CURCUMIN: A WONDER THERAPY FOR ORAL DISEASES

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ABSTRACT
Turmeric (Curcuma longa) is an ancient dye, flavouring and medical herb, widely used in Asian countries. It is a herb that has been used in Indian medicine, cookery, and cosmetics since a long time. Curcumin is a polyphenol derived from the Curcuma longa plant, which is commonly known as turmeric or Haldi in India. Curcumin is used extensively in Ayurvedic medicine for centuries, because of its nontoxic nature and has a variety of therapeutic properties including anti-oxidant, analgesic, anti-inflammatory and anti-septic activity. Also its anti-cancer effects are known now. This review article will highlight on the pharmacological actions and therapeutic role of this golden herb in dentistry.

KEYWORDS: Curcumin, Turmeric, Antioxidant, Dental infection.

INTRODUCTION
Turmeric is an ancient spice derived from rhizome ‘curcuma logna’. It is a perennial plant belonging to Zingiberaceae (ginger) family, popularly called as Haldi in India.[1] The components of turmeric are called as curcumoids which are comprised of curcumin (diferuloyl methane), demethoxycurcumin and bisdemethoxy curcumin. Curcumin was first isolated in 1815 and the chemical structure was recognised by Roughley and Whiting in 1973. Curcumin is cultivated in several parts of the Indian subcontinent as well as in South East Asia and South America. It is widely used in cookery as a spice herb, cosmetics, fabric dying and medicine for more than 2000 years.[2]

Chemistry and biological actions
It is soluble in ethanol and acetone but insoluble in water.[3] Curcumin(1,7-bis4-hydroxy-3-methoxyphenyl-1,6-heptadiene-3,5-Dione) is the most active polyphenolic constituent and is a powerful ingredient in the traditional herbal practices.[3] Curcumin has been used in Ayurveda since ages. In Ayurveda, it was used for the treatment of many medical probelms ranging from constipation to skin disease and in both Ayurvedic and Chinese medicine; it is used as a bitter digestive and carminative. In Unani, it is considered as blood purifier and safest herb of choice.[2] Curcumin exhibits therapeutic activity against a number of pathological processes mainly due to its chemical structure and unique physical and biological properties. It is believed that these chemical structural features are associated with the biological activity of curcumin. The o-methoxypheinol group and methylenic hydrogen are responsible for its antioxidant activity, and curcumin donates an electron/ hydrogen atom to reactive oxygen species.[4]

Biological activities of curcumin are as follows.
1. As an antioxidant
2. As an anti-inflammatory
3. As an immunomodulator
4. Anti tumorogenic
5. As a healing agent
6. As an antimicrobial agent
7. Antihelminthic property
8. Analgesic property
9. As an antifungal agent
10. Hepatoprotective effects
11. Cardioprotective effects

1. Antioxidant actions: following actions support the antioxidant role of curcumin[8,9,10]
   a. Curcumin is an effective scavenger of reactive oxygen species (ROS).
   b. It inhibits oxidative damage to the DNA
   c. It enhances the synthesis of glutathione which is an important intracellular antioxidant indirectly acting as an antioxidant.
d. It quenches the oxygen and makes it less available for oxidative reactions.
e. Curcumin interacts with oxidative cascade and prevents its outcome.
f. It has chelating action with iron and disarms it’s the oxidative properties.

2. Anti-inflammatory actions
a. Curcumin reduces the inflammatory mediators by regulating activation of transcription factors like activating protein-1 (AP-1) and NF-κB in stimulated monocytes and alveolar macrophages. Hence, blocking expression of cytokine gene expression.
b. Causes shrinkage by reducing inflammatory edema and vascular engorgement of connective tissues.
c. Lowers the levels of Histamine.
d. Increase the production of natural cortisone by adrenal glands.
e. Inhibits both biosynthesis of inflammatory prostaglandins from arachidonic acid and neutrophil function during inflammatory states.\(^\text{[11]}\)
f. They also reduce pain from arthritis, bursitis, tendonitis, stiffness of the joints.\(^\text{[2]}\)

3. As an immunomodulator: Curcumin increases the production of antibodies and enhances the proliferative capacity of T cells.\(^\text{[3]}\)

4. Anti tumorogenic actions
a. It induces cell cycle arrest and apoptosis.
b. Effects on biotransformation of enzymes involved in carcinogen metabolism as it inhibits tyrosine kinase c activity, inhibition of biotransformation of carcinogenesis & induction of Glutathione S transferase activity c. Inhibition of tumor invasion and metastasis.\(^\text{[12,13]}\) In addition, it causes suppression of inflammation, inhibition of cell proliferation, suppression of some oncogens, inhibition of transcription factors NF-KB & ap-1 suppressions of COX-2, inhibition of chromosomal damage, inhibition of tumor implantation.\(^\text{[14]}\)
c. It effectively inhibits metastasis (uncontrolled spread) of melanoma and may be especially useful in deactivating the carcinogens in cigarette smoke and chewing tobacco.\(^\text{[15]}\)

5. As a healing agent
Curcumin treated wounds were found to heal much faster as it shows improved rates of epithelialisation, wound contraction and increased tensile strength.\(^\text{[4]}\)

6. Curcumin as an antimicrobial agent
Curcumin and the oil fraction inhibits the growth of variety of bacteria like Streptococci, Staphylococci, Lactobacillus, etc and it also prevents Helicobacter pylori CagA + strains in vitro.\(^\text{[16]}\)

7. Antihelminthic property: Curcumin has anti-leishmania activity. (Koide et al. 2002)\(^\text{[5]}\)

8. As an Analgesic
The powdered form of the rhizome is effective in the treatment of sprain and inflammation (Khare, 2000). Turmeric paste mixed with a lime and applied hot, is a popular application to sprains (Nadkarni, 1976).\(^\text{[6]}\)

9. As an antifungal agent
Curcumin and materials derived from curcuma longa rhizomes have antifungal actions against several plant pathogenic fungi. Fungicidal actions of curcumin are comparable to that of the fungicidal agent chlorothalonil.\(^\text{[7]}\)

10. Hepatoprotective effects
Turmeric’s hepatoprotective effect is mainly a result of its antioxidant properties, as well as its ability to decrease the formation of pro inflammatory cytokines.\(^\text{[7]}\) Turmeric is effective in treating jaundice and is recommended in the diet of patients suffering from jaundice or even infective hepatitis.\(^\text{[5]}\)

11. Cardioprotective effects
Protective effect of turmeric on the cardiovascular system is because of its action of lowering the triglyceride and cholesterol levels to decline the susceptibility of low-density lipoprotein (LDL) to lipid peroxidation, and also hampers platelet aggregation. These effects are visible even with low doses of turmeric. The reason for Turmeric extract’s effect on cholesterol levels is thought to be due to increased transformation of cholesterol to bile acids in the liver and reduced cholesterol uptake in the intestines. Platelet aggregation Inhibition by curcumin is via potentiation of prostacyclin synthesis and inhibition of thromboxane synthesis.\(^\text{[7]}\)

Therapeutic applications in dentistry
\[ \text{d. Rinsing the mouth with turmeric water (boil 5 g of turmeric powder, two cloves and two dried leaves of guava in 200 g water) gives instant relief.} \]
\[ \text{e. Massaging the paining teeth with roasted turmeric powder reduces pain & swelling.} \]
\[ \text{f. Use of the powder of burnt turmeric and bishap weed seed on teeth and cleaning them makes the gums and strong teeth.} \]
\[ \text{g. Applying a paste made from 1 tsp of turmeric with ½ tsp of salt and ½ tsp of mustard oil provides relief from gingivitis and periodontitis. These are some of the ways of obtaining relief from dental problems by using turmeric that are reported in the literature.} \]

1. In Periodontal diseases
\[ \text{a. Prevention of plaque formation and gingivitis: Bhandari & Shankwalker used curcumin in the form of mouthwash and found it to be an effective anti-inflammatory agent. Curcumin has been found to possess antimicrobial property. It has been suggested that curcumin may be used as an alternative antimicrobial agent against severe bacterial infections.} \]
\[ \text{Mali Amitha in 2012 also concluded that turmeric mouthwash can be} \]
effectively used as an adjunct to mechanical plaque control methods in prevention of plaque and gingivitis.\(^{[19]}\)

b. As a subgingival irritant: Curcumin 1% as subgingival irrigant resulted in significant reduction in bleeding on probing and redness in comparison with chlorhexidine and saline group as an adjunctive therapy in periodontitis.\(^{[20,21]}\) It results resolution of inflammatory signs than chlorhexidine and saline irrigation, by selectively reducing the inflammatory mediators and by reducing inflammatory oedema and vascular engorgement of connective tissues causing shrinkage.\(^{[22]}\) It is also used as Dental – Plaque detection system.\(^{[23]}\)

**Dosage and form of curcumin used in periodontal diseases.**\(^{[4]}\)

- **Topical application:** 1 tsp of turmeric +1/2 tsp of salt +1/2 tsp mustard oil- Useful in Gingivitis and Periodontitis
- **Mouth wash:** 10 mg curcumin extract in 100 ml distilled H2O +0.005% peppermint – Reduces the microbial count and also has anti-inflammatory action
- **Local drug delivery system:** 2 % whole turmeric- Decreases gingival and plaque index, also improving pocket depth and relative attachment loss
- **Subgingival irrigant:** 1 % curcumin solution- useful because of its Anti-inflammatory actions.\(^{[4]}\)

2. Pit & Fissure Sealant

Pit and fissure sealants are normally used in children to prevent development of dental caries. The use of curcumin performs two roles in that, it gives a color tint to the pit and fissure sealant. Furthermore, it being antibacterial also prevents caries. These formulations contain a resin and in addition may contain extracts of other agents apart from curcumin.\(^{[2]}\) This sealant is comprising of 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.\(^{[23]}\)

3. Anticariogenic agent

The inhibitory effects of Curcuma longa on the cariogenic property of Streptococcus mutans is seen at concentrations from 0.5 to 4 mg/ml. And also exhibits the significant inhibition of S.mutans adherence to saliva coated hydroxylapatite beads and inhibited the formation of S.mutans at concentrations higher than 0.5 mg/ml.(24,25)

4. As an intracanal medicament in endodontics

Chemo mechanical preparation is an important step for infection control during root canal treatment. 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 including unpleasant taste ,toxicity, in ability to remove smear layer and limited antibacterial activity, detrimental effect on dentin macrophages structural integrity, elasticity and flexural strength.\(^{[26]}\)

5. Curcumin in treatment of precancerous lesions and conditions

a. In oral lichen planus: Pathogenesis of the OLP involves the cell mediated immunity to secondary antigenic change in oral mucous membrane where the host cells and antigen presenting langerhans cells seems to be the key cellular elements in the progression of the lesion. Curcumin has shown immunomodulatory effect involving activation of host macrophages and natural killer cells and modulation of lymphocytes mediated function.\(^{[27]}\)

b. Role of curcumin in OSMF: Myofibroblasts which are the activated fibroblasts have a major role in morphogenesis, oncogenesis, inflammation, wound healing and fibrosis. It is a consistent feature of fibrotic diseases like oral submucous fibrosis. Studies have proved that curcumin is used as a treatment modality in OSMF because of its following actions.

- It inhibits the proliferation of fibroblasts as well as myofibroblasts hence, reducing further fibrosis
- Inhibits cell cycle arrest in myofibroblast.
- Decreases the Bcl-2/Bax ratio in myofibroblasts intum inducing apoptosis in myofibroblast.
- Decreases the generation of type I and type III collagen in myofibroblasts.\(^{[28]}\)

6. Curcumin in oral cancer as a chemopreventive agent: Curcumin is an effective chemopreventive agent because of its anti-oxidative and anti-inflammatory, anti-cancerous effects. They carry this out by inducing cell cycle arrest and apoptosis, interrupting the NF-KB signaling at multiple levels, Inhibiting tumor invasion and neovascularization. Curcumin also inhibits deregulated cellular proliferation, de-differentiation and progression.\(^{[4,29]}\)

7. In Recurrent Aphthous Stomatitis: Curcumin gel is found to reduce pain intensity and size of aphthous ulcer.\(^{[7]}\)

8. Influence of Curcumin on Human Gingival Fibroblasts: Many studies have also shown apoptosis of human primary gingival fibroblasts (hPGF) cells at lower dose like 1, 10 and 25μM of curcumin but at higher doses like 50, 60, 75 and 100μM, was statistically significant high apoptosis was noted.\(^{[23]}\)

The disadvantages of curcumin are as follows.

- It has a lower bioavailability with high rate of metabolism leading to its rapid elimination from the body.
- It has a dose and time dependent induction of chromosomal aberrations
- Toxicity and carcinogenic properties of curcumin called turmeric oleorism.
• Curcumin which is an active chelator of iron, can also induce a state of overt iron deficiency anaemia.[100]

The negative effects of curcumin are probably mediated by its pro-oxidant properties like, formation of reactive oxygen species such as superoxide anion and hydrogen peroxide which can have inductive effects on malignant transformation of cells.

CONCLUSION
Curcumin is a safe, natural, non-toxic and effective alternative for many conventional drugs due to its diverse therapeutic properties and wide range of effects on various body systems. The only obstacle in using of curcumin is its lower bioavailability and its pro-oxidant properties like tendency of forming reactive oxygen species. Future research is required to determine the optimal dosage and efficacy as a therapeutic drug. But, Curcumin truly has a promising future for therapeutic applications in various fields including dentistry.

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