

Republic of Iraq
Ministry of higher education
and Scientific research
University of Baghdad
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Intracanal Medicaments

A Project Submitted to

The college of Dentistry, University of Baghdad, Department of Conservative
Dentistry in Partial Fulfillment for the Bachelor of Dental Surgery

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2021-2022

Certification of the supervisor

I certify that this project entitled "Intracanal medicaments" was prepared by the fifth- year student "Ali Saad Ghanem" under my supervision at the college of dentistry/University of Baghdad in partial fulfillment of the graduation requirements for the bachelor degree in dentistry.

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Date:

Dedication

I'd like to dedicate my work to Allah who was my greatest support, without god I would never have reached here. I'd also like to thank everyone who supported me including my family, professors and friends. Special Thanks to my parents for giving me all the emotional and financial support that helped me to reach the level I'm in now. I would also like to thank myself for the hard work and effort that I made to be here. A special thanks to my college and professors for being in my back and giving us all they had to help us become great dentists. My final thanks are for my beloved country Iraq.

Acknowledgment

I would like to express my special thanks and gratitude to my supervisor "Dr. Samar Abd al-hameed" for her guidance and support in completing my project.

I would also like to thank my Endodontic professors for providing me with all the information necessary for me to complete my project. A special thanks for my college for providing me with books that I needed for my project. I'm very proud of being one of its students and I'm willing to be one of its professors in the future.

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Introduction:

Are intracanal medicaments essential in modern endodontic treatment?

The main goal of endodontic treatment is the eradication of microorganisms and their byproducts from the root canal and complete sealing of the canals.

Disinfection of root canal is the elimination of microorganisms from the pulp space within the root canal system. This process of disinfection is considered as the most important and significant phase of endodontic therapy.

Modern endodontics focuses on chemo-mechanical preparation of the canals and is considered as more important than the use of intracanal medicaments.

The more modern meaning of intracanal dressing is for a blockade against coronal leakage from the gap between filling materials and cavity wall.

Pulp canal system is extremely complex and many variations exist. Root canal treatment is still one of the most difficult dental practices. Failures in endodontic treatments are contributed to the difficulty encountered in eradicating all harmful microorganisms inside the canals. In multiple visits endodontic therapy the use of intracanal medicament is strongly recommended.

Therefore, since it is believed since there is no entirely predictable way in one treatment session to ensure complete eradication of microorganisms, an antimicrobial agent is extremely important to predictably destroy and eradicate microorganisms from the canals.

Aims of this review:

1. understanding the role of intracanal medicament in root canal treatment.
2. studying the different intracanal medicament agents available.
3. studying the ideal requirements and indications of intracanal medicaments
4. studying the effects and side effects of these materials on the treated tooth in particular and the patient in general.
5. determining which cases require the use of intracanal medicaments and the prognosis of these cases.

Chapter 1
REVIEW OF LITERATURE

Microbial flora of pulp:

Endodontic pathogen definition should include every organism capable of inducing tissue destruction in apical periodontitis. The current knowledge of endodontic micro flora is based on the applications of several methods and procedures such as histopathological methods, correlative light and electronic microscopy, laser microscopy, culturing and biochemical and mechanical methods. PCR was proved to be a great method for detection of microorganism's species.^[1]

Bacterial species that penetrate the dentine are dominated by gram-positive rods and cocci. These include lactobacillus, streptococcus and propionibacterium.^{[1][3]}

The main reason for endodontic failure is the presence some species of bacteria that persists in the canals. Among these bacteria are Enterococcus faecalis. *E.faecalis* is a gram-positive facultative anaerobe commensal bacterium in the GIT.^{[1][4][10]}

The role of E.feacalis in the research of intracanal medicament:

E.faecalis has gained a lot of interest in recent years due to its ability to grow under almost any laboratory condition. *E.faecalis* has become the benchmark organism to test different irrigants, medicament and antiseptic solutions used in endodontic therapy in vivo studies and these studies have resulted in the acknowledgement of this organism as one of the main etiological factors in chronic endodontic infections.^{[1][4][12][16]}

In persistent endodontic infection and failed endodontic treatments, *E.faecalis* is the most isolated species. (Rodriguez-Niklitschek, 2015).

It is an extremely challenging task to eliminate *E.Faecalis* from the root canals because of its extraordinary capability to infect and colonize dentinal tubules to a considerable depth and its ability to bond to the dentinal collagen.^[4]

Features that make *E.faecalis* an exceptional survivor:

- Live and persist in poor nutrient environment of endodontically treated teeth.^{[1][3][10]}
- Survives in the presence of several medications such as sodium hypochlorite, clindamycin and even calcium hydroxide.^{[10][28]}
- Forms biofilm in medicated canals, invade and metabolize fluids within the dentinal tubules and adhere to the collagen fibers of the the dentine.^[3]
- Convert to into a viable but non-cultivable state.^{[1][2][3]}
- Endure prolonged periods of starvation.^[1]
- Establish mono-infections in medicated canals.^[3]
- Resistance to antibiotics.^[10]
- Survive in extreme environments such as low pH and high temperature.^{[1][4][10]}

Intracanal medicament:

Intracanal medicaments are used as an aid to improve the predictability and prognosis of endodontic treatment. Nowadays, intracanal medicaments are used to eliminate or to destroy the remaining microorganisms in the pulp space after the chemo-mechanical preparation of the canals. It may also be used to eliminate apical exudates and may act as physical barrier during inter-appointment dressings.^{[1][3]}

Its use may be questionable. Some authorities do not recommend the use of intracanal medicament after chemo-mechanical preparation except in some conditions.^[4]

These conditions include the following:

- To eliminate few microorganisms remaining in the root canal after chemo-mechanical preparation.^[1]
- Provide a barrier against leakage of coronal seal. This leakage may allow entry of microorganisms into the canal.^{[1][2][3]}
- To reduce inflammation of periapical tissues or to manage the remnants of vital pulp if time does not allow its complete removal.^[4]
- Help to dry persistently wet canals.^{[4][9]}

Inter-appointment intracanal medicament has been shown to result in better outcome of endodontic treatment. They are mostly needed in cases where bacterial infection persists and when full therapy can't be completed due to the presence of symptoms such as pain or continued exudates.^[8]

Ideal requirements of intracanal medicament:^{[1][2][4][5][6][7][19]}

- It should be an effective germicide and fungicide.
- It should be non-irritating to the periapical tissues.
- It should be stable in solutions.
- It should not stain tooth structure.
- It should have low surface tension.
- It Should have prolonged antimicrobial effect.
- It should be active in the presence of protein derivatives, blood and serum.
- It should have no interference with periapical tissues repair.
- It should not induce cell-mediated immune response.
- It should have no deleterious effects on vital tissues.
- It should not alter the host's physiological functions.
- It should be able to penetrate the dentinal tubules in order to eliminate the bacteria that reside inside them.
- It should reduce pain and sensitivity.
- It should induce healing and bone formation.
- It should eliminate periapical exudates.
- It should stop or at least control root resorption to a certain degree.
- It should have reasonable shelf-life.
- It should be available and not expensive.

Before an intracanal medicament is selected for use, it should be tested extensively by national and international standard organizations to maintain a possible balance between the therapeutic effect and tissue damage effect.

Indications of intracanal medicaments:

1. For eradication of deeply penetrating microorganisms such as *E.faecalis*.^{[1][4][10][27]}
2. To destroy existing microorganisms and inhibit their growth.^[3]
3. Elimination of apical exudates and control inflammatory root resorption.^[1]
4. Prevent contamination between visits as it acts as a physical barrier.^{[1][3]}
5. Help manage persistently weeping canals.^[4]
6. Stimulation of hard tissue bridge formation.^{[1][3][4][6][7][19]}
7. To help complete root formation.^{[1][4]}
8. As an obturating material for primary teeth following pulpectomy.^{[1][19]}

Classification of intracanal medicament:

1. Phenolic compounds:

Phenol or carbolic acid is a potent antimicrobial agent capable of destroying tissue cells by binding to cell membrane lipids and proteins.^[4]

Most common phenolic compounds that are used as intracanal medicament are aqueous parachlorophenicol, camphorated monochlorophenicol, cresatin and creosote. Of these camphorated monophenicol (CMCP) was the most commonly used intracanal medicament in early years, currently its use has been decreased over

the years. The antimicrobial action of CMCP is dependent on the volatility of the medicament by the diffusion of its vapors to spread the material throughout the root canal system and bring it into contact with microorganisms remaining in the canal. This makes it not reliable.^{[1][3][4]}

2. Essential oils:

Clove oil (eugenol) has some antibacterial effect but is considered as severe periapical irritant.^[19]

3. Aldehydes:

Formaldehyde, paraformaldehyde and glutaraldehyde are commonly used intracanal medicaments in endodontic therapy. They are water soluble protein denaturing agents and are considered as one of the best disinfectant agents.^{[7][19]}

Formocresol is considered as one of the most commonly used intracanal medicament. However it should be used with caution because it is carcinogenic, mutagenic and cytotoxic agent.^{[1][4]}

4. Halogens:

Chlorine which is the active ingredient of sodium hypochlorite is used as antiseptic agent in endodontic therapy. Iodine which is found in iodine-potassium iodine is another agent that has minimal toxicity and has bactericidal effect.^[4]

5. quaternary ammonium compounds:

They are mild antiseptic irrigants and intracanal medicament.^[3]

6. Antibiotics and corticosteroids:

Antibiotics are avoided nowadays due to fear of bacterial resistance development. US food and drug administration (USFDA) banned the use of PBSC (penicillin-bacitracin; streptomycin-caprylate) for endodontic use because of risks of sensitization and allergic reactions attributed to penicillin.^{[1][3][19]}

Antibiotic mixtures such as ciprofloxacin-metronidazole-minocycline have been used topical root canal antibiotic agent. Topical corticosteroids have also been used as anti-inflammatory agents for several decades. Studies have shown that they are effective in reducing pain of teeth with vital pulps but not with non-vital teeth. There are several combinations of antibiotics and corticosteroids such as septomixine, pulpomixine and ledermix paste. These mixtures should be used with caution because of the risk of bacterial resistance, drug's hypersensitization and the potential to mask certain etiological factors limit their benefits.^{[1][2][4]}

Now I will discuss some of the most common intracanal medicaments used in endodontics.

Calcium hydroxide:

Calcium hydroxide is the most popular intracanal medicament in use since its introduction by Hermann in 1920. Its use is related to antibacterial properties and the ability to induce repair and hard tissue formation. It has high pH so it is considered as a bactericidal agent. It is used as pulp capping material, intracanal medicament and as a component of many dental materials and pastes.^{[2][4][9]}

The lethality of calcium hydroxide is observed only when it comes into direct contact with the bacteria and this may not always be possible clinically.^[27]



Figure 1: pulpdent calcium hydroxide paste Kit. **Timea dako, Mihai Pop, Julia Kulop, Janos Kantor, Monica Monea 2020.**

Combinations of calcium hydroxide:

In order to improve the ability of calcium hydroxide to disinfect the canal, many attempts were made to combine it with other medicament such as potassium-iodine to produce synergistic effect. This combination has been proven to be better at eradicating *E.faecalis*.^{[11][27]}

another combination is calcium hydroxide and CMCP glycerin paste. This mix has been shown to rapidly eliminate bacteria in root canal. Few researchers have confirmed the excellent results of CA(OH)/CMCP in eradicating bacteria from the root canal.^{[4][11][27]}

calcium hydroxide was also combined with sodium hypochlorite and chlorhexidine which produced great results in eliminating bacteria. This mix was more effective than the separate treatment.^[11]

With limitations aside, calcium hydroxide remains the best single medicament currently available to reduce endodontic microorganisms.^{[1][2]}

Biological features of calcium hydroxide:^{[1][3]}

1. Biocompatibility due to its low solubility in water and limited diffusion.
2. Ability to induce formation and mineralization of hard tissues such as bone and dentine.
3. Stimulation of periapical healing.
4. Inhibition of root resorption.

Disadvantages of calcium hydroxide:

1. It is hard to remove it from the walls of the canals.^[25]
2. It alters the zinc-oxide eugenol cements by reducing its setting time.^[4]

The lethal effects of calcium hydroxide on bacteria lie in the following properties:

1. Its ability to act as a physical barrier to the ingress of bacteria.^[1]
2. Destroying the remaining bacteria by preventing substrates from reaching bacteria and by limiting the space for multiplication.^{[3][5][9]}
3. Direct damage to the bacterial cytoplasm by the action of hydroxyl ions.^{[1][2][27]}
4. Suppression of the enzyme activity by disruption of cellular metabolism.^{[1][4][11]}
5. Protein denaturation and Inhibition of DNA replication by splitting the DNA.^{[1][2][4][11]}
6. CA(OH) has tissue dissolving property due to which it aids in cleaning of canal walls by removing necrotic tissue remnants (Wadachi et al., 1998; Yang et al., 1995).

Calcium hydroxide is available in many forms, it is available as non-setting form which is dispensed inside the canal and removed for redressing or for obturation. It is also added and incorporated in presterile absorbant paper points which are used for delivering the material to the apical third of the canal.^[1]

Recently, single paste system which is injectable exists and is more preferable. These include centrix, calcijet and pyraxicalci.^[3]

Limitations of Calcium hydroxide:^{[1][9][11]}

1. Ineffective against *E.faecalis* and *C.albicans* unless combined with other agents.
2. Reduces microhardness of dentine.
3. Its remnants adversely affect zinc oxide eugenol sealers.
4. Alters physical properties of sealers.
5. Questionable healing of peri-radicular lesions.
6. Its antibacterial properties are largely dependent on the vehicle used (aqueous, oily or viscous).
7. 10 percentage of calcium hydroxide gets converted into calcium carbonate at the apical region.
8. No impact on post-operative pain.
9. Difficult to remove.
10. Less effective against gram-negative bacteria.

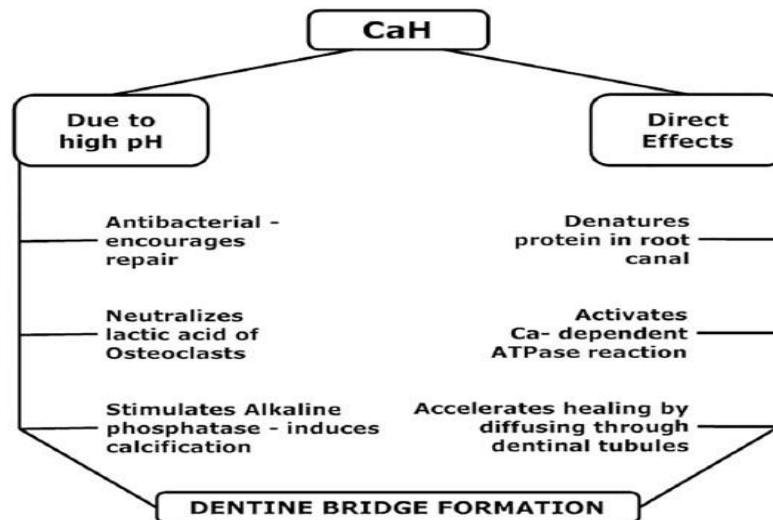


Figure 2: Mechanisms by which calcium hydroxide (CaOH_2) may form dentine bridge/reparative dentine. **GR Ravi and RV Subramanyam 2015.**

Triple antibiotic paste:

The triple antibiotic paste is a mixture of 3 antibiotics, metronidazole, ciprofloxacin and tetracycline(either minocycline or doxycycline). It is also known as hoshino's paste (Qiu and Wang, 2015). The paste is prepared by mixing these antibiotics powders in a ratio of 1:1:1 which is then mixed with a solvent in a ratio of 7:1.^[4]

In high concentration this paste can have toxic effect on the stem cells in the apical papilla, therefore it is used in low concentration only. In low concentration it is sufficient to eradicate *E.faecalis* (Alghilan et al., 2017; Ruparel et al 2012).

The antibacterial effect of this paste is attributed to the following.^{[4][24][27]}

1. The broad-spectrum antibacterial action of metronidazole.
2. The bactericidal effect of ciprofloxacin on gram-negative bacteria.
3. The bacteriostatic and anti-resorptive properties of tetracycline.

The combination of these drugs makes it effective against the polymicrobial nature of endodontic infections (Mohammadi et al., 2018).



Figure 3 : Triple antibiotic paste Kumar S, Desai K, Palekar A, Biradar B, Chatterjee A, Kumari K. 2020

Indications of Triple antibiotic paste:

1. Regenerative endodontic procedures to produce completely sterile environment for healing.^[22]
2. In primary teeth where non-instrumentation endodontic treatment known as "lesion sterilization and tissue repair" is the last resort treatment (Arangannal et al., 2019, Sain et al., 2018).
3. Necrotic teeth with or without periapical lesions.^[4]

Disadvantages:

1. Discoloration of teeth is the most common complaint associated with triple antibiotic paste use. This discoloration is due to minocycline. Minocycline chelates with calcium to form a compound that cannot be removed. Therefore minocycline was replaced with amoxicillin or cofactor in the triple antibiotic paste. An alternative is the use of double antibiotic paste which consists of metronidazole and ciprofloxacin only.^{[12][19][24]}



Figure 4: Discoloration of the tooth due to triple antibiotic paste. . **Zohaibkhurshid, Muhammad SohailZafar and ShariqNajeeb (2021).**

2. Reduces the microhardness of dentine when applied for prolonged period.^{[4][25]}
3. Toxic and cause damage to the stem cells in the apical papilla when applied in higher concentration.^{[4][7]}
4. Bacterial resistance. Although there is no clear evidence of triple antibiotic paste association with increased bacterial resistance.^{[2][27]}

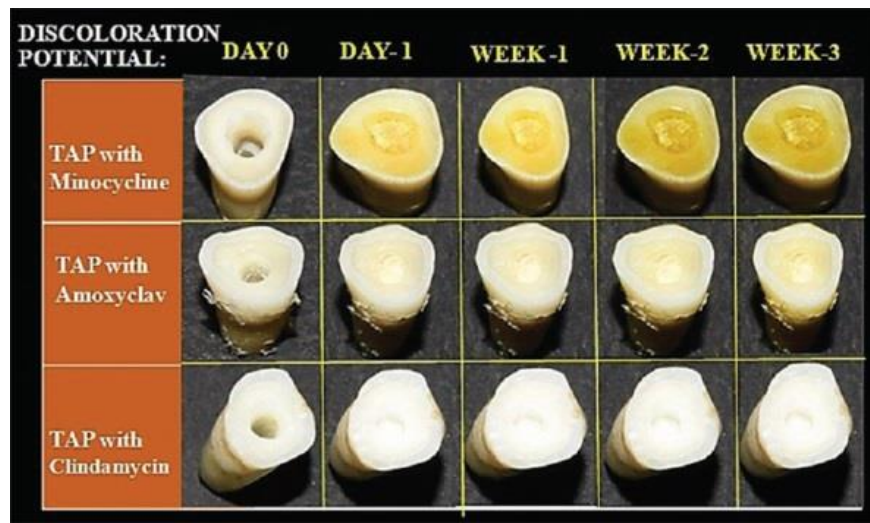


Figure 5: Discoloration of the teeth associated with the use of triple antibiotic paste with minocycline, amoxyclav and clindamycin to assess the discoloration potential of TAP. The discoloration was mostly associated with the use minocycline in the TAP. .

Zohaibkhurshid, Muhammad SohailZafar and ShariqNajeeb (2021).

Camphorated monochlorophenol (CMCP):

CMCP is a phenolic compound with antiseptic properties. It is composed of 35 percent Parachlorophenol and 65 percent camphor. Parachlorophenol is a solid that is liquefied by the addition of camphor. Although it is permitted by American dental association (ADA) parachlorophenol when used as intracanal medicament is a caustic agent and is more caustic than its combination with camphor.^[2]

The Antimicrobial effect of CMCP is attributed to its protein and lipid-binding property which destroys bacterial membrane. It is highly effective against *E.faecalis* therefore, it is used in combination with calcium hydroxide as I mentioned before.^[4]



Figure 6: camphorated mono-chlorophenol (CMCP) solution. **PD Swiss 2020.**

Disadvantages:

1. Less biocompatibility than other agents.
2. Toxicity to periodontal cells.
3. Genotoxic potential.

Other phenolic medicaments:

Eugenol, cresol, thymol and parachlorophenol are phenolic compounds that were used in the past for their antibacterial properties. Eugenol was used with formocresol in pulpotomy procedures in primary teeth. The adverse effects of these compounds are more than their healing effects. Therefore they are no longer used. These compounds are toxic to cells, have immunosuppressive effects and lack of supporting research studies.^[4]

Iodine potassium iodide (IKI):

IKI is a rapid acting antibacterial agent that has bactericidal effects reaching for a long distance due to the production of vapors. When a cotton pellet soaked with IKI is placed inside the pulp chamber, its fumes are able to reach and exert antibacterial effects at the apical region of the root canal (Aggarwal et al., 2018). It is also strongly effective against *E.faecalis*. to make IKI, 2 g of iodine is mixed with 4 g potassium iodide and then dissolved in distilled water.^{[1][2]}

The antibacterial effect of IKI is due to its ability to penetrate the cell wall of the bacteria and cause disruption in the synthesis and structural

orientation of proteins and alters then physical properties of the cell membrane lipids and makes it immobilized.^{[4][5]}

It has been suggested to use IKI in single visit root canal therapy and it was proven as effective as 2 or 3 visits procedure using calcium hydroxide. 10 min placement of IKI is enough to disinfect the canal.^{[4][6]}

The only disadvantage associated with IKI is its potential to cause allergy. It was reported that patients with allergy to sodium hypochlorite are also allergic to IKI.^[4]

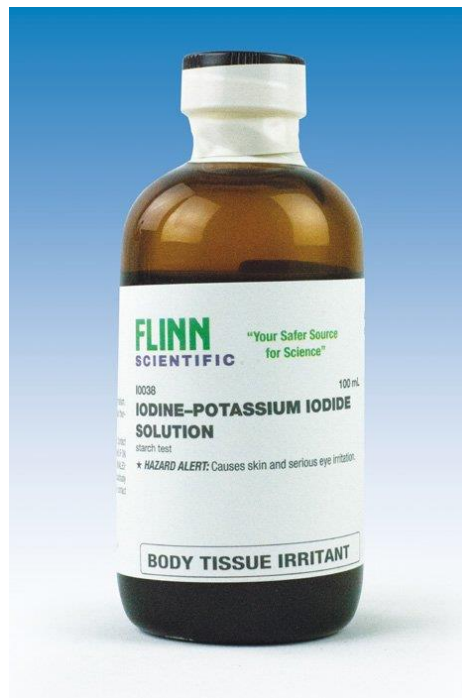


Figure 7: Iodine-potassium iodide solution.
Flinn scientific.

Ledermix paste:

Ledermix paste was developed in 1960 by Schroeder and Triandan. It is composed of demeclocycline HCL and triamcinolone acetonide with polyethene glycol paste.^[4]



Figure 8: Ledermix paste.
Ozdent 2020

The effects of ledermix paste are exerted through the anti-inflammatory effect of triamcinolone which reduces perapical inflammation and the ability of demeclocycline to impair the protein synthesis of bacterial cells by binding with the 30S ribosomal subunits. It was also reported that this paste has antiresorptive effect.^{[4][5]}

Ledermix is used as medicament in root canal procedures and as cement for pulp capping and pulpotomy procedures. It is also indicated to be used in cases of replantation of avulsed teeth to prevent external root resorption due to its antiresorptive properties. It is more effective than calcium hydroxide in preventing external root resorption. It is also effective in preventing post-operative pain between appointments due to its corticosteroid component while calcium hydroxide can't prevent post-operative pain.^[2]

The only disadvantage of ledermix paste is its potential to cause discoloration due to the presence of demeclocycline. This can be minimized by placement of the paste under CEJ.^{[1][2][4][5]}



Figure 9: tooth discoloration due to ledermix paste. .
**Zohaibkhurshid, Muhammad SohailZafar and
ShariqNajeeb (2021).**

Newly synthetic /engineered intracanal medicaments:

The shift from mechanical to biomechanical preparation of the root canal has resulted in the development of many agents that are biocompatible and less toxic to the stem cells of the apical dental papilla.^[4]

I will discuss the most common newly synthetic/engineered intracanal agents which includes the following:

Bio ceramic:

Bioceramic were used for different purposes in medicine. Their use in endodontics began in 1990. Initially they were used as root canal filling materials. Later they were modified and used as root canal sealers, root perforation repair materials and coated gutta-percha points.^{[6][7]}

The first introduced bioceramic material was mineral trioxide aggregate (MTA). Nowadays the MTA is considered as the golden standard in many endodontic procedures.^[2]

Classification of bioceramics:

Bioceramics are classified either on the basis of biological functions or on the basis of composition:

1. According to the biological functions:^{[4][6]}

- Bioinert.
- Bioactive.
- Biodegradable.

2. According to the composition:^{[4][6]}

- Calcium silicate based.
- Tricalcium silicate based cements.
- Hydraulic calcium silicate based.
- Calcium phosphate based.
- Tricalcium phosphate based.
- Hydroxyapatite based.
- Mixture of calcium silicate and calcium phosphate.

The antibacterial effect of bioceramic agents is controversial. Some authors attributed it to the ability of bioceramic materials to increase the pH due to the ionic dissolution from the glass surface on wetting. Other authors didn't find this increase in pH when bioceramic materials were applied at root dentine, therefore, they concluded that it is not related to pH (Zehnder et al., 2004).

Properties of bioceramic materials^{[2][4]}:

1. High biocompatibility.
2. Does not cause inflammatory root resorption.
3. Osteoconductive effect.
4. Effective against *E.faecalis*.
5. Superior antibacterial properties. Better than chlorhexidin and calcium hydroxide.

Some of the most famous bioceramic materials used nowadays are iRoot FM, S53P4, MTA Fillapex and endosequence root repair (ESP and ESS).^[4]

Odontopaste:

Odontopaste is an Australian product that was developed as a substitute to ledermix paste. It is zinc oxide eugenol based agent used as bacteriostatic and anti-inflammatory agent. It is composed of clindamycin HCL, triamcinolone acetonide and calcium hydroxide in a zinc oxide eugenol paste.[4]

The antibacterial action of odontopaste is attributed to the presence of clindamycin which is bacteriostatic against several pathogens. Odontopaste also has anti-inflammatory action and reduces pain by increasing pain threshold.[4][19][6]

It was used as a substitute to ledermix paste as it does not cause dental staining.[4]



Figure 10: Odontopaste. **Zohaibkhurshid, Muhammad SohailZafar and ShariqNajeeb (2021).**

Nanosilver:

Nanosilver use in endodontic begin with the use of gutta-percha points coated with nanosilver for enhanced antibacterial sealing. Nanosilver in high concentration is effective against several microbes including *E.faecalis*, *S.aureus*, *C.albican* and *E.coli*. Nanosilver gel was proven to be more effective than chlorhexidine, CMCP and calcium hydroxide.^{[4][12]}

The antibacterial effect of nanosilver is exerted by interfering with the bacterial cell membrane sulfur and phosphorus contained in the DNA.^[12]

Nanosilver was also used in combination with other intracanal medicaments such as calcium hydroxide and mesoporous calcium silicate nanoparticles.^[19]

Different studies have shown different results, in one study the combination of nanosilver and MCSNP was more effective against *E.faecalis* and less toxic. Another study has shown that it has reduced effectiveness as result of failure in the synthesis and release of silver nanoparticles. among the new nanosilver particles includes aveucal which mixed with calcium hydroxide and cavisept gel.^{[4][28]}

Other synthetic medicaments includes: MTAD, Octenidine, Mesoporous calcium silicate nanoparticles, Alendronate, and probiotics.^{[1][2]}

These synthetic materials have both antibacterial and anti-inflammatory activity. In addition to that they can be used in combination with other types of medications.^[4]

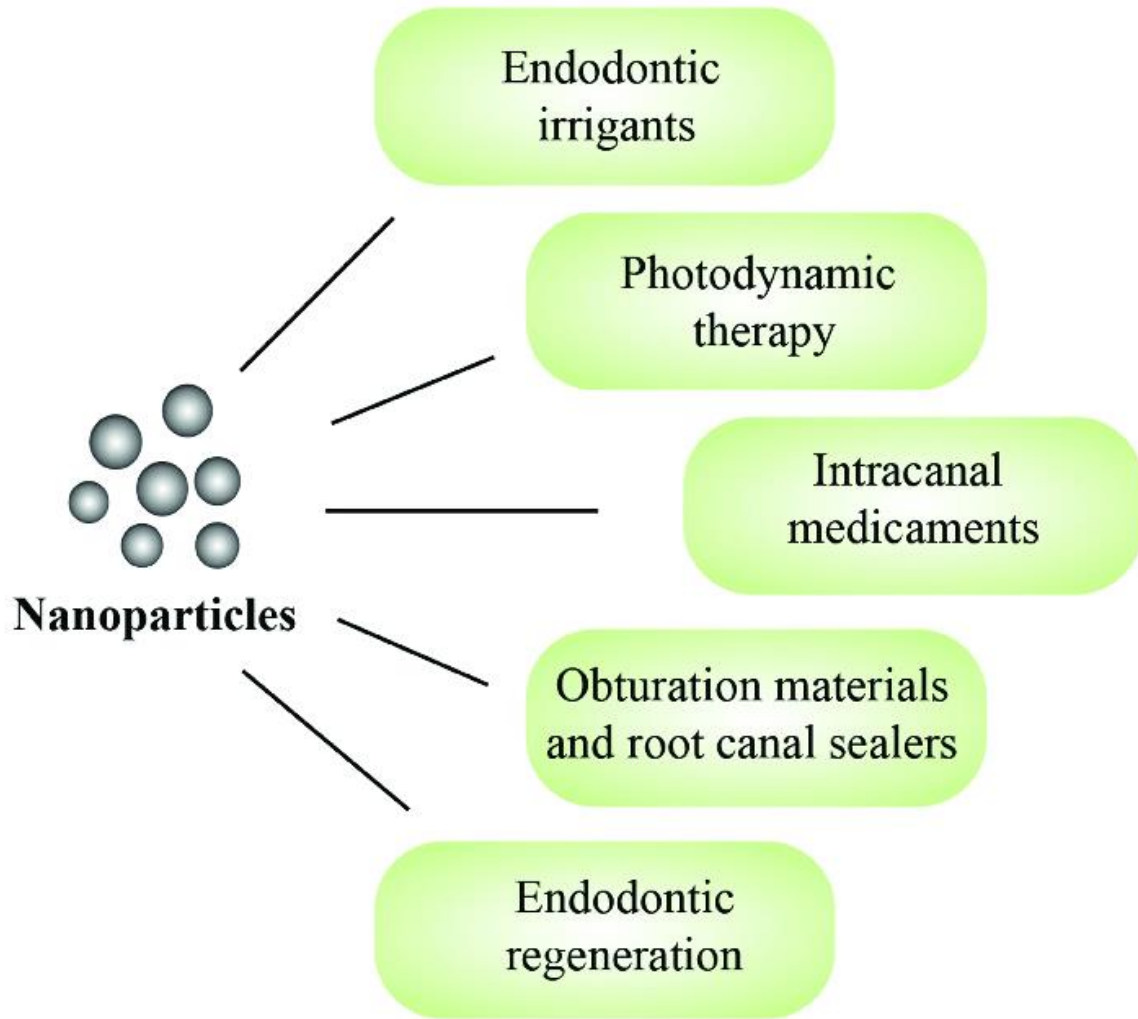


Figure 11: The applications of nanoparticles in endodontics. **Jazmine Wong, Ting Zou, Angeline Hui Cheng lee, Chengfei Zhang 2021.**

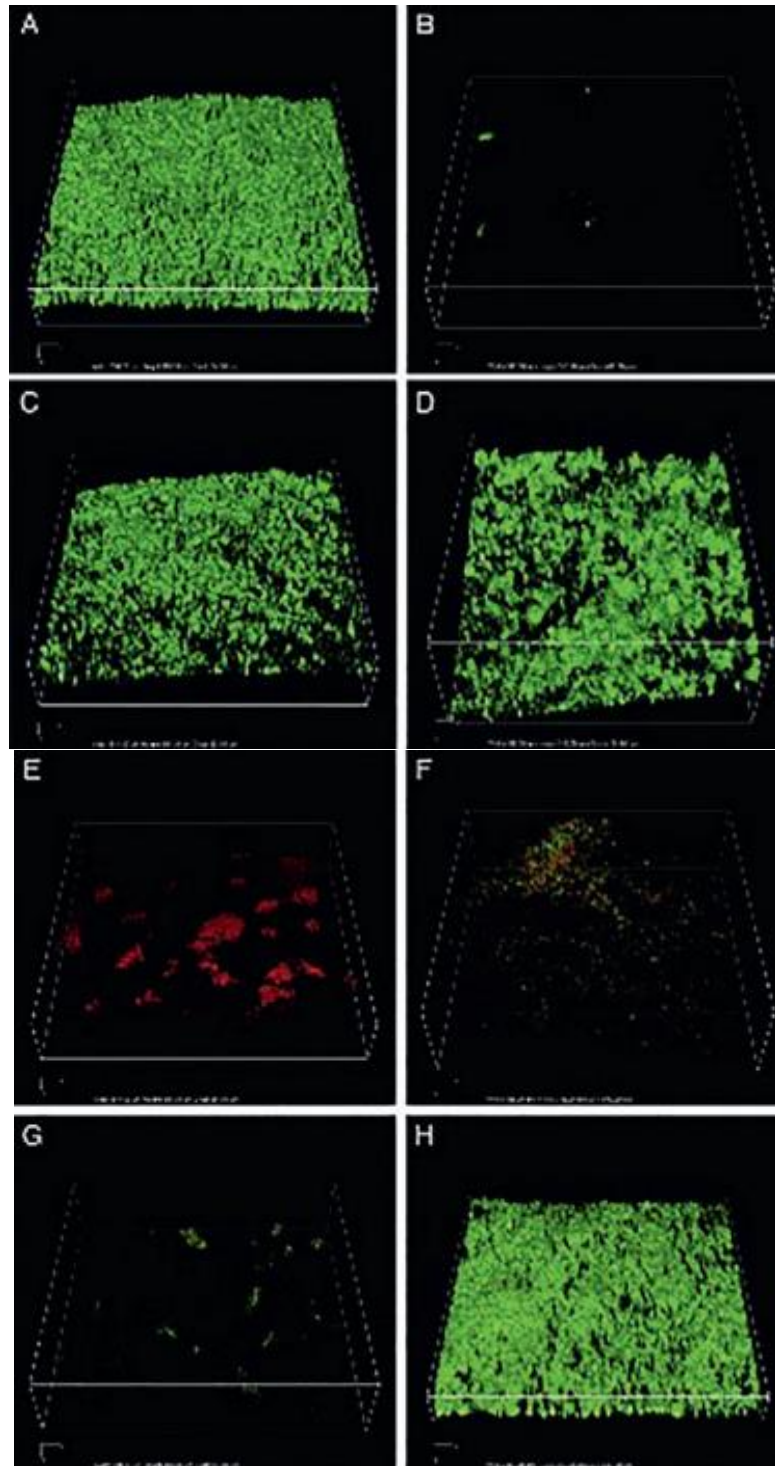


Figure 12: 3D reconstruction of *E-faecalis* biofilms after irrigation with medicaments. (A) control group. (B) 2% sodium hypochlorite irrigated group. (C) 0.1% silver nanoparticles solution irrigated group. (D) saline irrigated group. (E) biofilm treated with 0.02% silver nanoparticles gel for seven days. (F) Biofilm treated with 0.01% silver nanoparticles gel for 7 days. (G) Biofilm treated with CA(OH) for 7 days. (H) Biofilm treated with saline for 7 days. (Green: live cells, Red: dead cells. **Zohaibkhurshid, Muhammad SohailZafar and ShariqNajeeb (2021).**

Herbal/organic medicaments:

Bee glue (propolis):

Propolis is a resin-like natural product obtained from poplar and coniferous trees or clusiafowers by the honey bees. It is composed of more than 300 constituents related to flavonoids, phenolic acids and esters. These components are responsible for the immune stimulatory, antioxidant, anti-inflammatory and antimicrobial properties.^[4]



Figure 13: (A) premeasured propolis powder, 200 mg (0.2g). (B) propolis paste (propolis powder mixed with saline). . **Zohaibkhurshid, Muhammad SohailZafar and ShariqNajeeb (2021).**

The pH of the environment in which propolis is applied has little effect on its activity. Some authors found that this activity was better in slightly acidic environment. Propolis reduces the acid production of *S.mutans*. it also inhibits *C.albicans*, *Prevotella inetermedia* and *P.nigrescenes*.^{[15][16]}

It is more effective against *E.faecalis* than triple antibiotic paste and calcium hydroxide but less effective than chlorhexidine.^[18]

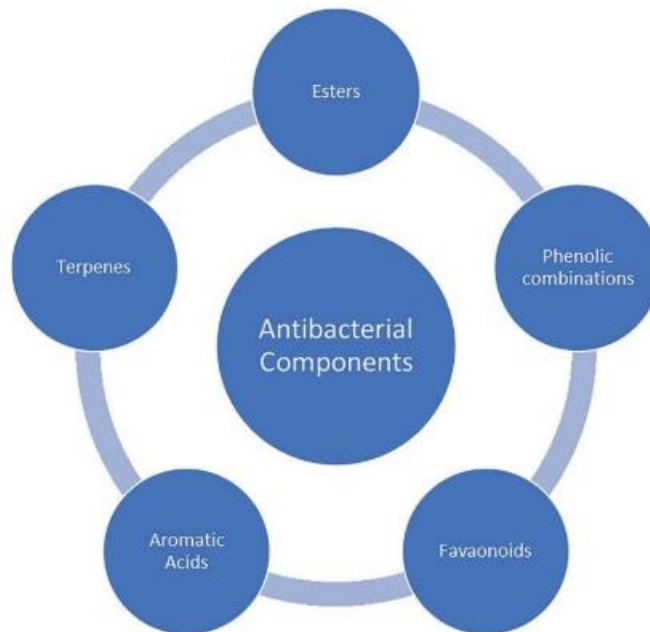


Figure 14: Suggested antibacterial constituents of the propolis. . **Zohaibkhurshid, Muhammad SohailZafar and ShariqNajeeb (2021).**

Since it is natural compound it is less cytotoxic and more biocompatible than other medicaments. It is also effective in preventing post-operative pain between visits.^{[4][18]}

Flavonoids and caffeic acid phenethyl ester are responsible for the anti-inflammatory and antibacterial effects. It was also shown that this agent has anti-resorptive activity as well. No significant side effects have been found with the use of propolis as intracanal medicament.^{[4][15][16][27]}



Figure 15: Suggested anti-inflammatory components of propolis. . **Zohaibkhurshid, Muhammad SohailZafar and ShariqNajeeb (2021).**

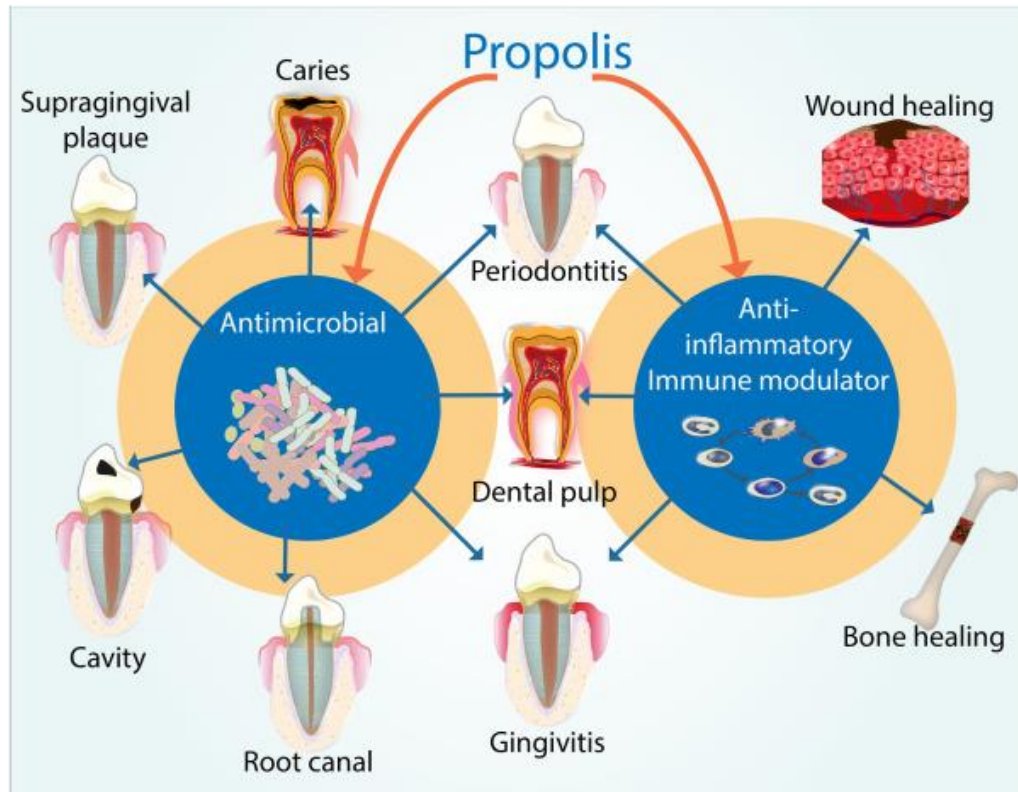


Figure 16: Antimicrobial and anti-inflammatory effects of propolis and its different uses in dentistry. **Felix Zuhendri Rafael Felitti, James Fearnley, Munir Ravalialia 2021.**

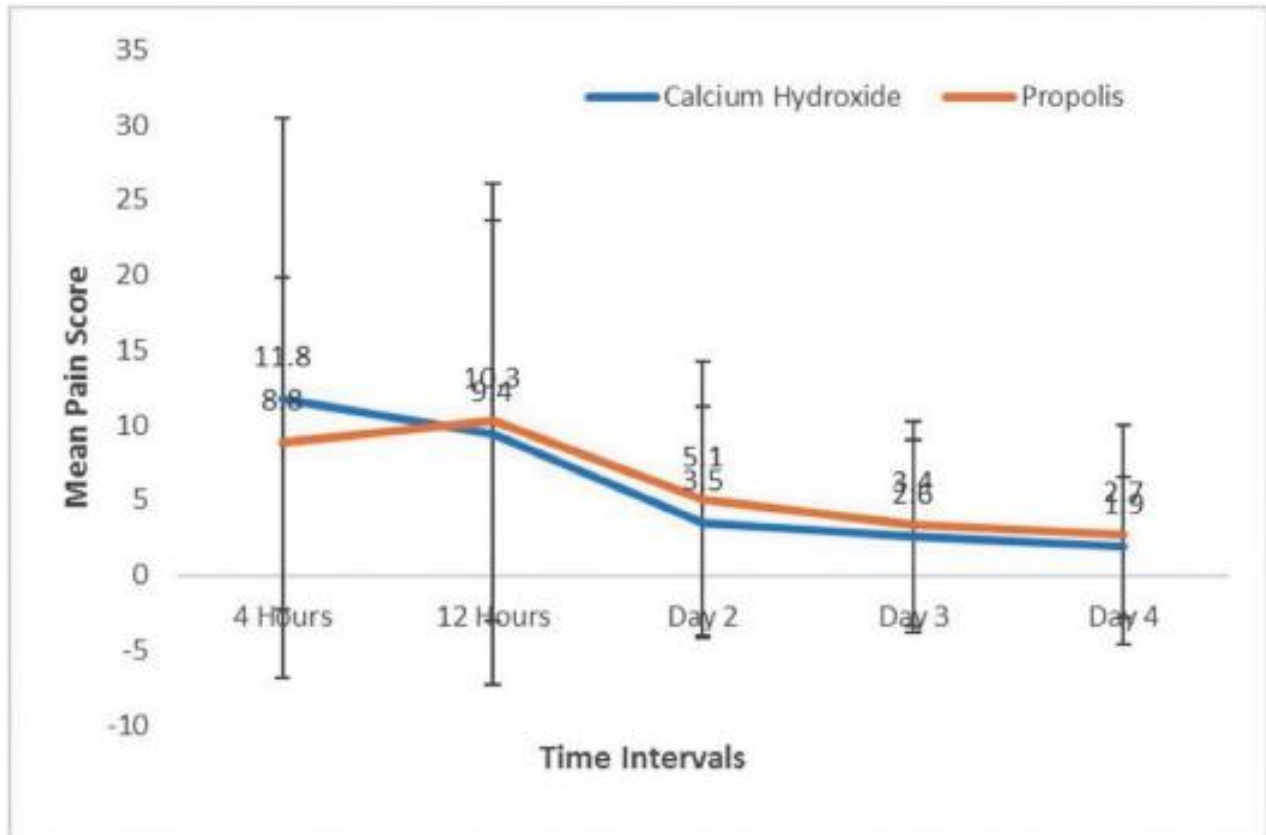


Figure 17: Graph showing pain scores according to time when either propolis or calcium hydroxide were used as intracanal medicaments. . **Zohaibkhurshid, Muhammad SohailZafar and ShariqNajeeb (2021).**

Aloe vera (Aloe barbadensis miller):

Aloe vera also known as babosa is a plant that is used widely in medicine. It is available as powder and gel. The gel is famous around the world for its antibacterial, anti-inflammatory and healing action.^[1]

It is highly effective against several species of bacteria but its effectiveness against *E.faecalis* is still controversial. It also diffuses easily through the dentinal tubules.^{[4][26]}

It has the ability to stimulate and intimate fibroblast proliferation and stimulation of keratinocyte growth factor 1, vascular endothelial growth factor and type 1 collagen expression.^[26]

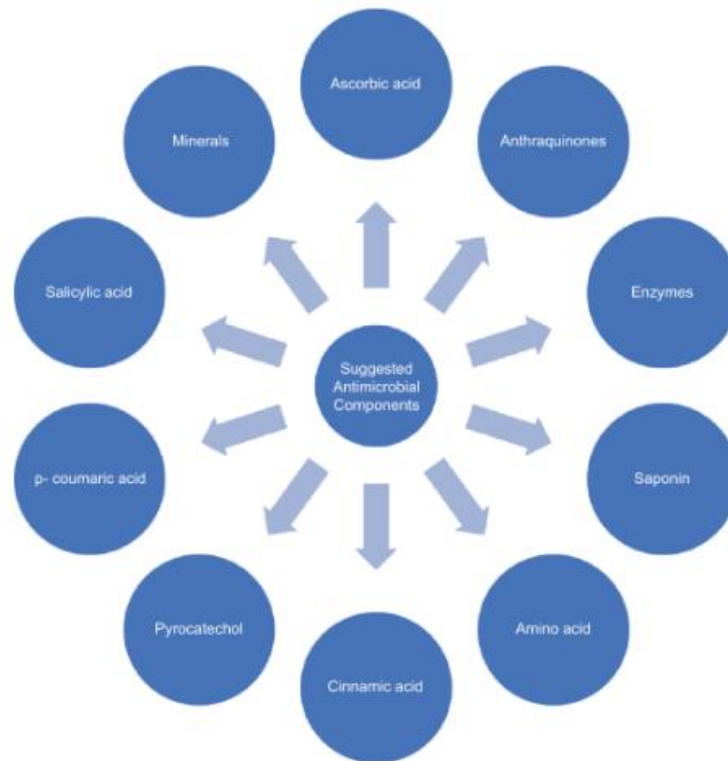


Figure 18: antibacterial constituents of Aloe vera.
Zohaibkhurshid, Muhammad SohailZafar and ShariqNajeeb (2021).

Chitosan:

Chitosan is a naturally occurring biopolymer. In the last few years chitosan has gained popularity in dentistry due to its biocompatibility, bioadhesion and biodegradability. It is non-toxic and extracted by alkaline deacetylation of chitin.^[30]

Nowadays, chitosan has wide range of uses in dentistry. This is mainly due to its properties which include biocompatibility, biodegradability and antibacterial effect.^{[14][17]}

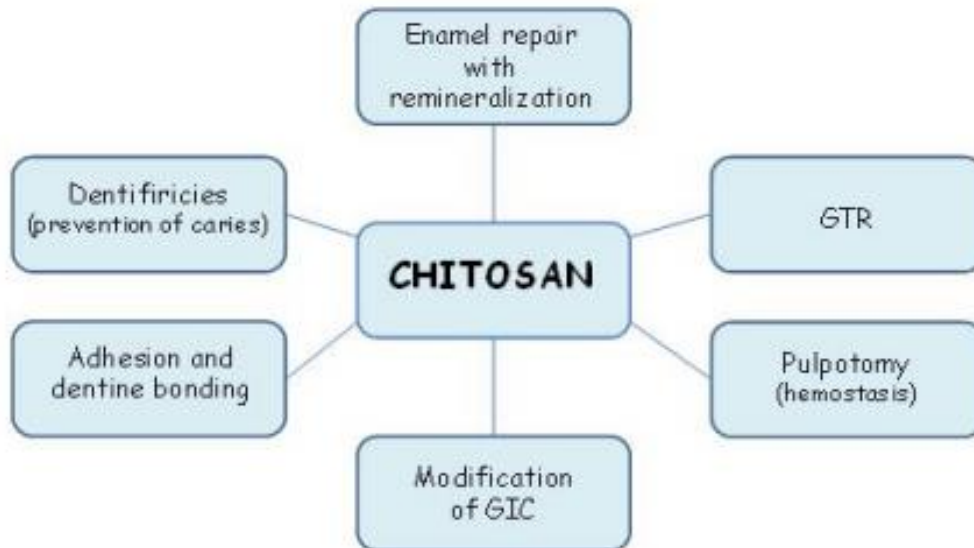


Figure 19: uses of Chitosan in dentistry. **Int. Biol. Biomed. J. Winter 2019; Vol 5, No 1**

Chitosan has wide range of antibacterial and antifungal effect. This effect is attributed to its cationic nature which reacts with negatively charged particles on the surface of bacteria and fungi resulting in the destruction of the bacterial cell and the leakage of their components. It also provides a barrier that prevents bacterial adherence to dentine surface.^{[4][14][17][30]}

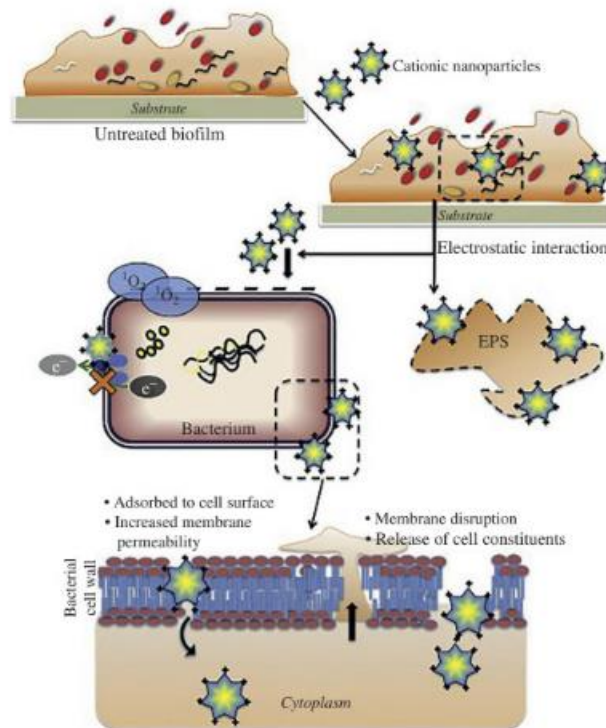


Figure 20: schematic diagram of showing mechanism of antibacterial action of Chitosan. Biofilm contains extracellular polymeric substance (EPS) and enclosed bacteria. The positively charged nanoparticles interact with both of them. The bactericidal effects are then exerted by lipid peroxidation by the formation of reactive oxygen species upon the contact. This result in the entrance of the nanoparticles inside the bacterial cells and damage to the cell membrane with the subsequent leakage of the cell constituents out of the cell. The EPS play a negative role in this mechanism. They interact with the nanoparticles and prevent them from coming into contact with the bacterial cells. **Zohaibkhurshid, Muhammad SohailZafar and ShariqNajeeb (2021).**

Curcumin (*Curcuma longa*):

In the last two decades, curcumin gained a lot of fame in medicine. It is used for the treatment of different diseases such as arthritis and osteoporosis in females which have great impact on movement and cause severe pain. In dentistry, the use of curcumin may be controversial but many researches were made to study the effects of curcumin on endodontic bacteria and how it affects the outcome of root canal treatment. Curcumin is the active ingredient of turmeric which is a popular food spice. Curcumin possesses antibacterial, anti-inflammatory and antioxidant activities. In addition to that curcumin is not toxic to vital cells such as stem cells and odontoblasts.^{[1][4]}

The antibacterial activity of curcumin is by inhibiting the proliferation of bacteria by deactivating the assembly dynamics of a specific gene required for the division of bacterial cells. It has a wide range of activity against gram-positive and gram-negative bacteria and it is effective against *E.faecalis*. Curcumin was modified and new light-activated curcumin was introduced. Studies have proven that curcumin has superior antibacterial properties to that of triple antibiotic paste. Light activation of curcumin results in the generation of hydrogen peroxide which has antibacterial effect that reaches a long distance. It also has no effect on the micro hardness of dentine.^{[4][27]}

The drawbacks of curcumin are that it works in a very specific pH which is estimated to be 6.5. It is highly unstable at neutral to basic pH. This means that even slight increase in pH will have adverse effects on the antibacterial effects of curcumin. However, curcumin use in endodontics is still in

research and in the future its use may be justified and it may replace the old triple antibiotic paste which has many adverse effects.^{[4][29]}

Other famous herbal products that are being studied as intracanal medicaments include Copaiba oil, Ginger, Eucalyptus Galbice, Gum (Acacia Nilotica), Garlic and Chlorophyll.^{[1][4][6]}

These natural herbal products have a wide range of antibacterial and anti-inflammatory effects that made them the targets of many researches to use them as intracanal medicaments.^[7]

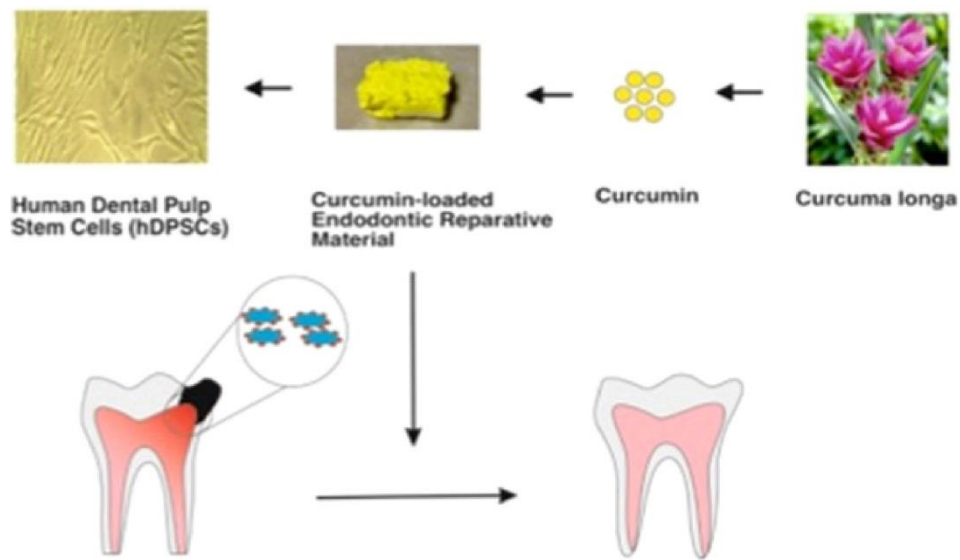


Figure 21: The use of Curcumin as endodontic reparative material. **Mahdieh Alipour, Sadaf Fadakar, Marziyeh Aghazadeh 2021.**

Techniques for the placement of intracanal medicaments:

1. Lentulospiral technique:

In this technique, a contra-angle handpiece is used to rotate the spiral in a clockwise motion at 1000 rpm. The medicament in paste form is applied to the lentulospiral. The paste should be thick enough to carry as many particles as possible but it should not be over dried to encourage continued dissociation in a moisturized state. The spiral is inserted in a vertical manner toward the apical region but it should be 2-3 mm shorter of the estimated working length. Up and down movements are followed by withdrawal of the spiral. The spiral should be rotating during the entire procedure.^[4]

This technique is easy and effective but it has many drawbacks. The difficulty in fitting the rubber stopper to the spiral is one of the disadvantages which leads to alteration in the working length and overextension of medicament out of the apical foramen which can lead to many destructive effects if the medicament is toxic such as CMCP. Another disadvantage is the fracture of the spiral inside the canal, therefore, this technique is effective when the canals are adequately shaped and cleaned.^[4]

Another instrument was designed called pastinject. It was found that this instrument is superior to lentulospiral.^[4]



Figure 22: lentulo-spiral on the left and astinject on the right. **Zohaibkhurshid, Muhammad SohailZafar and ShariqNajeeb (2021).**

2. Syringe technique:

This is considered as the conventional technique. This technique is considered better or equal to lentulospiral technique when performed correctly.^[4]

In this method the tip of the syringe is inserted inside the canal and the paste is then injected while the moving the syringe from the apical to the coronal region. One of the advantages of this technique over the lentulospiral technique is that it produces less porosity in the structure of the medicament.^[4]

One of the drawbacks of this technique includes the tendency overextension of the paste out of the canal as result of lack of control.^{[4][6]}

Several syringe systems were designed for this technique which includes calcicur syringe, ultracal tip and calasept system.^{[4][6][7]}



Figure 23: Ultracal syringe for the insertion of CA(OH) medicament inside the canal. The stopper at the tip is adjusted according to the working length of the canal. **Zohaibkhurshid, Muhammad SohailZafar and ShariqNajeeb (2021)**

3. Sonic activation technique:

This was first introduced by Clifford J. Ruddle in 2009. He suggested the use of endoActivator in inserting the intracanal medicament homogenously. It can be used with other techniques.^[4]

In this technique the intracanal medicament is inserted inside the canal with the help of hand file, then the endoActivator tip is placed 2 mm shorter of the working length and activated at 6000 rpm for 20 s. this sequence is repeated three times. This technique is inferior when compared to other techniques.^{[4][6][31]}

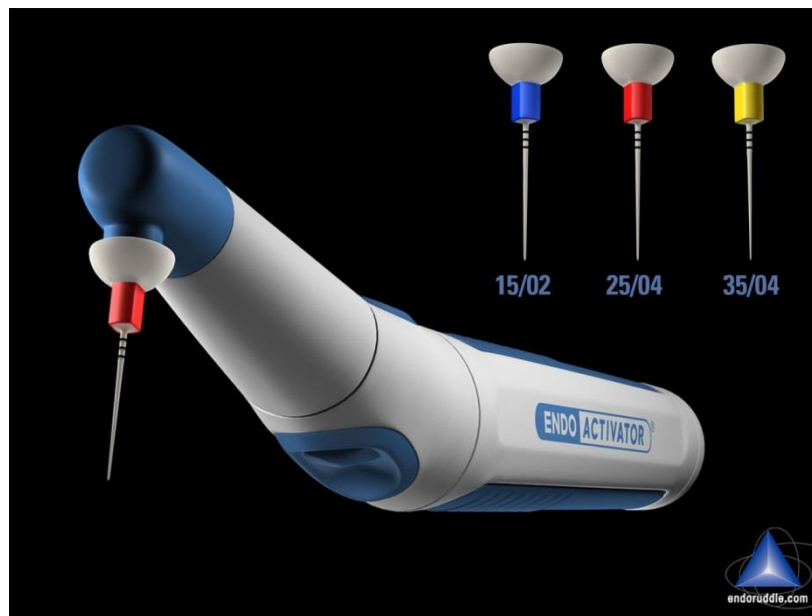


Figure 24: Endoactivator sonic irrigation system. **Bryce G, MacBeth N, Gulabivala K, Ng YL. 2018**

4. Specially designed carrier technique:

In this technique two needles are used, thin and thick needles. The medicament is inserted inside the canal via the thicker needle. Then the thin needle is inserted into the thicker needle to act as a condenser that condenses the medicament to the apex. This method is cost effective without tendency for overextension of the medicament. And is proven to be superior to the syringe and lentulospiral technique.^{[4][6][23]}



Figure 25: specially designed paste carrier technique. (A) sectioning of the needle with a diamond disc. (B) Lumen of the thinner needle sealed with cyanoacrylate. (c) checking for smooth fit and movement of the thinner needle through the thick needle. (D) Tapping the thick needle on the mixed CA(OH) paste. (E) the excess of CA(OH) paste extruding from the opening of the needle hub. (F) compaction of the paste into the canal with the stoppers on the needle. **Joseph Meng Ern Tan 2018.**

5. Amalgam carrier and endodontic plugger technique:

In this method amalgam carrier is used to put the medicament at the coronal portion of the canal. Then a plugger is used to condense the paste into the canal. This method is suitable to use when a dry mix is desired. Incremental deposition of the paste with amalgam carrier and pluggers of different sizes are used until the whole canal is filled.^{[2][4]}

6. McSpadden compactor technique:

In this technique the paste is placed inside the pulp chamber. A bur is then inserted about 3 mm short of the working length without rotation. It is then activated at constant speed with in and out movement for 3 seconds. Once the cervical part was filled a plugger is used to condense the medicament apically.^{[1][2][4]}

7. Manual hand file method:

In this method the medicament is placed with a hand file inside the canal till reaching the apex and removed by rotating the file counterclockwise so that the file is able to apply the medicament on the canal walls. This method is easy and operative friendly. Reamer can be used in curved and unprepared canals.^{[2][4]}

8. Combination of these methods.^[4]

Problems encountered during the use of intracanal medicament:^{[1][12]}

1. Extrusion of the medicament through the apical foramen. the effects of the extruded medicament ranges from mild to severe.
2. The use of inappropriate medicament for the individual case. Which might worsen the condition.
3. Poor placement technique.
4. Incomplete removal of the medicament.



Figure 26: Medicament extruded out of the canal as result of aggressive and poor placement technique. The effects of this extruded material may range from little or no effect to bone necrosis and root resorption. The medicament in the figure is CA(OH).
Zohaibkhurshid, Muhammad SohailZafar and ShariqNajeeb (2021).

Removal of intracanal medicament:

Intracanal medicaments are used as inter-appointment agents that must be removed prior to obturation. However, complete removal of these agents is not quite easy. Remnant of these materials might have adverse effects on the obturation process. These may interfere with the adaptability of penetrability of the sealers into the dentinal tubules. They also react with zinc oxide eugenol and make it brittle and granular.^{[1][25][31]}

Several techniques were developed to remove the medicaments. The most widely used methods include:

1. The use of master apical file (MAF), sodium hypochlorite irrigation and final rinse with EDTA. Other effective methods include the use of NiTi rotary systems, sonic and ultrasonic irrigation and EndoVac system.^[4]
2. **Laser-assisted irrigation:** it is another technique that is proven to be as effective as the other methods in the removal of medicaments.^{[2][4]}

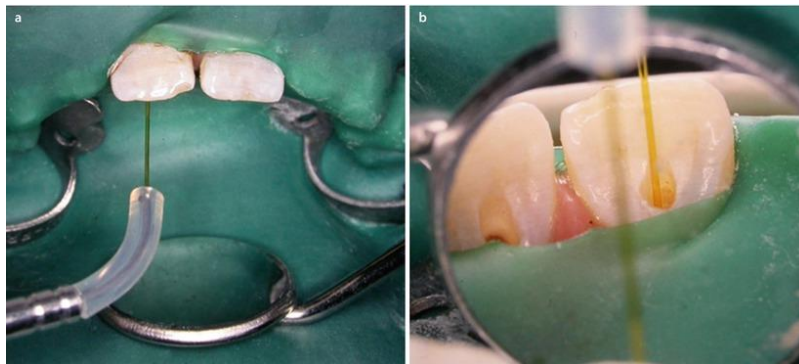


Figure 27: laser assisted irrigation system used to remove bacterial remnants, intracanal medicament and dentinal smear layer. **George R., Walsh L.J. (2017).**

3. Canal brush technique:

In this technique instrumentation and irrigation is done to remove the bulk of the medicament. This is followed by the use of specially designed endodontic brush. This brush is inserted inside the canal and rotated for 30 s at 600 rpm. This pushes the remnants into the apex therefore it is considered as a poor technique for the removal of medicaments.^{[4][31]}



Figure 28: Canal specially designed microbrushes used to remove the medicament. Gorduysus M, Yilmaz Z, Gorduysus O, Atila B, Karapinar SO. (2012)

4. Automated dynamic irrigation:

This method uses the RinsEndo system in which the irrigation solution is inserted automatically inside the canal and then with the suction of this system it is aspirated back from the canal. This method is effective in removal of the medicament from the apical third.^{[4][31]}

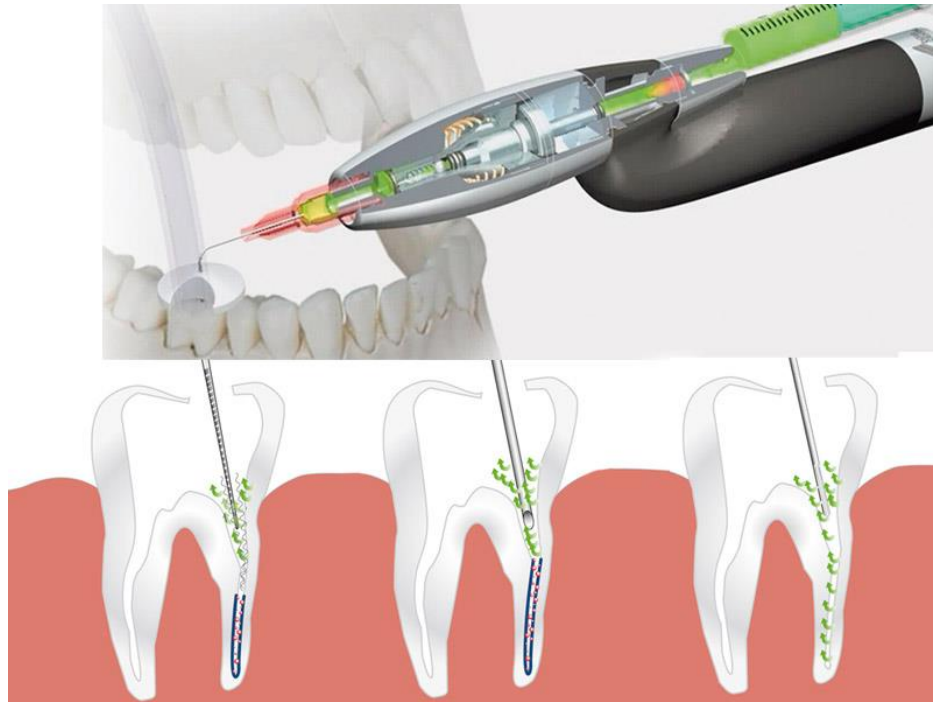


Figure 29: Rinsendo irrigation system for the removal of the intracanal medicament. (**Inside dentistry 2007**)

5. Some chemical agents which include the use of 17% EDTA and 7% maleic acid which have been shown to be very effective in the removal of calcium hydroxide. However, Maleic acid is more effective than EDTA (Palma et al., 2019). Phytic acid is another agent that is most effective for the removal of triple antibiotic paste from the root canal. Citric acid and Etidronate are also used to remove the intracanal medicaments with the effectiveness of Etidronate proven to be more superior to that of EDTA.^{[4][20]}

It should be emphasized that all of these techniques don't completely remove medicament from the root canal. Therefore, the removal of medicaments from the root canal is still a wide open topic for many scientific researches.^{[2][3]}

Chapter 2

Discussion

The main component for the success of endodontic treatment is the disinfection of the canal. The complex root canal systems may make this disinfection process difficult. This has led to the development of different materials to be used as intracanal medicaments and various techniques to place them.

However, these agents may also have adverse effects on the vital cells required for the process of healing. Because of that, several studies have focused on the proper concentration of medicaments to eliminate the pathogenic agents while maintaining the vitality of stem cells.

Nowadays, these agents are not used routinely by endodontists. The reason behind this lies in the difficulty in the removal of them and the effects they exert on the obturation process and the sealers. These factors render them unsuitable for routine use. However in complicated cases, their use is inevitable.

Post-operative pain between visits may be annoying to the patient and encourage the patient to discontinue the treatment. Studies have shown that the use of intracanal medicaments is effective in reducing this pain. Therefore, their use in multiple visits treatment may be necessary in cases where post-operative pain is predicted to occur.

Some of these agents have antiresorptive action. This makes them useful to prevent external root resorption in cases of trauma and teeth replantation.

These agents are frequently used in pulpotomy, apexification and apexogenesis of primary teeth.

In the last decades, the use of regenerative endodontic procedures has grown rapidly. More promising outcome has resulted with the use of intracanal medicaments.^[22]

The use of intracanal medicaments must be assessed carefully as their side effects may be severe and affect the treatment outcome. Therefore the dentist or endodontist must gain knowledge about the different types of materials available and their effects, side effects and their interactions with the dentine, sealers and various root canal materials.

Chapter 3
Conclusion

The use of intracanal medicament in routine endodontic practice is still controversial. Therefore, the decision to whether to use or not to use these agents is dependent on the difficulty of the case and the experience and skills of the endodontist in dealing with the different types of intracanal medicaments available. Different types of medicaments are available and different methods for their placement and removal have been developed to achieve the maximum efficiency from them. However, these materials vary considerably in their properties and interactions with the vital tissues and filling materials. Some of them are more effective compared to the others. In addition to the old medicaments, new synthetic and herbal medicaments are being developed and modified and are getting more popular as alternatives to the old toxic non-biocompatible materials. However, much is yet to be known about most of these medicaments before their use as intracanal medicaments.

A study of different intracanal medicaments has concluded the followings:^[2]

- Calcium hydroxide may be safe but may not be the most suitable medicament in all cases.
- Antibiotics may not be ideal as an active component for intracanal medicament. It also has many adverse effects such as teeth discoloration.
- The use of ledermix is debated.
- The conclusion from the in-vitro and in-vivo experiments of the antibacterial effects of the various medicaments is clear but it is poorer in the root canals than in the neutral conditions.
- No current medicament is able to achieve a bacterial-free pulp system.

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