish. Aloe-Vera: A nature's gift to children. Int J Clin Pediatr Dent. 2010;3(2):87-92. doi: 10.5005/jpjournals-10005-1059
- Gala-García A, Teixeira KIR, Mendes LL, Sobrinho APR, Santos VR, Cortes ME. Effect of Aloe vera on rat pulp tissue. *Pharm Biol.* 2008;46(5):302-8. doi: 10.1080/13880200801887138
- Lusby PE, Coombes A, Wilkinson JM. Honey. J Wound Ostomy Continence Nurs. 2002;29(6):295-300. doi: 10.1097/00152192-200211000-00008
- 36. Ahuja V, Ahuja A. Apitherapy A sweet approach to dental diseases. Part II: Propolis. J Adv Oral Res. 2011;2(2):1-8. doi: 10.1177/2229411220110201
- Newadkar U. Miraculous honey: A sweet and valuable remedy in dentistry!! SRM J Res Dent Sci. 2016;7(2):132. doi: 10.4103/0976-433X.182663
- Reddy GA, Sridevi E, Sai Sankar AJ, Pranitha K, Pratap Gowd MJS, Vinay C. Endodontic treatment of chronically infected primary teeth using triple antibiotic paste: an in vivo study. *J Conserv Dent*. 2017;20(6):405-10. doi: 10.4103/JCD.JCD\_161\_17
- 39. Molan PC. The evidence supporting the use of honey as a wound dressing. Int J Lower Extrem Wounds. 2006;5(1):40-54. doi: 10.1177/1534734605286014
- 40. Goker H, Haznedaroglu IC, Ercetin S, Kirazli S, Akman U, Ozturk Y, Firat HC. Haemostatic actions of the folkloric medicinal plant extract Ankaferd Blood Stopper<sup>®</sup>. J Int Med Res. 2008;36(1):163-70. doi: 10.1177/147323000803600121
- 41. Yaman E, Görken F, Pinar Erdem A, Sepet E, Aytepe Z. Effects of folk medicinal plant extract Ankaferd Blood stopper<sup>®</sup> in vital primary molar pulpotomy. *Eur Arch Paediatr Dent*. 2012;13(4):197-202. doi: 10.1007/ BF03262870
- 42. Cushley S, Duncan H, Lappin M, Chua P, Elamin A, Clarke M, El-Karim I. Efficacy of direct pulp capping for management of cariously exposed pulps in permanent teeth: a systematic review and meta-analysis. *Int Endod J.* 2021;54(4):556-71. doi: 10.1111/iej.13449
- 43. Abuelniel GM, Duggal MS, Kabel N. A comparison of MTA and Biodentine as medicaments for pulpotomy in traumatized anterior immature permanent teeth: a randomized clinical trial. *Dent Traumatol.* 2020;36(4):400-10. doi: 10.1111/edt.12553
- 44. Mousivand S, Sheikhnezami M, Moradi S, Koohestanian N, Jafarzadeh H. Evaluation of the outcome of apexogenesis in traumatised anterior and carious posterior teeth using mineral trioxide aggregate: a 5-year retrospective study. *Aust Endod J.* 2022;48(3). doi: 10.1111/aej.12583
- 45. Nicoloso GF, Goldenfum GM, Pizzol TdSD, Scarparo RK, Montagner F, de Almeida Rodrigues J et al. Pulp revascularization or apexification for the treatment of immature necrotic permanent teeth: systematic review and meta-analysis. J Clin Pediatr Dent. 2019;43(5):305-13. doi: 10.17796/1053-4625-43.5.1
- 46. Babaki D, Amoako K, Bahrami AR, Yaghoubi S, Mirahmadi M, Matin MM. MTA enhances the potential of adipose-derived mesenchymal stem cells for dentin-pulp complex regeneration. *Materials*. 2020;13(24):5712. doi: 10.3390/ma13245712
- 47. Gorni FG, Ionescu AC, Ambrogi F, Brambilla E, Gagliani MM. Prognostic factors and primary healing on root perforation repaired with MTA: a

14-year longitudinal study. *J Endod.* 2022;48(9):1092-9. doi: 10.1016/j. joen.2022.06.005

- 48. Jeong YN, Yang SY, Park BJ, Park YJ, Hwang YC, Hwang IN, Oh WM. Physical and chemical properties of experimental mixture of mineral trioxide aggregate and glass ionomer cement. J Korean Acad Conserv Dent. 2010;35(5):344-52. doi: 10.5395/JKACD.2010.35.5.344
- Osorio RM, Hefti A, Vertucci FJ, Shawley AL. Cytotoxicity of endodontic materials. J Endod. 1998;24(2):91-6. doi: 10.1016/S0099-2399(98)80084-8
- Nowicka A, Lipski M, Parafiniuk M, Sporniak-Tutak K, Lichota D, Kosierkiewicz A et al. Response of human dental pulp capped with biodentine and mineral trioxide aggregate. *J Endod.* 2013;39(6):743-7. doi: 10.1016/j.joen.2013.01.005
- Zhang H, Pappen FG, Haapasalo M. Dentin enhances the antibacterial effect of mineral trioxide aggregate and bioaggregate. *J Endod.* 2009;35(2):221-4. doi: 10.1016/j.joen.2008.11.001
- Chacko DV, Kurikose DS. Human pulpal response to Mineral Trioxide Aggregate (MTA): a histologic study. *J Clin Pediatr Dent.* 2006;30(3):203-9. doi: 10.17796/jcpd.30.3.38h13g5p84651652
- 53. Jahromi M, Nasri Z, Aminzadeh A. Clinical and histological response of human pulp tissue to direct pulp capping with mineral trioxide aggregate, Biodentine and propolis. *Dent Res J (Isfahan).* 2022;19(1):40. doi: 10.4103/1735-3327.344163
- 54. Witherspoon DE, Small JC, Harris GZ. Mineral trioxide aggregate pulpotomies. *J Am Dent Assoc.* 2006;137(5):610-8. doi: 10.14219/jada. archive.2006.0256
- 55. Eghbal MJ, Asgary S, Baglue RA, Parirokh M, Ghoddusi J. MTA pulpotomy of human permanent molars with irreversible pulpitis. Aust Endod J. 2009;35(1):4-8. doi: 10.1111/j.1747-4477.2009.00166.x
- Fridland M, Rosado R. MTA solubility: a long term study. J Endod. 2005;31(5):376-9. doi: 10.1097/01.DON.0000140566.97319.3e
- 57. Urist MR. Bone: formation by autoinduction. *Science*. 1965;150(3698):893-9. doi: 10.1126/science.150.3698.893
- Shirvani A, Asgary S. Mineral trioxide aggregate versus formocresol pulpotomy: a systematic review and meta-analysis of randomized clinical trials. *Clin Oral Investig.* 2014;18(4):1023-30. doi: 10.1007/ s00784-014-1189-2
- 59. Anthonappa RP, King NM, Martens LC. Is there sufficient evidence to support the long-term efficacy of mineral trioxide aggregate (MTA) for endodontic therapy in primary teeth? *Int Endod J.* 2012;46(3):198-204. doi: 10.1111/j.1365-2591.2012.02128.x
- Kaur M, Singh H, Dhillon JS, Batra M, Saini M. MTA versus Biodentine: review of literature with a comparative analysis. J Clin Diagn Res. 2017;11(8):ZG01-Z5. doi: 10.7860/JCDR/2017/25840.10374
- Malkondu O, Karapinar Kazandag M, Kazazoglu E. A review on biodentine, a contemporary dentine replacement and repair material. *Biomed Res Int.* 2014;2014:160951. doi: 10.1155/2014/160951
- Kunert M, Rozpedek-Kaminska W, Galita G, Sauro S, Bourgi R, Hardan L, et al. The cytotoxicity and genotoxicity of bioactive dental materials. *Cells.* 2022;11(20):3238. doi: 10.3390/cells11203238
- 63. Luo Z, Li D, Kohli MR, Yu Q, Kim S, He WX. Effect of Biodentine on the proliferation, migration and adhesion of human dental pulp stem cells. *J Dent*. 2014;42(4):490-7. doi: 10.1016/j.jdent.2013.12.011
- 64. Zanini M, Sautier JM, Berdal A, Simon S. Biodentine induces immortalized murine pulp cell differentiation into odontoblast-like cells and stimulates biomineralization. *J Endod.* 2012;38(9):1220-6. doi: 10.1016/j.joen.2012.04.018
- 65. Zhou HM, Shen Y, Wang ZJ, Li L, Zheng YF, Hakkinen L, Haapasalo M. In vitro cytotoxicity evaluation of a novel root repair material. *J Endod*. 2013;39(4):478-83. doi: 10.1016/j.joen.2012.11.026
- 66. Villat C, Grosgogeat B, Seux D, Farge P. Conservative approach of a symptomatic carious immature permanent tooth using a tricalcium silicate cement (Biodentine): a case report. *Restor Dent Endod*. 2013;38(4):258-62. doi: 10.5395/rde.2013.38.4.258
- Kashyap N, Bagchi P, Biswas S. Pulpotomy: Modern concepts and materials. *Int J Oral Health Dent*. 2021;7(4):245-52. doi: 10.18231/j. ijohd.2021.049