



REVIEW ARTICLE

Effects of EDTA as an irrigating solution alone or combined with NaOCl vs. other substances during treatment of the root canal system

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ABSTRACT

Introduction: effective disinfection of the root canal system depends on irrigation protocols capable of eliminating biofilms, tissue remnants, and smear layer, all of which directly influence the clinical success of endodontic treatment.

Objective: to examine differences between the use of ethylenediaminetetraacetic acid as a single irrigant or combined with sodium hypochlorite versus other irrigation solutions in root canal therapy.

Methods: a systematic documentary review was conducted following prisma guidelines, through searches in specialized databases from 2017 to 2023. High-impact and up-to-date sources were selected and analyzed to establish a pertinent approach to the topic.

Development: studies agree that ethylenediaminetetraacetic acid has strong chelating capacity, facilitates removal of the smear layer, and promotes exposure of dentinal tubules. Its effectiveness increases when combined with sodium hypochlorite, particularly for removing residual tissue and intracanal calcium hydroxide. Compared with solutions such as citric acid, maleic acid, or preparations combined with chlorhexidine and detergents, its performance varies depending on the root third evaluated. Some emerging alternatives, such as nanobubbles and new irrigation systems, show superior potential for apical cleaning without compromising dentin microhardness. The sequence, concentration, and activation of the irrigant significantly influence clinical outcomes.

Conclusions: ethylenediaminetetraacetic acid remains a key component of irrigation protocols, especially when used together with sodium hypochlorite. Currently, new technologies offer potential improvements, although further evidence is required to support their effectiveness.

Keywords: Endodontics; Chemical Compounds; Therapeutic Irrigation; Root Canal Therapy.

INTRODUCTION

Root canal treatment is a widely used procedure whose main goal is the effective elimination of intracanal biofilm, a structure formed by bacteria with resistance up to a thousand times greater than in their planktonic form due to the protective matrix that surrounds them, making disinfection difficult regardless of the instrumentation technique used and conditioning the preservation of the tooth. Although conventional endodontic techniques of the latest generation continue to be considered the gold standard, their ability to activate irrigants and optimize disinfection has limitations, which has driven the search for complementary alternatives. Among the most commonly used irrigants are sodium hypochlorite (NaOCl), chlorhexidine, ethylenediaminetetraacetic acid (EDTA), and citric acid; of these, NaOCl is the most preferred in chemomechanical debridement due to its broad - spectrum antimicrobial activity and its ability to dissolve organic and inorganic residues.⁽¹⁾

Instrumentation of root canals leads to the formation of a residual layer known as the smear layer, which adheres to the dentin walls; this can contain microorganisms and their by - products, serving as a substrate for biofilm formation.^(2,3) Vega and colleagues,⁽⁴⁾ state that since the smear layer contains irritating microorganisms, biofilms, and necrotic tissue remnants, it must be completely removed from the walls so that it does not act as a physical barrier between filling materials and dentin, preventing the entry and flow of irrigating solutions into the dentinal tubules and potentially leading to endodontic treatment failure.

The anatomical complexity of the root canal system can result in 35 – 50 % of it remaining intact through endodontic instrumentation, which is why it is necessary to use an irrigating solution capable of having antimicrobial action, as well as the ability to dissolve residual pulp tissue and to remove the smear layer and other waste products generated during instrumentation.⁽⁵⁾

Sodium hypochlorite is the most commonly used irrigating solution in endodontics, but it has limitations, including its insufficient ability to completely remove the smear layer and its lack of substantivity, a property that would allow an antimicrobial agent to adhere to tissues with hydroxyapatite and be released gradually. These limitations have motivated the incorporation of complementary substances aimed at enhancing its effectiveness. Therefore, the complementary use of a chelating agent such as ethylenediaminetetraacetic acid (EDTA) has been proposed to remove the layer of smear created after root canal preparation. It is usually used in concentrations of 10 % to 17 %; its pH is modified from a value of four to values of 8 to increase its chelating activity.^(5,6)

EDTA is a complex molecule with a structure similar to a claw that binds and captures divalent and trivalent metal ions such as calcium and aluminum to form a stable ring structure. EDTA removes proteins from the bacterial surface by combining with metal ions in the cell envelope, causing bacterial death. EDTA forms a stable complex with calcium. When all available ions have been bound, no further dissolution occurs; therefore, EDTA is self - limiting.⁽⁷⁾ Given this, it is understood that EDTA is a chelating agent and, therefore, is responsible for removing the smear layer. Additionally, it has an antibacterial effect, probably due to the chemical chelation involving the outer bacterial membrane; it has been reported that EDTA decalcifies dentin to a depth of 20 to 30 μm in 5 minutes.⁽⁶⁾

The combination of EDTA and NaOCl has been proposed as an effective irrigation protocol for removing organic and inorganic components during root canal therapy. However, controversies persist regarding the ideal sequence, volume, and application time. Usually, NaOCl is used during instrumentation and EDTA at the end to complete the removal of the smear layer. The literature indicates that using NaOCl before EDTA allows the hydroxyapatite layer to partially protect collagen fibers, while applying it after EDTA intensifies its dissolving action on the previously exposed collagen. Similarly, it has been observed that the sequence of use influences the opening of dentinal tubules and the degree of dentin erosion.⁽⁸⁾

Based on the above, the need arises to conduct a literature review with the objective of examining the differences between the use of ethylenediaminetetraacetic acid as a single irrigant or combined with sodium hypochlorite versus other irrigating solutions in root canal therapy.

METHODS

To conduct the following bibliographic review, a documentary methodology was employed. The material used to analyze the differences between the effects of EDTA as an irrigant alone or combined with NaOCl versus other irrigating substances consisted of 17 original articles. The period considered was from 2017 to 2023. These articles were obtained through an electronic search of databases such as Journal of Endodontics, International Endodontic Journal, American Journal of Materials Science, The Journal of Contemporary Dental Practice, Journal of Dental and Medical Sciences, The Cureus Journal of Medical Science, Multidisciplinary Digital Publishing Institute, PubMed, Wiley Online Library, and Iranian Endodontic Journal. Data were obtained through a content matrix and interpreted using content analysis. When searching for this information, the following keywords were used: "EDTA vs NaOCl"; "EDTA"; "irrigation solutions".

For the search, inclusion criteria were established to select only relevant and high - quality literature. Articles were considered if their abstract and/or full text were available, published between 2017 and 2023, written in English, and published in high - impact scientific journals such as MDPI, PubMed, Wiley Online Library, Journal of Endodontics, International Endodontic Journal, American Journal of Materials Science, and Journal of Dental and Medical Sciences, among others. Only studies with a direct and substantial relationship to the researched topic were included. Articles without access to their content, those that did not provide useful information for the study's objectives, and those not within the defined period for the review were excluded.

Taking into account the above, articles were selected, not all of which met the previously indicated parameters. Therefore, only 18 original articles with full text in English were used, all within the period from 2017 to 2023, which in turn are related to the objectives of the present bibliographic review. In this way, the existing problem was resolved, and the differences between the effects of EDTA as an irrigant alone or combined with NaOCl versus other irrigating substances during root canal treatment were determined. Figure 1 shows the flowchart developed in the process.

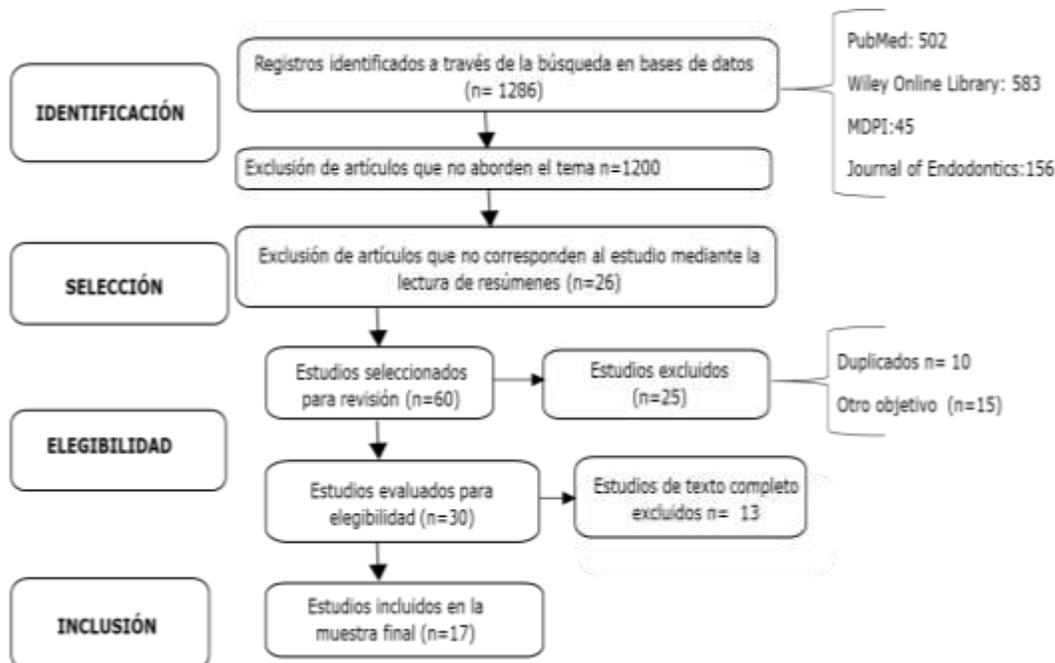


Fig. 1 Flowchart.

DEVELOPMENT

Endodontics has been transformed by continuous research, which has revolutionized both its diagnosis and treatment. The introduction of new tools and techniques has dramatically changed the way pulp diseases are approached. These technological advancements continue to raise the level of care in this field, resulting in a significant improvement in patients' quality of life and more reliable and lasting outcomes.

Table 1. Description of the articles used for the research.

Source	Results	Conclusions
(Boutsioukis et al., 2022) ⁽¹⁾	Although NaOCl is the primary irrigant due to its ability to dissolve organic tissue, it does not remove the smear layer, hence the need for EDTA at the end of instrumentation. Given its low antimicrobial action, EDTA must be complemented with NaOCl following a sequential protocol: NaOCl during preparation, EDTA to remove the smear layer, and a final rinse with NaOCl. While alternatives like synthetic antimicrobial peptides are being studied, the NaOCl-EDTA combination with ultrasonic activation remains the irrigation standard.	NaOCl and EDTA complement each other to be the standard method of irrigation protocols.

(Nogo-Zivanović et al., 2019) ⁽²⁾	This study compared smear layer removal and changes in dentin mineral composition after initial irrigation with 5.25% NaOCl and final irrigation with MTAD, Qmix, or 17% EDTA. No chelating solution completely removed the smear layer, although all were effective in the coronal and middle thirds. In the apical third, Qmix showed significantly greater smear layer reduction than EDTA and similar to MTAD, likely due to its combination of EDTA, CHX, and detergent. In terms of demineralization, MTAD caused the greatest mineral loss and greater collagen fiber exposure.	EDTA combined with Chlorhexidine and a detergent is effective in removing the smear layer in the coronal, middle, and apical thirds, unlike EDTA alone.
(Tosco et al., 2023) ⁽³⁾	In the comparison of the four irrigation systems, group D (ANP-EndoVac) was the only one that consistently showed satisfactory results in the coronal, middle, and apical thirds, achieving the highest efficacy in removing the smear layer. Group A used conventional needle irrigation combined with 5.25% NaOCl, saline solution, and 17% EDTA. Group B employed Irriflex with the same sequence of solutions. Group C combined Irriflex with ultrasonic activation using Z Activator and 5.25% NaOCl. However, none of these outperformed group D, which integrated the ANP system with 5.25% NaOCl and 17% EDTA.	Efficacy in removing the smear layer even in the apical third by combining 5.25% NaOCl + 17% EDTA.
(Mohammadi et al., 2017) ⁽⁵⁾	This review establishes that EDTA can cause NaOCl to lose its tissue - dissolving ability, while NaOCl cannot reduce EDTA's smear layer - removing capacity or alter EDTA's demineralization ability. EDTA's antimicrobial activity against Enterococcus faecalis and Candida albicans is greater compared to NaOCl.	EDTA is effective in removing the smear layer and is more effective against Enterococcus faecalis and Candida albicans compared to NaOCl.
(Doumani et al., 2017) ⁽⁷⁾	EDTA exhibits germicidal activity between 10% and 15%, effective against Candida albicans and E. faecalis. Its biocompatibility shows variable results: some studies observed no periapical damage after its extrusion, while others reported bone decalcification and macrophage function inhibition even at low concentrations. However, its use for 28 days following a pulpotomy did not cause pulp necrosis.	EDTA is effective against Enterococcus faecalis and Candida albicans and does not cause pulp necrosis after pulpotomy.
(Elbahary et al., 2020) ⁽⁸⁾	Effective sealing depends on proper adhesion, favored by smooth surfaces in chemical bonds and rough surfaces in micromechanical bonds. In 150 dentin sections, 17% EDTA alone or combined with 5.25% NaOCl for 10 minutes generated greater roughness than the control or NaOCl alone. Although NaOCl as the final irrigant increased roughness, the order of	Irrigation with 17% EDTA combined with 5.25% NaOCl provides greater surface roughness, offering better adhesive strength for the sealer compared to NaOCl alone.

	application did not significantly alter the results.	
(Zahed Mohammadi et al., 2019) ⁽⁹⁾	In a comparison between EDTA, MTAD, Tetracelan, citric acid, and Qmix, it was determined that QMix (EDTA + CHX + detergent) is as effective as EDTA in removing the smear layer after the application of 5.25% NaOCl. Several studies establish that EDTA is more effective than MTAD, while others propose that MTAD is more efficient than EDTA; controversy persists on this topic.	EDTA is effective in removing the smear layer, with no significant differences compared to its combination with chlorhexidine or detergents. Additionally, there is no consensus on whether it surpasses or is surpassed by MTAD in efficacy.
(Shekhar et al., 2023) ⁽¹⁰⁾	Smear layer removal improves sealer penetration into dentinal tubules. In the comparison between 17% EDTA, 10% citric acid, and 7% maleic acid, all three were equally effective in the coronal third. However, in the middle and apical thirds, citric acid and maleic acid achieved better smear layer removal and greater sealer penetration than EDTA.	EDTA is effective in removing the smear layer in the coronal third, while its efficacy decreases in the middle and apical thirds compared to citric acid and maleic acid.
(Alshwali et al., 2020) ⁽¹¹⁾	EDTA is fundamental in endodontics and promotes the release of growth factors for pulp regeneration at concentrations between 3% and 17%. However, its prolonged use can compromise the dentin matrix and reduce microhardness, unlike nanobubbles, which remove the smear layer without affecting dentin. In this study, 17% EDTA applied for 1 minute did not completely remove the smear layer or demineralize the peritubular dentin.	NB allows for more effective removal of the smear layer and exposure of dentin than 17% EDTA without affecting dentin microhardness as much as EDTA does.
(Tonelli et al., 2020) ⁽¹²⁾	Calcium hydroxide is the most commonly used intracanal dressing, but it must be completely removed to ensure proper sealing and avoid interference with apex locators. The combination of 17% EDTA with 5.25% NaOCl showed significantly superior removal compared to NaOCl alone, achieving more effective Ca(OH) ₂ removal and better lateral canal filling.	The combination of NaOCl with 17% EDTA enhances the removal of intracanal calcium hydroxide, thereby improving root canal filling.
(Mello I et al., 2008) ⁽¹³⁾	The study evaluated volumes of 5, 10, and 15 ml of 17% EDTA as a final rinse and compared them with a 1% NaOCl control. All three volumes of EDTA showed smear-free surfaces in all thirds, with no differences among them. In contrast, the control group presented a thick layer of smear, confirming the need for a chelating agent to remove inorganic components. It was concluded that low volumes of 17% EDTA are sufficient for effective smear layer removal.	Variations in the volume of 17% EDTA do not hinder the removal of the smear layer. There is a significant difference in the presence of smear layer when using a chelating agent in comparison to NaOCl alone.

(Grando CP., et al., 2019) ⁽¹⁴⁾	The study compared 2.5% NaOCl + 17% EDTA with 1% peracetic acid for removing the smear layer. Both regimens showed similar efficacy in antimicrobial action against <i>E. faecalis</i> and in removing the smear layer, although NaOCl - EDTA achieved greater removal in the middle third.	NaOCl - EDTA is effective in antimicrobial action against <i>E. faecalis</i> and in removing the smear layer.
(Álvarez-Sagües et al., 2021) ⁽¹⁵⁾	The study compared the antibacterial capacity of different irrigants activated with PUI: 17% EDTA, 9% HEDP + 5.25% NaOCl, and 17% EDTA + 5.25% NaOCl. The results showed that HEDP was the most effective, with no bacterial recovery, followed by EDTA mixed with NaOCl, and finally EDTA alone.	The combination of EDTA + NaOCl is more effective in eliminating bacteria compared to EDTA alone.
(Murugesan K, et al., 2022) ⁽¹⁶⁾	The efficacy in removing the smear layer was evaluated in 50 freshly extracted premolars, distributed into five groups: Group I - 17% EDTA, Group II - 5% NaOCl, Group III - Oxum, Group IV - ozonated water, and Group V - normal saline solution. Group I, treated with 17% EDTA, had the lowest smear layer scores compared to the other groups.	EDTA is the superior irrigant in removing the smear layer in root canal treatment.
(Wang et al., 2017) ⁽¹⁷⁾	EDTA alone has weak or no antimicrobial activity. In this study, the combination of the synthetic peptide DJK5 with EDTA showed equivalent efficacy to DJK5 alone against <i>E. faecalis</i> and biofilms grown on hydroxyapatite discs.	EDTA is equally effective as the enantiomeric peptide D against <i>E. faecalis</i> .

To contextualize the findings of the literature and support the analysis conducted, various studies examining the behavior of EDTA, either alone or in combination with other irrigants and activation systems, were collected and organized across different critical aspects of endodontic therapy. These works include narrative and systematic reviews, in vitro research, and comparative evaluations exploring its efficacy in removing the smear layer, modifying the dentin surface, sealer penetration, antimicrobial action, and its interaction with alternative solutions or emerging technologies. The following table synthesizes the most relevant contributions of each article, allowing for an integrated visualization of the available evidence and its relationship with the objectives of the present research.

Upon analyzing the research presented as the basis for this study, it is determined that EDTA is an effective substance for removing the smear layer, as there is sufficient evidence supporting this hypothesis provided by different authors,^(1,5,11,14,16) who agree on the efficacy of EDTA combined with 5,25 % NaOCl. It is also important to mention that these studies highlight the importance of the combination of NaOCl and EDTA as the standard method of irrigation protocols.

Similarly, some reports indicate that 17 % EDTA, when combined with Chlorhexidine and a detergent to form the QMix solution, is more effective in removing the smear layer in the coronal and middle thirds than EDTA alone. However, comparing these studies reveals a decreased efficacy in the apical third when using EDTA alone compared to QMix (which contains a mixture

of EDTA + CHX + detergent) and other solutions such as 10 % Citric Acid and 7 % Maleic Acid.^(2,5,10) In all these studies, the efficacy of EDTA at different volumes was evaluated, which can vary from 3ml, 5ml, 10ml, 15ml, and despite its variability, it was determined in the study presented by Mello et al.,⁽¹³⁾ that variations in the volume of 17 % EDTA do not hinder the removal of the smear layer.

On the other hand, it is important to mention that one of the objectives of root canal treatment is the elimination of biofilms and the microorganisms present in them, and EDTA meets one of these requirements, as established by Mohammadi et al.,⁽⁹⁾ and Wang et al.,⁽¹⁷⁾ who determine that the use of EDTA is effective in eliminating *Enterococcus faecalis* and *Candida albicans*. However, the research by Álvarez - Sagües et al.,⁽¹⁵⁾ and Doumani et al.,⁽⁷⁾ highlight that the combination of EDTA + NaOCl is more effective for bacterial elimination compared to EDTA or NaOCl alone.

Furthermore, EDTA has the ability to demineralize dentin, as established by Mohammadi et al.,⁽⁵⁾ however, in a study provided by Nogo - Živanović et al.,⁽²⁾ EDTA was compared with MTAD and it was determined that MTAD provides greater dentin demineralization and greater exposure of collagen fibers compared to EDTA. Similarly, Alshwali et al.,⁽¹¹⁾ mention that nanobubbles (NB) produced by a nanobubble generator obtained better results in removing the smear layer and exposing the dentin more effectively than 17 % EDTA.

Currently, the use of synthetic antimicrobial peptides in root canal treatment is being investigated; however, according to Boutsoukis et al.,⁽¹⁾ their efficacy does not surpass the combination of NaOCl + EDTA. This conclusion differs from that reported by Wang et al.,⁽¹⁷⁾ who state that EDTA is equally effective as the enantiomeric peptide D against *E. faecalis*. These discrepancies may be due to the fact that the first study evaluated the combination of NaOCl + EDTA, while the second focused solely on EDTA.

Another important aspect in endodontic treatment is achieving proper sealing and filling. Elbahary et al.,⁽⁸⁾ report that 17 % EDTA combined with 5,25 % NaOCl increases surface roughness, improving sealer adhesion compared to NaOCl alone. Similar results are supported by Tonelli et al.,⁽¹²⁾ who point out that this combination enhances the removal of intracanal calcium hydroxide, favoring more effective root canal filling compared to the isolated use of NaOCl.

CONCLUSIONS

EDTA enhances the irrigation of the root canal system by improving the removal of the smear layer, dentin debris, and other residues, as well as promoting sealer adhesion and root filling. Its antimicrobial efficacy is increased when combined with solutions such as NaOCl, being capable of eliminating microorganisms like *E. faecalis* and *C. albicans*. However, EDTA should be considered a complement to conventional treatment that combines agents for organic and inorganic residues, and not used in isolation. Although comparisons have been made between EDTA alone and NaOCl and their combination, further evidence is still required regarding its efficacy compared to other chelating agents such as citric acid, maleic acid, or QMix. These benefits highlight its importance in improving clinical outcomes in endodontics.

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