

Next-Generation Intracanal Medicaments: Deciphering Their Impact

Richa Wadhawan, VyomitaKushwah, Sayma Rizvi, Noor Zuber Mandal,
Anand Kumar, Rishav Saha

Professor, Department Of Oral Medicine, Diagnosis & Radiology, PDM Dental College & Research Institute,
Bahadurgarh, Haryana, India

General Dentist, Community Health Programs Inc, Massachusetts, United States Of America

Dental Surgeon, District Hospital, Betul, Madhya Pradesh

Dental Surgeon, Dr Zuber's Dental Care, Hojai, Assam

Dental Surgeon, Anandam Dental Clinic, Bhopal, Madhya Pradesh

Dental Surgeon, Saha Oral And Dental Care, Barpeta, Assam

Abstract:

Next-generation intracanal medicaments are set to revolutionize endodontic therapy, effectively overcoming the limitations of traditional treatments. Central to their transformative impact is their unparalleled ability to thoroughly disinfect the root canal and drastically reduce microbial load—key factors for successful treatment outcomes. Calcium hydroxide has long been regarded as the gold standard in endodontic treatment. However, recent innovations have introduced powerful alternatives that significantly improve both antimicrobial effectiveness and biocompatibility. These advanced agents not only target resistant bacterial strains with precision but also promote the healing and regeneration of periapical tissues, paving the way for significantly improved patient outcomes. This review offers a comprehensive examination of the various intracanal medicaments currently available, assessing their effectiveness through robust clinical studies and cutting-edge laboratory research. Ongoing investigations aimed at optimizing these treatments highlight their transformative potential, especially in managing non-vital teeth, periapical diseases, abscesses, and dental trauma. By enhancing disinfection processes and minimizing complications, these innovative medicaments elevate the overall patient experience and outcomes. Ultimately, the evolution of these intracanal agents represents a monumental leap forward in the pursuit of optimal endodontic care, emphasizing the critical need for continuous innovation in dental therapies. Embracing these advancements brings us closer to a future where endodontic treatment is not only more effective but also more compassionate, transforming the lives of patients and enhancing their journeys toward oral health.

Keywords: Intracanal medicaments, Endodontic treatment, Antimicrobial properties, Non-vital teeth, Disinfection, Calcium hydroxide, Triple antibiotic paste

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I. Introduction:

Pain is defined by the International Association for the Study of Pain (IASP) as an unpleasant sensory emotional experience associated with actual potential tissue damage or described in terms of such damage. It can greatly disrupt daily life, often leading patients to seek dental treatment for relief.¹ Discomfort between dental appointments is common and can sometimes be unexpected, influenced by various factors related to the patient and the dentist.² After endodontic treatment, the level of pain can vary significantly, with reports ranging from 1.7% to 70%.³ About half of the patients report discomfort after treatment for infected teeth.⁴ Factors that contribute to this post-treatment pain include the presence of bacteria, changes in pressure around the tooth, and chemical reactions.⁵ Poor disinfection can allow harmful bacteria to survive, highlighting the importance of using intracanal medicaments—substances placed inside the tooth canal to eliminate inflammation and target germs effectively.⁶ Common intracanal medicaments include calcium hydroxide, Ledermix paste, triple antibiotic paste, chlorhexidine gel, and various antibiotics (**Figure 1**).⁷

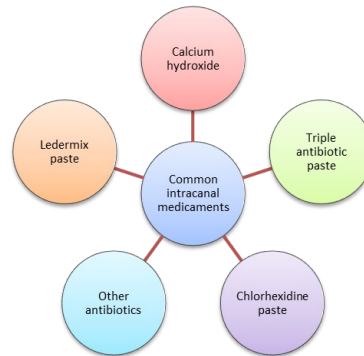


Figure 1: Key intracanal agents: powering successful root canal therapy

These medicaments play a crucial role because bacteria are major contributors to tooth and surrounding tissue diseases.⁸ Ongoing infections can lead to tissue death and inflammation at the root tip, putting the root canal treatment at risk.⁹ The main goal of root canal therapy is to remove bacteria and leftover materials after cleaning the canal.¹⁰ Successful endodontic treatment depends on three key steps: preparing the canal, thoroughly cleaning it, and properly sealing it afterward (**Figure 2**).¹¹

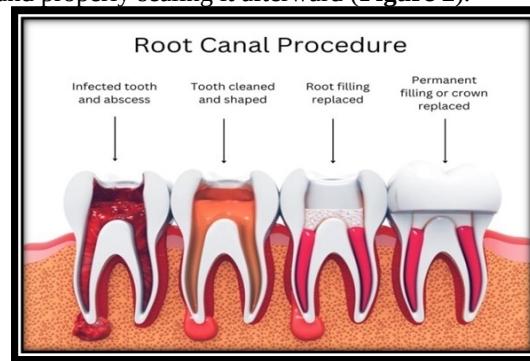


Figure 2: Mastering Root Canal Therapy: The Triad Of Success

Courtesy: <https://www.broadwayfamilydentalpc.com/general-cosmetic-dentist/root-canal-procedure-specialist-dentist/>

To prevent new infections and ensure effective antibacterial action, intracanal medicaments are essential in modern endodontics.¹² After sealing the canal, any remaining bacteria can rapidly proliferate due to nutrient depletion.¹³ Simple cleaning often fails to eradicate bacteria hidden in the tiny tubules within the tooth structure. If antiseptic medicaments aren't correctly applied between visits, surviving bacteria can multiply, undermining treatment success.¹⁴ This underscores the urgent need for effective medicaments that can penetrate these small tubules, eliminate bacteria, and reduce irritation—especially in multi-visit treatments.¹⁵ Recent advancements have led to innovative agents designed to enhance effectiveness, extend their action, and ensure patient safety, ultimately improving success rates in root canal treatments.¹⁶ Severe discomfort and swelling post-treatment, or the presence of a draining canal, may indicate an active infection at the root tip.¹⁷ In these critical circumstances, intracanal medicaments are vital for managing infections, fostering healing, and alleviating pain when applied directly to the infection site.¹⁸ By addressing discomfort and controlling infections, these medicaments promise greater patient comfort and improved clinical outcomes, fundamentally reshaping the landscape of dental care.¹⁹ The primary goal of endodontic treatment is the thorough elimination of bacteria, their byproducts, and pulpal remnants from infected root canals, followed by complete sealing.²⁰ While historically crucial in bacterial eradication, modern endodontics increasingly emphasizes shaping and cleaning as the foundation of disinfection.²¹ Biocompatibility and stability are essential characteristics for these agents, with intracanal dressing primarily serving to prevent coronal leakage.²² The trend toward single-visit endodontics is gaining traction, with studies indicating comparable clinical outcomes between single- and multiple-visit treatments. Although there's no compelling reason to oppose single-visit procedures, the application of an intracanal medicament is strongly advocated when multiple visits are necessary.²³ Success in endodontic treatment has traditionally relied on debridement, thorough disinfection, and obturation, all equally important (**Figure 3**).²⁴



Figure 3: Key Pillars: Debridement, Disinfection, Obtrurate Success
 Courtesy: <https://www.Omnidental.Com.Sg/Articles/What-Is-Root-Canal-Treatment/>

Today's effective root canal treatment encompasses broader principles, including diagnosis, treatment planning, and anatomical comprehension.²⁵ The evolution of protocols and enhanced chemomechanical preparation techniques has led to markedly improved outcomes, with access cavity preparation remaining essential.²⁶ The transition from "Extension for prevention" to "prevention of extension" highlights a focus on minimally invasive dentistry, aimed at conserving tooth structure.²⁷ Although intracanal medicaments remain crucial, particularly when treatment cannot be completed in one visit, their role has evolved.²⁸ They help inhibit bacterial regrowth and improve outcomes when strategically applied to reduce pathogen infiltration.²⁹ In situations involving pulpal necrosis and apical periodontitis, their importance is heightened, as numerous root canals may still contain viable microorganisms despite comprehensive preparation.³⁰ However, multiple appointments carry risks, such as temporary filling leaks and poor patient adherence.³¹ Despite the shift toward single-visit endodontics, research suggests comparable outcomes for both single- and multiple-visit procedures.³²

If multiple visits are required, the use of intracanal medicaments is highly recommended.³³ Once the "stars" of endodontic treatment, these agents have shifted to a secondary role but still maintain significant importance. As defined by Kawashima et al., intracanal medicaments are biocompatible substances temporarily placed in root canals to thwart bacterial intrusion.³⁴ The absence of an ideal medicament and variability in clinical practice regarding their application continue to be pertinent challenges in endodontic care.³⁵ This review article emphasizes the indications and properties of next-generation intracanal medicaments, highlighting their role in improving endodontic outcomes. It discusses their effectiveness in eradicating bacteria, promoting biocompatibility, and facilitating healing. Additionally, the review consolidates the challenges and advancements in their formulation and application. These innovations represent a transformative era in endodontics, enhancing the efficacy of root canal treatments and leading to better patient outcomes.³⁶

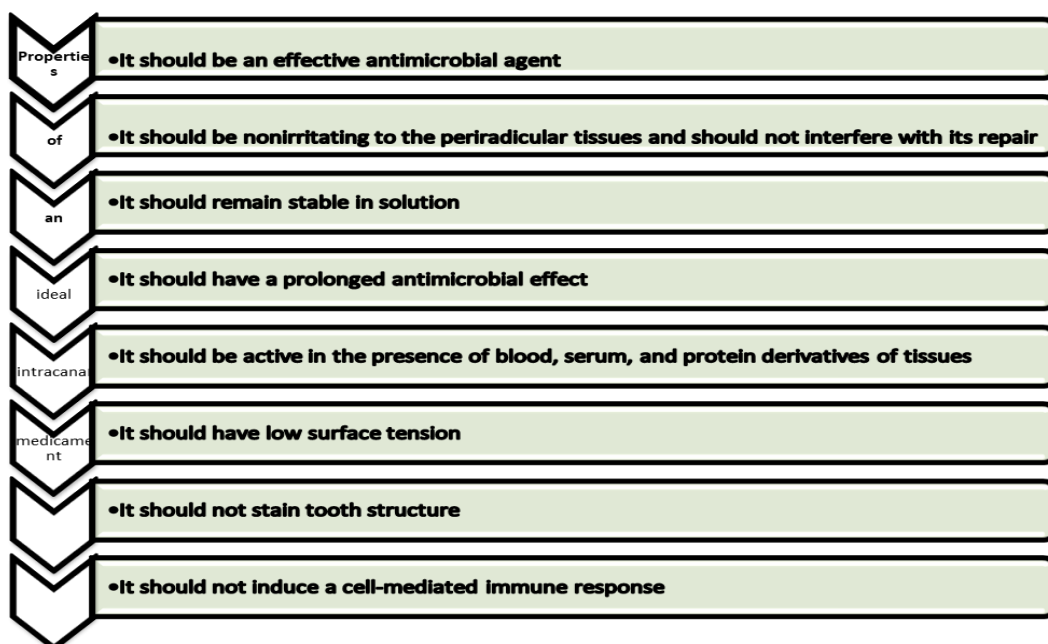


Figure 4: Properties of an ideal intracanal medicament

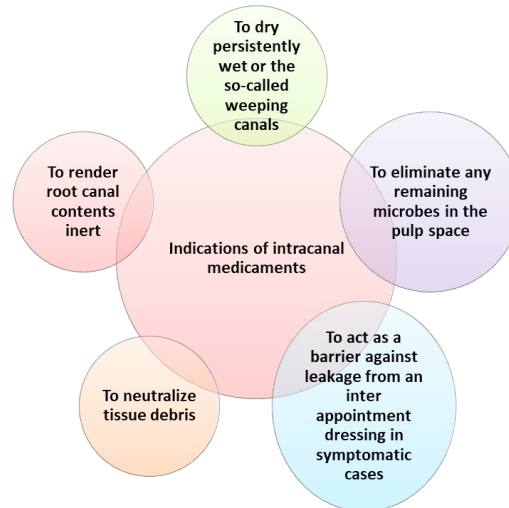


Figure 5: Indications of intracanal medicaments

II. Discussion:

Intracanal medicaments serve several important objectives in endodontic treatment. Firstly, they aim to destroy microorganisms by killing all viable pathogens in the canal space.³⁷ Secondly, these medicaments render the contents of the canal inert, effectively "mummifying" or deactivating any remaining tissue or debris, which helps eliminate residual bacteria.³⁸ Thirdly, they play a crucial role in preventing or controlling post-treatment pain by reducing inflammation through their antimicrobial action or by altering the inflammatory response, thereby alleviating pain associated with inflammation.³⁹ Additionally, they can enhance anesthesia, particularly in cases where the inflamed pulp is difficult to anesthetize, making subsequent procedures less painful.⁴⁰ Lastly, intracanal medicaments are vital for managing persistent periapical abscesses; they provide direct access to periapical lesions, helping to restore a healthy balance and alleviate significant pain and swelling that may occur after treatment (Figure 6).⁴¹

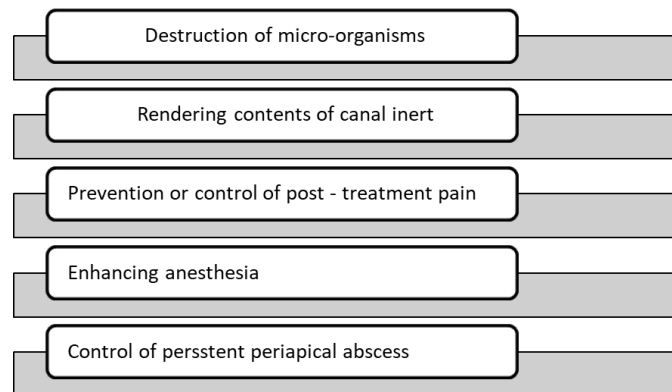


Figure 6: Objectives of intracanal medicaments

Classification:

According to Grossman intracanal medicament can be classified as ⁴²

1. Essential oils <ul style="list-style-type: none">• Eugenol
2. Phenolic compounds <ul style="list-style-type: none">• Phenol• Parachlorophenol• Camphorated parachlorophenol• Cresol• Formocresol• Creosote• Cresatin• Cresanol 3. N2
4. Salt of heavy metals <ul style="list-style-type: none">• Metaphen• Merthiolate• Mercuriofen
5. Halogens <ul style="list-style-type: none">• Sodium hypochlorite• Iodides• Chlorexidine
6. Quaternary ammonium compounds <ul style="list-style-type: none">• 9-aminoacidine
7. Fatty acids <ul style="list-style-type: none">• Propionic acid• Caproic acid• Cuprylic acid
8. Sulphonamides

Eugenol: It is the primary active ingredient in clove oil and shares some similarities with phenol. It serves as both an antiseptic and an anodyne, though it tends to be slightly more irritating than clove oil itself. Over time, eugenol can darken, appearing as a pale yellow liquid. It has mild anesthetic and antiseptic properties, along with a characteristic scent reminiscent of cloves (**Figure 7**).⁴³



Figure7: Eugenol

Courtesy: <https://Amplemeds.Com/Product/Vishal-Dentocare-Eugenol-Pure/>

Phenol: In 1867, Lord Lister transformed the landscape of medicine by introducing phenol as one of the first antiseptics, marking a groundbreaking shift in infection control. Derived from coal tar, phenol is a white crystalline substance known for its distinct odor and potent antiseptic properties.⁴⁴ When combined with camphor, menthol, or thymol, it forms carbolic acid—a powerful solution that has become a cornerstone in both medicine and dentistry. In the realm of dentistry, phenol's versatility is unmatched.⁴⁵ It acts as a sedative for pulp tissue, an effective treatment for root canals, and a disinfectant for cavity preparations. Its role extends to pre-surgical disinfection before periapical procedures and cauterizing stubborn tissue tags that defy conventional removal methods.⁴⁶ Moreover, phenol sets the standard for assessing the disinfectant efficacy of other antimicrobial agents, affirming its enduring relevance and unparalleled significance in modern dental practice. By revolutionizing infection control, phenol has cemented its legacy as a vital tool in the fight against infections, shaping the future of patient care and safety.⁴⁷

Parachlorophenol: It darkens when exposed to light and appears as colorless, needle-like crystals similar to phenol. Chlorine replaces one of the hydrogen atoms in phenol, leading to the formation of parachlorophenol (C_6H_4OHCl). The crystals of parachlorophenol are soluble in ether, alcohol, and alkalis. When ground with gum camphor, it converts into an oily liquid.⁴⁸

Camphorated Parachlorophenol: In 1891, Walkhoff introduced camphorated parachlorophenol (**Figure 8**), which combines para-chlorophenol and gum camphor in a 2:3 ratio for use as an intracanal antiseptic in dentistry.⁴⁹ This formulation is recognized for its distinct aromatic fragrance and appears as a transparent, light amber oily liquid. The camphor helps lessen the irritating effects of pure parachlorophenol, serving as both a diluent and a medium.⁵⁰ Grossman highlighted its antimicrobial properties compared to other root canal treatments.⁵¹ Wantulor and Brown demonstrated that the vapors of camphorated chlorophenol from cresatin can penetrate through the apical foramen.⁵²



Figure 8: Camphorated Parachlorophenol

Courtesy: <https://Thefuturedentistry.Com/Most-Important-Intra-Canal-Medicaments-Frequently-Asked/>

Camphorated Monoparachlorophenol (CMCP): It is prepared using mining crystals, which consist of a compound made from paramonochlorophenol and camphor in a 3:7 ratio when liquefaction occurs suddenly (Figure 9). This compound is less irritating, a more effective bactericidal agent than phenol, and does not coagulate albumin.⁵³



Figure 9: CMCP

Courtesy: https://www.Facebook.Com/Xenonbiomed/Posts/Camphor-X-Cmcp-Camphor-Phenol-For-Intracanal-Medication-It-Has-The-Following-Ben/1233896289960883/?_Rdr

Cresol (Tricresol): It is acquired from coal tar with or without containing a trace of phenol having properties like Ortho, Meta (Figure 10) and Para-isomeric cresol. It is found in phenolic odor and is colourless or pinkish liquid in nature. Cresol (C₆H₄OHCH₃) can substitute phenol considering its 3-times more powerful disinfectant capacity.⁵⁴



Figure 10: Metacresol

Courtesy: <https://www.Jaypeedigital.Com/Book/9789352500482/Chapter/Ch12>

Creosote: It filled the air of most dental orifices having sharp pungent aromatic odor in the form of clear yellowish oily liquid. Only the beechwood variety of creosote should be used in dentistry due to its better disinfectant, less irritant, and less toxic effect than phenol (**Figure 11**).⁵⁵

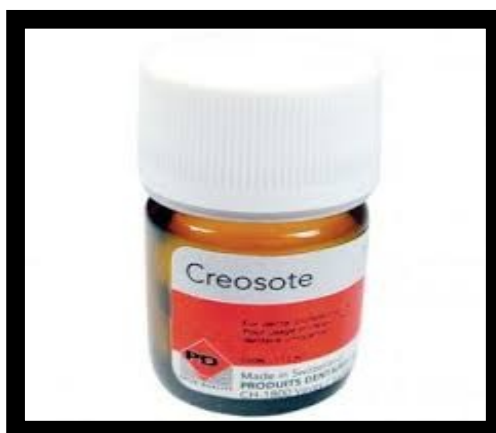


Figure 11: Creosote

Courtesy: <https://Dental.Bintang Saudara.Com/Product-Category/Endodontics/Endodontic-Medicament/Root-Canal-Treatment-Disinfection-Material/>

Cresatin: Metacresyl acetate, also referred to as cresatin (**Figure 12**), is a clear, stable, low-volatility oily liquid with a phenolic acetic scent. It acts as both an antiseptic and analgesic, exhibiting improved antibacterial effects due to its low surface tension and low vapor pressure, which prolongs its efficacy.⁵⁶ Research by Grossman suggests that cresatin's antimicrobial properties are less significant compared to other agents in its category. It is non-caustic, less irritating, and does not precipitate albumin.⁵⁷



Figure 12: Cresatin

Courtesy: <https://www.Humayundental.Com/Product/Tehno-Dent-Cresatin-Liquid-No-1-15ml/>

Cresanol: It is a compound of cresatin, P-chlorophenol and camphor in 1:1:2 ration. It is found more effective than cresatin as an antiseptic and less irritating than chlorophenol.⁵⁸

N2: It is used as intracanal medicament and as a sealer containing paraformaldehyde and phenyl mercuric borate as demonstrated by Sargenti and Richter.⁵⁹ The properties present in N2 have permanent disinfectant action and unusual antiseptic agent that are irritating and toxic with high degree of antimicrobial activity. It has been observed that the antibacterial effect of N2 is of short duration and degenerate in about 7 to 10 days.⁶⁰

Aldehydes

Formocresol: Introduced by Buckley in 1905, this compound typically contains a mixture of formaldehyde, cresol (in a 1:1 to 1:2 ratio), and glycerin, forming a transparent reddish liquid with a distinctive odor. The formulation often includes around 19% formaldehyde, 35% cresol, and 46% glycerin with water (**Figure 13**).⁶¹



Figure 13: Formecresol

Courtesy: <https://Dentestore.Com/Itemview/3550-0101008001/Maquira>

Heavy Metal Salts: Salts of heavy metals are protoplasmic poisons that can precipitate albumin, leading to staining of tooth structures. Historical use of ammoniated silver nitrate (**Figure 14**) for disinfecting root canals has diminished due to its staining effects.⁶²

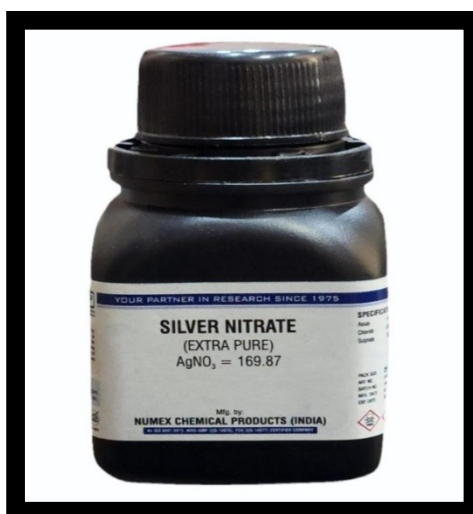


Figure 14: Silver Nitrate

Courtesy: <https://Www.Indiamart.Com/Proddetail/Silver-Nitrate-16534314073.Html?Mtd=1>

Organic Mercurial Salts: Compounds like Metaphen, Merthiolate, and Mercuraphen are strong disinfectants but are limited in endodontic use due to their potential to stain.⁶³

Halogens: Halogens, particularly chlorine, are renowned for their exceptional disinfectant properties. Among them, chlorine stands out as the most effective; making sodium hypochlorite (**Figure 15**) and chloramines vital in dental practices.⁶⁴ Sodium hypochlorite is the go-to irrigating solution in modern dentistry, utilized in concentrations ranging from 0.5% to 5.25%.⁶⁵ Its unmatched ability to dissolve necrotic tissue and debris during the biomechanical cleansing of root canals positions it as an indispensable tool in endodontics. By ensuring thorough disinfection and effective removal of harmful pathogens, sodium hypochlorite not only enhances treatment outcomes but also significantly contributes to the overall health and safety of patients.⁶⁶ Incorporating sodium hypochlorite into root canal procedures exemplifies how harnessing the power of halogens can lead to more effective and efficient dental care, setting a standard for excellence in infection control.⁶⁷



Figure 15: Sodium Hypochlorite

Courtesy: <https://Www.Dentganga.Com/Product/Sodium-Hypochoirite-500ml-Pack-Of-5>

Chloramine T: It is a potent active chlorine-releasing compound, boasts remarkable antimicrobial properties that make it a valuable asset in dental care. For patients with a history of iodine sensitivity, Chloramines at a concentration of 5% offers an excellent alternative for intracanal dressing, combining effectiveness with low toxicity.⁶⁸ Not only does Chloramine T (**Figure 16**) excel in treating root canals, but it is also effective for disinfecting gutta-percha points. Its versatile application underscores its importance in maintaining optimal hygiene and ensuring patient safety. By choosing Chloramine T, dental professionals can provide a reliable solution that addresses both infection control and patient comfort, making it an essential component of modern endodontic practice.⁶⁹



Figure 16: Chloramine T

Courtesy: <https://www.Indiamart.Com/Proddetail/Chloramine-T-Sd-500-Gm-23990048255.Html?Mtd=1>

Iodine: It has been recognized for its gentle effect on living tissue for many years. Iodine tincture, at a concentration of 5% in alcohol, is used to disinfect endodontic surgical fields, while iodine potassium iodide, consisting of 2% iodine, 4% potassium iodide, and 94% distilled water, is employed for intracanal medication. These are the two most common formulations of iodine used in dentistry.⁷⁰

Chlorhexidine: Chlorhexidine digluconate (**Figure 17**) is a potent synthetic cationic bis-guanide, consisting of two symmetric 4-chlorophenyl rings linked by a hexamethylene chain. Its unique positive, hydrophobic, and lipophilic properties allow it to effectively interact with the negatively charged phosphate groups of phospholipids and lipopolysaccharides in bacterial cell membranes.⁷¹ This interaction increases cell wall permeability, enabling Chlorhexidine to penetrate bacterial cells and disrupt osmotic balance.⁷² Clinically, it has become a top choice for root canal irrigation and intracanal medication, particularly in its 2% gel form or when combined with calcium hydroxide.⁷³ Research by Lindsog et al. emphasizes its therapeutic potential in reducing inflammatory root resorption in replanted infected teeth, showing significant improvements compared

to non-medicated controls.⁷⁴ Additionally, a study by Jose F. Siqueira et al. demonstrated that a mixture of Chlorhexidine and zinc oxide effectively eliminates *Candida albicans* infection from radicular dentin. These compelling findings highlight the efficacy of Chlorhexidine as a vital adjunct in endodontic therapy, transforming patient care and outcomes in dental practice.⁷⁵

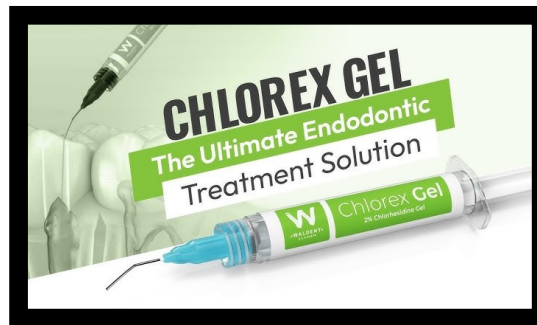


Figure 17: Chlorhexidine Digluconate

Courtesy: <https://www.Youtube.Com/Watch?App=Desktop&V=Otdjrcaufk>

Quaternary ammonium compounds: It is a cationic detergent and wetting agent that serves as a mildly effective disinfectant. It can be used for irrigating root canals without causing inflammation of the periapical tissue. It is considered foaming and is practically non-irritating in weak solutions at concentrations of 1:20,000 to 1:50,000. Its effectiveness is greater in alkaline media than in acidic conditions. This colorless and odorless stable compound has a lower surface tension in solutions.⁷⁶

Calcium hydroxide: In 1920, Hermann revolutionized dental treatment with calcium hydroxide (**Figure 18**), a highly alkaline compound known for promoting tissue formation. This medicament is invaluable for preventing root resorption, repairing perforations, treating horizontal root fractures, apexification, apexogenesis, and managing weeping canals.⁷⁷ Grossman also highlighted p-chloro-phenol-sodium caprylate (PBSC) in dental practice, which is now often replaced by Nystatin in formulations, resulting in p-chloro-phenol-sodium Nystatin (PBSN).⁷⁸ Both PBSC and PBSN can be injected into root canals or applied with paper points, requiring careful placement for effectiveness.⁷⁹ However, PBSC can interfere with culturing processes and inactivate penicillin, leading to decreased use due to sensitivity concerns and a decline in popularity of intracanal medicaments. This shift underscores the need for safe and effective treatment options in modern endodontics.⁸⁰

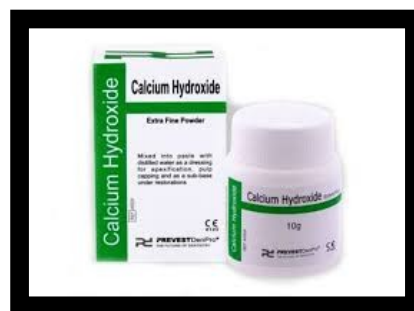


Figure 18: Calcium Hydroxide

Courtesy: <https://Thefuturedentistry.Com/Most-Important-Intra-Canal-Medicaments-Frequently-Asked/>

Ledermix paste: Developed by Schroeder and Tridon in 1960, Ledermix (**Figure 19**) is a revolutionary glucocorticoid antibiotic compound that plays a pivotal role in managing pain and inflammation in dental treatments.⁸¹ By combining Ledermix with an antibiotic, this formulation effectively mitigates potential corticosteroid-induced reductions in the host's immune response, ensuring comprehensive patient care.⁸² Formulated in polyethylene glycol, Ledermix features 3.2% demeclocycline hydrochloride and 1% triamcinolone acetoxido, creating a potent synergy that significantly enhances its efficacy against dental infections.⁸³ In contrast, sulfonamides act as bacteriostatic agents, disrupting bacterial metabolism and making pathogens more vulnerable to the body's natural defenses.⁸⁴ These medications are easily applied using moistened paper points or mixed with sterile distilled water. However, clinicians should note that sulfonamides may cause yellowish discoloration of teeth and are particularly effective for closing teeth left open due to acute periapical abscesses.⁸⁵ Despite their benefits, the effectiveness of sulfonamides can diminish in the presence of pus, protein breakdown products, tissue debris, and p-aminobenzoic acid.⁸⁶ Recognizing these limitations is

crucial for the optimal use of these therapeutic agents, ultimately enhancing patient outcomes in endodontic practice. This holistic approach highlights the transformative potential of innovative treatments in advancing dental care, reinforcing the commitment to providing the highest quality of patient-centered treatment.⁸⁷



Figure 19: Ledermix Paste

Courtesy: <https://Dentverses.Com/Ledermix-Paste-2>

Mode of application: The mode of application is a critical factor in selecting an intracanal medicament, with two primary methods for placement that can significantly impact treatment outcomes. The first method involves placing the medicament in the pulp chamber on a cotton pellet.⁸⁸ This requires careful preparation: the pulp chamber and root canals must be dried using sterile cotton pellets and paper points after the final recapitulation. To apply the medicament, the bottle is inverted to allow the liquid to adhere to the inside near the opening.⁸⁹ After removing the cap, a sterile cotton pellet is wiped against the interior to absorb the liquid, which is then squeezed onto a sterile gauze sponge.⁹⁰ The medicament remaining in the pellet is adequate for providing temporary antibacterial action when placed in the pulp chamber.⁹¹ The second method consists of flooding the root canal with the prepared medicament. A plastic instrument is used to transfer the paste into the pulp chamber, and it is then propelled apically with a plastic carrier. It's crucial to take precautions when sealing the pulp chamber to prevent recontamination due to marginal leakage or loss of the seal before the next appointment.⁹² Both methods require precision and care, as the effectiveness of the intracanal medicament hinges on proper application. This attention to detail not only enhances the medicament's antibacterial action but also safeguards the integrity of the treatment, ultimately leading to improved patient outcomes in endodontic practice.⁹³

Recent Advances in Intracanal Medicaments and Techniques:

1. Triple Antibiotic Paste: Root canal infections are often polymicrobial, necessitating a combination of antibiotics for effective treatment. The innovative use of metronidazole, ciprofloxacin, and minocycline has demonstrated remarkable efficacy in eliminating bacteria from deep dentin layers.⁹⁴ Research by Sato et al. revealed that after applying this triple antibiotic paste, no bacteria were recovered within 24 hours from the infected dentin, significantly reducing the risk of developing antibiotic-resistant strains (Figure 20).⁹⁵



Figure 20: Triple Antibiotic Paste

Courtesy: <https://www.youtube.com/watch?app=desktop&v=McuPt1-Ptm>

2. Medicated Gutta-Percha: New gutta-percha points (Figure 21) infused with calcium hydroxide (50-51% concentration) has revolutionized root canal procedures. This advancement simplifies the placement and removal of calcium hydroxide, enhancing treatment efficiency.⁹⁶

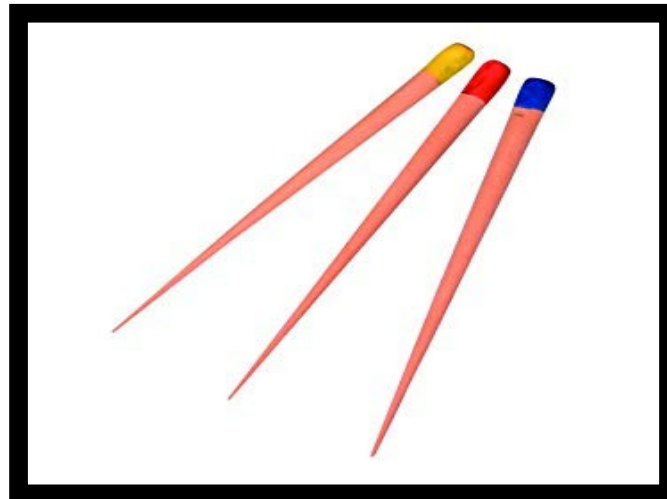


Figure 21: Medicated Gutta Percha Points
Courtesy: <http://Bsdinhvietthang.Com/100-2/>

3. Bioactive Glass: Bioactive glass is emerging as a promising intracanal medicament, consisting of 53% SiO₂, 23% Na₂O, 20% CaO, and 4% P₂O₅. It has demonstrated effective disinfection properties in root canals, and notably, its antimicrobial action is not dependent on pH. This characteristic suggests its potential for widespread use in endodontics.⁹⁷

4. Nisin: This natural antimicrobial peptide, derived from *Lactococcus lactis*, has been used as a food preservative for over 40 years. Nisin (**Figure 22**) works by disrupting bacterial cell membranes, leading to the leakage of intracellular contents. Its safety and effectiveness position it as a strong candidate for applications in endodontics.⁹⁸



Figure 22: Nisin

Courtesy: <https://www.Semanticscholar.Org/Paper/ANTIMICROBIAL-EFFICACY-OF-DIFFERENT-INTRACANAL-ON-%E2%80%93-Anirudhan/Ca572dcbef914412ede659e2875e0e10026fc001>

5. Photodynamic Therapy (PAD): Leveraging toloum chloride activated by a 635 nm red laser, PAD generates reactive oxygen species that target and damage microbial cells. This technique offers a powerful approach to combat biofilm-associated infections, enhancing overall treatment outcomes.⁹⁹

6. ENDOX System: This innovative endodontic system uses high-frequency electrical impulses to sterilize the root canal effectively. While it shows promise in eliminating pulp and bacteria, it is recommended as an adjunct to traditional mechanical cleaning rather than a standalone treatment.¹⁰⁰

7. Curcumin: Derived from turmeric, curcumin (**Figure 23**) possesses notable antimicrobial and anti-inflammatory properties. Recent studies suggest its potential as a viable alternative to triple antibiotic paste, particularly when combined with photoactivation to boost its antibiofilm effects.¹⁰¹



Figure 23: Curcumin

Courtesy: <https://www.Academia.Edu/34836856/>

[An_Investigation_Into_The_Potential_Use_Of_Dennkur_As_An_Intra_Canal_Irrigant_And_Medicament_In_Endodontics](#)

Syringe Injection Technique: Intracanal medicaments can be effectively delivered using an injection syringe system, ensuring precise placement within the root canal. To guarantee optimal insertion of the medicament into the apex, proper needle placement is crucial. Research has shown that filling can be achieved using this syringe system in straight or slightly curved root canals prepared to at least size 50.¹⁰² Notably, studies indicate that canal preparation with an apical size of 40 yields a more homogeneous distribution compared to the injection syringe method, resulting in less taper.¹⁰³ Furthermore, a study on calcium hydroxide dressings highlighted the differences in preparation and application modes, demonstrating that density and dissolution are enhanced by stimulated tissue pressure. These findings underscore the importance of careful technique in the application of intracanal medicaments for improved treatment outcomes.¹⁰⁴

Future Prospects: The field of endodontics is rapidly evolving with the introduction of next-generation intracanal medicaments. These advanced treatments promise improved efficacy in managing dental infections and promoting healing. Understanding their current impact and future prospects is essential for dental professionals and researchers alike.

1. **Enhanced Efficacy:** New medicaments demonstrate superior antimicrobial activity, effectively targeting resistant bacteria and biofilms.
2. **Improved Healing:** Many formulations support tissue regeneration, leading to better healing outcomes post-treatment.
3. **Patient Comfort:** Reduced side effects and irritation enhance patient experience during and after endodontic procedures.
4. **Biomimetic Approaches:** Future medicaments may mimic natural healing processes, incorporating biomaterials that encourage regeneration and repair.
5. **Personalized Medicine:** Tailoring treatments based on individual patient profiles and microbiomes could optimize outcomes.
6. **Nanotechnology:** The integration of nanoparticles may enhance drug delivery systems, improving penetration and sustained release within the canal.
7. **Smart Therapeutics:** Development of responsive medicaments that activate under specific conditions within the canal may revolutionize treatment.
8. **Integration with Digital Technologies:** Combining intracanal therapies with advanced imaging and diagnostic tools could facilitate more effective treatment planning and monitoring.

Next-generation intracanal medicaments hold significant promise for the future of endodontics. As research progresses, these innovations are expected to enhance treatment efficacy, patient comfort, and overall outcomes in dental care. Embracing these advancements will be crucial for dental professionals aiming to provide the best possible care.¹⁰⁵

III. Conclusion:

Next-generation intracanal medicaments represent a transformative leap in endodontic therapy, significantly improving treatment outcomes for patients facing non-vital teeth, periapical diseases, abscesses,

and trauma-related complications. These innovative medicaments are designed to effectively disinfect the root canal and reduce microbial load, thereby enhancing the prognosis for affected teeth. While calcium hydroxide has long stood as the gold standard due to its remarkable antimicrobial properties, its limitations have sparked a quest for more advanced alternatives. Recent breakthroughs in intracanal medicaments are addressing these challenges, equipping dental professionals with powerful tools that elevate root canal therapy to new heights. This review showcases the array of medicaments currently available for root canal treatment, underscoring the critical need for continuous research and development in this field. As advancements unfold, the integration of cutting-edge therapeutic agents promises to not only boost the efficacy of endodontic procedures but also to profoundly improve patient outcomes, revolutionizing the landscape of dental care. For dental practitioners, embracing these innovations is not just beneficial—it is essential. The future of endodontics hinges on the adoption of these advanced solutions, enabling practitioners to provide optimal care in an ever-evolving field. The potential for improved patient experiences and treatment success is immense, marking a new era in dental health.

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References:

- [1] Siqueira JF, Lopes HP. Mechanisms Of Antimicrobial Activity Of Calcium Hydroxide: A Critical Review. *Int Endod J.* 1999; 32(5):361–9.
- [2] Ingle JI, Bakland LK. *Endodontics*. 6th Edition, Bc Decker Inc., Hamilton, 2008; 1-1581.
- [3] Taylor GN. Advanced Techniques For Intracanal Preparation And Filling In Routine Endodontic Therapy. *Dent Clin North Am.* 1984; 28:819-832.
- [4] Almyroudi A, Mackenzie D, Mchugh S, et al. The Effectiveness Of Various Disinfectants Used As Endodontic Intracanal Medications: An In Vitro Study. *J Endod.* 2002; 28:163-167.
- [5] Relan K, Chandak M, Chaudhari SS, et al. Clinical Evaluation And Comparison Of Effectiveness Of Three Different Endodontic Irrigation Systems For Irrigant Delivery To Working Length Of Single Rooted Teeth Using Radiopaque Dye An Interventional Study. *Int J Pharm Res.* 2019; 11:1840–1843.
- [6] Walton RE. Intracanal Medicaments. *Dent Clin North Am.* 1984; 28:783-796.
- [7] Bhonde R, Ikhar A, Palsodkar P, et al. Comparative Clinical Evaluation Of Post Endodontic Pain In Retreatment Cases Using Calcium Hydroxide And Triple Anti Biotic Paste An Interventional Study. *Int J Pharma Res.* 2019; 11:1428–1430.
- [8] Chandak MG, Modi RR, Rathi BJJ, et al. In Vitro Comparative Assessment Of Diffusion Of Ion From Calcium Hydroxide With Three Different Phytomedicine Pastes Through Dentin. *World J Dent.* 2018; 9:366–371.
- [9] Hamidi MR, Mahmoudi E, Moghadamnia AA, et al. Effect Of Calcium Hydroxide And Chlorhexidine Medicaments On The Apical Seal. *Iran Endod J.* 2012; 7:15-19.
- [10] Berman L, Hahnel S, Langeland K. An Evaluation Of Calcium Hydroxide As An Antimicrobial Agent In Root Canal Therapy. *J Endod.* 1991; 17(8):370-373.
- [11] Sedgley C, Lenox J, Botero T, et al. Antimicrobial Properties Of Calcium Hydroxide In Endodontics: A Review. *J Endod.* 2015; 41(1):48-55.
- [12] Adl Alireza et al. A Comparison Between The Antimicrobial Effects Of Triple Antibiotic Paste And Calcium Hydroxide Against *Enterococcus Faecalis*. *Iran Endod. J.* 2012; 7:149-155.
- [13] Pai S, Vivekananda Pai AR, Thomas MS, et al. Effect Of Calcium Hydroxide And Triple Antibiotic Paste As Intracanal Medicaments On The Incidence Of Inter Appointment Flare Up In Diabetic Patients: An In Vivo Study. *J Conserv Dent.* 2014; 17:208-211.
- [14] Rosenberg B, Murray PE, Namerow K, et al. The Effect Of Calcium Hydroxide Root Filling On Dentin Fracture Strength. *Dent Traumatol* 2007; 23:26-29.
- [15] Lambrianidis T, Margelos J, Beltes P, et al. Removal Efficiency Of Calcium Hydroxide Dressing From The Root Canal. *J Endod.* 1999; 25:85-88.
- [16] Basrani B, Tjaderhane L, Santos JM, et al. Efficacy Of Chlorhexidine And Calcium Hydroxide Containing Medicaments Against *Enterococcus Faecalis* In Vitro. *Oral Surg Oral Med Oral Pathol Oral RadiolEndod.* 2003; 96:618-624.
- [17] Zhu J, Liang R, Sun C, Xie L, Wang J, Leng D, et al. Effects Of Nanosilver And Nanozinc Incorporated Mesoporous Calcium-Silicate Nanoparticles On The Mechanical Properties Of Dentin. *Plos One.* 2017; 12:E0182583.
- [18] Waltimo T, Trope M, Haapasalo M, et al. Clinical Efficacy Of Treatment Procedures In Endodontic Infection Control And One Year Follow Up Of Periapical Healing. *J Endod.* 2005; 31:863-866.
- [19] Zheng T, Huang X, Chen J, Feng D, Mei L, Huang Y, et al. A Liquid Crystalline Precursor Incorporating Chlorhexidine Acetate And Silver Nanoparticles For Root Canal Disinfection. *Biomater Sci.* 2018; 6:596–603.
- [20] Zerella JA, Fouad AF, Spångberg LS. Effectiveness Of A Calcium Hydroxide And Chlorhexidine Digluconate Mixture As Disinfectant During Retreatment Of Failed Endodontic Cases. *Oral Surg Oral Med Oral Pathol Oral RadiolEndod.* 2005; 100:756–61.
- [21] Krithika Datta J, Indira R, Dorothykalyani AL, et al. Disinfection Of Dentinal Tubules With 2% Chlorhexidine, 2% Metronidazole, Bioactive Glass When Compared With Calcium Hydroxide As Intracanal Medicaments. *J Endod.* 2007; 33:1473-1476.
- [22] Cohen S. *Instrument Materials And Device* 10th Edition, MosbyElsevier, 2011; 245-282.
- [23] Dahake PT, Baliga SM, Kumbar VM, et al. Cytotoxicity Of Novel Polymeric Gel Matrix Triple Antibiotic Paste An In Vitro Study. *Regen Eng Transl Med.* 2021; 7:21–29.
- [24] Khatod S, Ikhar A, Nikhade P, et al. Comparative Evaluation Of Different Irrigation Techniques With Conventional Irrigation Technique For The Removal Of Double Antibiotic Paste From Root Canal An In Vitro Study. *Int J Res Pharm Sci.* 2020; 11:5578–5583.

- [25] Mohammadi Z, Abbott PY. On The Local Applications Of Antibiotics And Antibiotic Based Agents In Endodontics And Dental Traumatology. *Int Endod J*.2009; 42:555-567.
- [26] Paredes-Vieyra J, Enriquez FJ. Success Rate Of Single- Versus Two-Visit Root Canal Treatment Of Teeth With Apical Periodontitis: A Randomized Controlled Trial. *J Endod*. 2012; 38:1164-9.
- [27] Parhizkar A, Nojehdehian H, Asgary S. Triple Antibiotic Paste: Momentous Roles And Applications In Endodontics: A Review. *Restor Dent Endod*. 2018; 43:e28.
- [28] Penesis VA, Fitzgerald PI, Fayad M, Wenckus CS, Begole EA, Johnson BR. Outcome Of One-Visit And Two-Visit Endodontic Treatment Of Necrotic Teeth With Apical Periodontitis: A Randomized Controlled Trial With One-Year Evaluation. *J Endod*. 2008; 34:251-7.
- [29] Petean IBF, K uchler EC, Soares IMV, Segato RAB, Silva LABD, Antunes LAA, et al. Genetic Polymorphisms In Rank And Rankl Are Associated With Persistent Apical Periodontitis. *J Endod*. 2019; 45:526-31.
- [30] Pirtskhalava M, Amstrong Aa, Grigolava M, Chubinidze M, Alimbarashvili E, Vishnepolsky B, et al. Dbaasp V3: Database Of Antimicrobial/Cytotoxic Activity And Structure Of Peptides As A Resource For Development Of New Therapeutics. *Nucleic Acids Res*. 2021; 49:D288-97.
- [31] Portenier I, Haapasalo H, Rye A, Waltimo T,  rstavik D, Haapasalo M. Inactivation Of Root Canal Medicaments By Dentine, Hydroxylapatite And Bovine Serum Albumin. *Int Endod J*. 2001; 34:184-8.
- [32] Portenier I, Haapasalo H,  rstavik D, Yamauchi M, Haapasalo M. Inactivation Of The Antibacterial Activity Of Iodine Potassium Iodide And Chlorhexidine Digluconate Against *Enterococcus Faecalis* By Dentin, Dentin Matrix, Type-I Collagen, And Heat-Killed Microbial Whole Cells. *J Endod*. 2002; 28:634-7.
- [33] Portenier I, Waltimo T,  rstavik D, Haapasalo M. Killing Of *Enterococcus Faecalis* By Mtd And Chlorhexidine Digluconate With Or Without Cetrimide In The Presence Or Absence Of Dentine Powder Or Bsa. *J Endod*. 2006; 32:138-41.
- [34] Tanomaru JM, Leonardo MR, Tanomaru Filho M, Bonetti Filho I, Silva LA. Effect Of Different Irrigation Solutions And Calcium Hydroxide On Bacterial LPS. *Int Endod J*. 2003; 36:733-9.
- [35] Tello-Barbaran J, Nakata HM, Salcedo-Moncada D, Bramante CM, Ordinola-Zapata R. The Antimicrobial Effect Of Iodine-Potassium Iodide After Cleaning And Shaping Procedures In Mesial Root Canals Of Mandibular Molars. *Acta Odontol Latinoam*. 2010; 23:244-7.
- [36] Tong Z, Huang L, Ling J, Mao X, Ning Y, Deng D. Effects Of Intracanal Irrigant Mtd Combined With Nisin At Sub-Minimum Inhibitory Concentration Levels On *Enterococcus Faecalis* Growth And The Expression Of Pathogenic Genes. *Plos One*. 2014; 9:E90235.
- [37] Torabinejad M, Kettering JD, Mcgraw JC, Cummings RR, Dwyer TG, Tobias TS. Factors Associated With Endodontic Interappointment Emergencies Of Teeth With Necrotic Pulp. *J Endod*. 1988; 14:261-6.
- [38] Tronstad L, Andreasen JO, Hasselgren G, Kristerson L, Riis I. Ph Changes In Dental Tissues After Root Canal Filling With Calcium Hydroxide. *J Endod*. 1981; 7:17-21.
- [39] Trope M. Flare-Up Rate Of Single-Visit Endodontics. *Int Endod J*. 1991; 24:24-6.
- [40] Trope M, Delano O, Orstavik D. Endodontic Treatment Of Teeth With Apical Periodontitis: Single Vs. Multivisit Treatment. *J Endod*. 1999; 25:345-50.
- [41] T rk n M, Cengiz T. The Effects Of Sodium Hypochlorite And Calcium Hydroxide On Tissue Dissolution And Root Canal Cleanliness. *Int Endod J*. 1997; 30:335-42.
- [42] Wang G, Li X, Wang Z. Apd3: The Antimicrobial Peptide Database As A Tool For Research And Education. *Nucleic Acids Res*. 2016; 44:D1087-93.
- [43] Weckwerth PH, Zapata RO, Vivan RR, Tanomaru Filho M, Maliza AG, Duarte MA. In Vitro Alkaline Ph Resistance Of *Enterococcus Faecalis*. *Braz Dent J*. 2013; 24:474-6.
- [44] Winfred SB, Meiyazagan G, Panda JJ, Nagendrababu V, Deivanayagam K, Chauhan VS, et al. Antimicrobial Activity Of Cationic Peptides In Endodontic Procedures. *Eur J Dent*. 2014; 8:254-60.
- [45] Wu D, Fan W, Kishen A, Gutmann JL, Fan B. Evaluation Of The Antibacterial Efficacy Of Silver Nanoparticles Against *Enterococcus Faecalis* Biofilm. *J Endod*. 2014; 40:285-90.
- [46] Ye Z, Aparicio C. Modulation Of Supramolecular Self-Assembly Of An Antimicrobial Designer Peptide By Single Amino Acid Substitution: Implications On Peptide Activity. *Nanoscale Adv*. 2019; 1:4679-82.
- [47] Ye Z, Aparicio C. Interactions Of Two Enantiomers Of A Designer Antimicrobial Peptide With Structural Components Of The Bacterial Cell Envelope. *J Pept Sci*. 2022; 28:E3299.
- [48] Ye Z, Ting S, Kun L, Nicholas GF, Isha M, Constanza E, et al. Hybrid Nanocoatings Of Self-Assembled Organic-Inorganic Amphiphiles For Prevention Of Implant Infections. *Acta Biomater*. 2022; 140:338-49.
- [49] Ye Z, Zhu X, Mutreja I, Boda SK, Fischer NG, Zhang A, et al. Biomimetic Mineralized Hybrid Scaffolds With Antimicrobial Peptides. *Bioact Mater*. 2021; 6:2250-60.
- [50] Yoldas O, Topuz A, IS I AS, Oztunc H. Postoperative Pain After Endodontic Retreatment: Single- Versus Two-Visit Treatment. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2004; 98:483-7.
- [51] Zapata RO, Bramante CM, Gomes DE Moraes I, Bernardineli N, Gasparoto Th, Graeff MS, et al. Confocal Laser Scanning Microscopy Is Appropriate To Detect *Enterococcus Faecalis* In Infected Dentin. *J Endod*. 2008; 34:1198-201.
- [52] Prestinaci F, Pezzotti P, Pantosti A. Antimicrobial Resistance: A Global Multifaceted Phenomenon. *Pathog Glob Health*. 2015; 109 (6):309-18.20.
- [53] Ricucci D, Candeiro GT, Bugea C, Siqueira JF. Complex Apical Intraradicular Infection And Extraradicular Mineralized Biofilms As The Cause Of Wet Canals And Treatment Failure: Report Of 2 Cases. *J Endod*. 2016; 42(4):509-15.
- [54] Ricucci D, Loghin S, Goncalves LS, R ças IN, Siqueira JF. Histobacteriological Conditions Of The Apical Root Canal System And Periapical Tissues In Teeth Associated With Sinus Tracts. *J Endod*. 2018; 44 (3):405-13.
- [55] Ricucci D, Russo J, Rutberg M, Burlelson Ja, Sp ngberg Ls. A Prospective Cohort Study Of Endodontic Treatments Of 1,369 Root Canals: Results After 5 Years. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2011; 112 (6):825-42.
- [56] Ricucci D, Siqueira JF. Biofilms And Apical Periodontitis: Study Of Prevalence And Association With Clinical And Histopathologic Findings. *J Endod*. 2010; 36 (8):1277-88.
- [57] Ricucci D, Siqueira JF. Fate Of The Tissue In Lateral Canals And Apical Ramifications In Response To Pathological Conditions And Treatment Procedures. *J Endod*. 2010; 36(1):1-15.
- [58] R ças IN, Siqueira JF. Root Canal Microbiota Of Teeth With Chronic Apical Periodontitis. *J Clin Microbiol*. 2008; 46 (10):3599-606.

- [59] Rojas B, Soto N, Villalba M, Bello-Toledo H, Meléndrez-Castro M, Sánchez-Sanhueza G. Antibacterial Activity Of Copper Nanoparticles (Cunps) Against A Resistant Calcium Hydroxide Multispecies Endodontic Biofilm. *Nanomaterials*. 2021; 11(9):2254.
- [60] Ruden S, Hilpert K, Berditsch M, Wadhvani P, Ulrich AS. Synergistic Interaction Between Silver Nanoparticles And Membrane-Permeabilizing Antimicrobial Peptides. *Antimicrob Agents Chemother*. 2009; 53(8):3538–40.
- [61] Safavi KE, Nichols FC. Effect Of Calcium Hydroxide On Bacterial Lipopolysaccharide. *J Endod*. 1993; 19 (2):76–8.
- [62] Safavi KE, Nichols FC. Alteration Of Biological Properties Of Bacterial Lipopolysaccharide By Calcium Hydroxide Treatment. *J Endod*. 1994; 20 (3):127–9.
- [63] Samiei M, Torab A, Hosseini O, Abbasi T, Abdollahi Aa, Divband B. Antibacterial Effect Of Two Nano Zinc Oxide Gel Preparations Compared To Calcium Hydroxide And Chlorhexidine Mixture. *Iran Endod J*. 2018; 13(3):305–11.
- [64] Sathorn C, Parashos P, Messer HH. Effectiveness Of Single- Versus Multiple-Visit Endodontic Treatment Of Teeth With Apical Periodontitis: A Systematic Review And Meta-Analysis. *Int Endod J*. 2005; 38 (6):347–55.
- [65] Chen Y, Yang H, Li Y, et al. A Meta-Analysis Of The Efficacy Of Sodium Hypochlorite And Chlorhexidine As Root Canal Irrigants. *J Endod*. 2015; 41(4):664-672.
- [66] Oliveira L, Ferreira M, Lima E, et al. A Comparison Of The Efficacy Of Calcium Hydroxide And Sodium Hypochlorite As Intracanal Medicaments: A Systematic Review. *J Endod*. 2018; 44(1):41-49.
- [67] Schilder H. Cleaning And Shaping The Root Canal. *Dent Clin North Am*. 1974; 18(2):269–96.
- [68] Shahmoradi S, Shariati A, Zargar N, Yadegari Z, Asnaashari M, Amini SM, et al. Antimicrobial Effects Of Selenium Nanoparticles In Combination With Photodynamic Therapy Against *Enterococcus Faecalis* Biofilm. *Photodiagnosis Photodyn Ther*. 2021; 35:102398.
- [69] Shuping GB, Ørstavik D, Sigurdsson A, Trope M. Reduction Of Intracanal Bacteria Using Nickel-Titanium Rotary Instrumentation And Various Medications. *J Endod*. 2000; 26(12):751
- [70] Silva LA, Leonardo MR, Assed S, Tanomaru Filho M. Histological Study Of The Effect Of Some Irrigating Solutions On Bacterial Endotoxin In Dogs. *Braz Dent J*. 2004; 15(2):109–14.
- [71] Savitha A, Srirekha A, Vijay R, Ashwija CC, Jaykumar T. An In Vivo Comparative Evaluation Of Antimicrobial Efficacy Of Chitosan, Chlorhexidine Gluconate Gel And Their Combination As An Intracanal Medicament Against *Enterococcus Faecalis* In Failed Endodontic Cases Using Real Time Polymerase Chain Reaction (Qpcr). *Saudi Dent J*. 2019; 31(3):360–6.
- [72] Silveira CFDSMPD, Malagutte KND, Nogueira BF, Reis FM, Rodrigues CDSA, Rossi DAA, ET AL. Assessment Of The Antibacterial Activity Of Calcium Hydroxide Combined With Chlorhexidine Paste And Other Intracanal Medications Against Bacterial Pathogens. *Eur J Dent*. 2011; 5(1):1–7.
- [73] Freire LG, Carvalho CN, Ferrari PH, et al. Influence Of Dentin On Ph Of 2% Chlorhexidine Gel And Calcium Hydroxide Alone Or In Combination. *Dent Traumatol*. 2010; 26:276-280.
- [74] Sinha N, Patil S, Dodwad PK, et al. Evaluation Of Antimicrobial Efficacy Of Calcium Hydroxide Paste, Chlorhexidine Gel, And A Combination Of Both As Intracanal Medicament: An In Vivo Comparative Study. *J Conserv Dent*. 2013; 16:65-70.
- [75] Sjögren U, Figdor D, Persson S, Sundqvist G. Influence Of Infection At The Time Of Root Filling On The Outcome Of Endodontic Treatment Of Teeth With Apical Periodontitis. *Int Endod J*. 1997; 30(5):297–306.
- [76] Southard DW, Rooney TP. Effective One-Visit Therapy For The Acute Periapical Abscess. *J Endod*. 1984; 10(12):580–3.
- [77] Sjögren U, Figdor D, Spangberg L, Sundqvist G. The Antimicrobial Effect Of Calcium Hydroxide As A Short-Term Intracanal Dressing. *Int Endod J*. 1991; 24(3):119–25.
- [78] Sundqvist G, Figdor D, Persson S, Sjögren U. Microbiological Analysis Of Teeth With Failed Endodontic Treatment And The Outcome Of Conservative Re-Treatment. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1998; 85(1):86–93.
- [79] Lima CO, Pereira R, Nunes J, et al. The Influence Of Calcium Hydroxide And Chlorhexidine On The Fracture Resistance Of Root-Filled Teeth. *J Endod*. 2015; 41(6):908-912.
- [80] SY K, Agossa K, Maton M, Chijcheapaza-Flores H, Martel B, Siepmann F, et al. How Adding Chlorhexidine Or Metallic Nanoparticles Affects The Antimicrobial Performance Of Calcium Hydroxide Paste As An Intracanal Medication: An In Vitro Study. *Antibiotics*. 2021; 10(11):1352.
- [81] Tordik PA, Gans KYA, Huynh-BAG, et al. Clinical Outcomes Of Root Canal Retreatment Using Calcium Hydroxide As An Intracanal Medicament. *J Endod*. 2017; 43(5):734-738.
- [82] Wang H, Wang X, Zhang C, et al. Effect Of Different Intracanal Medicaments On Postoperative Pain: A Systematic Review And Meta-Analysis. *J Endod*. 2016; 42(10):1571-1581.
- [83] Sweileh WM. Global Research Publications On Irrational Use Of Antimicrobials: Call For More Research To Contain Antimicrobial Resistance. *Global Health*. 2021; 17(1):94.
- [84] Sathorn C, Parashos P, Messer H. The Prevalence Of Postoperative Pain And Flare-Up In Single- And Multiple-Visit Endodontic Treatment: A Systematic Review. *Int Endod J*. 2008; 41(2):91–9.
- [85] Teles Rp, Lima C, Tavares R, et al. Antimicrobial Efficacy Of Different Concentrations Of Calcium Hydroxide And Chlorhexidine In Root Canals: An In Vitro Study. *J Conserv Dent*. 2013; 16(3):257-261.
- [86] Nascimento C, Lemos C, De Oliveira F, et al. Effects Of Calcium Hydroxide On The Apical Seal Of Root Canal Fillings: A Systematic Review. *Int Endod J*. 2014; 47(8):690-698.
- [87] Ghasemi N, Farahani A, Rajabi S, et al. Effect Of Different Irrigating Solutions On The Removal Of Calcium Hydroxide From Root Canals. *Iran Endod J*. 2015; 10(4):247-252.
- [88] Giardino L, Manzoli L, Sinjari B, et al. Comparative Analysis Of The Antimicrobial Activity Of Sodium Hypochlorite And Calcium Hydroxide Against *E. Faecalis* Biofilm. *J Endod*. 2014; 40(7):1047-1050.
- [89] Krishnan K, Teja M, Anjaneyulu K, et al. The Role Of Root Canal Filling Materials In The Prevention Of Apical Leakage: A Review. *J Conserv Dent*. 2014; 17(5):401-405.
- [90] Mohammadi Z, Jafarzadeh H, Shalavi S, et al. A Review On The Use Of Calcium Hydroxide In Endodontics. *J Endod*. 2015; 41(5):673-681.
- [91] Keleş A, Çelik D, Sönmez D, et al. The Effect Of Different Calcium Hydroxide Formulations On The Apical Seal Of Root Fillings. *J Endod*. 2016; 42(4):548-553.
- [92] Gomes B, Figueiredo J, Almeida J, et al. Analysis Of The Antimicrobial Activity Of Calcium Hydroxide In Endodontics: A Systematic Review. *J Endod*. 2017; 43(1):132-144.
- [93] Shahrbaf S, Lotfi M, Kooshki A, et al. Comparison Of The Antibacterial Effects Of Calcium Hydroxide, Sodium Hypochlorite, And Chlorhexidine Against *Enterococcus Faecalis*. *Iran Endod J*. 2017; 12(2):157-162.
- [94] Da Silva LA, Nelson-Filho P, Da Silva RA, Flores DSH, Heilborn C, Johnson JD, et al. Revascularization And Periapical Repair After Endodontic Treatment Using Apical Negative Pressure Irrigation Versus Conventional Irrigation Plus Triantibiotic

- Intracanal Dressing In Dogs' Teeth With Apical Periodontitis. *Oral Surg Oral Med Oral Pathol Oral RadiolEndod.* 2010; 109(6):779–87.
- [95] Ferraz C, Gomes B, Zaia A, et al. Effect Of Calcium Hydroxide On The Antimicrobial Activity Of Various Intracanal Medicaments. *J Endod.* 2001; 27(11):689-692.
- [96] Tavares B, De Almeida J, Sanches B, et al. Efficacy Of Calcium Hydroxide In Disinfecting Root Canals: A Systematic Review. *J Endod.* 2015; 41(10):1556-1565.
- [97] Ribeiro R, De Almeida A, Nascimento M, et al. The Influence Of Calcium Hydroxide On The Success Rate Of Endodontic Treatments: A Systematic Review. *J Endod.* 2016; 42(3):496-504.
- [98] Verma P, Kaur A, Goyal M, et al. Role Of Calcium Hydroxide In Endodontics: A Review. *J Conserv Dent.* 2018; 21(5):501-505.
- [99] Yamanaka A, Yasuda T, Hoshino E. Efficacy Of Calcium Hydroxide As An Intracanal Medicament In Endodontics. *J Endod.* 2000; 26(2):103-106.
- [100] Kahn F, Chechik H, Hoffer P, et al. Clinical Significance Of Calcium Hydroxide In Endodontics: An Overview. *J Endod.* 2004; 30(10):573-580.
- [101] Kumar H. An In Vitro Evaluation Of The Antimicrobial Efficacy Of Curcuma Longa, Tachyspermum Ammi, Chlorhexidine Gluconate, And Calcium Hydroxide On Enterococcus Faecalis. *J Conserv Dent.* 2013; 16:144-147.
- [102] Maziarz S, Pawluk A, Sroka A, et al. The Effectiveness Of Calcium Hydroxide Combined With Other Medications In Reducing Postoperative Pain After Root Canal Treatment: A Systematic Review. *J Endod.* 2018; 44(4):593-605.
- [103] Stojanovic J, Stojanovic D, Milojevic M, et al. The Impact Of Calcium Hydroxide And Chlorhexidine On The Success Rate Of Endodontic Treatments: A Systematic Review And Meta-Analysis. *J Endod.* 2020; 46(3):352-366.
- [104] Perinpanayagam H, Fothergill J, Koenig L. The Effectiveness Of Calcium Hydroxide As An Intracanal Medicament Against Enterococcus Faecalis: An In Vitro Study. *J Endod.* 2003; 29(6):370-373.
- [105] Sarri G, Ritchie D, Markowitz K, et al. The Effectiveness Of Calcium Hydroxide In The Disinfection Of Root Canals: A Systematic Review And Meta-Analysis. *J Endod.* 2020; 46(12):1915-1924.