REVIEW ARTICLE

Sodium Hypochlorite Interaction with Other Root Canal Irrigants: A Systematic Review

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Abstract

Background: The root canal system is essential for successful endodontic treatment, demanding effective irrigation and disinfection. Sodium hypochlorite, valued for its low viscosity, serves as a versatile agent with lubricating, antimicrobial, and pulp tissue dissolving properties. However, its increasing concentration correlates with heightened antibacterial efficacy and tissue dissolution, accompanied by increased toxicity. Combined root canal irrigant use is common to address individual limitations, necessitating an understanding of their chemical interactions and potential effects.

Methods: This systematic review adheres to PRISMA guidelines, with a registered protocol on PROSPERO. A thorough search strategy encompassed PubMed, Science Direct, and Google Scholar, focusing on English-language articles published from 2003 to 2023. Duplicate removal utilized Zotero, while title/abstract screening employed Rayyan online software. Two authors conducted full-text reviews and data extraction, addressing inclusion and exclusion criteria and resolving discrepancies through discussion.

Results: The review explores the chemical interactions of sodium hypochlorite with various agents, including chlorhexidine, alexidine, ethylenediaminetetraacetic acid (EDTA), citric acid, etidronate, octenidine, MTAD, Q mix and select natural products. Each interaction is analyzed for its implications on root canal treatment, encompassing potential benefits and adverse effects.

Conclusion: Understanding the interactions between sodium hypochlorite and diverse root canal irrigants is crucial for optimizing treatment outcomes. The review synthesizes current literature to provide insights into the complex interplay of these agents, facilitating informed decision-making in endodontic practice.

Keywords: Endodontic irrigants, Ethylenediaminetetraacetic acid, Root canal disinfection, Sodium hypochlorite.

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Introduction

Accomplishment of good endodontic treatment is feasible only with efficient irrigation subsequently with proper biomechanical preparation during the root canal procedure. Good biomechanical preparation can reduce the bacterial load in the root canal by 100–1000 folds. Irrigation plays a key role in reducing the friction between the instrument and dentin, and also improves the cutting efficiency of the files in the root canal. Proper irrigation is a requisite to prevent accumulation and extrusion of infected material and debris into the periapical region. About 35–50% of the canal system remains untouched by the endodontic instrument and hence usage of appropriate irrigant is obligatory for proper disinfection of the canal.[1] Of all the irrigants used in endodontics, sodium hypochlorite happens to be one of the most common irrigants in use.[2–4]

For any root canal irrigant to be considered ideal, it must possess certain properties such as prolonged antimicrobial effect, stability in solution, reduced surface tension, it must be non-irritating to the oral tissues, etc. Due to the fact that no irrigant possesses all the ideal properties, it is preferred to combine suitable irrigants in a sequential manner to enhance the antimicrobial, tissue dissolving and lubricant properties which is essential during biomechanical preparation of the root canal.[5]

During endodontic irrigation, various root canal irrigants interact with each other chemically and result in the formation of reactive precipitates and alter the chemical structure of each irrigant which may either have beneficial or adverse effects during the endodontic procedure.[6]

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Search Strategy

This systematic review follows PRISMA guidelines, with a PROSPERO-registered protocol (Fig. 1). A comprehensive search strategy covered PubMed, Science Direct, and Google Scholar for English-language articles published between 2003 and 2023. Duplicate removal used Zotero, and title/abstract screening employed Rayyan online software. Full-text review and data extraction based

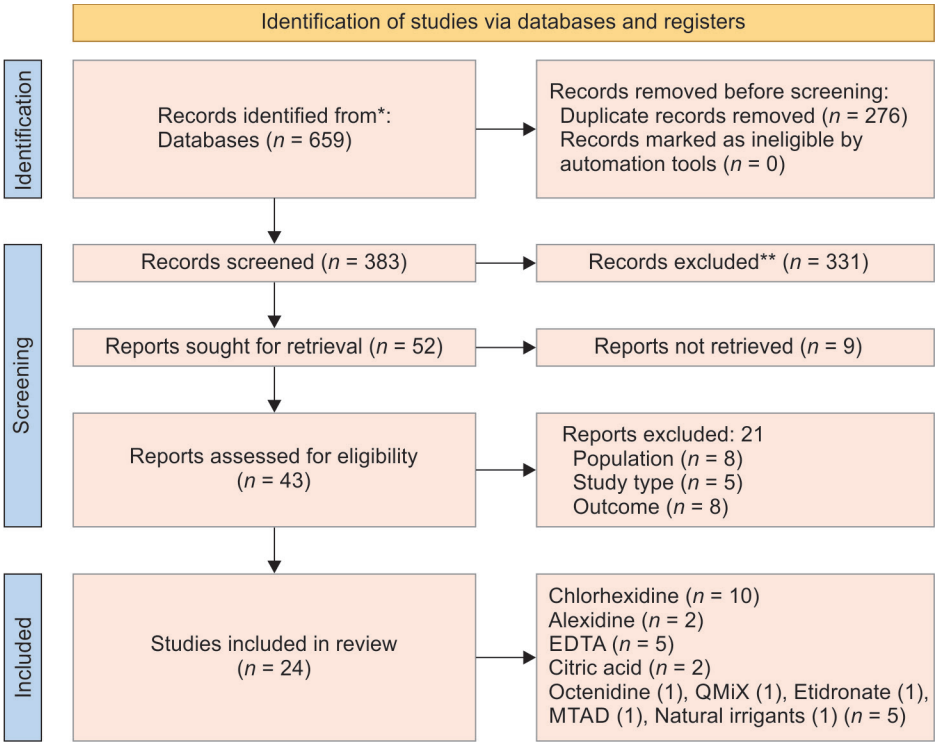

Fig. 1: PRISMA flowchart for search strategy

In total 24 articles are selected based on inclusion and exclusion criteria. *Signifies the record indentified from mutliple databases accross web; **Signifies the records removed from mutliple databses accross web

on inclusion and exclusion criteria involved two authors, resolving discrepancies through discussion (Supplementary data: Table 1).

Interactions between Sodium Hypochlorite and Chlorhexidine

Chlorhexidine is a known broad-spectrum antimicrobial agent widely used in endodontics for root canal disinfection.[7] The widespread use of chlorhexidine in dentistry was mainly after the 1970s. In endodontics, 2% chlorhexidine is most commonly used either in liquid or gel form.[8] Chlorhexidine mainly scores over many other root canal irrigants because of its substantivity.[7]

The lack of substantivity is a known drawback of sodium hypochlorite while the lack of the ability to dissolve organic matter happens to be the setback of chlorhexidine.[1,7] The combination of these two irrigants compensate the respective drawbacks that each of them possess. CHX binds to the hydroxyapatite of the enamel and dentin or the anionic groups of glycoproteins and is steadily released, prolonging its antimicrobial effects and hence accounting for its enhanced substantivity.[9]

Chemical Interaction between NaOCl and CHX

The combination of sodium hypochlorite with CHX has shown to form a reddish brown precipitate which contains parachlororaniline (PCA). Parachlororaniline is a known carcinogenic and has been found to cause methemoglobinemia in humans.[7,10] The formation of this precipitate is due to an acid–base reaction, occluding the dentinal walls with a thickness of 139–639 μm.[7] It has been reported that the higher the concentration of chlorides in the NaOCL, higher the levels of precipitate formed. The color of the precipitate formed varies according to the concentration of the NaOCL used along with CHX.[9]

Clinical Significance

This precipitate formed has been proven to occlude the dentinal tubules, as a consequence may result in the lack of penetration of intracanal medicaments and also result in poor seal of root canal obturating material. It moreover causes an undesirable color change in the crown portion of the tooth.[11]

The amount of PCA formed in the above-mentioned precipitate is directly dependent on the concentration of NaOCL used. It has been shown that if the canal has been irrigated with NaOCl first, followed by an intermediate irrigant and then irrigated with CHX as a final rinse, the precipitate formed, contains less of PCA.[11]

The use of an intermediate irrigant after irrigation with sodium hypochlorite but before irrigation with CHX has been proven to reduce the PCA present in the precipitate formed.[11]

Irrigation of the canal with large volumes of saline following irrigation with NaOCL, before final irrigation with CHX has proven to minimize the precipitate formation. The use of acetic acid had also shown dissolution of the precipitate; however, it did not remove the already established brown stain.[9]

In spite of the fact of precipitate formation on combining sodium hypochlorite and chlorhexidine, the antimicrobial effect of this combination, has been shown to better than that of any other combinations.[12]

Interactions of Sodium Hypochlorite with Alexidine

Alexidine, just like chlorhexidine is a biguanide.[13] Recently, Alexidine dihydrochloride has been proposed as a potential alternative to 2% chlorhexidine digluconate as an irrigating solution, as it possesses similar substantivity, antimicrobial

properties, and unlike chlorhexidine, Alexidine does not produce p-chloroaniline when mixed with sodium hypochlorite.[14]

Chemical Interactions between NaOCl and Alexidine

The reactive products of the interaction of sodium hypochlorite and alexidine, are yet being studied. Studies using ultrahigh performance liquid chromatography–mass spectrometry revealed that a yellowish precipitate was formed during this interaction. Moreover, this interaction resulted in the formation of aliphatic amines. Breaking bonds in the ALX chain or dehydrogenation caused by NaOCl leads to the formation of these amines.[14]

Clinical Significance

Earlier researches conducted to compare the efficacy of ALX alone as an irrigant and its efficacy in combination with NaOCl showed that ALX alone is a less effective irrigant, while when combined with NaOCl, its efficacy was similar to that of the CHX and NaOCl combination. It was also proved that the combination of ALX and NaOCl had a good potential of eliminating biofilms during endodontic procedures.[15]

It has been confirmed that the precipitate formed during the interaction of ALX and NaOCl is similar to that formed during interaction of CHX and NaOCl with the only difference that it does not contain PCA, however contains certain other harmful products and hence it is suggested that ALX and NaOCL should not be combined as per endodontic protocol.[14]

Another major clinical relevance of the precipitate formed during this reaction is that the observed color change is associated with tooth staining. It is found to stain the dentin and also remains as a residual film which is difficult to remove from the root canal.[13]

Sodium Hypochlorite and EDTA

Despite its great antimicrobial effect, sodium hypochlorite is ineffective in the removal of smear layer and therefore has to be used along with a chelator such as ethylenediaminetetraacetic acid (EDTA).[1] EDTA was invented in the mid-1930s in Germany. Usually, EDTA is used in the concentration of 17% in endodontics and is capable of removing the smear layer when in direct contact with the root canal walls for less than a minute.[16]

Chelating agents are complexes of metallic ions with organic substances, which are highly stable with ringed bonds. Chelators bind and inactivate metallic ions, hence are widely in use in medicine and dentistry.[17]

Chemical Interactions between NaOCl and EDTA

In aqueous solutions of NaOCl and EDTA, the resulting pH is neutral to slightly alkaline. The interaction between NaOCl and EDTA is basically a neutralization reaction with formation of hypochlorous acid (HOCl). This results in reduced levels of chlorine gas formations. At neutral pH, HOCl predominates, which enhances the antibacterial ability of sodium hypochlorite, whereas if the pH is above 9, hypochlorite ion predominates resulting in enhanced tissue dissolving ability. Chlorine gas is mainly formed when the pH is dropped below 4.[18]

Clinical Significance

As mentioned previously, at a lower pH, there is greater decline in the free available chlorine formed by dissociation of HOCl. The main clinical implication of this loss of free available chlorine is the reduced tissue dissolving ability of NaOCl. And hence, it is suggested that these irrigants should never be used in contact.[18] Despite the reduction in the tissue dissolving capacity of NaOCl, its disinfecting capacity and EDTA's chelating ability, remain unaltered.

It is a known fact that EDTA plays an essential role in the smear layer removal in endodontic therapy. In this case, it has been stated by Goldman et al. that on irrigation of the root canal with EDTA alone, only the inorganic component of the smear layer is removed, leaving an organic layer in the tubules. Moreover, it has been demonstrated that alternating use of EDTA and NaOCl removed the organic portion of the smear layer as well.[19]

Furthermore, NaOCl has certain oxidizing properties that reduce the chemical activity of EDTA. This limits the progressive demineralization and prevents weakening of the inorganic structure of the tooth.[19]

Even though this combination has its own adverse effects, it has been proven that the combination of NaOCl and EDTA increases the beneficial effect of the chelating agent.[20]

Sodium Hypochlorite and Citric Acid

Citric acid is a tricarboxylic acid, capable of removing the smear layer when combined with NaOCl. It is available in the range of concentrations from 1 to 40%. Due to the toxicity of EDTA, alternative biocompatible irrigants are being looked for in order to remove the inorganic components of the smear layer.[21]

Chemical Interactions of Sodium Hypochlorite and Citric Acid

When NaOCl and citric acid are mixed, the pH is considerably lower than that resulted when combining NaOCl and EDTA. It has been demonstrated that a 1:1 mixture of 2.5% NaOCl and 10% citric acid has pH of 3. The low pH levels favor chlorine gas formation.[18]

Clinical Significance

The major clinical implication of this chlorine formation and depletion of free available chlorine is that mixtures of NaOCl and citric acid lose their ability to dissolve organic tissue.[18]

The interactions between NaOCl and citric acid also demineralize the intertubular dentin, thus opening the dentinal tubules.[21]

And hence, even though, citric acid in combination with sodium hypochlorite does maintain its chelation and antimicrobial action, because of the decrease in tissue dissolving capacity, they should not be present together in root canal therapy, either sequentially or in admixed form.[18]

Octenidine and Sodium Hypochlorite

Octenidine is not just an antimicrobial and antibiofilm agent, but also has been proved to be a promising root canal irrigant in endodontic treatment.[22] In a study conducted to compare the effectiveness of octenidine with CHX as a root canal irrigant, it was demonstrated that octenidine was more effective than chlorhexidine for prolonged bacterial antiadhesive property.[23]

Interactions between Octenidine and NaOCl

When a study was conducted to detect the interactions of combining 5.2% sodium hypochlorite with octenidine by nuclear magnetic resonance (NMR) and mass spectroscopy (MS) analysis, it was found that a whitish precipitate was formed, which corresponded with the structure of phenoxyethanol (PE).[22]

Clinical Significance

PE has been proven to be effective against oral bacterial and subgingival plaque, hence this interaction or combination is encouraged in endodontic therapy. It moreover acts synergistically with various other antimicrobial agents.[22]

In contrast, PE was proved to partly occlude the dentinal tubules and therefore it hinders sealer penetration during obturation. This PE can be easily washed away by passive ultrasonic irrigation.[22]

Although octenidine (OCT) has significant antimicrobial property, additional studies will be needed to investigate its safety, biocompatibility and absence of unfavorable cosmetic and organoleptic properties.

Etidronate and Sodium Hypochlorite: Various Interactions

Hydroxyethylidine bisphosphonate (also known as Etidronate or Etidronic acid) has been recently used as a root canal irrigant. It has been suggested as a substitute for other chelators used in endodontic therapy, as it has fewer effects on the dentin structure.[24]

Apart from its use as a root canal irrigant, it is a substance known to reduce bone resorption and is used systemically in patients suffering from osteoporosis and Paget's disease.[24]

Chemical Interactions between NaOCl and Etidronate

When compared with the combination of NaOCl with EDTA or citric acid, free available chlorine is lost at a slower rate when sodium hypochlorite is combined with Etidronate. It has been demonstrated that a 1:1 mixture of 1% NaOCl: 9% etidronate maintains all its free available chlorine at 1 minute, declines to 80% after 1 hour, and then to 20% after 24 hours.[18]

Clinical Significance

The most significant clinical implication of this combination is that, with the maintenance of higher pH and free available chlorine levels, a therapeutic window of 1 hour exists, with a good level of organic tissue dissolution within this timeframe.[18]

As mentioned earlier, combining EDTA and NaOCl can affect the tissue dissolving capability of sodium hypochlorite, and hence, hydroxyethylidene bisphosphonate (HEBP) is used as an alternative chelating agent due to its alkalinity and does not produce any significant effect on combination with sodium hypochlorite.[18]

Moreover, a study conducted to determine the effectiveness of combining sodium hypochlorite with HEBP has shown that hard tissue debris accumulation during rotary instrumentation of root canal is greatly reduced.[25]

Interactions between Sodium Hypochlorite and MTAD

MTAD was introduced in the year 2003 by Torabinejad and Johnson as a mixture of a broad-spectrum antibiotic, that is, 3% Doxycycline, 4.25% citric acid, which is a demineralizing agent and a detergent Tween 80. MTAD has been proved to be quite effective as an irrigant and it is biocompatible. Recently, it has been reported that MTAD has great smear layer removal properties in comparison with the smear layer removing properties of EDTA and sodium hypochlorite.[26]

Chemical Interactions between NaOCl and MTAD

The reaction between NaOCl and MTAD is basically a redox reaction.[27]

Interestingly, it has been found that, when MTAD was used initially for irrigation followed by 5.25% NaOCl, a chemical reaction took place which resulted in the formation of a brownish solution in the canals. It was also found that addition of MTAD to NaOCl resulted in the formation of a yellow precipitate instantly. This precipitate slowly changed color from yellow to orange-yellow and then later formed a red color. This was stated to be an exothermic reaction.[27]

Clinical Significance

In a study conducted to determine the staining of endodontically treated teeth after irrigation with sodium hypochlorite and MTAD containing tetracycline, red purple staining of the light exposed dentin was noticed after irrigation with 1.3% NaOCl followed by use of MTAD for final irrigation.[27]

As a solution for this problem of staining of coronal dentin, it has been reported that an initial addition of 10% ascorbic acid for neutralizing the oxidizing effect of NaOCl and EDTA did not result in staining of the tooth.[27]

It has also been proved that the structure of the dentinal tubules was not altered after MTAD was used for smear layer removal following irrigation with NaOCl.[28]

Sodium Hypochlorite and QMiX

QMiX is one of the recently used irrigants in endodontics, which basically is composed of CHX, EDTA and a detergent. Certain studies conducted have shown that the combination of EDTA and CHX resulted in the formation of a white precipitate. QMiX has a certain chemical design that prevents the formation of this precipitate. QMiX is a ready-made solution with no requirement of chair-side mixing. In addition to that, a recent study has revealed that, QMiX is as effective as 9% NaOCl in eliminating *E. faecalis* in dentinal tubules.[29]

Reactions between QMiX and NaOCl

In a study conducted using time of flight secondary ion mass spectrometry (TOF-SIMS) analysis which is usually used in surface chemistry, the chemical interaction between QMiX and sodium hypochlorite resulted in no precipitate formation on the surface level of dentinal tubules. No color change was also observed during irrigation with sodium hypochlorite followed by QMiX.[29]

Clinical Significance

Due to the fact that a PCA containing precipitate is not formed during this interaction, the potential toxicity of PCA is avoided, this combination has an added up advantage. Nevertheless, just for the purpose of precaution, it is recommended to perform a saline irrigation after sodium hypochlorite and before irrigation using QMiX.[29]

Interactions of Sodium Hypochlorite with Natural Root Canal Irrigants

According to a recent study, a number of natural plant extracts have been found to be effective in dental treatment and this has been termed as phytotherapeutics or ethnopharmacology. *Triphala*,

honey, *neem* leaf extract, *tulsi*, and apple cider vinegar are some of the naturally used products in root canal treatment.[30]

Triphala is an ayurvedic herbal composition consisting mainly of tannic acid and three medicinal plant components*; Terminalia bellerica*, *Terminalia chebula*, and *Emblica officinalis*. *Triphala* has an advantage of great substantivity, absence of microbial resistance and minimal toxicity.[31]

An initial rinse of the root canal with 5.25% NaOCl followed by a final rinse of the canal with *triphala* solution was found to be very effective in smear layer removal almost as equivalent as rinsing the canal with NaOCl and EDTA.[31]

Conclusion

The combination of sodium hypochlorite with various root canal irrigants has resulted in the formation of precipitates in certain cases and color changes in others. The consequence of most precipitate formation is the occluding of dentinal tubules resulting in prevention of sealer penetration during the process of obturation. The color changes have mostly resulted in staining of the tooth structure, as in the case of interaction between NaOCl and MTAD. Apart from these negative consequences, certain combinations have been proved to have beneficial effects, such as more efficient smear layer removal with the combination of NaOCl and EDTA.

As mentioned earlier, no ideal irrigant exists for eradicating all the microorganisms present in the root canal, and hence we prefer combining various irrigants during the root canal procedure.

Proper irrigation with mechanical instrumentation of the root canal helps us in achieving a biofilm-free environment in the root canal.

Every combination of root canal irrigants have their own beneficial and adverse effects, and an ideal combination of root canal irrigants is yet to be discovered.

Supplementary Materials

All the supplementary materials are available online on the website of https://www.jodend.com/.

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References

1. Mohammadi Z, Shalavi S, Moeintaghavi A, et al. A review over benefits and drawbacks of combining sodium hypochlorite with other endodontic materials. Open Dent J 2017;11:661–669. DOI: 10.2174/1874210601711010661.
2. Kaur P. Role of irrigants in endodontics. J Dent Probl Solut 2020;7: 100–104. DOI: 10.17352/2394-8418.000093.
3. Haapasalo M, Shen Y, Wang Z, Gao Y. Irrigation in endodontics. Br Dent J 2014;216:299–303. DOI: 10.1038/sj.bdj.2014.204.
4. Kandaswamy D, Venkateshbabu N. Root canal irrigants. J Conserve Dent 2010;13:256–264. DOI: 10.4103/0972-0707.73378.
5. Shenoy A, Bolla N, Sayish, et al. Assessment of precipitate formation on interaction of irrigants used in different combinations: An in vitro study. Indian J Dent Res 2013;24:451–455. DOI: 10.4103/0970-9290.118392.
6. Almfudi M. The chemical interactions between endodontic irrigants: A literature review. University of Lisbon: 2019, pp. 1–32.
7. Siddique R, Sureshbabu NM, Somasundaram J, et al. Qualitative and quantitative analysis of precipitate formation following interaction of chlorhexidine with sodium hypochlorite, neem, and tulsi. J Conserv Dent 2019;22:40–47. DOI: 10.4103/JCD.JCD_284_18.
8. Gomes BP, Vianna ME, Zaia AA, et al. Chlorhexidine in endodontics. Braz Dent J 2013;24:89–102. DOI: 10.1590/0103-6440201302188.
9. Bernardi A, Teixeira CS. The properties of chlorhexidine and undesired effects of its use in endodontics. Quintessence Int 2015;46:575–582. PMID: 25918757.
10. Orhan EO, Irmak Ö, Hür D, et al. Does para-chloroaniline really form after mixing sodium hypochlorite and chlorhexidine? J Endod 2016;42:455–459. DOI: 10.1016/j.joen.2015.12.024.
11. Mortenson D, Sadilek M, Flake NM, et al. 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;45:878–882. DOI: 10.1111/j.1365-2591.2012.02048.x.
12. Krishnamurthy S, Sudhakaran S. Evaluation and prevention of the precipitate formed on interaction between sodium hypochlorite and chlorhexidine. J Endod 2010;36:1154–1157. DOI: 10.1016/j.joen.2010.01.012.
13. Jain K, Agarwal P, Jain S, et al. Alexidine versus chlorhexidine for endodontic irrigation with sodium hypochlorite. Eur J Dent 2018;12:398–402. DOI: 10.4103/ejd.ejd_180_17.
14. Czopik B, Ciechomska M, Zarzecka J, et al. Insight into the reaction of alexidine with sodium hypochlorite: A potential error in endodontic treatment. Molecules 2021;26:1623. DOI: 10.3390/molecules26061623.
15. da Silva TM, Alves FR, Lutterbach MT, et al. Comparison of antibacterial activity of alexidine alone or as a final irrigant with sodium hypochlorite and chlorhexidine. BDJ Open 2018;4:18003. DOI: 10.1038/bdjopen.2018.3.
16. Doumani M, HabibA, Doumani A.et al. A review: The applications of EDTA in endodontics (Part I). IOSR-JDMS.2017;9:83–85. DOI: 10.9790/0853-1609058385.
17. Hülsmann M, Heckendorff M, Lennon A. Chelating agents in root canal treatment: Mode of action and indications for their use. Int Endod J 2003;36:810–830. DOI: 10.1111/j.1365-2591.2003.00754.x
18. Wright PP, Kahler B, Walsh LJ. Alkaline sodium hypochlorite irrigant and its chemical interactions. Materials (Basel) 2017;10:1147. DOI: 10.3390/ma10101147.
19. Grande NM, Plotino G, Falanga A, et al. Interaction between EDTA and sodium hypochlorite: A nuclear magnetic resonance analysis. J Endod 2006;32:460–464. DOI: 10.1016/j.joen.2005.08.007.
20. Zaparolli D, Saquy PC, Cruz-Filho AM. Effect of sodium hypochlorite and EDTA irrigation, individually and in alternation, on dentin microhardness at the furcation area of mandibular molars. Braz Dent J 2012;23:654–658. DOI: 10.1590/s0103-64402012000600005.
21. Hardhitari R, Kamizar, Sumawinata N. Effects of 2.625% NaOCl - 20% citric acid and 2.625% NaOCl - 17% EDTA on cleanliness of smear layer on apical one third. J Phys Conf Ser.2018;1073:62023. DOI: 10.1088/1742-6596/1073/6/062023.
22. Thaha KA, Varma RL, Nair MG, et al. Interaction between octenidine-based solution and sodium hypochlorite: A mass spectroscopy, proton nuclear magnetic resonance, and scanning electron microscopy-based observational study. J Endod 2017;43:135–140. DOI: 10.1016/j.joen.2016.09.015.
23. Makkar S, Aggarwal A, Pasricha S, et al. Comparative evaluation of octenidine hydrochloride and chlorhexidine as antibacterial root canal irrigant. Indian J Oral Sci 2015;6:10–13.
24. Tartari T, de Almeida Rodrigues Silva E Souza P, Vila Nova de Almeida B, et al. A new weak chelator in endodontics: Effects of different irrigation regimens with etidronate on root dentin microhardness. Int J Dent 2013; 2013:743018. DOI: 10.1155/2013/743018.
25. Niyas FM, Subbarao C. Effectiveness of sodium hypochlorite and etidronic acid in combination as a root canal irrigant with varying

apical file sizes – an in vitro analyses. J Pharm Sci and Res 2017;5: 716–718. Corpus ID: 212575074.
26. Singla MG, Garg A, Gupta S. MTAD in endodontics: An update review. DOI: 10.1016/j.tripleo.2011.02.015.
27. Tay FR, Mazzoni A, Pashley DH, et al. Potential iatrogenic tetracycline staining of endodontically treated teeth via NaOCl/MTAD irrigation: A preliminary report. J Endod 2006;32:354–358. DOI: 10.1016/j.joen.2005.11.006.
28. Kolosowski KP, Sodhi RN, Kishen A, et al. Qualitative analysis of precipitate formation on the surface and in the tubules of dentin irrigated with sodium hypochlorite and a final rinse of chlorhexidine or QMiX. J Endod 2014;40(12):2036–2040. DOI: 10.1016/j.joen.2014.08.017.
29. Stojicic S, Shen Y, Qian W, et al. Antibacterial and smear layer removal ability of a novel irrigant, QMiX. Int Endod J 2012;45:363–371. DOI: 10.1111/j.1365-2591.2011.01985.x.
30. Sundaram D, Narayanan RK, Vadakkepurayil K. A comparative evaluation on antimicrobial effect of honey, neem leaf extract and sodium hypochlorite as intracanal irrigant: An ex-vivo study. J Clin Diagn Res 2016;10:88–91. DOI: 10.7860/JCDR/2016/19268.8311.
31. Susan AC, Bharathraj AR, Praveen M, et al. Intraradicular smear removal efficacy of triphala as a final rinse solution in curved canals: A scanning electron microscope study. J Pharm Bioallied Sci 2019;11:420–428. DOI: 10.4103/JPBS.JPBS_55_19.