Pharmacophore

ISSN-2229-5402



Journal home page: http://www.pharmacophorejournal.com

EVALUATION OF THE USE OF PHOTODYNAMIC THERAPY IN ENDODONTICS, LITERATURE REVIEW

Raymaa Abed G Alshareef^{1*}, Ghaidaa Ahmed Mobarki², May Mohammed Alshemaisi³, Yasser Mohammad Altkhais³, Bader Saeed Alotaibi³, Layan Saad Alshehri⁴, Lamees Annas H Zarei⁴, Aeshah Hassan S Abduljabar⁵, Farah Ahmed Alghenaim⁶, Alaa Shayem Alshammari⁷

- 1. Department of Dentistry, My Clinic Dental Center, Riyadh, KSA.
- 2. Faculty of Dentistry, Ibn Sina National College of Medicine, Jeddah, KSA.
- 3. Department of Dentistry, North of Riyadh Dental Center, Riyadh, KSA.
- 4. Faculty of Dentistry, King Abdulaziz University, Jeddah, KSA.
- 5. Faculty of Dentistry, Batterjy Medical College, Jeddah, KSA.
- 6. Faculty of Dentistry, Princess Nourah bint Abdulrahman University, Riyadh, KSA.
- 7. Department of Dentistry, Al-Wasayta Primary Health Care, Hail, KSA.

ARTICLE INFO

Received: 02 Aug 2021 Received in revised form: 24 Nov 2021 Accepted: 05 Dec 2021 Available online: 28 Dec 2021

Keywords: Photodynamic therapy, Photodynamic disinfection, Photodynamic antimicrobial chemotherapy, Endodontics

ABSTRACT

Photodynamic therapy treatment (PDT) was introduced in 1900. Uses for it in dentistry have been considered in order to decrease the infection level of the root canal system. This therapy regained popularity in the last decade due to its effectiveness in treating endodontic microbial infections, particularly because the most commonly used chemical irrigations such as chlorhexidine and sodium hypochlorite are not always 100% successful in eradicating the microbial flora in the infected root canal. Understanding of the mechanism of microbes and a total microorganism eradication from the system of the root canal. The Pubmed, Embase, NCBI, and Cochrane databases were searched for studies of photodynamic therapy and its effects in endodontic treatments. Both clinical and laboratory studies as well as *in vitro* and *in vivo* studies were analyzed. In recent years, studies that were done showed PDTs' antibacterial potential, however, most of them were unable to adequately confirm better disinfection when contrasted with regular chemomechanical formulation with NaOCI.

This is an **open-access** article distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License, which allows others to remix, tweak, and build upon the work non commercially, as long as the author is credited and the new creations are licensed under the identical terms.

To Cite This Article: Alshareef RAG, Mobarki GA, Alshemaisi MM, Altkhais YM, Alotaibi BS, Alshehri LS, et al. Evaluation of the Use of Photodynamic Therapy in Endodontics. Pharmacophore. 2021;12(6):37-42. https://doi.org/10.51847/ycTzG7tvJd

Introduction

'The light-induced inactivation of cells, microorganisms, or molecules' [1] has been used as a definition of Photodynamic therapy (PDT) [1]. PDT has been called several different names, including photodynamic antimicrobial chemotherapy (PACT), photodynamic disinfection (PD), and antimicrobial photodynamic therapy (APD) [2-4]. Multiple studies have demonstrated positive results in treating infection of the root canal. Indeed, photodynamic therapy in the treatment of microorganisms has proven to be quite useful in the treatment of periapical and pulpal infections. The quantifier of the successfulness of endodontic treatment is the relative eradication of root canal microbes [5]. However, it is an unfeasible task to perform the total eradication of microorganisms from the root canal system [6, 7].

Generally, gram-positive (G +) bacteria are the main composition of endodontic failure infections (secondary infections) that are caused by one or multiple species of bacteria. This being said, an apparent predominance of anaerobes or facultatives cannot be declared in them [8]. The microflora associated with the infected root canal is typically a mix of species with a predominance of gram-negative (G -) anaerobic rods.

This review aims to discuss Photodynamic therapy in endodontics management and how it helps in the dental industry.

Corresponding Author: Raymaa Abed G Alshareef; Department of Dentistry, My clinic Dental Center, Riyadh, KSA. E-mail: Raymaa.bds@gmail.com.

Pharmacophore, 12(6) 2021, Pages 37-42

Materials and Methods

The indicated keys were put to work in the mesh of the PubMed database for the choosing of articles (("Photodynamic therapy "[Mesh]) AND ("in endodontic management" [Mesh]) OR (Photodynamic therapy in endodontics management) Mesh])).

Article selection was based on the inclusion of certain topics that lined up with the objective as the ones that did not have the indicated key topics as their chief directive were not considered. The topics were: Photodynamic therapy in endodontics management.

Around 90 publications were chosen as the most clinically relevant out of 1,202 articles indexed in the previous two decades, and their full texts were evaluated. A total of 31 of the 90 were included after a thorough examination. Additional research and publications were found using reference lists from the recognized and linked studies. Expert consensus recommendations and commentary were added where relevant to help practicing physicians assess cirrhosis most simply and practically possible.

Results and Discussion

The consequences of microorganisms entering the root canal can range from reversible pulpitis to necrosis of the pulp, which leads to a periapical lesion [9]. Additionally, pulpal necrosis without the involvement of microorganisms does not always lead to periapical lesions [10]. When mechanical or thermal trauma occurs to the pulp, the lack of blood circulation and defense mechanisms create a welcoming environment for intruding microorganisms and the pulp doesn't stand much chance of remaining sterile for long.

A dye that has the ability to light source energy absorption and transference of this energy to another molecule is considered a photosensitizer (PS) [11]. Said photosensitizers are involved in photodynamic therapy. The most common are phenothiazine salts, used in clinical trials.

Photodynamic therapy is a two-stage treatment: the first stage involves the application of an applied PS compound to targeted tissues [12], which compound is then activated with exposure to light whose wavelengths are controlled to excite the compound. In the second step, light is emitted by a device used directly on the targeted tissue or directed to inner sites.

Photoactivated disinfection (PAD) is a therapy that consists of the contact between a light source and a photosensitive antibacterial agent. The photosensitizer generally used is a harmless dye combined with low-intensity visible light, which molecules attach to the bacteria membrane [13, 14]. In the presence of oxygen, it results in the production of certain cytotoxic species. Rupture of the microbial cell wall occurs when irradiation with a specific wavelength of light produces singlet oxygen [15, 16].

Treatment

In Oral Surgery and Periodontics, antimicrobial PDT represents a theoretical treatment alternative for peri-implantitis, postextraction pain, alveolar osteitis [17], and localized microbial periodontal infections [18-26]. It requires the use of a photosensitizer along with low-concentration laser light, together with fostering the destruction of harmful microorganisms by singlet oxygen molecules. Despite the fact that it was unsuccessful in eliminating bacteria, PDT nonetheless resulted in a significant bacterial reduction [27, 28].

Recently, PDT treatments with photosensitizing dyes combined with the usage of lasers or LEDs of different wavelengths have been explored as dental plaque removal treatments [28, 29] and to minimize dental caries that are conductive to aetiological factors [30].

The effectivity of this photodynamic approach has been seen in ridding the root canals of microorganisms both *in vitro* and *in vivo* [31]. The potential of PDT has been demonstrated by these studies alongside standard endodontic antimicrobial treatment. A wide range of irrigating and disinfecting solutions are used to help in debridement and scrubbing of the canal [32]. Indeed, complete cleaning of the root canal system cannot be achieved by mechanical instrumentation alone [33]; debridement of the endodontic space and poor disinfection, limited filling, untreated canals, and leaking of the coronal are all likely cases of post-treatment endodontic disease or failures that may cause bacteria to persist within the root canal system [34].

New methods and substances have recently been suggested to improve disinfection of the root canal, in replacement of conventional chemo-mechanical procedures or in addition to these procedures [35]. PDT was suggested as a promising addition to the clinical treatment of periapical lesions, alongside standard antimicrobial intracanal cleaning and shaping [36, 37], especially for teeth going through endodontic retreatment or treatment [35], Asnaashari *et al.* [38], Pourhajibagher *et al.* [39], Rabello *et al.* [40]. Indeed, when PDT parameters were optimized for the best photodynamic effect, colony-forming unit counts decreased by 99% in experimentally infected root canals of extracted teeth [31, 41].

Recently, positive results have been indicated in the use of PDT in root canal treatment when looked at in terms of the reduction of the bacterial load *in vivo* [40, 42-44], also *in vitro* [31, 45-47] and *ex vivo* [48].

Clinical Procedure

A non-intrusive method of treatment that involves photosensitizers, a specific wavelength of light, and the generation of reactive oxygen species (ROS) and singlet oxygen to eradicate unwanted pathogenic microorganisms is Photodynamic therapy (PDT). The highly reactive oxygen species (ROS) destroys the microorganisms.

Pharmacophore, 12(6) 2021, Pages 37-42

Viruses, fungi, and protozoa are among other microorganisms that are greatly reduced by PDT [48-50]. Additionally, toxicological tests have reported no negative side effects in the treatment with the applied photosensitizer [51].

Clinically, a PS solution flush that is done post canal preparation, is allowed to sit for approximately 60 seconds, in order for the solution to interact with the bacteria. Radiation is performed for 30 seconds on each canal, by the emitter which is placed in the root canal. This method has been clinically proven capable of killing high concentrations of the bacteria found in root canals [52]. However, it is crucial to ensure that the preparation completely floods the area; indeed, the solution must come into contact with all bacteria or the photosensitization will not be effective [53].

However, it has been mentioned by Kosarieh *et al.* [54] that irrigation lasting 2 minutes along with 17% EDTA improves photosensitizer penetration inside the dentinal tubules, possibly ensuring that the bacteria in deeper areas of the wall of the root canal are got to by the photosensitizer.

PDT is also an effective reducer of biofilm [55]. Indeed, advanced noninvasive PDT with an oxidizer/oxygen-based photosensitizer formulation disrupts the biofilm matrix and has been proven to allow the comprehensive disinfection and inactivation of endodontic biofilm that is matured [56].

According to laboratory studies performed by Nunes *et al.* [57], there is doubt concerning the necessity of light delivery as it does not drastically affect the antimicrobial action of PDT. It should therefore be effective with or without an intracanal fiber. Additionally, according to Pinheiro *et al.* [58], it appears there is also doubt concerning penetration depth of the fiber; indeed, PDT was administered before and after instrumentation and similar values were reported. This study also reports that when the canal's complete length is not penetrated by the probe, it prevents the removal of apical microbial pathogens. Lastly, Firmino *et al.* [59] noted accelerated healing of a periapical lesion, which is probably due to the fact that bone repair in permanent teeth with the periapical disease is heightened with the red spectrum's laser light [60].

The application of PDT has many advantages but also reports potential adverse effects. Indeed, there is no evidence of the bacteria developing resistance after PDT [61], even after multiple applications [50, 62, 63]. PDT is also effective against antibiotic-sensitive and antibiotic-resistant microorganisms.

However, the methylene blue photosensitizer causes tooth staining and discoloration [64, 65], and chemical smear layer is also formed while obliterating the dentinal tubules has led to microleakage root filling materials having a lesser bond strength to the dentine [66]. The potential cytotoxicity of PDT is also a cause for concern. *In ex vivo and vitro* studies are being done to look into the safety of PDT for future aspirations *in vivo* applications [67, 68].

Conclusion

PDT has several applications in dentistry because the basis of successful periodontal treatment is the removal of bacteria from the infected area. Phenothiazinium PSs are effective and safe for this purpose [69]. However, it is worth mentioning that to administer PDT, scaling and root planing should be performed beforehand.

PDT has significant antibacterial potential as highlighted by recent studies. However, most of these studies do not show significant improvement of disinfection as compared with conventional chemomechanical preparation with NaOCl. PDT is one among many strategies (using intracanal medicaments, e.g., calcium hydroxide, irrigation solutions, e.g., NaOCl and chlorhexidine) advocated as useful in increasing the level of disinfection of the root canal system [70, 71].

Acknowledgments: None

Conflict of interest: None

Financial support: None

Ethics statement: None

References

- Gursoy H, Ozcakir-Tomruk C, Tanalp J, Yılmaz S. Photodynamic therapy in dentistry: a literature review. Clin Oral Investig. 2013;17(4):1113-25.
- 2. Wainwright M. Photodynamic antimicrobial chemotherapy (PACT). J Antimicrob Chemother. 1998;42(1):13-28.
- 3. Takasaki AA, Aoki A, Mizutani K, Schwarz F, Sculean A, Wang C, et al. Application of antimicrobial photodynamic therapy in periodontal and peri-implant diseases. Periodontology. 2009;51(1):109-40.
- Souza RC, Junqueira JC, Rossoni RD, Pereira CA, Munin E, Jorge AO. Comparison of the photodynamic fungicidal efficacy of methylene blue, toluidine blue, malachite green and low-power laser irradiation alone against Candida albicans. Lasers Med Sci. 2010;25(3):385-9.
- Nair PNR, Sjogren U, Figdor D. Persistent periapical radiolucencies of root-filled human teeth, failed endodontic treatments, and periapical scars. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1999;87(5):617-27.
- Mohammadi Z, Abbott PV. On the local applications of antibiotics and antibiotic-based agents in endodontics and dental traumatology. Int Endod J. 2009;42(7):555-67.

Alshareef et al., 2021

Pharmacophore, 12(6) 2021, Pages 37-42

- 7. Mohammadi Z, Abbot PV. The properties and applications of chlorexidine in endodontics. Int Endod J. 2009;42(4):288-302.
- Siqueira Jr JF. Aetiology of root canal treatment failure: why well-treated teeth can fail (Literature review). Int Endod J. 2001;34(1):1-10.
- 9. Kakehashi S, Stanley HR, Fitzgerald RJ. The effects of surgical exposures of dental pulps in germ-free and conventional laboratory rats. Oral Surg Oral Med Oral Pathol. 1965;20(3):340-9. doi:10.1016/0030-4220(65)90166-0
- Özok AR, Persoon IF, Huse SM, Keijser BJF, Wesselink PR, CrielaardW, et al. Ecology of the microbiome of the infected root canal system: a comparison between apical and coronal root segments. Int Endod J. 2012;45(6):530-41. doi:10.1111/j.1365-2591.2011.02006.x
- 11. Plaetzer K, Krammer B, Berlanda J, Berr F, Kiesslich T. Photophysics and photochemistry of photodynamic therapy: fundamental aspects. Lasers Med Sci. 2009;24(2):259-68.
- Sharwani A, Jerjes W, Salih V, MacRobert AJ, El-Maaytah M, Khalil HSM, et al. Fluorescence spectroscopy combined with 5-aminolevulinic acid-induced protoporphyrin IX fluorescence in detecting oral premalignancy. J Photochem Photobiol B Biol. 2006;83(1):27-33.
- 13. Dai T, Huang YY, Hamblin MR. Photodynamic therapy for localized infections-state of the art. Photodiagnosis Photodyn Ther. 2009;6(3-4):170-88.
- 14. Hamblin MR, Hasan T. Photodynamic therapy: a new antimicrobial approach to infectious disease? Photochem Photobiol Sci. 2004;3(5):436-50.
- 15. Ochsner M. Photophysical and phnotobiological processes in the photodynamic therapy of Tumors. J Photochem Photobiol B. 1997;39(1):1-18.
- 16. Redmond RW, Gamlin JN. A compilation of singlet oxygen yields from biologically relevant molecules. Photochem Photobiol. 1999;70(4):391-475.
- Hayek RR, Araújo NS, Gioso MA, Ferreira J, Baptista-Sobrinho CA, Yamada Jr AM, et al. Comparative study between the effects of photodynamic therapy and conventional therapy on microbial reduction in ligature-induced peri-implantitis in dogs. J Periodontol. 2005;76(8):1275-81.
- Sarkar S, Wilson M. Lethal photosensitization of bacteria in subgingival plaque from patients with chronic periodontitis. J Periodontal Res. 1993;28(3):204-10.
- Soukos NS, Ximenez-Fyvie LA, Hamblin MR, Socransky SS, Hasan T. Targeted antimicrobial photochemotherapy. Antimicrob Agents Chemother. 1998;42(10):2595-601.
- Kömerik NU, Nakanishi H, MacRobert AJ, Henderson B, Speight P, Wilson M. In vivo killing of Porphyromonas gingivalis by toluidine blue-mediated photosensitization in an animal model. Antimicrob Agents Chemother. 2003;47(3):932-40.
- 21. Sigusch BW, Pfitzner A, Albrecht V, Glockmann E. Efficacy of photodynamic therapy on inflammatory signs and two selected periodontopathogenic species in a beagle dog model. J Periodontol. 2005;76(7):1100-5.
- 22. Zanin ICJ, Goncalves RB, Junior AB, Hope CK, Pratten J. Susceptibility of Streptococcus mutans biofilms to photodynamic therapy: an in vitro study. J Antimicrob Chemother. 2005;56(2):324-30.
- Zanin IC, Lobo MM, Rodrigues LK, Pimenta LA, Höfling JF, Gonçalves RB. Photosensitization of in vitro biofilms by toluidine blue O combined with a light-emitting diode. Eur J Oral Sci. 2006;114(1):64-9.
- 24. Metcalf D, Robinson C, Devine D, Wood S. Enhancement of erythrosine-mediated photodynamic therapy of Streptococcus mutans biofilms by light fractionation. J Antimicrob Chemother. 2006;58(1):190-2.
- 25. Wood S, Metcalf D, Devine D, Robinson C. Erythrosine is a potential photosensitizer for the photodynamic therapy of oral plaque biofilms. J Antimicrob Chemother. 2006;57(4):680-4.
- 26. Fontana CR, Abernethy AD, Som S, Ruggiero K, Doucette S, Marcantonio RC, et al. The antibacterial effect of photodynamic therapy in dental plaque-derived biofilms. J Periodontal Res. 2009;44(6):751-9.
- 27. Dörtbudak O, Haas R, Bernhart T, Mailath-Pokorny G. Lethal photosensitization for decontamination of implant surfaces in the treatment of peri-implantitis. Clin Oral Implants Res. 2001;12(2):104-8.
- Shibli JA, Martins MC, Theodoro LH, Lotufo RFM, Garcia VG, Marcantonio Jr E. Lethal photosensitization in microbiological treatment of ligature-induced peri-implantitis: a preliminary study in dogs. J Oral Sci. 2003;45(1):17-23.
- 29. Bevilacqua IM, Nicolau RA, Khouri S, Brugnera Jr A, Teodoro GR, Zângaro RA, et al. The impact of photodynamic therapy on the viability of Streptococcus mutans in a planktonic culture. Photomed Laser Surg. 2007;25(6):513-8.
- Nagata JY, Hioka N, Kimura E, Batistela VR, Terada RSS, Graciano AX, et al. Antibacterial photodynamic therapy for dental caries: evaluation of the photosensitizers used and light source properties. Photodiagnosis Photodyn Ther. 2012;9(2):122-31.
- Fimple JL, Fontana C R, Foschi F, Ruggiero K, Song X, Pagonis TC, et al. Photodynamic treatment of endodontic polymicrobial infection in vitro. J Endod. 2008;34(6):728-34.
- 32. Zehnder M. Root canal irrigants. J Endod. 2006;32(5):389-98.
- Peters MC, McLean ME. Minimally Invasive Operative Care: II. Contemporary Techniques and Materials: an Overview. J Adhes Dent. 2001;3(1).
- 34. Siqueira JF. Strategies to treat infected root canals. CDA. 2001;29(12):825-38.

Alshareef et al., 2021

Pharmacophore, 12(6) 2021, Pages 37-42

- 35. Rôças IN, Siqueira Jr JF. Comparison of the in vivo antimicrobial effectiveness of sodium hypochlorite and chlorhexidine used as root canal irrigants: a molecular microbiology study. J Endod. 2011;37(2):143-50.
- 36. Nagayoshi M, Nishihara T, Nakashima K, Iwaki S, Chen KK, Terashita M, et al. Bactericidal effects of diode laser irradiation on Enterococcus faecalis using periapical lesion defect model. Int Sch Res Notices. 2011;2011.
- 37. Garcez AS, Arantes-Neto JG, Sellera DP, Fregnani ER. Effects of antimicrobial photodynamic therapy and surgical endodontic treatment on the bacterial load reduction and periapical lesion healing. Three years follow up. Photodiagnosis Photodyn Ther. 2015;12(4):575-80.
- Asnaashari M, Ashraf H, Rahmati A, Amini N. A comparison between effect of photodynamic therapy by LED and calcium hydroxide therapy for root canal disinfection against Enterococcus faecalis: A randomized controlled trial. Photodiagnosis Photodyn Ther. 2017;17:226-32.
- Pourhajibagher M, Bahador A. Outer membrane protein 100 of Ag- gregatibacter actinomycetemcomitans act as a biopharmaceutical target for photodynamic therapy: an in silico analysis. Photodiagnosis Photodyn Ther. 2016;16:154-60.
- 40. Rabello DG, Corazza BJ, Ferreira LL, Santamaria MP, Gomes AP, Martinho FC. Does supplemental photodynamic therapy optimize the disinfection of bacteria and endotoxins in one-visit and two-visit root canal therapy? A randomized clinical trial. Photodiagnosis Photodyn Ther. 2017;19:205-11.
- 41. Tennert C, Drews AM, Walther V, Altenburger MJ, Karygianni L, Wrbas KT, et al. Ultrasonic activation and chemical modification of photosensitizers enhances the effects of photodynamic therapy against Enterococcus faecalis root-canal isolates. Photodiagnosis Photodyn Ther. 2015;12(2):244-51.
- 42. Bonsor SJ, Nichol R, Reid TMS, Pearson GJ. Microbiological evaluation of photo-activated disinfection in endodontics (an in vivo study). Br Dent J. 2006;200(6):337-41.
- 43. Garcez AS, Nuñez SC, Hamblin MR, Ribeiro MS. Antimicrobial effects of photodynamic therapy on patients with necrotic pulps and periapical lesion. J Endod. 2008;34(2):138-42.
- 44. Garcez AS, Nunez SC, Hamblim MR, Suzuki H, Ribeiro MS. Photodynamic therapy associated with conventional endodontic treatment in patients with antibiotic-resistant microflora: a preliminary report. J Endod. 2010;36(9):1463-6.
- 45. Foschi F, Fontana CR, Ruggiero K, Riahi R, Vera A, Doukas AG, et al. Photodynamic inactivation of Enterococcus faecalis in dental root canals in vitro. Lasers Surg Med. 2007;39(10):782-7.
- 46. Asnaashari M, Godiny M, Azari-Marhabi S, Tabatabaei FS, Barati M. Comparison of the antibacterial effect of 810 nm diode laser and photodynamic therapy in reducing the microbial flora of root canal in endodontic retreatment in patients with periradicular lesions. J Lasers Med Sci. 2016;7(2):99.
- 47. Soares FZM, Follak A, Da Rosa LS, Montagner AF, Lenzi TL, Rocha RO. Bovine tooth is a substitute for human tooth on bond strength studies: A systematic review and meta-analysis of in vitro studies. Dent Mater. 2016;32(11):1385-93.
- 48. Ng R, Singh F, Papamanou DA, Song X, Patel C, Holewa C, et al. Endodontic photodynamic therapy ex vivo. J Endod. 2011;37(2):217-22.
- 49. Jori G. Photodynamic therapy of microbial infections: state of the art and perspectives. J Environ Pathol, Toxicol Oncol. 2006;25(1-2).
- 50. Konopka K, Goslinski T. Photodynamic therapy in dentistry. J Dent Res. 2007;86(8):694-707.
- 51. Kömerik N, Wilson M. Factors influencing the susceptibility of Gram-negative bacteria to toluidine blue O-mediated lethal photosensitization. J Appl Microbiol. 2002;92(4):618-23.
- 52. Pourhajibagher M, Bahador A. An in vivo evaluation of microbial diversity before and after the photo-activated disinfection in primary endodontic infections: Traditional phenotypic and molecular approaches. Photodiagnosis Photodyn Ther. 2018;22:19-25.
- 53. Bonsor SJ, Nichol R, Reid TMS, Pearson GJ. An alternative regimen for root canal disinfection. Br Dent J. 2006;201(2):101-5.
- 54. Kosarieh E, Khavas SS, Rahimi A, Chiniforush N, Gutknecht N. The comparison of penetration depth of two different photosensitizers in root canals with and without smear layer: An in vitro study. Photodiagnosis Photodyn Ther. 2016;13:10-4.
- 55. George S, Kishen A. Advanced noninvasive light-activated disinfection: assessment of cytotoxicity on fibroblast versus antimicrobial activity against Enterococcus faecalis. J Endod. 2007;33(5):599-602.
- 56. George S, Kishen A. Photophysical, photochemical, and photobiological characterization of methylene blue formulations for light-activated root canal disinfection. J Biomed Opt. 2007;12(3):034029.
- Nunes MR, Mello I, Franco GCN, de Medeiros JMF, Dos Santos SSF, Habitante SM, et al. Effectiveness of photodynamic therapy against Enterococcus faecalis, with and without the use of an intracanal optical fiber: an in vitro study. Photomed Laser Surg. 2011;29(12):803-8.
- 58. Pinheiro ALB, Gerbi MEM, Ponzi EAC, Ramalho LMP, Marques AM, Carvalho CM, et al. Infrared laser light further improves bone healing when associated with bone morphogenetic proteins and guided bone regeneration: an in vivo study in a rodent model. Photomed Laser Surg. 2008;26(2):167-74.
- Firmino RT, Brandt LMT, Ribeiro GL, Dos Santos KSA, de Vasconccelos Catão MHC, de Castro Gomes DQ. Endodontic treatment associated with photodynamic therapy: Case report. Photodiagnosis Photodyn Ther. 2016;15:105-8.

Alshareef et al., 2021

Pharmacophore, 12(6) 2021, Pages 37-42

- 60. Yoshida T, Yamaguchi M, Utsunomiya T, Kato M, Arai Y, Kaneda T, et al. Low-energy laser irradiation accelerates the velocity of tooth movement via stimulation of the alveolar bone remodeling. Orthod Craniofac Res. 2009;12(4):289-98.
- 61. Komerik N, MacRobert AJ. Photodynamic therapy as an alternative antimicrobial modality for oral infections. J Environ Pathol Toxicol Oncol. 2006;25(1-2).
- 62. Wainwright M, Crossley KB. Photosensitising agents—circumventing resistance and breaking down biofilms: a review. Int Biodeterior Biodegradation. 2004;53(2):119-26.
- 63. Rossoni RD, Junqueira JC, Santos ELS, Costa ACB, Jorge AOC. Comparison of the efficacy of Rose Bengal and erythrosin in photodynamic therapy against Enterobacteriaceae. Lasers Med Sci. 2010;25(4):581-6.
- 64. Carvalho Edos S, Mello I, Albergaria SJ, Habitante SM, Lage-Marquez JS, Raldi DP. Effect of chemical substances in removing methylene blue after photodynamic therapy in root canal treatment. Photomed Laser Surg. 2011;29(8):559-63.
- 65. Ramalho KM, Cunha SR, Mayer-Santos E, de Paula Eduardo C, de Freitas PM, Aranha AC et al. In vitro evaluation of methylene blue removal from root canal after Photodynamic Therapy. Photodiagnosis Photodyn Ther. 2017;20:248-52.
- 66. Shahravan A, Haghdoost AA, Adl A, Rahimi H, Shadifar F. Effect of smear layer on sealing ability of canal obturation: a systematic review and meta-analysis. J Endod. 2007;33(2):96-105.
- 67. George S, Kishen A. Optimization of an advanced non-invasive light activated disinfection strategy. In European Conference on Biomedical Optics (p. 6633_43). Optical Society of America. 2007 June.
- 68. Xu Y, Young MJ, Battaglino RA, Morse LR, Fontana CR, Pagonis TC, et al. Endodontic antimicrobial photodynamic therapy: safety assessment in mammalian cell cultures. J Endod. 2009;35(11):1567-72.
- 69. Hohammadi Z, Shalavi S, Jafarzadeh H. Ethylenedia minetetraacetic acid in endodontics. Eur J Dent. 2013;7:S135-42.
- 70. Mohammadi Z, Jafarzadeh H, Shalavi S. Antomocrobial efficacy of chlorhexidine as a root canal irrigant: a literature review. J Oral Sci. 2014;56(2):99-103.
- 71. Sculean A, Aoki A, Romanos G, Schwarz F, Miron RJ, Cosgarea R. Is photodynamic Therapy an Effective Treatment for Periodontal and peri-Implant infections? Dent Clin North Am. 2015;59(4):831-58.