Review Article

A Review on Root Canal Irrigation Solutions in Endodontics

Zahed Mohammadi[1], Sousan Shalavi[2], Jun-Ichiro Kinoshita[3], Luciano Giardino[4], James L Gutmann[5], SeyedAhmad Banihashem Rad[6], Christopher I. Udoye[7], Hamid Jafarzadeh[8]

[1]Iranian Center for Endodontic Research (ICER), Research Institute of Dental Sciences, Shaheed Beheshti University of Medical Sciences, Tehran, Iran and Iranian National Elite Foundation, Tehran, Iran
[2]General Dental Practitioner, Hamedan, Iran
[3]Department of Conservative Dentistry, Showa University Dental Hospital, Tokyo, Japan
[4]School of Dentistry, Department of Endodontics, Università degli Studi di Torino; and Private Practice, Crotone, Italy
[5]Baylor College of Dentistry, Texas A&M Health Science Center, Dallas, Texas, USA
[6]Department of Restorative, Preventive and Pediatric Dentistry, School of Dental Medicine (ZMK Bern), University of Bern, Switzerland
[7]Department of Restorative Dentistry, College of Medicine, University of Nigeria, Enugu State, Nigeria
[8]Department of Endodontics, Mashhad University of Medical Sciences, Mashhad, Iran

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Abstract

Introduction: This paper aims to review the different characteristics of root canal irrigants including sodium hypochlorite (NaOCl), chlorhexidine (CHX), hydrogen peroxide (H_2O_2), iodine potassium iodide (IKI), antibiotic-based irrigants, photo-activated disinfection, electrochemically activated water, and QMix. The literature on root canal irrigation solutions in the context of endodontics up to June 2020 was reviewed using PubMed and MEDLINE. NaOCl was identified as the most likely effective irrigation solution that could be used for endodontics. Its antimicrobial activity is at least comparable or even greater than that of other common irrigants. Tetraclean was also proposed to be more effective than CHX against endodontic microorganisms. In addition, Hypoclean was suggested as the most potent and effective irrigant against *Candida albicans*. Similarly, IKI was introduced as a successful irrigant in killing *Candida albicans* and *Enterococcus faecalis*. MTAD is also known to be effective in smear layer removal as well as against the growth of *Enterococcus faecalis*. EDTA is also considered to have limited antimicrobial activity.

Keywords: Chlorhexidine, Iodine Compounds, MTAD, Root Canal Irrigation.

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Introduction

Many human and animal experiments have demonstrated the crucial role of microorganisms in the production of pulpo-periapical diseases (1-3). *In vitro* and clinical records have suggested that mechanical instrumentation of the canal does not debride all areas of the canal walls (4) and hence it seems impossible that microorganisms can be completely eliminated from the canal by mechanical preparation solely (5). Consequently, different irrigation techniques to eliminate and/or destroy microorganisms should be considered essential (6). Every dentist ought to be informed of irrigation solutions, their advantages, and their side effects.

The present review will discuss different aspects of some root canal irrigants such as sodium hypochlorite (NaOCl), chlorhexidine (CHX), hydrogen peroxide (H_2O_2), iodine potassium iodide (IKI), antibiotic irrigants, and QMix based on the existing literature guidelines.

Search Strategy

The literature on root canal irrigation solutions in the context of endodontics up to June 2020 was reviewed using PubMed and MEDLINE.

NaOCl

Mechanism of Action

NaOCl can function as a fat solvent that converts them into glycerol and fatty acids, thus decreasing the surface tension of the remaining solution (7). NaOCl can neutralize amino acids by a neutralization reaction and hence releasing salt and water. Hydroxyl ion release decreases pH. Because of the near interaction between NaOCl and organic tissues, hypochloric acid can perform as a solvent and generates chlorine, which can build chloramines combined with the amino protein group. Hypochlorite ions and hypochloric acid could trigger hydrolysis and degradation of the amino acids (8).

Antibacterial Activity

An *in vivo* analysis, Bystrom and Sundqvist (9) found that 12 out of 15 root canals were bacteria-free at the fifth examination when 0.5% of hypochlorite had been used. By contrast, in the saline group, 8 out of 15 root canals were bacteria-free. Siqueira et al. (10) suggested that 4% NaOCl would display substantial efficacy in comparing the saline solution in disinfecting the *Enterococcus faecalis* contaminated root canal. 5.25% NaOCl was more successful against *Enterococcus faecalis* than its lower concentrations (11). Ercan et al. (12) suggested that the microorganisms were greatly decreased using 5.25% NaOCl.

Antifungal Activity

Overall, the prevalence of fungi has been estimated to be 1-17% in contaminated canals (13, 14). Implementing cylindrical dentine tubes, Sen et al. (15) demonstrated that antifungal activity of NaOCl begins after 30 minutes in the absence of a smear layer. Another study by Waltimo et al. (16) revealed that NaOCl is able to destroy all *Candida albicans* in just 30 seconds at a concentration of 0.5% and 5%. Furthermore, Ferguson et al. (17) found that NaOCl even with substantial dilution was successful against *Candida albicans*. An analysis found that 6% NaOCl antifungal function was higher than 17% EDTA (18). Radcliffe et al. (19) found that, after 10 seconds, various NaOCl concentrations (0.5%, 1%, 2.5%, and 5.25%) reduced colony formation of *Candida albicans* below the detection level. Similarly, Ayhan et al. (20) had the same results.

Antibiofilm Activity

Biofilm microorganisms can have a 2-1000 times higher tolerance than planktonic form (21). A recent research found that 2.25% NaOCl is more successful against monoculture biofilms than other irrigants (22). Clegg et al. (23) found that 6% NaOCl has been the only irrigant with the potential to make the bacteria inviolable as well as physically eliminating the biofilm. Dunavant et al. (24) suggested that both 1% and 6% NaOCl is more successful in eliminating *Enterococcus faecalis* biofilm as opposed to other irrigants. Moreover, Giardino et al. (25) indicated that 5.25% NaOCl could destroy the biofilm at any time.

Tissue Solubility

Grossman (26) claimed that NaOCl would degrade the pulp tissue within 20 minutes to 2 hours by concentration at 5%. Moreover, Moorer and Naenni et al. (27) reported a sufficient potential of 1% NaOCl for tissue destruction. Clarkson et al. (28) reported that higher NaOCl concentrations produced quicker tissue dissolution, although a new study showed that applying a surfactant to NaOCl did not improve the ability to dissolve the tissue (29).

Toxicity

In an *in vitro* research, Pashley et al. (30) found that 1:1000 isotonic NaOCl concentration in saline could cause complete hemolysis of red blood cells. Kozol et al. (31) found that the solution of Dakin (composed of 0.4% to 0.5% NaOCl and 4% boric acid) was harmful to neutrophilic chemotaxis and toxic to endothelial cells and to fibroblasts. Heggers et al. (32) found that 0.025% NaOCl had been perfectly harmless as it had a bactericidal activity without toxicity to the tissue, whereas Zhang et al. (33) demonstrated that toxicity of NaOCl may have been dosage-dependent. Barnhart et al. (34) also reported that cytotoxicity of NaOCl was considerably greater than that of calcium hydroxide and IKI.

Complications Faced when using NaOCl

Most complications of NaOCl usage appears to be NaOCl accident involving unintended injection of NaOCl over apical foramen leading to aggressive tissue reactions associated with extreme pain and swelling, and perhaps even secondary infection (35). In an *in vitro* investigation, Brown et al. (36) proposed that filling coronal access cavity by NaOCl and pushing it into the canal space throughout instrumentation could lead to considerably less extrusion of irrigation solutions from

apical foramen compared to deep irrigant distribution through needles.

Activation of NaOCl using Ultrasonic

Ultrasound that is a sound energy with a frequency above 20 kHz appears to have cleaning properties in combination with NaOCl through cavitation. A further significant result is to drive the irrigant into inaccessible canal regions (37). Sjögren and Sundqvist (38) found that by using 0.5% NaOCl along with ultrasonic instrumentation would lead to more appropriate antibacterial activities than just hand preparation. Huque et al. (39) demonstrated the superiority of passive ultrasonic irrigation over irrigation of the syringe. In contrast, there was no marked difference between syringe irrigation and passive ultrasonic irrigation reported by Alves et al. (40) and Siqueira et al. (41). In an *in vitro* study, Tardivo et al. (42) indicated that there has been no difference between syringe irrigation, passive ultrasonic irrigation, and passive sonic irrigation in reducing *Enterococcus faecalis* through using 5.25% NaOCl. Also, some experiments have revealed the beneficial effect of irrigation by ultrasonic instruments on lowering the canal bacteria (43, 44).

Newer NaOCl-Based Irrigants

Chlor-XTRA consists of 5.85% NaOCl and a detergent, which can decrease surface tension. Its color is transparent pale yellow-green with a chlorine-like odor and is fully soluble in water. It is 2.6 times more digestive than typical NaOCl, and is 2.5 times higher than typical NaOCl wetting ability (26, 45). By using the agar diffusion test recently, it has been discovered that Chlor-XTRA has been the most powerful alternative against *Actinomyces Israeli* (46). Hypoclean is a recent root canal irrigant based on NaOCl comprised of 5.25% NaOCl and two disinfectants. Hypoclean substantivity could be seen for up to 4 weeks (45). Recently, agar diffusion test has shown that Hypoclean has become the most efficient irrigation solution against certain bacteria, such as *Candida albicans*, *Pseudomonas aeroginosa*, and *Lactobacillus casei* (46).

CHX

Mechanism of Action

CHX is a lipophilic and hydrophobic substance that connects with the membrane of bacterial cells, and can therefore penetrate the bacteria (6). CHX, through positively charging the molecule, will change the osmotic balance of the cells. CHX is bacteriostatic at 0.2% concentration due to potassium and phosphorous leakage from the bacterial cell membrane. By contrast, 2% CHX has a bactericidal function due to cytoplasmic material precipitation (47).

Antibacterial Aactivity

Basson and Tait (48) conducted an *in vitro* research indicating that the only irrigant capable of fully disinfecting the channels contaminated with *Actinomyces Israeli* even after two months has been a 2% CHX solution. Oncag et al. (49) found, in another *in vitro* research, that after 5 minutes and 48 hours, 2% CHX was more successful against *Enterococcus faecalis* than 5.25% NaOCl. Ercan et al. (12) reported that 2% CHX was successful in minimizing the volume of microbes in teeth with necrotic pulp, periapical disease or even both According to Tanomaru et al. (50), the endotoxin *in vivo* was not inactivated by 2% CHX along with biomechanical preparation.

Antifungal activity

Waltimo et al. (16) found that in just five minutes, 0.5% CHX-acetate could destroy all seven strains of *Candida albicans*. After only one hour, the contaminated bovine dentine treated with CHX conjugated in zinc oxide paste may be disinfected (51). Ferguson et al. (17) confirmed that CHX-digluconate was successful against *Candida albicans*.

Antibiofilm Activity

Clegg et al. (23) found that biofilm could not be damaged by 2% CHX. Dunavant et al. (24) reported that there is no disparity in the killing of *Enterococcus faecalis* biofilm between 1 minute and 5 minutes application of 2% CHX. Moreover, the percentage of bacteria destroyed was 60%. In contrast, Lima et al. (52) found that one-day and three-day *Enterococcus faecalis* biofilms can be completely removed by substances comprising 2% CHX.

Substantivity

The *in vitro* and *in vivo* researches represented the antimicrobial substantivity of 2% CHX solution for 72 (53) and 48 (54) hours. Few other studies found that CHX substantivity would last from 4 (55) to 12 (56) weeks. Lately, CHX solvent and gel have recently been found to be maintained in dentine for up to 90 days (56). The time taken for the dentine treatment to trigger substantivity is still controversial. Though other studies have shown that 5-10 minutes of dentin treatment may cause substantivity (54, 55, 57). Others (58, 59) linked CHX substantivity to its capacity to adsorb dentin in the first hour. Studies lately suggest that there has been a connection between the duration of dentine therapy and the substantive irrigant (60). Moreover, CHX delayed canal

recontamination through the coronal pathway (61). In another study, Mohammadi et al. (62) stated that the substantivity of CHX makes it an excellent choice for final canal rinsing.

Buffering Effect of Dentine and Canal Contents on CHX

One research displayed that the dentin powder prevented antibacterial function of 0.5% and 0.05% CHX acetate (63). Portenier et al. (64) illustrated that bovine serum albumin suppressed 0.05% CHX and slowed down by dentin. Yet CHX seemed to have little inhibition from hydroxyapatite. It was shown that the most powerful inhibitors of CHX can be heat-killed bacterial cells and even the dentin matrix; nevertheless, pretreatment of dentin by EDTA or citric acid has led to the minor inhibition activity. At 1 hour, dentine showed certain inhibition but after 24 hours it has no effect (65). It has been shown that the existence of dentine or bovine serum albumin can trigger a substantial delay in CHX destroying *Enterococcus faecalis* (66, 67). Mohammadi and Shalavi (68) have shown that both heat-killed *Candida albicans* and dentine powder have greatly reduced the function of 2% CHX against *Enterococcus faecalis* and *Streptococcus sanguis*.

Tissue Solubility

Okino et al. (69) found that the pulp could not be dissolved within 6 hours by 2% CHX-digluconate (aqueous solution) and 2% CHX digluconate (gel). In addition, Naenni et al. (27) have noted that 10% CHX has no significant ability to remove tissue.

Toxicity of CHX

Sanchez et al. (70) demonstrated that high CHX concentrations with bactericidal activity were harmful to embryonic fibroblasts, while non-cytotoxic CHX concentrations permitted bacterial growth. Tatnall et al. (71) observed that CHX concentrations prescribed for wound cleaning might also have adverse effects such as fibroblast destruction and basal keratinocyte removal.

Babich et al. (72) suggested that the toxic effects of CHX to gingival cells largely depends on the duration of exposure. Similarly, Boyce et al. (73) reported that the 0.05% CHX was harmful to human cells and microorganisms. However, Ribeiro et al. (74) demonstrated that CHX does not have genotoxicity against hamster cells.

Allergic Reactions to CHX

Sensitivity to CHX was confirmed to be uncommon but contact dermatitis could be a side effect (75). Some other adverse effects including tooth discoloration, gingivitis, sensitivity to light, and occasional anaphylactic reactions have been mentioned (76, 77).

New CHX-Based Irrigants

CHX-Plus

A newer type of CHX, called CHX-Plus (Vista Dental Products, Racine, WI, USA) has recently been released that includes surface modifiers. Studies on CHX-Plus are very limited. Utilizing a 3-dimensional quantitative study, Shen et al. (78) showed that, at 1 minute, 3 minutes and 10 minutes, CHX-Plus was more successful than CHX against spirochetes biofilms. A survey was performed by Bidar et al. (79) to evaluate the antimicrobial activity of 2% CHX, 2.5% NaOCL, and 2% CHX MUMS. All the aforementioned irrigants have been tested on *Enterococcus faecalis*, *Streptococcus mutans*, *Candida Albicans*, *Lactobacillus casei*. Results suggested that MUMS containing CHX demonstrated antimicrobial properties much like the effect of CHX on *Escherichia Coli*, *Streptococcus mutans*, *Candida Albicans*, *Enterococcus faecalis*, and *Lactobacillus casei* in preventing incubation of all these microorganisms. NaOCl is not successful against *Enterococcus faecalis* and *Candida Albicans* in 15, 30, and 45 minutes incubated as well as *Enterococcus faecalis* within 15 minutes (80).

Q-Mix

Q-Mix is also another root canal irrigant base on CHX, which contains CHX, EDTA, saline, and a detergent (81). Chemical property of Q-Mix prohibits precipitation of CHX as the orange-brown precipitate is not formed along with EDTA and mixing with NaOCl. the capability of Q-Mix to eliminate smear layer was found to be equal with that of 17% EDTA (82) and its antibacterial efficacy was higher than 1%, 2% NaOCl, and 2% CHX. Mohammadi et al. (83) also reported that Qmix should be used at the final rinse and is assumed to be as successful as EDTA.

MTAD

In 2003, Torabinejad et al. (84) proposed a new substance named MTAD that is composed of 4.25% citric acid, 3% doxycycline, and 0.5% polysorbate which acts as a detergent.

Antimicrobial Activity

MTAD will break down the smear layer and is able to perform successfully against *Enterococcus faecalis* based on some studies by Torabinejad et al. (84-87). One study (87) demonstrated that MTAD is a better alternative than 5.25% NaOCl for canal disinfection. In comparison, Kho and Baumgartner (88) claimed that

the usage of a combination of the 1.3% NaOCl/MTAD left 50% of the canals contaminated with *Enterococcus faecalis*. Another survey by Newberry et al. (89) revealed that MTAD inhibited the production of *Enterococcus faecalis* when diluted.

Substantivity of MTAD

Another component of MTAD is Doxycycline and is in charge of antimicrobial activity (84). Mohammadi and Shahriari (55) stated that the substantivity of MTAD was greater than that of CHX and NaOCl in 4 weeks period. In another research, the substantivity of 100% MTAD was higher than other concentrations of MTAD (90). Tay et al. (91) ended up finding that, when added to NaOCl-irrigated dentin, MTAD antimicrobial substantivity reduced by 1.3%.

MTAD and Biofilms

Based on the findings of Clegg et al. (23), 6% NaOCl was the only irrigant capable of making bacteria inviable and physically eliminating the biofilm. Dunavant et al. (24) indicated that MTAD removed 16% of microbial pathogens in *Enterococcus faecalis* biofilm. In contrast, Giardino et al. (25) demonstrated that MTAD was unable to destroy bacterial biofilm.

Effect on Dentine and Smear Layer Removal

Torabinejad et al. (84) reported that MTAD is an appropriate choice for eliminating the smear layer. When MTAD was used after irrigation of the canal with NaOCl as a final rinse, it did not significantly alter the composition of the dentinal tubule. However, Lotfi et al. (92) have shown that MTAD has not removed the smear layer. Another study by Tay et al. (93) has shown that MTAD is able to create a thicker demineralized dentine matrix than EDTA. De-Deus et al. (94) observed that demineralization induced by MTAD was comparatively quicker than demineralization induced by EDTA. Machnick et al. (95) suggested there was little disparity between MTAD and saline in the flexural intensity of the dentin.

MTAD and Dentin Bonding

Machnick et al. (96) displayed that the MTAD applied throughout the root canal therapy did not require additional dentine preparation before dentin bonding was implemented. Another survey by Garcia-Godoy et al. (97) showed that the thickness of MTAD hybrid layer was approximately 17% greater than EDTA. In comparison with NaOCl, neither MTAD nor EDTA improved the strength of the bond between epiphany and dentin (98). A further research by Yurdaguven et al. (99) showed that MTAD reduced the connection of Clearfil SE Bond to coronal dentine.

Toxicity of MTAD

Zhang et al. (33) considered MTAD to be less cytotoxic than 3% H_2O_2, 5.25% NaOCl, eugenol, calcium hydroxide, and EDTA; but perhaps more cytotoxic than 2.6% and 0.66% NaOCl, in turn. MTAD also displayed less cytotoxicity than other irrigation products based on a study by Yasuda et al. (100).

Tetraclean

Tetraclean is a relatively new substance, which was first introduced in Italy and is a mixture of 50 mg/ml doxycycline, acid, and a detergent, which is polypropylene glycol. The surface tension of NaOCl and EDTA is much more than that of Tetraclean (101).

Antibacterial Activity

In an *in vitro* experiment, Neglia et al. (102) showed that Tetraclean was a successful option against *Enterococcus faecalis*. Similarly, Ardizzoni et al. (103) highlighted that Tetraclean had been fully successful against *Enterococcus faecalis* at specific concentration (up to 1:256). Moreover, Giardino et al. (104) proposed that Tetraclean would be more successful than CHX against endodontic microorganisms. Similarly, Pappen et al. (105) indicated that Tetraclean was more successful against *Enterococcus faecalis* than MTAD. According to reports from Poggio et al. (106), the Tetraclean efficacy against *Streptococcus mutans* and *Enterococcus faecalis* was substantially higher than NaOCl.

Substantivity of Tetraclean

Mohammadi et al. (107) reported that Tetraclean substantivity was significantly higher than MTAD and even 5.25% NaOCl and is able to stay in dentin for 4 weeks at minimum (108). Tetraclean has made a direct relation between substantivity and time of dentine treatment (109). In addition, pretreatment of dentin with NaOCl is thought to greatly minimize Tetraclean substantivity (110).

Smear Layer Removal Ability

Poggio et al. (111) reported that Tetraclean capacity for demineralization was markedly higher than 17% EDTA.

Iodine Compounds

Mechanism of action

It would appear that the precise mechanism of action of iodine compounds is the iodine attack to the proteins.

Molecular iodine is in charge of the action against bacteria. A critical form of iodine complexes is IKI, which is produced by combining iodine into potassium iodide; dissolved in distilled water afterward (112).

Antibacterial Activity

Peciuliene et al. (113) suggested that 2% IKI was successful in disinfecting the root canal system with 4% potassium iodide. Abdullah et al. (114) reported that application of 10% povidone-iodine in 30 minutes ended in a 100% decrease in *Enterococcus faecalis*. In a model using the contaminated bovine teeth with *Enterococcus faecalis*, Baker et al. (115) revealed that the agents comprising iodine were considerably stronger than calcium hydroxide. Shurrab (116) considered povidone iodine to be particularly efficient against *Enterococcus faecalis*, and its minimum active concentration in contaminated canals was 1%.

Antifungal Activity

Waltimo et al. (16) illustrated that IKI would destroy all *Candida albicans* in just 30 seconds. It has been reported that two weeks after the application of 2% iodine-iodate solution as an intra-canal medication destroyed half of the *Candida albicans* cells (117). Peciuliene et al. (113) also observed that 4% potassium iodide could eliminate all *Candida albicans* cells in 30 seconds; while ten-fold dilution would destroy all cells after 5 minutes.

Buffering Effect of Dentine

Dentine demonstrates some inhibitory effects on iodine solutions activity. Haapasalo et al. (63) found that dentine powder inhibited the impact of 0.4% potassium iodide; although, dentine powder inactivation of 4% potassium iodide has been very poor. Portenier et al. (64) found that hydroxyapatite caused limited inhibition in dentine, whereas collagen matrix efficiently inhibited 0.1% IKI.

Cytotoxicity

Barnhart et al. (34) suggested that IKI was considerably less cytotoxic than NaOCl. Using cultivated Chinese hamster lung cells, Iwasaki et al. (118) demonstrated that povidone-iodine cytotoxicity appeared in dose- and time-dependent ways, and that povidone-iodine induced cell synthesis inhibition of DNA, RNA, and protein, along with therapy that did not affect cell viability. In an *in vitro* analysis to determine the cytotoxicity of povidone-iodine mouth-rinse on gingival fibroblasts, Wilken et al. (119) observed that 20% povidone-iodine fixed cells instantly. Another research by Cabral and Fernandes (120) has demonstrated that CHX has greater cytotoxicity than iodine povidone.

EDTA

Structure and Smear Layer Removal

EDTA is a colorless chelating agent and soluble in water. It is synthesized primarily from ethylenediamine, sodium cyanide, and formaldehyde (121).

Wu et al. (122) found that 17% EDTA was substantially more effective than MTAD and 20% citric acid for smear layer elimination. If 5.25% NaOCl is used as a preliminary irrigant, Dai et al. (80) have demonstrated that 17% EDTA was as successful as Q-Mix in eliminating smear layers. Rodig et al. (123), Mancini et al. (124), and da Silva et al. (125) have stated that EDTA is a great substitute for eliminating the smear layer.

Antimicrobial Activity

Patterson (126) showed that antimicrobial activity of EDTA was limited. This is the consequence of cations being chelated from the outer bacterial membrane. Kotula and Bradshaw (127) revealed that the antimicrobial activity of EDTA was preserved for as long as there was no bond with metal ions. Heling et al. (128) have found that the antibacterial activity improved by rising temperature from 10 to 45°C. In another study, Ørstavik and Haapasalo (129) challenged the antimicrobial activity of 17% EDTA and Ordinola-Zapata et al. (130) stated that EDTA has no considerable effect on the biofilm. According to these observations, even after one hour, Arias-Moliz et al. (131) demonstrated no influence of EDTA on *Enterococcus faecalis*. Bystrom and Sundqvist (132) reported that EDTA and NaOCl together had greater antimicrobial activity than NaOCl alone. However, Sen et al. (133) discovered that EDTA was successful against *Candida albicans*. Mohammadi et al. (134) proposed that the combination of CH with NaOCl, CHX and IKI would improve the antimicrobial efficacy of these compounds. It should be emphasized that the interactions between canal irrigants and dentin should be focused (135, 136).

Conclusion

Irrigants have a key role in the eradication of microbes from the root canal system. Some parameters such as antibacterial, antifungal, and antibiofilm activity, toxicity, tissue solubility, substantivity, impact on dentin and smear layer, and side effects such as allergic reactions can affect the choice of an appropriate irrigant. NaOCl has been regarded in several studies as the most successful irrigation solution for endodontic treatment. Its antimicrobial activity is at least comparable or even greater than that of other popular irrigants. It is the only irrigant able to remove and eliminate the microbial

biofilm from the canal. It could be used as a strong agent with the highest dissolving tissue capacity as an irrigant.

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Corresponding Author
Hamid Jafarzadeh
Department of Endodontics, Mashhad University of Medical Sciences, Mashhad, Iran
Tel: +98-51-38829501
Email: hamid_j365@yahoo.com &
JafarzadehBH@mums.ac.ir