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Inhibition of Root Canal Medicaments by Dentin and Its Implication

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Abstract

Disinfection of root canal using root canal medicaments is considered to be an essential step for a successful endodontic treatment. Ideal requisite of intracanal madicaments is the disinfection of the root canal and rendering it free of bacteria without causing harm to the tooth and oral tissues. Most commonly used intracanal medicaments are calcium hydroxide, chlorhexidine and iodine potassium iodide. Sodium chloride is not preferred as a medicament due to its property of irritating the surrounding tissues. Dentin has an inherent inhibiting effect on intracanal medicaments as it has the buffering effect which tends to neutralise the pH of the medicaments rendering them with decreased antibacterial property. The antibacterial effect of a medicament indicates its level of action. More the antibacterial action, less the dentinal inhibition. A review of scientific literature was done using databases such as pubmed, google scholar, MESH and so on. The time frame of the articles taken is between 2000 to 2020. The results are based on previous studies done on this topic. Newer methods such as bioactive glass, photon induced acoustic streaming and gentlewave system were introduced to overcome this discrepancy in disinfecting the root canal. Even though the success rates of endodontic treatments are high, it can be improved by researching and using newer and better materials for elimination of bacteria. Thus, in this review we have analysed the relation between root canal medicaments and their inhibition by dentin.

Keywords: *Root Canal Medicaments; Chlorhexidine; Calcium Hydroxide; Iodine Potassium Iodide; Inhibition; Enterococcus Faecalis; Antibacterial Property.*

Introduction

Success or failure of an endodontic treatment depends on many factors. One of the most important prerequisites is the disinfection of the root canal and rendering it free of bacteria. One of the common etiologies of periapical diseases is the invasion of the infected root canal by bacteria which can be the result of periapical inflammation which is also caused by bacterial infection[1]. Disinfection of the root canal using medicaments is considered to be an essential step for a successful endodontic treatment. In the modern days however, shaping and cleaning is preferred more as a means of disinfection[2]. But, cleaning and shaping, use of rotary and hand instrumentation, alone is not enough in cases of severe infections and in root canals with complex anatomies[3]. Instrumentation of canals with such anatomy, such as, oval shaped canals, can lead to buccal and lingual recesses or extensions which serves as a collection point for necrotic debris and biofilms[4–7]. This can lead to the failure of the treatment and recurrent infections[8,9]. Further disinfection after instrumentation is required in order to increase the success of the endodontic treatment. Usage of phenols and its derivatives and compounds of formaldehyde and formocresol, previously preferred, are now not used due to their action as irritants[10]. Formocresol is also said to lead to brain injury by anaphylactic shock. Biocompatibility and stability are properties important for root canal medicaments. The long acting activity and stability of calcium hydroxide has made it one of the most widely used medicaments. For a root canal treatment, a single visit treatment is considered advantageous over multiple visits[11]. In case of multiple visit treatment, calcium hydroxide is the most preferred medicament. Root canal medicaments act by disinfecting the root canal and rendering it clean and free of bacteria and infected

tissues[12,13]. The antibacterial effects of medicaments can be analysed by their action against microorganisms such as Enterococcus faecalis and Candida albicans. The more the antibacterial action, the lesser is the dentinal inhibition. Some of the most commonly used root canal medicaments are calcium hydroxide, chlorhexidine and iodine potassium iodide[14].

Chlorhexidine is widely used as an irrigant and disinfectant and is mainly available in form of salts[15]. The original salts were CHX acetate and CHX hydrochloride. Both were replaced with CHX digluconate due to their insufficient solubility in water. CHX is a cationic molecule with a pH of 5.5 - 7[16]. It has a central hexamethylene chain which connects two biguanide groups and has two symmetric 4-chlorophenyl rings in the sides. It acts better against gram positive bacteria than gram negative bacteria[17]. The bacterial cell wall is destroyed by the attachment of CHX to the surface of the bacteria rendering it permeable. The subsequent entering of the medicament into the bacteria causes the precipitation of the cytoplasm damaging the self repair mechanism. The function is usually bacteriostatic. Chlorhexidine was found to be inhibited by dentine powder Invitro. However, at higher concentrations, the effect of inhibition was not observed[18].

Calcium hydroxide is the most commonly used root canal medicament. It has a high ph, 12.5 to 12.8, and has less solubility in water compared to tissue fluids[19]. It is not soluble in alcohol. When in the oral cavity, calcium hydroxide gets soluble in the tissue fluids on direct contact with the tissues. Calcium hydroxide exerts antimicrobial action by direct contact and high pH. It creates an alkaline environment which is not not suitable for microorganisms by release and diffusion of hydroxyl ions[20]. However, the rate of diffusion is slow due to the inhibitive and buffering action of the dentin. Some microorganisms are not susceptible to the action of calcium hydroxide. These include Enterococcus faecalis and Candida albicans[21]. CHX is usually used in combination with calcium hydroxide to improve its antimicrobial property[22]. Calcium hydroxide is inhibited in the dentin by the buffering action of dentin which neutralises the pH and reduces the antibacterial property[23].

Iodine potassium iodide (IKI) when used as a 2% solution, acts as a root canal disinfectant. When compared to sodium hydroxide, which is not used as a disinfectant much these days die to their bad odour, taste, cytotoxicity, damaging effect on dentin, harmful effects on the mechanical properties of nickel titanium instruments and its negative effect on the bond strength of bonding system, IKI has a pleasant odour, taste and lower toxicity[24]. IKI can penetrate deep until 1000 μm when irrigated in dentin for 5 minutes. It has rapid microbial activity against Enterococcus faecalis, Streptococcus sanguis, Fusobacterium, Pseudomonas aeruginosa, Bacillus subtilis, Escherichia coli, Staphylococcus aureus and Candida albicans[25]. It is generally used in concentrations ranging from 1% to 5% with the minimum active concentration of IKI being 1%. IKI also shows less toxicity and tissue irritation than chlorhexidine, camphorated monoparachlorhenol, formocresol and sodium hypochlorite. Combination of IKI with calcium hypochlorite tends to increase its antimicrobial properties[26]. The mechanism of action of IKI has not been clearly understood. The level of inhibition of dentin is dependent on the concentration of the medicament. However, IKI showed high antimicrobial properties in both high and low concentrations[27]. But, at diluted concentrations of 0.2% - 0.4%, the dentin exhibited strong inhibitory effect and if IKI is preincubated in dentin for 1 hour, the bactericidal effect was completely abolished. It is a possibility that dentin has limited capacity to inactivate IKI and a solution of stronger concentration remained viable and killed the bacteria in 5 minutes. In previous studies, the rapid loss of antibacterial activity has also been noted[28].

Finally, this review is aimed at assessing the inactivation of root canal medicaments by dentin and its implications.

Materials and Methods

A review of scientific literature was done in preparation of the manuscript. The relevant articles were collected from databases such as pubmed, google scholar, MESH etc. The Time frame of the articles are between the year 2000 to 2020. Around 25 articles were collected, analysed and reviewed. The articles were collected on the basis of containing keywords such as

root canal medicaments, inactivation, antimicrobial properties, dentin powder etc. All topics irrelevant to the subject are excluded. The results of this review are based on previous studies done by other esteemed authors.

INHIBITIVE AND BUFFERING ACTION OF DENTIN:

Calcium hydroxide is one of the main medicaments which displays its antimicrobial activity due to its high pH. A few earlier studies indicate that Enterococcus faecalis may survive in the root canal disinfected by calcium hydroxide, due to the buffering mechanism of dentin[29]. This action of dentin is against the pH rise by alkaline medicaments. The mechanism of action of calcium hydroxide medicaments is the ability of the medicament to dissociate and release calcium and hydroxyl ions which leads to increase in pH and ultimately results in bacterial cell toxicity[30]. However the dentinal structure has a buffering effect which causes pH variations and reduces the antimicrobial action of calcium hydroxide in the root canal. Such interaction between alkaline medicaments and dentine leads to negative impact on their performance and impaired disinfection of the canal[31]. In a previous study, it was observed that invitro inhibition of root canal medicaments such as calcium hydroxide was observed when the medicament was incubated with dentin taken from the canal walls as it reduced the pH significantly. On the other hand, dentin taken from the pulp chamber floor did not play such an active role of inhibiting the alkaline medicaments[32]. A 1.8% dentine powder prevented the eradication of Enterococcus faecalis by saturated calcium hydroxide solution.

TIME DEPENDENT INHIBITION OF MEDICAMENTS BY DENTIN:

It is a generalised opinion that medicaments tend to get inhibited and use their activity in the root canal environment. The inhibitory effect of dentin on calcium hydroxide due to its buffering action is seen to decrease with time[33]. In previous studies it was seen that the pH of the dentin located in the root canal was seen to increase from 6.2 to 7.4 in about 1 hour of placement and increased upto 10.8 within 24 hours of placement of the medicament[34]. The antibacterial property of calcium hydroxide is mainly mediated by the release of hydroxide ions into the surrounding aqueous environment and the rate of such ionic dissociation tends to increased time[35–38]. The synergistic effect of the hydroxide ions and iodoform aids in overcoming the buffering activity of the dentin leading to the rise in pH[39].

INHIBITION OF IODINE POTASSIUM IODINE AND CHLORHEXIDINE DIGLUCONATE BY DENTIN:

The most effective inhibitors of chlorhexidine digluconate were seen to be dentin matrix and heat killed microbial cells[40]. Dentin which is pretreated with citric acid or EDTA tended to display only a slight inhibition of the medicament[41]. Similar to calcium hydroxide, while dentin displays inhibition of the medicament within 1 hour of administration, the level of inhibition decreases with time and no inhibition is seen at 24 hours of application of the disinfectant. IKI can also be inhibited by dentin, dentinal matrix and heat killed microbial cells and application of EDTA to dentin lead to little or no inhibitory effect[42]. IKI is a strong medicament and does not get inhibited at high and medium concentrations[43,44]. Different components of the dentin are responsible for inhibition in divergent patterns of the antibacterial activity of chlorhexidine digluconate and potassium iodide. Inorder to lessen the inhibitory effect, it is better to chemically heat dentin before application of medicaments[45].

ASSESSING THE ERADICATION OF *Enterococcus faecalis* BY MEDICAMENTS IN PRESENCE OF DENTIN:

In most medicaments, the inhibitory effect of dentin would not be observable at a higher concentration[46]. Calcium hydroxide tends to completely lose activity against Enterococcus faecalis in presence of dentin[47]. Presence of dentin induces a strong inhibitory effect on diluted iodine potassium iodide whereas a stronger solution of IKI displayed reduced activity against Enterococcus faecalis[48]. While chlorhexidine digluconate showed reduced activity against dentin initially, extended incubation, upto 24 hours, leads to loss of 99% viability of bacteria. Sodium hypochlorite also displays inhibition by dentine and is also not much preferred as a disinfecting agent[11].

NEWER METHODS OF ROOT CANAL DISINFECTION:

Newer and better methods of root canal disinfection are developed in order to get better results[49]. Bioactive glass can be used as an alternative to calcium hydroxide[50]. Bioactive glass which contains silicon dioxide, sodium oxide, calcium oxide and phosphorus pentoxide has a superior disinfecting effect. It does not irritate or affect dentin and can induce dentin mineralisation[51]. It is also used as an intracanal dressing. The antibacterial effect of bioglass increases when mixed with dentin unlike other medicaments which get inhibited[52,53]. Chitosan nanoparticles act synergistically with chlorhexidine inorder to eliminate qmore number of colony forming units[54]. Photon induced acoustic streaming of antibacterial fluid within the canal by creating successive shockwaves[55]. Another system known as Gentlewave system aids in cleaning the root canal by generation of various broad spectrum sound waves through different physical, chemical and biological mechanisms[56].

Limitations:

Even though studies have been made to analyse the inhibition of medicaments by dentine, no adequate quantitative data is available. Since disinfection is a technique which has been used for a longer time, dental practitioners are skeptical to try newer products. The mechanism of action and inhibition of some medicaments are not yet available and have to be researched upon.

FUTURE SCOPE:

Further research can aid in discovery of newer products with better properties and functions. Usage of newer techniques can create better treatment plans and treatment success rates. Since disinfectants are commonly used materials for endodontic procedures, ways to overcome inhibition can go a long way for success of the treatment in the long run. Awareness must be created among dentists about the availability of newer products that can help expand their horizons and aid in doing better clinical treatments.

Conclusion

The success rates of endodontic treatments are high and can be improved by using newer and better materials for elimination of bacteria. Consideration of the medicament's therapeutic action and level of inhibition based on the type of treatment is crucial. Newer materials can be researched upon as many of the commercial preparations fail to fulfil the requirements for an ideal root canal medicament. Thus, we have analysed the relation between root canal medicaments and their inhibition by dentin.

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References

1. Portenier I, Haapasalo H, Rye A, Waltimo T, Ørstavik D, Haapasalo M. Inactivation of root canal medicaments by dentine, hydroxylapatite and bovine serum albumin. Int Endod J. 2001 Apr;34(3):184–8.
2. Kawashima N, Wadachi R, Suda H, Yeng T, Parashos P. Root canal medicaments. Int Dent J. 2009 Feb;59(1):5–11.
3. Ragul P, Dhanraj M, Jain AR. Irrigation technique used in cleaning and shaping during endodontic treatment-A review. Drug Invention Today [Internet]. 2018;10(5). Available from: https://www.researchgate.net/profile/Ashish_Jain52/publication/326030915_Irrigation_technique_used_in_cleaning_and_shaping_during_endodontic_treatment_-_A_review/links/5b3e266d0f7e9b0df5f4db7d/Irrigation-technique-used-in-cleaning-and-shaping-during-endodontic-treatment-A-review.pdf
4. Ramamoorthi S, Nivedhitha MS, Divyanand MJ. Comparative evaluation of postoperative pain after using endodontic needle and EndoActivator during root canal irrigation: A randomised controlled trial [Internet]. Vol. 41, Australian Endodontic Journal. 2015. p. 78–87. Available from: http://dx.doi.org/10.1111/aej.12076
5. Ramanathan S, Solete P. Cone-beam Computed Tomography Evaluation of Root Canal Preparation using Various Rotary Instruments: An in vitro Study. J Contemp Dent Pract. 2015 Nov 1;16(11):869–72.

6. Kumar D, Antony S. Calcified Canal and Negotiation-A Review. Research Journal of Pharmacy and Technology. 2018;11(8):3727–30.
7. Teja KV, Ramesh S. Shape optimal and clean more. Saudi Endodontic Journal. 2019 Sep 1;9(3):235.
8. Alves FRF, Almeida BM, Neves MAS, Moreno JO, Rôças IN, Siqueira JF Jr. Disinfecting oval-shaped root canals: effectiveness of different supplementary approaches. J Endod. 2011 Apr;37(4):496–501.
9. Wu M-K, van der Sluis LWM, Wesselink PR. The capability of two hand instrumentation techniques to remove the inner layer of dentine in oval canals. Int Endod J. 2003 Mar;36(3):218–24.
10. Peters OA, Peters CI, Basrani B. Cleaning and shaping of the root canal system. Pathways of the Pulp. 2006;9:290–357.
11. Sathyaprasad S, Jose BK, Chandra HS. Antimicrobial and antifungal efficacy of Spilanthes acmella as an intracanal medicament in comparison to calcium hydroxide: An in vitro study. Indian J Dent Res. 2015 Sep;26(5):528–32.
12. Manohar M, Sharma S. A survey of the knowledge, attitude, and awareness about the principal choice of intracanal medicaments among the general dental practitioners and nonendodontic specialists [Internet]. Vol. 29, Indian Journal of Dental Research. 2018. p. 716. Available from: http://dx.doi.org/10.4103/ijdr.ijdr_716_16
13. Nandakumar M, Nasim I. Comparative evaluation of grape seed and cranberry extracts in preventing enamel erosion: An optical emission spectrometric analysis. J Conserv Dent. 2018 Sep;21(5):516–20.
14. Jaju S, Jaju PP. Newer root canal irrigants in horizon: a review. Int J Dent. 2011 Nov 30;2011:851359.
15. Kanisavaran ZM. Chlorhexidine gluconate in endodontics: an update review. Int Dent J. 2008 Oct;58(5):247–57.
16. Basrani BR, Manek S, Sodhi RNS, Fillery E, Manzur A. Interaction between sodium hypochlorite and chlorhexidine gluconate. J Endod. 2007 Aug;33(8):966–9.
17. Portenier I, Haapasalo H, Ørstavik D, Yamauchi M. Inactivation of the antibacterial activity of iodine potassium iodide and chlorhexidine digluconate against Enterococcus faecalis by dentin, dentin matrix, type-I collagen …. Journal of [Internet]. 2002; Available from: https://www.sciencedirect.com/science/article/pii/S0099239905604487
18. Taur S, Sugandhan S, Prabhakar AR, Hadakar S. Comparison of Antibacterial Efficacy of Calcium Hydroxide Paste, 2% Chlorhexidine Gel and Turmeric Extract as an Intracanal Medicament and their Effect on Microhardness of Root Dentin: An in vitro Study [Internet]. Vol. 6, International Journal of Clinical Pediatric Dentistry. 2013. p. 171–7. Available from: http://dx.doi.org/10.5005/jp-journals-10005-1213
19. Tang G, Samaranayake LP, Yip H-K. Molecular evaluation of residual endodontic microorganisms after instrumentation, irrigation and medication with either calcium hydroxide or Septomixine. Oral Dis. 2004 Nov;10(6):389–97.
20. Athanassiadis B, Abbott PV, Walsh LJ. The use of calcium hydroxide, antibiotics and biocides as antimicrobial medicaments in endodontics. Aust Dent J. 2007 Mar;52(1 Suppl):S64–82.
21. Pacios MG, Silva C, López ME, Cecilia M. Antibacterial action of calcium hydroxide vehicles and calcium hydroxide pastes [Internet]. Vol. 3, Journal of Investigative and Clinical Dentistry. 2012. p. 264–70. Available from: http://dx.doi.org/10.1111/j.2041-1626.2012.00147.x
22. Gomes BPF de A, Ferraz CCR, Vianna ME, Rosalen PL, Zaia AA, Teixeira FB, et al. In vitro antimicrobial activity of calcium hydroxide pastes and their vehicles against selected microorganisms. Braz Dent J. 2002;13(3):155–61.
23. Cavalcanti A, Limeira FR, Sales ELS, Oliveira AG, Lima DB, Castro R. In vitro antimicrobial activity of root canal sealers and calcium hydroxide paste [Internet]. Vol. 1, Contemporary Clinical Dentistry. 2010. p. 164. Available from: http://dx.doi.org/10.4103/0976-237x.72784
24. Hülsmann M, Hahn W. Complications during root canal irrigation–literature review and case reports. Int Endod J [Internet]. 2000; Available from: https://onlinelibrary.wiley.com/doi/abs/10.1046/j.1365-2591.2000.00303.x
25. Barnhart BD, Chuang A, Lucca JJD, Roberts S, Liewehr F, Joyce AP. An in vitro evaluation of the cytotoxicity of various endodontic irrigants

on human gingival fibroblasts. J Endod. 2005 Aug;31(8):613–5.

26. Peciuliene V, Balciuniene I, Eriksen HM, Haapasalo M. Isolation of Enterococcus faecalis in previously root-filled canals in a Lithuanian population. J Endod. 2000 Oct;26(10):593–5.
27. Erdemir A, Ari H, Gungunes H, Belli S. Effect of Medications for Root Canal Treatment on Bonding to Root Canal Dentin [Internet]. Vol. 30, Journal of Endodontics. 2004. p. 113–6. Available from: http://dx.doi.org/10.1097/00004770-200402000-00013
28. Lin S, Kfir A, Laviv A, Sela G, Fuss Z. The in vitro antibacterial effect of iodine-potassium iodide and calcium hydroxide in infected dentinal tubules at different time intervals. J Contemp Dent Pract. 2009 Mar 1;10(2):59–66.
29. Haapasalo M, Qian W, Portenier I, Waltimo T. Effects of dentin on the antimicrobial properties of endodontic medicaments. J Endod. 2007 Aug;33(8):917–25.
30. Rajakeerthi R, Ms N. Natural Product as the Storage medium for an avulsed tooth–A Systematic Review. Cumhuriyet Dental Journal [Internet]. 2019; Available from: https://dergipark.org.tr/en/pub/cumudj/issue/45584/525182
31. Semenov A. SURFACE DISINFECTION OF BOVINE DENTIN SAMPLES INFECTED WITH ESCHERICHIA COLI FOR THE ASSESSMENT OF ENDODONTIC IRRIGANTS [Internet]. 17th International Multidisciplinary Scientific GeoConference SGEM2017, Nano, Bio and Green □ Technologies for a Sustainable Future. 2017. Available from: http://dx.doi.org/10.5593/sgem2017h/63/s25.046
32. Agrafioti A, Tzimpoulas NE, Kontakiotis EG. Influence of dentin from the root canal walls and the pulp chamber floor on the pH of intracanal medicaments. J Endod. 2013 May;39(5):701–3.
33. M.r. G, Ganesh MR, Baranwal S, Chauhan N. INFLUENCE OF DIFFERENT VEHICLES ON THE ANTIBACTERIAL/ ANTIMICROBIAL EFFECTS OF CALCIUM HYDROXIDE [Internet]. Vol. 2, Journal of Evolution of Medical and Dental Sciences. 2013. p. 7598–600. Available from: http://dx.doi.org/10.14260/jemds/1346
34. Ajitha P, Rao CVN, Lakshminarayanan L. Time dependent inhibitory effect of dentin on various calcium hydroxide medicaments-An in vitro study. Endodontology. 2003;15(2):7–11.
35. Hussainy SN, Nasim I, Thomas T, Ranjan M. Clinical performance of resin-modified glass ionomer cement, flowable composite, and polyacid-modified resin composite in noncarious cervical lesions: One-year follow-up. J Conserv Dent. 2018 Sep;21(5):510–5.
36. Teja KV, Ramesh S, Priya V. Regulation of matrix metalloproteinase-3 gene expression in inflammation: A molecular study. J Conserv Dent. 2018 Nov;21(6):592–6.
37. Janani K, Palanivelu A, Sandhya R. Diagnostic accuracy of dental pulse oximeter with customized sensor holder, thermal test and electric pulp test for the evaluation of pulp vitality: an in vivo study. Brazilian Dental Science. 2020;23(1):8.
38. Jose J, P. A, Subbaiyan H. Different Treatment Modalities followed by Dental Practitioners for Ellis Class 2 Fracture – A Questionnaire-based Survey [Internet]. Vol. 14, The Open Dentistry Journal. 2020. p. 59–65. Available from: http://dx.doi.org/10.2174/1874210602014010059
39. Turkistani J, Hanno A. Recent trends in the management of dentoalveolar traumatic injuries to primary and young permanent teeth. Dent Traumatol. 2011 Feb;27(1):46–54.
40. Gunasekaran G, Geetha RV. Evaluation of the effect of Glycyrrhiza glabra as root canal disinfectant-An in vitro study. Drug Invention [Internet]. 2019; Available from: http://search.ebscohost.com/login.aspx?direct=true&profile=ehost&scope= site&authtype= crawler&jrnl= 09757619&AN=1371539

61&h=0zS2cjJ% 2 FYC OuCb7SoNFtQuqZgIC4Z Of CyhNZmKHQO17 CsOSpNMB7kg6myaq Efuc9o YJlDxC1ECjNbVQGfxj TSQ%3D%3D&crl=c

41. Manojkanna K, Chandana CS, Gayathri R, Priya VV. Evaluation of biocompatibility of irrigants used for root canal disinfection. Drug Invention Today [Internet]. 2018;10. Available from: http://search.ebscohost.com/ login.aspx? direct= true&profile= ehost&scope= site& authtype= crawler&jrnl= 09757619&AN= 133549324&h= FMiz61cFIPkYdLv Gq1J51fBRgwz CFi6ERWw8X0Yrl91 NMSbzy0Va% 2F0d3af 3Sxx0QF6KZLw0W3mK7 CyJq2P pIfw%3D%3 D&crl=c

42. Crri RK. Cytotoxicity of Root Canal Disinfecting Agents against Stem Cells of Apical Papilla--A Review. Res J Pharm Biol Chem Sci. 2017;9(11):2052–5.

43. Noor S, Others. Chlorhexidine: Its properties and effects. Research Journal of Pharmacy and Technology. 2016;9(10):1755–60.

44. Siddique R, Jayalakshmi S. Assessment of Precipitate Formation on Interaction of Chlorhexidine with Sodium Hypochlorite, Neem, Aloevera and Garlic: An in vitro Study [Internet]. Vol. 10, Indian Journal of Public Health Research & Development. 2019. p. 3648. Available from: http://dx.doi.org/10.5958/0976-5506.2019.04155.x

45. Parthasarathy P, Antony SDP. Awareness and Knowledge of Dentists about Laser Technique Used in Endodontic Disinfection. Journal of Pharmaceutical [Internet]. 2017; Available from: https://www.researchgate.net/profile/Delphine_ Priscilla_Selvanayagam/ publication/316877036_ Awareness_and_Knowledge_of_Dentists_about_ Laser_Technique_Used_in_ Endodontic_ Disinfection/links/ 59154c3ea6fdcc963e825b98/ Awareness-and- Knowledge-of- Dentists-about-Laser-Technique-Used-in-Endodontic-Disinfection.pdf

46. Neelakantan P, Subbarao C, Sharma S, Subbarao CV, Garcia-Godoy F, Gutmann JL. Effectiveness of curcumin against Enterococcus faecalis biofilm. Acta Odontol Scand. 2013 Nov;71(6):1453–7.

47. Devaraj S, Jagannathan N, Neelakantan P. Antibiofilm efficacy of photoactivated curcumin, triple and double antibiotic paste, 2% chlorhexidine and calcium hydroxide against Enterococcus fecalis in vitro. Sci Rep. 2016 Apr 21;6:24797.

48. Sivakumar NAP, Ganapathy D, Others . Awareness of triple antibiotic paste among dental students. Drug Invention Today [Internet]. 2019;12(10). Available from: http://search. ebscohost.com/login.aspx?direct=true&profile= ehost&scope= site& authtype= crawler&jrnl=09757619&AN=139446017&h= DywqSVoISwf%2 FgU0PadxMa%2 B F s T y H D v z G S 2 y y U B q 6 R w V 7 mK0Rh9p XxpcXyN%2 Ff1C6PRJLafkOUR5ClMfBFaC7bHEQ%3 D%3 D&crl=c

49. Subhashini MHR, Raj JD. Nanoparticle disinfection of root canals. pdfs. semanticscholar. org [Internet]. Available from: https://pdfs.semanticscholar.org/69a5/ 70cbfb81ac931cae746551cc1a60c2eb29cb.pdf

50. Sheik R, Nasim I. Newer root canal irrigants-A review. Research Journal of Pharmacy and Technology. 2016;9(12):1451–6.

51. Susila AV, Sugumar R, Chandana CS, Subbarao CV. Combined effects of photodynamic therapy and irrigants in disinfection of root canals. J Biophotonics. 2016 Jun;9(6):603–9.

52. Rajendran R, Kunjusankaran RN, Sandhya R, Anilkumar A, Santhosh R, Patil SR. Comparative Evaluation of Remineralizing Potential of a Paste Containing Bioactive Glass and a Topical Cream Containing Casein Phosphopeptide-Amorphous Calcium Phosphate: An in Vitro Study. Pesqui Bras Odontopediatria Clin Integr [Internet]. 2019;19. Available from: http://www.scielo.br/ scielo.php?pid= S1983-46322019000100364& script=sci_arttext

53. Ravinthar K, Jayalakshmi. Recent Advancements in Laminates and Veneers in Dentistry [Internet]. Vol. 11, Research Journal of Pharmacy and Technology. 2018. p. 785. Available from: http:// dx.doi.org/10.5958/0974-360x.2018.00148.8

54. Jayashree RS, Radhika AK. Dental laser education and knowledge among final year dental students at Saveetha dental college-A questionnaire study. Int

J Adv Res. 2015;3:556–61.

55. Korkut E, Torlak E, Gezgin O, Özer H, Şener Y. Antibacterial and smear layer removal efficacy of Er: YAG laser irradiation by photon-induced photoacoustic streaming in primary molar root canals: a preliminary study. Photomed Laser Surg. 2018;36(9):480–6.

56. Neelakantan P, Cheng CQ, Mohanraj R, Sriraman P, Subbarao C, Sharma S. Antibiofilm activity of three irrigation protocols activated by ultrasonic, diode laser or Er:YAG laser in vitro. Int Endod J. 2015 Jun;48(6):602–10.