

## CURCUMA LONGA IN THE MANAGEMENT OF INFLAMMATORY DISEASES – A REVIEW

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### ABSTRACT

*Curcuma longa* (turmeric) has a long history of use in Ayurvedic medicine as a treatment for inflammatory conditions. Turmeric constituents include the three curcuminoids: curcumin (diferuloylmethane; the primary constituent and the one responsible for its vibrant yellow color), demethoxycurcumin, and bisdemethoxycurcumin, as well as volatile oils (tumerone, atlantone, and zingiberone), sugars, proteins, and resins. While numerous pharmacological activities, including antioxidant and antimicrobial properties, have been attributed to curcumin, this article focuses on curcumin's anti-inflammatory properties and its use for inflammatory conditions.

This property of curcumin acting as anti inflammatory has been taken under consideration to treat the inflammatory response of gums with positive results according to various studies.

**Keywords:** Curcuma longa, Gingivitis, Periodontitis, Herbal medicine, Ayurveda

### INTRODUCTION

Curcumin is the active ingredient in the herbal remedy and dietary spice turmeric (*Curcuma longa* Linn). Curcumin was identified to be responsible for most of the biological effects of turmeric.<sup>28</sup> Turmeric in English, Haridra in Sanskrit, Haldi in Hindi, Paspu in Telugu, Manjal in Tamil, Halada in Gujarati, Halade in Marathi, Mannal in Malayalam and Arishina in Kannada. Turmeric (*Curcuma longa*) is native to tropical South Asia and needs a considerable amount of annual rainfall to thrive. Turmeric is a sterile plant and does not produce seed. It is thought to

have arisen by selection and vegetative propagation of a hybrid between turmeric, native India, Sri Lanka, eastern Himalayas and some other closely related species. The whole plant of turmeric mainly rhizomes, roots and leaves are used for medicinal purposes.<sup>1</sup> Fig. 1

This ancient remedy is used to treat dental diseases, digestive disorders such as dyspepsia and acidity, indigestion, flatulence, ulcers, as well to alleviate the hallucinatory effects of hashish and other psychotropic drugs. Fig.2

### Botanical classification<sup>1</sup> of curcumin:

Kingdom	Plantae – Plants
Subkingdom	Tracheobionta
Superdivision	Spermatophyta
Division	Magnoliophyta
Class	Liliopsida
Subclass	Zingiberidae
Order	Zingiberales
Family	Zingiberaceae
Genus	Curcuma

### HISTORY

In the latter half of the 20th century, Curcumin was identified as responsible for most of the biological effects of turmeric. The exact origin of turmeric or species is not known but it originates from south or south East Asia, most probably from western India. Turmeric is a sterile plant and does not produce seed.

It is thought to have arisen by selection and vegetative propagation of a hybrid between turmeric, native India, Sri Lanka and the eastern Himalayas and some other closely related species. It is commonly distributed in stream banks in marshy places.<sup>2</sup> Turmeric has been cultivated in India, from very ancient times for its cultivation. The crop cannot stand water logging or alkalinity in the soils. The largest supplies of turmeric are obtained from Guntur district of Andhra Pradesh. Orissa is the next important growing area for turmeric where production is concentrated in the districts of Annam, Phulbani and Karaput in Maharashtra, the main centres of turmeric production are in Gujarat and Khandesh districts, Tiruchirapalli, Salem and Coimbatore districts of Tamilnadu are also important turmeric growing areas. Other important states for this crop are Uttar Pradesh, west Bengal, Rajasthan and the Punjab. The total average under turmeric in India has been estimated variously from 60,000 to 1,

00,000 acres and the production is nearly 1, 00,000 tonnes of rhizomes per annum.<sup>3</sup>



Fig. 1 Whole Plant of Curcumin



Fig. 2 Forms of Curcumin

### COMPOSITION

Turmeric contains a number of phytoconstituents namely (6.3%) of proteins, (5.1%) of fat, (3.5%) Minerals, (5%) of diaryl heptanoid colouring material known curcuminoids. Volatile oil (5%), Sesquiterpenes (25%) (alcohols and ketones), Monoterpenes. Rhizomes contain free Arabinose (1%), Fructose (12%), Glucose (2%), Zingiberous starch grains (it was 30-60  $\mu$ m long). The rhizomes contain curcuminoids, curcumin, demethoxy curcumin, bis-demthoxycurcumin, 5-methoxycurcumin and dihydrocurcumin which are found to be natural antioxidants. A new curcuminoid, cyclocurcumin, was isolated from the nematocidally active fraction of turmeric. The fresh rhizomes also contain two new natural phenolics which possess antioxidant and anti-inflammatory

activities and also two new pigments. Several sesquiterpenes, germacrone, turmerone, ar-(+)-, a-, -turmerones, -bisabolene, a-curcumene, zingiberene, -sesquiphellandene, bisacurone, curcumenone, dehydrocurdinone, procurcumadiol, bis-acumol. curcumenol, isoprocurcumenol, epiprocurcumenol, procurcumadiol, zedoaronediol, curlone, and turmeronol A and turmeronol B, have been recorded from the rhizomes. The rhizomes are also reported to contain four new polysaccharides- unkonas – having activity on the Reticuloendothelial system, along with stigmasterol, -sitosterol, cholesterol and 2-hydroxymethyl anthraquinone.

The essential oil from the rhizome contains d-a-phellandrene, d-sabinene, cineol, borneol, zingiberene, sesquiterpenes (turmerones). The crystalline colouring matter, curcumin, is diferuloyl methane. It dissolves in concentrated sulphuric acid giving yellow-red coloration.<sup>1</sup>

Pharmacokinetic studies in animals have demonstrated that 40-85 percent of an oral dose of curcumin passes through the gastrointestinal tract unchanged, with most of the absorbed flavonoid being metabolized in the intestinal mucosa and liver. Due to its low rate of absorption, curcumin is often formulated with bromelain for increased absorption and enhanced anti-inflammatory effect.<sup>4</sup>

### **CURCUMIN PROCESSING**

Curcumin is extracted from the dried root of the rhizome *Curcuma Longa*. The process of extraction requires the raw material to be ground into powder, and washed with a suitable solvent that selectively extracts colouring matter. This process after distillation of the solvent yields an oleoresin with colouring matter content in the region of 25-35 percent

along with volatile oils and other resinous extractives. The oleoresin so obtained is subjected to further washes using selective solvents that can extract the curcumin pigment from the oleoresin. This process yields a powdered, purified food colour, known as curcumin powder, with over 90 percent colouring matter content and very little volatile oil and other dry matter of natural origin.<sup>5</sup>

### **ABSORPTION OF CURCUMIN**

Animal studies have shown curcumin is rapidly metabolized, conjugated in the liver, and excreted in the feces, therefore having limited systemic bioavailability. A 40 mg/kg intravenous dose of curcumin given to rats resulted in complete plasma clearance at one hour post dose. An oral dose of 500 mg/kg given to rats resulted in a peak plasma concentration of only 1.8 ng/mL, with the major metabolites identified being curcumin sulfate and curcumin glucuronide.<sup>6</sup>

Data on the pharmacokinetics, metabolites, and systemic bioavailability of curcumin in humans, mainly conducted on cancer patients, are inconclusive.

A phase I clinical trial conducted on 25 patients with various precancerous lesions demonstrated oral doses of 4, 6, and 8 g curcumin daily for three months yielded serum curcumin concentrations of only  $0.51 \pm 0.11$ ,  $0.63 \pm 0.06$ , and  $1.77 \pm 1.87 \mu\text{M}$ , respectively, indicating curcumin is poorly absorbed and may have limited systemic bioavailability. Serum levels peaked between one and two hours post-dose and declined rapidly. This study did not identify curcumin metabolites and urinary excretion of curcumin was undetectable.<sup>7</sup>

Another phase I trial, involving 15 patients with advanced colorectal cancer, used curcumin at doses between 0.45 and

3.6 g daily for four months. In three of six patients given the 3.6 g dose, mean plasma curcumin measured after one hour on day 1 was  $11.1 \pm 0.6$  nmol/L. This measurement remained relatively consistent at all time points measured during the first month of curcumin therapy. Curcumin was not detected in the plasma of patients taking lower doses. Glucuronide and sulfate metabolites of curcumin were detected in plasma of all six patients in the high-dose group at all measurement points in the study.<sup>8</sup> Curcumin levels reported in this study are approximately 1/45 of the levels reported by Cheng et al, who used a similar dose of curcumin (4 g).<sup>8</sup> The reason for the discrepancy is unclear.

While systemic distribution of curcumin tends to be low, Garcea et al demonstrated that 3.6 g curcumin given to 12 patients with varying stages of colorectal cancer for seven days resulted in pharmacologically efficacious levels of curcumin ( $12.7 \pm 5.7$  nmol/g) in both malignant colorectal tissue and normal colorectal tissue ( $7.7 \pm 1.8$  nmol/g), perhaps accounting for the anti-inflammatory benefits of curcumin observed in diseases of the gastrointestinal tract.<sup>9</sup>

Although research on curcumin pharmacokinetics in healthy subjects is limited, one study using high doses (10 and 12 g in a single oral dose) in 12 healthy subjects measured serum curcumin as well as its sulfate and glucuronide metabolites at various time points up to 72 hours post-dose. As in previous studies, curcumin was rapidly cleared (only one subject had detectable free curcumin in the serum) and subsequently conjugated in the gastrointestinal tract and liver. Area under the curve (AUC) for curcumin conjugates was surprisingly higher ( $35.33 \pm 3.78$

$\mu\text{g/mL}$ ) for the 10-g dose than for the 12-g dose ( $26.57 \pm 2.97$   $\mu\text{g/mL}$ ), perhaps indicating saturation of the transport mechanism in the gut for free curcumin. Maximum serum concentration ( $C_{\text{max}}$ ) for the 10-g dose was  $2.30 \pm 0.26$   $\mu\text{g/mL}$  compared to  $1.73 \pm 0.19$   $\mu\text{g/mL}$  for the 12-g dose.<sup>10</sup>

Because of curcumin's rapid plasma clearance and conjugation, its therapeutic usefulness has been somewhat limited, leading researchers to investigate the benefits of complexing curcumin with other substances to increase systemic bioavailability. One substance that has been studied is the alkaloid piperine, a constituent from black pepper and long pepper (*Piper nigrum* and *Piper longum*, respectively). In humans 20 mg piperine given concomitantly with 2 g curcumin increased serum curcumin bioavailability 20-fold, which was attributed to piperine's inhibition of hepatic glucuronidation and intestinal metabolism.<sup>11</sup>

Another method currently being investigated is complexing curcumin with a phospholipid, known as a phytosome. The phosphatidylcholine-curcumin complex (Meriva) is more readily incorporated into lipophilic cell membranes, making it significantly more bioavailable than unbound curcumin. In rats, peak plasma concentration and AUC were five times higher for Meriva than for unbound curcumin.<sup>14</sup> One small unpublished, single-dose trial demonstrated 450 mg of Meriva curcuminoids complexed with phosphatidylcholine was absorbed as efficiently as 4 g unbound *Curcuma longa* (95% curcumin), reflecting a significant increase in bioavailability for Meriva complex.<sup>12</sup>

## PROPERTIES OF CURCUMIN

Turmeric plant has several benefits in medical as well traditional medicines like ayurvedic and unani medicines. It has found application in canned beverages, baked products, dairy products, ice cream, yogurt, yellow cakes, orange juices, biscuits, popcorn colour, sweets, cake icings, cereals, sauces, gelatin, etc. It is significant ingredient in most commercial curry powders. In ayurvedic medicine used as readily available antiseptic for cuts, burns and brushes and used in cosmetics preparation. It is also used as poor fabric dye, commercially in Indian clothing, such as saris. Turmeric plant extract should have like anti-inflammatory, anti-arthritis, anti oxidant, anti-microbial, anti-leishmanial, hepato protective, anti-cancer, anti-ulcer and anti diabetic.<sup>1</sup> Fig. 3

**1. Anti inflammatory agent:-** The volatile oil and also the petroleum ether, alcohol and water extracts of *C. longa* show anti-inflammatory effects. The suppression of activation of transcription factors like NF- $\kappa$ B which regulates most of the proinflammatory gene expression. Down regulation of activity and synthesis of cyclo oxygenase-2 (COX-2).

**2. Anti-cancer activity:-**The effect of Curcumin, Chlorogenic acid, Caffeic acid and Ferulic acid on tumour promotion in mouse skin by 12-O-tetradecanoyl-13-acetate (TPA), observed that all these compounds inhibit the epidermal ornithine decarboxylase (ODC) and epidermal DNA synthesis, being curcumin the most efficient. Curcuma has chemopreventive and chemo protective action. Anti cancer activity of curcuma is by inhibiting tumour cell proliferation, induction of apoptosis, inhibition of transformation of normal cells to tumour cells and inhibition of invasion of metastasis.

**3. Role in arthritis :-** Different in vitro and clinical studies with curcumin suppresses symptoms associated with arthritis by suppressing TNF production and blocking action of TNF topical application of curcumin also shows activity for arthritis. The cytokine macrophage migration inhibitory factor (MIF) has recently emerged as a crucial factor in the pathogenesis of rheumatoid arthritis.

**4. Role in diabetes:-** Administration of ethanolic extract of curcuma in animals reduces blood sugar level, Haemoglobin and glycosylated haemoglobin levels. Curcumin also reduces oxidative stress in diabetic induced rats having increased NADPH/NADP ratio as well as increased activity of oxidative enzymes. Curcumin prevents galactose-induced cataract formation at very low doses.

**5. Role in cardiovascular diseases:-** Ethanolic extract of curcuma helps in prevention of myocardial infarction, cardio toxicity and atherosclerosis. Oral administration of curcumin significantly decreases the lipid peroxides (33%), increased HDL cholesterol (29%), decreased total serum cholesterol (11-12%).

**6. Anti ulcer activity: -** An oral dose of the ethanolic extract of turmeric produced significant antiulcerogenic activity subjected to hypothermic-resistant stress and pyloric ligation. The extract had highly significant protective effect against cytodestructive agents.

**7. Anti oxidant activity:-** Curcumin is the natural anti oxidant from turmeric, an Indian spice, and its derivatives have significant abilities to protect plasmid Pbr 322 DNA against single strand breaks induced by singlet oxygen, a reactive oxygen species with genotoxic/mutagenic properties. The observed anti oxidant



activity was both time and concentration dependent. Curcumin can significantly inhibit the generation of reactive oxygen species (ROS) like superoxide anions, H<sub>2</sub>O<sub>2</sub> and nitrite radical generation by activated macrophages, which play an important role in inflammation. It acts as a scavenger of oxygen free radicals. It can protect haemoglobin from oxidation.

**8. Alzheimer's disease:** - Alzheimer's disease involves amyloid (A $\beta$ ) accumulation, oxidative damage and inflammation. The phenolic yellow curry pigment curcumin has potent anti-inflammatory and antioxidant activities and can suppress oxidative damage, inflammation, cognitive deficits, and amyloid accumulation. Curcumin reduces amyloid levels and plaque burden. Hence, curcumin directly binds small amyloid species to block aggregation and fibril formation in vitro and in vivo.

**9. Antivenom activity:** - potent antivenom was tested against snakebite. The fraction consisting of ar-turmerone, isolated from *C. longa* L., neutralized both the hemorrhagic activity and lethal effect of venom in mice. In this study ar-turmerone was capable of abolishing the hemorrhagic activity of *Bothrops* venom and about 70% of the lethal effect of *Crotalus* venom. Ar-turmerone can act as an enzymatic inhibitor in the case of venom enzymes, with proteolytic and hemorrhagic activities.<sup>1</sup>

**10. Curcumin in dentistry:** - Curcumin can be used in following ways offer relief from dental problems.

-Rinsing the mouth with turmeric water (boil 5g of turmeric powder, two cloves, and two dried leaves of guava in 200g water) gives instant relief.

-Massaging the aching teeth with roasted, ground turmeric eliminates pain and swelling.

-Applying the powder of burnt turmeric pieces and bisop's weed seed on the teeth and cleaning them makes the gums and teeth strong.<sup>13</sup>



Fig.3 Properties of Curcumin

### 11. Curcumin in Periodontal diseases :-

Anti-inflammatory property and wound healing property of Curcumin by virtue of which it reduces the inflammatory mediators generated via arachidonic acid pathway and causes shrinkage by reducing inflammatory oedema and vascular engorgement of connective tissue. It also promotes migration of various cells including fibroblasts in wound bed and thus results in reduction of vascularization by bringing about fibrosis of connective tissue. Curcumin promotes migration of epithelial cells to wounded sites by promoting localization of TGF-1 thus helping re-epithelization. Trend for reduction in pocket depth and gain in relative attachment levels by curcumin can be contributed to ability of curcumin in enhancing regeneration after traumatic injury. Curcumin also showed a significant reduction in *Porphyromonas gingivalis*, *Porphyromonas intermedia*, *Fusobacterium species* count. It has antibacterial action against various microorganisms.<sup>14</sup>

Applying a paste made from 1 tsp of turmeric with half tsp of salt and half tsp of mustard oil provides relief from gingivitis and periodontitis. Rub the teeth and gums with this paste twice daily.<sup>13</sup>

## CONCLUSION

The plant *curcuma longa* has several significant biological activities and chemical compounds like curcuminoids, volatile oils and sugars. The extracts should be carried from different parts like rhizomes, roots, leaves and whole plant is used.

*Curcuma longa* (turmeric) has a long history of use in Ayurvedic medicine as a treatment for inflammatory conditions. Turmeric constituents include the three curcuminoids: curcumin (diferuloylmethane; the primary constituent and the one responsible for its vibrant yellow color), demethoxycurcumin, and bisdemethoxycurcumin, as well as volatile oils (tumerone, atlantone, and zingiberone), sugars, proteins, and resins. While numerous pharmacological activities, including antioxidant and antimicrobial properties, have been attributed to curcumin, this article focuses on curcumin's anti-inflammatory properties and its use for inflammatory conditions.

This property of curcumin acting as anti inflammatory has been taken under consideration to treat the inflammatory response of gums with a positive results according to various studies.

The most important goal of periodontal therapy is to arrest the inflammatory disease process, and to maintain periodontal health. Scaling and root planning has been shown to be effective in resolving inflammation, reducing pocket depth and gaining periodontal attachment levels. Although

mechanical therapy significantly decreases the load of subgingival micro-organisms, it does not necessary eliminate all pathogens.

Several antimicrobial and antiseptic agents, delivered by rinsing, irrigation, systemic administration and local drug delivery systems have been used to overcome the limited efficacy of conventional therapy.

This review will help to further explore the medical potential and efficacy of curcumin in general and dental health.

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