REVIEW ARTICLE

Recent advances in curcumin: An integrative overview of its mode of action, pharmacological properties, and health benefits

Arvind Kumar, Saket Singh Chandel, Aayush Vaishnaw, Roshan Sonwani, Vijay Kumar Patel

Department of Pharmaceutical Sciences, Dr. C.V. Raman University, Kota, Bilaspur, Chhattisgarh, India

Abstract

Turmeric (*Curcuma longa*) is used as a spice, preservative, and coloring matter and has a wide range of medicinal and pharmacological applications. Curcumin, a polyphenolic herbal product, well-known shows healing hobby for some of the diseases, attributed specially to its chemical shape and specific physical, chemical, and organic properties. The oxidative damage and inflammation have been pointed out as the root cause of many chronic diseases such as cancer, diabetes, hypertension, and Alzheimer's disease. Curcumin and its analogs prevent oxidative damage and inhibit the binding of toxic metabolites to DNA. The safety studies indicate that turmeric is well tolerated at a very high dose (0.5–1.5 g/day/person) without any toxic effects. Epidemiological and clinical studies of curcumin suggested that cancer could be prevented or significantly reduced by treatment with anti-oxidant and anti-inflammatory drugs, therefore, Curcumin, an anti-oxidant and anti-inflammatory compound found in turmeric (a curry spice), could be a promising option for the prevention and/or treatment of cancer and other chronic diseases. Curcumin, a highly pleiotropic drug with a great safety profile and strong molecular evidence targeting various diseases, could not attain its optimal therapeutic effect in previous clinical studies, owing to its limited solubility and poor absorption. Curcumin can be developed as a medicinal medication by enhancing its absorption and cellular uptake through better formulation qualities or delivery mechanisms. This review focuses on the properties, chemistry, toxicity studies, dosage, and the possibilities of the therapeutic application of curcumin for the prevention and/or treatment of several diseases, and their safety profile.

Key words: Curcuminoids, safety profile, therapeutic activities, toxicity studies, turmeric

INTRODUCTION

Curcumin, a turmeric pigment, is one of the few potential natural products that has been studied both abiologically and biochemically by scientists. It is the most frequent derivative of the turmeric spice used in India.[1] Turmeric is a herbal plant (*Curcuma longa*) of the ginger family (*Zingiberaceae*) having medical benefits. Curcumin (chemical name: Diferuloylmethane) is an active, yellow-colored component obtained from rhizomes of turmeric, *C. longa* Linn. (Family: *Zingiberaceae*).[2,3] It is a perennial herb that grows primarily in tropical and subtropical climates. The fat-soluble polyphenolic pigments also called curcuminoids are mainly responsible for the yellow color of curcumin. It was isolated 200 years ago after that structure was described in 1910 and has a vast history of being used as a medicine in the treatment of many diseases.[4] The present review is focused on recent advances in chemistry, pharmacological/biological activities, pharmacokinetics, toxicological studies, side effects, and suitable dosage of curcumin moiety.

PROPERTIES OF CURCUMIN

The curcuminoids include curcumin as the main bioactive component, which is non-toxic and non-mutagenic.[5]

Address for correspondence:
Dr. Saket Singh Chandel, Department of Pharmaceutical Sciences, Dr. C.V. Raman University, Kota, Bilaspur, Chhattisgarh, India. E-mail singhpharma@gmail.com

Received: 29-05-2022
Revised: 08-08-2022
Accepted: 19-08-2022

The unique structure of curcumin, which has the phenolic hydroxyl groups, heptadiene chain, and diketone moiety[6] [Figure 1] is responsible for all the therapeutic activities of curcumin such as anti-inflammatory, antitumor, anticancer, anti-HIV, antibacterial, antidiabetic, antioxidant, a wound-healing agent, Alzheimer's disease, and as an antidepressant agent. First, turmeric lowers the production of inflammation-inducing histamine. Second, turmeric promotes circulation, pushing toxins out of small joints where cellular wastes and inflammatory substances are usually trapped, and it also boosts and prolongs the function of the body's natural anti-inflammatory adrenal hormone, cortisol. Turmeric's digestive advantages have also been proved through research. Turmeric is a cholagogue, meaning it stimulates bile secretion, aiding digestion and removing toxins from the liver.[1-5]

ISOLATION OF CURCUMIN

Curcumin was separated using an organic solvent because it is insoluble in water. Ground turmeric is heated in dichloromethane with stirring and refluxed for 1 h to extract curcumin. After being suction-filtered, the filtrate was concentrated in a hot-water bath maintained at 50°C. After being triturated with hexane, the reddish-yellow oil residue was captured by suction filtration. Curcumin is extracted from turmeric powder using a mixture of ethanol and acetone as a solvent. Chemical analyses have shown that turmeric contains carbohydrates (69.4%), moisture (13.1%), protein (6.3%), fat (5.1%), and minerals (3.5%). The essential oil (5.8%) obtained by steam distillation of the rhizomes contains a-phellandrene (1%), sabinene (0.6%), cineol (1%), borneol (0.5%), zingiberene (25%), and sesquiterpenes (53%), curcumin (3–6%) is responsible for the yellow color.[6-8]

CHEMISTRY

It melts at 176–177°C and reacts with alkalis to generate red-brown salts. Curcumin is water insoluble but soluble in ethanol, alkalis, ketone, acetic acid, and chloroform. Curcumin has an aliphatic main chain that is unsaturated, and the aryl group can be substituted or not.[2] The active constituents of turmeric are flavonoid curcumin (diferuloylmethane) and various volatile oils, including tumerone, at lantone, and zingiberone. Other constituents include sugars, proteins, and resins. Curcumin, which makes up 0.3–5.4 percent of raw turmeric, is the most well-studied active component.[9]

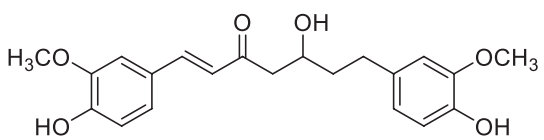

Figure 1: Chemical structure of Curcumin

PHARMACOLOGICAL ACTIVITIES OF CURCUMIN

Turmeric exhibits a wide range of pharmacological activities. Curcumin is the primary polyphenolic active ingredient in turmeric responsible for its biological activity. A wide range of therapeutic effects has been demonstrated for curcumin, the active ingredient in turmeric.[10] Curcumin has been used extensively in Ayurvedic and traditional medicine for centuries, as it is non-toxic and has a variety of therapeutic properties [Figure 2] including Anti-Parkinson activity and Anti-Alzheimer Activity [Table 1], Wound Healing [Table 2], Anti-arthritis Activity and Anti-inflammatory [Table 3], Anti- Bacterial activity and Antifungal [Table 4], Anti-viral activity and Anti-HIV [Table 5], Anti-cancer Activity [Table 6], Antidiabetic [Table 7], Cardiovascular Activity [Table 8], Gastrointestinal Activity [Table 9], Hepatoprotective Activity [Table 10], Eye disease treatment [Table 11], Lupus Nephritis Treatment [Table 12], and Miscellaneous Activities of Curcumin [Table 13].

PHARMACOKINETICS OF CURCUMIN

Curcumin pharmacokinetics and bioavailability studies have indicated low intestinal absorption. Oral administration of 400 mg of curcumin shows an absorption rate of 60–66% and rapid clearance from the body. Curcumin's clinical use is limited largely because it has low solubility and fast metabolism that leads to low bioavailability. It is permeable across the blood-brain barrier.[33]

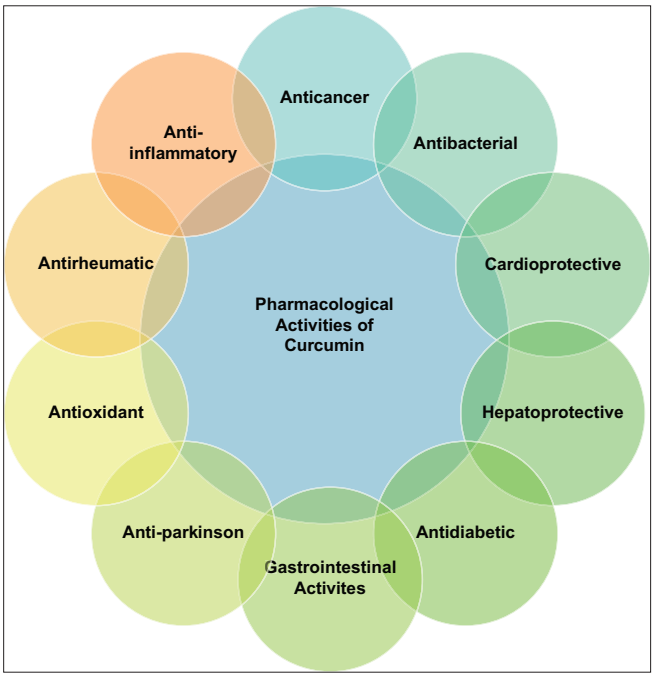

Figure 2: The pharmacological activity of Curcumin

Table 1: Pharmacological activity of curcumin on the central nervous system

Pharmacological activities	Mode of Action	Ref
Anti-Parkinson activity	• Curcumin restores depletion of GSH levels, protects against protein oxidation, and preserves mitochondrial complex I activity which normally is impaired due to GSH loss. • Curcumin can alleviate αs induced toxicity, reduce intracellular reactive oxygen species ROS levels and protect cells against apoptosis.	[11]
Anti-Alzheimer activity	• The inhibition of the accumulation of amyloid β-peptide (Aβ) and the formation of β-amyloid fibrils (fAβ) from Aβ, • The destabilization of preformed fAβ in the central nervous system.	[11]

Table 2: P Pharmacological activity of curcumin on wound

Wound Healing	• Repair of tissues is a complex process that involves inflammation, granulation, and remodeling of the tissue. • The mechanisms of action of the wound healing effect of curcumin include: immunohistochemical localization of transforming growth factor-β1 showed an increase in curcumin-treated wounds as compared with untreated wounds and modulating collagen and decreasing reactive oxygen species. • Curcumin showed earlier reepithelialization, improved neovascularization, increased migration of various cells including dermal myofibroblasts, fibroblasts, and macrophages into the wound bed, and higher collagen content.	[11]

Table 3: Pharmacological activity of curcumin on arthritis and inflammation

Pharmacological activities	Mode of Action	Ref.
Anti-arthritis activity	• Curcumin's antioxidant, antiproliferative, anti-inflammatory, and immunosuppressive activities are shared in the improvement of symptoms in patients suffering from rheumatoid arthritis. • One of the important consequences of rheumatoid arthritis could be decreased apoptosis. • Exposure of the synovial fibroblasts to curcumin resulted in growth inhibition and the induction of apoptosis, as measured by MTT assay, fluorescent microscopy, and Annexin-V-based assay. These results show that curcumin might help against hyperplasia of the synovial fibroblasts in rheumatoid arthritis	[11]
Anti-inflammatory	• Exert its anti-inflammatory activity by inhibiting several different molecules that play a role in inflammation. • Curcumin regulates numerous transcription factors, cytokines, protein kinases, adhesion molecules, redox status, and enzymes that have been linked to inflammation.	[12,13]

TOXICOLOGICAL ASPECTS OF CURCUMIN

Curcumin has minimal toxicity in both humans and animals. Curcumin is thought to be consumed by adults in India in the range of 80–200 milligrams per day. In phase-I clinical research with 25 volunteers, up to 8000 mg of curcumin per day for three months produced no noticeable side effects. Five other clinical trials in which humans were given 1125–2500 mg curcumin per day confirmed the apparent safe of the substance.[34] There are no reports of adverse effects of either curcumin or its analogs except for rare cases of contact dermatitis.[35] One of which occurred as an occupational illness of a miller working in a spice shop. Many Indian women app.ly turmeric to their skin to minimize unwanted hair growth, but few experience dermatitis. One of the 62 patients treated with the topical application of curcumin for skin and mucous membrane cancers reported an adverse effect of itching their scalp during the 18-month study.[36] Curcumin was one of eleven colorants detected in an analysis of the colorants that may be included in the transferable picture tattoos used by children. However, based on the findings, the colorant's risk of causing an allergic reaction appeared to be low.[31] Curcumin was given orally to rats at levels up to 5 g/kg with no obvious evidence of harm. Turmeric is classified as a menstruation stimulant by the American Herbal Association, and some sites advise against using curcumin during pregnancy. It is not suggested for usage while breastfeeding because the effects on nursing infants are unknown. Turmeric may have antiplatelet properties, and when used with anticoagulants, it may have a synergistic impact. Although there have been no instances of this in humans, it should be avoided in individuals

Table 4: Pharmacological Activity of Curcumin on Bacterial and Fungal infections

Pharmacological activities	Mode of Action	Ref.
Anti-bacterial activity	• Curcumin inhibits the growth of a variety of periodontopathic bacteria and Porphyromonas gingivitis Arg- and Lys-specific proteinase (RGP and KGP, respectively) activities. • Curcumin suppressed *P. gingivitis* homotypic and Streptococcus Gordonii biofilm formations in a dose-dependent manner. • Bacterial growth was suppressed almost completely at very low concentrations of curcumin. • A concentration of 20 µg/mL of curcumin inhibited these *P. gingivitis* biofilm formations by more than 80%. On the other hand, 100 µg/mL of curcumin did not suppress the growth of *Aggregatibacter actinomycetemcomitans*. Furthermore, at relatively high concentrations, curcumin targets bacterial membranes (*Escherichia coli*). • In addition, many features of a bacterial apoptosis-like response were observed after treatment with curcumin at the MIC, including membrane depolarization, Ca 2+ influx, PS exposure, and DNA fragmentation. • A bacterial apoptosis-like response, induced by curcumin, by causing reactive oxygen species generation and DNA damage. • The study on *E. coli* and *B. subtilis* demonstrated that curcumin by the inhibitory effect against FtsZ polymerization could suppress the FtsZ assembly leading to disruption of prokaryotic cell division.	[11]
Anti-fungal	• The curcumin powder in plant tissue culture showed that curcumin at the 0.8 and 1.0 g/L had appreciable inhibitory activity against fungal contaminations. • The mechanism underlying the mentioned antifungal effect was found to be downregulation of desaturase (ERG3) leading to a significant reduction in ergosterol of fungal cells. Reduction in production of ergosterol results in accumulations of biosynthetic precursors of ergosterol which leads to cell death through generation of ROS. • Reduction in proteinase secretion and alteration of membrane-associated properties of ATPase activity are other possible critical factors for the antifungal activity of curcumin. • The study of curcumin, against 14 strains of Candida, showed that curcumin is a potent fungicide compound against Candida species with MIC values ranging from 250 to 2000 µg/mL. • Curcumin exhibited a potent antifungal effect via mechanisms associated with disruption of the plasma membrane in Candida albicans.	[11]

Table 5: Pharmacological activity of curcumin on viruses

Anti-viral activity	• The lack of effective therapeutics for most of the viral diseases, the emergence of antiviral drug resistance, and the high cost of some antiviral therapies necessitate finding new effective antiviral compounds. • The existing antiviral therapies are not always well-tolerated or quite effective and satisfactory. Hence, the increasing requirement for antiviral substances will be highlighted. • Plants as a rich source of phytochemicals with different biological activities including antiviral activities are in the interest of scientists.	[11]
Anti -HIV	• Cyclohexanone derivative of curcumin was the strongest human HIV-1 protease inhibitor *in vitro*. • Curcumin is a modest inhibitor of HIV-1 and HIV-2 proteases.	[13]

with bleeding disorders or bile duct obstruction, and should only be used in patients with gallstones under the guidance of a physician.[37]

SIDE EFFECTS OF CURCUMIN

Curcumin has a long-established safety record as per The Joint United Nations and World Health Organization Expert Committee on Food Additives and European Food Safety Authority reports, the Allowable Daily Intake value of curcumin is 0–3 mg/kg of body weight. Curcumin's safety and efficacy have been proven in a number of studies on healthy people. Despite the fact that the drug's safety has been verified, several negative side effects have been documented. In a dose-response trial, seven participants who received 500–12000 mg and were observed for 72 hours had diarrhea, headache, rash, and yellow stool. In another trial, some

Table 6: Pharmacological activity of curcumin on cancer

Pharmacological activities	Mode of Action	Ref.
Anti-cancer activity	Breast cancer • The frequency of BRCA1 mutation is 55–65% whereas for the BRCA2 mutation is 45%. • A combination of 45mg of DMSO (dimethyl sulfoxide) and Curcumin inhibited the development of intestinal adenomas and reduced the frequency of mutation in BRCA genes.	[14]
	Colorectal cancer • In combination treatment IC50 value were 71.8 μm (20.5 μm curcumin+51.3 μm Resveratrol) for DLD-1 cell lines and 66.21μm (18.9μm curcumin+47.3μm Resveratrol) for CaCo-2 cell lines, respectively.	[14]
	Head and neck squamous cell carcinoma • Curcumin with Docetaxel, Doxorubicin (DOX), 5-Fluorouracil (5-FU), and Cisplatin (diamine dichloroplatinum (II), CDDP) may increase the efficiency of these chemotherapeutic drugs and reduce toxicity. • Curcumin exhibited a significant effect on cell growth and enhanced apoptosis in NT8e cancer cell lines with a combination of 5-FU or DOX. This combination shows cell cycle growth arrest at the G1/S phase.	[14]
	Pancreatic cancer • A combination of nano-formulated curcumin with the drug Gemcitabine has been used to control tumor growth.	[14]
	Prostate cancer • The combinatorial treatment of docetaxel (10 nm) and curcumin (20 μm) for 48 h significantly inhibited the rapid cell growth and apoptosis in DU145 and PC3 cell lines of prostate cancer. • These are the dietary phytochemicals that target inflammatory signaling pathways including Stat3 and NF-κB and hindered cancer development and progression.	[14]
	Cervical cancer • Curcumin decreases the expression and activity of many enzymes that facilitate metastasis and invasion such as matrix metalloproteinases (MMP-2) and (MMP-9). • Curcumin inhibits telomerase activity in cervical cancer and this effect could be superior to other anticancer effects of curcumin in cervical cancer.	[15,16]
	Liver cancer • One group of mice received a diet containing 0.2% curcumin, from 4 days before DENA injection until the end of the study. At the age of 42 weeks, the curcumin group exhibited an 81% reduction in the multiplicity and a 62% reduction in the incidence of hepatocarcinoma compared with the non-treated group. • Busquets studied the chemopreventive potential of curcumin in rats that were inoculated with Yoshida AH-130 ascites hepatoma, a fast-growing tumor that results in a fatality in~10 days after inoculation. • Curcumin significantly decreased tumor growth by 31%.	[17-19]
	Lung cancer • Curcumin suppresses the activation of NF-kB. On activation by carcinogens, this nuclear factor can suppress apoptosis and induce cellular transformation, proliferation, invasion, metastasis, chemoresistance, radioresistance, and/or inflammation.	[20]
	Ovarian cancer • Curcumin alone induced a 49–55% reduction in mean tumor growth compared with control animals, • The combination of curcumin with docetaxel resulted in a 77% reduction in mean tumor growth compared with the controls. • In both cases, curcumin induced a decrease in proliferation and microvessel density and a significant increase in tumor cell apoptosis. • The combination of curcumin and triptolide was able to synergistically inhibit ovarian cancer cell growth.	[21,22]
	Skin cancer • Topical application of curcumin combined with the tumor promoter TPA, twice per week for 20 weeks, to female CD-1 mice, markedly inhibited papilloma formation. • Low doses of curcumin (20 or 100 nmol) markedly abrogated TPA-induced tumor promotion.	

(Contd...)

Table 6: *(Continued)*

Pharmacological activities	Mode of Action	Ref.
	• Topical application of commercial-grade curcumin (containing~77% curcumin, 17% demethoxycurcumin, 3% bis-demethoxycurcumin), pure curcumin or demethoxycurcumin exhibited almost equipotent inhibitory effects on TPA-induced tumor promotion in DMBA-initiated mouse skin carcinogenesis. Furthermore, in female Swiss mice, dietary administration of 2% turmeric significantly inhibited DMBA and TPA-induced skin tumor formation. • In a benzo[a] pyrene-initiated and TPA-promoted two-stage skin tumorigenesis model, curcumin reduced the number of tumors per mouse and decreased the number of tumor-bearing mice. • Huang demonstrated that curcumin inhibited UV-induced dermatitis in mouse skin.	[23-25]

Table 7: Pharmacological activity of curcumin on metabolic disease

Pharmacological activities	Mode of action	Ref.
Anti-diabetic	• The effect of antidiabetic activity could be attributed to the antioxidant property of curcumin. • Improvement of diabetes-induced endothelial dysfunction by decreasing superoxide production and vascular protein kinase C inhibition. • The ability of curcumin can directly quench reactive oxygen species (ROS) that can contribute to oxidative damage. • Curcumin attenuates cell death caused by oxidative stress, indirectly through induction and/or activation of antioxidant/ cytoprotective enzymes, such as heme oxygenase-1 (HO-1).	[12,26]

Table 8: Pharmacological activity of curcumin on cardiovascular system

Pharmacological activities	Mode of action	Ref.
Cardiovascular Activity	• Due to the antioxidant property of turmeric which generates a protective effect on the cardiovascular system includes lowering cholesterol and triglyceride levels, decreasing susceptibility of low-density lipoprotein (LDL) to lipid peroxidation, and inhibiting platelet aggregation. • Turmeric extract being given to 18 atherosclerotic rabbits at a low dose (1.6–3.2 mg/kg body weight daily) shows decreasing susceptibility of LDL to lipid peroxidation, • It lowers plasma cholesterol and triglyceride levels. • The higher dose decreases cholesterol and triglyceride levels but it did not decrease lipid peroxidation of LDL. • Turmeric extract has its potential effect on cholesterol levels may possibly be due to decreased cholesterol uptake in the intestines and increased • Conversion of cholesterol to bile acids in the liver. • Curcuma longa inhibits platelet aggregation to be via the potentiation of prostacyclin synthesis and inhibition of thromboxane synthesis.	[15]

Table 9: Pharmacological activity of curcumin on gastrointestinal tract

Pharmacological activities	Mode of action	Ref.
Gastrointestinal activity	• The constituents of Curcuma longa, namely, Sodium curcuminate and p-tolymethylcarbinol have several protective effects on the gastrointestinal tract. • Sodium curcuminate exhibits the characteristics of inhibition of intestinal spasm and p-tolymethylcarbinol, which increases gastrin, secretin, bicarbonate, and pancreatic enzyme secretion. • Turmeric has also been seen that it can inhibit ulcer formation caused by stress, alcohol, indomethacin, pyloric ligation, and reserpine, considerably increasing gastric wall mucus in rats applied to these gastrointestinal insults.	[12]

Table 10: Pharmacological activity of curcumin on hepatic system

Pharmacological activities	Mode of action	Ref.
Hepatoprotective activity	• Turmeric has both hepatoprotective and reno-protective characteristics similar to silymarin mainly due to its antioxidant properties, as well as its ability to decrease the formation of pro-inflammatory cytokines. • Animal studies have revealed that turmeric's hepatoprotective effects from a variety of hepatotoxic insults, including carbon tetrachloride ($CCl4$), galactosamine, and acetaminophen (paracetamol), and Aspergillus aflatoxin. • It is noticed that in rats with $CCl4$-induced acute and subacute liver injury, administration of curcumin drastically decreased liver injury in test animals compared to controls. • Extract of turmeric is very effective which inhibits the production of fungal aflatoxin by 90% when tested on ducklings infected with Aspergillus parasiticus preventing and treating cholelithiasis possible due to sodium curcumin, a salt of curcumin, also exerts choleretic effects by increasing biliary excretion of bile salts, cholesterol, and bilirubin, as well as increasing bile solubility.	[27]

Table 11: Pharmacological activity of curcumin on the ophthalmic system

Pharmacological activities	Mode of action	Ref.
Eye disease treatment	• Clinical trials on the subject of curcumin's effect on various ophthalmological disorders demonstrated high efficacy of this compound, when either locally or systemically applied, by oral intake. • It has been reported that a 15-day eye drops application containing turmeric can improve symptoms of conjunctivitis, conjunctival xerosis (dry eye), acute dacryocystitis, and degenerative conditions (pterygium or pinguecula), and post-operative cataract patients. • In patients with uveitis, marked symptoms improvement in all treated patients. • Reduces eye discomfort and number of relapses • After oral curcumin intake for 12 weeks and 18 months, respectively.	[28,29]

Table 12: Pharmacological activity of curcumin on nephron

Pharmacological activities	Mode of action	Ref.
Lupus nephritis treatment	• Lupus nephritis is an autoimmune disease characterized by polyclonal B cell hyperactivity and defective T cell function. The disease is responsive to immunosuppressive and steroid therapy, but sometimes the disease relapses. • The effect of oral turmeric supplementation on 24 patients with relapsing or refractory biopsy-proven lupus nephritis was investigated in a randomized and placebo-controlled study. • Short-term turmeric supplementation can decrease proteinuria, hematuria, and systolic blood pressure in patients with relapsing or refractory lupus nephritis and can be used as safe adjuvant therapy for such patients. Long-term clinical trials with larger numbers of patients are required to further clarify these effects of turmeric.	[30,31]

people who took 0.45–3.6 g of curcumin every day for one to four months had nausea and diarrhea, as well as an elevation in serum alkaline phosphatase and lactate dehydrogenase levels.[38,39]

SAFETY AND DOSAGE OF CURCUMIN

The administration of turmeric powder, extracts, or curcumin at high doses no significant toxicity has been reported in. There were no symptoms of toxicity in Asians who drank 0.5–1.5 g of turmeric per day per person. After administration of turmeric at greater doses (2.5 g/kg body weight), the appearance and weight of kidney, liver, and heart in male and female guinea pigs, monkeys, and Wistar rats showed no changes. In a phase-I human experiment including 25 patients who were given up to 8000 mg of curcumin per day for three months, no damage was seen. Curcumin was also found to be safe in five further human trials including doses ranging from 1125 to 2500 mg per day.[38,39]

Table 13: Miscellaneous activities of curcumin

Pharmacological activities	Mode of action	Ref.
Radioprotective activity	• Curcumin is effective in inhibiting radiation-induced protein kinase C (PKC) activity and was potentially useful as a chemopreventive agent. • Activation of PKC is reported to be the means of conferring radioresistance on a tumor cell. Therefore suppression of PKC by curcumin may be means of preventing the development of radioresistance following radiotherapy. • It is beneficial in reducing the risk of developing cancer; it has also a protective effect on radiation-induced toxicity and also probably against the harmful effects of organochlorine pesticides. • Curcumin is potentially useful in preventing the development of radioresistance following radiotherapy. I the protective action of curcumin to reduce the incidence of mammary and pituitary tumors against the long-term effect of radiation in pregnant rats. • Curcumin (3.75 μM) exhibits radio-sensitizing effects on squamous cell carcinoma (SCC) cells. C • Curcumin and its mononuclear copper complex is very effective in protecting the cells against radiation-induced suppression of glutathione peroxidase, catalase, and superoxide dismutase (SOD) activities.	[13]
Anti-oxidant	• Curcumin demonstrated the antioxidant activity by evaluating curcumin using various in-vitro antioxidant assays such as 1,1-diphenyl-2-picryl-hydrazyl free radical (DPP.H) scavenging, 2,2′-azino-bis (3-ethylbenzthiazoline-6-sulfonic acid) (ABTS) radical scavenging activity, N, N-dimethyl-p-phenylenediamine dihydrochloride (DMPD) radical scavenging activity, total antioxidant activity determination by ferric thiocyanate, total reducing ability determination by the Fe3+ – Fe2 + transformation method, superoxide anion radical scavenging by the riboflavin/methionine/illuminate system, hydrogen peroxide scavenging and ferrous ions (Fe2+) chelating activities.	[11,12]
Anti-coagulant	• Anticoagulant activity by inhibiting platelet aggregation induced by arachidonate, adrenaline, and collagen, *in vitro* as well as in vivo, in rat thoracic aorta.	[32]
Anti-fertility	• Incubation of sperm with curcumin caused a concentration-dependent decrease in forwarding motility of sperm, capacitation/acrosome reaction, and murine fertilization in vitro. • A complete block of sperm motility and function within 5–15 min at higher concentrations of curcumin. • Intravaginal administration of curcumin caused a significant reduction in fertility. • Curcumin inhibits 5a-reductase, which converts testosterone to 5a-dihydrotestosterone, thereby inhibiting the growth of flank organs in hamsters. • Curcumin also inhibits human sperm motility and has the potential for the development of a novel intravaginal contraceptive.	[33]

CONCLUSION

Numerous studies of curcumins' effect on cell tissues and animals, as well as clinical studies, have shown its multiple medical benefits (more than 10,000 published papers in the last 10 years). Turmeric's coloring notion is curcumin, a yellow-colored compound that is the plant's primary component. Curcumin is a yellow pigment found in curry powder, turmeric, and ginger to a lesser extent. Turmeric's health benefits have typically been obtained through long-term food intake, even at modest doses. The appropriate use of turmeric in the treatment of human diseases necessitates a thorough understanding of effective dose, safety, and mechanism of action. The activities of turmeric include antibacterial, antiviral, anti-inflammatory, antidiabetic, antioxidant, anti-HIV, antimicrobial, antifertility, anti-Parkinsonian, antifungal, anticoagulant, cardioprotective, hepatoprotective, neuroprotective, radioprotective, and digestive activities and also effective in various types of cancer such as breast cancer, liver cancer, lung cancer, and colorectal cancer. The major drawbacks of curcumin are poor solubility in water since it is a phenolic compound and its poor stability and biodegradability within the living organism. Curcumin, a main component of turmeric (*C. longa* L.), has been found to have considerable anti-cancer and antibacterial capabilities, yet it is not enough to cure the problem. As a result, treating these disorders with a combination of drugs is the superior option.

FUTURE PROSPECT

Curcumin is important for human beings for the treatment and management of diseases such as cancer, diabetes, arthritis, cardiovascular diseases, viral and bacterial/fungal diseases, and neurological diseases with no side effects. However, it

has low solubility and fast metabolism which leads to low bioavailability. Thus there is a need to develop various novel derivatives of curcumin that have high biostability; as a result, the curcumin derivative has a more beneficial pharmacological effect. Curcumin can be developed as a therapeutic drug through improvement in formulation properties or delivery systems, enabling its enhanced absorption and cellular uptake.

REFERENCES

1. Gilani N, Basharat H, Qureshi H. Curcumin a review on multipotential phytocompound. J Coast Life Med 2017;5:455-8.
2. Urošević M, Nikolić L, Gajić I, Nikolić V, Dinić A, Miljković V. Curcumin: Biological activities and modern pharmaceutical forms. Antibiotics 2022;11:135.
3. Damarla SR, Komma R, Bhatnagar U, Rajesh N, Mulla SM. An evaluation of the genotoxicity and subchronic oral toxicity of synthetic curcumin. J Toxicol 2018;2018:6872753.
4. Kumari A, Kaur M, Sharma S. A review on curcumin and its medicinal properties. Acta Sci Pharm Sci 2021;4:31-7.
5. Sokmen M, Khan MA. The antioxidant activity of some curcuminoids and chalcones. Inflammopharmacology 2016;24:81-6.
6. Rathore S, Mukim M, Sharma P. Curcumin: A review for health benefits. Int J Res Rev 2000;7:273-90.
7. Bagchi A. Extraction of curcumin. IOSR J Environ Sci Toxicol Food Technol 2012;1:1-16.
8. Mem I, Cruz O, Janeiro RD. Biological activities of *Curcuma longa* Linn. Mem Inst Oswaldo Cruz 2001;96:723-8.
9. Abhijeet A. Curcumin pharmacological actions and its role in oral submucous fibrosis: A review. J Clin Diagn Res 2015;9:1-3.
10. Ali A, Jaber N. Pharmacological aspects of curcumin: Review article. Int J Pharmacogn 2018;5:313-26.
11. Singh A. Role and application of curcumin as an alternative therapeutic agent. HSOA Adv Microbiol Res 2020;4:1-7.
12. Chereddy KK, Coco R, Memvanga PB, Ucakar B, des Rieux A, Vandermeulen G, *et al*. Combined effect of PLGA and curcumin on wound healing activity. J Control Release 2013;171:208-15.
13. Panchatcharam M, Miriyala S, Gayathri VS, Suguna L. Curcumin improves wound healing by modulating collagen and decreasing reactive oxygen species. Mol Cell Biochem 2006;290:87-96.
14. Clarke MA, Wentzensen N, Mirabello L, Ghosh A, Wacholder S, Harari A, *et al.* Human papilloma virus DNA methylation as a potential biomarker for cervical cancer. Cancer Epidemiol Biomarkers Prev 2012; 21:2125-37.
15. Momtazi-Borojeni AA, Mosafer J, Nikfar B, Ekhlasi-Hundrieser M, Chaichian S, Mehdizadehkashi A, *et al.* Curcumin in advancing treatment for gynecological cancers with developed drug- and radiotherapy-associated resistance. Rev Physiol Biochem Pharmacol 2019;176:107-29.
16. Singh M, Singh N. Curcumin counteracts the proliferative effect of estradiol and induces apoptosis in cervical cancer cells. Mol Cell Biochem 2011;347:1-11.
17. Busquets S, Carbó N, Almendro V, Quiles MT, López-Soriano FJ, Argilés JM. Curcumin, a natural product present in turmeric, decreases tumor growth but does not behave as an anticachectic compound in a rat model. Cancer Lett 2001;167:33-8.
18. Surh YJ, Chun KS. Cancer chemopreventive effects of curcumin. Adv Exp Med Biol 2007;595:149-72.
19. Shishodia S, Potdar P, Gairola CG, Aggarwal BB. Curcumin (diferuloylmethane) down-regulates cigarette smokeinduced NF- activation through inhibition of I a kinase in human lung epithelial cells: Correlation with suppression of COX-2, MMP-9 and cyclin D1. Carcinogenesis 2003;24:1269-79.
20. Menon LG, Kuttan R, Kuttan G. Inhibition of lung metastasis in mice induced by B16F10 melanoma cells by polyphenolic compounds. Cancer Lett 1995;95:221-5.
21. Cai YY, Lin WP, Li AP, Xu JY. Combined effects of curcumin and triptolide on an ovarian cancer cell line. Asian Pac J Cancer Prev 2013;14:4267-71.
22. Huang MT, Wang ZY, Georgiadis CA, Laskin JD, Conney AH. Inhibitory effects of curcumin on tumor initiation by benzo[a]pyrene and 7,12-dimethylbenz[a] anthracene. Carcinogenesis 1992;13:2183-6.
23. Huang MT, Wang ZY, Georgiadis CA, Laskin JD, Conney AH. Effects of curcumin, demethoxycurcumin, bisdemethoxycurcumin and tetrahydrocurcumin on 12-O-tetradecanoylphorbol-13-acetate-induced tumor promotion. Carcinogenesis 1995;16:2493-7.
24. Huang MT, Smart RC, Wong CQ, Conney AH. Inhibitory effect of curcumin, chlorogenic acid, caffeic acid and ferulic acid on tumor promotion in mouse skin by 12-O-tetradecanoylphorbol-13-acetate. Cancer Res 1988;48:5941-6.
25. Goel RK, Agrawal S. Curcumin and its protective and therapeutic uses. Natl J Physiol Pharm Pharmacol 2013;6:1-8.
26. Alsamydai A, Jaber N. Pharmacological aspects of curcumin: Review article. Int J Pharmacogn 2018;5:313-26.
27. Gupta SC, Patchva S, Aggarwal BB. Therapeutic roles of curcumin: Lessons learned from clinical trials. Am Assoc Pharm Sci J 2013;15:195-218.
28. Allegri P. Management of chronic anterior uveitis relapses: Efficacy of oral phospholipidic curcumin treatment. Clin Ophthalmol 2010;4:1201.
29. Mazzolani F, Togni S. Oral administration of a curcumin-phospholipid delivery system for the treatment of central serous chorioretinopathy. Clin Ophthalmol 2013;7:939.
30. Shoskes D, Lapierre C, Cruz-Correa M, Muruve N,

Rosario R, Fromkin B, *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.
31. Ahsan R, Arshad M, Khushtar M, Ahmad MA, Muazzam M, Akhter MS, *et al.* A comprehensive review on physiological effects of curcumin. Thieme 2020;70:441-7.
32. Commandeur JN, Vermeulen NP. Cytotoxicity and cytoprotective activities of natural compounds, The case of curcumin. Biochem Biophys Res Commun 1996;295:667-80.
33. Chainani-Wu N. Safety and anti-inflammatory activity of curcumin: A component of turmeric (*Curcuma longa*). J Altern Complement Med 2003;9:161-8.
34. Lamb SR, Wilkinson SM. Contact allergy to tetrahydrocurcumin. Contact Dermatitis 2003;48:227.
35. Kuttan R, Sudheeran PC, Joseph CD. Turmeric and curcumin as topical agents in cancer therapy. Tumori 1987;73:29-31.
36. Rastogi SC, Johansen JD. Colourants in transferable picture tattoos for the skin. Contact Dermatitis 2005;53:207-10.
37. Nawaz A, Khan GM, Hussian A, Khan A, Safdar M. Curcumin: A natural product of biological importance. Gomal Univ J Res 2011;27:7-14.
38. Hewlings SJ, Kalman DS. Curcumin: A review of its' effects on human health. Food 2017;6:92.
39. Niranjan A, Prakash D. Chemical constituents and biological activities of turmeric (*Curcuma longa* L) a review. J Food Sci Technol 2008;45:119-6.

Source of Support: Nil. **Conflicts of Interest:** None declared.