A comprehensive review on *Curcuma longa* Linn.: Phytochemical, pharmacological, and molecular study

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Abstract

*Curcuma longa* Linn. is well-known and valued medicinal plant. It has a long history of traditional uses ranging from folk medicine to several culinary preparations. The phytochemical, pharmacological, and molecular studies of *C. longa* are reviewed. The rhizome is rich in essential oils, and various numbers of chemical constituents with biomedical significance have been isolated from it. The management of indigenous knowledge by appropriate documentation is recommended. This review was compiled to provide recent consolidated information covering different aspects of the plant, phytochemical, pharmacological, and molecular study to provide a basis on which to plan future studies and to promote sustainable use of *C. longa*.

Key words: Antidiabetic, *Curcuma longa*, curcuminoids, random amplification polymorphism DNA

INTRODUCTION

Turmeric (*Curcuma longa* L.) belongs to the family Zingiberaceae includes more than 80 species of rhizomatous perennial herbs and has widespread existence in the tropics of Asia, Africa, and Australia.¹ It is a perennial herbaceous plant, which reaches a stature of up to 1 m. There are highly branched, yellow-to-orange, cylindrical, aromatic rhizomes. *C. longa*, commonly known as turmeric (Haldi), is a well-known plant which is used as a drug in Ayurvedic and Unani system of medicine.² Others various common name includes *Curcuma* (Sp. It. Fr.), acafrão da India (port.), geelwortel (Dutch), kurkum (Arab), Manjano (East Africa [KiSwahili]), manjal (Tamil), kunyit (Indonesia), temukunyit (Malaysian), and iyu-chin (Chin.). The most important chemical components of turmeric are a group of compounds called curcuminoids, which include curcumin (diferuloylmethane), demethoxycurcumin, and bisdemethoxycurcumin.³⁻⁵ India is the largest producer, consumer, and exporter of turmeric in the world and contains highest diversity (40 species) of *C. longa*.² The World Health Organization has suggested the use of turmeric as a spice.⁶ Comprehensively, *Curcuma* is attainment importance as a growing source of new drug (s) to fight a variety of ailments as the species contain molecules validated with anti-fungal properties,⁷ anti-inflammatory, hepatoprotective, antitumor, antiviral,⁸ and anticancer activities.⁹ The structure of curcuminoids are shown in Figure 1.

In recent year, several studies have come out in the literature about this plant, and this may imitate the status of the subject and its common use as a spice and a medicinal plant. From the literature, it was found that very few or no review is available which correlates the data of phytochemical, pharmacological, and molecular properties of turmeric together. Here, the aim was to recapitulate the more recent and common actions including the phytochemical, pharmacological, and molecular aspect of *C. longa*.

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Chemical Constituents of Turmeric

Phytochemical investigations carried out on C. longa revealed the presence of many rich sources of polyphenolic curcuminoids, i.e., curcumin, demethoxycurcumin, and bisdemethoxycurcumin. Curcuminoids contain curcumin the principal curcuminoids (about 80%), and other two curcuminoids are demethoxycurcumin (about 12%) and bisdemethoxycurcumin along with other one’s protein (6.3%), fat (5.1%), minerals (3.5%), carbohydrates (69.4%), and moisture (13.1%). The essential oil (5.8%) obtained by steam distillation of rhizomes has a-phellandrene (1%), sabinene (0.6%), cineol (1%), borneol (0.5%), zingiberene (25%), and sesquiterpenes (53%).

Medicinal Uses

As part of the ancient Indian medical system, Ayurveda, a poultice of turmeric paste is used to treat common eye infections and to dress wounds, treat bites, burns, acne, and various skin diseases. In northern India, women are given a tonic of fresh turmeric paste with powder of dried ginger roots and honey in a glass of hot milk to drink twice daily after childbirth. Johnson and Johnson (An American Pharma Company) makes turmeric band-aids for the Indian market. A poultice of turmeric is also applied to the perineum to aid in the healing of any lacerations in the birth canal. Powdered turmeric when taken with boiled milk is helpful in curing cough and related respiratory ailment, and roasted turmeric is an ingredient used as an antisynergic for children. Turmeric is also used in the treatment of dental diseases, digestive disorders such as dyspepsia and acidity, indigestion, flatulence, ulcers, antioxidant, antifertility as well to alleviate the hallucinatory effects of hashish, and other psychotropic drugs. In food and manufacturing, curcumin is currently used in perfumes and as a natural yellow-coloring agent, as well as an approved food additive to flavor various types of curries and mustards. Recent emphasis on the use of natural and complementary medicines in western medicine has drawn the notice of the scientific community to this ancient remedy. Current researches have revealed that curcumin has a surprisingly wide range of beneficial properties, including anti-inflammatory, antioxidant, and chemopreventive and chemotherapeutic activity. These activities have been demonstrated both in cultured cells and animal models and have paved the way for ongoing human clinical trials.

Adulteration

Turmeric and other spices are commonly the potential exist for powders of toxic, cheaper agents with a similar color to be added, such as lead (II, IV) oxide, giving turmeric an orange-red color in its place of its native gold-yellow. Metanil yellow (also known as acid yellow 36) is another common adulterant in turmeric. It is believed to be an illegal dye for use in foods by the British Food Standards Agency.

PHYTOCHEMICAL ANALYSIS

A curcuminoids are a linear diarylheptanoid, with molecules such as curcumin or derivatives of curcumin with different chemical groups. These compounds are natural phenols and produce a pronounced yellow color. Many curcumin characters are incompatible for use as drugs by themselves. They have a meager solubility in water at acidic and physiological pH and also hydrolyze rapidly in alkaline solutions. Therefore, curcumin derivatives are synthesized to increase their solubility and hence bioavailability. Curcuminoids are soluble in dimethyl sulfoxide, acetone, and ethanol but are poorly soluble in lipids. The solubility of curcuminoids is enhanced in the aqueous phase with the application of surfactants or cosurfactants. Several studies have been reported to separate curcuminoids pigments by thin-layer chromatography (TLC), high-performance TLC (HPTLC), and column chromatography. Silica gel is used as a most common stationary phase with different solvent systems including benzene, ethyl acetate, ethanol, chloroform, acetic acid, hexane, and methanol for chromatographic separations. A HPTLC method was developed for the simultaneous determination of curcuminoids in turmeric plant extract using chloroform:methanol (95:5) as the mobile phase. They separated at the Rf value 0.69, 0.44, and 0.29 for curcumin, demethoxycurcumin, and bisdemethoxycurcumin.
respectively.[27] In another experiment, analysis of curcuminoids in Chinese herbal medicine was carried out using MEEKC. They are separated using uncoated fused-silica capillary column with a buffer consisting of 25 mM hydroxypropyl-β-CD, 10% MeOH, 0.04 M sodium borate, and 0.04 M sodium dodecylsulfate at pH 9.50 <10 min. The recoveries obtained were in the range of 95.7 – 106.3%. The calibration curves exhibited good linearity in the range of 90 – 1220 µg/mL with r of 0.9996 for C, 80 – 1120 µg/mL with r of 0.9998 (DMC), and 80 – 1200 µg/mL with r of 0.9998 (BDMC).[29] Analysis of curcuminoids in some Curcuma genus which are indigenous to Indonesia, namely, C. manga Val. and v. Zijp, C. heyneana Val. and v. Zijp, C. aeruginosa Roxb., and C. soloensis Val. was carried out using high-performance liquid chromatography (HPLC) with PDA detector at 425 nm. The separation was achieved using Zorbax Eclipse XDB C18 (250 × 4.6 mm i.d.; 5 µm) with mobile phase consisted of a mixture of MeOH:H₂O (containing 0.1% trifluoroacetic acid)-acetonitrile (39:5:350:468, v/v/v/v). The developed method gives the accuracy of 100.4 ± 0.92% (C), 99.8 ± 0.80% (DMC), and 99.9 ± 0.57% (BDMC), with limit of detection of 0.044 µg for C, 0.048 µg for DMC, and 0.058 µg for BDMC.[29] Payton et al.[30] carried out study on nuclear magnetic resonance (NMR) study of the solution structure of curcumin. The solution structure of curcumin was determined on the basis of NMR techniques including DEPT, HMOC, HMBC, and COSY. The results of the NMR studies showed that curcumin exists in solution as keto–enol tautomers. In another experiment, a HPTLC method for the determination of curcuminoids in turmeric plant extract has been reported by Paramasivam et al.[31] In this method, different solvents were tried for the extraction of curcuminoids, and ultimately, methanol gave the maximum extraction of the compound. The separations of the curcuminoids were performed with chloroform:methanol (48:2, v/v) as the mobile phase. The assay combined the separation and quantification of analyts on silica gel 60GF254 HPTLC plates with visualization under ultraviolet (UV) and scanned at 425 nm. Zhang et al.[32] have achieved successful separation of curcuminoids within 30 min by a Cadenza CD-C18 column (250 × 4.6 mm; i.d., 3 mm) with a mixture of 0.1 M of acetate buffer (pH 4.0) and CH₃CN (=57:43, v/v) as a mobile phase. The retention times of BDMC, DMC, and C were 19, 22, and 25 min, respectively. The developed method was also validated to determine its accuracy and precision by carrying out linearity and recovery experiment. In most cases, HPLC methods with UV/visible detection at around 260 or 450 nm were used, and these methods require simple instruments and are sufficiently sensitive to determine curcuminoids in rhizomes of Curcuma species.[33] Paramapojn and Gritsanapan[34] have carried out the determination of curcuminoids in turmeric plant extract by HPLC method and were found to be sensitive, precise, and accurate in the extract of rhizome C. longa. In another study, Herebian et al.[35] showed for the first time a gas chromatography–mass spectrometry-based method for metabolic profiling of the hydrophilic extract. They also identified 61 polar metabolites as TMS derivatives. In another study, HPLC–UV–MS experiment was performed on an Agilent series 1100 HPLC system including a quaternary pump, a variable wavelength detector, an autosampler, and a column compartment. The separation was performed on a YMC ODS-A C18 reversed column (250 4.6 mm i.d., 5 µm) equipped with an Agilent Zorbax SB-C18 guard column (12.5 4.6 mm i.d., 5 µm) at 30°C. The mobile phase consisted of acetonitrile (CH₃CN, A) and 0.1% formic acid in water (B) using a gradient program of 40–50% (A) in 0–30 min, 50–65% (A) in 30–35 min, 65–70% (A) in 35–42 min, 70% (A) in 42–55 min, and 70–100% (A) in 55–60 min. The mobile phase flow rate was 1.0 mL/min. The UV detector was monitored at 270 nm for fingerprinting analysis and 380 nm for quantitative analysis.[36] Ashraf et al. reported variations in content of curcumin in C. longa by HPTLC methods across Indian subcontinent. Linear concentration of curcumin was found to be 50–1000 ng/mL. The mobile phase consisting of toluene:chloroform:methanol (5:4:1, v/v/v) gave a sharp and well-defined peak at Rₚ value of 0.31. The lowest amount of curcumin, which was limit of detected, was 50 ng/spot. The lowest amount of curcumin, which was limit of quantified, was found to be 200 ng/spot.[3] Recently, Ashraf et al. have carried out determination of curcuminoids in different samples of C. longa by UPLC/MS method.[37] Mudge et al. have carried out analysis of curcuminoids in turmeric roots and supplements. The method was optimized and validated and also reported that this validated method is suitable for quantitation of individual curcuminoids in turmeric raw materials and finished products.[39] In another study, Dhakal et al. have applied Fourier Transform-Raman (FT-Raman) and FT-infrared (FT-IR) spectroscopy as separate but complementary methods for detecting metanil yellow adulteration of turmeric powder in turmeric. Spectral analysis showed that the FT-IR method in this study could detect the metanil yellow at the 5% concentration, while the FT-Raman method appeared to be more sensitive and could detect the metanil yellow at the 1% concentration.[39] Recently, Sahne et al. have carried out comparative study of extraction of bioactive compound curcumin from turmeric (C. longa) through different routes.[40] In this experiment, extraction of curcumin was carried out through different extraction methods such as microwave-assisted, ultrasound-assisted, and enzyme-assisted extractions. These were used as modern extraction routes to extract curcumin from turmeric powder, and the yield was investigated. The presence of curcumin in the extracted samples was confirmed by UV-visible spectroscopy, and quantification of curcumin was carried out by HPLC analysis. Result showed that Soxhlet method gives the highest yield. In another recent study, Osorio-Tobón et al. carried out fast analysis of curcuminoids from turmeric (C. longa L.) by high-performance liquid chromatography using a fused-core column. They developed and validated the method as well. In this method, they used different extracts of turmeric rhizome and products in their formulation.[41] Monton et al. have carried out quantitation of curcuminoids contents, dissolution profile, and volatile oil content of
Turmeric capsules produced at some secondary government hospitals. In a very recent study, Jin et al. have reported an integrated strategy for establishment of curcuminoids profile in turmeric using two LC–MS/MS platforms. Some of the phytochemical analysis work has been summarized in Table 1.

**PHARMACOLOGICAL ACTIONS**

Turmeric powder, curcumin demethoxycurcumin, and bisdemethoxycurcumin were found to be bioactive. Pharmacological action of *C. longa* is mainly due to its main active constituent curcumin present in *C. longa*. Different extract of turmeric such as ethanolic, aqueous, ether, and petroleum ether shows different types of activities.

**Action on Gastrointestinal System**

Turmeric powder increases mucin secretion in rabbits and may thus act as gastroprotectant against irritants. It also shows both anti-ulcer and ulcerogenic activities. They also observed antiflatulent activity in both in vivo and in vitro experiments in rats. Curcumin was also found to increase intestinal lipase, sucrase, and maltase activity. Lin et al. have reported that curcumin suppresses intestinal fibrosis by inhibition of PPAR-α-mediated epithelial-mesenchymal transition. Zhang et al. have carried out experiment on the protective effect of curcumin on TNBS-induced intestinal inflammation which is mediated through the JAK/STAT pathway and reported excellent results.

**Dyspepsia and Gastric Ulcer**

Curcumin has significant effect on dyspepsia and gastric ulcer. In a clinical trial phase II experiment, 45 subjects with endoscopically diagnosed peptic ulcers were given 600 mg curcumin 5 times daily for 12 weeks. It was seen that ulcers were absent in 12 patients (48%) after 4 weeks, 18 patients after 8 weeks, and 19 patients (76%) after 12 weeks. The remaining 20 patients, also given curcumin, had no noticeable ulcerations at the start of the study but were symptomatic-erosions, gastritis, and dyspepsia. Abdominal pain and other symptoms had decreased significantly within 1–2 weeks. Kim et al. discovered the defensive effect of turmeric ethanolic extract against gastric ulcers by blocking H2 histamine receptors (H2R) of male Sprague–Dawley (pylorus-ligated) rats. The effect of *C. longa* extract was compared to the properties of ranitidine. *Curcuma* was found to protect the gastric mucosal layer as effective as ranitidine. Orally administered ethanolic extract is believed to inhibit gastric acid, gastric juice secretion, and ulcer formation comparable to the properties of ranitidine. Rafatullah et al. examined the antiulcer activity of an ethanolic extract of turmeric. Administration of turmeric extract led to a noteworthy decrease in ulcer index and acidity of stomach contents. Pre-treatment 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.

**Action on Cardiovascular System**

Turmeric acts as a protective action on the cardiovascular system. It causes lowering cholesterol and triglyceride levels, falling susceptibility of low-density lipoprotein (LDL) to lipid peroxidation, and preventing platelet aggregation. Turmeric extract also causes to decrease predisposition of LDL to lipid peroxidation, furthermore to lower plasma cholesterol and triglyceride levels. Turmeric extract 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 through potentiation of prostacyclin synthesis and inhibition of thromboxane synthesis. Curcumin also causes protection against oxidative damage produced during atherosclerosis development by mobilizing α-tocopherol from adipose tissue. It also increases VLDL cholesterol transport in plasma, which results in increasing levels of α-tocopherol. Curcumin mobilizes α-tocopherol from adipose tissue, thus protecting their body against oxidative damage produced during the development of atherosclerosis. The study showed that increasing levels of α-tocopherol in plasma are due to more LDL cholesterol transportation. As a whole, the fatty acids in the animals were less susceptible to oxidation in the vessel wall. In another experiment, it was observed that oral intake of 500 mg/d curcumin for 7 days resulted in a significant decrease in the level of serum lipid peroxides (33%), increase in high-density lipoprotein cholesterol (29%), and a decrease in level of total serum cholesterol (12%). LDL in plasma and total cholesterol level in liver were found to decrease by action of curcumin. It also increases α-tocopherol level in rat plasma, suggesting in vivo interaction between curcumin and α-tocopherol. The fatty acid content was found to increase after ethanol-induced liver damage is significantly decreased by curcumin treatment. Curcumin causes the severity of pathological changes, and thus, it protects the damage of the heart from myocardial infarction. Calcium transport was improved by curcumin helps in pharmacological interventions to correct the defective Ca2+ homeostasis in the cardiac muscle. Curcumin has significant hypocholesteremic effect in hypercholesteremic rats.

**Antidepressant Properties and Effect on Nervous System**

The antidepressant effect of curcumin was explored in chronic mild stress (CMS) model. In assessment with normal rats, rats suffering from the CMS procedure have a considerable
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HPLC: High-performance liquid chromatography, HPTLC: High-performance thin-layer chromatography, *C. longa*: *Curcuma longa*
lower consumption of sucrose, increased interleukin (IL-6), tumor necrosis factor alpha (TNF-α) levels, CRF, and cortisol levels. Ethanolic extract of turmeric causes to increase the sucrose intake to normal control levels reduced the CMS-induced increase in serum IL-6 and TNF-α level 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. Antidepressants properties of turmeric are mediated through inhibition of monoamine oxidase A.\(^{[76]}\) Ethanol extract of C. longa causes to reverse the decrease in serotonin, noradrenaline, and dopamine concentrations as well as the increase in serotonin turnover, cortisol levels, and serum corticotrophin-releasing factor.\(^{[77]}\) Xu et al.\(^{[78]}\) examined the consequence of orally directed curcumin on behavior in a long-lasting stress model of depression in rats. The antidepressant imipramine was used as a control. Administration of curcumin exhibited similar properties as imipramine. These discoveries propose that the properties of chronic administration of curcumin on the conduct of chronic stressed rats may be connected to the controlling properties of the dysfunction of the hypothalamic-pituitary-adrenal axis, through a discerning increase in brain-derived neurotrophic factor in the frontal cortex and the hippocampus of the rats. A direct effect of curcumin in decreasing the amyloid pathology of Alzheimer’s disease (AD) has been shown by an experimental model of AD.\(^{[79]}\) Several studies showed that curcumin possessed multiple actions in the brain. It can be a future drug of therapy for the treatment of various neurological disorders such as major depression, tardive dyskinesia, and diabetic neuropathy.\(^{[80]}\) Curcumin and manganese complex of curcumin affectionate defensive acts next to vascular dementia by showing antioxidant activity.\(^{[81,82]}\)

**Anti-inflammatory Activity**

C. longa plays very vital role in reducing inflammatory swelling. Oral administration of curcumin was found to be as effective as cortisone or phenylbutazone in acute inflammation. Anti-inflammatory properties of C. longa may be endorsed to its skill to restrain both biosynthesis of inflammatory prostaglandins from arachidonic acid and neutrophil function during inflammatory states. Curcuminoids also prevent LOX, COX, phospholipases, leukotriene’s, prostaglandins, thromboxone, nitric oxide elastase, hyaluronidase, collagenase, monocyte chemoattractant protein-1, interferon-inducible protein, TNF, and IL-12. It also decreases prostaglandin formation and inhibits leukotriene biosynthesis through the lipoxygenase pathway.\(^{[83]}\) Carrageenan-induced edema in rats and mice experiment was done to check the anti-inflammatory effect of curcumin and found to be effective.\(^{[84-87]}\) FHM and BHM (natural analogs of curcumin) also possess anti-inflammatory activity. Another study showed that petroleum ether, alcohol water, and more importantly volatile oil extract of C. longa have anti-inflammatory effect.\(^{[88,89]}\) The anti-inflammatory effect of curcumin has acted through inhibition of NFkB activation.\(^{[90]}\) Curcumin also enhances wound healing in diabetic rats and mice.\(^{[91]}\)

**Antioxidant Effect**

Several works have been done in the past for the antioxidant property of curcumin. Sharma\(^{[92]}\) supported antioxidant property of curcumin. It acts as a scavenger of oxygen free radicals.\(^{[93,94]}\) It can protect hemoglobin from oxidation.\(^{[95,96]}\) In vitro, curcumin can significantly reduce speed of the production of reactive oxygen species such as superoxide anions, hydrogen peroxide, and nitrite radical production. This is done by activated macrophages, which take part in a vital job in inflammation.\(^{[97]}\) Different extracts of turmeric such as water and fat soluble and its curcumin component exhibit strong antioxidant activity. Pre-treatment of curcumin causes and decreases ischemia-induced changes in the heart.\(^{[98]}\) In another study in vitro measuring, the effect of curcumin on endothelial heme oxygenase-1, an inducible stress protein, was carried out by utilizing bovine aortic endothelial cells.\(^{[99]}\) Curcumin was found to reduce the testicular damage caused by exposure to di-n-butyl phthalate, by an increase in glutathion (GSH), testosterone levels, and glucose-6-phosphate dehydrogenase activity and decrease in malondialdehyde (MDA) levels. These properties may be due to intrinsic antioxidative abilities of curcumin.\(^{[100]}\) Curcumin is only antimutagenic against mutagens which require metabolic activation. Curcumin was found to block cyclosporine A-resistant phosphor myristate acetate + anti-CD28 pathway of T-cell proliferation.\(^{[101]}\) Clinical research on curcumin’s therapeutic advantage for pancreatitis is inadequate and has mainly focused on its antioxidant properties. However, research indicates that the inflammatory response plays a critical role in the development of pancreatitis and subsequent tissue damage. Consequently, it appears 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.\(^{[102]}\) Action consequence on pain patterns as well as erythrocyte MDA (MDA; an indicator of lipid peroxidation) and GSH was evaluated at baseline and after 6 weeks. In the curcumin group, there was a significant drop in MDA levels. Further research is needed to determine the role of lipid peroxidation in pain and other symptomology associated with pancreatitis.\(^{[102]}\)

**Anticarcinogenic Effect - Induction of Apoptosis**

Curcumin plays an important role as anti-carcinogenic agent. Apoptosis by induction plays a significant task in its anti-carcinogenic effect. Actually, apoptosis was caused by this and block cell-cycle series, both of which are involved in reducing cancerous cell enlargement in rat aortic smooth muscle cells.\(^{[103]}\) Although curcumin may act differently.
on different cell lines. However, leukemia, breast, colon, hepatocellular, and ovarian carcinoma cells go away through apoptosis in the occurrence of curcumin, lung, prostate, kidney, cervix, and central nervous system malignancies and melanoma cells illustrate fight to cytotoxic effect of curcumin. Curcumin also decreases the production of rat thymocytes. These powerfully involve that cell growth and cell death contribute to a common lane.

In vitro and in vivo studies clearly indicated that turmeric and curcumin are proficient of suppressing the activity of several common mutagens and carcinogens in a variety of cell types. The direct antioxidant and free-radical scavenging properties of turmeric and curcumin caused anticarcinogenic effect 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. Supplementation with turmeric and curcumin may not be without harm. Laboratory findings show that dietary turmeric may actually inhibit the antitumor activity of chemotherapeutic agents such as cyclophosphamide and doxorubicin. The use of both curcumin and turmeric extract during carcinogenesis and promotion resulted in less papilloma production, compared to controls. This specifies that both curcumin and turmeric extracts produce their best properties during tumor promotion. The effect of C. longa on myocardial apoptosis in experimentally induced myocardial ischemia-reperfusion injury was also investigated. C. longa demonstrated significant antiapoptotic property, which might contribute to the observed preservation in cardioprotective properties and cardiac function. Some evidence showed that curcumin inhibits the action of certain chemotherapy drugs. Research discloses curcumin decreased camptothecin-induced death of cultured breast cancer cells and prevented cyclophosphamide-induced breast tumor regression in mice. 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.

Antimicrobial Properties

Composition and antimicrobial activity of the essential oil from leaves of C. longa L. kasur variety was investigated. The antimicrobial properties of leaves of C. longa were tested by disc diffusion method against various human pathogens, including eight fungal and five bacterial strains. Essential oil showed maximum resistance against Fusarium minitormes MAY 3629 followed by Bacillus subtilis ATCC 6633, whereas it exhibited least resistance against Fusarium oxysporum ATCC 48122. Another study, in which guinea pigs were infected with dermatophytes, pathogenic molds, or yeast, found that topically applied turmeric oil inhibited dermatophytes and pathogenic fungi. Lesions developments were detected in the dermatophyte- and fungi-infected guinea pigs, and it disappeared at 7 days post-turmeric application. Curcumin has also been found to have moderate activity against Plasmodium falciparum and Leishmania major organisms. Khattak et al. studied the antifungal, antibacterial, phytotoxic, cytotoxic, and insecticidal activity of an ethanolic extract of turmeric. The extract exhibited antifungal activity toward Trichophyton longifusus and Microsporum canis and meager antibacterial activity against Staphylococcus aureus. Toxic activity was detected against Lemma minor. The C. longa-treated rabbit group showed a notable higher mean value for the decline of the wound related to controls. Furthermore, the wounds showed less inflammation and an increasing trend in the formation of collagen.

Antimutagenic Activity

Curcumin shows together pro- and anti-mutagenic effects. Curcumin is shown to decrease the numeral of abnormal cells in cyclophosphamide-induced chromosomal aberration in Wistar rats at 100 and 200 mg/kg body wt doses. Turmeric also prevents mutation in urethane (a powerful mutagen) models.

Anticoagulant Activity

Curcumin has found to possess anticoagulant activity. Its mechanism of action is to inhibit collagen and adrenaline-induced platelet aggregation in vitro as well as in vivo in rat thoracic aorta. Grag reported antifertility activity about 100% in rats when fed orally in petroleum ether and aqueous extracts of turmeric rhizomes. Again Garg et al. also reported that implantation is totally repressed by these extracts. Curcumin is also found to inhibit 5a-reductase, which changes testosterone to 5a-dihydrotestosterone, in that way inhibiting the enlargement of flank organs in hamster. Curcumin also inhibits human sperm motility, and it is a sign of possible for the progress of a novel intra-vaginal contraceptive.

Antidiabetic Effect

A number of experiments carried out in the past which showed the antidiabetic property of curcumin. A hexane extract (containing ar-turmerone), ethanolic extract (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. In this experiment, it was found that ethanolic extract of turmeric containing both curcuminoids and sesquiterpenoids is more powerfully hypoglycemic than either curcuminoids or...
Wickenberg et al. studied the effects of turmeric on postprandial plasma glucose and insulin in healthy subjects; they found that the ingestion of 6 g Curcuma longa had no considerable effect on the glucose response. The alteration in insulin reported was appreciably higher 30 min and 60 min after the OGTT including Curcuma longa. The insulin AUCs were also significantly higher after the ingestion of Curcuma longa after the OGTT. Turmeric was found to reduce blood sugar level in alloxan-induced diabetes in rat. In another experiment, it showed that, at very low dose, curcumin prevents galactose-induced cataract formation. Turmeric (curcumin) and its oil portion suppress growth of a number of bacteria such as Streptococcus, Staphylococcus, and Lactobacillus.

The aqueous extract of turmeric rhizomes is reported to act as antibacterial effects.

Antifungal Effect

Due to wide traditional use of turmeric in food products, several studies have been done to study the turmeric and curcumin with the aspect of regulatory fungal related spoilage and fungal pathogens. Concentration of curcumin plays very important role in prevention of growth of fungus. Addition of turmeric powder in plant tissue culture at the 0.8 and 1.0g/L had considerable inhibitory activity against fungal infections. The methanol extract of turmeric showed antifungal activity against Cryptococcus neoformans and Candida albicans with minimum inhibitory concentration (MIC) values of 128 and 256 µg/mL, respectively. Hexane extract of Curcuma longa at 1000 mg/L confirmed antifungal activity against Rhizoctonia solani, Phytophthora infestans, and Erysiphe graminis. The study also revealed that 1000 mg/L of ethyl acetate extract of Curcuma longa shown inhibitory effect against R. solani, P. infestans, Puccinia recondita, and Botrytis cinerea. At the concentration of 500 mg/L, curcumin displayed antifungal activity against R. solani, P. recondita, and P. infestans.

Curcumin and turmeric oil showed antifungal effect against two phytophagous fungi, namely, Fusarium solani and Helminthosporium sporium. Oil of turmeric showed the most effective antifungal activity against F. solani and H. oryzae with IC_{50} of 19.73 and 12.7 µg/mL, respectively. The methanol extract of C. longa has inhibitory effect against some clinical isolates of dermatophytes. It was established that 18-month-old and freshly distilled oil isolated from rhizome of Curcuma longa exhibited the most potent antifungal effect against 29 clinical isolates of dermatophytes with MIC values of 7.2 and 7.8 mg/mL, respectively. Trichophyton rubrum, T. mentagrophytes, Epidermophyton floccosum, and Microsporum gypseum were suppressed by 1:40–1:320 dilutions of turmeric oil. In another in vivo study conducted on infected guinea pigs with T. rubrum, dermal application of turmeric oil (dilution 1:80) induced an improvement in healing of the lesions after 2–5 days which were and it caused the lesions after 6–7 days of consumption to vanish. Turmeric oil also showed activity against pathogenic molds such as Sporothrix schenckii, Exophiala jeaneselmei, Fonsecaea pedrosii, and Scedosporium apiospermum with MIC values of 114.9, 459.6, 459.6, and 114.9 µg/mL, respectively. However, curcumin showed more potent significant effect against Paracoccidioides brasiliensis than fluconazole, though it did not affect the growth of Aspergillus species.

Antiviral Effect

Curcumin also plays important role as an antiviral agent. It acts as an inhibition of Epstein–Barr virus key activator BamH fragment z left frame 1 protein transcription in RajiDR-LUC cells. It also restrains UV light-induced HIV gene expression. Plants as a rich source of phytochemicals with different biological activities including antiviral activities are of interest of scientists. Due to the absence of successful therapeutics for the most of viral diseases, rise of antiviral drug resistance and high cost of some antiviral therapies require finding new effective antiviral compounds. Moreover, the offered antiviral therapies are not always well-tolerated or to a certain extent effective and satisfactory. Henceforth, in recent days, the increasing requirement for antiviral substances is more emphasized. It has been well-known that curcumin as a plant derivative has a widespread range of antiviral activity against different viruses. An enzyme called inosine monophosphate dehydrogenase (IMPDH) is suggested as a therapeutic target for antiviral and anticancer compounds. Curcumin in the course of inhibitory activity against IMPDH effect in either noncompetitive or competitive way is flexible as a potent antiviral compound through this process among the 15 different polyphenols. One study showed curcumin to be an effective compound to inhibit the HIV-1 LTR-directed gene expression without any major effects on cell viability. It was also found that curcumin and its derivatives, specifically, reduced curcumin, allyl-curcumin, and tocopheryl-curcumin, discovered 70–85% inhibition in Tat protein transactivation of HIV-1 LTR measured by β-galactosidase activities of HeLa cells which in HIV-1 LTR was fused to the indictor of lac Z gene. Furthermore, curcumin reserved the acetylation of Tat protein of HIV significantly by p300 related with invasion of HIV-1 multiplication. Curcumin by targeting the acetyltransferase proteins of p300/CREE binding protein can be a potent compound for combinatorial HIV therapeutics.

Molecular Marker Analysis in Curcuma longa

Curcuma longa is well-known and valued medicinal plant. Several molecular studies have been reported for the assessment of different accessions. Authentication and genuinely of plant is essential part in marker analysis of plant. As dissimilar parts of the same species can be used as different drugs and as the same drug comes from several species that lead to confusion on the taxonomy of these Curcuma species. Besides this, by
distributing this species in a large area, phenotypic variation of morphological characters of rhizomes and leaves is very common in this species that lead to phenotypic plasticity of the species and wrong taxonomic treatment of individuals. However, the correct identity is important to confirm the sources of origin of herbal drugs within the genus.[141,142] It is necessary to adopt various methods to identify the sources of origin of different Curcuma species and evaluate their genetic relationship.[143] Among all markers, random amplification polymorphism DNA (RAPD)-based molecular marker is the best approach for identification and genetic diversity analysis in turmeric plant. The declining number of natural populations and rapid fragmentation of natural habitat may have severe impact on the genetic potential of this species.[144] Besides this, taxonomic identity of the species is also confusing. Their potential use, genetic diversity at species, and population level are also unfamiliar. Taxonomic identity of the species is important to search and confirm the origins of different potential. Extending to that knowledge of genetic diversity, it will greatly help to utilize and conserve C. longa genetic resource of the country. Even though germplasm collections represent the main source of variability for turmeric genetic improvement studies which is mostly restricted to phenotypic makers. However, the use of phenotypic traits in germplasm characterization may be limited due to the small number of descriptors available and the influence of environment and genotype x environment interactions. Molecular marker techniques may overcome many restrictions of the morphological and biochemical markers for the inequity of turmeric cultivars by providing genetic background for the observed phenotypic variability since they are not affected by the environment or developmental stage and can detect variation at the DNA level.[145] Hussain et al.[146] studied RAPD analysis for 30 accessions of 5 Curcuma species including Curcuma latifolia, Curcuma malabarica, Curcuma manga, Curcuma Rakatakanta, and 13 C. longa conserved morphotypes. Their RAPD data corroborated the morphological classification of the morphotypes. The efficiency of individual RAPD primers was also compared showing that RAPD markers were highly informative in discriminating the germplasm of Curcuma. Islam et al.[147] had reported that existence of a high level of genetic diversity within populations of Curcuma zedoaria may be present due variations in ecological conditions. However, RAPD markers are known to yield low levels of polymorphism when compared to other molecular markers, such as microsatellites (simple sequence repeats, SSR).[148,149] In recent study, ISSRs, SSRs, and chloroplast or nuclear markers (matK, rbCL, rpl16, and trnK) were used for characterization of inter- and intra-specific diversity of turmeric cultivars.[150] The genetic fingerprints of 15 Curcuma species using RAPD and ISSR markers were done by Syamkumar and Sasikumar[151] A RAPD-based assay was carried out and reported that the genetic diversity of C. zedoaria was maintained to a greater extent in hilly populations than in plain and plateau populations.[152] RAPD analysis of genetic divergence in 20 accessions of C. longa showed a small divergence between accessions.[153] A simple and rapid molecular identification method for six medicinal Curcuma species from China using the trnK nucleotide sequences was reported by Cao and Komats.[154] Khan et al.[155] reported that the ecology of the species varied so much that their habitat ranges from sea level (sandy coastal habitat) to high altitude such as above 2000 m in the Himalayas. Isozyme polymorphism in a germplasm collection of C. longa was done by using acid phosphatase, superoxide dismutase, esterase, polyphenol oxidase, peroxidase, and catalase, and it showed good polymorphism in the 15 accessions.[156] An isozyme polymorphism was used to identify some early seven flowering Curcuma species.[157] RAPD markers are markers of choice, because of its simplicity and low-cost nature, rapid, inexpensive, and effective system for studying plant genetic relationships.[153,158] The RAPD markers could also be used in the study of genetic variability of species or natural populations.[147,159] This could also be used in the study of genotype identification.[160-162] In another study, Sasaki and Nagumo reported rapid identification of C. longa and C. aromatica by LAMP method.[163] A study conducted by Sigrist et al. showed genetic diversity of turmeric germplasm (C. longa; Zingiberaceae) using microsatellite markers to discover genetics and molecular research.[164] Sasikumar et al. carried out polymerase chain reaction (PCR)-based detection of adulteration in the market samples of turmeric powder.[165] In another experiment, Hayakawa et al. carried out molecular identification of turmeric (C. longa, Zingiberaceae) with high curcumin content.[166] Das et al.[167] have reported genetic relationship of Curcuma species from northeast India using PCR-based markers. They elucidated intra- and inter-specific genetic diversity important for utilization, management, and conservation. In another experiment, identification of different Curcuma species using RAPD markers were carried out by Donipati and Sreeramulu[168] They established relationships among six medicinal species of Curcuma assessed by RAPD markers. Recently, ISSR fingerprinting of genetic relationship of Curcuma sp. of Tripura was carried out by Saha et al.[169] Molecular fingerprints of four different species of Curcuma, namely, Curcuma amada, Curcuma caesia, Curcuma Longa, and Curcuma zedoaria found in Tripura were developed using inter simple sequence repeats. Twenty ISSR primers generated 116 loci amplified in the range of 200–5000 bp with an average of 5.8 alleles and 1.6 effective alleles per locus. The percentage of polymorphic band was found to be 86.29 with an average of 5.15 per primer.

CONCLUSION

The present review attempts to summarize and document the phytochemical, pharmacological, and molecular work done on turmeric. Turmeric and many of its chemical constituents were shown to have useful pharmacological actions to treat various types of disease. Curcumin is one such phytoconstituent and nutraceutical substance with
numerous pharmacological activities verified experimentally and clinically. It has been recognized advantageous in treating anti-inflammatory, anti-allergic, antioxidant, anti-hyperglycemic, and anticancer properties. Molecular study of turmeric including fingerprinting by RAPD, SCAR, ISSR, and AFLP plays an important role in the development of molecular marker for authenticity and diversity of plants. Different marker analysis shows that there is a high level of polymorphism among different accessions and pattern varied with respect to environmental factors and genetic parameters.

**FUTURE PERSPECTIVE OF C. LONGA**

Comprehensive traditional knowledge on turmeric can be validated by modern pharmacological studies emphasizing the chemical nature of turmeric, its effects on various parameters and detailed studies of the mechanisms of the observed biological actions and molecular study. Although this information alone is not adequate to provide proof for safety and efficacy of a natural product and requires further exploration. Studies on molecular, phytochemical, and pharmacological effects allow greater perceptive of the factors sustaining the safe use of the medicine, including interactions with other drugs or nutritional factors. If the whole of these results endorses and explains the traditional uses, a clinical study in volunteers or patients may be vindicated for the specific outcome being projected.

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