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Medicinal and pharmacological properties of Turmeric (*Curcuma longa*): A review

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Abstract

Turmeric or *Curcuma longa*, is a perennial herb and member of the Zingiberaceae (ginger) family, and is cultivated extensively in Asian countries. The rhizome, the portion of the plant used medicinally as a yellow powder which is used as a flavor in many cuisines and as a medicines to treat many diseases particularly as an anti-inflammatory and for the treatment of flatulence, jaundice, menstrual difficulties, hematuria, hemorrhage, and colic or can be applied as an ointment to treat many skin diseases. The active constituents of turmeric are the flavonoid curcumin (diferuloylmethane) and various volatile oils, including tumerone, atlantone, and zingiberone. Water and fat soluble extracts of turmeric and its curcumin component exhibit strong antioxidant activity, comparable to vitamins C and E. Turmeric's hepatoprotective effect is mainly a result of its antioxidant properties resulting in enhanced cellular resistance to oxidative damage as well as its ability to decrease the formation of proinflammatory cytokines. Curcumin administration significantly decreased liver injury in test animals compared to controls and Turmeric extract also inhibited fungal aflatoxin production by 90% in addition to the role of turmeric and curcumin in reversing biliary hyperplasia, fatty changes, and necrosis. Studies showed that oral administration of curcumin in instances of diabetes, cancers, gastrointestinal disorders and neurological diseases. Curcumin may also be applied topically to counteract inflammation and irritation associated with inflammatory skin conditions and allergies. Curcumin's ability to inhibit carcinogenesis at three stages: tumor promotion, angiogenesis, and tumor growth.This review focuses on the medicinal and pharmacological benefits of turmeric in prevention and treatment of diseases. The information was collected from articles that have been published in pubmed and which are available online.

Key words: Medicinal plant, Anticancer, Anti-inflammatory, Antioxidant, Hepatoprotective agent.

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1. INTRODUCTION

Curcuma longa, or turmeric is a perennial herb and member of the Zingiberaceae (ginger) family and is cultivated extensively in Asia mostly in India and China. The rhizome, the portion of the plant used medicinally, yields a yellow powder. Dried *Curcuma longa* is the source of turmeric, the ingredient that gives curry powder its characteristic yellow color. It has many names such as Curcum in the Arab region, Indian saffron, Haridra (Sanskrit, Ayurvedic), Jianghuang (yellow ginger in Chinese), Kyoo or Ukon (Japanese) [1].

Turmeric has been used in Asian cuisines for both its flavor and color and in the Chinese and Ayurvedic medicine particularly as an anti-inflammatory and for the treatment of jaundice, menstrual difficulties, hematuria, hemorrhage, and colic. It is official in the Pharmacopoeia of China as well as in other Asian countries such as Japan and Korea and its

usage covers a wide range of health indications. In China it is ingested orally and applied topically for urticaria and skin allergy, viral hepatitis, inflammatory conditions of joints, sore throat and wounds [2].

Oral administration is the main route of administration for *Curcuma longa,* it can also be used topically and via inhalation (Ayurvedic tradition) or can be applied topically for the treatment of acne, wounds, boils, bruises, blistering, ulcers, eczema, insect bites, parasitic infections, hemorrhages and skin diseases like herpes zoster and pemphigus [3].

The active constituents of turmeric are the flavonoid Curcuminoids which is a mixture of curcumin (diferuloylmethane), monodexmethoxycurcumin and bisdesmethoxycurcumin Curcumin makes up approximately 90% of the curcuminoid content in turmeric. Other constituents include sugars, proteins, and resins. The best-researched active constituent is curcumin, which comprises 0.3-5.4% of raw turmeric [4].

Turmeric is comprised of a group of three curcuminoids: curcumin (diferuloylmethane), demethoxycurcumin, and bisdemethoxycurcumin (Fig.1), as well as volatile oils (tumerone, atlantone, and zingiberone), sugars, proteins, and resins. The Curcumin is a lipophilic polyphenol that is nearly insoluble in water but is quite stable in the acidic pH of the stomach [5].

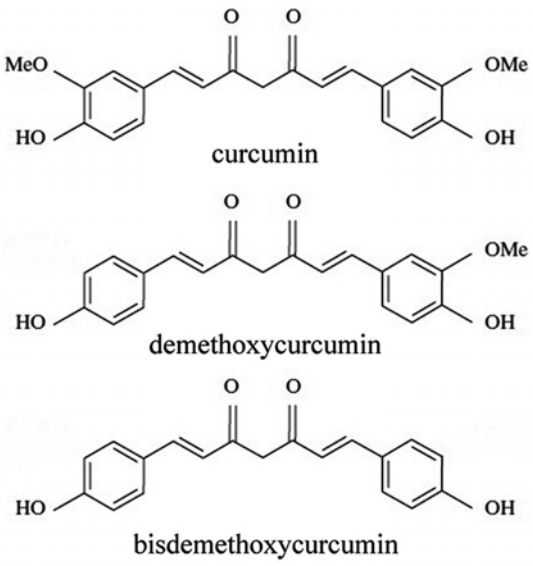

Fig.1.Structural formula of three curcuminoids

The phenolic groups in the structure of curcumin explain the ability of curcumin to eliminate oxygen-derived free radicals. The free radicals which can be eliminated by curcumin are hydroxyl radical, singlet oxygen, superoxide radical , nitrogen dioxide and NO [6].

With regard to pharmacokinetic, studies have demonstrated that 40-85% of an oral dose of curcumin passes through the gastrointestinal tract unchanged. Due to its low rate of absorption, curcumin is often formulated with bromelain for increased absorption and enhanced anti-inflammatory effect [7].

This review focuses on the medicinal and pharmacological properties of turmeric as anti-inflammatory, antioxidant, hepatoprotective, anticarcinogenic, antidiabetic, antimicrobial, antidepressant in addition to its use in cardiovascular disease, gastrointestinal and neurological disorders.

2. MEDICINAL AND PHARMACOLOGICAL PROPERTIES OF TURMERIC

2.1. Anti-inflammatory properties

Oral administration of curcumin in instances of acute inflammation was found to be as effective as cortisone or phenylbutazone. Oral administration of *Curcuma longa* significantly reduced inflammatory swelling [8]. *C. longa's* anti-inflammatory properties may be attributed to its ability to inhibit both biosynthesis of inflammatory prostaglandins from arachidonic acid, and neutrophil function during inflammatory states.

Curcuminoids also inhibit LOX, COX, phospholipases, leukotrienes, prostaglandins, thromboxane, nitric oxide elastase, hyaluronidase, collagenase, monocyte chemoattractant protein-1, interferon inducible protein, TNF and interleukin-12. They also decrease prostaglandin formation and inhibit leukotriene biosynthesis via the lipoxygenase pathway [9].

An RCT investigated the effect of a combination of 480mg curcumin and 20mg quercetin (per capsule) on delayed graft rejection (DGR) in 43 kidney transplant patients. Of 39 participants who completed the study, two of 14 in the control group experienced DGR compared to zero in either treatment group. Early function (significantly decreased serum creatinine 48 hours post-transplant) was achieved in 43% of subjects in the control group, 71% of those in the lowdose treatment group. Since the amount of quercetin in the compound was minimal, the majority of benefit is thought to be due to curcumin's anti-inflammatory and antioxidant activity. Likely mechanisms for improved early function of transplanted kidneys include induction of the hemeoxygenase enzyme, and proinflammatory cytokines, and scavenging of free radicals associated with tissue damage [10].

2.2. Antioxidant properties

Water and fat-soluble extracts of turmeric and its curcumin component exhibit strong antioxidant activity, comparable to vitamins C and E. A study of ischemia demonstrated that curcumin pretreatment decreased ischemia-induced changes in the heart [11]. An *in vitro* study measuring the effect of curcumin on endothelial heme oxygenase-1, an inducible stress protein, was conducted

utilizing bovine aortic endothelial cells. Incubation with curcumin resulted in enhanced cellular resistance to oxidative damage [12].

Nagabhushan *et al.* 1987 [13] tested curcumin against tobacco products and several environmental mutagens in a Salmonella/microsome test with or without Aroclor 1254-induced rat liver homogenate (S-9 mix), in order to determine the difference between mutagens. Curcumin inhibited the mutagenicity of bidi smoke condensate, cigarette smoke condensate and masheri (a tobacco product) and tobacco extracts in a dose-dependent manner. Curcumin is only antimutagenic against mutagens which require metabolic activation.

Curcumin was found to block cyclosporine A-resistant phorbol myristate acetate + anti-CD28 pathway of T-cell proliferation [14]. In addition, curcumin reduces the testicular damage caused by exposure to di-n-butylphthalate (DBP), by increase in Glutathion (GSH), testosterone levels and glucose-6-phosphate dehydrogenase (G6PD) activity and decrease in malondialdehyde (MDA) levels. These properties may be due to intrinsic antioxidative abilities of curcumin [15].

Farombi *et al.* 2007 carried out a study to determine the ameliorative properties of curcumin and kolaviron (a biflavonoid from the seeds of *Garcinia kola*) on the di-n-butylphthalate (DBP)-induced testicular damage in rats The level of glutathione (GSH), the glucose-6-phosphate dehydrogenase (G6PD) activity and the decreased testosterone levels were significantly increased. The increased levels of malondialdehyde (MDA) were decreased, which is in agreement with [16]. This may be due to the intrinsic antioxidative abilities to combat oxidative damage induced by DBP.

Mice exposed to human prostate cancer cells were treated with curcumin. The curcumin-treated animals showed a decrease in microvessel density and cell proliferation and an increase in apoptosis compared to controls [17]. Incubation of endothelial cells from bovine aorta with curcumin (in a concentration range of 5-15μM) showed induction of heme oxygenase expression. Heme oxygenase is an enzyme that reacts to oxidative stress, by producing the antioxidant biliverdin, and it enhances resistance to oxidative damage to cells [18].

Clinical research on curcumin's therapeutic benefit for pancreatitis is limited and has primarily focused on its antioxidant properties. However, research indicates the inflammatory response plays a critical role in development of pancreatitis and subsequent tissue damage. For this reason, it seems likely an anti-inflammatory agent like curcumin, effective against a variety of inflammatory molecular targets and shown to decrease inflammatory markers in an animal model of pancreatitis. One pilot study examined the effect of curcumin for tropical pancreatitis in patients [19].

Treatment effect on pain patterns as well as erythrocyte malonylaldehyde (MDA; an indicator of lipid peroxidation) and glutathione (GSH) were assessed at baseline and after six weeks. In the curcumin group there was a significant reduction in MDA levels. Further research is needed to determine the role of lipid peroxidation in pain and other symptomology associated with pancreatitis [20].

2.3. Hepatoprotective properties

Turmeric is known to have a hepatoprotective characteristic similar to silymarin. Studies have demonstrated turmeric's hepatoprotective properties from a variety of hepatotoxic injuries, including carbon tetrachloride (CCl_4) [21] galactosamine and acetaminophen (paracetamol) [22]. Turmeric's hepatoprotective effect is mainly a result of its antioxidant properties, as well as its ability to decrease the formation of proinflammatory cytokines. Curcumin administration significantly decreased liver injury [23].

Turmeric reduced infection with *Aspergillus parasiticus* and inhibited fungal aflatoxin production by 90%. Turmeric and curcumin also reversed biliary hyperplasia, fatty changes, and necrosis induced by aflatoxin production. Sodium curcuminate, a salt of curcumin, also exerts choleretic properties by increasing biliary excretion of bile salts, cholesterol, and bilirubin, as well as increasing bile solubility, therefore possibly preventing and treating cholelithiasis. Curcumin also protects cells against lipid peroxidation induced by paracetamol. This may be due to the antioxidative properties of the phenolic groups of curcumin [24].

Curcumin was found to decrease serum aspartate transaminase and alkaline phosphatase activity, and free fatty acid, cholesterol and phospholipid levels. Tacrine is known for its T-cell destructive activity and hepatotoxicity. In a study with cultures of human hepatocytes, which had been destroyed by tacrine, curcumin showed to be nearly ten times more effective than the regular treatment, ascorbic acid [25].

The effect of curcumin on alcohol induced hepatotoxicity in alcoholic rats was studied by Rajakrishnan *et al.*1998 [26]. Curcumin administration resulted in a decrease of serum aspartate transaminase and alkaline phosphatase activity. The levels of serum free fatty acids, cholesterol and phospholipids decreased as well.

2.4. Anticarcinogenic properties

Animal research demonstrates inhibition at all three stages of carcinogenesis-initiation, promotion, and progression. During initiation and promotion, curcumin modulates transcription factors controlling phase I and II detoxification of carcinogens; [27] down-regulates proinflammatory cytokines, free radical-activated transcription factors, and arachidonic acid metabolism vicyclooxygenase and lipoxygenase pathways; and scavenges free radicals [28].

Studies involving rats and mice, as well as *in vitro* studies utilizing human cell lines, have demonstrated curcumin's

ability to inhibit carcinogenesis at three stages: tumor promotion, angiogenesis, and tumor growth [29]. Turmeric and curcumin are also capable of suppressing the activity of several common mutagens and carcinogens in a variety of cell types in both *in vitro* and *in vivo* studies [30]. The anticarcinogenic properties of turmeric and curcumin are due to direct antioxidant and free-radical scavenging properties, as well as their ability to indirectly increase glutathione levels, thereby aiding in hepatic detoxification of mutagens and carcinogens, and inhibiting nitrosamine formation and Curcumin also induces apoptosis of cancer cells and it inhibits angiogenesis [31].

The efficacy of curcumin or turmeric extract in reducing chemically-induced tumours was studied by [32]. Application of both curcumin and turmeric extract during carcinogenesis and promotion resulted in less papilloma production, compared to controls. This indicates that both curcumin and turmeric extract produce their best properties during tumour promotion.

The effect of dietary curcumin (0.2% and 1.0%) on 7,12-dimethylbenz (a) anthracene (DMBA) and 12,0-tetradecanoylphorbol-13-acetate (TPA)-promoted skin tumor formation was investigated by Limtrakul *et al.* They found a significant lower number of papillomas in the curcumin treated group compared to the control group. The enhanced expression of ras-p21 and fos-p62 oncogenes were decreased dose dependently in the curcumin treated group [33].

The effect of *Curcuma longa* on myocardial apoptosis in experimentally induced myocardial ischemic-reperfusion injury was investigated by Mohanty *et al.* 2006 [34]. *Curcuma longa* demonstrated significant anti-apoptotic property, which might contribute to the observed preservation in cardioprotective properties and cardiac function.

Azuine *et al.* investigated the protective effect of turmeric extract on chemically induced mutagenicity in *Salmonella typhimurium* strains and clastogenicity in mammalian bone marrow in female Swiss mice. The anticarcinogenic properties were assessed in the benzo (a) pyrene induced forestomach neoplasia model. Aqueous turmeric extract exhibited antimutagenic activity against direct acting mutagens and also inhibited the mutagenicity of benzo (a) pyrene in *Salmonella typhimurium* strains. Treatment with the aqueous tumeric extract inhibited the development of forestomach tumors induced by benzo (a) pyrene significantly. These findings were all dose-dependent [35].

There is some evidence that curcumin inhibits the activity of certain chemotherapy drugs. Research reveals curcumin decreased camptothecininduced death of cultured breast cancer cells and prevented cyclophosphamide-induced breast tumor regression in mice [36]. Curcumin might also interfere with the absorption and efficacy of the chemotherapy drug irinotecan, which is used to treat colon cancer. On the other hand, curcumin may enhance the effects of some chemotherapy drugs. In a mouse xenograft model of human breast cancer, curcumin in conjunction with paclitaxel (Taxol) significantly inhibited breast cancer metastasis to the lung to a greater degree than either curcumin or paclitaxel alone [37].

2.5. Antidiabetic properties

A hexane extract (containing ar-turmerone), ethanolic extract (containing containing ar-turmerone, curcumin, demethoxycurcumin and bisdemethoxycurcumin) and ethanolic extract from the residue of the hexane extraction (containing curcumin, demethoxycurcumin and bisdemethoxycurcumin) were found to dose-dependently stimulate adipocyte differentiation. The results indicate that turmeric ethanolic extract containing both curcuminoids and sesquiterpenoids is more strongly hypoglycemic than either curcuminoids or sesquiterpenoids [38].

Wickenberg *et al.* 2010 [39] studied the effects of turmeric on postprandial plasma glucose and insulin in healthy subjects; they found out that the ingestion of 6g *C. longa* had no significant effect on the glucose response. The change in insulin was significantly higher 30min and 60min after the OGTT including *C. longa*. The insulin AUCs were also significantly higher after the ingestion of *C. longa* after the OGTT.

2.6. Antimicrobial properties

Turmeric extract and the essential oil of *Curcuma longa* inhibit the growth of a variety of bacteria, parasites, and pathogenic fungi. A study of chicks infected with the caecal parasite *Eimera maxima* demonstrated that diets supplemented with turmeric resulted in a reduction in small intestinal lesion scores and improved weight gain [40]. Another study, in which guinea pigs were infected with eitherdermatophytes, pathogenic molds, or yeast, found that topically applied turmeric oil inhibited dermatophytes and pathogenic fungi. Improvements in lesions were observed in the dermatophyte- and fungi-infected guinea pigs, and at seven days post-turmeric application the lesions disappeared. Curcumin has also been found to have moderate activity against *Plasmodium falciparum* and *Leishmania major* organisms [41].

Khattak *et al.* 2005 [42] studied the antifungal, antibacterial, phytotoxic, cytotoxic and insecticidal activity of an ethanolic extract of turmeric. The extract showed antifungal activity towards *Trichophyton longifusus* and *Microsporum canis* and weak antibacterial activity against *Staphylococcus aureus*. Toxic activity was observed against *Lemna minor*.

The *Curcuma longa* treated rabbit group showed a significant higher mean value for contraction of the wound compared to controls. Furthermore the wounds showed less inflammation and an increasing trend in the formation of collagen [43].

2.7. Antidepressant properties

The effect of curcumin was investigated in chronic mild stress (CMS) model. In comparison with normal rats, rats suffering the CMS procedure have a significant lower intake of sucrose, increased IL-6, TNF-α levels, CRF- and cortisol levels. Treatment with ethanolic extract increased the sucrose intake to normal control levels, reduced the CMS-induced increase in serum IL-6 and TNF-α levels and reduced the CRF levels in serum and medulla oblongata to lower than normal. It also lowered the cortisol levels in serum to normal levels. Turmeric has antidepressant properties mediated through inhibition of monoamine oxidize A [44]. *Curcuma longa* ethanolic extract reversed the decrease in serotonin, noradrenalin and dopamine concentrations as well as the increase in serotonin turnover, cortisol levels and the in serum corticotrophin-releasing factor [45].

Xu *et al.* 2006 [46] investigated the effect of orally administered curcumin on behavior in a chronic stress model of depression in rats. The antidepressant imipramine was used as a control. Curcumin administration showed similar properties as imipramine. These findings suggest that the properties of chronic administration of curcumin on the behavior of chronic stressed rats may be related to the modulating properties of the dysfunction of the hypothalamic-pituitary-adrenal (HPA) axis, through selective increase in brain-derived neurotropic factor in the frontal cortex and the hippocampus of the rats.

2.8. Cardiovascular diseases

Turmeric's protective properties on the cardiovascular system include lowering cholesterol and triglyceride levels, decreasing susceptibility of low density lipoprotein (LDL) to lipid peroxidation and inhibiting platelet aggregation [47]. Turmeric extract demonstrated decreased susceptibility of LDL to lipid peroxidation, in addition to lower plasma cholesterol and triglyceride levels. Turmeric extract's effect on cholesterol levels may be due to decreased cholesterol uptake in the intestines and increased conversion of cholesterol to bile acids in the liver. Inhibition of platelet aggregation by *C. longa* constituents is thought to be via potentiation of prostacyclin synthesis and inhibition of thromboxane synthesis [48].

Curcumin mobilizes α-tocopherol from adipose tissue, this results in protection against oxidative damage produced during atherosclerosis development. Curcumin increases VLDL cholesterol transport in plasma, which results in increasing levels of α-tocopherol. Curcumin has shown to mobilize α-tocopherol from adipose tissue, thus protecting their body against oxidative damage produced during the development of atherosclerosis. Also more LDL cholesterol could be transported in plasma, increasing levels of α-tocopherol. Overall the fatty acids in the animals were less susceptible to oxidation in the vessel wall [49]. It was observed that oral intake of 500mg/d curcumin for 7 days resulted in a significant decrease in the level of serum lipid peroxides (33%) and increase in HDL cholesterol (29%) and a decrease in level of total serum cholesterol (12%) [50].

2.9. Gastrointestinal disorders

Curcumin's anti-inflammatory properties and therapeutic benefit have been demonstrated for a variety of gastrointestinal disorders, including dyspepsia, *Helicobacter pylori* infection, peptic ulcer, irritable bowel syndrome, Crohn's disease, and ulcerative colitis.

2.9.1. Dyspepsia and gastric ulcer

In a phase II clinical trial involving 45 subjects with endoscopically diagnosed peptic ulcers were given 600mg curcumin five times daily for 12 weeks. Ulcers were absent in 12 patients (48%) after four weeks, in 18 patients after eight weeks, and in 19 patients (76%) after 12 weeks. The remaining 20 patients, also given curcumin, had no detectable ulcerations at the start of the study, but were symptomatic-erosions, gastritis, and dyspepsia. Within 1-2 weeks abdominal pain and other symptoms had decreased significantly [51].

Kim *et al.* 2005 [52] investigated the protective effect of turmeric ethanolic extract against gastric ulcers by blocking H_2 histamine receptors (H_2R) of male Sprague-Dawley (pylorus-ligated) rats. The effect of *Curcuma longa* extract was compared to the properties of ranitidine. Curcuma was found to protect the gastric mucosal layer as effective as ranitidine. Orally administerd ethanolic extract inhibited gastric acid, gastric juice secretion and ulcer formation comparable to the properties of ranitidine.

Rafatullah *et al.* 1990 [53] investigated the antiulcer activity of an ethanolic extract of turmeric. Administration of turmeric extract led to a significant decrease in ulcer index and acidity of stomach contents. Pretreatment with the turmeric extract reduced the intensity of ulceration. Hypothermic-restraint stress reduction of gastric wall mucus was inhibited by turmeric extract treatment and reduced the severity of lesions induced by various necrotizing agents.

2.9.2. Irritable bowel syndrome

In patients with irritable bowel syndrome (IBS) the most common symptoms are abdominal pain, bloating, altered bowel habits, and increased stool frequency. In an eight-week pilot study of IBS patients. After four weeks, those groups experienced a 53% and 60% reduction in IBS prevalence. In post-study analysis, abdominal pain and discomfort scores were reduced by 22 and 25% [54].

2.9.3. Inflammatory bowel disease

Crohn's disease (CD) and ulcerative colitis (UC) are the two primary forms of inflammatory bowel disease (IBD).

Holt *et al.,* 2005 [55] conducted a pilot study to examine the effect of curcumin therapy in patients with IBD who had previously received standard UC or CD therapy. Hematological and biochemical blood analysis, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) (the latter two inflammatory indicators), sigmoidoscopy, and biopsy were all performed at baseline and at the study end. Crohn's Disease Activity Index (CDAI), CRP, ESR, hematological blood analysis, and kidney function was assessed in all patients at baseline and end of study. In the proctitis group all five patients improved by study's end as indicated by a global score, and all five subjects demonstrated normal ESR, CRP, and serologic indices of inflammation after two months. In the CD group, CDAI scores decreased by an average of 55 points, and CRP and ESR decreased in four of five patients. The authors concluded that curcumin plus standard therapy was more effective in maintaining remission than placebo plus standard UC treatment [56].

2.10. Neurological disorders

Studies in animal models of Alzheimer's disease (AD) indicate a direct effect of curcumin in decreasing the amyloid pathology of AD [57]. Based on many studies, results have shown that curcumin possessed multiple actions in brain. Curcumin can be a future drug of therapy for the treatment of various neurological disorders such as major depression, tardive dyskinesia and diabetic neuropathy [58].

2.11. Pregnancy/neonates

Singh and Aggarwal 1995 [59] studied curcumin on hepatic biotransformation system enzymes. Turmeric and curcumin induced a significant increase in hepatic levels of glutathione S-transferase (GST) and sulfhydryl (SH) levels. Cytochrome b5 and cytochrome P450 levels were significantly elevated as well. This indicates that turmeric and/or curcumin metabolites can be transferred through lactation.

3. CONCLUSION

Curcumin can be considered a great potential therapeutic agent for a variety of inflammatory conditions and cancer types. Consequently, there is extensive interest in its therapeutic potential as evidenced by the number of ongoing phase II and III clinical trials. The primary obstacle to utilizing curcumin therapeutically has been its limited systemic bioavailability, but researchers are actively involved in trying to find the most efficient method of application.

CONFLICTS OF INTEREST

The authors declare that they have no affiliations with or involvement in any organization or entity with any financial interest, or non-financial interest in the subject matter or materials discussed in this manuscript.

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