

An Investigation into the Medicinal and Pharmaceutical Properties of Turmeric

Vishal Srivastava¹ and Dr. Tushar Treembakshelke²

Research Scholar, Department of Pharmacy¹

Research Guide, Department of Pharmacy²

Sunrise University, Alwar, Rajasthan, India

Abstract: *Curcuma longa*, or turmeric, is a perennial Zingiberaceae (ginger) plant. Asia grows it extensively. The rhizome's yellow powder is used as an ointment to treat skin diseases or as an anti-inflammatory and pharmaceutical to treat colic, hematuria, jaundice, flatulence, and menstruation issues. Curcumin, also known as diferuloylmethane, and volatile oils including tumerone, atlantone, and zingiberone are turmeric's active components. Turmeric and curcumin in fat- and water-soluble extracts have antioxidant activity comparable to vitamins C and E. Turmeric's hepatoprotective benefits come from its antioxidant properties, which boost cellular resistance to oxidative damage and suppress proinflammatory cytokines. Curcumin decreased liver damage in test animals compared to controls. Turmeric extract prevented biliary hyperplasia, lipid changes, and necrosis and inhibited aflatoxin formation in fungus by 90%. Curcumin may be used orally for diabetes, cancer, gastrointestinal difficulties, and neurological disorders, according to research. Turmeric may be used topically to decrease inflammation and discomfort from inflammatory skin conditions and allergies. Curcumin may inhibit tumor proliferation, angiogenesis, and growth. The medicinal and pharmacological uses of turmeric in disease prevention and therapy are the focus of this research. The data came from Pubmed-published online articles.

Keywords: Medicinal plant, Anticancer, Anti-inflammatory.

I. INTRODUCTION

Curcuma longa, the scientific name for turmeric, is a perennial plant that is extensively cultivated across Asia, mainly in China and India. It belongs to the family Zingiberaceae, which includes ginger. The rhizome, or medicinal portion of the plant, yields a yellow powder. Dried *Curcuma longa* is the source of turmeric, which is what gives curry powder its characteristic yellow color. There are many names for it: Indian saffron, Japanese Kyoo or Ukon, Sanskrit Haridra, Jianghuang (yellow ginger), Curcum in the Arab world [1]. Turmeric's flavor and color have long been appreciated in Asian cuisines. It is also used in Chinese and Ayurvedic medicine, particularly as an anti-inflammatory and for the treatment of jaundice, menstrual issues, hematuria, bleeding, and colic. It is listed in the pharmacopoeia of China and other Asian countries, such as Japan and Korea, and is acknowledged for use in a wide range of medicinal purposes. In China, it is used topically and orally to treat wounds, sore throats, joint inflammation, viral hepatitis, urticaria, and skin allergies [2]. In accordance with Ayurvedic tradition, *curcuma longa* is mainly taken orally, but it can also be applied topically, inhaled, and used to treat a range of skin conditions, such as eczema, acne, wounds, boils, bruises, blistering, ulcers, insect bites, parasitic infections, hemorrhages, and skin diseases like zoster and herpes [3]. Among the other constituents are carbohydrates, proteins, and resins. Curcumin, which makes up 0.3-5.4% of raw turmeric, is the active component that has been researched the most [4]. Turmeric is made up of three curcuminoids (curcumin (diferuloylmethane), demethoxycurcumin, and bisdemethoxycurcumin), as well as volatile oils (tumerone, atlantone, and zingiberone), carbohydrates, proteins, and resins (Fig. 1). Curcumin is a lipophilic polyphenol that exhibits remarkable stability in the acidic pH of the stomach, while being almost entirely soluble in water [5].

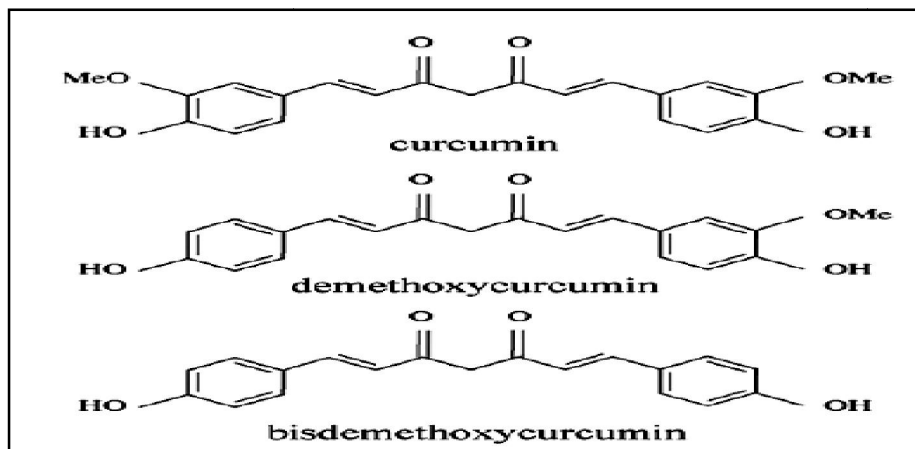


Fig.1. Structural formula of three curcuminoids

The phenolic groups included in curcumin's structure are responsible for its ability to eliminate oxygen-produced free radicals. The following free radicals may be eliminated by curcumin: nitrogen dioxide, superoxide radical, hydroxyl radical, singlet oxygen, and NO [6]. According to studies on pharmacokinetics, the digestive tract absorbs 40–85% of an oral dose of curcumin intact. Bromelain is often added to curcumin formulations to enhance absorption and enhance the anti-inflammatory properties of the slow-absorbing curcumin [7]. This study focuses on the medical and pharmacological aspects of turmeric, including its anti-inflammatory, antioxidant, hepatoprotective, anticarcinogenic, antidiabetic, antibacterial, and antidepressant properties. Turmeric is also used in the treatment of cardiovascular disease, gastrointestinal disorders, and neurological issues.

Medicinal And Pharmacological Properties of Turmeric

Anti-inflammatory properties

Oral curcumin therapy was shown to be as efficacious as cortisone or phenylbutazone in instances of acute inflammation. When taken orally, curcuma longa significantly reduced inflammatory swelling [8]. *C. longa* is believed to have anti-inflammatory properties since it may inhibit the production of pro-inflammatory prostaglandins from arachidonic acid and reduce neutrophil activity in inflammatory situations. Curcuminoids also suppress TNF, interleukin-12, phospholipases, thromboxane, nitric oxide elastase, hyaluronidase, collagenase, monocyte chemoattractant protein-1, and interferon inducible protein. They also inhibit the lipoxygenase pathway, which lowers the synthesis of prostaglandin and stops the production of leukotrienes [9]. An RCT looked at the effects of 480 mg curcumin and 20 mg quercetin (per capsule) on delayed graft rejection (DGR) in 43 patients of kidney transplants. Two of the 14 participants in the control group, out of the 39 who completed the experiment, developed DGR, but none of the participants in the treatment group did. In the control group, 43% of individuals had achieved early function, as measured by a significantly decreased blood creatinine 48 hours after transplant, while 71% of those in the lowdose treatment group had done so. The low concentration of quercetin in the molecule is thought to be the main cause of curcumin's antioxidant and anti-inflammatory effects. The activation of hemeoxygenase, the scavenging of free radicals associated with tissue damage, and proinflammatory cytokines are probably the reasons for the improved early function of transplanted kidneys [10].

Antioxidant properties

Turmeric and curcumin in fat- and water-soluble extracts have antioxidant activity comparable to vitamins C and E. An ischemia study found that curcumin pretreatment delayed cardiac changes [11]. In vitro, curcumin was tested on endothelial heme oxygenase-1, an inducible stress protein, in bovine aortic endothelial cells. Curcumin incubation strengthened cells against oxidative damage [12].

Nagabhushan et al. 1987 [13] used a Salmonella/microsome experiment with or without an Aroclor 1254-induced rat liver homogenate (S-9 mix) to compare curcumin to tobacco products and many environmental mutagens. Curcumin

reduced the mutagenicity of tobacco extracts, bidi smoke condensate, cigarette smoke condensate, and masheri dose-dependently. Curcumin is exclusively antimutagenic against metabolically activated mutagens.

Curcumin inhibits the cyclosporine A-resistant phorbol myristate acetate + anti-CD28 T-cell proliferation pathway [14]. Curcumin also reduces malondialdehyde (MDA) and enhances glutathione (GSH), testosterone, and glucose-6-phosphate dehydrogenase (G6PD) activity, reducing testicular injury from di-n-butylphthalate. Curcumin may have these properties due to its antioxidant properties [15].

Farombi et al. investigated the therapeutic effects of curcumin and kolaviron, a biflavonoid from *Garcinia kola* seeds, on rats' di-n-butylphthalate-induced testicular damage in 2007. Increased GSH, G6PD activity, and decreased testosterone were observed. Despite rising, MDA levels decreased, as expected [16]. DBP may induce oxidative damage, which innate antioxidants may combat. Mouse-exposed to human prostate cancer cells received curcumin. Curcumin reduced microvessel density, cell proliferation, and apoptosis in mice [17]. Endothelial cells from the bovine aorta were treated with curcumin (5-15 μ M) to promote heme oxygenase production. The antioxidant biliverdin produced by heme oxygenase in response to oxidative stress strengthens cells [18]. Most curcumin research on pancreatitis has focused on its antioxidant properties. However, pancreatitis and tissue damage seem to be largely induced by inflammation. Curcumin, an anti-inflammatory medication that lowers inflammatory indicators in an animal model of pancreatitis and targets many inflammatory molecular targets, may be the reason. Curcumin was tested for tropical pancreatitis in a pilot study [19]. MDA, an indicator of lipid peroxidation, and glutathione (GSH) were assessed at baseline and six weeks into therapy, along with pain patterns. Curcumin significantly reduced MDA levels. Lipid peroxidation's role in pancreatitis pain and symptoms needs additional study [20].

Hepatoprotective properties

Like silymarin, turmeric protects the liver. Turmeric protects the liver against CCl₄, galactosamine, and paracetamol [21, 22]. Antioxidant and proinflammatory cytokine-reducing turmeric protects the liver. Curcumin greatly decreased liver damage [23].

Turmeric reduced aflatoxin and *Aspergillus parasiticus* infection by 90%. Curry and curcumin treated aflatoxins-induced biliary hyperplasia, fatty changes, and necrosis. Cholelithiasis may be avoided and treated with sodium curcumin, a curcumin salt that improves biliary excretion of bile salts, cholesterol, and bilirubin and bile solubility. Paracetamol-induced lipid peroxidation is prevented by curcumin. Curcumin's phenolics may be antioxidant [24]. Curcumin decreased serum aspartate transaminase, alkaline phosphatase, free fatty acid, cholesterol, and phospholipids. Toxicity and T-cell destruction define tacrine. Curcumin restored tacrine-damaged human hepatocyte cultures 10 times better than ascorbic acid [25]. Rajakrishnan et al. 1998 studied curcumin's effect on rat alcohol-induced hepatotoxicity [26]. ALP and aspartate transaminase were decreased by curcumin. Reduced serum cholesterol, phospholipids, and FFA.

Anticarcinogenic properties

Studies conducted on animals demonstrate that the three phases of carcinogenesis—initiation, promotion, and progression—are blocked. Curcumin scavenges free radicals [28], down-regulates proinflammatory cytokines, free radical-activated transcription factors, and the cyclooxygenase and lipoxygenase pathways involved in arachidonic acid metabolism. It also regulates transcription factors that control phase I and II detoxification of carcinogens during initiation and promotion.

Studies involving rats and mice, as well as in vitro studies

Curcumin suppresses tumor promotion, angiogenesis, and proliferation in human cell lines [29]. Turmeric and curcumin reduce the effects of several mutagens and carcinogens in multiple cell types in vitro and in vivo [30]. By directly antioxidant and free-radical scavenging and indirectly boosting glutathione, turmeric and curcumin assist the liver detoxify mutagens and carcinogens and limit nitrosamine production. Curcumin inhibits angiogenesis and kills cancer cells [31].

Turmeric extract inhibits chemically-induced cancers [32]. Compared to controls, curcumin and turmeric extract decreased papilloma growth during carcinogenesis and promotion. It seems that curcumin and turmeric extract promote tumor growth best.

Limtrakul et al. tested 0.2% and 1.0% dietary curcumin on DMBA and TPA-induced skin cancers. Curcumin substantially reduced papillomas compared to the control group. Curcumin dose-dependently suppressed ras-p21 and fos-p62 oncogenes [33].

In experimental ischemic-reperfusion injury, Mohanty et al. 2006 evaluated *Curcuma longa*'s effect on myocardial apoptosis [34]. Anti-apoptotic properties may explain *curcuma longa*'s cardioprotective and heart function benefits. Azuine et al. tested turmeric extract's protection against chemically generated *Salmonella typhimurium* mutagenicity and bone marrow clastogenicity in female Swiss mice. Anticarcinogenicity was tested in benzo (a) pyrene-induced forestomach neoplasia. In *Salmonella typhimurium* strains, aqueous turmeric extract reduced benzo (a) pyrene and direct mutagens. Aqueous turmeric extract significantly decreased benzo (a) pyrene-induced forestomach cancers. All outcomes were dose-dependent [35]. It seems that curcumin inhibits numerous chemotherapeutics. In mice, curcumin inhibited camptothecin-induced breast cancer cell death and cyclophosphamide-induced tumor regression [36]. Curcumin may impair irinotecan absorption and efficacy. However, curcumin may enhance chemotherapy. Curcumin plus paclitaxel (Taxol) inhibited lung metastases more than either alone in a mouse xenograft model of human breast cancer [37].

Antidiabetic properties

A hexane extract (containing ar-turmerone), ethanolic extract (containing ar-turmerone, curcumin, demethoxycurcumin, and bisdemethoxycurcumin), and ethanolic extract from the residue hexane extraction dose-dependently stimulated adipocyte differentiation. Turmeric ethanolic extract with curcuminoids and sesquiterpenoids is more hypoglycemic than either alone [38].

Wickenberg et al. 2010 [39] reported that 6g *C. longa* had no impact on postprandial plasma glucose and insulin in healthy participants. Post-OGTT insulin changes were substantially greater 30 and 60 minutes, including *C. longa*. After the OGTT, *C. longa* dramatically increased insulin AUCs.

Antimicrobial properties

Curcuma longa essential oil and turmeric extract resist bacteria, parasites, and harmful fungi. In *Eimeria maxima*-infected chicks, turmeric-supplemented meals reduced small intestine lesion scores and enhanced weight growth [40]. In guinea pigs with dermatophytes, pathogenic molds, or yeast, turmeric oil suppressed both. Seven days of turmeric treatment eliminated lesions in dermatophyte- and fungi-infected guinea pigs. Curcumin suppresses *Plasmodium falciparum* and *Leishmania major* somewhat [41].

Khattak et al. 2005 tested ethanolic turmeric extract for antifungal, antibacterial, phytotoxic, cytotoxic, and insecticidal properties [42]. The extract has mild antibacterial and antifungal activity against *Staphylococcus aureus*, *Trichophyton longifusus*, and *Microsporum canis*. Toxicity affected *Lemna minor*. *Curcuma longa* contracted rabbit wounds more than controls. Less inflammation and more collagen in wounds [43].

Antidepressant properties

This CMS study examined curcumin. CMS-treated rats exhibit reduced sucrose intake, elevated IL-6, TNF- α , CRF-, and cortisol levels relative to controls. Ethanolic extract treatment reduced CMS-induced IL-6 and TNF- α levels, normalized sucrose consumption, and lowered blood and medulla oblongata CRF levels. Also, serum cortisol normalized. Monoamine oxidizes Turmeric prevents depression [44]. The *curcuma longa* ethanolic extract lowered serotonin, cortisol, and serum corticotrophin-releasing factor [45]. In a chronic stress depression paradigm, Xu et al. 2006 [46] examined oral curcumin's effects on rats. Control: imipramine. Curcumin resembled imipramine. Chronic curcumin may improve hypothalamic-pituitary-adrenal (HPA) axis dysfunction in stressed rats by increasing brain-derived neurotropic factor in the frontal cortex and hippocampus.

Cardiovascular diseases

Turmeric reduces cholesterol, triglycerides, LDL lipid peroxidation, and platelet aggregation [47]. Triglycerides, plasma cholesterol, and LDL lipid peroxidation decreased with turmeric extract. By lowering intestinal cholesterol absorption and enhancing hepatic cholesterol-to-bile acid conversion, turmeric extract may decrease cholesterol. *C. longa* components may prevent platelet aggregation by increasing prostacyclin and inhibiting thromboxane [48].

Curcumin prevents atherosclerosis-related oxidative damage by mobilizing α -tocopherol from adipose tissue. Curcumin increases plasma VLDL cholesterol transport, resulting in increased α -tocopherol levels. Curcumin may prevent atherosclerosis-related oxidative damage by releasing α -tocopherol from adipose tissue. Additionally, elevated plasma LDL cholesterol transport may raise α -tocopherol levels. Overall, vessel wall oxidation affected animal fatty acids less [49]. Oral 500mg/d curcumin for 7 days reduced blood lipid peroxides (33%), raised HDL cholesterol (29%), and lowered total serum cholesterol (12%) [50].

Gastrointestinal disorders

Curcumin is effective in treating dyspepsia, *Helicobacter pylori* infection, peptic ulcer, irritable bowel syndrome, Crohn's disease, and ulcerative colitis due to its anti-inflammatory characteristics.

Dyspepsia and gastric ulcer

In a phase II clinical investigation, 45 endoscopically diagnosed peptic ulcer patients got 600mg curcumin five times a day for 12 weeks. After four weeks, 12 (48%) had no ulcers, 18 after eight, and 19 after 12 weeks. The remaining 20 curcumin study participants developed erosions, gastritis, and dyspepsia but no ulcers. Stomach pain and other symptoms vanished after 1-2 weeks [51]. Kim et al. 2005 [52] inhibited H2R in male Sprague-Dawley (pylorus-ligated) rats to investigate turmeric ethanolic extract's stomach ulcer prevention. Ranitidine and curcuma *longa* extract were compared. Curcuma and ranitidine protected stomach mucosa. Like ranitidine, oral ethanolic extract reduced stomach acid, juice, and ulcers.

Rafatullah et al. 1990 evaluated ethanolic turmeric extract for antiulcer activity [53]. Turmeric extract dramatically lowered ulcer index and GI acidity. Treatment with turmeric extract reduced ulceration. Necrotizing agent-induced lesions and hypothermic-restraint stress were alleviated by turmeric extract.

Irritable bowel syndrome

Abdominal discomfort, bloating, changed bowel habits, and increased stool frequency are the most frequent symptoms of IBS. IBS patient eight-week pilot trial. After four weeks, IBS prevalence dropped 53% and 60% in those groups. In post-study analysis, stomach pain and discomfort dropped 22 and 25% [54].

Inflammatory bowel disease

IBD is mostly Crohn's and ulcerative colitis. A pilot study by Holt et al., 2005 [55] examined curcumin administration in IBD patients who had taken traditional UC or CD medication. Hematological and biochemical blood tests, ESR, CRP, sigmoidoscopy, and biopsy were done at baseline and study end. All patients had baseline and end-of-study CDAI, CRP, ESR, hematological blood analysis, and renal function assessed. A global score improved in all five proctitis patients, and ESR, CRP, and serologic inflammatory markers were normal after two months. The average CDAI score reduced 55 points, and four of five CD patients had lower CRP and ESR. Curcumin with standard treatment sustained remission better than placebo + UC [56].

Neurological disorders

In animal models of Alzheimer's disease (AD), curcumin directly reduces amyloid pathology [57]. Many studies have demonstrated that curcumin has numerous brain effects. Curcumin may cure serious depression, tardive dyskinesia, and diabetic neuropathy [58].

Pregnancy/neonates

Hepatic biotransformation system enzymes were examined with curcumin by Singh and Aggarwal 1995 [59]. GST and SH levels in the liver increased significantly with turmeric and curcumin. Cytochrome b5 and P450 levels also increased dramatically. This suggests breastfeeding may transmit turmeric and curcumin metabolites.

II. CONCLUSION

Curcumin has considerable promise as a therapeutic agent for a range of cancer types and inflammatory diseases. As a result, a large number of phase II and III clinical studies are now underway, indicating the high level of interest in its medicinal potential. Curcumin's poor systemic bioavailability has been the main barrier to its therapeutic use, however researchers are constantly working to identify the most effective way to use the drug.

CONFLICTS OF INTEREST

The authors hereby declare that they have no connections to, or engagement with, any institution or group that has a financial or non-financial interest in the topics covered in this work or the materials described in it.

IV. REFERENCES

- [1]. Goel A, Kunnumakkara AB, Aggarwal BB. Curcumin as "Curecumin": From kitchen to clinic. *Biochemical Pharmacology*. 2008;75(4):787-809.
- [2]. Kapoor LD. *Handbook of Ayurvedic medicinal plants*. Boca Raton, FL: CRC Press, 1990.
- [3]. WHO. *Rhizoma Curcumae Longae*, WHO monographs on selected medicinal plants Vol 1: World Health Organisation 1999.
- [4]. Heath DD, Khwaja F, Rock CL. Curcumin content of turmeric and curry powders. *FASEB J*. 2004;18:A125.
- [5]. Wang YJ, Pan MH, Cheng AL, Lin LI, Ho YS, Hsieh CY et al. Stability of curcumin in buffer solutions and characterization of its degradation products. *J Pharm Biomed Anal*. 1997;15:1867-76.
- [6]. Sreejayan N, Rao MNA, Priyadarsini KI, Devasagayam TP. Inhibition of radiation induced lipid peroxidation by curcumin. *Int J Pharm*. 1997; 151:127-30.
- [7]. Ravindranath V, Chandrasekhara N. Absorption and tissue distribution of curcumin in rats. *Toxicol*. 1980;16:259-265.
- [8]. Cronin, J.R. Curcumin: Old spice is a new medicine. *Journal of Alternative & Complementary Therapies*. 2003;9(1):34-8.
- [9]. Bundy R, Walker AF, Middleton RW, Booth J. Turmeric extract may improve irritable bowel syndrome symptomology in otherwise healthy adults: a pilot study. *J Altern Complement Med*. 2004;10:1015-8.
- [10]. Shoskes D, Lapiere C, Cruz-Corerra M, Muruve R, Rosario B, Fromkin M. et al. Beneficial effects of the bioflavonoids curcumin and quercetin on early function in cadaveric renal transplantation: a randomized placebo controlled trial. *Transplantation*. 2005;80:1556-9.
- [11]. Dikshit M, Rastogi L, Shukla R, Srimal RC. Prevention of ischaemia- induced biochemical changes by curcumin and quinidine in the catheart. *Indian J Med Res*. 1995;101:31-35.
- [12]. Mortellini R, Foresti R, Bassi R, Green CJ. Curcumin, an antioxidant and anti-inflammatory agent, induces heme oxygenase-1 and protects endothelial cells against oxidative stress. *Free Radic Biol Med*. 2000;28:1303-12.
- [13]. Nagabhushan M, Amonkar AJ, Bhide SV. In vitro antimutagenicity of curcumin against environmental mutagens. *Food Chem Toxicol*. 1987;25(7):545-547.
- [14]. Ranjan D, Johnston TD, Wu G, Elliott L, Bondada S, Nagabhushan M. Curcumin blocks cyclosporine A-resistant CD28 costimulatory pathway of human T-cell proliferation. *J Surg Res*. 1998;77(2):174-8.
- [15]. Okamoto T, Yamagishi S, Inagaki Y, Amano S, Koga K, Abe R et al. Angiogenesis induced by advanced glycation end products and its prevention by cerivastatin. *Faseb J*. 2002;16(14):1928-30.
- [16]. Ishihara M, Itoh M, Miyamoto K, Suna S, Takeuchi Y, Takenaka I et al. Spermatogenic disturbance induced by di-(2-ethylhexyl) phthalate is significantly prevented by treatment with antioxidant vitamins in the rat. *Int J Androl*. 2000;23(2):85-94.

- [17]. Arbiser JL, Klauber N, Rohan R, van Leeuwen R, Huang MT, Fisher C et al. Curcumin is an in vivo inhibitor of angiogenesis. *Mol Med.* 1998;4(6):376-83.
- [18]. Motterlini R, Foresti R, Bassi R, Green CJ. Curcumin, an antioxidant and anti-inflammatory agent, induces heme oxygenase-1 and protects endothelial cells against oxidative stress. *Free Radic Biol Med.* 2000;28(8):1303-12.
- [19]. Gukovsky I, Reyes CN, Vaquero EC, Gukovskaya AS, Pandol SJ. Curcumin ameliorates ethanol and nonethanol experimental pancreatitis. *Am J Physiol Gastrointest Liver Physiol.* 2003;284:G85-G95.
- [20]. Durgaprasad S, Pai CG, Vasanthkumar, Alvres JF, Namitha S. A pilot study of the antioxidant effect of curcumin in tropical pancreatitis. *Indian J Med Res.* 2005;122:315-8.
- [21]. Ruby J, Kuttan G, Babu KD, Rajashekharan KN, Kuttan R. Antitumor and oxidant activity of natural curcuminoids. *Cancer Lett.* 1995;94:79- 83.
- [22]. Rao CV, Desai D, Rivenson A, Simi B, Amin S, Reddy BS. Chemoprevention of colon carcinogenesis by phenylethyl-3- methylcaffeate. *Cancer Res.* 1995;55(11):2310-5.
- [23]. Park EJ, Jeon CH, Ko G, Kim J, Sohn DH. Protective effect of curcumin in rat liver injury induced by carbon tetrachloride. *J Pharm Pharmacol.* 2000;52:437-40.
- [24]. Soni KB, Rajan A, Kuttan R. Reversal of aflatoxin induced liver damage by turmeric and curcumin. *Cancer Lett.* 1992;66:115-21.
- [25]. Song EK, Cho H, Kim JS, Kim NY, An NH, Kim JA et al. Diarylheptanoids with free radical scavenging and hepatoprotective activity in vitro from *Curcuma longa*. *Planta Med.* 2001;67(9):876-7.
- [26]. Rajakrishnan V, Menon VP, Rajashekaran KN. Protective role of curcumin in ethanol toxicity. *Phytotherapy Research.* 1998;12:55-6.
- [27]. Garg R, Gupta S, Maru GB. Dietary curcumin modulates transcriptional regulators of phase I and phase II enzymes in benzo[a]pyrene-treated mice: mechanism of its anti-initiating action. *Carcinogenesis.* 2008;29:1022-32.
- [28]. Hong J, Bose M, Ju J, Ryu JH, Chen X, Sang S. et al. Modulation of arachidonic acid metabolism by curcumin and related beta-diketone derivatives: effects of cytosolic phospholipase A(2), cyclooxygenases and 5-lipoxygenase. *Carcinogenesis.* 2004;25:1671-9.
- [29]. Shao ZM, Shen ZZ, Liu CH, Sartippour MR, Go VL, Heber D et al. Curcumin exerts multiple suppressive effects on human breast carcinoma cells. *Int J Cancer.* 2002;98(2):234-40.
- [30]. Boone CW, Steele VE, Kelloff GJ. Screening of chemopreventive (anticarcinogenic) compounds rodents. *Mut Res.* 1992;267:251-5.
- [31]. Thaloor D, Singh AK, Sidhu GS, Prasad PV, Kleinman HK, Maheshwari RK. Inhibition of angiogenic differentiation of human umbilical vein endothelial cells by curcumin. *Cell Growth Differ.* 1998;9(4):305-12.
- [32]. Khar A, Ali AM, Pardhasaradhi BV, Varalakshmi CH, Anjum R, Kumari AL. Induction of stress response renders human tumor cell lines resistant to curcumin-mediated apoptosis: role of reactive oxygen intermediates. *Cell Stress Chaperones.* 2001;6(4):368-76.
- [33]. Limtrakul P, Anuchapreeda S, Lipigorngoson S, Dunn FW. Inhibition of carcinogen induced c-Ha-ras and c-fos proto-oncogenes expression by dietary curcumin. *BMC Cancer.* 2001;1:1.
- [34]. Mohanty I, Arya DS, Gupta SK. Effect of *Curcuma longa* and *Ocimum sanctum* on myocardial apoptosis in experimentally induced myocardial ischemic-reperfusion injury. *BMC Complement Altern Med.* 2006;6:3.
- [35]. Azuine MA, Kayal JJ, Bhide SV. Protective role of aqueous turmeric extract against mutagenicity of direct-acting carcinogens as well as benzo [alpha] pyrene-induced genotoxicity and carcinogenicity. *J Cancer Res Clin Oncol.* 1992;118(6):447-52.
- [36]. Sakano K, Kawanishi S. Metal-mediated DNA damage induced by curcumin in the presence of human cytochrome p450 isozymes. *Arch Biochem Biophys.* 2002;405:223-30.
- [37]. Frank N, Knauff J, Amelung F, Nair J, Wesch H, Bartsch H. No prevention of liver and kidney tumors in Long-Evans Cinnamon rats by dietary curcumin, but inhibition at other sites and of metastases. *Mutat Res.* 2003;523-524:127-35.

- [38]. Nishiyama T, Mae T, Kishida H, Tsukagawa M, Mimaki Y, Kuroda M et al. Curcuminoids and sesquiterpenoids in turmeric (*Curcuma longa* L.) suppress an increase in blood glucose level in type 2 diabetic KK- Ay mice. *J Agric Food Chem.* 2005;53(4):959-63.
- [39]. Wickenberg J, Ingemansson SL, Hlebowicz J. Effects of *Curcuma longa* (turmeric) on postprandial plasma glucose and insulin in healthy subjects. *Nutr J.* 2010;9:43.
- [40]. Allen PC, Danforth HD, Augustine PC. Dietary modulation of avian coccidiosis. *Int J Parasitol.* 1998;28:1131-40.
- [41]. Rasmussen HB, Christensen SB, Kvist LP, Karazami A. A simple and efficient separation of the curcumins, the antiprotozoal constituents of *Curcuma longa*. *Planta Med.* 2000;66:396-8.
- [42]. Khattak S, Saeed ur R, Ullah Shah H, Ahmad W, Ahmad M. Biological effects of indigenous medicinal plants *Curcuma longa* and *Alpinia galanga*. *Fitoterapia.* 2005;76(2):254-7.
- [43]. Kundu S, Biswas TK, Das P, Kumar S, De DK. Turmeric (*Curcuma longa*) rhizome paste and honey show similar wound healing potential: a preclinical study in rabbits. *Int J Low Extrem Wounds.* 2005;4(4):205- 13.
- [44]. Yu ZF, Kong LD, Chen Y. Antidepressant activity of aqueous extracts of *Curcuma longa* in mice. *J Ethnopharmacol.* 2002;83(1-2):161-5.
- [45]. Xia X, Cheng G, Pan Y, Xia ZH, Kong LD. Behavioral, neurochemical and neuroendocrine effects of the ethanolic extract from *Curcuma longa*
- [46]. L. in the mouse forced swimming test. *J Ethnopharmacol.* 2007;110(2):356-63.
- [47]. Xu Y, Ku B, Tie L, Yao H, Jiang W, Ma X et al. Curcumin reverses the effects of chronic stress on behavior, the HPA axis, BDNF expression and phosphorylation of CREB. *Brain Res.* 2006;1122(1):56-64.
- [48]. Ramirez-Tortosa MC, Mesa MD, Aguilera MC, Quiles JL, Baro L, Ramirez-Tortosa, CL et al. Oral administration of turmeric extract inhibits LDL oxidation and has hypocholesterolemic effects in rabbits with experimental atherosclerosis. *Atherosclerosis.* 1999;147:371-8.
- [49]. Srivastava R. Inhibition of neutrophil response by curcumin. *Agents Actions.* 1989;28:298-303.
- [50]. Lee HS. Antiplatelet property of *Curcuma longa* L. rhizome-derived ar- turmerone. *Bioresour Technol.* 2006;97(12):1372-6.
- [51]. Soni KB, Rajan A, Kuttan R. Reversal of aflatoxin induced liver damage by turmeric and curcumin. *Cancer Lett.* 1992;66:115-21.
- [52]. Prucksunand C, Indrasukhsri B, Leethochawalit M, Hungspreugs K. Phase II clinical trial on effect of the long turmeric (*Curcuma longa* Linn) on healing of peptic ulcer. *Southeast Asian J Trop Med Public Health.* 2001;32:208-15.
- [53]. Kim DC, Kim SH, Choi BH, Baek NI, Kim D, Kim MJ et al. *Curcuma longa* extract protects against gastric ulcers by blocking H2 histamine receptors. *Biol Pharm Bull.* 2005;28(12):2220-4.
- [54]. Rafatullah S, Tariq M, Al-Yahya MA, Mossa JS, Ageel AM. Evaluation of turmeric (*Curcuma longa*) for gastric and duodenal antiulcer activity in rats. *J Ethnopharmacol.* 1990;29(1):25-34.
- [55]. Barbara G, De Giorgio R, Stanghellini V, Cremon C, Corinaldesi R. A role for inflammation in irritable bowel syndrome? *Gut.* 2002;51(1):i41-i44.
- [56]. Holt PR, Katz S, Kirshoff R. Curcumin therapy in inflammatory bowel disease: a pilot study. *Dig Dis Sci.* 2005;50:2191-3.
- [57]. Hanai H, Iida T, Takeuchi K, et al. Curcumin maintenance therapy for ulcerative colitis: randomized, multicenter, double-blind, placebocontrolled trial. *Clin Gastroenterol Hepatol.* 2006;4:1502-6.
- [58]. Ringman JM, Frautschy S, Cole GM, Masterman DL, Cummings JL. A potential role of the curry spice curcumin in Alzheimer's disease. *Curr Alzheimer Res.* 2005;2(2):131-6.
- [59]. Kulkarni SK, Dhir A. An overview of curcumin in neurological disorders. *Indian J Pharm Sci.* 2010;72(2):149-54.
- [60]. Singh S, Aggarwal BB. Activation of transcription factor NF- kappa B is suppressed by curcumin (diferuloylmethane) [corrected]. *J Biol Chem.* 1995;270:24995-5000.