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Endodontics

THERAPEUTIC EFFECTS OF CURCUMIN IN ROOT CANAL PROCEDURE - A REVIEW

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ABSTRACT Successful Endodontic therapy aims at thorough debridement of root canals and complete elimination of microorganisms from the root canals. Currently, research in the field of herbal products has increased due to its varied advantages. Curcumin, a phytochemical obtained from rhizomes of Curcuma longa, shows broad spectrum antimicrobial activity. It is a natural polyphenol that is commonly used as a spice and coloring and flavoring agent in South Asian countries. Over the last decade, Curcumin is becoming popular in Endodontics due to its excellent pharmacological attributes like antimicrobial, antifungal, antiviral, antiseptic and anti-oxidant properties. Curcumin also acts as a natural photosensitizer with the ability to provide targeted therapy and has good photophysical properties. It is less cytotoxic compared to sodium hypochlorite and is cost-effective. There is a quest for newer treatment strategies to prevent endodontic failures and Post-treatment apical periodontitis, caused by persistent intraradicular infection. Photodynamic therapy is one such adjunctive therapy found to be effective in the treatment of secondary infections with several invitro studies showing curcumin as an effective photosensitizer in root canal disinfection against resistant gram-positive bacterial species. This review article is a collection of invitro studies describing applications of curcumin in endodontics, its photosensitizing properties, functions and effects of curcumin in Endodontic therapy.

KEYWORDS : Antimicrobial Photodynamic therapy, Curcumin, E.faecalis, Herbal therapy, Photosensitizer.

INTRODUCTION

Pulpal and periapical pathosis are biofilm mediated infections, requiring endodontic therapy. Adequate root canal disinfection is the primary requisite in endodontic treatment. Thus, the goal of endodontic therapy is the complete elimination of multispecies biofilm present within the root canal system. Conventional disinfection strategies apply sodium hypochlorite for canal irrigation and eradication of microorganisms. However, due to the complexities of the root canal system and tenacious structure of the biofilm, conventional root canal irrigants show reduced penetration in the biofilm structure and within the dentinal tubules of the root canal system. Sodium hypochlorite is also cytotoxic and shows inability to completely remove the smear layer.[1] It also has detrimental effects on the mechanical properties of the root dentin like reduced dentin microhardness, structural integrity, elasticity and flexural strength.[2,3] Hence, a lot of research is being undertaken for the use of herbal products in endodontics due to their proven antimicrobial properties and reduced toxic effects.

Herbal therapy is also an alternative treatment for recalcitrant conditions in the body and one such commonly used natural compound is Curcumin. [4] It is a polyphenol obtained from rhizomes of Curcuma longa, a commonly used Indian spice and coloring agent. It shows broad spectrum antimicrobial activity, has good biocompatibility, is less toxic and cost effective. Curcumin is shown to have photosensitizer properties as well. It has characteristics like strong absorption of light in the wavelength range of 430-480nm and has substantial oxidative properties.[5] It is lethal to the bacteria without being in close proximity or binding to the bacteria. Also it shows less discoloration when compared to other conventional photosensitizers used in Endodontics like methylene blue and toluidine blue ortho.[6]

Thus, this review aims to discuss all the research based applications of curcumin in endodontics and also the effect of curcumin application on the structures of the root canal system performed within the last decade.

Several research studies showing the use of curcumin in Endodontics are detailed below. They are -

1. Curcumin as an Intracanal irrigant
2. Curcumin as a Photosensitizer in:
   a. Antibacterial agent in endodontic irrigation
   b. In Revascularization procedures as an irrigant and intracanal medicament.
   c. As Curcumin Nanoparticles in Disinfection of root canal.
3. Antifungal agent in biofilm eradication

1. Curcumin As An Intracanal Irrigant -

Curcumin was first studied as an endodontic antimicrobial irrigant in an in-vitro study by Prasanna Neelakantan and coworkers in 2013. They used 2.5mg/mL of curcumin in dimethyl sulphoxide(DMSO) vehicle. They compared conventional irrigants such as 3% sodium hypochlorite and 2% chlorhexidine with the experimental curcumin solution on 2nd day, 2nd week and 8th week of E.faecalis biofilm formed on instrumented, extracted single rooted teeth. They found that 2.5mg/mL of curcumin and 3% sodium hypochlorite solution showed complete eradication of the biofilm. And, amongst the three solutions sodium hypochlorite completely removed E.faecalis biofilm from the tooth samples at 8 weeks. This study also revealed that 2% Chlorhexidine was inefficient in complete eradication of biofilm at all time intervals. They concluded that at 2 day and 2 week biofilm, curcumin showed better penetration and anti-biofilm activity against gram positive and gram negative bacteria whereas with 8 weeks biofilm, curcumin did not show complete eradication of E.faecalis. They attributed it to the thickness and complex dynamic nature and structure of the biofilm.[7]

2. The Antimicrobial Photodisinfection Property Of Curcumin:

A. Antibacterial Agent In Endodontic Irrigant -

i. Prasanna Neelakantan et al in 2015 carried out the first study in endodontics using curcumin as a photosensitizer molecule and its antimicrobial action. Here, they compared the effect of Photoactivated and ultrasonically activated curcumin and sodium hypochlorite against E.faecalis biofilm. The E faecalis biofilm was grown on root dentin in brain heart infusion agar and incubated anaerobically for 4 weeks. 3% NaOCl and 2.5mg/mL curcumin were tested for both light activation for 4 minutes with blue light of 1200mW/cm2 intensity and also with ultrasonic activation for 30 second cycles for 4 minutes using Irrisafe files. They proved that Photoactivated curcumin had maximum effect on the bacterial biofilm when compared to Photoactivated sodium hypochlorite because of the photo-oxidative properties of curcumin, although ultrasonic activated sodium hypochlorite was better than ultrasonic activated curcumin because ultrasonic activation of curcumin did not enhance the antibacterial properties of curcumin.[8]

ii. A study by Maryam Pourhajibagher et al in 2018 evaluated the antimicrobial and anti-biofilm effect of traditional irrigants like 5.25% sodium hypochlorite, 0.2% and 2% chlorhexidine against planktonic

and biofilm forms of E.faecalis in comparison to aPDT with curcumin and indocyanine green (ICG) photosensitizers. Different concentrations of photosensitizer and wavelength of light was used in this study. 40mM of curcumin dissolved in 0.05% dimethyl sulfoxide and 1000 µg/mL ICG was dissolved in 1.0 mL of sterile distilled water. This study concluded that the irrigating solutions showed maximum reduction in the colony forming units with curcumin aPDT, ICG aPDT also showing high potential for reduction in E.faecalis bacteria and its biofilm. This is attributed to the detoxification property of these photosensitizer dyes[9]

iii. Sh. Farkhonde Masoule et al in 2018, studied the effect of curcumin PDT, curcumin irrigant and LED light on cell viability and biofilm degradation of endodontic pathogens. E.faecalis and P.aeruginosa biofilms were inoculated anaerobically on brain heart infusion broth. This study proved that PDT with Curcumin photosensitizer using LED light of 450nm wavelength and 1000–1400 Mw/Cm2 intensity was effective against E faecalis and P aeruginosa species in both planktonic and biofilm mode. Although curcumin PDT showed 1.2 times greater phototoxic effect on E.faecalis biofilm as compared to P.aeruginosa biofilm. This is due to the relatively porous peptidoglycan layer in their cell wall structure of gram positive bacteria and also due to the complex composition (i.e high magnesium content) of the outer membrane of gram negative bacteria, which acts as a barrier for penetration of the photosensitizers.[10]

iv. Again in 2018, Maryam Pourhajibagher and team compared the effect of PDT with different photosensitizers like Indocyanine green (ICG), methylene blue (MB), Toluidine Blue Ortho (TBO) and curcumin on E.faecalis strains that were cultured in the laboratory. These photosensitizers were compared with and without light irradiation using their corresponding wavelength of activation. Diode laser was used for TBO, MB and ICG PSs while LED light was used for curcumin PS. They concluded that PDT with curcumin and Indocyanine green had greater anti-biofilm action than toluidine blue and methylene blue PDT in reduction of E.faecalis.[11]

v. In 2020, Ali Mozayeni et al compared photodynamic therapy using various photosensitizers such as 0.5mg/mL of Toluidine blue, methylene blue and curcumin after 2.5% NaOCl canal irrigation of single rooted extracted teeth following instrumentation. These groups were also compared to irrigating solutions like 0.5mg/mL of curcumin dissolved in a mixture of 1% ethanol and 1% bovine serum albumin with saline, which was the control group. FotoSan 630 was the light unit used in the study. It is an LED device that emits light in the red spectrum of 630 nm wavelength and output intensity of 2000-4000mW/cm2. The light tip of 0.5mm diameter was introduced upto half the length of the root canal. The results of this study showed that 2.5% NaOCl irrigation followed by Toluidine blue PDT was most effective followed by 2.5% NaOCl with curcumin PDT, this could be attributed to the right concentration of Toluidine blue photosensitizer and the corresponding red spectrum of Light source used. Toluidine blue shows maximum absorption of light of 630 nm wavelength. On the contrary, curcumin PDT was less effective as red light LED of 660 nm was used in the study whereas curcumin shows maximum absorption of light at 450 nm as proven by the earlier studies.[12]

B. Revascularization Procedures-

I) As An Intracanal Medicament In Immature Necrotic Teeth-

Successful pulp revascularization procedures primarily depend on the complete debridement and disinfection of the canals. Thus, in 2015, P Neelakantan et al compared the use of various intracanal medicaments like Triple Antibiotic Paste (TAP), Double Antibiotic Paste (DAP), Chlorhexidine (CHX), Calcium hydroxide (CaOH) with Curcumin PDT for debridement of immature teeth with necrotic canals. In 2012, Ruparel et al have shown that conventional intracanal medicaments like TAP and DAP could be cytotoxic to the cells of apical papilla and also have deleterious effects on the root dentin. while CaOH is proven to be ineffective against E faecalis biofilms. CHX is also toxic to the stem cells of dental pulp and shows reduced anti-biofilm activity. This study was designed to understand the anti-biofilm effect of curcumin PDT and its effect on the dentin matrix of immature roots. They found that 2.5mg/mL of Curcumin in 5% aqueous polyethylene glycol vehicle with aPDT using visible light for 4 minutes was most effective in reducing the viable bacterial count as it showed dentinal tubule penetration upto 400 microns and also showed reduced detrimental effects on the canal walls and untoward effects on the cells of apical papilla.[13]

II) Curcumin Modified Electrospun Fibers For Disinfection Of Immature Pulpless Teeth-

Regenerative procedures commonly require the use of triple antibiotic or double antibiotic paste for disinfection procedures. But they cause tooth discoloration and stem cell toxicity. Thus. there was a need for an alternative disinfection procedure. In 2019, Julian Sotomil et al tested the effectiveness of Curcumin-modified Electrospun fibers and curcumin-free electrospun fibers against Actinomyces naeslundii bacteria frequently found in the root canals of immature necrotic teeth. The fibers were prepared using Polydioxanone polymer solutions mixed with curcumin dissolved in ethanol. They were stirred overnight and then loaded into 5mL of plastic syringes. These syringes were put into the syringe pump. After the electrospinning procedure, the fibers were dried under vacuum. They showed that NaOCl and CHX irrigants followed by Curcumin Irrigant were better when compared to PDT using Curcumin-modified fibers for disinfection purposes. Although these fibers were effective compared to the control saline group.[14]

C. Curcumin Nanoparticles In Disinfection-

In 2020, Maryam Pourhajibaugher initiated the use of nano-curcumin particles for Photodynamic therapy, they tested the use of curcumin nanoparticles with a novel metformin and indocyanine green complex. This is because nanotechnology provides an efficient solution as it increases the solubility of curcumin in aqueous solution. It improves the bioavailability, penetrability and localization of curcumin within the bacterial cell. They used dual wavelength irradiation using LED at 450 nm and Diode Laser at 810nm with 60J/cm2 and 31.2J/cm2 energy density respectively for 5 minutes. 10 microlitre of Nano-curcumin doped with metformin and indocyanine was compared with 10 microlitre of 2.5% NaOCl and saline. They observed that the combination of both LED and Diode LASER for aPDT with this complex was more effective than when LED and Diode laser was used individually for aPDT. Nano-curcumin showed improved properties like better penetration and localization of the photosensitizer within the dentinal tubules and improved solubility. Metformin, a well-known oral hypoglycemic, provides a synergistic advantage and increases the photosensitivity of curcumin photosensitizer. Indocyanine, an anionic photosensitizer, showed better effectiveness when combined with nano-curcumin particles.[15]

3. Antifungal Agent In Biofilm Eradication

In 2021, Prasanna Neelakantan et al showed that Curcumin with nano-lipid complexes like sophorolipids obtained from the non-pathogenic yeasts could be used as a vehicle for curcumin delivery. They may prevent hyphal and fungal biofilm formation. Thus, curcumin sophorolipid complexes were effective against the Candida albicans present in the root canals in conjugation with E faecalis due to their ability to bind to the membrane ergosterol and prevent filamentation. This CU-SL complex also downregulates the ERG11 gene responsible for hyphae formation.[16]

4. Enhancing Photosensitizer Property

In 2014, Mathew da frota studied 20 microns of curcumin as a photosensitizer with light source of 450nm with energy power of 100mW/cm2 and irradiation time of 5 and 10 minutes with pre-irradiation of canals for 5 and 10 minutes in each group, where photosensitizer was placed within the canal. They explained that pre-irradiation of the canals prior to photodynamic therapy for maximum antimicrobial effect.They concluded that 5 minutes of pre-irradiation of the canals followed by 5 minutes of curcumin antimicrobial Photodynamic therapy(aPDT) was proven the most effective for bacterial biofilm than 10 minutes of PDT due to biphasic dose response.[17]

5. Effect Of Curcumin Photosensitizer On Periapical Cells

As sodium hypochlorite is a known cytotoxic agent, Gomes Filho et al in 2016 tested the effect of Curcumin on the gingival fibroblast cell viability and IL-1Beta and IL-6 cytokine release when used during photodynamic therapy. They found that Curcumin PDT showed less than 25% inhibition of gingival fibroblasts whereas NaOCl showed greater than 75% reduction in cell viability. NaOCl and Curcumin expressed both Interleukin 1-beta and Interleukin 6 similarly during the 6,12 and 48 hours of experimental period. Hence, they proved that curcumin PDT was not cytotoxic and did not limit the cell viability and release of cytokines.[18]

6. Curcumin PDT On Mechanical Properties Of Root Dentin

In 2019, Henrico Sahyon et al studied the effect of aPDT with

curcumin of two different concentrations at 500 mg/L and 1000 mg/L on the mechanical properties of root dentin and showed that higher concentration of curcumin without light activation (CUR-1000 mg-WL) showed better mechanical properties like higher Martens Hardness and Elastic Indentation modulus followed by lower concentration of curcumin with light activation (CUR-500 mg- L) when compared with other groups.[19]

7. Bond Strength Of Different Materials Using Curcumin PDT -

A. Effect Of Curcumin As A Photosensitizer On The Bond Strength Of Glass Fiber Posts -

In 2019, Henrico Sahyon et al studied the effect of aPDT with curcumin of two different concentrations at 500 mg/L and 1000mg/L on the push-out bond strength of glass fiber posts at different thirds of the root. They found that curcumin alone without light activation had better bond strength values at cervical thirds whereas at the middle and apical third, there was no statistical significant difference between the groups.[19]

B. Effect Of Curcumin Pdt On The Extrusion Bond Strength Of Different Sealers -

In 2021, Mazen Alkatany et al have studied the effect of curcumin aPDT on Extrusion bond strength of root canal sealers like AH plus,a resin-based sealer, Sealapex, a CaOH based sealer and MTA Fillapex, bioceramic based sealer following NaOCl and EDTA irrigation. They found that extrusion bond strength of resin-based sealers reduced when compared to CaOH and bioceramic-based sealers, also showed no significant difference in the EBS when Curcumin aPDT was used.[20]

Limitations Of The Review

The major limitations are the heterogeneity of information available in the literature regarding the use of photodynamic therapy as an adjunct for disinfection of root canals. The application of the parameters for photodynamic therapy used for these invitro biofilm based studies needs more clinical trials for utilization of PDT in endodontics.

CONCLUSION

Today in the Era of evidenced-based practice, herbal products are gaining importance due to their varied applications and advantages. The above mentioned studies prove Curcumin is an effective root canal disinfectant provided the right parameters are followed. Photodynamic property of Curcumin is said to be maximum at a concentration of 2.5mg/mL with a suitable aqueous vehicle for 4 - 5 minutes, at a wavelength of 430-480nm with 1000-1200mW/cm2 intensity with 5 minutes of pre-irradiation.

Further research is warranted in understanding the role of Photodynamic therapy in effective disinfection of the root canal system. More clinical studies are required to learn the effect of curcumin PDT on Sealer bond strength, Sealer penetration into dentinal tubule, Effect on obturating material, Root dentin properties and Bioavailability of curcumin. The existing literature on Photodynamic Therapy, Curcumin appears to be the most efficacious photosensitizer when compared to other conventional photosensitizers against endopathogens.

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