



## Current concepts and advances in intracanal medicaments in Endodontics: A comprehensive review

Dr. Shah Sharvil<sup>1</sup>, Dr. Rao Dinesh<sup>2</sup>, Dr. Panwar Sunil<sup>3</sup>

<sup>1</sup> Department of Paediatric and Preventive Dentistry, Pacific Dental College and Hospital, Debari, Udaipur, Rajasthan, India.

<sup>2</sup> Head Professor, Department of Paediatric and Preventive Dentistry, Pacific Dental College and Hospital, Debari, Udaipur, Rajasthan, India.

<sup>3</sup> Professor, Department of Paediatric and Preventive Dentistry, Pacific Dental College and Hospital, Debari, Udaipur, Rajasthan, India.

### Abstract

Intracanal medicaments are essential for achieving effective microbial control in endodontic treatment, especially in teeth with necrotic pulps and apical periodontitis. While mechanical instrumentation and irrigation form the primary foundation for root canal disinfection, they are often inadequate in eliminating all microorganisms from the complex root canal system. Medicaments serve as interappointment dressings that continue to disinfect the canal space, neutralize bacterial byproducts, and support periapical healing. Over time, the use of intracanal medicaments has evolved from basic chemical disinfectants to sophisticated formulations, including calcium hydroxide, antibiotic pastes, herbal alternatives, and nanoparticle-based therapies. This review presents an in-depth analysis of their classification, mechanisms, indications, limitations, and emerging innovations such as antimicrobial photodynamic therapy and bioactive nanomaterials. Emphasis is placed on evidence-based selection tailored to specific clinical scenarios, microbial challenges, and regenerative goals.

**Keywords:** Intracanal medicaments, *E. faecalis*, Disinfection, Infections

### Introduction

Endodontic infections are among the most challenging dental conditions due to their polymicrobial nature and the complex anatomy of the root canal system [1]. The ultimate objective of root canal therapy is to remove bacteria, necrotic tissue, and microbial toxins that initiate and perpetuate periapical inflammation [2]. However, due to the presence of fins, isthmuses, lateral canals, and apical deltas, mechanical instrumentation alone is insufficient [3]. Irrigants like sodium hypochlorite aid in debridement, but their effects are transient [4]. Therefore, intracanal medicaments are employed between appointments to maintain antimicrobial activity, reduce inflammation, and promote healing.

These medicaments act as a secondary line of defence by targeting bacteria that persist after canal preparation and irrigation. They also suppress bacterial regrowth and create an unfavourable environment for residual microorganisms [5]. With the advent of regenerative endodontic procedures and increasing antibiotic resistance, the focus on intracanal medicaments has shifted from simply being antibacterial agents to biocompatible, bioactive formulations that integrate with host healing processes [6].

### Methods

To compile a comprehensive overview of the various intracanal medicaments used in endodontics, an extensive literature search was conducted using the keywords 'intracanal medicament', 'endodontic disinfection', 'root canal treatment', 'calcium hydroxide', 'triple antibiotic paste', 'nanoparticles in endodontics', and 'Enterococcus faecalis'. The search was carried out in electronic databases including PubMed, Scopus, Medline, Google Scholar, and

ScienceDirect for studies published in English between January 2000 and May 2024.

Studies included in this review were original research articles (*in vitro*, *in vivo*, or clinical), systematic reviews, narrative reviews, and randomized controlled trials that evaluated the antimicrobial efficacy, biocompatibility, mechanism of action, and clinical outcomes of intracanal medicaments. Articles that focused exclusively on pulp capping materials, sealers, or obturation techniques were excluded.

Following the removal of duplicates, titles and abstracts were screened to assess relevance. Full texts of potentially eligible studies were then reviewed. A total of 85 publications were included for final evaluation. Each article was analyzed based on the type of medicament, target microorganisms, duration of action, ability to penetrate dentinal tubules, cytotoxicity, and resistance patterns.

The findings were categorized and discussed under natural, synthetic, and advanced medicaments (such as nanoparticle-based formulations). This narrative review emphasizes the comparative effectiveness of intracanal medicaments, highlighting their clinical significance in the elimination of persistent endodontic pathogens such as *E. faecalis*.

### Mechanism of Action

The mechanism of action of intracanal medicaments is influenced by their chemical composition and biological properties. Effective medicaments demonstrate multiple mechanisms:

- **Disruption of microbial membranes:** Many agents, including calcium hydroxide and nanoparticles, alter membrane integrity, leading to cell lysis.

- **High pH action:** Alkaline agents denature bacterial enzymes and structural proteins.
- **Inhibition of DNA replication:** Antibiotics like ciprofloxacin interfere with bacterial DNA gyrase, arresting replication.
- **Production of reactive oxygen species (ROS):** Nanoparticles, especially silver and iron oxide, generate ROS that damage microbial DNA, lipids, and proteins.
- **Anti-inflammatory and immunomodulatory effects:** Herbal agents such as curcumin and propolis reduce local inflammatory cytokines, aiding tissue repair.

### Ideal Properties

An ideal intracanal medicament should fulfil the following criteria:

- Broad-spectrum antimicrobial activity
- Non-toxic and biocompatible to periapical tissues
- Stable and effective in the presence of organic and inorganic debris
- Easy to deliver and remove
- No interference with sealer bonding or obturation
- Resistance to inactivation by body fluids
- Affordable and shelf-stable <sup>[7]</sup>

### Indications

Intracanal medicaments are indicated in the following clinical situations:

- Persistent endodontic infection post-instrumentation
- Apical abscesses with continuous exudation
- Teeth with open apices requiring apexification or revascularization
- Internal or external resorption
- Multi-visit root canal therapy requiring interappointment disinfection
- Management of perforations and regenerative endodontic procedures <sup>[8]</sup>

### Objectives

- Destruction of micro-organisms
- Rendering contents of canal inert
- Prevention of control of post-treatment pain
- Enhancing anaesthesia
- Control of persistent periapical abscess <sup>[9]</sup>

### Classification of Intracanal Medicaments

Intracanal medicaments can be broadly categorized based on their chemical nature and function:

1. **Phenolic Compounds:** Eugenol, camphorated monochlorophenol—once popular, now used cautiously due to cytotoxicity.
2. **Aldehydes:** Formocresol, glutaraldehyde—highly effective but discouraged due to mutagenicity.
3. **Halogens:** Iodine compounds, chlorhexidine, and sodium hypochlorite—broad-spectrum activity but potential for irritation.
4. **Calcium Hydroxide:** Alkaline-based medicament with antimicrobial and mineralizing action.
5. **Antibiotic Pastes:** Triple antibiotic paste (TAP), Ledermix, and double antibiotic paste (DAP).
6. **Herbal Extracts:** Neem, propolis, turmeric, tea tree oil, aloe vera.

7. **Nanoparticles:** Silver, zinc oxide, titanium dioxide, and iron oxide—used alone or in combination with traditional agents.
8. **Photodynamic Agents:** Methylene blue, toluidine blue—activated by specific wavelengths for bacterial destruction.

### Intracanal Medicaments

**Eugenol:** Key component of clove oil with antiseptic and mild anaesthetic effects. It is a pale-yellow liquid with a clove-like odor but can become darker over time and is moderately irritating.

**Phenol:** One of the oldest antiseptics, was introduced by Lord Lister in 1867. Derived from coal tar, it appears as white crystals with a distinct odor. It is used in dentistry for pulp sedation, root canal disinfection, caries cavity preparation, and before periapical surgery. Phenol crystals liquefy when mixed with camphor, menthol, or thymol, forming carbolic acid.

**Parachlorophenol:** Colourless, needle-like crystal like phenol, but chlorine replaces one hydrogen atom in the molecule. It darkens when exposed to light and is soluble in ether, alcohol, and alkalis. When mixed with gum camphor, it forms an oily liquid <sup>[10]</sup>.

**Camphorated Parachlorophenol (CPC):** Introduced in 1891, is a mixture of parachlorophenol and gum camphor (2:3 ratio). It has an aromatic odor and light amber colour. Camphor reduces the irritation caused by parachlorophenol and acts as a vehicle. CPC's antimicrobial effectiveness is well documented, and its vapours can penetrate through the apical foramen.

**Camphorated Monoparachlorophenol (CMCP):** With a ratio of 3:7 para-monochlorophenol to camphor, is less irritating and more bactericidal than phenol, without causing albumin coagulation <sup>[7]</sup>.

**Cresol (Tricresol):** Coal tar derivative with phenolic odor, existing in three isomeric forms. It is a powerful disinfectant, reportedly three times more effective than phenol.

**N<sub>2</sub>:** Intracanal medicament containing paraformaldehyde and phenyl mercuric borate. It has strong antimicrobial activity but is irritating and toxic. Its antibacterial effect lasts only 7-10 days <sup>[10]</sup>.

**Formocresol:** A mix of formalin and cresol (ratios vary 1:2 to 1:1), was introduced in 1905. It is a reddish transparent liquid containing formaldehyde (19%), cresol (35%), glycerine (46%), and water. It is bactericidal due to protein bonding but highly irritating and toxic. Formaldehyde is now classified as carcinogenic, and its use in dentistry is discouraged, especially in children due to genotoxicity risks <sup>[7]</sup>.

**Halogens:** (Chlorine-based) Have disinfectant properties inversely related to atomic weight. Chlorine is the most effective. Sodium hypochlorite and chloramines are commonly used for short-term root canal dressings.

**Sodium Hypochlorite:** Primary irrigant used today (0.5–5.25% concentration). It dissolves necrotic tissue and debris during root canal treatment.

**Iodine preparations:** Such as iodine tincture (5% in alcohol) and iodine potassium iodide, are used for surgical field disinfection and intracanal medication <sup>[11]</sup>.

**Chlorhexidine:** Synthetic cationic bis-guanide with positive charge that disrupts bacterial cell membranes, increasing permeability and killing bacteria <sup>[12]</sup>.

**Quaternary Ammonium Compounds:** Mildly effective cationic detergents and wetting agents, non-irritating in weak solutions, and more effective in alkaline media. <sup>[10]</sup> PBSC (phenyl benzoate sodium caprylate) and PBSC-Nystatin were widely used pastes, but their use is now obsolete due to potential antibiotic sensitivity and interference with culturing <sup>[13]</sup>.

**Ledermix Paste:** Combines corticosteroids (triamcinolone acetonide 1%) and antibiotics (demeclocycline) to reduce inflammation and pain in root canals. It is water-soluble, non-setting, and releases medication gradually. It has shown better healing outcomes compared to gutta-percha fillings <sup>[7]</sup>.

**Sulphonamides:** Bacteriostatic agents interfering with bacterial metabolism. They are used for infected open teeth but are ineffective in the presence of pus and tissue debris. Their use can cause yellowish tooth discoloration <sup>[10]</sup>.

### Calcium Hydroxide

Calcium hydroxide is the most extensively used intracanal medicament, especially in multi-visit root canal therapy. Its alkaline pH (~12.5) is lethal to most microorganisms by denaturing cellular enzymes and damaging cytoplasmic membranes. It also promotes mineralized tissue formation by stimulating alkaline phosphatase activity and hard tissue deposition. <sup>126</sup>

### Clinical Applications

- Apexification in immature teeth
- Management of internal resorption
- Inhibition of inflammatory root resorption
- Neutralization of lipopolysaccharides (LPS)

### Limitations

- Incomplete effectiveness against *Enterococcus faecalis* and *Candida albicans*
- Limited action in acidic pH or exudative environments
- Potential to weaken dentin when used long-term

To enhance its efficacy, calcium hydroxide is often combined with chlorhexidine or incorporated into nanoparticle formulations <sup>[14]</sup>.

### Triple Antibiotic Paste (TAP)

TAP consists of a combination of ciprofloxacin, metronidazole, and minocycline. It is particularly useful in regenerative endodontic procedures (REPs) for disinfection of immature teeth with necrotic pulps. TAP has shown high success in reducing bacterial load in root canals prior to revascularization <sup>[15]</sup>.

### Advantages

- Broad-spectrum action against anaerobes and facultative bacteria
- Synergistic effect of three different antibiotics
- Useful in cases of resistant infections

### Drawbacks

- Minocycline-related tooth discoloration
  - Risk of antibiotic resistance
  - Cytotoxic effects on stem cells and apical papilla cells
- Modifications like DAP (without minocycline) or the use of calcium hydroxide as an alternative are being investigated for safer regenerative outcomes. <sup>[16]</sup>

### Herbal Medicaments

**Propolis (Beeswax):** Propolis contains bioactive compounds like flavonoids, phenolics, and aromatic acids. It has demonstrated antimicrobial, anti-inflammatory, antioxidant, and cytotoxic activities. Due to its effectiveness against *Enterococcus faecalis*, it is used both as an intracanal medicament and irrigant, often in combination with calcium hydroxide to enhance disinfection <sup>[17]</sup>.

**Aloe Vera (*Aloe barbadensis miller*):** Aloe vera gel contains active compounds like aloin and aloe-emodin. It exhibits significant antibacterial, antifungal, and anti-inflammatory effects. These properties make it suitable for use in endodontics as both an intracanal medicament and an irrigating solution <sup>[18]</sup>.

**Ginger (*Zingiber officinale*):** Ginger is known for its anti-inflammatory, analgesic, antipyretic, and antimicrobial actions. It has shown high antibacterial activity against *E. faecalis*, even outperforming chlorhexidine and garlic extract in some studies, making it a promising alternative in root canal disinfection <sup>[19]</sup>.

**Neem (*Azadirachta indica*):** Neem is a widely used medicinal herb in naturopathy. Its extracts possess strong antimicrobial and antioxidant properties. As an irrigant, neem offers biocompatibility and minimal toxicity compared to sodium hypochlorite, making it a safer option for root canal irrigation <sup>[20]</sup>.

**German Chamomile (*Matricaria recutita*):** Extracted from the dried flowers of German chamomile, this herbal agent contains various acids such as capric, coumaric, and caprylic acids. It has antimicrobial, anti-inflammatory, and antioxidant effects and is effective in smear layer removal due to its mild acidity (pH ~7.6) <sup>[21]</sup>.

### Nanoparticles in Intracanal Medicaments

Nanotechnology enhances drug delivery and disinfection by exploiting particles <100 nm in size with a large surface area-to-volume ratio.

### Common Types

- **Silver nanoparticles (AgNPs):** Strong antimicrobial action; may be cytotoxic at high concentrations.
- **Zinc oxide nanoparticles:** Biocompatible and antimicrobial; can be incorporated into sealers.
- **Iron oxide nanoparticles (Fe<sub>3</sub>O<sub>4</sub>):** Generate ROS; have shown synergy when combined with calcium hydroxide.

### Advantages

- Effective against biofilm-forming organisms like *E. faecalis*
- Can penetrate dentinal tubules
- May be engineered for controlled release

The incorporation of nanoparticles into conventional medicaments (e.g., IONPs + CH) significantly boosts efficacy while reducing required concentrations [22].

### Antimicrobial Photodynamic Therapy (aPDT)

aPDT involves applying a non-toxic photosensitizer to the root canal, which, upon activation with a specific light wavelength, generates singlet oxygen that destroys microbial cells.

### Mechanism

1. Application of photosensitizer (e.g., methylene blue)
2. Light activation (typically laser or LED)
3. ROS production leading to bacterial lysis

### Benefits

- Targets bacteria in biofilms and inaccessible canal areas
- Non-antibiotic; no resistance development
- Enhances outcomes in conjunction with traditional irrigation

### Limitations

- Equipment cost and learning curve
- Limited penetration in large or complex canal systems [23].

### Drawbacks of Intra-Canal Medicaments

**Discoloration of Tooth:** Iodoform-containing calcium hydroxide (CH) pastes can discolor the crown, especially with prolonged use. Similarly, Triple Antibiotic Paste (TAP) causes staining due to minocycline binding with calcium in dentine. Alternatives like Double Antibiotic Paste (DAP), or substituting minocycline with clindamycin, cefaclor, or augmentin can prevent this. Sealing dentinal tubules or internal bleaching can also manage discoloration.

**Dentine Weakening:** TAP reduces dentine microhardness and flexural strength due to its low pH and minocycline's chelating effect. High concentrations (1g/ml) show significant damage. Using methylcellulose-based low-concentration TAP (1mg/ml) is recommended. CH also reduces dentine strength over time [24].

**Cytotoxicity to Stem Cells:** High concentrations of TAP (1g/ml) negatively affect apical papilla stem cells. Safer concentrations between 0.1–2 mg/ml are preferred to reduce cytotoxic effects.

**Difficulty in Removal:** TAP binds tightly to dentine, making removal difficult. Techniques like the Endovac, Endoactivator, XP-Endo Finisher, and use of 1.5% NaOCl with EDTA help but don't ensure complete removal. CH also presents similar removal challenges, affecting canal sealing [16].

Further *in vivo* research and clinical trials are needed to validate these promising approaches for daily practice.

### Conclusion

Intracanal medicaments are a cornerstone of effective root canal therapy, particularly in cases involving complex anatomy, resistant infections, or regenerative goals. From the classic efficacy of calcium hydroxide to the innovative potential of nanotechnology and photodynamic therapy, the selection of intracanal medicaments should be based on clinical context, microbial profile, and biocompatibility. The ongoing development of safer, more effective, and biologically integrated medicaments heralds a new era in endodontic disinfection and healing.

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