

Review Article

Efficacy of enzyme-based irrigants in endodontics

Osamah Ahmed Qawass^{1*}, Abdullah Khalid Albaz², Abdulrahman Saleh Aldamook³,
Deema Abdulrahman Alhassan², Abdulaziz Hmoud Aloreifi⁴, Motaz Abdullah Alowein²

¹Department of Endodontics, King Fahad Armed Force Hospital, Jeddah, Saudi Arabia

²Department of Dentistry, Prince Sultan Military Medical City, Riyadh, Saudi Arabia

³Department of Dentistry, Comprehensive Care Clinic of MOI, Jeddah, Saudi Arabia

⁴Department of Dentistry, Ministry of Interior, Riyadh, Saudi Arabia

Received: 15 October 2025

Accepted: 30 October 2025

*Correspondence:

Dr. Osamah Ahmed Qawass,

E-mail: tm.akkad@gmail.co

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ABSTRACT

Effective root canal therapy depends on a combination of mechanical instrumentation and chemical irrigation to eliminate bacteria, necrotic tissue, and debris from the complex anatomy of the root canal system. Traditional irrigants such as sodium hypochlorite and EDTA are widely used due to their antimicrobial properties and ability to dissolve organic and inorganic matter. However, these agents carry disadvantages including cytotoxicity, unpleasant taste, tissue irritation, and the potential to weaken dentinal structure. In response to these limitations, enzyme-based irrigants have been introduced as a biologically compatible alternative with selective action on organic components. Enzymes such as papain, bromelain, subtilisin, ficin, and keratinase act by breaking peptide bonds in denatured proteins, leading to the degradation of tissue remnants and the disruption of microbial biofilms. These irrigants have demonstrated effective smear layer modification without aggressive erosion of dentin and have shown compatibility with passive irrigation systems. Their activity under physiological pH conditions, combined with low toxicity and reduced risk of periapical irritation, makes them particularly useful in patients with open apices, complex canal morphology, or heightened sensitivity. Despite these advantages, limitations persist. Enzymatic efficiency may vary depending on tissue type, pH fluctuations, and anatomical challenges. Storage requirements, formulation stability, and compatibility with other endodontic materials remain areas of concern. Some studies have also noted incomplete tissue clearance when used as a sole irrigant. Current evidence supports their use as adjuncts rather than replacements in most clinical settings. Ongoing research is focused on improving formulation consistency, delivery mechanisms, and integration into standardized irrigation protocols. Enzyme-based irrigants present a promising evolution in endodontic disinfection strategies, offering a more tissue-friendly alternative that aligns with minimally invasive and biologically respectful treatment goals.

Keywords: Enzyme-based irrigants, Endodontics, Biofilm disruption, Proteolytic enzymes, Root canal disinfection

INTRODUCTION

Successful root canal therapy hinges on the complete debridement and disinfection of the root canal system, a complex anatomical space often inaccessible to mechanical instrumentation alone. Chemical irrigation is therefore essential to enhance microbial eradication, dissolve tissue remnants, and eliminate smear layers. Traditionally, sodium hypochlorite (NaOCl) and

ethylenediaminetetraacetic acid (EDTA) have been widely used due to their strong antimicrobial and tissue-dissolving properties. However, these agents are associated with significant cytotoxicity, unpleasant taste, and the potential to weaken dentinal walls, prompting the search for safer yet equally effective alternatives.¹

In recent years, enzyme-based irrigants have emerged as promising adjuncts or alternatives in endodontic

disinfection. These agents, derived from biological sources, include proteolytic enzymes such as papain, bromelain, and trypsin, which break down organic matter including necrotic pulp tissue and microbial biofilms. Enzymes act by hydrolyzing peptide bonds in proteins, effectively degrading the structural integrity of biofilm matrices and facilitating bacterial removal.² Unlike conventional irrigants, enzyme-based solutions offer the advantage of biocompatibility, biodegradability, and reduced risk of allergic or adverse tissue reactions, aligning with the principles of minimally invasive and patient-centered care.

One of the major challenges in root canal disinfection is the presence of persistent biofilms, particularly those composed of *Enterococcus faecalis*, a bacterium known for its resistance to conventional treatment methods. Studies have shown that enzyme-based formulations can disrupt these biofilms by targeting the extracellular polymeric substances (EPS) that provide structural support and protection to microbial communities. For example, a bromelain-based irrigant demonstrated significant antibiofilm activity and enhanced dentinal tubule penetration, outperforming even NaOCl in certain *in vitro* settings.³ This has sparked interest in their potential integration into standard irrigation protocols, either alone or in combination with traditional agents to achieve synergistic effects.

Furthermore, enzyme-based irrigants exhibit potential in smear layer removal, an essential step for effective sealing and bonding of obturation materials. The smear layer, composed of organic and inorganic debris, can harbor residual bacteria and interfere with sealer penetration. Some enzyme-based solutions have shown the ability to dissolve organic components of the smear layer without altering the physical integrity of dentin, a benefit over the erosive action seen with EDTA.⁴ Such findings underscore their relevance in enhancing root canal cleanliness while preserving structural stability.

Despite promising laboratory results, the clinical efficacy of enzyme-based irrigants remains under-explored. Limited human trials and lack of standardized formulations hinder definitive conclusions. Nevertheless, their incorporation into multi-agent irrigation strategies and their natural origin make them an appealing subject for ongoing research in endodontics.

Enzyme-based irrigants have shown increasing promise as alternatives or adjuncts to conventional irrigants in endodontics, particularly due to their biodegradability and minimal cytotoxic effects. Their proteolytic action enables effective breakdown of necrotic pulp tissues and disruption of biofilms, addressing one of the most challenging aspects of endodontic disinfection. Bromelain and papain, in particular, have demonstrated the ability to dissolve organic material and inhibit bacterial growth, including *E. faecalis*, a pathogen often associated with persistent periapical infections.^{5,6}

Unlike sodium hypochlorite, which can damage periapical tissues if extruded, enzyme-based irrigants offer a gentler biological profile, making them suitable for patients with tissue sensitivity. Additionally, they have shown potential in smear layer removal by degrading organic residues without causing dentinal erosion, a limitation observed with EDTA and other chelating agents.⁷ However, enzyme stability, optimal concentration, and effective delivery into complex root canal anatomy remain challenges that need further investigation. While *in vitro* studies support their efficacy, robust clinical trials are necessary to validate their performance *in vivo*. Integration of enzymatic agents into current irrigation protocols may provide synergistic benefits, enhance disinfection while preserving dentin integrity and improving long-term outcomes.

EFFICACY VS. CONVENTIONAL IRRIGANTS

The operational capacity of endodontic irrigants in clinical settings is largely defined by their antimicrobial efficacy, ease of delivery, biocompatibility, and overall tissue response. Sodium hypochlorite (NaOCl) has served as a dominant agent in endodontic irrigation for decades. Its reputation for organic tissue dissolution and broad-spectrum antimicrobial activity is well documented. However, the issue with NaOCl lies not in its efficacy but in its risk profile. Accidental extrusion beyond the apex can cause severe cytotoxic effects, including tissue necrosis and inflammatory reactions, which compromise procedural safety.⁸ Clinicians also report unpleasant odor, taste, and dentinal weakening, especially in repeated exposures and variables that impact its occupational usability during root canal therapy.

Enzyme-based irrigants are gradually earning ground as viable options in practice settings where tissue sensitivity, operator safety, and patient comfort are prioritized. Bromelain, papain, and other proteolytic enzymes operate through targeted breakdown of necrotic pulp remnants and biofilm structures, without the aggressive oxidative mechanisms observed with NaOCl. In one experimental setup, papain-based formulations demonstrated strong performance in smear layer removal and biofilm disruption, all while maintaining low cytotoxicity to periodontal ligament fibroblasts.⁹ This safety profile enhances their usability during procedures, reducing the anxiety surrounding apical extrusion and post-operative discomfort.

From an occupational perspective, enzyme-based agents are associated with less aerosol generation compared to traditional irrigants when used with passive ultrasonic activation or syringe irrigation, contributing to safer operatory conditions. Moreover, their shelf stability and non-corrosive behavior toward endodontic instruments make them less demanding in terms of operatory maintenance and instrument lifespan. These seemingly subtle benefits have real implications for day-to-day endodontic workflows, especially in clinics managing

high patient throughput or operating under constraints of minimal invasive protocols.

On the microbial front, enzyme-based irrigants lack the sheer bactericidal potency of high-concentration NaOCl, but they compensate by effectively breaking down the extracellular polymeric substance matrix in biofilms, exposing pathogens to subsequent antimicrobial agents when used in combination therapies. In a comparative study involving bromelain and NaOCl, bromelain showed meaningful reduction in *E. faecalis* colony counts, although not complete elimination. The mechanical disruption, however, made bacterial clusters significantly more vulnerable to follow-up disinfection.¹⁰

The occupational handling properties of enzyme-based irrigants for improved operator focus and procedural endurance in longer cases. In pediatric or geriatric endodontics, where patient compliance is fragile, enzyme-based formulations minimize intraoperative complications and are more forgiving in case of unintended extrusion. Compared to the irritating effects of chlorhexidine and EDTA, their application remains smoother and less prone to triggering soft tissue reactions, which is especially valuable in anatomically complex or inflamed canals.¹¹

MECHANISM OF ENZYMATIC ACTION

Enzyme-based irrigants function through a targeted biochemical process rather than relying on the broad-spectrum cytotoxicity typical of conventional agents. Their effectiveness is based on the activity of proteolytic enzymes that cleave peptide bonds in organic material. This allows them to degrade necrotic pulp tissue and disrupt biofilm structures while preserving healthy periapical tissues. Enzymes such as bromelain and papain are commonly used due to their high substrate specificity and minimal irritation to surrounding structures.¹²

Bromelain, derived from the stem of the pineapple plant, consists of thiol proteases that degrade denatured proteins in the root canal system. It has been shown to act efficiently on collagen fibers and fibrin remnants without damaging the dentin. Studies have reported that bromelain retains its enzymatic activity in the presence of calcium and phosphate, which are abundant in the pulp chamber during decomposition. This stability under ionic conditions allows for predictable action in variable canal environments and improves performance when mechanical instrumentation is limited or incomplete.¹³

Papain, an enzyme extracted from the papaya plant, has broad proteolytic capabilities and targets both terminal and internal bonds in denatured proteins. It is particularly effective at dissolving soft tissues and has demonstrated activity against structural proteins in bacterial biofilms. Its sulfhydryl group-rich active site makes it reactive under physiological pH conditions, making it suitable for integration into gentle irrigation regimens. When used in

combination with surfactants or chloramine derivatives, papain shows enhanced penetration into dentinal tubules. This increased diffusion contributes to more effective sub-surface disinfection compared to conventional irrigants that rely solely on chemical concentration gradients.¹⁴

Microbial fermentation-derived proteases represent another promising category. These enzymes are engineered during production to have specific substrate targets and high stability under varied pH conditions. Their activity remains effective in a pH range from 6 to 9, which is especially useful in endodontic infections where bacterial metabolism alters the pH of the canal environment. Some studies have examined the use of these proteases alongside chelating agents like EDTA. In such combinations, the chelators expose the tubules by removing inorganic smear layer components, while the enzymes hydrolyze residual organic debris and proteinaceous biofilm remnants. This synergistic effect simplifies the irrigation protocol and reduces the need for aggressive chemical agents.¹⁵

Rather than removing the smear layer completely, enzyme-based irrigants tend to selectively break down its organic component. This approach weakens the structural integrity of the smear layer and reduces its potential to harbor bacteria, while maintaining the mineral content needed for sealer adhesion. As a result, the root canal is left in a condition that supports both microbial control and mechanical integrity. The specificity of enzymatic action allows these agents to balance effective disinfection with preservation of dentinal structure, making them well-suited for biologically respectful endodontic practice.

CLINICAL RELEVANCE AND LIMITATIONS

Translating the performance of enzyme-based irrigants from laboratory experiments into clinical scenarios involves several contextual shifts. The *in vitro* success of these agents in removing tissue remnants and disrupting biofilms does not always replicate *in vivo*, where anatomical complexity, fluid dynamics, and host responses introduce multiple variables. Clinical application demands not just efficacy under controlled conditions, but predictability within irregular canal systems, patient-specific microbial profiles, and procedural time constraints.

The influence of these irrigants on post-operative symptoms remains a topic of debate. In a randomized trial evaluating a papain-based solution, patients exhibited comparable pain scores to those treated with sodium hypochlorite, suggesting no increase in inflammatory response or soft tissue irritation. The same study, however, highlighted slower onset of tissue dissolution when compared to NaOCl, raising concerns in acute necrotic cases where rapid debridement may be necessary.¹⁴ This delay becomes particularly relevant in

cases involving purulent exudate or extensive tissue breakdown, where procedural time is already extended due to complexity.

In pediatric and geriatric endodontics, enzyme-based solutions offer favorable handling properties. Their low toxicity and reduced likelihood of accidental extrusion make them appealing in cases with wide apical foramina or open apex conditions. One observational report on their use in primary molars indicated that enzyme-based irrigants produced fewer reports of adverse taste and soft tissue irritation, which improved cooperation during multi-visit sessions. However, clinicians also noted the need for more mechanical assistance during irrigation, especially in canals with pulp stones or dense tissue remnants that resist enzymatic action alone.¹⁶

Cost and availability pose additional limitations. Many enzyme-based formulations remain in the investigational or niche commercial phase, with limited access in general clinical practice. Some require refrigeration or pH adjustments before use, complicating their integration into routine chairside workflows. A cross-sectional study among general practitioners found that despite interest in alternatives to NaOCl, most continued using traditional irrigants due to uncertainty regarding storage protocols, compatibility with obturation materials, and lack of clinical guidelines.⁹ These logistical concerns hinder wider adoption, even among practitioners inclined toward biological irrigation protocols.

Interactions with other materials used during root canal therapy can also impact their clinical performance. Certain adhesives or sealers may show altered setting times or bonding properties when exposed to residual enzymatic activity. A controlled laboratory investigation tested this hypothesis by measuring sealer penetration depth after enzyme-based irrigation and found inconsistent adaptation in cases where rinsing was insufficient. This result pointed to the necessity of incorporating final rinse protocols and carefully calibrating irrigation volumes to avoid residual enzyme interfering with downstream obturation steps.¹⁷ Such considerations emphasize that while enzyme-based irrigants present unique advantages, they also introduce a new set of operational demands that require procedural adjustments and clinical awareness.

CONCLUSION

Enzyme-based irrigants offer a biologically compatible alternative to traditional endodontic solutions, with promising outcomes in tissue dissolution and biofilm disruption. Their selective mechanism of action supports structural preservation while enhancing disinfection in complex canal systems. Clinical translation, however, requires standardized protocols and broader accessibility. Continued investigation will determine their long-term value in routine endodontic care.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

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Cite this article as: Qawass OA, Albaz AK, Aldamook AS, Alhassan DA, Aloreifi AH, Alowein MA. Efficacy of enzyme-based irrigants in endodontics. *Int J Community Med Public Health* 2025;12:5274-8.