

CURCUMIN- PHARMACOLOGICAL ACTIONS AND ITS ROLE IN DENTISTRY

SHARMILA DEVI DEVARAJ, PRASANNA NEELAKANTAN*

Saveetha Dental College and Hospitals, Saveetha University, Chennai, India

* Author for correspondence: prasanna_neelakantan@yahoo.com**This paper is available online at www.jprhc.in****ABSTRACT**

Turmeric (*Curcuma longa*) is an ancient dye, flavouring and medical herb, widely used in Asian countries. It is a herb that has been widely used in Indian medicine, cookery, and cosmetics. The main component of turmeric is curcumin. Curcumin has a surprisingly wide range of beneficial properties includes anti inflammatory, antioxidant, chemopreventive, chemotherapeutic activity etc. The activity of curcumin derived from its complex chemistry as well as its ability to influence the multiple signalling pathways. This review article is to highlight the pharmacological action and its therapeutic role in dentistry.

KEY WORDS: Curcumin, Turmeric, Antibiotic, Antioxidant, Oral health, Dental infection.**INTRODUCTION**

Phytotherapy i.e., the use of herbal agents as medicines is gaining interest in medicine and dentistry. These ethnopharmacological therapies have claimed wide attention globally. One very widely used home remedy which has been an area of focus in medicine is turmeric (*Curcuma longa*). The active component of turmeric is curcumin. A member of the Zingiberaceae family, it is cultivated in several parts of the Indian subcontinent, South East Asia and South America^{1,2}. It has widely used in cookery, cosmetics, fabric dyeing and medicine for more than 2000 years. The dimensions of this rhizome range between 2.7 - 7 cm in length and about 2.5 cm in diameter².

Curcumin (diferuloylmethane), the main yellow active component of turmeric has been to have a wide spectrum of biological actions³. Turmeric has held an important position in India's traditional ayurvedic medicine². In Ayurveda, it was prescribed for treatment of many medical problems ranging from constipation to skin disease and in both Ayurvedic and Chinese medicines, it is considered to be a bitter digestive and carminative¹. In Unani, turmeric is considered as blood purifiers and safest herb of choice². It is an excellent anti inflammatory herb, used in treatment of arthritis, rheumatoid arthritis, injuries, trauma. Curcumin exhibits a big promise as a therapeutic agents and is currently in human trails for a variety of conditions like multiple myeloma, pancreatic cancer, colon cancer, myelodysplastic syndromes, psoriasis, Alzheimer's disease⁴, diabetic nephropathy³. It also play important role in dentistry in treating periodontal disease, to maintain good oral hygiene, oral cancers. It can also be used as a component in local drug delivery system in gel form⁵.

CHEMISTRY OF TURMERIC

Curcumin(1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-Dione) is the most active polyphenolic constituent, powerful ingredient in the traditional herbal practices⁵.

Chemical composition of turmeric

Turmeric includes protein (6.3%), fat (5.1%), minerals (3.5%), carbohydrates (69.4%), moisture (13.1%). The essential oil obtained from the steam distillation of rhizomes has alpha-phellandrene (1%), sabinene (0.6%), cineol (1%), bornol (0.5%), zingiberene (25%), sesquiterpenes (53%)⁶.

Components of turmeric

The components of turmeric are known as curcuminoids comprised of curcumin (diferuloyl methane), demethoxycurcumin and bisdemethoxycurcumin⁷. Curcumin was first isolated in 1815, the chemical structure was found by Roughley and Whiting in 1973. The melting point of curcumin is 184°C. It is soluble in ethanol and acetone but insoluble in water. They also exists as keto-enol tautomers. Most recent available preparation of curcumin includes approximately of 77% diferuloylmethane, 18% demethoxycurcumin, 5% bis-demethoxycurcumin.

Pharmacokinetics

Curcumin has shown therapeutic efficacy against many human diseases, one of the major concerns with curcumin is its poor oral bioavailability that can be attributed due to its poor absorption, high rate of metabolism in the intestines and rapid systemic elimination from body⁸. Efforts have been made to improve curcumin's bioavailability and reduce their toxicity⁶. Adjuvants that can block the metabolic pathway of curcumin have been most extensively used to increase the bioavailability of the polyphenol. For instance, in humans receiving a dose of 2g curcumin alone, serum levels have been either undetectable or very low, but concomitant administration of piperine was associated with an increase of 2000% in the bioavailability of curcumin³. Other advance approaches to increase the bioavailability of curcumin based on nanotechnology include use of nanoparticles, liposomes, micelles, phosphor lipid complexes and structural analogues³.

PHARMACOLOGICAL ACTIONS

The variety of human disorders against which curcumin has potential has been revealed by numerous clinical trials³. The roles relevant to dentistry has been discussed below:

Anti-inflammatory effects

Curcumin has the ability to suppress the acute and chronic inflammation⁴. It reduces inflammation by lowering histamine levels and by possibly increasing the production of natural cortisone by adrenal glands⁶. They also reduces pain from arthritis, bursitis, tendonitis, stiffness of joints¹. It also inhibits the biosynthesis of inflammatory prostaglandins from the arachidonic acid and neutrophil function. Curcumin has been found to be superior to placebo and NSAID¹.

Anticarcinogenic effects

Curcumin potentially helps to prevent the new cancers that are caused by chemotherapy or radiation used to treat existing cancers. It effectively inhibits metastasis (uncontrolled spread) of melanoma and may be especially useful in deactivating the carcinogens in cigarette smoke and chewing tobacco¹.

Antimicrobial effects

Curcumin and the oil fraction inhibits the growth of variety of bacteria like Streptococci, Staphylococci, Lactobacillus, etc and also prevents Helicobacter pylori CagA + strains in vitro³. It is also effective against Enterococcus faecalis, and will serve to be useful as root canal medicaments in endodontics¹⁰. It also acts as antifungal agent which is active against Aspergillus flavus, A.parasiticus, Fusarium moniliforme, Penicillium digitatum. It has antiprotozoan activity against E.histolytica, Leishmania, Plasmodium falciparum¹¹⁻¹³. It also has antiviral effect which inhibits HIV in test tube studies¹ and also inhibits UV light induced HIV gene expression.

Photodynamic effects

Curcumin (1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-Dione) has potential as a photo sensitizer for photo dynamic treatment of localised superficial infection in eg: the mouth or skin. In vitro studies reveals that aqueous preparations of curcumin has phototoxic effects against certain bacteria like Enterococcus faecalis, Streptococcus intermedius, E.coli. Also photo dynamic inactivation of Candida albicans in a murine model of Oral candidiasis has been noted^{12,13}.

Antihyperalgesic effect

Curcumin has diverse therapeutic effects as anti oxidant, anti inflammatory, anti-cancer, etc it also exhibits antihyperalgesic effect. The vanilloid moiety of curcumin is considered most important for activation of the Transient Receptor Potential Vanilloid 1 (TRPV1) which have anti nociceptive effects under behavioural studies and in vitro whole cell patch-clamp recordings in the trigeminal system¹⁴.

Therapeutic role in dentistry

Turmeric has been recommended to be used in following ways to relief from the dental pain¹

- As a mouth rinse: 5g of turmeric powder in 200 mL boiling water, mixed with two cloves and dried leaves of guava has been claimed to offer gives instant pain relief.
- Paste form: Mixing 1 tsp of turmeric with salt (1/2 tsp) and mustard oil (1/2 tsp) gives a paste, which when massaged over the gums offers relief from gingivitis and periodontitis.

Pit & Fissure Sealant

Pit and fissure sealants are normally used in children to prevent development of dental caries. They may be colored for easy identification on future recalls. The use of curcumin serves two roles in that, it gives a color tint to the pit and fissure sealant. Furthermore, being antibacterial, curcumin would also serve to prevent caries. These formulations contain a resin and in addition may contain extracts of other agents apart from curcumin¹⁵.

Dental –Plaque detection system

Dental Plaque is usually colourless and may not be easily detected. Dental plaques detection system involves an agent (dye, usually in solution or tablet form), which stains plaque and allows its detection. It includes dental plaque staining agent with yellow pigment of beni- koji, turmeric extracts, curcumin and a light-emitting apparatus which have outputs light having a wavelength within a range of 200 – 500 nm to an object in the oral cavity where the dental plaque staining agent is attached^{1,15}.

Anticariogenic effect

The inhibitory effects of an essential oil isolated from *Curcuma longa* on the cariogenic property of *Streptococcus mutans* has been observed at concentrations from 0.5 to 4 mg/ml. And also exhibits the significant inhibition of *S.mutans* adherence to saliva coated hydroxyl apatite beads and inhibited the formation of *S.mutans* at concentrations higher than 0.5 mg/ml^{17,18}.

Prevention of plaque and gingivitis

Anti inflammatory property of turmeric has been studied and demonstrated significant reduction of inflammation⁹. Curcumin oil used as a treatment modality in Recurrent Aphthous Stomatitis¹⁹. An orally applicable composition for treatment and prevention of periodontal diseases using a bio adhesive formulation comprises curcuminoids as an active agent. has been described in the literature, composed of curcumin, tetra hydro curcumin, bishydro curcumin, crude drug and solvents extracts of *Curcuma longa*, one or more bio adhesive polymers such as hydroxyl propyl cellulose, hydroxyl propyl methyl cellulose, sodium carboxy methyl cellulose, hydroxyl ethyl cellulose and carbomers and sodium chloride, sodium bicarbonate or mixtures and one or more excipients^{19,20}.

Mouth wash

Turmeric mouth wash can be effectively used as an adjunct to mechanical plaque control methods. Ten mg of curcumin can be dissolved in 100 mL distilled water. The flavor may be enhanced by using peppermint oil. The pH of these mouthwashes have been adjusted to 4 and a study has shown that this mouthwash is as effective as a chlorhexidine mouth wash^{19,21}

Local drug delivery system

Local drug delivery system containing 2 % whole turmeric gel form as an adjunct to scaling and root planning treatment showed significant reduction in plaque index, gingival index, sulcus bleeding index, probing, pocket depth and gain in relative attachment loss. There was significant reduction in trypsin – like enzyme activity of “red complex” micro organisms, namely *Bacteroides forsythus*, *Porphyromonas gingivalis* and *Treponema denticola*²¹

As a subgingival irrigant in periodontics

Curcumin 1% as sub gingival irrigant resulted in significant reduction in bleeding on probing and redness, when compared with chlorhexidine and saline group as an adjunctive therapy in periodontitis patients^{19,21}. They can cause better resolution of inflammatory signs than chlor hexidine and saline irrigation, by selectively reducing the inflammatory mediators and causing shrinkage by reducing inflammatory oedema and vascular engorgement of connective tissues⁷. Curcumin also enhances wound healing by causing increase in fibronectin and transforming growth factor transcription²². One fraction of crude polysaccharides extracted from the rhizomes of wild turmeric, *Curcuma aromatic Salisb* (Zingiberaceae) can significantly induce human gingival fibroblasts cells proliferation by 30 % while the other fraction could inhibits gingival fibroblast cells proliferation by 92%²².

As an intra canal medicament in endodontics

Chemo mechanical preparation is a pivotal step for infection control during root canal treatment. During the stages of cleaning and shaping, instrumentation, irrigation promotes microbial reduction¹⁰. Effectiveness of Curcumin against *E.faecalis* biofilm in root canals are studied and compared to that with sodium hypochlorite, Curcumin over comes the disadvantages of NaOCl includes unpleasant taste, toxicity, in ability to remove smear layer and limited anti bacterial activity, detrimental effect on dentin macrophages structural integrity, elasticity and flexural strength Future scope and research warranted that Curcumin can be used as an irrigant and intra canal – medicament¹⁰.

In precancerous lesions

Curcumin has its role in the treatment of various pre cancerous conditions like Oral submucous fibrosis, leukoplakia, oral lichen planus. Turmeric extract and oil have demonstrated oncopreventive activity in in vitro and in vivo animal experiments. Curcuminoids at doses of 6000 mg/d in 3 divided doses were well tolerated and may prove efficacy in controlling signs and symptoms of oral Lichen planus²³. Curcumin also holds a promising future in the treatment of oral submucous fibrosis.

CONCLUSIONS

Curcumin is considered a safe, non-toxic and effective alternative for many conventional drugs due to its distinguished therapeutic properties and multiple effects on various systems on the human body. Future research is required to determine the optimal dosage, bioavailability and bioefficacy of curcumin-based drugs. As the number of research studies on therapeutic effects of Curcumin keeps on increasing across the globe, it appears that Curcumin truly holds a promising future in therapeutic applications including dentistry.

REFERENCES

1. Chaturvedi TP. Uses of turmeric in dentistry: An update. *Indian J Dent Res* 2009;20:107-9.
2. Hatcher H, Planalp R, Cho J, Torti FM, Torti SV. Curcumin: from ancient medicine to current clinical trails. *Cell Mol Life Sci* 2008;65:1631-52.

3. Chattopadhyay I, Biswas K, Bandhopadhyay U, Banerjee R. Turmeric and curcumin: Biological actions and medicinal applications. *Current science* 2004;87:44-53.
4. Baum I and Ng A. Curcumin interaction with copper and iron suggests one possible mechanism of action in Alzheimer's disease animal models. *J Alzheimers Dis* 2004;6:367-77
5. Nagpal M, Sood S. Role of curcumin in systemic and oral health: An overview. *J Nat Sci Biol Med* 2013;4:3-7.
6. Mukhopadhyay A, Basu N, Ghatak N. Anti-inflammatory and irritant activities of curcumin analogues in rats. *Agents Actions* 1982;12:508-15
7. Abe Y, Hashimoto S, Horie T. Curcumin inhibition of inflammatory cytokine production by human peripheral blood monocytes and alveolar macrophages. *Pharmacol Res* 1999; 39: 41 -47.
8. Joe B and Lokesh BR. Role of capsaicin, curcumin and dietary n-3 fatty acids in lowering the generation of reactive oxygen species in rat peritoneal macrophages. *Biochim Biophys Acta* 1994;1224:255-63
9. Mortellini R, Foresti R, Bassi R, Green CJ. Curcumin, an antioxidant and anti-inflammatory agent, induces heme oxygenase-1 and protects endothelial cells against oxidative stress. *Free Radic Biol Med* 2000;28:1303-12.
10. Neelakantan P, Subbarao C, Sharma S, Subbarao CV, Garcia-Godoy F, Gutmann JL. Effectiveness of curcumin against *Enterococcus faecalis* biofilm. *Acta Odontologica Scandinavica* 2013;71:1453-7
11. Haukvik T, Bruzell S, Kristensen S, Tonnesen HH. Photokilling of bacteria by curcumin in selected polyethylene glycol 400 (PEG 400) preparations. *Studies on curcumin and curcuminoids*, XLI *Pharmazie* 2010;65:600-6.
12. Haukvik T, Bruzell S, Kristensen S, Tonnesen HH. A screening of curcumin derivatives for antibacterial phototoxic effects. *Studies on curcumin and curcuminoids*. XLIII. *Pharmazie* 2011;66:69-74.
13. Dovigo LN, Carmello JC, de Souza Costa CA, Vergani CE, Brunetti IL, Bagnato VS, Pavarina AC. Curcumin mediated Photodynamic Inactivation of *C. albicans* in a murine model of Oral Candidiasis. *Med Mycology* 2013;51:243-51.
14. Yeon KY, Kim SA, Kim YH, Lee MK, Ahn DK, Kim HJ, Kim JS, Jung JS, Oh SB. Curcumin produces an antihyperalgesic effect via antagonism of TRPV1. *J Dent Res*.2010;89:170-4.
15. Lawande SA. Therapeutic applications of turmeric (*Curcuma longa*) in dentistry: A promising future. *J Pharm Biomed Sci* 2013; 27: 586-591.
16. Lee KH, Kim BS, Keum BS, Yu HH, Kim YH, Chang BS, Ra JY, Moon HD, Seo BR, Choi NY, You YO. Essential oil of *Curcuma longa* inhibits *Streptococcus mutans* biofilm formation. *J Food Sci* 2011;76:226-30.
17. Antharjanm RSD, Anita B: Curcumin as a treatment modality in recurrent aphthous stomatitis. *Case Report. Kerala Dental Journal* 2009; 32: 206-208
18. Kumar P, Ansari SH, Ali J. Herbal remedies for the treatment of periodontal disease- a patent review. *Recent Patents on Drug Delivery & Formulation* 2009;3:221-8.
19. Waghmare PF, Chaudhary AU, Karhadkar VM, Jamkhande AS. Comparative evaluation of turmeric and chlorhexidine gluconate mouthwash in prevention of plaque formation and gingivitis: A clinical and microbiological study. *J Contemp Dent Pract*. 2011;12:221-2
20. Behal R, Mali MA, Gilda SS, Paradkar AR. Evaluation of local drug delivery system containing 2% whole turmeric gel used as an adjunct to scaling and root planning in chronic periodontitis: A clinical and microbiological study. *J Indian Soc Periodontol* 2011;15:35-8
21. Suhag A, Dixit J, Dhan P. Role of curcumin as a subgingival irrigant: a pilot study. *PERIO* 2007;4:115-21.
22. Niyomploy P, Thunyakitpisal P, Karchanatat A, Sangvanich P. Cell proliferative effect of polyxyloses extracted from the rhizomes of wild turmeric, *Curcuma aromatic*, *Pharmaceutical Biology* 2010;48:932-7.
23. Chainani-Wu N, Madden E, Lozzaada Nur F, Silverman S Jr. High dose curcuminoids are efficacious in the reduction in symptoms and signs of oral lichen planus. *J Am Acad Dermatol* 2012;66:752-60.