

The Effect of Curcumin (Turmeric) on Oral and Periodontal Diseases

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1. Introduction

Herbal medicines have been used for thousands of years in developing countries and more than 80% of population relies on their use for health care needs. Turmeric, neem, aloe Vera, clove, cinnamon are among the common herbal products used in dentistry, turmeric has been used traditionally as a remedy for skin, stomach, liver etc. Since turmeric has antimicrobial, Antioxidant and other useful properties, it is useful in dentistry also[1]

The most active part of turmeric named curcumin, its responsible for turmeric vibrant yellow color, first identified in 1910 by Lampe and Milobedzka[2].

Periodontal disease is One of the most common diseases affecting human race Prevalence rates range from 25 to 54 percent in gingivitis (early disease with no attachment loss) to 43 percent with chronic periodontitis determined by one or more sites of attachment loss [3] according to American Academy of Periodontology(2000)defined Chronic Periodontitis as, "inflammation of the gingiva extending into the adjacent attachment apparatus.The disease is characterized by loss of clinical attachment due to destruction of the periodontal ligament and loss of the adjacent supporting bone" [4]

Periodontitis is a bacterial initiated but host modulated chronic infection that leads to destruction of the connective tissue supporting the teeth [5]

Non – surgical therapy has been the main stay of periodontal disease management with mechanical removal of plaque being the predominant method, However the use of antimicrobial adjunctive treatment is widely investigated with minimum resistance and adverse effect.

This has led to renewed interest in the discovery of novel anti-infective natural compounds derived from turmeric [6] Curcumin has anti-inflammatory, antimicrobial and has action in suppressing the activity of Toll like receptor (TLRS) has initiated great interest in identifying and expanding its therapeutic potential in limiting the destruction in periodontitis [7]

Medicinal and Pharmacological Properties of curcumin

Anti-Inflammatory Effects

Curcumin has anti_ inflammatory effects via interrupting several inflammatory pathways [8] inhibits the production of the inflammatory cytokines tumor necrosis factor-alpha (TNF-a) interleukin(IL-1, -2, -6, -8, and -12),down-regulating the activity of cyclooxygenase-2 (COX-2),

lipooxygenase and inducible nitric oxide synthase (iNOS) enzymes.[9], curcumin regulates activation of certain transcription factors such as activating protein-1 (AP-1) and NF-κB in stimulated monocytes and alveolar macrophages, thereby blocking expression of cytokine gene expression. Down-regulation of intercellular signaling proteins, such as protein kinase C, may be another way in which curcumin inhibits cytokine production[10]

Anti-oxidant effects

Water-and fat-soluble extracts of turmeric and its curcumin component exhibit strong antioxidant activity, study of ischemia in the feline heart demonstrated that curcumin pre-treatment decreased ischemia-induced changes in the heart. Evaluating the outcome of curcumin by an *in vitro* study on endothelial heme oxygenase-1, an inducible stress protein, which was carried out by utilizing bovine aortic endothelial cells. Incubation (18 h) with curcumin ensued in intensified cellular resistance to oxidative damage[11]

Anti-microbial effects

Curcumin possesses antibacterial activity against periodontopathic bacteria and may be a potent agent for preventing periodontal diseases Curcumin inhibited the growth of *P. gingivalis*, *Prevotella intermedia*, *Fusobacterium nucleatum*, and *Treponema denticola* in a dose-dependent manner[12]

Hepatoprotective effects

Turmeric has been found to have a hepatoprotective characteristic by down-regulation of NF-transcription factorso an improvement of hepatic fibrosis in alcoholic [13]liver injuries[14], an increase of the survival rates in animals[15] and a reduction of damage in experimental steatohepatitis [16]

The herbal formulation comprising of *C. longa* and *Tinospora cordifolia* was found to prevent anti-tuberculosis treatment-induced hepatotoxicity significantly without causing any toxic effects [17]

Anti-carcinogenic effects

Curcumin has potential to hamper carcinogenesis at three stages: tumor promotion, angiogenesis, and tumor growth., Curcumin has also been found to have potential against head and neck cancer, which generally arises in the paranasal sinuses, nasal cavity, oral cavity, pharynx and larynx[18]

Cardiovascular effects

Turmeric's protective effects on the cardiovascular system include lowering cholesterol and triglyceride levels,

decreasing susceptibility of low density lipoprotein (LDL) to lipid peroxidation [19]

Antiplatelet aggregation effects

It has been shown to prevent platelets from clumping together, which in turn improves circulation. Inhibition of platelet aggregation by curcumin[20]

Gastrointestinal effects

On the gastrointestinal tract the constituents of *C. longa* has several beneficial effects. Bicarbonate, pancreatic enzyme, secretin, and gastrin, secretion enhanced by p-tolymethylcarbinol, a turmeric component and intestinal spasm reduced by sodium curcuminatate [21]

Effect of curcumin on macrophages

Macrophages play an important role in the immune system. They help the body to fight against foreign proteins and then effectively clear them. Curcuminoids enhance amyloid-beta uptake by macrophages of Alzheimer's disease patients[22]

Iron chelator

A study was conducted by Yan Jiao in 2005 to evaluate iron chelation in the biological activity of curcumin. Mice that were fed diets supplemented with curcumin exhibited a decline in levels of ferritin protein in the liver. These results suggest that iron chelation may be an additional mode of action of curcumin [23]

Skin wound healing

A study done at Baghdad college of dentistry by application of curcumin powder and essential oil on skin wound of rabbits and the histological examination observed good response and enhancement of wound healing [24]

2. Application of Curcumin in Dentistry

Relief from dental problems

Rinsing the mouth with turmeric water (boil 5 g of turmeric powder, two cloves and two dried leaves of guava in 200 g water) gives instant relief. Massaging the aching teeth with roasted ground turmeric eliminates pain & swelling. Applying the powder of burnt turmeric pieces and bishop's weed seed on teeth and cleaning them makes the gingiva and teeth strong.[1]

Pit and fissure sealant

It has been found that tinted pit and fissure sealant is useful for applying to tooth surfaces for the prevention or reduction of dental caries. This sealant can be produced from a composition comprising a polymerizable resin system containing acrylic monomer and at least one colorant selected from the group consisting of Annatto extract, turmeric extract and L-Apo-8-Carotenol [25]

Use of curcumin in dental- plaque detection system

Dental plaques are not easy to identify by the naked eye. So plaques are generally stained with dental-plaque staining agents, which contain dyes, to reveal their location. The dental-plaque detection system includes a dental-plaque staining agent, which contains turmeric extracts and curcumin; and a light-emitting apparatus, which gives out light having a wavelength within a range of 250 to 500 nm

to an object in the oral cavity where the dental-plaque staining agent is, attached [25]

Curcumin and Aphthous Ulcers

Manifar studied a randomized, two weeks double blind clinical study on patients between 18 and 65 years old, with minor Aphthous ulcers. Twenty eight- patients were randomly allocated to Curcumin gel containing (2% Curcumin) and 29 patients were allocated to placebo gel. The patients used the medication twice per day using a swap. After enrolment, the size of ulcers were measured by the investigator, and pain was evaluated by the patients based on Perceived Pain Rating Scale before drug application (day 0) and at days 4, 7, and 14. Patients overall satisfaction were assessed at the end of treatment. The results have shown that Curcumin gel significantly reduced pain intensity and size of aphthous ulcer compare to placebo[26]

Curcumin as a Treatment Modality in Recurrent Aphthous Stomatitis

Recurrent Aphthous Stomatitis (RAS) is an inflammatory condition of unknown etiology affecting the oral mucosa. Approximately 20% of the population suffers from RAS sometime in their lives. The disease mainly involves non-keratinized mucosal surfaces and is characterized by single or multiple painful ulcers with periodic recurrence and healing. Patients who used curcumin oil reported that ulcers started healing earlier than in previous attacks; there was also early reduction in pain. A followup for one year has shown no recurrence in these patients[27]

Curcumin as obturating material for primary teeth

Curcumin was able to demonstrate complete eradication of *E. faecalis* in a study conducted by [28] so it is used as obturating material in primary teeth[29]

The Anti-Adhesive Effect of Curcumin on *Candida albicans* Biofilms on Denture Materials

Curcumin Adsorption Reduces *Candida albicans* Adhesion, it has been shown that curcumin has the capacity to adsorb to denture relevant substrates and to inhibit *C. albicans* adhesion, rather than actively kill or inhibit the microorganisms.

Interestingly, *C. albicans* exposed to curcumin induced cellular aggregation, and the effect also reduced its adhesion capacity [30]

Curcumin and Mucositis

Patil evaluated the efficacy and safety of curcumin mouthwash in reducing the severity of signs and symptoms of radio-chemotherapy induced oral mucositis in cancer patients[31] Curcumin mouthwash was well tolerated and effective in controlling the signs and symptoms of induced oral mucositis[32]

3. Periodontal Application of Curcumin

Prevention of plaque formation and gingivitis

Waghmare Conducted a study on about 100 subjects, which were randomly selected. On 0, 14, and 21 days both plaque

index and gingival index were recorded. In addition to mechanical plaque control for the prevention of gingivitis, a very effective role of turmeric as well as chlorhexidine gluconate has been observed. When compared with chlorhexidine mouthwash, turmeric mouthwash, which was prepared by dissolving 10 mg of curcumin extract in 100 ml of distilled water and 0.005% of flavoring agent peppermint oil with pH adjusted to 4 was equally effective [33]

Another study by Mali Amita concluded that chlorhexidine gluconate as well as turmeric mouthwash can be effectively used as an adjunct to mechanical plaque control in prevention of plaque and gingivitis. Both the mouthwashes have comparable anti-plaque, anti-inflammatory, and antimicrobial properties. Turmeric mouthwash was biocompatible and well accepted by all the subjects without side effects [34]

Sub gingival irrigant

Suhag conducted a study in which periodontal sites were treated by scaling and root planning and later selected sites were irrigated (triple irrigation regimen) with chlorhexidine (0.2%), curcumin (1%), saline (0.9%), or control sites (non-irrigated). As a subgingival irrigant, the inflammatory signs were better resolved by 1% curcumin solution when compared to saline and chlorhexidine irrigation [35]

Curcumin gel

Curcumin gel containing 2% whole turmeric gel can be used as an adjunct to scaling and root planning. Curcumin gel has reduced gingival inflammatory signs and promotes healing with reduced pocket depth [36]

4. Curcumin Local Drug Delivery

Curcumin-loaded nanoparticles

A new promising approach has been reported by Mazzarino and co-authors developed mucoadhesive films containing nanoparticles loaded with Curcumin aiming to prolong the residence time of the dosage form in the oral cavity [37]

In addition to increase drug absorption through the buccal mucosa for the treatment of periodontal diseases that requires a sustained drug delivery Gottumukkla described a comparative study to evaluate the therapeutic efficacy of gold standard chlorhexidine (CHX) chips (Pericol-CG) and the developed local drug delivery module, indigenous curcumin (CU) based collagen as adjuncts to scaling and root planning in the nonsurgical management of chronic periodontitis. The clinical parameters - plaque index, gingival index, probing pocket depth (PPD), and clinical attachment level (CAL) of the selected target site were recorded prior to the placement of the drug at baseline, 1, 3 and 6 months post operatively. Subgingival plaque was analyzed for periodonto-pathological anaerobic microorganisms from the samples collected from the selected sites by using BANA reagent strip. The results demonstrated that, both the groups (CHX and CU) produced a significant reduction in all the clinical and microbiological parameters. However, at the end of the study period, CHX group showed greater improvement [38]

Influence on Human Gingival Fibroblasts

Antharjanm R study revealed apoptosis of human primary gingival fibroblasts (hPGF) cells at lower dose like 1, 10 and 25 μ M of curcumin but at higher doses like 50, 60, 75 and 100 μ M, was statistically significant high apoptosis was noted. They have also found that the effect of curcumin treated normal human fibroblasts and micro-vascular endothelial cells (hMVEC) using MTT assay and observed that lower doses of Curcumin stimulated the proliferation of normal human fibroblasts and hMVED, whereas higher doses inhibited it [39]

According to other authors Curcumin treated hPGF cells exhibited maximum and significant apoptosis at 75 μ M and showed decrease in cell population and shrinkage of cell size and morphologic alterations in basal cell carcinoma cells after treatment with 50 nM Curcumin & found cell shrinkage, disappearance of microvilli and appearance of membrane blebbing [40][41]

Curcumin Suppresses the Production of Interleukin-6 in *Prevotella intermedia* Lipopolysaccharide- Activated Raw 264.7 Cells

Periodontal disease is a chronic inflammatory process accompanied by destruction of surrounding connective tissue and alveolar bone, and sometimes loss of teeth [42] The primary causative agents of periodontal disease are particularly gram-negative anaerobic bacteria that accumulate in the gingival sulcus. *P. intermedia* is a major periodontal pathogen that is dominant in the subgingival flora of patients with adult periodontitis [43]

Acute necrotizing ulcerative gingivitis and pregnancy gingivitis [44]

Lipopolysaccharide (LPS) is a major component of the outer membrane of gram-negative bacteria, including *P. intermedia*. It can trigger a number of host cells to produce and release a wide variety of proinflammatory cytokines, including tumor necrosis factor alpha (TNF- α), IL-1 α , IL-6, and IL-8. LPS preparations extracted from oral black pigmented bacteria including *P. intermedia* have been reported to possess unique chemical and immunobiological properties quite different from those of the classical LPSs from the family *Enterobacteriaceae* such as *Escherichia coli* and *Salmonella* species [45]

According to Sung-Jo Kim curcumin strongly suppresses IL-6 production induced by LPS from *P. intermedia* in macrophages [46]

Surgical Wound Healing

Habiboallah performed a study to compare the effects of Curcuma longa – ghee formulation and hyaluronic acid on gingival wound healing following surgery in beagle dogs. A significant difference in the inflammatory and repair parameters of the healing process as regards to case treated with curcuma longa was observed. The results suggested a positive potential therapeutic effect on surgical wound healing particularly improvement of periodontal treatment consequences after surgery [47]

5. Conclusion

Turmeric, a rhizome of *Curcuma longa*, is an herb known for its medicinal properties and is a more acceptable option for a common man. *Curcumin* has been found to have antioxidant, anti-tumor, anti-inflammatory, antibacterial, antifungal properties, analgesic, anti-allergic and thus has a potential against various disease in the body and so that curcumin include in treatment of periodontal diseases it is found in many form like a mouth wash, irrigate material, local drug delivery.

Curcumin is safe, non-toxic, effective and economical alternative with no side effects for many traditional drugs used in oral infection and periodontal diseases. Mechanism of curcumin in modulating periodontal inflammation has shown to suppress or inhibits cytokines such as TNF-, IL-1, -2, -6, -8, -12., It also has shown to down regulate enzymes like the inducible nitric oxide synthase (iNOS), cyclooxygenase-2 (COX-2) (The main target of curcumin is NF- κ B whose modulation following Toll like receptor (TLR4) activation by lipopolysaccharide (LPS) could be the main mechanism involved in affecting periodontal disease. Some pathogens like *P. gingivalis* evade TLR4 and activate TLR2 for their protection. Curcumin can inhibit the activity of TLR2, 4 and 9 and would be potent to prevent excess connective tissue loss in periodontitis initiated by various pathogens.

It inhibits NF- κ B activation, matrix metalloproteinase (MMP-1, -9, -13) secretion. Curcumin was also found to decrease gene expression of mitochondrial DNA (mt DNA), and mitochondrial transcription factor A (Tfam). Thus, curcumin suppresses inflammation through multiple pathways.

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