

# Endodontic Irrigation: From Current Concepts to Future Innovations

## Introduction

Successful endodontic therapy depends on effective elimination of microorganisms, organic tissue remnants, and smear layer from the root canal system. However, the intricate anatomy of root canals, including fins, isthmuses, lateral canals, and apical deltas, limits the effectiveness of mechanical instrumentation alone. Consequently, chemical irrigation plays a critical role in achieving adequate disinfection and enhancing long-term treatment outcomes.<sup>1</sup>

Sodium hypochlorite (NaOCl) remains the primary irrigant in contemporary endodontics because of its broad-spectrum antimicrobial activity and unique ability to dissolve organic tissue. Nevertheless, its cytotoxicity, unpleasant characteristics, and inability to remove the inorganic component of the smear layer highlight the need for adjunctive solutions.<sup>2</sup> Chelating agents such as ethylenediaminetetraacetic acid (EDTA) are therefore used to remove the inorganic smear layer, while chlorhexidine (CHX) contributes substantivity and additional antimicrobial coverage.<sup>3</sup> Despite these combined protocols, persistent intraradicular infections, particularly those involving *Enterococcus faecalis* biofilms, continue to challenge predictable disinfection.<sup>4</sup>

In response to these limitations, contemporary research has focused on enhancing irrigant delivery and antimicrobial efficacy. Activation systems such as passive ultrasonic irrigation, laser-activated irrigation, and apical negative pressure have demonstrated improved irrigant penetration, smear layer removal, and short-term reduction in postoperative pain compared with conventional syringe irrigation.<sup>5,6</sup> At the same time, novel irrigant formulations—including nanoparticle-based systems, herbal extracts, electrochemically activated solutions, and multifunctional “all-in-one” irrigants have emerged with the goal of improving biofilm disruption while minimizing cytotoxicity.<sup>7,8</sup>

Recent umbrella reviews and systematic analyses emphasize that although activated irrigation and advanced formulations improve short-term antimicrobial and cleaning outcomes, evidence regarding superior long-term periapical healing remains inconclusive.<sup>9</sup> Additionally, the shift toward minimally invasive endodontics has introduced new challenges, as conservative canal preparations may restrict irrigant exchange and fluid dynamics.<sup>10</sup> These evolving clinical paradigms necessitate irrigation strategies that combine chemical potency, biological safety, and effective hydrodynamic activation.

Therefore, modern endodontic irrigation is transitioning from conventional mono-solution protocols toward integrated, technology-driven approaches designed to maximize disinfection while preserving tooth structure. This review aims to examine current concepts in endodontic irrigation and explore recent innovations shaping the future of root canal disinfection.

44  
45  
46

## 47 **Keywords**

48 Endodontic irrigation, Root canal disinfection, smear layer removal, Biofilm disruption, Sodium  
49 hypochlorite (NaOCl), Ethylenediaminetetraacetic acid (EDTA), Chlorhexidine (CHX), Irrigation  
50 activation, Passive ultrasonic irrigation (PUI), Normal saline, Multisonic ultracleaning  
51 (GentleWave), Laser-activated irrigation

52  
53

## 54 **Conventional Irrigants: Mechanisms and Limitations**

### 55 **Sodium Hypochlorite (NaOCl)**

56 Sodium hypochlorite (NaOCl) continues to be extensively used as an endodontic irrigant due to  
57 its broad antimicrobial efficacy and its distinctive ability to dissolve organic and necrotic tissues  
58 within an intracanal environment throughout the root canal system.<sup>2</sup> Its antimicrobial action is  
59 primarily driven by an oxidative chain of reactions that disrupt microbial biofilms.<sup>11</sup> Despite a  
60 substantial reduction in microbial load through the combination of instrumentation and irrigation,  
61 complete eradication of bacteria and canal disinfection are not reliably achieved and residual  
62 bacteria at obturation may compromise treatment success.<sup>2</sup>

63 The bacterial elimination capacity, proteolytic activity and biological toxicity of NaOCl are  
64 influenced by several clinical variables including concentration, contact time, volume and  
65 temperature. Lowering the concentration limits cytotoxic effects but leads to a decline in  
66 antimicrobial efficacy and organic tissue dissolution. Prolonged exposure is especially essential  
67 in necrotic canals to maximize antimicrobial efficacy, while higher volume promotes bacterial  
68 elimination by facilitating intracanal flushing. Thermal activation of NaOCl enhances its tissue-  
69 dissolving efficacy, as solutions heated to approximately 45°C demonstrated effects comparable  
70 to 5.25% NaOCl at room temperature, with reduced systemic toxicity.<sup>15</sup>

71 Although NaOCl offers several clinical benefits, its ineffectiveness against inorganic  
72 components of the smear layer means it cannot achieve complete smear layer elimination when  
73 used alone.<sup>11</sup> Furthermore, accidental apical extrusion through apical foramen can lead to  
74 significant risk of cytotoxic reactions associated with intense pain, hemorrhage, swelling,  
75 ecchymosis, tissue damage and possible neurosensory complications.<sup>13</sup> NaOCl presents with  
76 several limitations including undesirable taste and odor, corrosive properties, compromising  
77 dentin biomechanical integrity and impaired dental pulp stem cell viability at high  
78 concentrations.<sup>12,14</sup> As a result, implementation of carefully regulated irrigation protocols that  
79 include activation techniques or final EDTA rinse is widely recommended to maximize  
80 antimicrobial effectiveness while minimizing adverse effects.<sup>2</sup>

### 81 **Normal Saline**

82 Normal saline is commonly utilized in endodontic practice due to its excellent biocompatibility  
83 with periapical tissues. However, saline-assisted mechanical instrumentation alone does not  
84 provide adequate elimination of pulp tissue, dentinal debris and microbial biofilms from the canal  
85 system. Saline primarily provides mechanical debridement and lubrication but lacks inherent  
86 chemical disinfecting properties, therefore is not suitable as a primary irrigant. The commonly  
87 used 0.9% w/v solution is used in conjunction with chemically active irrigants.<sup>15</sup>

88 Saline serves as an intermediate or terminal rinse following elimination of irrigants residual after  
89 canal preparation and minimizing the risk of harmful irrigant interactions.<sup>15</sup> Although saline lacks  
90 intrinsic bactericidal properties, saline has been shown to result in significant reduction in  
91 microbial counts when it is used as control irrigant, highlighting the importance of mechanical  
92 preparation and hydrodynamic flushing in the reduction of bacterial counts. Saline effectiveness  
93 is enhanced by passive ultrasonic activation resulting in improved removal of planktonic  
94 microorganisms compared with conventional syringe irrigation. Because of its excellent  
95 biocompatibility, saline is commonly used as a final rinse in endodontic procedures to promote  
96 dental pulp stem cell adhesion and regeneration after stronger chemical irrigants.<sup>15</sup>

### 97 **Chlorhexidine (CHX)**

98 Chlorhexidine gluconate (CHX) is frequently employed in endodontic practice due to its  
99 extensive antimicrobial spectrum against Gram-positive and Gram-negative bacteria. In root  
100 canal treatment, it is generally applied at a 2% concentration and demonstrates bactericidal  
101 effects at higher concentrations and bacteriostatic effects at lower concentrations. One of the  
102 key advantages of CHX is its substantivity attributed to strong affinity for dentin and enabling  
103 extended antimicrobial release, with 2% CHX demonstrating prolonged effectiveness lasting  
104 several weeks.<sup>15</sup>

105 CHX is incapable of dissolving organic tissue or adequately disrupting mature biofilms, which  
106 restricts its capacity in accomplishing total canal debridement when used independently. The  
107 antimicrobial properties are further reduced in the presence of organic matter and its ability to  
108 penetrate into well-established biofilms remains limited. The sequential application of CHX with  
109 NaOCl or EDTA leads to precipitate formation which can obstruct dentinal tubules causing tooth  
110 discoloration and compromise apical sealing.<sup>17</sup> Despite its established biocompatibility,  
111 inadvertent extrusion into periapical tissues can induce inflammatory reactions and has been  
112 associated with alteration in tooth color, oral tissue pigmentation, gingival epithelial  
113 desquamation and unpleasant metallic taste.<sup>15</sup> Strategies including heating CHX or addition of  
114 surfactants can improve antimicrobial activity and dentinal diffusion, however, the clinical safety  
115 of these methods is not yet well-established.<sup>17</sup> Consequently, CHX is more appropriately used  
116 as a supplementary or final irrigant instead of primary irrigating solution.

### 117 **Chelating Agent (EDTA)**

118 Successful root canal disinfection requires elimination of both the organic and inorganic  
119 components of the smear layer, given that no single irrigant can effectively target both

120 components simultaneously. Since NaOCl is limited to dissolving organic matter, the use of  
121 chelating agents like ethylenediaminetetraacetic acid (EDTA) is necessary to achieve  
122 comprehensive smear layer elimination. The application of chelating agents was first introduced  
123 by Nygaard-Østby in 1957, originally suggesting a 15% EDTA solution, whereas modern clinical  
124 practice protocols predominantly utilize a neutralized 17% EDTA formulation.<sup>15</sup>

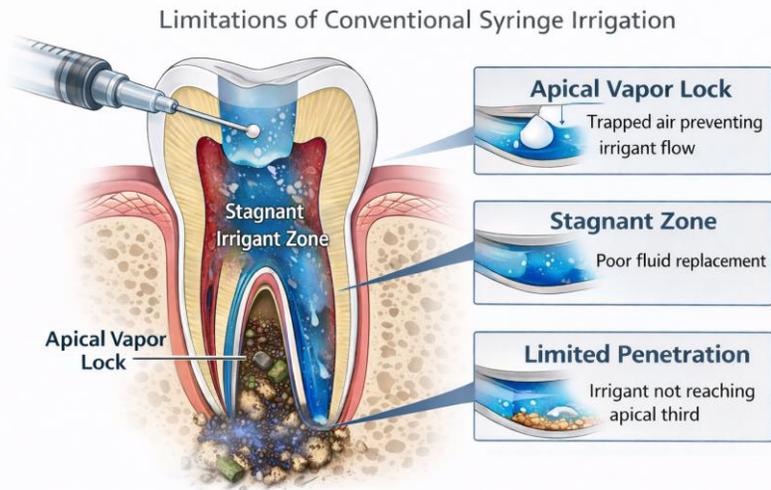
125 EDTA eliminates the smear layer by binding to calcium ions in dentin to form soluble calcium  
126 complexes, with demineralization stopping once the chelating capacity is exhausted. Studies  
127 indicate that final irrigation with 17% EDTA for 1-3 minutes effectively removes the smear layer,  
128 while ultrasonic activation particularly in the apical third of the canal system, significantly  
129 improves its action.<sup>15</sup> Beyond smear layer elimination, EDTA promotes the release of growth  
130 factors from the dentin matrix and attenuates NaOCl cytotoxic effects, making it particularly  
131 relevant in regenerative endodontics.<sup>11</sup> EDTA demonstrates limited antimicrobial properties,  
132 and excessive contact can lead to dentinal erosion and reduction in microhardness, potentially  
133 weakening tooth structure.<sup>12</sup>

### 134 **Limitations of Conventional Irrigation Delivery**

135 Conventional syringe-and-needle-based irrigation provides limited irrigant penetration into the  
136 apical third region, accessory canals and complex canal anatomy, often resulting in inadequate  
137 debridement and microbial control. Passive syringe irrigation results in low flow velocities and  
138 low shear stress, which diminishes debris clearance and biofilm disruption along canal walls.<sup>16</sup>  
139 Computer-based fluid flow analyses reveal the presence of stagnation zones and uneven  
140 irrigant distribution, particularly in apical areas, which reduce effective irrigant exchange and  
141 antimicrobial activity.<sup>5</sup>

142 A key limitation of conventional irrigation is the apical vapor lock phenomenon, in which trapped  
143 air obstructs the delivery of fresh irrigant from reaching the length and compromises  
144 antimicrobial action in the apical third region.<sup>16</sup> Additionally, syringe irrigation offers insufficient  
145 irrigation renewal, leading to rapid depletion of chemically active components and reduced  
146 antibacterial efficacy over time.<sup>5</sup> [Figure 1].

147



148

149 *Figure 1. Limitations of Conventional Syringe Irrigation*

150 From a procedural standpoint, the performance of syringe-based irrigation is influenced by  
 151 certain factors such as needle gauge, irrigant volume, delivery frequency, temperature, canal  
 152 diameter and dimensions, and irrigant age; however, conventional techniques cannot  
 153 simultaneously optimize all variables. Although smaller-diameter needles may enhance  
 154 penetration depth, they commonly create a stagnant zone near the apex, limiting effective  
 155 irrigant exchange.<sup>15</sup>

156 Conventional irrigation methods present a risk of apical extrusion, especially under excessive  
 157 pressure or in presence of compromised apical anatomy, potentially resulting in periapical tissue  
 158 damage. Overall, these shortcomings indicate that syringe irrigation alone is insufficient for  
 159 predictable canal disinfection results, thereby indicating the need for adjunctive activation  
 160 techniques or advanced delivery systems.<sup>16</sup>

161

## 162 **Advanced Endodontic Irrigants**

163

### 164 **Nanoparticles:**

165 Endodontic infections are polymicrobial in nature, with *Enterococcus faecalis* being the most  
 166 prevalent Gram-positive facultative anaerobe in persistent intraradicular infections. Its  
 167 elimination is challenging due to the complex root canal anatomy that limits mechanical  
 168 instrumentation, as well as its ability to penetrate dentinal tubules and form biofilms. Regular  
 169 root canal disinfectants don't kill all bacteria effectively, especially tough ones hiding in biofilms.  
 170 Here is where nanoparticles emerged as alternatives.<sup>4</sup>

171 The complex anatomy of the root canal system makes effective cleaning and shaping difficult,  
 172 allowing bacteria to persist despite the use of various irrigants and intracanal medicaments.

173 Increasing microbial resistance to conventional agents has led to the introduction of antibacterial  
 174 nanoparticles in endodontics.

175 In endodontics, nanoparticles have been explored for multiple applications, including biofilm  
176 elimination, dentin hypersensitivity management, tissue regeneration, reinforcement of the  
177 compromised dentinal matrix, and incorporation into irrigants, intracanal medicaments, sealers,  
178 and restorative materials to enhance antimicrobial efficacy.<sup>18</sup>

179 Pulpal and periradicular diseases are primarily caused by polymicrobial endodontic infections  
180 that develop as biofilms within the root canal system. These biofilms consist of bacterial cells  
181 embedded in an extracellular polymeric matrix that provides mechanical stability, nutrient  
182 support, and increased resistance to conventional irrigants and medicaments. Altered bacterial  
183 growth patterns and gene expression within the biofilm further enhance microbial virulence and  
184 antimicrobial resistance. Owing to these challenges, nanoparticles have recently gained  
185 attention as promising antimicrobial agents due to their enhanced antibiofilm properties.<sup>18</sup>  
186

### 187 **Nano versus bulk materials:**

188 Unlike bulk materials, nanoparticles not only damage bacterial cell walls but also interfere with  
189 essential bacterial enzymes involved in DNA replication and RNA synthesis, ultimately leading  
190 to bacterial death.<sup>18</sup>

191 Antibacterial mechanisms of nanoparticles:

192 Nanoparticles exert antibacterial effects through multiple mechanisms. First, they bind to  
193 bacterial cell membranes via electrostatic interactions, disrupting membrane integrity, polarity,  
194 and essential functions such as respiration, nutrient transport, and energy production, leading to  
195 cell death. Second, nanoparticles generate reactive oxygen species (ROS), which damage  
196 proteins and DNA and impair bacterial survival. Additionally, metal-based nanoparticles disrupt  
197 metal ion homeostasis and metabolic functions, causing irreversible cellular damage.

198 Nanoparticles also induce protein and enzyme dysfunction by oxidizing amino acid side chains,  
199 resulting in loss of catalytic activity. Furthermore, their interaction with cellular biopolymers  
200 interferes with DNA replication and signal transduction, ultimately inhibiting bacterial growth or  
201 causing cell death.

202 Chitosan nanoparticles have demonstrated significant antibiofilm activity against *Enterococcus*  
203 *faecalis*, particularly when combined with zinc oxide, in a time- and concentration-dependent  
204 manner. Their ability to penetrate dentinal tubules makes them suitable for disinfecting complex  
205 root canal systems. Unlike conventional antimicrobials, chitosan nanoparticles are not affected  
206 by bacterial efflux pump mechanisms and retain efficacy in the presence of dentin and dentin  
207 matrix. Studies have also shown enhanced antimicrobial effects when chitosan nanoparticles  
208 are combined with chlorhexidine, supporting their potential use as an endodontic irrigant or  
209 irrigant adjunct.<sup>18</sup>

210 Poly (lactic-co-glycolic acid) nanoparticles loaded with methylene blue enhance light-activated  
211 antimicrobial therapy, significantly reducing bacterial counts in infected root canals, indicating  
212 their potential as an adjunct to conventional endodontic irrigation.<sup>18</sup>  
213

214 Silver nanoparticles (Ag Np) and zinc oxide nanoparticles (ZnO Np) have shown strong ability to  
215 kill bacteria (antimicrobial effect) and break down bacterial communities stuck together in layers  
216 (antibiofilm effect). When silver nanoparticles were added to dental materials or used inside root  
217 canals: They improved disinfection during root canal treatment, they could be used either as an  
218 intracanal dressing (left inside the canal between visits) or as an irrigant (liquid used to flush the

219 canal). Zinc oxide nanoparticles were found to prevent *Enterococcus faecalis* (a bacteria  
220 commonly responsible for failed root canals) from sticking to the dentin walls and breaking apart  
221 and destroying existing biofilms formed by this bacteria.<sup>4</sup>

222  
223 Metal nanoparticles such as silver (Ag-NPs) and zinc oxide (ZnO-NPs) have shown significant  
224 antibiofilm activity against *Enterococcus faecalis* in root canals, highlighting their potential as  
225 adjunctive endodontic irrigants.<sup>4</sup> Ag-NPs disrupt bacterial cell membranes, interfere with DNA  
226 and protein function, and increase cell permeability, while ZnO-NPs exert bactericidal effects  
227 through high pH, cell wall disruption, cytoplasmic leakage, and zinc ion-mediated metabolic  
228 interference<sup>18</sup>. Both nanoparticles reduce bacterial counts comparably to conventional irrigants,  
229 particularly when combined with passive ultrasonic activation. Although highly effective against  
230 planktonic bacteria and partially against biofilms, neither achieves complete eradication, and  
231 clinical use is limited by concerns such as dentin discoloration, cytotoxicity, and the need for  
232 further in vivo validation.<sup>18</sup> Magnesium oxide (MgO) and magnesium-halogen nanoparticles  
233 exhibit strong antibacterial activity against endodontic pathogens, including *E. faecalis*, *S.*  
234 *aureus*, and *Candida albicans*. These nanoparticles disrupt bacterial membrane potential,  
235 induce DNA binding and lipid peroxidation, and generate reactive superoxide anions, leading to  
236 cell death. When incorporated into irrigant solutions, MgO nanoparticles enhance the  
237 antibacterial efficacy of conventional irrigants such as sodium hypochlorite and chlorhexidine,  
238 supporting their potential use as adjunctive endodontic irrigants.<sup>18</sup>

239 Studies by Bukhari et al. demonstrated that iron oxide nanoparticles (IO-NPs) combined with  
240 hydrogen peroxide ( $H_2O_2$ ) provide superior disinfection of dentinal tubules compared to  
241 conventional irrigants. Microbial infection of dentinal tubules is a primary cause of apical  
242 periodontitis and endodontic treatment failure. Conventional irrigants like NaOCl and CHX  
243 mainly disinfect superficial dentin, leaving many bacteria viable in tubules. Iron oxide  
244 nanoparticles (IO-NPs) combined with  $H_2O_2$  show superior antimicrobial activity against *E.*  
245 *faecalis*, especially in middle and outer dentin zones. This works via pH-dependent  
246 nanocatalysis, where IO-NPs activate  $H_2O_2$  to generate free radicals that rapidly kill bacteria  
247 while remaining safe at physiological pH. Other nanoparticles, such as silver and chitosan, also  
248 show antimicrobial effects but require prolonged contact, limiting their use as irrigants.<sup>19</sup>

249 Effect of Nanoparticles on Fracture Resistance:

250 Studies have shown that roots irrigated with nanoparticles—silver (SNPs), titanium (TNPs), and  
251 zinc oxide (ZNPs)—exhibit higher fracture resistance (FR) compared to those treated with  
252 saline, chlorhexidine (CHX), or sodium hypochlorite (NaOCl). While NaOCl effectively dissolves  
253 biofilms, it cannot remove the smear layer, may be inactivated by organic matter, and weakens  
254 dentin by degrading its organic matrix, reducing FR, microhardness, and elasticity. CHX  
255 preserves dentin strength, maintains resin-sealer bonding, forms less smear layer, and helps  
256 prevent microleakage. Metal nanoparticles have gained attention for their antibacterial  
257 properties and potential use as root canal irrigants. Their small size allows deeper penetration  
258 into biofilms and complex canal anatomy, overcoming limitations of conventional irrigants. SNPs  
259 provide sustained broad-spectrum antibacterial activity via silver ion release, ZNPs retain  
260 activity against *E. faecalis* even after aging and inhibit MMPs, and TNPs generate free radicals  
261 to prevent bacterial adhesion. Pre-treatment with EDTA removed the smear layer, improving  
262 nanoparticle penetration and sealer bonding. Enhanced FR observed with nanoparticles may

263 also be due to their high surface area, energy, and improved contact with dentin and collagen,  
264 though this requires further study. Their nanoscale size allows deeper penetration into dentinal  
265 tubules (~1 µm), potentially providing sustained antibacterial effects and inhibiting bacterial  
266 adherence. However, limitations such as prior EDTA use, testing only one sealer, and lack of  
267 long-term antibacterial and systemic assessments exist, and further research is needed to  
268 evaluate nanoparticles' effects on dentin wettability, sealer bonding, and root integrity.<sup>20</sup>  
269

### 270 **Herbal Irrigants:**

271 Herbal products show considerable potential in endodontics due to their antimicrobial efficacy,  
272 biocompatibility, low cost, ease of use, and minimal risk of microbial resistance. They may serve  
273 as effective alternatives to conventional irrigants and medicaments, helping overcome  
274 limitations such as cytotoxicity and limited penetration into dentinal tubules. Although in vitro  
275 findings are promising, comprehensive preclinical and clinical studies are required to confirm  
276 their safety, biocompatibility, and clinical effectiveness. Herbal agents are generally safe when  
277 used correctly; however, improper use may lead to adverse effects. Therefore, further evidence-  
278 based research is essential before their routine clinical application in endodontic practice.<sup>21</sup>  
279 Successful endodontic therapy relies on effective access preparation, biomechanical cleaning,  
280 disinfection, and three-dimensional obturation of the root canal system. Due to the complex  
281 canal anatomy, persistent biofilms often remain, making chemical irrigants essential alongside  
282 mechanical instrumentation for removal of necrotic tissue, biofilm, and smear layer. An ideal  
283 irrigant should be antimicrobial, capable of dissolving organic tissue and smear layer,  
284 biocompatible, non-toxic, non-irritating to periapical tissues, and should not compromise sealer  
285 adhesion. Sodium hypochlorite is widely used because of its strong antimicrobial and tissue-  
286 dissolving properties, but its drawbacks include toxicity, allergic potential, unpleasant taste, risk  
287 of extrusion injuries, and inability to remove the smear layer. Other conventional irrigants such  
288 as chlorhexidine, EDTA, and citric acid also have limitations, including tooth discoloration and  
289 reduced dentin microhardness. Owing to these disadvantages, there has been a growing  
290 interest—particularly in India's traditional medicinal systems—in herbal endodontic irrigants.  
291 Phytochemical agents offer advantages such as high antimicrobial efficacy, anti-inflammatory,  
292 antioxidant and antiseptic properties, biocompatibility, cost-effectiveness, easy availability,  
293 minimal tooth staining, lower toxicity, and reduced microbial resistance, especially against  
294 *Enterococcus faecalis*, making them promising alternatives to synthetic irrigants.<sup>22</sup>  
295 Herbal root canal irrigants have been studied for their functional properties and can be classified  
296 based on their actions. Many herbal extracts, such as neem, Triphala, garlic, green tea, tulsi,  
297 miswak, and turmeric, have demonstrated significant antimicrobial activity against common  
298 endodontic pathogens. A subset of these agents also exhibits chelating ability, allowing effective  
299 removal of the smear layer, while some possess both antimicrobial and chelating properties.  
300 Additionally, a few herbal extracts, including garlic and *Sapindus mukorossi*, have shown the  
301 capacity to dissolve pulp tissue. These findings highlight the multifaceted potential of herbal  
302 irrigants as safe, biocompatible, and cost-effective alternatives or adjuncts to conventional  
303 endodontic solutions.<sup>22</sup>

304 Primary endodontic infections are mainly caused by obligate anaerobic bacteria, which can  
305 persist in complex areas of the root canal, making complete eradication difficult. Effective  
306 disinfection requires mechanical preparation combined with chemical irrigation, influenced by

307 factors such as microbiota, access cavity design, canal preparation, irrigant type, volume,  
308 contact time, and needle design. Sodium hypochlorite (NaOCl) is the primary irrigant for its  
309 antibacterial and tissue-dissolving properties, though high concentrations can weaken dentin,  
310 while EDTA is used for chelation. Herbal irrigants are being explored as alternatives, but  
311 standardized protocols for contact time, concentration, and volume are lacking. Needle design  
312 and flow rate are also critical for effective disinfection.<sup>7</sup>

313 This systematic review assessed studies comparing NaOCl with herbal agents for antimicrobial  
314 efficacy. Herbal agents investigated included triphala, green tea polyphenols, Morinda citrifolia,  
315 neem, oregano extract, carvacrol, tulsi, cinnamon, Syzygium aromaticum, and Zataria multiflora.  
316 Among these, triphala was most effective, followed by green tea, while Morinda citrifolia was  
317 least effective. Results for neem and oregano were inconsistent. Due to heterogeneity in study  
318 design, concentration, and type of irrigant, no single herbal agent can be recommended as an  
319 alternative to NaOCl. Overall, most herbal agents showed inferior antimicrobial activity  
320 compared to NaOCl, with only oregano and Zataria multiflora showing comparable efficacy.<sup>7</sup>  
321 Future studies should standardize concentration, volume, contact time, and assess fresh versus  
322 stored extracts, potential precipitate formation, and discoloration. While herbal agents are  
323 promising adjuncts, they cannot currently replace NaOCl for effective root canal disinfection.<sup>7</sup>  
324

## 325 **Alternative Irrigants:**

326

### 327 **Ozone as irrigant**

328 Ozone, particularly in its aqueous form, has been investigated for root canal disinfection due to  
329 its strong antimicrobial properties. Studies show that ozonated water can significantly reduce  
330 bacterial load, including *E. faecalis* and *C. albicans*, though its efficacy is generally slightly lower  
331 than sodium hypochlorite (NaOCl). In some lab studies, higher ozone concentrations, longer  
332 application times, or using it with ultrasonic activation or other irrigants (NaOCl or chlorhexidine)  
333 achieved comparable results, but these cases were exceptions. Ultrasonic activation improves  
334 ozone's effectiveness, with manual irrigation showing lower microbial reduction. Aqueous ozone  
335 is less cytotoxic than NaOCl or gaseous ozone and is biologically safe, with additional benefits  
336 such as tissue oxygenation and immune modulation that may aid healing. It works by oxidizing  
337 bacterial membranes and intracellular components, increasing permeability and causing cell  
338 lysis. While effective, its antimicrobial efficacy is generally slightly lower than sodium  
339 hypochlorite, and activation (e.g., ultrasonic) improves results. Most evidence is in vitro, with no  
340 standardized clinical protocols, so ozone cannot yet fully replace traditional irrigants but may  
341 serve as a safe adjunct<sup>23</sup> and less cytotoxic.<sup>24</sup>  
342

342

### 343 **Photodynamic therapy (PDT)**

344 Photodynamic therapy (PDT) is an adjunct to conventional endodontic treatment that enhances  
345 bacterial elimination. It involves applying non-toxic photosensitizers, such as methylene blue,  
346 which are activated by specific wavelengths of light in the presence of oxygen. This activation  
347 produces toxic oxygen species, including singlet oxygen and free radicals, which primarily target  
348 microbial cell walls and membranes, and can also damage DNA. Phenothiazine-derived  
349 photosensitizers are commonly used in endodontic PDT studies.

350 Conventional irrigation with a syringe often fails to clean the apical and complex areas of the  
351 canal, so agitated irrigation methods like passive ultrasonic irrigation (PUI) and the XP Endo  
352 Finisher have been developed to enhance disinfectant penetration and remove debris. The XP  
353 Endo Finisher is a flexible, non-tapered file that adapts to the root canal's shape, cleaning  
354 irregular areas effectively. This study is the first to investigate the combined use of PDT, PUI,  
355 and XP Endo for root canal disinfection.  
356 Photodynamic therapy (PDT) alone is insufficient to eliminate *E. faecalis* in root canals, but  
357 when combined with irrigation solutions like NaOCl, it significantly improves bacterial reduction.  
358 The XP Endo Finisher with PDT showed the highest effectiveness (~98–99%). Ultrasonic  
359 activation also enhanced results. While promising as an adjunct, PDT cannot replace  
360 conventional irrigation, and further in vivo studies are needed to confirm its efficacy across  
361 different canal anatomies.<sup>25</sup>

### 362 **MTAD (Mixture of Tetracycline, Acid, and Detergent)**

364 Biopure mixture of tetracycline acid and detergent (MTAD) (Tulsa, Dentsply) contains 3%  
365 doxycycline (tetracycline isomer) 150 mg/5 ml, 4.25% citric acid, 0.5% polysorbate 80  
366 (surfactant). The main goal of endodontics is thorough root canal disinfection, but bacteria like  
367 *Enterococcus faecalis* often persist due to virulence and biofilm formation. Standard irrigants  
368 (NaOCl, CHX, EDTA, IKI) are effective, with 5.25% NaOCl plus 17% EDTA as the gold  
369 standard, though this can weaken dentin. MTAD is used as a final rinse but shows no clear  
370 advantage over NaOCl/EDTA. Surfactants like cetrimide (CTR) and SDS enhance antimicrobial  
371 activity by reducing surface tension and disrupting bacterial membranes. This study found that  
372 combining CHX with CTR or SDS improved *E. faecalis* eradication compared to CHX alone,  
373 offering effective disinfection while potentially lowering the need for higher, more toxic irrigant  
374 concentrations. Further studies on biofilms, cytotoxicity, and tooth models are needed.<sup>26</sup>

### 375 **QMix:**

377 QMix is commonly presented as an advanced final irrigant that combines smear-layer removal  
378 and antimicrobial activity in one solution. Its formulation is described in the literature as including  
379 EDTA (for chelation/smear-layer removal), antimicrobial components with chlorhexidine-like  
380 behavior, and a surfactant to reduce surface tension and improve wetting and penetration into  
381 dentinal tubules. This positions QMix primarily for use in the final irrigation phase, when the aim  
382 is to optimize dentin surface cleanliness and reduce residual microbes prior to obturation.<sup>28</sup>  
383 A clinically important aspect highlighted in the open-access evidence is endotoxin reduction. In  
384 infected canal models, QMix has been shown to reduce lipopolysaccharide (LPS) levels, which  
385 matters because endotoxin is implicated in periapical inflammatory responses. This adds a  
386 rationale for QMix use beyond simple “bacterial count reduction,” supporting its role in improving  
387 the chemical environment of the canal system near the end of treatment.<sup>29</sup>

388  
389 At the same time, QMix should be placed correctly in the sequence because it is not a substitute  
390 for NaOCl's tissue dissolution. The evidence base treats QMix as a finishing irrigant: it is used  
391 after NaOCl has performed the heavy lifting in organic tissue dissolution and bulk antimicrobial  
392 action, and then QMix helps address smear layer/inorganic aspects and residual disinfection  
393 goals to support improved conditions for obturation.<sup>28,32</sup>

394

395 **Calcium hydroxide pastes / solutions:**

396 Calcium hydroxide is primarily used as an intracanal medicament because its high pH supports  
397 antimicrobial activity and can neutralize bacterial by-products during inter-appointment dressing.  
398 Clinically, it is usually placed as a paste, and its effectiveness as a medicament is well  
399 accepted; however, the persistent issue is not whether it works as a medicament but how  
400 reliably it can be removed before obturation, especially from the apical third and anatomical  
401 irregularities.<sup>30,32</sup>

402 Experimental evidence demonstrates that conventional syringe irrigation alone often leaves  
403 calcium hydroxide remnants, particularly in complex anatomy and challenging canal shapes.  
404 This is clinically important because residual  $\text{Ca}(\text{OH})_2$  can interfere with sealer  
405 penetration/adaptation and may compromise the quality of obturation. Therefore, removal is  
406 treated as a critical step—not optional cleanup—before sealing the canal system.<sup>30</sup>

407 Evidence supports a “chemistry + activation” approach: using chelators such as EDTA and  
408 applying activation techniques (e.g., ultrasonic/sonic agitation) improves calcium hydroxide  
409 removal compared with non-activated syringe irrigation, although complete removal is still  
410 difficult to achieve consistently. The realistic clinical conclusion is that protocols should be  
411 designed to maximize removal in hard-to-clean regions, using activation as standard practice  
412 when calcium hydroxide medicament has been used.<sup>30</sup>

413

414 **Photo-activated irrigants (photoactivated disinfection / antimicrobial  
415 photodynamic therapy):**

416 Photoactivated disinfection (PAD), also termed antimicrobial photodynamic therapy (aPDT), is  
417 based on a triad: a photosensitizer, light at a matching wavelength, and oxygen. Light activation  
418 triggers energy transfer processes that generate reactive oxygen species (ROS), particularly  
419 singlet oxygen and free radicals, which exert antimicrobial effects through oxidative damage to  
420 cell membranes, proteins, and nucleic acids. In endodontics, methylene blue and toluidine blue  
421 O are among the most frequently described photosensitizers, and activation is commonly  
422 achieved using diode lasers or LEDs, with clinical relevance tied to the ability to reach bacteria  
423 in dentinal tubules and complex anatomical areas that conventional approaches may not  
424 completely disinfect.<sup>27,31</sup>

425 Evidence synthesis in the PAD literature consistently positions this method as adjunctive: it can  
426 add microbial reduction after conventional chemo-mechanical preparation, but it does not  
427 replace sodium hypochlorite because it lacks organic tissue dissolution and cannot reliably  
428 replicate NaOCl's combined tissue-dissolving and broad antimicrobial role. Reviews describing  
429 modern canal disinfection emphasize PAD's usefulness in reducing residual microbial burden  
430 (often studied with *E. faecalis*) while also stressing that PAD's effect depends heavily on  
431 successful delivery of all three components—photosensitizer distribution, appropriate light  
432 delivery, and oxygen availability.<sup>27,32</sup>

433 Technique factors strongly influence results. Parameters such as photosensitizer concentration,  
434 contact time, canal cleanliness (smear layer and debris can impede penetration), irradiation  
435 time, wavelength, and the practicality of delivering light into the full canal space all shape  
436 efficacy. Because ROS effects occur locally, limitations in penetration and activation can lead to  
437 inconsistent outcomes, which is why PAD is commonly recommended as a final supplementary

438 disinfection step once shaping/cleaning has already reduced debris and improved access to the  
439 canal system.<sup>27,31</sup>

440

#### 441 **Reactive solutions (oxidation-based irrigants):**

442 Reactive irrigant solutions aim to disinfect using oxidative chemistry that damages microbial  
443 structures and genetic material. This broad category includes approaches such as ozonated  
444 water, electrochemically activated (ECA) solutions (electrolyzed saline), and other oxidizing  
445 mixtures that rely on reactive oxygen/chlorine species for antimicrobial effect. The rationale for  
446 investigating these agents is typically framed around improved biocompatibility compared with  
447 stronger sodium hypochlorite concentrations, while maintaining meaningful antimicrobial action  
448 as part of irrigation regimens and/or activation protocols.<sup>1,32</sup>

449 Across endodontic irrigation reviews, a consistent limitation is that oxidative solutions often  
450 show more variable performance in the real canal environment, especially when organic load is  
451 present. Organic debris, dentin remnants, and biofilm architecture can reduce antimicrobial  
452 impact, and many reactive solutions do not provide meaningful organic tissue dissolution—an  
453 important clinical differentiator because removal of necrotic tissue and organic debris is central  
454 to debridement. As a result, reactive solutions are generally not framed as drop-in replacements  
455 for NaOCl but rather as adjuncts or alternatives in selected contexts.<sup>1</sup>

456 From a practical “evidence-safe” standpoint, the literature supports using reactive solutions with  
457 realistic expectations: they can contribute antimicrobial action, and activation methods can  
458 enhance performance, but NaOCl remains the most consistently effective irrigant when both  
459 antimicrobial action and tissue dissolution are needed. Therefore, reactive solutions are best  
460 positioned as adjunctive disinfectants, alternative options when NaOCl use is limited, or  
461 components within broader activation-supported irrigation strategies rather than the core irrigant  
462 for routine chemo-mechanical preparation.<sup>1</sup>

463

#### 464 **Electrolyzed water / super-oxidized water in endodontics:**

465 Electrolyzed water, often referred to as electrochemically activated (ECA) water or super-  
466 oxidized water, is produced by the electrolysis of a dilute saline solution, resulting in solutions  
467 rich in reactive chlorine and oxygen species, most notably hypochlorous acid. These reactive  
468 species exert antimicrobial effects by causing oxidative damage to bacterial cell membranes,  
469 enzymes, and nucleic acids. In endodontics, electrolyzed and super-oxidized water have been  
470 investigated as irrigant solutions due to their antimicrobial properties combined with  
471 comparatively favorable biocompatibility profiles. The primary rationale for their use is to  
472 achieve microbial reduction with lower cytotoxicity than higher concentrations of sodium  
473 hypochlorite.<sup>1,33</sup>

474 Experimental studies and reviews demonstrate that electrolyzed and super-oxidized water  
475 exhibit antimicrobial activity against common endodontic pathogens, including *Enterococcus*  
476 *faecalis*. However, their antimicrobial efficacy is highly dependent on factors such as solution  
477 concentration, exposure time, and the presence of organic matter. When organic debris, dentin  
478 remnants, or mature biofilms are present, the antimicrobial effectiveness of these solutions is  
479 significantly reduced. This limitation is particularly relevant in infected root canal systems, where  
480 organic load is almost always present during treatment. As a result, their performance is  
481 generally less predictable than sodium hypochlorite under clinically realistic conditions<sup>1,33</sup>.

482 Another important limitation of electrolyzed and super-oxidized water is their minimal organic  
483 tissue-dissolving capacity. Unlike sodium hypochlorite, these solutions do not effectively  
484 dissolve necrotic pulp tissue or organic debris, which is a critical requirement for thorough canal  
485 debridement. Consequently, while electrolyzed and super-oxidized water may contribute to  
486 microbial reduction, they cannot fulfill the dual role of disinfection and tissue dissolution that  
487 defines sodium hypochlorite as the primary irrigant in endodontics. Current evidence therefore  
488 supports their use mainly as adjunctive irrigants or as alternative solutions in selected clinical  
489 situations where sodium hypochlorite use is contraindicated or must be limited.<sup>1</sup>

490

## 491 **Irrigation Activation Systems**

### 492 **A) PASSIVE ULTRASONIC IRRIGATION (PUI)**

#### 493 **Definition and Mechanism**

494 Passive ultrasonic irrigation can be performed with a small file or smooth wire (size 10-20)  
495 oscillating freely in the root canal to induce powerful acoustic microstreaming.<sup>34</sup> PUI functions  
496 without simultaneous instrumentation, and ultrasonic irrigation has proved to be more powerful  
497 than sonic activation in eliminating debris.<sup>35</sup>

#### 498 **Clinical Protocol (2025 ESE Guidelines)**

499 The European Society of Endodontology 2025 S3 guidelines place PUI at the heart of the  
500 irrigation protocol, with ultrasonic activation of warmed sodium hypochlorite, a final chelation  
501 step with EDTA, and a neutralizing rinse.<sup>36</sup> Randomized controlled trials report greater than 99%  
502 bacterial reduction, markedly better smear-layer removal, and a significant drop in postoperative  
503 pain compared with conventional syringe irrigation.<sup>36</sup>

#### 504 **Clinical Efficacy**

- 505 ● **Bacterial Reduction:** Two 2024 studies showed significantly better smear layer  
506 removal in the apical third, and a 2023 randomized trial found a 38% drop in moderate  
507 post-operative pain.<sup>36</sup>
- 508 ● **Cost-Effectiveness:** A dedicated ultrasonic unit and tips pay for themselves in fewer  
509 than 40 cases if retreatments fall from 8% to 2%.<sup>36</sup>
- 510 ● **Cleaning Efficacy:** Compared with traditional syringe irrigation, PUI removes more  
511 organic tissue, planktonic bacteria and dentine debris from the root canal.<sup>34</sup>

#### 512 **Technical Considerations**

513 The taper and diameter of the root canal were found to be important parameters in determining  
514 the efficacies of dentine debris removal, and irrigation with sodium hypochlorite is more effective  
515 than with water.<sup>37</sup> However, in severely curved canals, the ultrasonic activation tip's

516 performance may be compromised since contact of the tip with the curved canal wall is  
517 inevitable, with high risk of straightening or otherwise damaging the original canal curvature.<sup>38</sup>

518

## 519 **B) LASER-ACTIVATED IRRIGATION (LAI)**

### 520 **Photon-Induced Photoacoustic Streaming (PIPS)**

521 **Technology and Mechanism:** PIPS is not a thermal event but rather sub ablative, creating  
522 turbulent photoacoustic agitation of irrigants that move fluids three dimensionally throughout the  
523 root canal system even to the apical terminus, using extremely low energy (20 mJs or less)  
524 below the threshold of ablation for dentin.<sup>39</sup>

525 The laser-activated irrigation technique is based on the creation of cavitation phenomena and  
526 acoustic streaming in intracanal fluids related to the photomechanical effects of lasers at low  
527 settings, with Er:YAG laser used with sub-ablative energy and ultra-short pulses (50  $\mu$ s) leading  
528 to intracanal cavitation and shockwaves.<sup>40</sup>

### 529 **Clinical Advantages:**

- 530 • Investigations from a histological study found half of the samples treated with the PIPS  
531 irrigation protocol to be rendered completely free from infection, with the group having a  
532 99.5% median reduction in bacterial count.<sup>41</sup>
- 533 • Irrigation using PIPS increased the canal volume and eliminated debris from the canal  
534 system 2.6 times greater than standard needle irrigation.<sup>42</sup>
- 535 • PIPS creates improved cleaning and debridement of organic and inorganic tissue left by  
536 instrumentation, with the tip activated in the access cavity outside the root canal  
537 system.<sup>39</sup>

538 **SWEEPS (Shock Wave-Enhanced Emission Photoacoustic Streaming):** SWEEPS is  
539 based on the emission of a couple of consecutive laser pulses, with the second subsequent  
540 laser pulse shooting into the liquid at an optimal delay time from the first pulse when the initial  
541 bubble is in the final phase of its collapse, producing acceleration of laser-induced bubbles'  
542 collapse and leading to shock wave emission even in narrow root canals

543 SWEEPS and EDDY exhibited superior bacterial killing efficacy within dentinal tubules, with  
544 SWEEPS, PIPS, and EDDY achieving the highest biofilm removal rates of 99.56%, 99.46%, and  
545 99.46% respectively in main canal spaces.<sup>36</sup>

### 546 **Postoperative Pain Reduction**

547 Diode LAI demonstrated superior efficacy to needle irrigation in reducing pain 6-48 hours post-  
548 treatment, though the impact of PIPS was unclear with no difference observed between PIPS

549 and needle irrigation, while PIPS mitigated post-endodontic pain better than manual dynamic  
550 activation, sonic and ultrasonic activation.<sup>43</sup>

551

## 552 **Comparative Studies**

553 Er:YAG LAI and PIPS outperformed other methods in 33 of 59 articles reviewed, though there  
554 was great variety in study designs including bacterial incubation time, laser parameters,  
555 irrigation protocols, and irrigating solution used.<sup>40</sup>

## 556 **Safety Considerations**

557 Diode laser and PIPS caused less bacterial extrusion compared to passive ultrasonic  
558 irrigation.<sup>41</sup>

## 559 **C) NEGATIVE PRESSURE AND MULTISONIC SYSTEMS**

### 560 **1. APICAL NEGATIVE PRESSURE IRRIGATION (EndoVac System)**

561 **Mechanism of Action:** EndoVac uses suction to pull irrigant down the root canal and then up  
562 and away into the high-vacuum suction unit, eliminating the need for applying positive pressure,  
563 with no risk of pushing sodium hypochlorite beyond the apical foramen.<sup>38</sup>

564 **System Components:**The EndoVac system is composed of three basic components: Master  
565 Delivery Tip (MDT) that delivers irrigant to the pulp chamber and evacuates it concomitantly; a  
566 Macrocannula made of flexible polypropylene with an open end of 0.55 mm diameter used to  
567 suction irrigants to the middle segment; and a Microcannula with closed end and external  
568 diameter of 0.32 mm with 12 microholes (0.1 mm diameter each) that can be used in canals  
569 enlarged to size 35 or larger and should be taken to working length.

### 570 **2. MULTISONIC ULTRACLEANING SYSTEM (GentleWave)**

571 **Technology Overview:**The GentleWave Procedure utilizes Multisonic Ultracleaning  
572 technology, which enables procedure fluids to reach through the entire root canal system; unlike  
573 ultrasonic wavelength technology which uses a single wavelength, this system generates  
574 multiple acoustic frequencies simultaneously.<sup>44</sup>

575 The interplay of Multisonic energy, vortical fluid dynamics, and chemistry of the treatment fluid  
576 result in enhanced dissolution and removal of organic matter including pulp tissue and biofilm  
577 from the root canal system.<sup>45</sup>

### 578 **Clinical Performance:**

- 579
- 580
- 581
- 582
- 583
- 584
- 585
- 586
- 587
- 588
- **Tissue Dissolution:** Tissue dissolution efficacy of the GentleWave System was compared with different conventional and contemporary endodontic systems at different temperatures and concentrations of NaOCl.<sup>45</sup>
  - **Biofilm Removal:** The residual biofilm removal effect of GentleWave is superior to passive ultrasonic activation in the isthmus and apical region, which is known to have complex root canal anatomy.<sup>54</sup>
  - **Minimal Instrumentation:** Because the GentleWave System has the ability to clean in such a comprehensive way, less traditional instrumentation is required, creating potential to dramatically reduce procedure time and remove less structural dentin, helping preserve structural integrity of the tooth.<sup>46</sup>

589 **Comparative Efficacy:** Previous in vitro and in vivo studies evaluated the ability of different  
590 instrumentation techniques and irrigation protocols to eliminate lipopolysaccharides, and given  
591 their limited effectiveness, supplemental treatments with passive ultrasonic irrigation and  
592 photodynamic therapy have been investigated.<sup>47</sup>

593 Er:YAG and Er,Cr:YSGG lasers were highly promising with results close to multisonic  
594 ultracleaning, and needle irrigation and passive ultrasonic activation may not be able to provide  
595 competent debridement in treating necrotic oval root canals.<sup>48</sup>

## 596 **Comparative Summary:**

### 597 **Advantages by System:**

#### 598 **PUI:**

- 599
- 600
- 601
- 602
- 603
- Widely adopted and evidence-based
  - Cost-effective
  - Significant bacterial reduction (>99%)
  - Better smear layer removal
  - Reduced postoperative pain

#### 604 **LAI (PIPS/SWEEPS):**

- 605
- 606
- 607
- 608
- 609
- 610
- Highest bacterial reduction (99.5% median)
  - Superior tissue dissolution
  - 2.6x better debris removal vs conventional
  - Minimal instrumentation required
  - Lowest postoperative pain
  - No thermal damage to dentin

#### 611 **Negative Pressure (EndoVac):**

- 612
- 613
- Maximum safety (no apical extrusion)
  - Effective apical irrigation

- 614 • Overcomes vapor lock
- 615 • Comparable antimicrobial efficacy to conventional

616 **Multisonic (GentleWave):**

- 617 • Superior biofilm removal in complex anatomy
- 618 • Minimal instrumentation
- 619 • Preserves tooth structure
- 620 • Single-visit treatment
- 621 • Comprehensive cleaning of isthmuses and lateral canals

622 **Limitations:**

623 **PUI:** Technique-sensitive, risk of canal damage in curved canals, instrument contact issues

624 **LAI:** High equipment cost, limited in vivo studies, technique variability in literature

625 **Negative Pressure:** Requires canal enlargement to size 35+, equipment cost

626 **Multisonic:** Highest equipment cost, limited long-term clinical data

627

628 **Clinical Outcomes of activated irrigation systems**

629 Activated irrigation systems have been introduced to enhance the clinical effectiveness of root  
630 canal disinfection by improving irrigant penetration, hydrodynamic activity, and debris  
631 disruption.<sup>5,6</sup> Clinical investigations evaluating these systems have focused on both patient-  
632 centered outcomes, such as post-operative pain, and treatment-related outcomes including  
633 canal cleanliness, antibacterial efficacy, irrigant delivery to working length, and periapical  
634 healing.<sup>6</sup>

635 Across multiple clinical studies, activated irrigation has demonstrated a consistent short-term  
636 advantage over conventional needle-syringe irrigation in reducing post-operative pain,  
637 particularly within the first 24–48 hours following treatment.<sup>6</sup> A range of activation techniques—  
638 including ultrasonic, sonic, apical negative pressure, and mechanically assisted systems—were  
639 associated with lower pain scores and reduced analgesic intake compared with conventional  
640 irrigation.<sup>6</sup> This benefit is likely related to enhanced debris removal and reduced apical extrusion  
641 achieved through controlled hydrodynamic activation, especially in systems operating under  
642 negative pressure.<sup>6</sup> However, differences in pain outcomes were not sustained beyond the early  
643 post-operative period, indicating that the analgesic benefit of irrigant activation is predominantly  
644 short-lived.<sup>6</sup>

645 With respect to debridement efficacy and canal cleanliness, activated irrigation systems  
646 generally outperformed conventional irrigation methods.<sup>6</sup> Histological and microscopic analyses  
647 consistently demonstrated improved removal of dentinal debris and smear layer, particularly in

648 anatomically complex regions such as the apical third and canal isthmuses.<sup>6</sup> Ultrasonic  
649 activation was frequently associated with superior canal and isthmus cleanliness, while apical  
650 negative pressure systems showed enhanced apical debris removal with a reduced risk of  
651 irrigant extrusion.<sup>6</sup> These findings support the role of hydrodynamic forces, acoustic streaming,  
652 and mechanical agitation in disrupting debris and biofilm adherent to canal walls beyond the  
653 capabilities of needle irrigation alone.<sup>6</sup>

654 Evidence regarding antibacterial efficacy remains variable. Several randomized clinical trials  
655 reported greater reductions in cultivable bacterial counts with activated irrigation—particularly  
656 passive ultrasonic activation—when compared with conventional needle irrigation.<sup>5</sup> Mechanical  
657 activation using systems such as XP-endo finisher also demonstrated improved bacterial  
658 reduction relative to needle irrigation and some other agitation devices.<sup>5</sup> However, other studies  
659 reported no statistically significant difference between activated and conventional irrigation  
660 techniques.<sup>6</sup> In some instances, activated irrigation was associated with increased detectable  
661 bacterial counts immediately after activation, a finding attributed to the mechanical disruption of  
662 biofilms and smear layers that may transiently increase recoverable microorganisms without  
663 necessarily compromising overall disinfection.<sup>6</sup>

664 The effectiveness of activated irrigation systems in delivering irrigants to the working length has  
665 been evaluated in a limited number of clinical studies.<sup>6</sup> Available evidence suggests that both  
666 passive ultrasonic irrigation and apical negative pressure systems achieve improved irrigant  
667 penetration to working length compared with conventional needle irrigation.<sup>6</sup> Nonetheless,  
668 differences between activation techniques were not always statistically significant, and the  
669 scarcity of clinical data limits definitive conclusions regarding comparative efficacy.<sup>6</sup>

670 Long-term clinical outcomes, particularly periapical healing assessed radiographically, have not  
671 shown a significant difference between activated and conventional irrigation methods.<sup>6</sup> Studies  
672 using periapical radiographs and cone-beam computed tomography reported comparable rates  
673 of lesion reduction and resolution irrespective of irrigation technique.<sup>6</sup> Variables such as pre-  
674 operative lesion size and master apical file size appeared to exert a greater influence on healing  
675 outcomes than the method of irrigant activation.<sup>6</sup> These findings suggest that while activated  
676 irrigation improves short-term procedural and symptomatic parameters, its impact on long-term  
677 periapical healing remains limited.<sup>6</sup>

678 Overall, current clinical evidence indicates that activated irrigation systems provide measurable  
679 benefits in short-term outcomes, including reduced post-operative pain, improved canal  
680 cleanliness, enhanced debridement, and, in some cases, greater bacterial reduction compared  
681 with conventional irrigation.<sup>6</sup> However, heterogeneity in study design, activation protocols,  
682 irrigant formulations, and outcome assessment methods limits direct comparison across studies.  
683 Further well-designed randomized clinical trials with standardized methodologies and long-term  
684 follow-up are required to clarify the role of activated irrigation systems in improving sustained  
685 endodontic treatment outcomes.<sup>5,6</sup>

686

## 687 **Future Innovations and Research Directions**

688

689 Traditional irrigants such as sodium hypochlorite remain cornerstones; however, their  
690 limitations, including cytotoxicity and corrosive nature have driven research toward  
691 multifunctional irrigants with broad antimicrobial efficacy, tissue-dissolving capacity, biofilm  
692 disruption, smear layer removal and improved biocompatibility. Advancements in irrigant  
693 formulations are expected to simplify treatment protocols, while improving antimicrobial  
694 properties. Whereas traditional techniques require multi-step application of sodium hypochlorite  
695 and chelating agents, multifunctional irrigants aim to integrate desirable properties of  
696 conventional irrigants into a single formulation. In a comparative study evaluating such solutions  
697 mainly Triton and Endojuice, Triton demonstrated better tissue dissolution, closely matching the  
698 performance of sodium hypochlorite. Endojuice excelled in smear layer removal and exhibited  
699 significantly lower cytotoxicity and genotoxicity than Triton, however, it requires prior sodium  
700 hypochlorite application for optimal smear layer dissolution and biofilm removal.<sup>8</sup>

701

702 The long-term success of a tooth following root canal treatment is strongly influenced by the  
703 remaining tooth structure. Minimally invasive endodontics is guided by this principle, focusing on  
704 preserving as much healthy tissue as possible. It prioritizes preservation of peri-cervical dentin  
705 and structural integrity, and presents a distinct challenge for irrigation protocols to accomplish  
706 deeper disinfection within more conservative canal preparations. The shift towards minimally  
707 invasive endodontics creates a unique challenge for irrigation efficacy as conservative canal  
708 preparations may constrain the volume and flow of irrigants.<sup>10</sup>

709

710 Recent research highlights the significant potential of non-thermal plasma (NTP) for endodontic  
711 irrigation, particularly through underwater discharge plasma, which operates by creating plasma  
712 directly in a liquid medium.<sup>51</sup> The antimicrobial action of underwater discharge plasma (UDP) is  
713 primarily mediated by reactive oxygen and nitrogen species, leading to cell membrane  
714 disruption, protein denaturation and biofilm degradation.<sup>6</sup> Cold plasma technologies, which  
715 enable microbial inactivation, biostimulation and surface modulation are transforming the  
716 medical field<sup>51</sup>. Nevertheless, their clinical superiority and safety in endodontics remain to be  
717 validated through further research.<sup>51</sup>

718

719 Artificial intelligence has brought significant advancements across multiple sectors and in the  
720 field of dentistry, particularly endodontics, AI contributes to improved diagnostic accuracy and  
721 enhanced clinical outcomes. The integration of artificial intelligence with irrigation systems will  
722 depend on interdisciplinary collaboration and well-designed studies.<sup>49</sup>

723

724 Current research primarily relies on culture-based methods that fail to detect many endodontic  
725 microbes, necessitating more advanced diagnostics for accurate antimicrobial testing.<sup>1</sup> Despite  
726 in vitro studies, there is a persistent lack of high quality clinical studies to ensure long term  
727 efficacy and widespread clinical adoption of new formulations as in vitro studies are limited in  
728 their ability to replicate the clinical conditions.<sup>52</sup> Future research must prioritize establishing the  
729 safety and biocompatibility of irrigants.<sup>8</sup> Large, multicenter randomized clinical trials are  
730 necessary to compare irrigants, evaluate irrigation protocols and measure long term outcomes  
731 across diverse patient populations.<sup>50</sup>

732

## 733 **Conclusion**

734 Endodontic irrigation remains the cornerstone of successful root canal therapy, compensating  
735 for the anatomical and biological limitations of mechanical instrumentation. Conventional  
736 irrigants such as sodium hypochlorite, chlorhexidine, and EDTA continue to form the backbone  
737 of chemo-mechanical preparation due to their well-established antimicrobial and chelating  
738 properties. However, none of these agents independently fulfills all the criteria of an ideal  
739 irrigant, particularly with respect to simultaneous tissue dissolution, smear layer removal, biofilm  
740 disruption, and optimal biocompatibility.<sup>9</sup>

741  
742 Emerging irrigant technologies, including nanoparticles, herbal formulations, ozone,  
743 photodynamic therapy, QMix, and electrochemically activated solutions—represent promising  
744 attempts to address the shortcomings of traditional protocols. Nanoparticle-based systems  
745 demonstrate enhanced antibiofilm activity and deeper dentinal penetration, although concerns  
746 regarding cytotoxicity, discoloration, and limited long-term clinical validation persist.<sup>4,19</sup> Herbal  
747 irrigants offer attractive biocompatibility profiles and reduced toxicity but currently lack sufficient  
748 standardized clinical evidence to replace sodium hypochlorite.<sup>7</sup> Similarly, ozone, reactive  
749 solutions, and photoactivated disinfection have shown encouraging antimicrobial effects but  
750 remain adjunctive rather than primary disinfection strategies.<sup>23,27</sup>

751  
752 Activation systems have significantly improved the effectiveness of irrigation by enhancing  
753 irrigant penetration and hydrodynamic disruption. Passive ultrasonic irrigation, laser-activated  
754 irrigation (PIPS and SWEEPS), apical negative pressure systems, and multisonic ultracleaning  
755 technologies consistently demonstrate superior debris removal and improved smear layer  
756 elimination compared to conventional syringe irrigation.<sup>50,53</sup> Short-term clinical benefits,  
757 particularly in reducing postoperative pain and enhancing canal cleanliness, are well  
758 documented. However, current evidence suggests that these activation systems do not  
759 consistently translate into superior long-term periapical healing outcomes.<sup>6</sup>

760  
761 Future innovations are shifting toward multifunctional irrigants capable of integrating  
762 antimicrobial, chelating, and tissue-dissolving properties within a single formulation.<sup>8</sup> Advances  
763 in minimally invasive endodontics further necessitate highly efficient irrigation systems capable  
764 of achieving deep disinfection within conservative canal preparations.<sup>10</sup> Novel technologies such  
765 as non-thermal plasma, artificial intelligence-guided irrigation protocols, and bioengineered  
766 antimicrobial systems represent the next frontier in endodontic disinfection.<sup>49,51</sup> Nevertheless,  
767 the transition from promising in vitro findings to routine clinical adoption requires robust,  
768 multicenter randomized controlled trials with standardized methodologies and long-term follow-  
769 up.<sup>9,52</sup>

770  
771 In summary, while sodium hypochlorite remains the gold standard irrigant, the future of  
772 endodontic irrigation lies in synergistic integration, combining advanced chemical formulations  
773 with sophisticated activation technologies to achieve safer, deeper, and more predictable canal  
774 disinfection. Continued interdisciplinary research will be essential to translate emerging  
775 innovations into clinically reliable, biologically sound protocols that enhance long-term treatment

776 success.

777

778

779

## References:

- 780 1. Gomes BPFA, Aveiro E, Kishen A. Irrigants and irrigation activation systems in  
781 endodontics. *Braz Dent J.* 2023;34(4):1–33.
- 782 2. Karataş E, Ayaz N, UlukÖylü E, Baltacı MÖ, AdigÜzel A. Effect of final irrigation with  
783 sodium hypochlorite at different temperatures on postoperative pain level and  
784 antibacterial activity: a randomized controlled clinical study. *J Appl Oral Sci.* 2021 Feb  
785 10;29:e20200502.
- 786 3. Drews DJ, Nguyen AD, Diederich A, Gernhardt CR. The Interaction of Two Widely Used  
787 Endodontic Irrigants, Chlorhexidine and Sodium Hypochlorite, and Its Impact on the  
788 Disinfection Protocol during Root Canal Treatment. *Antibiotics.* 2023 Mar 16;12(3):589.
- 789 4. de Almeida, Josiane<sup>1,2</sup>; Cechella, Bruna Casagrande<sup>1</sup>; Bernardi, Anarela Vassen<sup>1</sup>; de  
790 Lima Pimenta, Andrea<sup>3,4</sup>; Felipe, Wilson Tadeu<sup>1</sup>. Effectiveness of Nanoparticles  
791 Solutions and Conventional Endodontic Irrigants against *Enterococcus Faecalis* Biofilm.  
792 *Indian Journal of Dental Research* 29(3):p 347-351, May–Jun 2018
- 793 5. Tonini R, Salvadori M, Audino E, Sauro S, Garo ML, Salgarello S. Irrigating Solutions  
794 and Activation Methods Used in Clinical Endodontics: A Systematic Review. *Frontiers in*  
795 *Oral Health.* 2022 Jan 31;3
- 796 6. Nivedhitha MS, Shankar S, Ramaprabha S, Rajan R, Krithikadatta J.  
797 Clinical efficacy of activated irrigation techniques in endodontic treatment: a systematic  
798 review. *Restor Dent Endod.* 2021;46(1):e10
- 799 7. Teja KV, Janani K, Srivastava KC, Shrivastava D, Jose J, Marya A, Karobari MI.  
800 Comparison of herbal agents with sodium hypochlorite as root canal irrigant: a  
801 systematic review of in vitro studies. *Evidence- Based Complementary and Alternative*  
802 *Medicine.* 2021;2021(1):8967219.
- 803 8. Ballal NV, et al. Biological and chemical properties of new multi-functional root canal  
804 irrigants. *J Dent.*2025;153:105551.
- 805 9. Orozco-Gallego MJ, Pineda-Vélez EL, Rojas-Gutiérrez WJ, Rincón-Rodríguez ML,  
806 Agudelo-Suárez AA. Effectiveness of Irrigation Protocols in Endodontic Therapy: An  
807 Umbrella Review. *Dent J (Basel).* 2025;13(6):273.
- 808 10. Marvaniya J, et al. Minimal invasive endodontics: A comprehensive narrative review.  
809 *Cureus.* 2022;14(6):e25984.
- 810 11. Kaplan T, Kaplan SS, Sezgin GP. The effect of different irrigation and disinfection  
811 methods on post-operative pain in mandibular molars: a randomised clinical trial. *BMC*  
812 *Oral Health.* 2022 Dec 13;22(1):601
- 813 12. Kendre SB, Bhatane AU, Dadpe MV, Kale YJ, Dahake PT. Comparative evaluation of  
814 antibacterial efficacy of sequential herbal irrigation with conventional irrigation in  
815 endodontic therapy of primary teeth: A randomized controlled trial. *J Indian Soc Pedod*  
816 *Prev Dent.* 2025 Jul 1;43(3):410-417.

- 817 13. Magni E, Scianna A, Connert T, Leontiev W, Weiger R, Eggmann F. A Novel  
818 Educational Approach for Safe Endodontic Syringe Irrigation: A Randomized Controlled  
819 In Vitro Study. *EurEndod J.* 2024 Aug 19;9(3):279-286.
- 820 14. Machareonsap H, Chompu-Inwai P, Chaipattanawan N, Manmontri C, Nirunsittirat A,  
821 Phinyo P. Normal Saline or Sodium Hypochlorite Irrigation for Vital Pulp Therapy? A  
822 Non-Inferiority Randomized Controlled Trial. *EurEndod J.* 2024 Aug 22;9(3):180-190
- 823 15. li A, Bhosale A, Pawar S, Kakti A, Bichpuriya A, Agwan MA. Current Trends in Root  
824 Canal Irrigation. *Cureus.* 2022 May 8;
- 825 16. Dioguardi M, Di Gioia G, Illuzzi G, Laneve E, Cocco A, Troiano G. Endodontic irrigants:  
826 Different methods to improve efficacy and related problems. *European Journal of*  
827 *Dentistry [Internet].* 2018;12(3):459–66
- 828 17. Neelakantan P, Herrera DR, Pecorari VGA, Gomes BPFA. Endotoxin levels after  
829 chemomechanical preparation of root canals with sodium hypochlorite or chlorhexidine:  
830 a systematic review of clinical trials and meta-analysis. *International Endodontic Journal*  
831 *[Internet].* 2019 Jan 1;52(1):19–27
- 832 18. Chandak PG, Chandak MG, Relan KN, Chandak M, Rathi C, Patel A. Nanoparticles in  
833 endodontics-a review. *J Evol Med Dent Sci.* 2021 Mar 29;10(13):976-82.
- 834 19. Bukhari S, Kim D, Liu Y, Karabucak B, Koo H. Novel endodontic disinfection approach  
835 using catalytic nanoparticles. *Journal of endodontics.* 2018 May 1;44(5):806-12.
- 836 20. Jowkar Z, Hamidi SA, Shafiei F, Ghahramani Y. The effect of silver, zinc oxide, and  
837 titanium dioxide nanoparticles used as final irrigation solutions on the fracture resistance  
838 of root-filled teeth. *Clinical, cosmetic and investigational dentistry.* 2020 Apr 22:141-8.
- 839 21. Karobari MI, Adil AH, Assiry AA, Basheer SN, Noorani TY, Pawar AM, Marya A, Messina  
840 P, Scardina GA. Herbal medications in endodontics and its application—a review of  
841 literature. *Materials.* 2022 Apr 25;15(9):3111.
- 842 22. Kale PP, Raut AW. A proposed classification system for herbal endodontic irrigants.  
843 *Journal of Conservative Dentistry and Endodontics.* 2021 May 1;24(3):293-5.
- 844 23. Shetty N, Mathew T, Shetty A, Hegde MN, Attavar S. Ozonated water as an irrigant in  
845 disinfecting root canal systems-a systematic review. *Evidence-Based Dentistry.* 2022  
846 Sep 8:1-5.
- 847 24. Silva EJ, Prado MC, Soares DN, Hecksher F, Martins JN, Fidalgo TK. The effect of  
848 ozone therapy in root canal disinfection: a systematic review. *International endodontic*  
849 *journal.* 2020 Mar;53(3):317-32.
- 850 25. de Vasconcelos Neves G, Dos Santos KS, de Souza Sales EA, de Moura RQ, Barros  
851 DG, Gominho LF, de Castro Gomes DQ. Antibacterial effect of photodynamic therapy on  
852 root canal disinfection combined with different irrigation protocols. *Iranian Endodontic*  
853 *Journal.* 2020;15(2):90.
- 854 26. Ravinanthanan M, Hegde MN, Shetty V, Kumari S, Al Qahtani FN. A Comparative  
855 Evaluation of Antimicrobial Efficacy of Novel Surfactant-Based Endodontic Irrigant  
856 Regimen's on *Enterococcus faecalis*. *Contemporary Clinical Dentistry.* 2022 Jul  
857 1;13(3):205-10.
- 858 27. Ali IAA, Neelakantan P. Light activated disinfection in root canal treatment: a focused  
859 review. *Dent J (Basel).* 2018;6(3):31.

- 860 28. Shalavi S, Mohammadi Z. An overview on a promising root canal irrigation solution:  
861 QMix. *Iran Endod J.* 2021;16(2):71–77.
- 862 29. Gründling GL, Melo TA, Montagner F, Scarparo RK, Vier-Pelisser FV. QMix® irrigant  
863 reduces lipopolysaccharide levels in an in vitro model. *J Appl Oral Sci.* 2015;23(4):431–  
864 435.
- 865 30. Shi L, Wu S, Yang Y, Wan J. Efficacy of five irrigation techniques in removing calcium  
866 hydroxide from simulated S-shaped root canals. *J Dent Sci.* 2022;17(1):128–134.
- 867 31. Diogo P, Gonçalves T, Palma P, Santos JM. Photodynamic antimicrobial chemotherapy  
868 for root canal system asepsis: a narrative literature review. *Int J Dent.*  
869 2015;2015:269205.
- 870 32. Mohammadi Z, Jafarzadeh H, Shalavi S, Palazzi F. Recent advances in root canal  
871 disinfection: a review. *Iran Endod J.* 2017;12(4):402–406.
- 872 33. Rossi-Fedele G, Figueiredo JA, Steier L, Canullo L, Steier G, Roberts AP. Evaluation of  
873 the antimicrobial effect of super-oxidized water (Sterilox®) and sodium hypochlorite  
874 against *Enterococcus faecalis* in a bovine root canal model. *J Appl Oral Sci.*  
875 2010;18(5):498–502.
- 876 34. Paula Perlea, Cosmin Stefanescu, Madalina-Georgiana Dalaban, Alexandru-Eugen  
877 Petre- Experimental study on dimensional variations of 3D printed dental models based  
878 on printing orientation/Wiley Online Library/March 2024
- 879 35. Mohammed H Alyami , Alexander Muacevic, John R Adler- The Applications of 3D-  
880 Printing Technology in Prosthodontics: A Review of the Current Literature/PubMed  
881 Central/September 2024
- 882 36. Mi-Kyoung Jun1,Jong-Woo Kim2,Hye-Min Ku3- Three-Dimensional Printing in Dentistry:  
883 A Scoping Review of Clinical Applications, Advantages, and Current  
884 Limitations/MDPI/April 2025
- 885 37. Naveen Gopi Chander , Anup Gopi -. Trends and future perspectives of 3D printing in  
886 prosthodontics/PubMed Central/June 2024
- 887 38. Fereshte Rezaie , Masoud Farshbaf , Mohammad Dahri , Moein Masjedi , Reza Maleki ,  
888 Fatemeh Amini , Jonathan Wirth , Keyvan Moharamzadeh , Franz E Weber , Lobat  
889 Tayebi -3D Printing of Dental Prostheses: Current and Emerging Applications/PubMed  
890 Central April 2024
- 891 39. Poom Narongdej , Mana Hassanpour, Nicolas Alterman, Frederick Rawlins-Buchanan ,  
892 Ehsan Barjasteh - Advancements in Clear Aligner Fabrication: A Comprehensive Review  
893 of Direct-3D Printing Technologies/PubMed Central January 2024
- 894 40. Gianluca M Tartaglia , Andrea Mapelli , Cinzia Maspero , Tommaso Santaniello , Marco  
895 Serafin , Marco Farronato , Alberto Caprioglio - Direct 3D Printing of Clear Orthodontic  
896 Aligners: Current State and Future Possibilities/PubMed Central April 2021
- 897 41. Christina Erbe , Björn Ludwig , Maximilian Bleilöb -. Unlocking the biological insights of  
898 3D printed aligners: A look at current findings/Science Direct February 2025
- 899 42. Talar Torkomian , Fernando de la Iglesia , Andreu Puigdollers -3D-printed clear aligners:  
900 An emerging alternative to the conventional thermoformed aligners? - A systematic  
901 review/ PubMed/April 2025
- 902 43. ChenyangNiu,Chenyang Niu1Dongwen Li,Dongwen Li1,2†Yujia ZhangYujia  
903 Zhang1Yunkai WangYunkai Wang1Shangbo Ning,Shangbo Ning1,2Gang Zhao,Gang

- 904 Zhao1,Zhahui Ye,Zhahui Ye1,2Yu Kong,-Prospects for 3D-printing of clear aligners—a  
905 narrative reviewUpdated/Frontier /July 2024
- 906 44. José Evando da Silva-Filho,Júlia Magalhães-Saldanha,Francisco Samuel Rodrigues  
907 Carvalh0,Fábio de Almeida Gomes,Eduardo Diogo Gurgel-Filho -Evaluation of the  
908 Efficacy of Passive Ultrasonic Irrigation Versus Conventional Methods in Endodontic  
909 Therapy Outcomes: A Scoping Review/ Journal of Advances in Medicine and Medical  
910 Research/2024 Volume 36
- 911 45. Sandra Mozo , Carmen Llena , Leopoldo Forner-Review of ultrasonic irrigation in  
912 endodontics: increasing action of irrigating solutions/PubMed Central
- 913 46. L W M van der Sluis 1, M Versluis, M K Wu, P R Wesselink-Passive ultrasonic irrigation  
914 of the root canal: a review of the literature/PubMed
- 915 47. Glen A. Roberson,Pramod K. Sinha-3D printing in orthodontics: A practical guide to the  
916 printer technology and selection/Science Direct/June 2022
- 917 48. Renato Piai Pereira DDS, MSc , Clovis Monteiro Bramante DDS, PhD \*, Marco Antonio  
918 Hungaro Duarte DDS, PhD \*, Murilo Priori Alcalde DDS, PhD , Cristiane de Gusmão  
919 Silva Piai DDS , Rodrigo Ricci Vivan DDS, PhD -Postoperative Pain After Using Passive  
920 Ultrasonic Irrigation and EasyClean Device, Irrigation Activation Techniques: A  
921 Randomized Clinical Trial /Science Direct/June 2023
- 922 49. Kumar MSS, Rai A, Singh N, et al. Artificial Intelligence (AI) in Endodontics: A Review. J  
923 Pharm Bioallied Sci. 2025;17(Suppl 1):S96-S98.
- 924 50. Boutsoukis C, Arias-Moliz MT. Present status and future directions - irrigants and  
925 irrigation methods. Int Endod J. 2022;55 Suppl 3(Suppl 3):588-612.
- 926 51. Lyu JH, Kim YH, Chung HS, et al. Clinical Evaluation of Underwater Discharge Plasma  
927 as a Root Canal Irrigant: A Randomized Pilot Study on Efficacy and Safety.  
928 *Biomedicines*. 2025;13(10):2343.
- 929 52. Sheng X, Yu J, Liu H, Wang Z, Deng S, Shen Y. Dual effectiveness of a novel all-in-one  
930 endodontic irrigating solution in antibiofilm activity and smear layer removal. *Front*  
931 *BioengBiotechnol*. 2023;11:1254927
- 932 53. van der Sluis LWM, et al. Passive ultrasonic irrigation of the root canal: a review. Int  
933 Endod J. 2007.
- 934 54. Kim KH, Lévesque C, Malkhassian G, Basrani B. Efficacy of the GentleWave System in  
935 the removal of biofilm from the mesial roots of mandibular molars before and after  
936 minimal instrumentation: An ex vivo study. International Endodontic Journal. 2024 Feb  
937 19;57(7):922–32.
- 938
- 939