



## Use of ethylenediaminetetraacetic acid as an irrigating solution in root canals

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### ABSTRACT

**Introduction:** ethylenediaminetetraacetic acid (EDTA) is a chelating agent used in endodontics to facilitate cleaning and disinfection of root canals by removing the smear layer and improving the sealing of obturation materials.

**Objective:** to present the benefits of EDTA as a root canal irrigant.

**Methods:** a systematic literature review was conducted. A search strategy was developed across multiple databases, and relevant information was retrieved, analyzed, synthesized, and selected based on relevance and pertinence.

**Development:** ethylenediaminetetraacetic acid is a hexadentate chelating agent capable of forming stable complexes with metal ions, especially calcium, giving it efficacy in removing the smear layer during endodontic irrigation. Its use as a 17 % solution for 1–3 minutes opens dentinal tubules and improves permeability, enhancing the penetration of antimicrobial agents. However, prolonged exposure may weaken dentin and reduce its resistance. Although direct clinical evidence is limited, in vitro studies and systematic reviews support its routine incorporation into endodontic protocols, with an acceptable safety profile and extensive accumulated clinical experience.

**Conclusions:** as an endodontic irrigant, ethylenediaminetetraacetic acid optimizes the removal of residual dentin debris, pulpal remnants, and bacteria, improving canal preparation. However, its lack of biocompatibility requires clinical caution to protect the patient's soft tissues during the procedure.

**Keywords:** Smear Layer; Endodontics; Iron Chelating Agents.

## INTRODUCTION

Endodontic therapy aims for complete disinfection of root canals through mechanical instrumentation and irrigating solutions. Mechanical preparation generates an irregular layer known as the smear layer, composed of organic and inorganic debris—including necrotic pulp tissue, bacteria, and dentinal particles. Its removal requires irrigants: sodium hypochlorite is effective against organic components, while 17 % ethylenediaminetetraacetic acid (EDTA) dissolves the inorganic fraction. The combination of both agents enables comprehensive root canal cleaning, optimizing clinical outcomes and ensuring greater success in endodontic treatments.<sup>(1)</sup>

Ethylenediaminetetraacetic acid (EDTA) is a tetracarboxylic organic acid derived from ethane through methylene group amination followed by diacetylation of each amino group. Its primary chemical property—and the basis for its use in dentistry—is its ability to act as a metal ion chelating agent. A coordination group consists of a chemical group and a metal ion bonded via a coordinate (dative) covalent bond. The reaction that forms such groups is called chelation, and substances capable of forming more than one coordinated bond with a metal ion are known as chelating agents.<sup>(2)</sup>

The coordination compounds formed by chelating agents and metal ions are called chelates, in which various chemical groups of the chelator form coordinate bonds with the metal, surrounding it like a claw—hence the term “chelate,” from the Greek *khele* (claw). Among chelating agents, EDTA stands out as hexadentate due to its ability to coordinate octahedrally through six functional groups, enabling effective binding of ions such as Ca, Mg, Mo, Fe, Cu, and Zn. Thanks to this property, EDTA is used to remove trace metals from distilled and purified water and in complexometric chemical analyses, where the stability of its chelates ensures precise and reliable results.<sup>(3,4)</sup>

EDTA is widely used in biomedical research as an enzyme inhibitor, as it can bind  $\text{Co}^{2+}$ ,  $\text{Fe}^{2+}$ ,  $\text{Cu}^{2+}$ , or  $\text{Zn}^{2+}$  ions located in the active sites of various enzymes (metalloenzymes), abolishing their catalytic activity, inactivating them, and inhibiting the reactions they catalyze.<sup>(5)</sup> For example, EDTA inhibits the sequential hydrolysis of peptide bonds in proteins from the C-terminal end mediated by carboxypeptidase A by chelating the  $\text{Zn}^{2+}$  ion in the enzyme’s active site. Similarly, EDTA’s chelation of blood calcium allows its use as an anticoagulant, as calcium is essential for the coagulation cascade—specifically, divalent cationic bridges mediated by  $\text{Ca}^{2+}$  ions are required for the binding of coagulation factors.<sup>(6)</sup> Based on the above, this review was conducted to present the benefits of EDTA as a root canal irrigant.

## METHODS

A systematic review of the scientific literature on the benefits of EDTA as a root canal irrigant was performed. Preliminary searches were conducted in November 2023 in PubMed and Google Scholar. To optimize information retrieval, controlled descriptors and additional keywords—both MeSH and DeCS—related to EDTA use in endodontic practice were included alongside the main terms “EDTA” and “endodontics.” These included: “Ethylenediaminetetraacetic Acid,” “Root Canal Irrigants,” “Chelating Agents,” “Smear Layer Removal,” “Root Canal Preparation,” “Endodontic Irrigation,” and “Dentin Conditioning.” Combining these terms with Boolean operators (AND, OR) enhanced search sensitivity and ensured identification of a robust set of relevant studies.

The initial search identified 569 potentially relevant articles. After removing duplicates and screening titles and abstracts, 200 articles were pre-selected for detailed evaluation. Finally, 28 studies met the inclusion criteria (articles in Spanish or English, published within the last five years) and demonstrated the highest methodological quality and clinical relevance. Case reports, editorials without original data, and studies with high risk of methodological bias were excluded.

Evidence synthesis was organized according to key aspects of endodontic treatment related to EDTA use. Information was categorized into thematic areas including: chemical and chelating properties of EDTA, efficacy in smear layer removal, interactions with other irrigants, effects on dentin structure, irrigation protocols and application times, and emerging alternatives to conventional chelating agents.

## DEVELOPMENT

Ethylenediaminetetraacetic acid is a synthetic organic compound belonging to the aminopolycarboxylic acid family, with the molecular formula  $C_{10}H_{16}N_2O_8$  and a molecular weight of 292.24 g/mol. Its chemical structure features two amino groups ( $-NH_2$ ) linked by an ethylene bridge, each substituted by two acetic acid groups ( $-CH_2COOH$ ), resulting in four carboxylic groups. This configuration gives EDTA its remarkable ability to act as a multidentate chelating agent.<sup>(7)</sup>

The most relevant property of EDTA in endodontics is its ability to form stable coordination complexes with metal cations, particularly divalent ions such as calcium ( $Ca^{2+}$ ), magnesium ( $Mg^{2+}$ ), iron ( $Fe^{2+}$ ), and zinc ( $Zn^{2+}$ ). The term "chelation" derives from the Greek *khele* (claw), reflecting how the EDTA molecule wraps around a metal ion via multiple coordination bonds. EDTA can form up to six bonds with a single metal ion (two nitrogen and four oxygen atoms from carboxyl groups), making it a hexadentate chelating agent.<sup>(8)</sup>

Chelation occurs when EDTA donates electron pairs from its nitrogen and oxygen atoms to vacant orbitals of the metal ion, forming coordinate covalent bonds that create a closed heterocyclic ring called a chelate. This complex exhibits far greater thermodynamic stability than complexes with monodentate ligands. For instance, the EDTA-calcium chelate has a stability constant ( $\log K = 10.7$ ), demonstrating high affinity for calcium ions in dentinal hydroxyapatite. In aqueous solution, EDTA exists in various protonation states depending on pH; the tetrasodium form ( $Na_4EDTA$ ) is most commonly used in endodontic formulations due to its high water solubility. At neutral or slightly alkaline pH—the conditions under which it is most reactive for calcium chelation—it maximizes its effectiveness on mineralized dentin.<sup>(9,10)</sup>

EDTA's mechanism of action on radicular dentin is based on its selective chelation of calcium ions from hydroxyapatite crystals [ $Ca_{10}(PO_4)_6(OH)_2$ ], the main mineral component of dentin. Upon contact, EDTA molecules preferentially interact with calcium ions in the hydroxyapatite lattice, forming soluble calcium-EDTA complexes that disperse into the irrigant solution, thereby progressively demineralizing the superficial dentin layer.<sup>(11)</sup>

The smear layer generated during biomechanical instrumentation has two structural components: a superficial amorphous layer 1–2 micrometers thick covering instrumented dentin, and a deeper extension penetrating dentinal tubules up to 40 micrometers. The superficial portion consists of approximately 50 % inorganic material (mainly fragmented hydroxyapatite crystals) and 50 % organic matter (denatured collagen, pulpal remnants, microorganisms). EDTA efficiently acts on the mineral fraction of both components, dissolving it and enabling mechanical removal during irrigation.<sup>(12,13)</sup>

EDTA's chelating action not only removes the smear layer but also significantly affects peritubular and intertubular dentin. Recent studies show that highly mineralized peritubular dentin is especially vulnerable to EDTA-induced demineralization. This process opens and widens dentinal tubules, increasing tissue permeability and facilitating the diffusion of antimicrobial solutions into deeper dentin layers.<sup>(14,15)</sup>

Scanning electron microscopy (SEM) analyses have shown that irrigation with 17 % EDTA for brief intervals (1–3 minutes) achieves nearly complete smear layer removal, exposing a surface with open, unobstructed dentinal tubules. However, recent research indicates that exposure times exceeding 5 minutes cause marked demineralization of peritubular dentin, resulting in dentin loss and risk of structural weakening of root canal walls.<sup>(16)</sup>

The most widely used and validated EDTA concentration in endodontics remains the 17 % (w/v) solution. Recent studies confirm that this formulation—introduced in clinical practice in the mid-20th century—remains effective for smear layer removal without causing significant structural changes in radicular dentin, provided exposure time is controlled. EDTA 17 % is available in both liquid and gel forms, with comparable efficacy but different physical properties affecting distribution within the canal system.<sup>(17)</sup>

Lower EDTA concentrations (10 % and 5 %) have been proposed to reduce the risk of excessive dentin erosion without compromising chelating capacity. In vitro comparative studies suggest that 10 % EDTA requires slightly longer application times to achieve smear layer removal comparable to 17 % EDTA, though it offers a more favorable safety profile for dentin preservation. However, clinical evidence supporting the superiority of these lower concentrations remains limited.<sup>(18,19)</sup>

On the other hand, EDTA gel formulations have gained relevance in recent years due to their operational advantages in terms of handling and retention within the root canal. Although they maintain the active concentration at 17%, they incorporate thickening agents—such as carbopol or hydroxypropyl methylcellulose—that increase their viscosity and slow down their diffusion, allowing for a more controlled application, especially in wide canals or those with complex anatomies. Moreover, their consistency facilitates introduction through endodontic files, promoting an active application that combines chemical and mechanical action.<sup>(20)</sup>

The optimal EDTA application protocol has been extensively studied, and current consensus recommends its use as a final irrigant—after complete biomechanical instrumentation and thorough sodium hypochlorite irrigation. This sequence ensures sodium hypochlorite first acts on organic components (pulp tissue, organic smear layer, microbes), while EDTA subsequently removes the inorganic smear layer fraction.<sup>(21)</sup>

Regarding application time, scientific evidence suggests 1–3 minutes is sufficient for effective smear layer removal without excessive dentin erosion. SEM studies show that 1 minute of 17 % EDTA exposure significantly opens dentinal tubules and removes the superficial smear layer, while 3 minutes achieves more complete intratubular cleaning. Exposure beyond 5 minutes offers no additional cleaning benefit and may increase the risk of excessive peritubular dentin demineralization.<sup>(22,23)</sup>

EDTA irrigation induces structural and morphological changes in radicular dentin—removing the smear layer and opening dentinal tubules—thereby increasing dentin permeability and facilitating antimicrobial penetration into deeper layers.<sup>(24,25,26)</sup> SEM studies show that 1–3 minutes of 17 % EDTA exposure causes selective demineralization of highly mineralized peritubular dentin, resulting in tubular widening and exposure of the organic collagen matrix.<sup>(21)</sup>

Consequently, dentin experiences a significant reduction in surface microhardness, as documented by micro- and nano-indentation tests compared to untreated dentin.<sup>(27)</sup> Ultimately, EDTA-induced demineralization may compromise dentin's biomechanical properties; various studies report reduced fracture resistance when the smear layer is fully removed and dentin is exposed to chelators—especially in teeth with thin root walls or widely instrumented canals.<sup>(28)</sup> Therefore, appropriate concentrations and application times are essential. Many studies agree exposure should not exceed a few minutes to maximize canal cleaning without compromising tooth structural integrity.<sup>(29)</sup>

EDTA's biocompatibility has been extensively studied and generally shows a favorable safety profile at standard concentrations and clinically recommended exposure times. Cytotoxicity studies show moderate effects on fibroblasts, periodontal ligament cells, and osteoblasts—less severe than those caused by sodium hypochlorite. Toxicity is time- and concentration-dependent, increasing if protocols are exceeded. In animal models, small amounts extruded beyond the apex cause only transient, mild inflammation—less severe than NaOCl. Clinically, prolonged use should be avoided to prevent dentin weakening, and apical extrusion must be minimized using appropriate needles and controlled pressure. No significant systemic allergic reactions have been reported, and basic protective measures suffice during handling. In case of accidental soft tissue contact, copious irrigation with water or saline is recommended.<sup>(1,8,24)</sup>

Clinical evidence supporting EDTA use in endodontics primarily comes from in vitro studies, animal models, and limited controlled human trials. In vitro studies have significantly advanced understanding of EDTA's mechanisms, dentin effects, and protocol optimization. However, extrapolating these findings to clinical practice requires caution due to inherent limitations of in vitro models.<sup>(6,8)</sup>

Systematic literature reviews conclude that including EDTA as a final irrigant in endodontic protocols results in significantly more effective smear layer removal than sodium hypochlorite alone. This benefit translates into greater tubular opening, increased dentin permeability, and potentially improved penetration of intracanal medicaments or sealers. However, direct evidence linking EDTA use to improved long-term clinical success rates remains limited and warrants further research.<sup>(9,10)</sup>

Randomized clinical trials directly comparing protocols with and without EDTA in terms of objective clinical outcomes (radiographic success, absence of symptoms, periapical tissue preservation) are scarce. The few available generally report favorable trends in the EDTA group, though differences are not always statistically significant.<sup>(1,2,8,14,24)</sup>

pite these limitations in high-level clinical evidence, current professional consensus strongly supports routine inclusion of EDTA in endodontic irrigation protocols, based on robust experimental evidence of its smear layer removal efficacy, acceptable safety profile, and decades of favorable clinical experience. Future research should focus on well-designed, multicenter clinical trials with long-term follow-up to more precisely quantify EDTA's impact on long-term endodontic outcomes.<sup>(9,15,22,30)</sup>

## CONCLUSIONS

The role of an irrigant in endodontics is crucial for root canal treatment, and EDTA's properties significantly enhance the procedure by enabling optimal removal and disintegration of elements within root canals—such as residual dentin, pulpal remnants, and bacteria. However, it is important to emphasize that EDTA is not fully biocompatible with the human body; therefore, clinical caution is essential to protect the patient's soft tissues during the procedure.

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