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Turmeric - The Serendipitous Herb : A Review

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ABSTRACT

Phytotherapy, the use of herbal agents as medicines has become the focus of research in the recent years. This increased interest in the discovery of natural compounds is due to the various adverse effects of allopathic drugs and emergence of resistant strains of common pathogens. Turmeric or curcumin is one of the oldest spices that has been a vital part of Ayurvedic medicine, and has proven properties like anti-inflammatory, anti-oxidant, anti-microbial, antiseptic and antimutagenic properties making it a very viable and economical substitute. The objective of this article is to provide a brief overview of the plethora of research regarding the health benefits of curcumin and its uses in dentistry.

Key words: *Dry Eye Syndrome, Tarpana, Shatavarighrita, Shushkakshipaka.*

INTRODUCTION

The frequent use and most importantly misuse of the therapeutic agents and drugs have led to the rise of resistant strains of common pathogens not to mention increased incidence of adverse effects associated with their usage. Hence, the search for an alternative continues, and natural phytochemicals used as traditional medicines are considered as a good alternative source.

Turmeric (*haldi*), originally from India is a rhizome herbaceous perennial plant of *Curcuma longa*. Its Latin name is derived from Persian word, *kirkum* meaning saffron in reference to the yellow-orange colour of the spice. Curcumin has been used extensively in Ayurvedic medicine and as a home remedy measure for centuries. As it is non-toxic and has a variety of therapeutic properties like being an antioxidant, anti-inflammatory, antiseptic and anticarcinogenic because of which it has been gaining popularity in modern medicine and dentistry.[1],[2]

Turmeric can play a crucial role in dentistry as a naturoceutical agent in treating periodontal diseases and oral cancer and can be used in pit and fissure sealant, mouthwash, subgingival irrigant, local irrigant delivery system and in other endodontic applications.

Common Name: Turmeric / Turmeric root / Indian saffron.

Latin Name: *Curcuma aromatica, Curcuma domestica, Curcuma longa*

History:

Turmeric has been used as a medicine for more than 2500 years in Ayurveda, Unani, Siddha and Chinese medicine.

Marco Polo mentioned about turmeric in his writings of 1280 journey to China and India and it was first introduced to Europe in the 13th century by Arab traders. During 15th century, after Vasco de Gama's visit to India, spices were introduced to the West. It was during the rule of British in India that turmeric

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was combined with various other spices and renamed "Curry powder," as it is called in the West.[3]

Chemical Properties

In 1815, Roughley isolated *C. longa* while its chemical structure was determined in 1973 by Whiting. The structure has 2 aromatic rings are connected by two α-α-unsaturated carbonyl groups.

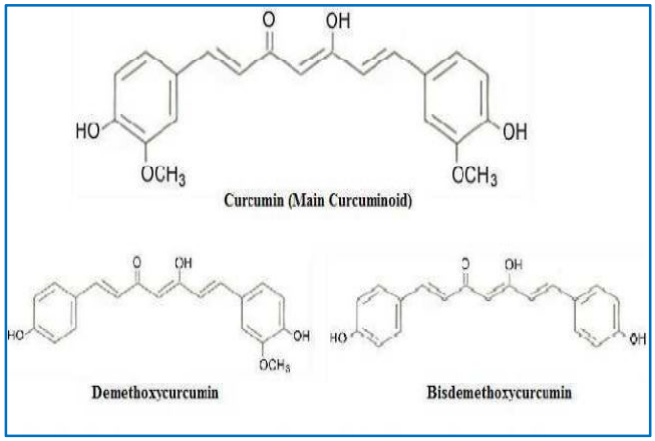

Figure 1: Structures of Curcumin (Diferuloylmethane), Demethoxy curcumin, and Bisdemethoxy curcumin.[3]

Components of turmeric is named curcuminoids, which include mainly (Figure 1)

- Curcumin/diferuloyl methane (1,7-bis(4-hydroxy-3-methoxyphenyl)-1, 6-heptadiene-3,5-dione)
- Demethoxycurcumin
- Bisdemethoxycurcumin and
- Various volatile oils including tumerone, atlantone and zingiberone.

Active constituent of turmeric is curcumin or diferuloylmethane (3-4%), this acts as the key ingredient in turmeric that adds to its medicinal values. The curcumin found is comprised of 3 types - Curcumin I (94%), curcumin II (6%) & curcumin III (0.3%).[4-6]

Turmeric contains protein (6.3%), fat (5.1%), minerals (3.5%), carbohydrates (69.4%) and moisture (13.1%).[7]

Curcumin with a melting point of 184°C is a lipophilic polyphenol that is nearly insoluble in water but is quite stable in the acidic pH of the stomach. They also exist as keto-enol tautomer.[3]

Most recent available preparation of curcumin includes approximately of 77% diferuloylmethane, 18% demethoxy curcumin, 5% bis-demethoxy curcumin.[3,8]

Pharmacokinetics

Curcumin has poor oral bioavailability because of its poor intestinal absorption, high metabolic rate and rapid elimination from the body. About 40-80% of curcumin given in the oral route passes through the gastrointestinal tract unchanged, with most of the absorbed flavonoid being metabolized in the intestinal mucosa and liver. To compensate for the poor absorption, curcumin is often formulated with bromelain or piperine (the major active component of black pepper) which in turn increases the bioavailability of curcumin by 2000%. Curcumin is fat soluble, so when taken with a fatty meal increases its absorption.[9-13]

Dosages

Curcuminoids have been approved by the US Food and Drug Administration (FDA) as "Generally Recognized As Safe" (GRAS), good tolerability and safety profiles have been shown by clinical trials, even at doses between 4000 and 8000 mg/day and of doses up to 12,000 mg/day of 95% concentration of three curcuminoids: curcumin, bisdemethoxy curcumin and demethoxy curcumin.[14],[15]

According to JECFA (The Joint United Nations and World Health Organization Expert Committee on Food Additives) and EFSA (European Food Safety Authority) reports, the Allowable Daily Intake (ADI) value of curcumin is 0–3 mg/kg body weight.[5]

Currently available preparations of curcumin are in capsule form for oral administration and oil form for topical application.[16]

Therapeutic actions of Turmeric

There are a wide range of therapeutic actions of curcumin.

- Antioxidant as it protects against free radical damage.[17]

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- Anti-inflammatory[8]
- Hepatoprotective[18]
- Antimicrobial[19,20]
- Anti-platelet action by preventing the clumping of platelets.[21]
- Antimutagenic action by inhibiting metastasis especially in deactivating the carcinogens in cigarette smoke and chewing tobacco.[22,23]
- Curcumin is also useful for reducing inflammation and symptoms such as pain and stiffness in the joints. Turmeric in the diet reduces pain from arthritis, bursitis and tendonitis.[24]
- A separate double-blind clinical trial found that curcumin was superior to placebo or phenylbutazone [a non-steroidal anti-inflammatory drug (NSAID)] for alleviating post-surgical inflammation.[25]
- Oral curcumin supplementation for chronic anterior uveitis (inflammation of the iris and middle coat of the eyeball).[26]
- Prevention of formation of cholelithiasis.[27]
- When applied to the skin and exposed to sunlight, turmeric is strongly anti-bacterial.[28]
- Fresh juice from the rhizome or a paste prepared from turmeric or decoction is often used for local application as well as internally in the treatment of leprosy, snake bites, and vomiting associated with pregnancy.[29]
- In case of smallpox and chickenpox, turmeric is applied as a powder or as a paste to facilitate the process of scabbing.[30,31]
- Although curcumin is proven to inhibit HIV in test tube cultures, human clinical testing is needed to determine the effectiveness in treating the condition.[32]

Mechanisms of action

Antioxidant

The antioxidant properties of curcumin depend on the presence of both central methylene hydrogens and the phenolic hydrogens.

The mechanism of action is by:

- Efficient scavenger of peroxyl radicals due to its lipophilic nature which shows a typical radical trapping ability as chain breaking antioxidant properties.[33]
- Chelates with iron and disarm the oxidative properties.[33]
- Increases serum activities of antioxidants such as superoxide dismutase (SOD), catalase, as well as serum concentrations of glutathione peroxidase (GSH) and lipid peroxides reducing oxidative stress.[34,35]
- It can scavenge different forms of free radicals, such as reactive oxygen and nitrogen species (ROS and RNS, respectively).[36]
- It can inhibit ROS-generating enzymes such as lipoxygenase/cyclooxygenase and xanthine hydrogenase/oxidase.[37]

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.[3]

Anti-Inflammatory

Inflammatory cells liberate several reactive species at the site of inflammation leading to oxidative stress, which is a key factor in development of chronic diseases like Alzheimer's disease, cardiovascular disease, cancer, allergy, asthma, bronchitis, colitis, arthritis, diabetes mellitus to name a few.[38]

The anti-inflammatory effect can be explained by various mechanisms;

- Tumor necrosis factor α (TNF-α) is a major mediator of inflammation in most diseases, and this effect is regulated by the activation of a transcription factor, nuclear factor (NF)-ḳB. The activation of (NF)-ḳB is activated by most inflammatory cytokines; gram-negative bacteria; environmental pollutants; chemical, physical, mechanical, and psychological stress; high glucose; fatty acids; ultraviolet radiation; and

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cigarette smoke. Curcumin has shown to reduce the anti-inflammatory action by many mechanisms the most accepted being its ability to block NF-ķB activation.[39]

- By lowering histamine levels and possibly by increasing the production of natural cortisone by the adrenal glands.[40]
- It also inhibits the biosynthesis of inflammatory prostaglandins from the arachidonic acid and neutrophil function by down regulating of the cyclooxygenase and lipoxygenase pathways.[8,36,41]
- Modulates the inflammatory response by down-regulating the activity of cyclooxygenase-2 (COX-2), lipoxygenase, and inducible nitric oxide synthase (iNOS) enzymes; inhibits the production of the inflammatory cytokines tumor necrosis factor-alpha (TNF-a), interleukin (IL) -1, -2, -6, -8, and -12, monocyte chemoattractant protein (MCP), and migration inhibitory protein; and down regulates mitogen-activation and Janus kinases.[41]

Antiplatelet action

Antiplatelet action of curcumin is by the potentiation of prostacyclins synthesis and inhibition of thromboxane synthesis.[21]

Antimutagenic

The antimutagenic effects of curcumin are due to direct antioxidant and free-radicals scavenging effects and their ability to indirectly increase glutathione levels, thereby aiding in hepatic detoxification of mutagens and carcinogens and in inhibiting nitrosamine formation.[42] It causes suppression of inflammation, inhibition of cell proliferation, suppression of certain oncogens, inhibition of transcription factors NF-KB & ap-1 suppressions of COX-2, inhibition of chromosomal damage, inhibition of tyrosine kinase C activity, and inhibition of biotransformation of carcinogenesis.[43]

Curcumin has been also found to effect biological pathways involved in mutagenesis, oncogene expression, cell cycle regulation, apoptosis, tumorigenesis, and metastasis. It is an enhancer of radiotherapy. Also, it is found to arrest carcinomatous cells in the G2/M phase of cell cycle, in which cells are more susceptible to cytotoxic effects of radiotherapy.[4]

Antimicrobial

Turmeric extract and the essential oil of Curcuma longa inhibits the growth of a variety of bacteria, parasites and pathogenic fungi. Curcumin and the oil fraction inhibit the growth of variety of bacteria like *Streptococci, Staphylococci, Lactobacillus* and *Helicobacter pylori* Cag A + strains in vitro.[44] It is also effective against Enterococcus faecalis and will serve to be useful as root canal medicaments in endodontics.[20] It also acts as antifungal agent which is active against Aspergillus flavus, *A. parasiticus*, and *Fusarium moniliforme*.[32] It has moderate antiprotozoal activity against *E.histolytica, Leishmania, Plasmodium falciparum*. It also has antiviral effect which inhibits HIV in test tube studies and inhibits UV light induced HIV gene expression.[45]

Hepatoprotective

Turmeric's hepatoprotective effect is mainly a result of its antioxidant properties as well as its ability to decrease the formation of proinflammatory cytokines and protects liver from toxic products like carbon tetrachloride (CCl4), galactosamine, acetaminophen, and Aspergillus aflatoxin. Sodium curcuminate, a salt of curcumin, also exerts choleretic effects by increasing biliary excretion of bile salts, cholesterol, and bilirubin as well as by increasing bile solubility, therefore, possibly preventing the formation of cholelithiasis.[18,46-50]

Cardiovascular effects

Protective effect of turmeric is by lowering the triglyceride and cholesterol levels to decline the susceptibility of low-density lipoprotein (LDL) to lipid peroxidation, and hampers platelet aggregation. The reason for this may be due to increased conversion of cholesterol to bile acids in the liver and reduced cholesterol uptake in the intestines.[41]

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Anti-hyperalgesia 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 system.[32]

Dental application of curcumin

1. Dental pain

Turmeric can be used in following ways to offer relief from dental problems:

- Rinse the mouth with turmeric water (boil 5 g of turmeric powder, two cloves, and two dried leaves of guava in 200 g water) to have an instant relief.
- Massage the aching teeth with roasted, ground turmeric to eliminate pain and swelling.
- Apply a paste made from 1 tsp. of turmeric with ½ tsp. of salt and ½ tsp. of mustard oil to provide relief from gingivitis and periodontitis. Rub the teeth and gums with this paste twice daily.[51]

2. Dental plaque detection system

Dental plaque is one of the cardinal factors for the occurrence of dental caries and periodontal diseases and its removal from the teeth surfaces is crucial. However, it's not easy to identify by naked eye and is arduous to precisely locate its attachment site and extent. To bridle this dental plaque is generally stained with dental plaque staining agents which contain dyes, to accurately reveal their locations.

Plaque disclosing solutions which are traditionally used can be substituted by dental plaque staining agent, which contains at least one selected from yellow pigment of beni-koji, turmeric extracts, and curcumin; and a light-emitting apparatus, which outputs light of wavelength within a range of 250 to 500 nm to an object in the oral cavity where the dental-plaque staining agent is attached.[52]

3. 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 β- Apo-8.-Carotenal.[53]

Curcumin serves two roles; it gives a colour tint to the pit and fissure sealant and has anti-bacterial action.[52,54]

4. Subgingival irrigation

Curcumin also enhances wound healing by causing increase in fibronectin and transforming growth factor transcription. One fraction of crude polysaccharides extracted from the rhizomes, Curcuma aromatic Salisb (*Zingiberaceae*) can significantly induce human gingival fibroblasts cells proliferation by 30% while the other fraction could inhibit gingival fibroblast cells proliferation by 92%.[55,56]

The studies conducted by Suhag et.al.[57] and Gottumukkala et al.[58] showed that curcumin (1%) can be used as subgingival irrigant as it reduces the inflammation and mean probing pocket depth. In the study, 20 patients with chronic periodontitis underwent scaling and root planning. Following instrumentation, they were irrigated with triple irrigation regimen i.e. chlorhexidine (0.2%), curcumin (1%), saline (0.9%) or control (non-irrigated) on baseline (day 0). It was followed by the same regimen on 5 consecutive days and then day 15 and 20. The probing pocket depth, bleeding on probing, and redness were recorded for 200 sites. On days 2, 3, 4 and 5 there was better results in the study group than in the non-irrigated group for all parameter. There was a significant reduction in redness (96%) and bleeding on probing (100%) by curcumin group as compared to other groups on day 5.

5. Mouthwash

In a study by Waghmare et.al.[59] about 100 subjects were randomly selected. Both gingival index and plaque index were recorded at 0, 14 and 21 days. It was concluded that chlorhexidine gluconate as well as turmeric mouthwash can be effectively used as an adjunct to mechanical plaque control methods in

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prevention of plaque and gingivitis. Turmeric mouthwash prepared by dissolving 10 mg of curcumin extract in 100 mL of distilled water and 0.005% of flavouring agent peppermint oil with pH adjusted to 4 is found to be as effective as most widely used chlorhexidine mouthwash, though, chlorhexidine gluconate has been found to be more effective when antiplaque property was considered. The effect of turmeric observed may be because of its anti-inflammatory action. Reduction in total microbial count was observed in both the groups.

In a recent study turmeric mouthwash with 10 mg curcumin extract dissolved in 100 ml of water with a peppermint flavouring agent added was found to be as potent as a solution made from chlorhexidine gluconate, the gold standard compound for plaque build-up in dentistry.[60]

6. Precancerous Lesions

Its use in the treatment of various precancerous conditions like oral submucous fibrosis, leucoplakia, and lichen planus has also been studied where the local symptoms of burning sensation and pain were reduced and partial reversal of opening of the mouth were observed.[61]

Curcumin can be used for treatment of oral lichen planus and has shown immunomodulatory effect involving activation of host macrophages and natural killer cells and modulation of lymphocytes mediated function.[4]

In the treatment of oral submucous fibrosis curcumin acts by;

- Cell proliferation in fibroblasts and myofibroblasts reduced.
- Cell cycle arrest in myofibroblasts is inhibited.
- Reduce the Bcl-2/Bax ratio in myofibroblasts and hence induces apoptosis in myo-fibroblasts.
- Type I and type III collagen in myofibroblasts production is diminished. [33,61]

7. Influence on human gingival fibroblasts

Study conducted by Suhag et.al.[57] shows the apoptosis of human primary gingival fibroblasts (hPGF) cells at lower doses like 1, 10 and 25µM of curcumin but higher doses like 50, 60, 75 and 100 µM was statistically significant high apoptosis was seen. The ability of curcumin to treat microvascular endothelial cells and normal fibroblast using MTT assay (used for assessing cell metabolic activity) were studied, hPGF cells treated with curcumin exhibit significant and maximum apoptosis at 75µM and showed a decrease in cell population and shrinkage of cell size and morphologic alterations in basal cell carcinoma cells and after treatment with 50Nm curcumin, cell shrinkage, disappearance of microvilli and appearance of membrane blebbing was seen.[54]

8. Recurrent apthous stomatitis (RAS)

RAS is an inflammatory condition of unknown aetiology mainly involving non-keratinized mucosal surfaces and is characterized by single or multiple painful ulcers with periodic recurrence and healing. Reports have shown that in patients who used conventional antiseptic gel, the lesion healed only after the periods of time as in previous attacks irrespective of whether the gel was applied or not. They experienced no early reduction in pain or frequency of recurrence. The patients who used the curcumin oil reported that ulcers started healing earlier than in previous attacks with early reduction in pain. Curcumin oil initiated healing effects as soon as applied. A follow-up for one-year has shown no recurrence in these patients.[62,63]

9. Local drug delivery system

Turmeric (2%) can be used as a local drug delivery system in addition to scaling and root planning in the treatment of periodontitis, reducing the pocket depth and gaining the clinical attachment levels.

In a study conducted by Behal et.al., thirty subjects with chronic localized or generalized periodontitis with pocket depth of 5-7 mm were enrolled in a split-mouth study design. Control sites received scaling and root planning (SRP) alone, while experimental sites received SRP plus 2% whole turmeric gel. Both groups demonstrated statistically significant reduction in plaque index, gingival index, sulcus bleeding index, probing pocket depth, and gain in relative attachment loss. There was a significant reduction in the trypsin-

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like enzyme activity of "red complex" microorganisms. Greater reduction was observed in all parameters in the experimental group in comparison to those in the control group. It was concluded that the local drug delivery system containing 2% whole turmeric gel can be used as an adjunct to scaling and root planning.[60,54]

Another study included thirty chronic periodontitis patients with an age range of 20–50 years with probing pocket depth (PPD) of 4-6 mm. Curcumin and chlorhexidine gel was applied in the contralateral disease sites at baseline and day 15. The clinical parameters like PPD, clinical attachment level (CAL), gingival index (Loe and Silness) and plaque index (Turesky Gillmore modification of Quigley Hein) were recorded and colony forming units (CFU) were assessed microbiologically at baseline, 15 and 30. Curcumin was found to have equivalent benefit to chlorhexidine, and it was concluded that curcumin be an alternative to chlorhexidine due to minimal adverse effects.[65]

10. Surgical wound healing

The mechanism of action of Curcumin may be considered as multicentric since it acts as a prostaglandin inhibitor, stabilizer of the liposomal membrane, inhibitor of the activity of leukotrienes and thromboxane B4 without effecting the synthesis of prostacyclines, stimulator of adrenal steroidogenesis, substance P depletor in nerve terminals, analgesic, anti-oxidant.[33]

Alveolar osteitis also called dry socket is the most common post extraction complication of teeth, most commonly occurring in 40-45 years of age. Traumatic extraction, aggressive curettage and irrigation, oral microorganisms, remaining fragments of bone and root in extraction wound, dislodgement of blood clot by excessive mouth rinsing and gargles by patient, oral contraceptives and smoking are important etiologic factors responsible for dry socket. A clinical study conducted by Lon et.al. on 178 patients diagnosed clinically of dry socket. One group was given turmeric dressing with mustard oil was given and other group received Zinc oxide eugenol dressing. The results showed wound healing was seen faster in the turmeric group than dressing with zinc oxide eugenol.[66]

Habiboallah et.al.[67] 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 in cases treated with *Curcuma longa* was observed. The results suggested a positive therapeutic effect on surgical wound healing, particularly improvement of periodontal treatment after surgery.

11. Dental caries

Najah et.al. conducted a study to evaluate the inhibitory effects of curcumin were studied against *Streptococcus mutans* and *Streptococcus pyogens* growth in comparison with antibiotic ciprofloxacin using well diffusion method on fifty-six patients. Minimum Inhibitory Concentration (MIC) showed curcumin inhibited the growth with inhibition zones. Thus, the study concluded that curcumin can be used for controlling dental biofilms and subsequently dental caries. Curcumin acts as an anti-cariogenic agent as it coats to hydroxyapatite crystals and inhibits the adherence of *Streptococcus mutans.*[44]

An in vitro study conducted by M. Ranjinikanth et.al.[68] compared the antibacterial property of ten phytochemicals by measuring the zone of inhibition in nutrient agar media. The study showed no zone of inhibition for turmeric thus refuting its use as an anti-caries agent contradicting all the other studies conducted till date.

12. Intra canal medicament and irrigant

Enterococcus faecalis, a facultative anaerobic gram-positive coccus is the most common species cultured from the non-healing endodontic cases. The species adhere to root canals, accumulate and form colonies making them more resistant to antibiotics.[69]

Effectiveness of Curcumin against *E. faecalis* biofilm in root canals was studied and compared to that with sodium hypochlorite and chlorhexidine. Ninety-six extracted tooth were instrumented and treated with

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30 minutes of test solutions and the colony forming units of *E. faecalis* were counted on 2nd day, 2nd week and 8th week. The study showed that the maximum antibacterial effect was seen with sodium hypochlorite group followed by curcumin and chlorhexidine. Considering the effectiveness and the minimum to none adverse effects curcumin can be substituted to the more conventional irrigants.[70]

Sixty deciduous teeth with single root canal were made into standardized segments and infected with *Enterococcus faecalis*. They were treated with a paste made of either turmeric extract, calcium hydroxide and saline for one week. Dentinal shavings were collected from within the canal, suspended in solution and spread on MRS broth. Colony forming units (CFU) were enumerated using a digital colony counter. The pH of the medicaments used was measured with the help of pH meter. Curcumin is effective against *E. faecalis* with approximately 50% reduction the microbial load and can be substituted for calcium hydroxide.[71]

Prasanna *et.al.,* (2011)[72] conducted an *in vitro* study to evaluate the antimicrobial efficacy of curcumin against *E. faecalis* considering sodium hypochlorite (3%) as reference for comparison. The result of his study revealed that curcumin had significant antibacterial activity against *E. faecalis* he concluded that the antibacterial activity of curcumin was similar to sodium hypochlorite and thus herbal medicine can be used in endodontics for root canal failure.

Adverse Effects

Intake of turmeric is generally considered safe, but may cause gastric irritation, stomach upset, nausea, diarrhoea, allergic skin reaction, yellow stool and antithrombotic activity.[2,15]

Curcumin can induce DNA damage and chromosomal alterations both in vitro and in vivo at concentrations like those reported to exert beneficial effect. Lower concentrations of curcumin induce antioxidant effects, higher concentrations of this compound increase the cellular levels of ROS (reactive oxygen species). Curcumin has also been shown to inhibit the activity of the drug-metabolizing enzymes cytochrome P450, glutathione-S-transferase, and UDP glucuronosyl transferase. The inhibition of these enzymes in people taking curcumin may lead to an undesirable increase in the plasma concentrations of some drugs and cause toxicity.[3]

CONCLUSION

Turmeric is considered a safe, nontoxic, easily available and effective alternative for many conventional drugs due to its distinguished therapeutic properties and effects on multiple systems of the body. Its antimutagenic role is promising especially in treating oral carcinoma as it is more cost effective especially for the lower economic strata of the society. However, there is scarcity of information and research, more research is required for regular implementation of curcumin in dentistry.

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