
ENDODONTIC IRRIGATION

Tsvetelina Borisova-Papancheva, Slavena Svetlozarova, Natalia Kostadinova

*Department of Conservative Dentistry and Oral Pathology, Faculty of Dental Medicine,
Medical University of Varna*

ABSTRACT

INTRODUCTION: The removal of pulp tissue and dentin debris from the root canal system, as well as the chemical and mechanical cleaning of the root canal system, are all necessary for an endodontic procedure to be successful. It is challenging to completely treat the dentinal surface of the root canal due to the complex root-canal shape, extra lateral canals, and the characteristics of the apical delta. Large portions of the main canal are still untreated and uncleaned according to numerous studies. The canal contents are evacuated to varied degrees and part of it is pushed apically and towards the walls during the shaping of the canal space without irrigants, resulting in the formation of a dense contaminant layer. Because of this, irrigation plays an essential role in endodontic therapy. The irrigant must be delivered to the prepared root space in order to be distributed to all areas, including mechanically untreated ones.

AIM: The primary goal of this article is to investigate the properties of various types of irrigation solutions, the concentrations at which they are used in modern dentistry, and how their effectiveness can be increased.

MATERIALS AND METHODS: For this research investigation, data were gathered from online databases.

RESULTS: Some of the most widely used irrigation solutions are sodium hypochlorite, EDTA, sterile water or saline, citric acid, and other combined solutions.

CONCLUSION: The main issues with using irrigation solutions are their inability to reach the most complex anatomical structures in the apical third, the clinical usage time, and their toxicity to the periapical tissues.

Keywords: *irrigation, sodium hypochlorite, EDTA, citric acid*

Address for correspondence:

*Tsvetelina Borisova-Papancheva
Faculty of Dental Medicine
Medical University of Varna
84 Tzar Osvoboditel Blvd
9002 Varna
e-mail: dr_borisova@abv.bg*

Received: September 3, 2022

Accepted: December 7, 2022

INTRODUCTION

Endodontic Therapy

The removal of pulp tissue and dentin debris from the root canal system, as well as the chemical and mechanical cleaning of the root canal system, are all necessary for an endodontic procedure to be successful. It is challenging to completely treat the dentinal surface of the root canal due to the complex root-canal shape, extra lateral canals, and the

characteristics of the apical delta. Large portions of the main canal are still untreated and uncleaned, according to numerous studies. The canal contents are evacuated to varied degrees and part of it is pushed apically and towards the walls during the shaping of the canal space without irrigants, resulting in the formation of a dense contaminant layer. Because of this, irrigation plays an essential role in endodontic therapy. The irrigant must be delivered to the prepared root canal space and from there—to spread it to all areas, including those that have remained mechanically untreated. The purpose of irrigation is:

- ◆ to reach all parts of the root canal anatomy
- ◆ to remove the smear layer from the dentinal tubules
- ◆ to reduce friction between the instrument and the root canal walls
- ◆ to improve the cutting efficiency of the instrument (lubricant)
- ◆ to exert its antibacterial effect
- ◆ to dissolve organic matter
- ◆ to penetrate to canal periphery

The effect of irrigants depends on:

- ◆ their chemical composition
- ◆ the degree of expansion of the root canal
- ◆ the taper of the canal
- ◆ the canal content/affected surface (treated or not mechanically)
- ◆ the dynamics of irrigation.

Microflora in the Root Canal

The bacterial microflora in the root canal contains aerobes and facultative anaerobes. As the disease progresses, the ecosystem changes as a result of:

- ◆ the presence of oxygen in the canal, which is open during its treatment
- ◆ the use of irrigants that change the pH of the canal
- ◆ the use of various medications—Ca(OH)₂, antibiotic pastes, etc.

In the root canal, microbes form communities (biofilm). When the bacteria are part of a biofilm, they can survive even in very extreme conditions. In the structure of the biofilm, microorganisms (MO) cooperate with each other and this allows them to act as a whole. In the composition of the biofilm, microorganisms produce extracellular polysaccharides (EPS) that protect them against environmental factors. For this reason, they are much more resistant to antibiotics (1-4). Bacteria communicate with each other through signaling molecules. This is the so-called quorum sensing. Microbes respond to these quorum-sensing molecules by regulating their metabolism and physiology, e.g., by increasing their toxin and EPS production (5).

Solutions Used in the Root Canal Irrigation

Due to the fact that irrigation serves a number of fundamental mechanical, chemical, and (micro) biological purposes, it plays a significant role in root canal therapy:

- ◆ **Mechanical:** Rinsing the root canal and removing microorganisms, tissue debris and den-

Table 1. Properties of irrigants.

Irrigants	Efficacy on Organic Residues	Efficacy on Inorganic Residues	Antibacterial Activity	Damage to the Periodontal Tissues	Manageability	Cost	Enlargement of Dentinal Tubules
NaOCl	Yes	No	Yes	Yes	Bad	Low	High
EDTA	No	Yes	No	Very low	Good	Low	High
Citric acid	Yes	Yes	Yes	Yes	N/A	Low	Low
CHX	No	No	Yes	No	Good	Low	No influenced
Tetraclean	Yes	Yes	Yes	No	Good	High	High
MTDA	Yes	Yes	Yes	No	Good	High	High
QMix	Yes	Yes	Yes	No	Good	High	High

tin filings; lubrication of the canal reduces the friction of the instrument and decreases the removal of dentin; prevention of the formation of apical plugs and extrusion of infected substances in the periapex.

- ◆ **Chemical:** Prevention of the formation of a smear layer; dissolution of organic (dentin collagen, pulp residues, biofilm) and inorganic (dentin) materials.
- ◆ **Biological:** High efficacy to anaerobic and facultative microorganisms; inactivation of endotoxins; prevention of the weakening of the tooth structure; prevention of toxic and caustic reactions in contact with vital tissues.

Most of the researches on endodontic irrigation are targeted at the removal of the smear layer (6–9). But the smear layer can be eliminated easily when we irrigate according to the correct protocol. However, the most challenging areas of the root canal anatomy may be those which were not touched by the files (such as fins, isthmuses and large lateral canals, large areas in the oval, and flat canals) (10). These areas contain tissue and biofilm residues that can only be removed by chemical irrigation. The apical part of the root canal is a challenge for irrigation as a balance between safety and efficiency (11).

AIM

The primary goal of this article is to investigate the properties of various types of irrigation solutions, the concentrations at which they are used in modern dentistry, and how their effectiveness can be increased.

MATERIALS AND METHODS

For this research investigation, data were gathered from Web of Science and PubMed online databases. Three reviewers from the dental clinic of the Medical University of Varna conducted the search in a standardized manner. *Endodontic irrigants, apical extrusion and root canal irrigants, or sodium hypochlorite activation and endodontic irrigants activation* have all been used as search terms to provide the desired results. Reviews, clinical trials, and in vitro research were among the article types chosen. In addition, all of their abstracts were examined to weed out any that were unnecessary or not in English. Many articles from endodontic peer-reviewed journals, in-

cluding the International Endodontic Journal and Journal of Endodontics, have been taken into consideration for the discussion. Every article listed in the references has been thoroughly read and debated.

RESULTS

Sodium Hypochlorite

Irrigation solutions are used for removal and destruction of microorganisms, necrotic and inflamed tissue and dentin debris (10). One of the most commonly used irrigants is sodium hypochlorite (NaOCl). NaOCl is one of the best disinfectant solutions in root canal treatment (12–14) due to its ability to dissolve both organic (pulpal remnants and collagen) and necrotic tissues. It affects a wide range of microorganisms in a non-specific way (15–17). It also destroys spores and viruses. Hypochlorite has a strong antimicrobial effect and in direct contact kills bacteria immediately, even in low concentrations. In endodontics the most commonly used concentrations are: 0.5% to 6% (20–23). The literature has a wide range of opinions about the antibacterial properties of NaOCl. Even at low concentrations, in some publications, hypochlorite is said to kill the target microorganisms in a matter of seconds, but other studies have found that the same species can be killed in much longer amounts of time (28–30). The presence of organic matter during irrigation has a great effect on the antibacterial activity of NaOCl. Haapasalo and colleagues (31) showed that the presence of dentin causes severe delaying the killing of *Enterococcus faecalis* by 1% NaOCl. Early research has documented that the presence of organic matter (such as inflammatory exudate, tissue remnants, microbial biomass) reduces the effectiveness of irrigation with NaOCl. To increase the effectiveness of hypochlorite, the solution should be frequently refreshed and kept in motion by continuous irrigation (18,19). Bystrom and Sundqvist (32,33) investigated root canal irrigation in necrotic and anaerobic bacterial mixtures. According to the study, irrigation with 0.5% or 5% NaOCl, with or without ethylenediaminetetraacetic acid (EDTA), significantly reduces the amount of bacteria in the root canal. However, it is difficult to clear the root canal of bacterial infection despite repeated irrigation sessions using just one irrigant (34). Studies show that antimicrobial activity is concentra-

tion-independent, but tissue and biofilm degradation is dependent.

In aqueous solutions at body temperature, active chlorine can exist in 2 forms: hypochlorite (OCl) or hypochlorous acid (HOCl). In what form it will act depends on the acidity of the solution. In water, NaOCl ionizes to form the ions Na and OCl, which are in equilibrium with HOCl. The major form of chlorine at acidic and neutral pH is HOCl. OCl predominates at high pH levels of 9 and above (24). It is HOCl that has an antibacterial effect. Because HOCl interferes with the microbial cell's essential processes, the cell dies (25,26). Without the addition of NaOCl, irrigations are unlikely to be successful. However, because it solely destroys the organic component, hypochlorite alone is unable to eliminate the smear layer. To completely remove the smear layer, we must combine the use of hypochlorite with EDTA and citric acid.

Disadvantages of hypochlorite are bad taste, toxicity, and the difficulty to remove the smear layer on its own. The lower in vivo performance, in comparison to in vitro, is likely brought about by difficulties in penetrating the root canal system's furthest reaches, including the fins, anastomoses, apical canal, lateral canals, and dentin canals. Additionally, the presence of certain substances renders NaOCl ineffective, such as periapical exudate, pulp tissue, dentin collagen, and microbial biomass (31). Recent research has revealed that continuous exposure of dentin to high concentrations of hypochlorite causes dentin to lose its flexibility and elasticity (35- 36).

In conclusion, NaOCl is the most significant irrigation solution and the only one that has the ability to dissolve organic tissue, including biofilm and the organic component of the smear layer. Throughout the instrumentation phase, it should be applied.

EDTA and Citric Acid

During the instrumental treatment of root canals, in addition to the removal of the organic component (from NaOCl), it is also necessary to remove the inorganic dentin particles and prevent the formation of a smear layer on the root canal surface. Also, calcifications and narrowing may be observed during root canal treatment due to their complex anatomy. Therefore, the use of chelators is needed. The chelators which we are using frequently are: EDTA

(17%) and citric acid (CA). They successfully remove inorganic matter, including hydroxyapatite (6–9). They also do not affect organic substances, and they do not work as an antibacterial agent by themselves. The most used EDTA concentrations are 17% (neutralized solution, pH 7) and 10–50% for CA concentrations.

During root canal instrumentation, the chelator causes demineralization of the dentin. Its effectiveness depends on the duration of its action. EDTA and CA are highly biocompatible (36). In addition to their cleaning ability, chelators may detach biofilms adhering to the root canal walls. It has been found that after 5 minutes of application of 15% solution of EDTA, the size of the demineralization zone around the luminal canal is about 20–30 micrometers, but does not exceed 50 micrometers even after 24–48 hours. This layer is separated from the underlying dentin by a demarcation line. This is a proof that the process is self-limiting, i.e., the process continues until the solution is saturated and there are no free ions (38,39). Neutral and alkaline EDTA solutions have been shown to have the most optimal effect.

After NaOCl irrigation and at the termination of instrumentation, EDTA and CA are applied for 2 to 3 minutes. In deeper layers of dentin, smear layer removal with EDTA or CA enhances the antibacterial effects of locally applied disinfectants (40,41). The effect of the chelators is different on the individual sections of the root canal and certainly decreases in the direction from the orifices to the apex. The result is influenced by the amount and concentration of the solutions used, as well as by the size of the root canal surface on which they act. Chelators reduce the amount of smear layer during the preparation of the duct surfaces by affecting the inorganic component. After removal of this layer, the walls of the canal are clean, the dentinal tubules are clearly visible, and their orifices are enlarged due to the dissolution of the peritubular dentin. Chelating agents are available in the form of liquids and pastes. The use of liquid forms is recommended as they enter the root canals more easily, affect all walls, and are easier to remove from the canal space (22,42). The combined use of chelators and NaOCl reduces the amount of Cl in the NaOCl solution, so it becomes less effective against bacteria and necrotic tissues. Therefore, the use of chelators in the early stages of treatment is

not desirable, especially in the preparation of infected root canals.

Citric acid removes the smear layer by reacting with calcium and phosphate ions, but has a weak antibacterial effect. The concentration at which it is used varies between 1% and 50%. The antibacterial effect is proportional to the concentration. Highly concentrated solutions cause dentinal erosions (25%, 50%). Therefore, the most commonly used concentration is 10% solution for 2–3 minutes at the end of the instrumental treatment and after irrigation with NaOCl. Alternating washes with 15% CA and 1% NaOCl during root canal preparation enhance the antibacterial effect in the presence of infection and bring it closer to 5.25%.

Guidelines for the use of chelating agents: The mechanical instrumentation of root canal can be done in the presence of chelators in the form of a paste, which is introduced with the instrument. The canal needs to be pre-washed with NaOCl to dissolve tissue debris. Paste chelators are used as lubricating agents and reduce the risk of endodontic instrument fracture. More NaOCl should be used during the preparation of the root canal because of its better antibacterial and lysing properties. The final rinsing with a chelating solution reduces the amount of smear layer, improves the cleaning of the canal walls and the adaptation of the filling. Substances containing EDTA should be used for 1 to 5 minutes.

Chlorhexidine Digluconate

Chlorhexidine digluconate (CHX) is a powerful antiseptic, which is widely used in the form of 0.1–0.2% solutions for chemical control of dental plaque. In endodontics it is used for irrigation in 2% concentration. It is widely used as an irrigant and as an intracanal medicament because of its well-defined antibacterial action against G+/G- microorganisms and yeasts (42,43). It is more active against G+, and some types of G- bacteria are less sensitive to it, such as: *Proteus*, *Pseudomonas*, *Enterobacter*, *Actinobacter*, *Klebsiella* (44,45). One of the reasons for the popularity of CHX is its substantivity (i.e., continued antimicrobial effect). The CHX molecule is cationic, which allows it to attach to the negatively charged surfaces of bacteria, enter their cell wall or outer membrane, and target their cytoplasm or inner membrane (24). Depending on its concentration, it may be bacteri-

cidal or bacteriostatic. In high concentrations it coagulates the intracellular elements and has a bactericidal effect. In low concentrations it has a bacteriostatic effect by irreversibly damaging the cell as a result of the extraction of potassium and phosphorus (46). In order to maximize the antibacterial effect at the completion of the chemomechanical preparation, 2% CHX may be a viable option because it does not erosively dissolve dentin like NaOCl does (40). Some studies suggest that the CHX gel performs significantly better than the CHX liquid, although the causes of any differences are unknown (48).

Mixtures of Irrigants

The smear layer is better cleaned by adding surfactants to EDTA and CA. Drugs with increased antibacterial activity by the addition of the antibiotic doxycycline are MTAD and TetraClean. Doxycycline, detergent, and CA are all ingredients in both products. They differ in terms of detergent kind and acid concentration. After using NaOCl as a pre-treatment and following mechanical and chemical treatment, they are intended for irrigation. In terms of excellent smear layer removal, less associated undesirable effects on dentine, and strong biocompatibility, MTAD exhibits potential as an endodontic irrigant (48). However, the use of these combination products raises some questions about the doxycycline content in them because it may lead to tooth discoloration or development of resistance. The use of MTAD is supported by scant clinical data (49).

The QMix 2-in-1 solution have all the requirements for effective irrigation after rinsing with NaOCl. It contains EDTA and CHX, which successfully remove the smudged layer and have a good antibacterial effect. Compared to 17% EDTA and CHX alone, QMix has a gentle effect on dentinal canals and has a strong bactericidal effect, especially against resistant bacteria such as *Enterococcus faecalis*. However, because this solution will not dissolve organic matter, it only has a narrow range of uses.

Irrigating Solution Interactions

NaOCl and EDTA are the two most often utilized irrigants. When combined with NaOCl, EDTA (and CA) immediately reduces the amount of chlorine, which causes the loss of NaOCl activity. These solutions should not be combined (50).

Chlorhexidine and hypochlorite must not be combined. They combine to create a precipitate of parachloroaniline, which is thought to be carcinogenic, may discolor teeth, and will prevent further irrigation by blocking the canal and tubules (51).

The effectiveness of EDTA to remove the smear layer is reduced when CHX and EDTA are combined right away because a white precipitate is created.

Increasing the Efficiency of Irrigation Solutions

An increase in efficiency can be achieved by increasing the temperature of the low concentration solutions. Warmed solutions improve their lysing effect on organic matter, better remove organic debris and increase their antibacterial properties. Studies have shown that each increase in the temperature of the solution by 5 degrees doubles the bactericidal effect. Therefore, the lysing action of 1% NaOCl solution at 37 degrees is equal to that of 5.25% solution at 22 degrees (52). When the solution is warmed, its toxicity has been shown to decrease. The longer the irrigant is in contact with the root surfaces, the greater the chance that microorganisms will be successfully killed, and the bacterial concentration will be decreased.

Another way of increasing the efficiency of the solution is achieved by using ultrasonic and sonic activation. Ultrasonic irrigation produces high oscillation frequencies, but with low amplitudes. The files are designed to work with an ultrasonic frequency of 25–30 kHz. Their vibration is transverse, alternating points with the lowest and highest amplitude along the entire length (53). By increasing the flow's turbulence, this enhances irrigant dispersion, isthmus penetration, and tissue disintegration. Once shaping is complete and an ISO 20 or 15 file has been passively inserted, this must be done. Ultrasonic irrigation can be classified into two categories: In the first type, root canal preparation and irrigation are performed simultaneously. The second type is the so-called passive ultrasonic irrigation. Three 20-second cycles of passive ultrasonic irrigation (PUI) per canal have been recommended as part of the treatment, and the file may be applied in an in-out motion (54).

Compared to rinsing with an ordinary syringe and needle, the ultrasonic activation of the solution leads to better cleaning of pulp residues and debris.

And this is due to the larger volume and higher speed of movement of the solution, which can reach hard-to-reach places in the root canal. The use of ultrasonic irrigation in NaOCl and EDTA improves the cleaning of the walls, the smeared layer in all parts of the canal, and reduces the number of bacteria. This can be due to 2 main factors:

- ◆ Due to the acoustic vortexing of the solution, deagglomeration of the biofilm occurs, single bacteria become more susceptible to the action of NaOCl.
- ◆ Cavitation causes weakening of the cell membranes of MO, which again facilitates the penetration of NaOCl.

Sonic irrigation uses a lower frequency (1–6 kHz), which causes less stress. The oscillation amplitude is higher, as a result of which the back-and-forth movement on the tip of the instrument is more pronounced. The oscillation generated by the device has its own characteristics. At the point of attachment, the oscillation has the lowest amplitude, while at the top, the amplitude is the highest. When movement is restricted, the lateral vibration disappears and becomes a longitudinal oscillation. This model of vibration has proven to be the most effective in cleaning root canals (55). The EndoActivator (Dentsply) combines a battery-operated handpiece and disposable polymeric tips with length indications. The handpiece that generates the sonic vibrations in the system can be conveniently attached to tips in 3 various sizes. EndoActivator helps the irrigant in the canal renew itself by allowing it to penetrate deeper into the canal. It does not really bring new irrigant to the canal. According to studies, using EndoActivator instead of needle irrigation increases irrigant penetration and mechanical cleansing with no increase in the danger of irrigant extrusion through the apex (56,57).

Vibringe is a new irrigation system that combines the qualities of sonic activation with traditional syringe and needle flushing. It has a built-in microchip that controls the generation of sonic energy, with vibrations of about 9,000 cpm.

EndoVac is a revolutionary technology that uses a negative-pressure approach to deliver the irrigant rather than a needle. The irrigant is placed in the pulp chamber and is sucked down the root canal and

back up again using a thin needle with a unique design. There is proof that the EndoVac technology significantly reduces the hazards connected with irrigation close to the apical foramen (57). A good apical cleaning at the level of 1 mm can be another benefit of the reverse flow of irrigants. (58–61).

CONCLUSION

The main issues with using irrigant solutions are their inability to reach the most complex anatomical structures in the apical third, the clinical usage time, and their toxicity to the periapical tissues. They are also affected by the presence of infected organic and inorganic debris, which can reduce their effectiveness. These issues can be resolved by using photoactivation or ultrasonic activation methods, which enhance reaction rate, shear stress, and antibacterial activity (60). But both can enhance the chance of hypochlorite apex extrusion (61).

REFERENCES

- Nair PN. Pathogenesis of apical periodontitis and the causes of endodontic failures. *Crit Rev Oral Biol Med.* 2004;15(6):348-81. doi: 10.1177/154411130401500604.
- Sundqvist G, Fidgor D. Life as an endodontic pathogen. Ecological differences between the untreated and root-filled root canals. *Endod Topics.* 2003;6(1):3-28. doi: 10.1111/j.1601-1546.2003.00054.x.
- Siqueira JF Jr, Rôças I. Present status and future directions in endodontic microbiology. *Endod Topics.* 2014;30(1):3-22. doi: 10.1111/etp.12060.
- Ricucci D, Siqueira JF Jr. Biofilms and apical periodontitis: study of prevalence and association with clinical and histopathological findings. *J Endod.* 2010;36(8):1277-88. doi: 10.1016/j.joen.2010.04.007.
- Casadevall A, Pirofski L. Virulence factors and their mechanisms of action: the view from a damageresponse framework. *J Water Health.* 2009;7 Suppl 1:S2-S18. doi: 10.2166/wh.2009.036.
- Loel DA. Use of acid cleanser in endodontic therapy. *J Am Dent Assoc.* 1975;90(1):148-51. doi: 10.14219/jada.archive.1975.0010.
- Baumgartner JC, Brown CM, Mader CL, Peters DD, Shulman JD. A scanning electron microscopic evaluation of root canal debridement using saline, sodium hypochlorite, and citric acid. *J Endod.* 1984; 10(11):525-31. doi: 10.1016/S0099-2399(84)80137-5.
- Baumgartner JC, Mader CL. A scanning electron microscopic evaluation of four root canal irrigation regimens. *J Endod.* 1987;13(4):147-57. doi: 10.1016/S0099-2399(87)80132-2.
- Czonstkowsky M, Wilson EG, Holstein FA. The smear layer in endodontics. *Dent Clin North Am.* 1990;34(1):13-25.
- Haapasalo M, Shen Y, Qian W, Gao Y. Irrigation in endodontics. *Dent Clin North Am.* 2010;54(2):291-312. doi: 10.1016/j.cden.2009.12.001.
- Park E, Shen Y, Khakpour M, Haapasalo M. Apical pressure and extent of irrigant flow beyond the needle tip during positive-pressure irrigation in an in vitro root canal model. *J Endod.* 2013;39(4):511-5. doi: 10.1016/j.joen.2012.12.004.
- Siqueira JF Jr, Rôças I N, Favieri A, Lima KC. Chemomechanical reduction of the bacterial population in the root canal after instrumentation and irrigation with 1%, 2.5%, and 5.25% sodium hypochlorite. *J Endod.* 2000;26(6):331-4. doi: 10.1097/00004770-200006000-00006.
- Dunavant TR, Regan JD, Glickman GN, Solomon ES, Honeyman AL. Comparative evaluation of endodontic irrigants against *Enterococcus faecalis* biofilms. *J Endod.* 2006;32(6):527-31. doi: 10.1016/j.joen.2005.09.001.
- Williamson AE, Cardon JW, Drake DR. Antimicrobial susceptibility of monoculture biofilms of a clinical isolate of *Enterococcus faecalis*. *J Endod.* 2009;35(1):95-7. doi: 10.1016/j.joen.2008.09.004.
- Beltz RE, Torabinejad M, Pouresmail M. Quantitative analysis of the solubilizing action of MTAD, sodium hypochlorite, and EDTA on bovine pulp and dentin. *J Endod.* 2003;29(5):334-7. doi: 10.1097/00004770-200305000-00004.
- Cobankara FK, Ozkan HB, Terlemez A. Comparison of organic tissue dissolution capacities of sodium hypochlorite and chlorine dioxide. *J Endod.* 2010;36(2):272-4. doi: 10.1016/j.joen.2009.10.027.
- Stojic S, Zivkovic S, Qian W, Zhang H, Haapasalo M. Tissue dissolution by sodium hypochlorite: effect of concentration, temperature, agitation, and surfactant. *J Endod.* 2010;36(9):1558-62. doi: 10.1016/j.joen.2010.06.021.

18. Klyn SL, Kirkpatrick TC, Rutledge RE. In vitro comparisons of debris removal of the EndoActivator system, the F file, ultrasonic irrigation, and NaOCl irrigation alone after hand-rotary instrumentation in human mandibular molars. *J Endod.* 2010;36(8):1367-71. doi: 10.1016/j.joen.2010.03.022.
19. Johnson M, Sidow SJ, Looney SW, Lindsey K, Niu LN, Tay FR. Canal and isthmus debridement efficacy using a sonic irrigation technique in a closed-canal system. *J Endod.* 2012;38(9):1265-8. doi: 10.1016/j.joen.2012.05.009.
20. Harrison JW, Hand RE. The effect of dilution and organic matter on the anti-bacterial property of 5.25% sodium hypochlorite. *J Endod.* 1981;7(3):128-32. doi: 10.1016/S0099-2399(81)80127-6.
21. Gomes BP, Ferraz CC, Vianna ME, Berber VB, Teixeira FB, Souza-Filho FJ. In vitro antimicrobial activity of several concentrations of sodium hypochlorite and chlorhexidine gluconate in the elimination of *Enterococcus faecalis*. *Int Endod J.* 2001;34(6):424-8. doi: 10.1046/j.1365-2591.2001.00410.x.
22. Zehnder M. Root canal irrigants. *J Endod.* 2006;32(5):389-98. doi: 10.1016/j.joen.2005.09.014.
23. Clegg MS, Vertucci FJ, Walker C, Belanger M, Britto LR. The effect of exposure to irrigant solutions on apical dentin biofilms in vitro. *J Endod.* 2006;32(5):434-7. doi: 10.1016/j.joen.2005.07.002.
24. McDonnell G, Russell D. Antiseptics and disinfectants: activity, action, and resistance. *Clin Microbiol Rev.* 1999;12(1):147-79. doi: 10.1128/CMR.12.1.147.
25. Barrette WC Jr, Hannum DM, Wheeler WD, Hurst JK. General mechanism for the bacterial toxicity of hypochlorous acid: abolition of ATP production. *Biochemistry.* 1989;28(23):9172-8. doi: 10.1021/bi00449a032.
26. McKenna SM, Davies KJA. The inhibition of bacterial growth by hypochlorous acid. Possible role in the bactericidal activity of phagocytes. *Biochem J.* 1988;254(3):685-92. doi: 10.1042/bj2540685.
27. Radcliffe CE, Potouridou L, Qureshi R, Hababeh N, Qualtrough A, Worthington H, et al. Antimicrobial activity of varying concentrations of sodium hypochlorite on the endodontic microorganisms *Actinomyces israelii*, *A. naeslundii*, *Candida albicans* and *Enterococcus faecalis*. *Int Endod J.* 2004;37(7):438-46. doi: 10.1111/j.1365-2591.2004.00752.x.
28. Vianna ME, Gomes BP, Berber VB, Zaia AA, Ferraz CC, de Souza-Filho FJ. In vitro evaluation of the antimicrobial activity of chlorhexidine and sodium hypochlorite. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2004; 97(1):79-84. doi: 10.1016/s1079-2104(03)00360-3.
29. Waltimo TM, Ørstavik D, Siren EK, Haapasalo MP. In vitro susceptibility of *Candida albicans* to four disinfectants and their combinations. *Int Endod J.* 1999; 32(6):421-9. doi: 10.1046/j.1365-2591.1999.00237.x.
30. Haapasalo HK, Siren EK, Waltimo TM, Ørstavik D, Haapasalo MP. Inactivation of local root canal medicaments by dentine: an in vitro study. *Int Endod J.* 2000; 33(2):126-31. doi: 10.1046/j.1365-2591.2000.00291.x.
31. Byström A, Sundqvist G. Bacteriologic evaluation of the effect of 0.5 percent sodium hypochlorite in endodontic therapy. *Oral Surg Oral Med Oral Pathol.* 1983; 55(3):307-12. doi: 10.1016/0030-4220(83)90333-x.
32. Byström A, Sundqvist G. The antibacterial action of sodium hypochlorite and EDTA in 60 cases of endodontic therapy. *Int Endod J.* 1985;18(1):35-40. doi: 10.1111/j.1365-2591.1985.tb00416.x.
33. Siqueira JF Jr, Rocas IN, Santos SR, Lima KC, Magalhães FA, de Uzeda M. Efficacy of instrumentation techniques and irrigation regimens in reducing the bacterial population within root canals. *J Endod.* 2002;28(3):181-4. doi: 10.1097/00004770-200203000-00009.
34. Sim TP, Knowles JC, Ng YL, Shelton J, Gulabivala K. Effect of sodium hypochlorite on mechanical properties of dentine and tooth surface strain. *Int Endod J.* 2001;34(2):120-32. doi: 10.1046/j.1365-2591.2001.00357.x.
35. Marending M, Luder HU, Brunner TJ, Knecht S, Stark WJ, Zehnder M. Effect of sodium hypochlorite on human root dentine—mechanical, chemical and structural evaluation. *Int Endod J.* 2007; 40(10):786-93. doi: 10.1111/j.1365-2591.2007.01287.x.
36. Coons D, Dankowski M, Diehl M, et al. Performance in detergents, cleaning agents and personal care products: detergents. In: Falbe J, ed.

- Surfactants in consumer products. Berlin: Springer-Verlag; 1987.
37. Perdigao J, Eiriksson S, Rosa BT, Lopes M, Gomes G. Effect of calcium removal on dentin bond strengths. *Quintessence Int.* 2001;32(2):142-6.
 38. Apostolopoulos AX, Buonocore MG. Comparative dissolution rates of enamel, dentin and bone. *J Dent Res.* 1966;45(4):1093-100. doi: 10.1177/00220345660450041201.
 39. Haapasalo M, Ørstavik D. In vitro infection and disinfection of dentinal tubules. *J Dent Res.* 1987;66(8):1375-9. doi: 10.1177/00220345870660081801.
 40. Ørstavik D, Haapasalo M. Disinfection by endodontic irrigants and dressings of experimentally infected dentinal tubules. *Endod Dent Traumatol.* 1990;6(4):142-9. doi: 10.1111/j.1600-9657.1990.tb00409.x.
 41. Hulsmann M, Heckendorff M, Lennon A. Chelating agents in root canal treatment: mode of action and indications for their use. *Int Endod J.* 2003;36(12):810-30. doi: 10.1111/j.1365-2591.2003.00754.x.
 42. Heling I, Chandler NP. Antimicrobial effect of irrigant combinations within dentinal tubules. *Int Endod J.* 1998;31(1):8-14.
 43. Vahdaty A, Pitt Ford TR, Wilson RF. Efficacy of chlorhexidine in disinfecting dentinal tubules in vitro. *Endod Dent Traumatol.* 1993;9(6):243-8. doi: 10.1111/j.1600-9657.1993.tb00280.x.
 44. Buck RA, Eleazer PD, Staat RH, Scheetz JP. Effectiveness of three endodontic irrigants at various tubular depths in human dentin. *J Endod.* 2001;27(3):206-8. doi: 10.1097/00004770-200103000-00017.
 45. Jeansonne MJ, White RR. A comparison of 2.0% chlorhexidine gluconate and 5.25% sodium hypochlorite as antimicrobial endodontic irrigants. *J Endod.* 1994;20(6):276-8. doi: 10.1016/S0099-2399(06)80815-0.
 46. Russell AD, Day MJ. Antibacterial activity of chlorhexidine. *J Hosp Infect.* 1993;25(4):229-38. doi: 10.1016/0195-6701(93)90109-d.
 47. Ferraz CC, Gomes BP, Zaia AA, Teixeira FB, Souza-Filho FJ. In vitro assessment of the antimicrobial action and the mechanical ability of chlorhexidine gel as an endodontic irrigant. *J Endod.* 2001; 27(7):452-5. doi: 10.1097/00004770-200107000-00004.
 48. Singla MG, Garg A, Gupta S. MTAD in endodontics: an update review. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2011;112(3):e70-6. doi: 10.1016/j.tripleo.2011.02.015.
 49. Malkhassian G, Manzur AJ, Legner M, Fillery ED, Manek S, Basrani BR, et al. Antibacterial efficacy of MTAD final rinse and two percent chlorhexidine gel medication in teeth with apical periodontitis: a randomized doubleblinded clinical trial. *J Endod.* 2009;35(11):1483-90. doi: 10.1016/j.joen.2009.08.003.
 50. Zehnder M, Schmidlin P, Sener B, Waltimo T. Chelation in root canal therapy reconsidered. *J Endod.* 2005;31(11):817-20. doi: 10.1097/01.don.0000158233.59316.fe.
 51. Basrani B, Haapasalo M. Update on endodontic irrigating solutions. *Endod Topics.* 2012;27(1):74-102. doi: 10.1111/etp.12031.
 52. Cunningham WT, Balekjian AY. Effect of temperature on collagen-dissolving ability of sodium hypochlorite endodontic irrigant. *Oral Surg Oral Med Oral Pathol.* 1980;49(2):175-7. doi: 10.1016/0030-4220(80)90313-8.
 53. Ahmad M, Pitt Ford TR, Crum LA. Ultrasonic debridement of root canals: acoustic streaming and its possible role. *J Endod.* 1987;13(10):490-9. doi: 10.1016/S0099-2399(87)80016-x.
 54. De Moor RJ, Meire M, Goharkhay K, Moritz A, Vanobbergen J. Efficacy of ultrasonic versus laser-activated irrigation to remove artificially placed dentin debris plugs. *J Endod.* 2010;36(9):1580-3. doi: 10.1016/j.joen.2010.06.007.
 55. Jensen SA, Walker TL, Hutter JW, Nicoll BK. Comparison of the cleaning efficacy of passive sonic activation and passive ultrasonic activation after hand instrumentation in molar root canals. *J Endod.* 1999;25(11):735-8. doi: 10.1016/S0099-2399(99)80120-4.
 56. Townsend C, Maki J. An in vitro comparison of new irrigation and agitation techniques to ultrasonic agitation in removing bacteria from a simulated root canal. *J Endod.* 2009; 35(7):1040-3. doi: 10.1016/j.joen.2009.04.007.
 57. Desai P, Himel V. Comparative safety of various intracanal irrigation systems. *J Endod.* 2009;35(4):545-9. doi: 10.1016/j.joen.2009.01.011.
 58. Hockett JL, Dommisch JK, Johnson JD, Cohenca N. Antimicrobial efficacy of two irrigation techniques in tapered and nontapered canal

- preparations: an in vitro study. *J Endod.* 2008; 34(11):1374-1377. doi: 10.1016/j.joen.2008.07.022.
59. Nielsen BA, Craig Baumgartner J. Comparison of the EndoVac system to needle irrigation of root canals. *J Endod.* 2007;33(5):611-5. doi: 10.1016/j.joen.2007.01.020.
60. Virdee SS, Seymour DW, Farnell D, Bhamra G, Bhakta S. Efficacy of irrigant activation techniques in removing intracanal smear layer and debris from mature permanent teeth: A systematic review and meta analysis. *Int Endod J.* 2018;51(6):605-21. doi: 10.1111/iej.12877. Epub 2017 Dec 22.
61. Muhammad OH, Chevalier M, Rocca JP, Brulat Bouchard N, Medioni E. Photodynamic therapy versus ultrasonic irrigation: Interaction with endodontic microbial biofilm, an ex vivo study. *Photodiagnosis Photodyn Ther.* 2014;11(2):171-81. doi: 10.1016/j.pdpdt.2014.02.005.