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CURCUMIN: THERAPEUTIC APPLICATIONS IN SYSTEMIC AND ORAL HEALTH

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ABSTRACT

Numerous treatment modalities are available for variety of systemic and dental diseases; however, the main drawback of conventional medicinal therapies is its various side effects causing harm to the patient. This diverted the interest of researchers towards an alternative approach where natural compounds derived from plants could be used for treating those patients. Curcumin is such an alternative which exhibits a number of medicinal properties and has been used from the centuries. This article discusses the efficacy of curcumin in maintenance of oral health, in particular, and overall health, in general. Curcumin (diferuloylmethane) is a polyphenol derived from the curcuma longa plant, commonly known as turmeric, is a herb known for its medicinal properties. It has a variety of therapeutic properties like anti-inflammatory, anti-oxidant, anti-microbial, hepatoprotective, immunostimulant, anti-septic, anti-angiogenic, apoptotic and anti-mutagenic. All these beneficial properties makes this compound quite more useful in dental field especially in treating periodontal diseases and cancers involving head and neck region and oral cavity. It can also be formulated as a pit and fissure sealant, mouth wash, and subgingival irrigant in different preparations in different dosages and also as a component in local drug delivery system in gel form.

Key Words: Antimicrobial, Medicine, Mouthwash, Oral health, Turmeric.

INTRODUCTION

Most of the anti-cancer drugs are very toxic, highly inefficient for cancer treatment or highly expensive. Thus, these drugs show their limited potential in cancer therapy and beyond the reach of the majority of affected individuals. Hence, an alternative medicinal product without exhibiting such drawbacks will be good option as an anti-cancer drug. Natural phytochemicals isolated from plants used as traditional medicines are referred as such sources. Curcumin, derived from the dried rhizome of the East Indian turmeric plant (*Curcuma longa*), a perennial herb belonging to the Zingiberacae (ginger) family of botanicals, has drawn attention as alternative source in cancer therapy. This turmeric plant is 3 feet in height and has lance-shaped leaves and spikes of yellow flowers, which grow in a fleshy rhizome or in underground stem. The rhizome (or root) of this turmeric plant, is processed into turmeric powder, which is 2% to 5% curcumin (Chainani‑Wu, 2003). It has been used for thousands of years as a healing medicine for variety of illnesses. It is the most active ingredient of turmeric, which is cultivated extensively in south and southeast tropical Asia. Turmeric is widely consumed through foods in the Indian subcontinent, south Asia, and Japan (Brouk, 1975). It is a popular dietary spice and pigment especially for curry and often used a folk medicine for treating various illnesses (Srimal & Dhawan, 1973). Besides, it is employed in textile industries and pharmaceutical companies and in several Hindu religious ceremonies (Srimal & Dhawan, 1973). Ayurveda and traditional Chinese medicines mention the benefits of turmeric in preventing and curing several health related problems.

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Curcumin, which is an orange–yellow crystalline powder, is practically insoluble in water and ether but soluble in ethanol, dimethylsulfoxide, and acetone (Aggarwal *et al*, 2003; Aggarwal *et al*, 2007). It was first isolated in 1815 by Vogel (Vogel and Pelletier, 1815). It was isolated in 1870 as a crystalline form and identified as 1, 6-heptadiene-3, 5-dione-1, 7-bis (4-hydroxy-3-methoxyphenyl)-(1E, 6E) or diferuloylmethane (Daube, 1870). Feruloylmethane skeleton of curcumin was confirmed (Lampe *et al*, 1910; Lampe & Milobedzka, 1913). Curcumin, a polyphenol has a melting point of 183°C; its molecular formula is $C_{21}H_{20}O_6$ and molecular weight 368.37. Besides curcumin, turmeric contains other chemical constituents known as the curcuminoids, which impart the characteristic yellow color to turmeric (Srinivasan, 1952). The major curcuminoids in turmeric are demethoxycurcumin, bisdemethoxycurcumin, and the recently identified cyclocurcumin (Kiuchi, 1993).

Curcumin has been used extensively in ancient ayurvedic medicine for centuries, as it is nontoxic and has a variety of therapeutic properties. These beneficial effects are due to its anti-oxidant, analgesic, anti-inflammatory, anti-septic activity, and anti-carcinogenic activity (Çıkrıkçı *et al*, 2008). As a natural product, turmeric extract i.e. curcumin is nontoxic and has diversified effects in various systemic and oral diseases. About 40-85% of an oral dose of curcumin passes through the gastrointestinal tract unchanged in its form, 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 to enhance its absorption and anti-inflammatory effect (Wahlstrom & Blennow, 1978; Ravindranath & Chandrasekhara, 1980).

CURCUMIN AND ITS THERAPEUTIC APPLICATIONS

Curcumin, the active constituent of turmeric, has been shown to have widespread therapeutic applications in medicine field. It exhibits antioxidant, anti-inflammatory, hepatoprotective, anti-microbial, anti-mutagenic, anti-angiogenic, apoptotic and anti-platelet aggregation properties.

Curcumin: Antioxidant Effects

The chemical structure of curcuminoid is the seldom factor responsible for their antioxidant behavior. Curcuminoids consist of two methoxylated phenols linked via two a, B unsaturated carbonyl groups which is a stable enol form (Sreejayan Rao, 1994). The mechanism of curcumin was attributed towards its antioxidant effect (Masuda *et al*, 2001). Curcumin inhibit lipid peroxidation using linoleate, a polyunsaturated fatty acid that is able to be oxidized and form a fatty acid radical. It also acts as a chain-breaking antioxidant at the 3' position, resulting in an intramolecular Diels-Alder reaction and neutralization of the lipid radicals. Other authors also tried to demonstrate the curcumin's mechanism of action towards antioxidant property using rat peritoneal macrophages as a model (Joe *et al*, 2004; Joe & Lokesh, 1994). Curcumin demonstrated its free radical-scavenging activity, where it has been shown to scavenge various reactive oxygen species produced by macrophages including superoxide anions, hydrogen peroxide and nitrite radicals.

Inducible nitric oxide synthase (iNOS), an enzyme present in macrophages generates large amounts of NO providing 'oxidative burst' necessary for defense against pathogenic microorganisms. This iNOS is induced in response to an oxidative environment, and the NO thus, produced can react with superoxide radicals to form peroxynitrite, which is highly toxic to cells. It has been demonstrated that curcumin downregulates the iNOS action in macrophages, thus reducing the amount of reactive oxygen species (ROS) produced in response to oxidative stress (Brouet & Ohshima, 1995; Chan *et al*, 1998). Some authors[21-23] (Jung *et al*, 2006; Ray & Lahiri, 2009; He *et al*, 2010) performed additional studies in microglial cells and demonstrated reduced NO production and protection of neural cells from oxidative stress after curcumin therapy. These studies showed curcumin's use in reducing the neuroinflammation associated with degenerative conditions such as Alzheimer's disease.

The strong antioxidant effect of curcumin was demonstrated (Ramirez-Bosc *et al*, 1995). They observed a decrease in the blood lipid peroxide levels of human subjects, thus protecting against free redical damage. Antioxidative compounds was isolated from rhizome of *curcuma longa* and the water- and fat-soluble extracts of turmeric and its curcumin component possessed a strong antioxidant action comparable to that of vitamins C and E (Toda *et al*, 1985). The effect of curcumin on bovine aortic endothelial heme oxygenase-1 (an inducible stress protein) led to an enhanced cellular resistance to oxidative damage after an incubation period of 18 hours (Mortellini *et al*, 2000).

Curcumin: Anti-inflammatory Effect

Several studies (Chan, 1995; Singh & Aggarwal, 1995; Brennan & O'Neill, 1998; Jobin *et al*, 1999) have demonstrated that the curcumin suppress the activation of NF-_B, an inducible transcription factor that regulates the expression of a host of genes [cyclooxygenase-2 (COX-2), I_Ba, TNF-a, cyclin D1, ICAM-1, c-myc, Bcl-2, MMP-9, inducible nitric oxide synthase (iNOS))], and interleukins including IL-6 and IL-8 involved in inflammation, cellular proliferation and cell survival. Activation of NF-_B is increased in many cancers, and is associated with various steps involved in the development of malignancy such as expression of anti-apoptotic genes, angiogenesis, tumor promotion and metastasis (Garg & Aggarwal, 2002). NF-_B, a heterodimeric protein is activated with the appropriate chemical signals. Curcumin exhibits its inhibitory effect on the NF-_B pathway providing the compound with its anti-inflammatory properties. Studies have revealed the potential action of curcumin on various pathways of inflammation including decrease in production of inflammatory markers[28-33] (Chan, 1995; Singh & Aggarwal, 1995; Brennan & O'Neill, 1998; Jobin *et al*, 1999; Garg & Aggarwal, 2002; Han *et al*, 2002; Plummer *et al*, 1999), inhibition of the production of inflammatory cytokines (Abe, 1999; Rao, 2007), decrease in metabolism of arachadonic acid (Huang *et al*, 1991; Zhang *et al* 1999), and inhibition of prostaglandin E2 biosynthesis (Koeberle, 2009). Several authors investigated the anti-inflammatory behavior of curcumin in variety of diseases including Alzheimer's disease, cardiovascular disease, diabetes, asthma, inflammatory bowel disease, arthritis, pancreatitis and renal disease (Lim *et al*, 2001; Yang *et al*, 2005; Hanai *et al*, 2006; Yadav *et al*, 2009; Yeh *et al*, 2005; Yang *et al*, 2006; Babu & Srinivasan, 1995; Meghana *et al*, 2007; Ram *et al*, 2003; Moon *et al*, 2008; Onodera *et al*, 2000; Mun *et al*, 2009; Gukovsky *et al*, 2003; Durgaprasad, 2005; Jones & Shoskes, 2000; Chiu *et al*, 2009; Aggarwal & Harikumar, 2009).

The anti-inflammatory and irritant actions of curcumin analogues were evaluated in rodents (Mukhopadhyay *et al*, 1982). They observed that oral administration of curcumin was effective compared to cortisone or phenylbutazone in acute and chronic inflammations. The authors attributed this anti-inflammatory effect exhibited by curcumin to its potential to inhibit both biosynthesis of inflammatory prostaglandins from arachidonic acid and neutrophil function during inflammatory conditions. The mechanism of anti-inflammatory actions of curcumin and boswellic acids was further discussed (Ammon *et al*, 1993). The authors proposed that curcumin reduces inflammation by lowering histamine levels and possibly by increasing the production of natural cortisone by the adrenal glands.

Curcumin: Hepatoprotective Effect

Several reaserchers (Deshpande *et al*, 1998; Park *et al*, 2000; Kiso *et al*, 1983; Donatus *et al*, 1990; Soni *et al*, 1992) reported hepatoprotective effects of curcumin against various toxic compounds such as carbon tetrachloride (CCl4), galactosamine, acetaminophen (paracetamol), and Aspergillus aflatoxin. The researchers attributed this hepatoprotective mechanism to its antioxidant behavior and its potential to decrease the formation of proinflammatory cytokines. The quantitative change in the bile constituents induced by sodium curcuminate was evaluated (Ramprasad & Sirsi, 1957). They noted choleretic effects of sodium curcuminate, a salt of curcumin and postulated that this salt increased biliary excretion of bile salts, cholesterol, and bilirubin as well as increased bile solubility, which prevented cholelithiasis. Curcumin possessed choleretic ability which increases bile output and solubility indicating its beneficial therapeutic application in the treatment of gallstones.

Curcumin: Antiplatelet Aggregation Effect

The effects of curcumin on platelet aggregation and vascular prostacyclin synthesis was evaluated and was observed that the ability of curcumin prevent platelets from clumping together, which further improves circulation (Srivastava *et al*, 1986). They attributed this effect to its potential of prostacyclin synthesis and inhibition of thromboxane synthesics.

Curcumin: Antimutagenic Effect

Certain authors (Mehta et al, 1997; Menon et al, 1991) revealed antimutagenic potential of curcumin (diferuloylmethane) preventing development of new cancers that are caused by chemotherapy or radiation therapy employed to treat existing cancers. They observed their effective inhibition towards metastasis of melanoma cells indicating their therapeutic role in deactivating the carcinogens in cigarette smokers and tobacco chewers. Several researchers (Kawamori *et al*, 1999; Thaloor *et al*, 1998; Limtrakul *et al*, 1997) conducted animal and *in vitro* studies to evaluate the antimutagenic potential of curcumin and observed that curcumin inhibited carcinogenesis at various stages of cancer such as tumor promotion or progression, angiogenesis, and tumor growth. Curcumin has revealed its potential role in inhibiting cell proliferation and tumor growth in colon and prostate cancer (Hanif *et al*, 1997; Dorai *et al*, 2001). This anticarcinogenic behavior of turmeric and curcumin are attributed to their direct antioxidant and free-radical scavenging actions and their potential to indirectly increase glutathione levels. These effects lead to hepatic detoxification of mutagens and carcinogens and inhibition of nitrosamine formation.

Curcumin: Antimicrobial Effect

The antifungal activity of turmeric oil extracted from curcuma longa was demonstrated (Apisariyakul *et al*, 1995). This turmeric extract and the extracted essential oil of curcuma longa inhibited the growth of variety of microorganisms including bacteria, parasites, and pathogenic fungi. The authors noticed drastic improvements in the lesions of dermatophyte- and fungi-infected guinea pigs, after a period of 7 days of turmeric application on these lesions. Other study (Rasmussen *et al*, 2000) also reported a moderate activity of curcumin administration against *Plasmodium falsiparum* and *Leishmania major*.

Curcumin: Cardiovascular Effects

The beneficial and protective effects of curcumin on the cardiovascular system were demonstrated in rabbits with experimental atherosclerosis (Ramirez-Tortosa *et al*, 1999). Oral administration of curcumin lowered cholesterol and triglyceride levels, which further decreased susceptibility of low density lipoprotein (LDL) to lipid peroxidation. Inhibition of platelet aggregation also contributes to its cardiovascular effects (Srivastava *et al*, 1986). These cardiovascular actions have been observed even with low doses of turmeric (1.6-3.2 mg/kg body weight, daily), which was administered in 18 atherosclerotic rabbits. Decreased susceptibility of LDL to lipid peroxidation in addition to lower plasma cholesterol and triglyceride levels was note in these experimental rabbits. However, increase of dose did not decrease lipid peroxidation of LDL, but cholesterol and triglycerie level decreased. Curcumin's effect on cholesterol levels may be attributed to decreased cholesterol uptake in the intestines and increased conversion of cholesterol to bile acids in the liver (Ramprasad & Sirsi, 1957).

Curcumin: Apoptotic Effects

Apoptosis establishes a natural balance between cell death and cell renewal in animals by destroying excess, damaged, or abnormal cells. The major mechanism by which curcumin induces cytotoxicity in tumor cells is induction of apoptosis. It has been shown that curcumin decreases the expression of antiapoptotic members of the Bcl-2 family and elevates the expression of p53, Bax, and procaspases-3, -8, and -9 (Aggarwal, 2004). Some authors (Shishodia *et al*, 2005; Bharti *et al*, 2003) suggested that curcumin suppresses the constitutive expression of Bcl-2 and Bcl-XL in mantle cell lymphoma and multiple myeloma cell lines. The serine/threonine protein kinase PKB/Akt and PI3K/Akt has been considered playing a critical role in mammalian cell survival signaling and is active in breast and other type of cancers (Clarke, 2003; Chang *et al*, 2003). This activated Akt has been reported to promote cell survival by activating the NF-_B signaling pathway and by inhibiting apoptosis through inactivation of several proapoptotic factors (Bad, Forkhead transcription factors, and caspase-9) (Ozes *et al*, 1999; Romashkova & Makarov, 1999; Brunet *et al*, 1999; Cardone *et al*, 1998). Curcuminoids downregulate expression of cell proliferation and antiapoptotic and metastatic gene products through suppression of IKK and Akt activation (Aggarwal *et al*, 2006). Several other researchers (Squires *et al*, 2003; Woo *et al*, 2003) have demonstrated that curcumin has molecular targets within the Akt signaling pathways, and that inhibition of Akt activity may facilitate inhibition of proliferation and induction of apoptosis in cancer cells. Curcumin completely inhibited Akt activation in the human prostate cancer cell lines and suppressed the growth of several T-cell leukemia cell lines (Chaudhary & Hruska, 2003; Hussain *et al*, 2006). The induction of early apoptosis and ROS (reactive oxygen species) generation activity in human gingival fibroblasts (HGF) and human submandibular gland carcinoma (HSG) cells has been reported after administration of curcumin therapy (Atsumi *et al*, 2006). The role of ROS on suppression of growth in follicular lymphoma cells was also supported by other study (Skommer *et al*, 2006). They performed flow cytometry and western blotting analysis and found that curcumin shifted the equilibrium of Bcl-2 family members toward apoptosis and initiated caspase-mediated cell death in these cell lines.

Gurcumin: Anti-angiogenic Effects

The tumor angiogenesis was explained as the proliferation of a network of blood vessels that penetrates into a cancerous growth, supplying nutrients and oxygen and removing waste products (Folkman, 2001). This phenomenon is essential for tumor growth and metastasis in variety of solid tumors. Tumor cells release certain angiogenic molecules including different proteins (eg, bFGF, EGF, granulocyte colony-stimulating factor, IL-8, PDGF, TGF-_, TNF, VEGF) and smaller molecules (eg, adenosine, prostaglandin E) that send signals to surrounding normal host tissue. Curcumin suppresses the proliferation and cell cycle progression of human umbilical vein endothelial cells (Singh *et al*, 1996). Curcuminoid inhibited the inhibition of the angiogenic response stimulated by fibroblast growth factor-2, including expression of matrix metalloproteinase gelatinase B (Mohan *et al*, 2000). Curcumin therapy inhibited angiogenesis in a subcutaneous Matrigel plug model in mice and caused the preformed tubes to break down (Thaloor *et al*, 1998). There was an irreversible inhibition of CD13/aminopeptidase N (APN) caused by curcumin's binding ability to APN (Shim *et al*, 2003)). Several investigators (Arbiser *et al*, 1998; Dorai *et al*, 2001) reported in their *in vivo* studies that curcumin inhibits proliferation and angiogenesis of LNCaP prostate cancer cells. cDNA microarray analysis showed that curcumin inhibits cell cycle progression of endothelial cells by up-regulating cyclin-depenent kinase inhibitor (Park *et al*, 2002).

Curcumin: Local Effects

Paste prepared from turmeric or turmeric decoction or fresh juice from turmeric is most commonly employed as a local application. Also, this preparation is used internally in the treatment of various illnesses such as leprosy, snake bites, and pregnancy associated vomiting (Snow, 1995).

Curcumin: Gastric Effects

Curcumin exhibited a significant role in patients affected with peptic ulcers (Prucksunand *et al*, 2001). They conducted an open, phase II clinical trial on 25 patients to evaluate the effect of the long turmeric on healing of peptic ulcers. These participants were diagnosed with gastric ulcer confirmed after endoscopic examination and were given 600 mg powdered turmeric, five times daily. About, 48% patients showed complete healing of ulcers after 4 weeks of period and 76% patients were ulcer free after 12 weeks of therapy. The success rate of therapy was increased with the period of curcumin's administration, without any significant adverse reactions or blood abnormalities found in participants (Prucksunand *et al*, 2001).

Curcumin: Chronic anterior uveitis

The beneficial therapeutic effects of curcumin were noted in patients affected with chronic anterior uveitis (Lal *et al*, 1999). They administered a dose of 375 mg curcumin 3 times daily in 32 patients affected with chronic anterior uveitis for a period of 12 weeks. The participant patients were divided into two groups: one group of 18 patients received curcumin only, whereas the other group of 14 patients' receieved antitubercular therapy. In both groups of patients, the uveitis started improving after 2 weeks of curcumin therapy. Authors noted improvement in all the patients who received curcumin alone, whereas the patients' receieving antitubercular treatment along with curcumin showed a response rate of 86%. After 3-years, a recurrence rate of 55% and 36% was observed in first and second groups respectively. Loss of vision was reported by 22% and 21% of the patients from the first and the second groups respectively. This was because of various complications such as vitritis, macular edema, central venous block, cataract formation, glaucomatous optic nerve damage. Curcumin's administration was as effective as corticosteroid therapy, which is at present is the only available standard therapy for chronic anterior uveitis. None of the patients reported side effects while undergoing curcumin therapy which is its greatest advantage compare with corticosteroids (Lal *et al*, 1999).

CURCUMIN AND ITS DENTAL APPLICATIONS

Turmeric and its extract can be used several ways to offer relief from dental problems. The biological activity of curcuminoids isolated from Curcuma longa was evaluated on dental related pain and suggested massaging the aching teeth with roasted and ground turmeric for the elimination of pain and swelling associated with teeth (Çikrikçi *et al*, 2008). Also, a paste prepared from 1 tsp of turmeric with ½ tsp of salt and ½ tsp of mustard oil can be applied topically providing relief from gingivitis and periodontitis. The authors suggested the topical application of this turmeric paste twice daily on to the affected teeth and gums. A comparative evaluation of turmeric and chlorhexidine gluconate mouthwash was conducted to investigate their contribution in prevention of plaque formation and gingivitis (Waghmare *et al*, 2011). They selected about 100 participants randomly, in which gingival and plaque indexes were recorded at 0, 1 week, and 3 weeks interval. Turmeric mouthwash was 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. This turmeric mouthwash was found to be as effective as the most widely used chlorhexidine mouthwashes that were given to those participants. The authors recommended both these mouthwashes along with mechanical plaque control methods in prevention of plaque and gingival inflammation. However, in view of antiplaque property, chlorhexidine gluconate was considered to be more effective. The effect of curcumin was attributed to its potential of anti-inflammatory action. Both the studied groups showed a significant reduction in total microbial count. A clinico-microbiological study was conducted in 30 individuals affected with chronic periodontitis in which a local drug delivery system (LDDS) containing 2% whole turmeric gel was experimented (Behal *et al*, 2011). These participants with chronic localized or generalized periodontitis exhibited pocket depth of 5-7 mm. The control group received scaling and root planning (SRP), whereas experimental group received SRP plus 2% whole turmeric gel LDDS. Both control and experimental groups showed statistically significant reduction in plaque index, gingival index, sulcus bleeding index, probing pocket depth, and gain in relative attachment loss. Authors noted a significant reduction in the trypsin-like enzyme activity of 'red complex' microorganisms and a greater reduction in all parameters in the experimental group compared to control one. This study suggested the 2% LDDS as an adjunct therapy to SRP in prevention of gingival problems. A pilot study was conducted in which 1% curcumin was administered for subgingival irrigation in 20 patients with chronic periodontitis (Suhag *et al*, 2007). They observed a significant improvement in bleeding on probing, redness and probing pocket depth. They suggested that 1% curcumin solution can reduce inflammatory signs more effectively than those most widely use chlorhexidine and saline irrigation media. Some authors (Cikrikci *et al*, 2008) suggested that the pit and fissure sealant can be prepared from ploymerizable resin containing acrylic monomer and a colorant from annatto extract, turmeric extract and β‑Apo‑8′‑Carotenal. The role of curcumin in the treatment of head and neck squamous cell carcinoma was reviewed (Wilken *et al*, 2011). Curcumin exhibited anticancer potential due to its effect on a variety of biological pathways involved in mutagenesis, oncogene expression, cell cycle regulation, apoptosis, tumorigenesis, and metastasis. Curcumin has been found enhancing the effect of chemotherapy and radiotherapy in squamous cell carcinomas. It also arrest cancer cells in the G2/M phase of cell cycle, in which cells are more susceptible to cytotoxic effects of radiotherapy. The efficacy of curcumin and turmeric oil was compared as chemoprotective agents in various precancerous conditions such as oral submucous fibrosis (OSMF), leukoplakia, and lichen planus (Deepa *et al*, 2010). Curcumin and turmeric oil have demonstrated their oncopreventive potential in animal studies. The authors, in their clinico-histopathological evaluation observed a reduction in burning sensation and pain and partial reversal of opening of the mouth in OSMF patients (Deepa *et al*, 2010).

Several researchers have studied the role of curcumin in multiple human human carcinomas such as melanoma, and cancers involving head and neck, breast, colon, pancreas, prostate and ovary. An epidemiological investigation of digestive tract cancers in India was conducted and reported that the low incidence of colon cancer can be attributed to the chemopreventive and antioxidant behavior of curcumin rich diets consumed in the country (Mohandas *et al*, 1999). Curcumin exhibits potent anti-oxidant and free-radical quenching activity, which causes inhibition of the compound on the initial stages of carcinogenesis. It has shown that the curcumin exhibits a potential of suppressing UV irradiation-induced DNA mutagenesis and inducting cellular SOS functions (Oda, 1995). It has been reported that the curcumin inhibit the Phase I enzymes (including cytochrome p450 isoforms and p450 reductase) creating carcinogenic metabolites that participate in DNA adduct formation (Thapliyal & Maru, 2001). However, other author (Iqbal & colleagues, 2003) observed that curcumin induces the Phase II metabolizing enzymes such as glutathione S-transferase, glutathione peroxidase and glutathione reductase in male mice. Several authors (Krishnaswamy *et al*, 1998; Inano *et al*, 1999; Collett *et al*, 2001) have reported curcumin's inhibitory potential on carcinogenesis in various animal models of various tumor types including oral cancer, mammary carcinoma and intestinal tumors.

CURCUMIN: FUTURE PERSPECTIVES

The major concern in the development of curcumin's clinical efficacy is related to its low oral bioavailability. This can be attributed to its poor absorption, high rate of metabolism in the intestines, and rapid elimination from the body. A little data is available on determining the curcumin's safety in higher doses, when used for therapeutic purposes. A novel polymeric based nanoparticle - encapsulated curcumin (Nanocurcumin) has been explored worldwide for treating human cancer (Bisht *et al*, 2007).

CONCLUSION

Curcumin is considered a safe and non-toxic alternative treatment approach for many conventionally prescribed medicines. Curcumin exhibits a variety of distinguished properties and actions on various systems of the human body. Recently, various clinical research and investigations experiments have revealed curcumin's great potential in the prevention and cure of cancer and proved its promising role in cancer therapy. However, future reaserch investigations are required to determine the optimal dosage, bioavailability, and bioefficacy of curcumin-based medicines. Oral administration of curcumin displays its poor bioavailability and tissue accumulation without compromising its therapeutic effects. Other structural analogs of curcumin, which are more bioavailable and effective, could be designed adjoined with large and well-controlled clinical trials.

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