IDR International Dental Research

Review Article

Endodontic Irrigation Solutions: A Review

Celaletin Topbas[1], Ozkan Adiguzel[2]

[1] Istanbul Aydin University, Faculty of Dentistry, Department of Endodontics, Istanbul, Turkey
[2] Dicle University, Faculty of Dentistry, Department of Endodontics, Diyarbakir, Turkey

Correspondence:
Dr. Celalettin TOPBAS
Istanbul University, Faculty of Dentistry, Department of Endodontics, Istanbul, TURKEY.
E-mail:celalettintopbas@aydin.edu.tr

Received 14 August 2017
Accepted 19 October 2017

Access Online

DOI
10.5577/intdentres.2017.vol7.no3.2

Abstract

The goal of endodontic treatment is to remove all the vital and necrotic tissues, microorganisms and microbial byproducts from root canal system. This goal can be achieved through chemical and mechanical debridement of root canals. This article narrates the specifics and requirements of the irrigation solutions. Sodium hypochlorite is proposed as the primary irrigant by virtue of its organic tissue dissolution capacity and broad antimicrobial properties. On the other hand, chelation solutions are recommended as auxiliary solutions to remove the smear layer or to hinder its formation on dentin surface. Thus, it's hoped that sealers and root canal fillers can penetrate to dentin tubules and obturate the canals hermetically. There are new studies on traditional irrigants especially on some irrigants that can replace sodium hypoclorite. This article reviews the new irrigants which can be used in future endodontic practice, and their advantages and limitations. Moreover, actions and interactions of recently used irrigants are adverted.

Keywords: Irrigation solutions, chelators, sodium hypochlorite, smear layer, disinfection

How to cite this article: Topbas C, Adiguzel O. Endodontic Irrigation Solutions: A Review. Int Dent Res 2017;7:54-61.

Introduction

The goal of endodontic treatment is to remove all vital and necrotic tissues, microorganisms, and microbial byproducts from the root canal system. This goal can be accomplished by chemical and mechanical cleaning of the root canal system. The anatomy of the root canal system is extremely complex and variable, and effective cleaning and disinfection are not always possible.

Root canals are usually shaped under constant irrigation with hand instruments and rotary systems (1). In a study of micro-CT images obtained before and after root canal shaping, 35% or more of the root canal surface (including the isthmus) was found to be untouched, regardless of the canal preparation technique. Therefore, the importance of irrigation and the complete disinfection of root canals has been emphasized (2). In addition, irrigation solutions should aid removal of the smear layer. As no single solution has all of the desired properties, a combination of two or more solutions is required for safe and effective irrigation.

Properties of an ideal irrigant are: (3, 4).

- Bactericidal, germicidal, and fungicidal effects
- Ability to serve as a lubricant during instrumentation
- Ability to dissolve organic dentinal tissues (pulp tissue, collagen, and biofilm)
- Ability to dissolve inorganic dentinal tissues
- No irritation of periapical tissues
- Solution stability
- Prolonged and sustainable antibacterial activity after use
- Activity in an environment in which blood, serum, and tissue protein products are present
- Ability to remove the smear layer completely
- Low surface tension
- Disinfection of dentin and dentinal tubules
- No interference with periapical tissue healing
- No staining of tooth tissues
- No weakening of tooth tissues
- No triggering of a cell-mediated immune response
- No antigenic, toxic, or carcinogenic effect on the peripheral tissue cells of the tooth
- No negative effect on the physical properties of the exposed dentin
- No negative effect on the sealing abilities of sealers
- Ease of application and low cost
- Long shelf life.

Sodium Hypochlorite (NaOCl)

NaOCl is the most widely used irrigation solution. It is ideal compared with other irrigation solutions because it is the only solution that possesses most required properties. The first chemically produced liquid chlorine solution was potassium hypochlorite, discovered in France by Berthollet (1748-1822). The chemist Labarraque (1777-1850) proposed the use of NaOCl for the prevention of puerperium and other infectious diseases (5).

Based on controlled laboratory studies conducted by Koch and Pasteur, the use of NaOCl as a disinfectant became extremely widespread in the late 19th century. During World War I, the chemist Henry Drysdale Dakin and the surgeon Alexis Carrel used buffered 0.5% NaOCl to wash and disinfect infected wounds, based on Dakin's study of the effectiveness of different solutions on infected necrotic tissues (5, 6).

NaOCl has a broad antibacterial spectrum and is sporicidal and viricidal. Its tissue-dissolving activity is greater for necrotic tissue than for vital tissue. These valuable properties have encouraged the use of liquid NaOCl as a basic irrigation solution in endodontics since the early 1920s (5).

Pécora et al have shown that when NaOCl is in a reaction with water, it reaches a dynamic equilibrium as shown below (7).

$$NaOCl + H_2O \leftrightarrow NaOH + HOCl \leftrightarrow Na^+ + OH^- + H^+ + OCl^-$$

NaOCl reacts with organic tissue, resulting in saponification, amino acid neutralization, and chloramine reactions. Owing to its solvent effect on necrotic tissues, NaOCl has become the most widely used irrigation solution in endodontics (8). However, the appropriate concentration for NaOCl solutions used in endodontics is a matter of much debate.

Organic matter (inflammatory exudate, tissue residue, and microbial mass) in root canals reduces the effect of NaOCl. High concentrations of NaOCl have better tissue-dissolving effects. Low concentrations used in high volumes have potency equivalent to that of high concentrations (9). In addition, higher concentrations of NaOCl are more toxic than lower concentrations (10).

As the anatomy of the root canal system enables limited application to the root alone, NaOCl can be used safely and reliably in high concentrations during root canal treatment if it is not introduced into the periapical tissues. The achievement of NaOCl contact with all canal surfaces for an optimal duration is much more important than the NaOCl concentration (11).

The necrotic tissue-dissolving property of NaOCl is unique (11). Its activity increases with the concentration, temperature, and duration of application (12). When NaOCl is used as the first irrigant, its dentinal organic tissue-dissolving effect is not very strong, as hydroxyapatite in the smear layer covers the collagen surface. However, when a decalcifying agent is used prior to NaOCl, hydroxyapatite dissolves readily and the underlying collagen fibrils become clear. When NaOCl is used in this stage, it acts directly on collagen, leading to the rapid destruction of collagen in the superficial dentin (13). After chemomechanical preparation, erosion of the dentin has been demonstrated when irrigation with NaOCl is followed by the use of ethylenediaminetetraacetic acid (EDTA) or citric acid (CA) (14).

The tissue-dissolving capacity of NaOCl solutions can be increased by increasing the solution temperature, by ultrasonic activation, and by prolongation of the working time (5). One of the most frequently used methods of increasing activity is to increase the temperature of a low-concentration NaOCl solution. The tissue-dissolving capacity of a 1% NaOCl solution at 45°C was found to be equivalent to that of a 5.25% solution at 20°C. In addition, the systemic toxicity of heated low-density NaOCl solutions is less than that of unheated, higher-concentration ones (15).

The antibacterial and tissue-dissolving effects of a 5.25% NaOCl solution are diminished when the solution is diluted (15). When NaOCl is mixed with water, the following reaction occurs:

$NaOCl + H_2O \rightarrow NaOH + HOCl$ (hypochlorous acid) [1.]

The hypochlorous acid in aqueous solution dissolves to hypochlorite anion (OCl^-):

$HOCl \leftrightarrow H + OCl^-$ [2.]

Hypochlorous acid (HOCl) is a stronger oxidant than the hypochlorite ion (OCl^-). The dissociation of HOCl depends on pH [2.reaction]. A balance exists between HOCl and OCl^-. HOCl has a germicidal effect. At a pH of 10, essentially all chlorine is OCl^-; at a pH of 4.5, all chlorine is HOCl. The disinfecting properties of hypochlorite solutions decrease with increasing pH, whereas their antimicrobial efficacy increases with decreasing pH.[15] Moorer and Wesselink found that mechanical agitation with NaOCl is very important for the generation of a tissue-dissolving effect (9). Ultrasonic agitation increased the activity of a 5% NaOCl solution in the apical third of the root canal wall (16). When NaOCl is activated with an ultrasonic device, it must be used after the completion of root canal preparation.

Compared with a device that contacts the root canal wall, a device that oscillates freely has more ultrasonic effects on the irrigation solution (17). The use of NaOCl for irrigation was found to reduce the bond strength between the adhesive system and the dentinal wall. NaOCl is thought to remove collagen fibrils from the dentin surface, thereby inhibiting the formation of the hybrid layer, as required to achieve a dentin–adhesive link (18).

Interactions of NaOCl

The reaction between NaOCl and chlorhexidine (CHX) produces para-chloroaniline (PCA), which is carcinogenic. This reaction product covers the surfaces of root canals, blocking the dentinal tubules and compromising the root canal seal (19).

With the aim of reducing PCA formation, Mortenson et al. investigated the use of an alternative intermediate irrigation solution in root canal treatment. They found that CA led to less PCA formation than did sterile saline or EDTA (20).

Grawehr et al. found that a solution of EDTA mixed with NaOCl retained calcium-binding capacity, but showed a sudden and rapid decrease in the amount of chlorine in NaOCl, significantly reducing the ability of NaOCl to degrade tissue (21). Many mishaps, such as the splashing of NaOCl into the patient's or dentist's eye, damaging of the patient's clothes, extrusion of NaOCl beyond the apical foramen, inadvertent injection of irrigants instead of anesthesia, or allergic reaction to the irrigation solution, can occur during root canal treatment (22). However, NaOCl solutions are inexpensive and easy to use, and they have a long shelf life (23).

Ethylenediaminetetraacetic Acid (EDTA)

Complete cleaning of the root canal system requires the combined use of organic and inorganic tissue-dissolving irrigation solutions. As NaOCl effectively dissolves only organic tissue, other solutions should be used to remove the smear layer and debris from the root canal system. The use of demineralizing agents, such as EDTA and CA, as auxiliary solutions during root canal treatment is recommended. In 1957, Nygaart-Ostby proposed the use of chelating agents to aid in the preparation of narrow and calcified root canals. The first recommended EDTA solution had a concentration of 15% and a pH of 7.3 (24, 25).

EDTA is used most commonly as a 17% neutralized solution. The solution reacts with the calcium ions in the dentin and forms soluble calcium chelates. Decalcification is a self-limiting process that eventually stops due to the lack of a chelator that will react quickly enough (26).

Calt and Serper showed that 1 min irrigation with 10 ml of 17% EDTA solution effectively removed the smear layer from the canal wall. They observed that dentin demineralization increased with the contact time, the EDTA concentration (from 10% to 17%), and the pH (from 7.5 to 9) (27).

The ultrasonic application of 17% EDTA for 1 min is very effective for removal of the smear layer, especially from the apical third of the root, and the continuous use of liquid EDTA during root canal treatment is recommended (28). Under normal conditions, CHX solutions are insoluble in EDTA. The resulting precipitate is a salt formed by electrostatic neutralization of the cationic CHX by the anionic EDTA.

The ionic equation is:

$$2HEDTA^{3-}_{(aq)} + 3H_2CHX^{2+}_{(aq)} \leftrightarrow (HEDTA)_2(H_2CHX)_{3\,(S)}$$

The clinical implications of this precipitate are not known widely. It is known to reduce the ability of EDTA to remove the smear layer (29).

Citric Acid (CA)

CA is also available on the market and is used at concentrations ranging from 1% to 50%. The use of 10% CA as a final irrigation solution yielded very good results in terms of smear layer removal (30). CA has shown slightly better performance than EDTA at similar concentrations, although both solutions are highly effective in removing the smear layer from root canal walls (31). In vitro studies have provided insight into the cytotoxicity of chelators. A 10% CA solution was proven to be more biocompatible than a 17% EDTA solution (32). In one study, a 25% CA solution failed to destroy *Enterococcus faecalis* biofilms in 1-, 5-, and 10-min applications (33).

Hydroxyethylidene Bisphosphonate (HEBP)

HEBP, also known as etidronic acid or etidronate, is a decalcifying agent that has little interaction with NaOCl. It has been proposed as an alternative to EDTA or CA (31). HEBP prevents bone resorption, and thus is used as a systemic drug in the treatment of osteoporosis and Paget's disease (34). However, additional studies are needed to determine whether this solution improves or shortens the duration of endodontic irrigation. Demineralization with 9% or 18% HEBP is slower than that with 17% EDTA (35).

Chlorhexidine (CHX)

CHX is a powerful antiseptic used commonly for the chemical control of plaque in the oral cavity. Whereas 0.1%–0.2% aqueous solutions are used as mouthwash, a 2% concentration is used for root canal irrigation in endodontic treatment. The antimicrobial activity of CHX depends on the achievement of an optimal pH (5.5–7) (38). CHX is bacteriostatic at lower concentrations and bactericidal at higher concentrations (39).

CHX is active against Gram-positive and Gram-negative bacteria, bacterial spores, lipophilic viruses, yeast, fungi, and dermatophytes (40). As with other endodontic disinfectants, however, these effects are greatly reduced in the presence of organic matter, as the activity of CHX is dependent on pH (38). Although CHX kills bacteria, it is ineffective in removing biofilm and other organic substances (19). A 2% solution of CHX is appropriate to achieve the desired maximal antibacterial effect at the end of chemomechanical preparation. This solution is used commonly as an intracanal medicament with calcium hydroxide ($Ca(OH)_2$) (41).

One reason for the widespread use of CHX is its prolonged antibacterial effect; CHX binds to hard tissues and maintains its antimicrobial action. This effect is due to the number of CHX molecules interacting with dentin (42). White et al. reported that the effect of 2% CHX persisted for 72 h to 12 weeks (43). The main disadvantage of CHX is the lack of tissue solubility (44).

CHX is a broad-spectrum matrix metalloproteinase (MMP) inhibitor (anticollagenolytic effect). Attachment of CHX to the dentin surface increases resin infiltration into the dentinal tubules, thereby increasing the bond strength (45).

The toxic potency of CHX depends on the size and structure of the region exposed to it. Although CHX does not cause long-term damage to host tissues, it can cause an inflammatory response if it is extruded from root canals or injected inadvertently (46).

CHX has several rarely occurring side effects, such as desquamative gingivitis, dental and oral pigmentation, and disgusting (bad-metallic taste in the mouth) (42). The heating of a low-concentration CHX solution increases total antimicrobial efficacy while maintaining low systemic toxicity (47). CHX can be used in the disinfection of gutta percha. The addition of surface-active agents to a CHX product (CHX-Plus) reduces the surface tension, significantly increasing the activity against bacteria and biofilms. However, no study has examined complications that may arise when an irrigation solution with surfactant overflows from the periapical tissues in clinical practice (48).

QMix is an irrigation solution developed for use in the final root canal cleaning. A combination of CHX with an added surfactant and EDTA is used to increase penetration to the dentinal tubules (4, 49).

Mixture of Tetracycline Isomer, Acid, and Detergent (MTAD)

Torabinejad et al. introduced a combination of 3% doxycycline, 4.25% CA, and detergent (Tween-80) as an alternative to EDTA with the aim of improving smear layer removal. This mixture acts as a chelator and has antimicrobial activity. As it has no organic tissue-dissolving effect, its use after NaOCl at the end of chemomechanical preparation is recommended (49).

MTAD is a mixture of three substances expected to affect bacteria synergistically (50). Its bactericidal effect on *E. faecalis* biofilm is less than that of NaOCl solution at concentrations of 1%–6%. The CA in the MTAD solution enables smear layer removal and allows doxycycline to enter the dentinal tubules and exert antibacterial effects (51). In a canal filled with AH Plus and gutta percha, the use of MTAD as a final irrigation solution significantly reduces bond strength compared with the use of EDTA (52). When MTAD is used instead of EDTA, resistance to tetracycline can develop in bacteria isolated from root canals (53).

Generally, the use of antibiotics instead of biocides, such as NaOCl and CHX, is not recommended because antibiotics have been developed for systemic use, rather than for local wound healing, and they have a narrower spectrum than do biocides (54).

Tetraclean

Like MTAD, Tetraclean (Ogna Laboratori Farmaceutici, Muggiò (Mi), Italy) is a mixture of CA, doxycycline (at a lower concentration than MTAD), and detergent. The concentration of antibiotic (doxycycline-50 mg / ml) and the type of detergent (propylene glycol) differ from those in MTAD. Tetraclean does not dissolve organic tissue, and its use after NaOCl at the end of chemomechanical preparation is recommended (49, 55).

Tetraclean exhibits high activity against anaerobic and facultative anaerobic bacteria. Compared with MTAD, Tetraclean is more effective against planktonic cultures of *E. faecalis* and in vitro biofilms composed of mixed species (56).

Maleic Acid (MA)

MA is a mild organic acid used to roughen enamel and dentin surfaces in adhesive dentistry (57). It removes the smear layer effectively at concentrations of 5% and 7%. In addition, when used at concentrations of 10% or higher, it causes demineralization and erosion of the root canal wall. Ballal et al. reported that 1 min application of 7% MA as the final irrigation agent removed the smear layer more effectively than did 1 min irrigation with 17% EDTA, especially in the apical third of the root canal system (57).

Compared with 17% EDTA, 7% MA has been reported to cause more surface roughening of root canal walls. However, before routine clinical endodontic use, the effects of MA on periapical tissues, its biocompatibility, and appropriate usage techniques need to be investigated (58).

Chlorine Dioxide (ClO_2)

Patients use ClO_2, which is chemically similar to NaOCl and chlorine, as a whitening agent in their homes. An in vitro study showed that the organic tissue-dissolving capacities of NaOCl and ClO_2 were similar (59).

Silver Diamine Fluoride

A 3.8% silver diamine fluoride ($Ag[NH_3]_2F$) solution was developed for use as an irrigation solution in root canal treatment. This solution is the 1:10-diluted form of the original 38% solution of $Ag[NH_3]_2F$, which was developed for the treatment of root canal infection (60).

Triclosan and Gantrez

Triclosan is a Gram-positive and Gram-negative bactericide, as well as a broad-spectrum agent effective against fungi and viruses. Nudera et al. investigated the minimum inhibitory and bacterial concentrations of triclosan and triclosan with Gantrez against *Prevotella intermedia*, *Fusobacterium nucleatum*, *Actinomyces naeslundii*, *Porphyromonas gingivalis*, and *E. faecalis*. The addition of Gantrez to triclosan increased bacterial activity. Both preparations showed bactericidal activity against the five major endodontic pathogens examined (61, 62).

Herbal Alternatives

Many plant species have been tested to determine their abilities to disinfect the root canal system in root canal treatment. Root canal disinfection with propolis, miswak, neem tree, *Morinda citrifolia* (MC), *Myrtus communis, Myristica fragrance*, turmeric, chamomile, babool, garlic, aloe vera, triphala, green tea polyphenols (GTP), and other terrestrial plant products has been attempted. The main advantages of the use of herbal alternatives in root canal treatment are that the products are easy to acquire and inexpensive, have long shelf lives and low toxicity, and cause no microbial resistance (63, 64). The most commonly used alternatives include the following.

Triphala: Triphala is a plant blend created by drying and pulverizing the fruit of three plants (*termina bellerica, termina chebula, and emblica officinalis*) used for medicinal purposes. Triphala kills 100% of *E. faecalis* within 6 min. When used at different rates, its effects can be increased synergistically.

Triphala contains fruit rich in CA, which can aid smear layer removal (65).

Green Tea Polyphenols (GTP): GTP are derived from fresh leaves of tea (*Camellia sinensis*), an important component of traditional Japanese and Chinese cultures. They have shown significant antibacterial activity in *E. faecalis* biofilms grown on dental culture, killing *E. faecalis* completely within 6 min (65, 66).

Morinda Citrifolia (MC): MC (noni fruit) has a wide range of therapeutic effects, such as antibacterial, antiviral, antifungal, antitumor, antihelminthic, analgesic, hypotensive, anti-inflammatory, and immune-developmental effects (67, 68). MC contains L-asperuloside and alizarin, which have antibacterial properties Murray et al. compared the abilities of 6% MC and 6% NaOCl irrigation solutions to remove the smear layer. As a final irrigating agent, 17% EDTA was used after both solutions. The two solutions were found to have equivalent smear layer removal capabilities (68). The use of MC for endodontic irrigation may be advantageous because it is a more biocompatible antioxidant. In addition, it has no harmful effect on the patient or the environment, which is relevant in the context of NaOCl irrigation accidents (68).

Electrochemically Activated Water (Superoxidized Water)

Electrochemically activated solutions (ECA) are produced from tap water and salt solutions with low concentrations (69). Anolyte solutions include combinations of oxidizing agents with microbicidal activity against bacteria, viruses, fungi, and protozoa (70). They are referred to as superoxidized water or oxidative potential water (71). They do not damage vital biological tissues and are not toxic (72). Electrochemical activation has produced promising results in terms of effective root canal irrigation (69).

Ozonated Water

Even at a low concentration (0.01 ppm), ozone (O_3) can effectively kill bacteria, including spores (73). It can be produced easily with an ozone generator. Ozone dissolves easily and rapidly in water (73). In one study, the researchers compared the microbicidal activities of ozonated water and 2.5% NaOCl under sonic activation. They reported that ozonated water did not neutralize *Escherichia coli* or lipopolysaccharides in root canals and that the amount of remaining lipopolysaccharides may have biological effects, such as the induction of apical periodontitis (74, 75). Before its routine clinical use for root canal treatment, ozonated water needs to be investigated further.

Recommended Irrigation Method

NaOCl solution should be used during root canal preparation. Between fillings, root canals should be irrigated with copious amounts of NaOCl solution. After the completion of shaping, the canals should be irrigated with liquid EDTA or CA.

Generally, each canal should be irrigated for at least 1 min with 5–10 ml of chelating solution. After smear layer removal, irrigation with an antiseptic solution is helpful. CHX is one of the most promising solutions for final irrigation in this context.

CHX has high affinity for dental hard tissues and its antimicrobial activity persists for a long time once it is bound to the surface. After the introduction of MTAD irrigants to the market, a new irrigation method was recommended: initial irrigation with 1.3% NaOCl for 20 min, followed by final irrigation with MTAD for 5 min.

Conclusion

Future studies of irrigants should focus on the production of a single solution that is biocompatible, has tissue-solubilizing properties, removes the smear layer, and has antibacterial effects.

Acknowledgments

The authors deny any conflicts of interest related to this study.

References

1. Paque F, Ganahl D, Peters OA. Effects of root canal preparation on apical geometry assessed by micro-computed tomography. J Endod 2009;35:1056-9. Crossref
2. Peters OA, Scheonenberger K, Laib A. Effects of four Ni–Ti preparation techniques on root canal geometry assessed by micro-computed tomography. Int Endod J 2001;34:221-30. Crossref
3. Basrani B, Haapasalo M. Update on endodontic irrigating solutions-Endodontic topics 2012;27:74-102. Crossref

4. Agrawal Vineet S, Rajesh M, Sonali K and Mukesh P. A Contemporary Overview of Endodontic Irrigants - A Review. J Dent App. 2014;1(6):105-15.
5. Zehnder M. Root canal irrigants. J Endod 2006;32:389-98. Crossref
6. Dakin HD. On the use of certain antiseptic substances in treatment of infected wounds. Br Med J 1915;2:318-20. Crossref
7. Spanó JC, Barbin EL, Santos TC, Guimarães LF, Pécora JD. Solvent action of sodium hypochlorite on bovine pulp and physico-chemical properties of resulting liquid. Braz Dent J 2001;12:154-7.
8. Martinho FC, Gomes BP. Quantification of endotoxins and cultivable bacteria in root canal infection before and after chemomechanical preparation with 2.5% sodium hypochlorite. J Endod 2008;34:268-72. Crossref
9. Moorer W, Wesselink P. Factors promoting the tissue dissolving capability of sodium hypochlorite. Int Endod J 1982;15:187-96. Crossref
10. Spångberg L, Engström B, Langeland K. Biologic effects of dental materials. 3. Toxicity and antimicrobial effect of endodontic antiseptics in vitro. Oral Surg Oral Med Oral Pathol 1973;36:856-71.
11. Grossman LI, Meiman BW. Solution of pulp tissue by chemical agents. J Am Dent Assoc 1941;28:223-5. Crossref
12. Naenni N, Thoma K, Zehnder M. Soft tissue dissolution capacity of currently used and potential endodontic irrigants. J Endod 2004;30:785-7. Crossref
13. Grigoratos D, Knowles J, Ng YL, Gulabivala K. Effect of exposing dentine to sodium hypochlorite and calcium hydroxide on its flexural strength and elastic modulus. Int Endod J 2001;34:113-9. Crossref
14. Haapasalo M, Shen Y, Qian W, Gao Y. Irrigation in endodontics. Dent Clin North Am 2010;54:291-312. Crossref
15. Sirtes G, Waltimo T, Schaetzle M, Zehnder M. The effects of temperature on sodium hypochlorite short-term stability, pulp dissolution capacity, and antimicrobial efficacy. J Endod 2005;31:669-71. Crossref
16. Paragliola R, Franco V, Fabiani C. Final Rinse Optimization: Influence of Different Agitation Protocols. J Endod 2010;36:282-5. Crossref
17. Roy RA, Ahmad M, Crum LA. Physical mechanisms governing the hydrodynamic response of an oscillating ultrasonic file. Int Endod J 1994;27:197-207. Crossref
18. Nikaido T, Takano Y, Sasafuchi Y, Burrow MF, Tagami J. Bond strengths to endodontically-treated teeth. Am J Dent 1999;12:177-80.
19. Bui TB, Baumgartner CJ, Mitchell CJ. Evaluation of the interaction between sodium hypochlorite and chlorhexidine gluconate and its effect on root dentin. J Endod 2008;34:181-5. Crossref
20. Mortenson D. The effect of using an alternative irrigant between sodium hypochlorite and chlorhexidine to prevent the formation of para-chloroaniline within the root canal system. Int Endod J 2012;45:878-82. Crossref
21. Grawehr M, Sener B, Waltimo T, Zehnder M. Interactions Of Ethylenediamine Tetraacetic Acid With Sodium Hypochlorite In Aqueous Solutions. Int Endod J 2003;36:411-7. Crossref
22. Topbaş C, Büyükbayram IK, Toker T, Budak N, Subay RK. Endodontik sodyum hipoklorit komplikasyonlarının değerlendirilmesi ve bir olgu bildirisi. Aydın Dental Journal 2017;3(1):35-42.
23. Frais S, Ng YL, Gulabivala K. Some factors affecting the concentration of available chlorine in commercial sources of sodium hypochlorite. Int Endod J 2001;34:206-15. Crossref
24. Nygaard-Ostby B. Chelation in root canal therapy. Odontol Tidskr 1957;65:3-11.
25. Loel DA. Use of acid cleanser in endodontic therapy. J Am Dent Assoc 1975;90:148-51. Crossref
26. Von Der Fehr FR, Nygaard-Ostby B. Effect of EDTAC and sulfuric acid on root canal dentine. Oral Surg Oral Med Oral Pathol 1963;16:199-205. Crossref
27. Calt S, Serper A. Time-dependent effects of EDTA on dentin structures. J Endod 2002;28:17-9. Crossref
28. Kuah HG, Lui JN, Tseng PS, Chen NN. The Effect of EDTA with and without Ultrasonics on Removal of the Smear Layer. J Endod 2009;35:393-6. Crossref
29. Rasimick BJ, Nekich M, Hladek MM, Musikant BL, Deutsch AS. Interaction between chlorhexidine digluconate and EDTA. J Endod 2008;34:1521-3. Crossref
30. Smith J, Wayman B. An evaluation of the antimicrobial effect of citric acid as root canal irrigants. J Endod 1986;12:54-8. Crossref
31. Zehnder M, Schmidlin P, Sener B, Waltimo T. Chelation in root canal therapy reconsidered. J Endod 2005;31:817-20. Crossref
32. Sceiza MF, Daniel RL, Santos EM, Jaeger MM. Cytotoxic effects of 10% citric acid and EDTA-T used as root canal irrigants: An In vitro analysis. J Endod 2001;7:741-3.
33. Moliz MT, Luque CM, García ME, Baca P. Enterococcus faecalis biofilms eradication by root canal irrigants. J Endod 2009;35:711-4. Crossref
34. Russell RG, Rogers MJ. Bisphosphonates: from the laboratory to the clinic and back again. Bone 1999;25:97-106. Crossref
35. De-Deus G, Zehnder M, Reis C, Fidel S, Fidel RA. Longitudinal co-site optical microscopy study on the chelating ability of etidronate and EDTA using a comparative single-tooth model. J Endod 2008;34:71-5. Crossref
36. Addy M, Moran JM. Clinical indications for the use of chemical adjuncts to plaque control: chlorhexidine formulations. Periodontol 2000 1997;15:52-4. Crossref
37. Morris MD, Lee KW, Agee KA, Bouillaguet S, Pashley DH. Effect of sodium hypochlorite and RC-prep on bond strengths of resin cement on endodontic surfaces. J Endod 2001;27:753-7. Crossref
38. Siqueira JF, Paiva SS, Rocas IN. Reduction in the cultivable bacterial populations in infected root canals by a chlorhexidine-based antimicrobial protocol. J Endod 2007;33:541-7.
39. Jones C.G. Chlorhexidine: is still the gold standard? Periodontology 2000;15:55-62.
40. Denton GW. Chlorhexidine. In: block SS. Disinfection, sterilization and preservation. 4th ed. Philadelphia: lea &febiger 1991:274-89. Crossref
41. Russell AD, Day MJ. Antibacterial activity of chlorhexidine. J Hosp Infect 1993;25:229-38. Crossref
42. Zamany A, Safavi K, Spangberg LS. The effect of chlorhexidine as an endodontic disinfectant. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2003;96:578-81. Crossref
43. White RR, Hays GL, Janer LR. Residual antimicrobial activity after canal irrigation with chlorhexidine. J Endodod 1997;23:229-31. Crossref
44. Gomes PFA. Chlorhexidine in Endodontics. Braz Dent J 2013;24:89-102. Crossref
45. Gendron R, Grenier D, Sorsa T, Mayrand D. Inhibition of the activities of matrix metalloproteinases 2, 8, and 9 by chlorhexidine. Clin Diagn Lab Immunol 1999;6:437-9.
46. Babich H, Wurzburger BJ, Rubin YL, Sinensky MC, Blau L. An in vitro study on the cytotoxicity of chlorhexidine digluconate to human gingival cells. Cell Biology & Toxicology 1995;11:79-88. Crossref
47. Evanov C, Liewehr F, Buxton TB, Joyce AP. Antibacterial efficacy of calcium hydroxide and chlorhexidine gluconate irrigants at 37 degrees C and 46 degrees C. J Endod 2004;30:653-7. Crossref
48. Shen Y, Qian W, Chung C, Evaluation of the effect of two chlorhexidine preparations on biofilm bacteria in vitro: a three-dimensional quantitative analysis. J Endod 2009;35:981-5. Crossref
49. Torabinejad M, Khademi AA, Babagoli J, Cho Y, Johnson WB. A new solution for removal of smear layer. J Endod 2003;29:170-5. Crossref

50. Haapasalo M, Qian W, Portenier I, Waltimo T. Effects of dentin on the antimicrobial properties of endodontic medicaments. J Endod 2007;33:917-25. Crossref
51. Torabinejad M, ChoY, Khademi AA, Bakland LK, Shabahang S. The effect of various concentrations of sodium hypochlorite on the ability of MTAD to remove the smear layer. J Endod 2003;29:233-9. Crossref
52. Hashem AA, Ghoneim AG, Lufty RA, Fouda MY. The effect of different irrigating solutions on bond strength of two root canal filling systems. J Endod 2009;35:537-40. Crossref
53. Dahlén G, Samuelsson W, Molander A, Reit C. Identification and antimicrobial susceptibility of Enterococci isolated from the root canal. Oral Microbiol Immunol 2000;15:309-12. Crossref
54. McDonnell G, Russell AD. Antiseptics and disinfectants: activity, action, and resistance. Clin Microbiol Rev 1999;12:147-79.
55. Giardino L, Ambu E, Becce C, Rimondini L, Morra M. Surface tension comparison of four common root canal irrigants and two new irrigants containing antibiotic. J Endod 2006;32:1091-3. Crossref
56. Pappen FG, Shen Y, Gian W, Leonardo MR, Giardino L. In vitro antimicrobial action of Tetraclean, MTAD and five experimental irrigation solutions Int Endod J 2010;43:528-35. Crossref
57. Ballal NV, Kandian S, Mala K, Bhat KS. Comparison of the efficacy of maleic acid and ethylenediaminetetraacetic acid in smear layer removal from instrumented human root canal: A Scanning Electron Microscopic Study. J Endod 2009;35:1573-6. Crossref
58. Ballal NV, S. Kandian, Kundanbala Mala, K S Bhat. Evaluation of the effect of maleic acid and EDTA on micro-hardness and surface roughness of human root canal dentin. J Endod 2010;36:1385-8. Crossref
59. Cobankara FK, Ozkan HB, Terlemez A. Comparison of organic tissue dissolution capacities of sodium hypochlorite and chlorine dioxide. J Endod 2010;36:272-4. Crossref
60. Eto JN, Niu W, Takeda FH, Kimura Y, Matsumoto K. Morphological and atomic analytical changes of root canal wall dentin after treatment with thirty eight percent Ag(NH3)2F solution and CO2 laser. J Clin Laser Med Surg 1999;17:19-24.
61. Zambon JJ, Reynolds HS, Dunford RG, Bonta CY. Effect of a triclosan/ copolymer/ fluoride dentifrice on the oral microflora. Am J Dent 1990;3:27-34.
62. Nudera WJ, Fayad MI, Johnson BR, Zhu M, Wenckus CS, et al. Antimicrobial effect of triclosan and triclosan with gantrez on five common endodontic pathogens. J Endod 2007;33:1239-42. Crossref
63. Sahni A, Chandak MG. Herbal usage in root canal irrigation: A review. Int J Dent Health Sci 2015;2(1):76-82.
64. Jain P, Ranjan M. Role of herbs in root canal irrigation - A review. IOSR Journal of Pharmacy and Biological Sciences 2014;9(2):6-10. Crossref
65. Prabhakar J, Senthilkumar M, Priya MS, Mahalakshmi K, Sehgal PK, et al. Evaluation of antimicrobial efficacy of herbal alternatives (Triphala and Green Tea Polyphenols), MTAD, and 5% sodium hypochlorite against enterococcus faecalis biofilm formed on tooth substrate: An in vitro study. J Endod 2010;36:83-6. Crossref
66. Hamilton-Miller JM. Anti-cariogenic properties of tea (Camellia sinensis). J Med Microbiol 2001;50:299-302. Crossref
67. Wang MY, Su C. Cancer preventive effect of morinda citrifolia (Noni). Ann N Y Acad Sci 2001;952:161-8. Crossref
68. Murray PE, Farber RM, Namerow KM, Kuttler S, Godoy FG. Evaluation of Morinda citrifolia as an endodontic irrigant. J Endod 2008;34:66-70. Crossref
69. Solovyeva AM, Dummer PMH. Cleaning effectiveness of root canal irrigation with electrochemically activated anolyte and catholyte solutions: A pilot study. Int Endod J 2000;33:494-504. Crossref
70. Prilutskii VI, Bakhir VM, Popov AI. The disinfection of water, water supply systems, tanks and pools by using an electrochemically activated solution of a neutral anolyte. Vopr Kurortol Fizioter Lech Fiz Kult 1996;(4):31-2.
71. Selkon JB, Babb JR, Morris R. Evaluation of the antimicrobial activity of a new super-oxidized water(Sterilox) for the disinfection of endoscopes. J Hosp Infect 1999;41:59-70. Crossref
72. Shraev TI, Legchilo AN. Use of electrochemically activated 0.8% potassium chloride solutions in the treatment of empyema and parietal abscesses of the lung. Grudn Khir 1989;4:64-8.
73. Broadwater WT, Hoehn RC, King PH. Sensitivity of three selected bacterial species to ozone. Journal of Appl Microbiol 1973;26:391-3.
74. Huth KC, Quirling M, Maier S, Kamereck K. Effectiveness of ozone against endodonto-pathogenic microorganisms in a root canal biofilm model. Int Endod J 2009;42:3-13. Crossref
75. Nogales CG, Ferrari PA, Kantorovich EO, Lage-Marques JL. Ozone therapy in medicine and dentistry. J Contemp Dent Pract 2008;(9)4:75-84.