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REVIEW

Multitargeting by turmeric, the golden spice: From kitchen to clinic

Subash C. Gupta[1], Bokyung Sung[1], Ji Hye Kim[1], Sahdeo Prasad[1], Shiyou Li[2] and Bharat B. Aggarwal[1]

[1] Cytokine Research Laboratory, Department of Experimental Therapeutics, The University of Texas MD Anderson Cancer Center, Houston, TX, USA
[2] National Center for Pharmaceutical Crops, Arthur Temple College of Forestry and Agriculture, Stephen F. Austin State University, Nacogdoches, TX, USA

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Although much has been published about curcumin, which is obtained from turmeric, comparatively little is known about turmeric itself. Turmeric, a golden spice obtained from the rhizome of the plant *Curcuma longa*, has been used to give color and taste to food preparations since ancient times. Traditionally, this spice has been used in Ayurveda and folk medicine for the treatment of such ailments as gynecological problems, gastric problems, hepatic disorders, infectious diseases, and blood disorders. Modern science has provided the scientific basis for the use of turmeric against such disorders. Various chemical constituents have been isolated from this spice, including polyphenols, sesquiterpenes, diterpenes, triterpenoids, sterols, and alkaloids. Curcumin, which constitutes 2–5% of turmeric, is perhaps the most-studied component. Although some of the activities of turmeric can be mimicked by curcumin, other activities are curcumin-independent. Cell-based studies have demonstrated the potential of turmeric as an antimicrobial, insecticidal, larvicidal, antimutagenic, radioprotector, and anticancer agent. Numerous animal studies have shown the potential of this spice against proinflammatory diseases, cancer, neurodegenerative diseases, depression, diabetes, obesity, and atherosclerosis. At the molecular level, this spice has been shown to modulate numerous cell-signaling pathways. In clinical trials, turmeric has shown efficacy against numerous human ailments including lupus nephritis, cancer, diabetes, irritable bowel syndrome, acne, and fibrosis. Thus, a spice originally common in the kitchen is now exhibiting activities in the clinic. In this review, we discuss the chemical constituents of turmeric, its biological activities, its molecular targets, and its potential in the clinic.

Keywords:
Chronic diseases / Modern uses / Spice / Traditional uses / Turmeric

1 Introduction and traditional uses of turmeric

Since ancient times, "Mother Nature" has been a fertile source for drugs used to treat human diseases. One such remedy is the spice turmeric, which has been used for at least 2500 years, mostly in Asian countries. Turmeric is derived from the plant *Curcuma longa* L., which belongs to the Zingiberaceae family [1]. This species is an herbaceous perennial that is extensively cultivated in the tropical areas of Asia and to a lesser extent in Africa. In India, it is popularly known as haldi. The rhizomes of the plant are oblong, ovate, pyriform, often short branched, and a good source of turmeric [2]. Some other sources of turmeric are *C. phaeocaulis*, *C. xanthorrhiza*, *C. mangga*, *C. zedoaria*, and *C. aromatica*. Although India is the primary exporter, turmeric is also cultivated in

Correspondence: Dr. Bharat B. Aggarwal, Cytokine Research Laboratory, Department of Experimental Therapeutics, Unit 1950, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, TX 77030, USA
E-mail: aggarwal@mdanderson.org
Fax: +1-713-792-0362

Abbreviations: CSF-1, colony stimulating factor-1; **DMBA**, 7,12-dimethylbenz(a)anthracene; **GGT**, gamma glutamyl transpeptidase; **HO-1**, heme oxygenase-1; **IBS**, irritable bowel syndrome; **NDEA**, nitrosodiethylamine; **NF-κB**, nucler factor-kappaB; **Nrf2**, NF-E2-related factor 2; **PGE_2**, prostaglandin E_2; **RANKL**, receptor activator of nuclear factor kappa-B ligand; **STAT3**, signal transducers and activators of transcription 3; **STZ**, streptozotocin; **TNF-α**, tumor necrosis factor-α; **TPA**, 12-*O*-tetradecanoylphorbol-13-acetate

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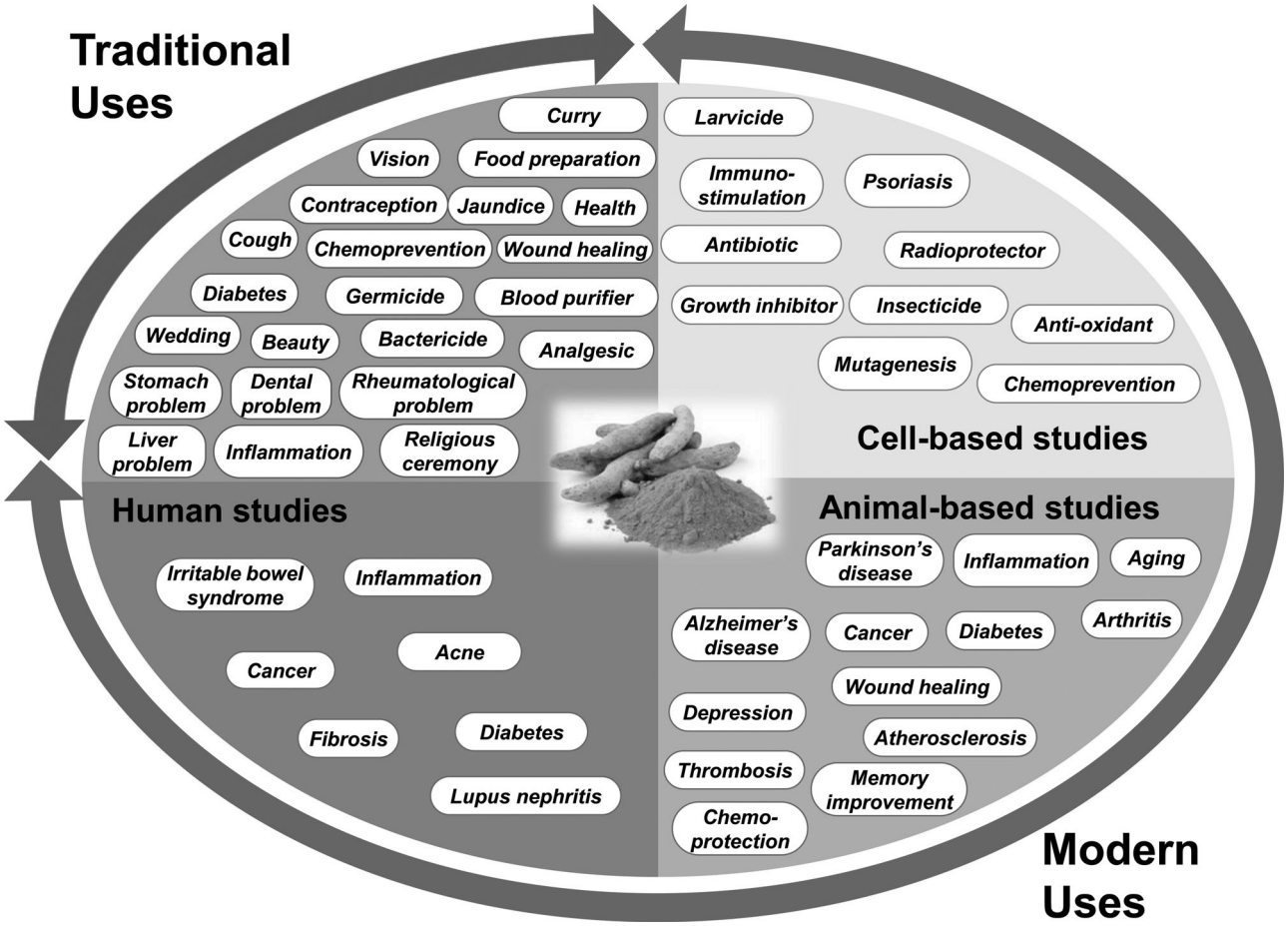

Figure 1. Schematic representation for the traditional and modern uses of turmeric.

Bangladesh, China, Indonesia, islands of the Caribbean, and South America [3]. The most active component of turmeric is curcumin, which makes up to 2–5% of the spice.

Turmeric has been used for numerous purposes since ancient times (Fig. 1). It has been used to flavor and color both vegetarian and nonvegetarian food preparations, especially in South Asian cuisine [3,4]. Turmeric is one of the principle ingredients of curry powder. In the Western world, it is used in sauces, mustard blends, and pickles. Turmeric tea is popular in certain areas of Japan, particularly in Okinawa. Turmeric has also been traditionally recognized as an agent of beauty and health [5]. For instance, turmeric paste is applied on the face and skin as a mask to improve skin appearance and to aid in the fading of blemishes. Turmeric is considered highly auspicious in India and has been used extensively in various Indian ceremonies for millennia. It is used in every part of India during weddings and other religious ceremonies.

Turmeric has a long tradition of use in both the Chinese and Indian systems of medicine. It has been used as an anti-inflammatory agent to treat gas, colic, toothaches, chest pains, and menstrual difficulties. This spice was also used to help with stomach and liver problems and to heal wounds and lighten scars [6]. It also has been used for digestive problems such as gastritis and acidity, helping to increase mucus production and to protect the stomach lining. Turmeric is a good antibacterial for those chronically weak or ill, with a name in Sanskrit that translates as "germicide." It helps to purify the blood and stimulates the formation of new blood tissue. Turmeric has been shown to improve gynecological problems as well. For instance, it helps to regulate the female reproductive system and purifies the uterus and breast milk. Turmeric has also been shown to help relieve pain during labor. Turmeric is believed to make the eyes clean and can improve the vision [7,8]. However, scientific evidence proving these health benefits of turmeric is lacking. The Ayurvedic Indian medicine claims the use of turmeric against biliary disorders, anorexia, coryza, cough, diabetic wounds, jaundice, stomach tumor, rheumatism, and sinusitis [9]. Turmeric has also been used to support liver function and to treat jaundice in both Ayurvedic and Chinese herbal medicine.

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Turmeric has been shown to offer relief from dental problems in numerous ways [10]. For instance, rinsing the mouth with turmeric water has been reported to provide instant relief. Additionally, massaging aching teeth with roasted, ground turmeric eliminates pain and swelling. The application of turmeric powder to the teeth makes the gums and teeth strong. The application of a paste made from 1 teaspoon of turmeric with 0.5 teaspoon of salt and 0.5 teaspoon of mustard oil provides relief from gingivitis and periodontitis [11].

Although initially it was believed that the activities of turmeric are mainly due to curcumin, research during the past decade has identified numerous chemical entities from turmeric, and modern science has provided a logical basis for the safety and efficacy of turmeric against human diseases. Epidemiologic data indicate that some extremely common cancers in the Western world are much less prevalent in regions (Southeast Asia, e.g.) where turmeric is widely consumed in the diet [12, 13]. This spice has been found well tolerated at gram doses in humans. Dietary turmeric contains over 300 different components, only curcumin has been extensively investigated, however [14, 15]. A recent study indicated that curcumin-free aqueous turmeric extract has the potential to suppress benzo[a]pyrene-induced tumorigenesis in mice [16]. In another study, curcumin-free turmeric inhibited 7,12-dimethylbenz(a)anthracene (DMBA) -induced mammary tumorigenesis in rats [17]. These reports suggest that components other than curcumin may also contribute to the anticancer activities of turmeric. Only limited studies have compared the potential of turmeric with curcumin. In our own lab, we found that turmeric is more potent in inhibiting colorectal cancer growth in comparison to curcumin using cell-based studies [18]. Ramachandran et al. reported a superior toxicity of turmeric in comparison to curcumin against pancreatic cancer cells [19]. In another study, turmeric exhibited better potential in comparison to curcumin in reversing thyroid hormone (T3)-induced oxidative stress and hyperplasia in wistar rats [20]. In vitro studies of this spice have shown potential of antimicrobial, insecticidal, larvicidal, antimutagenic, radioprotective, and antigrowth activities (Fig. 1). In animal studies, this golden spice exhibits activities against inflammatory conditions, cancer, neurodegenerative diseases, depression, diabetes, and atherosclerosis. It has also been shown to offer protection from numerous chemical insults. Some clinical trials have already evaluated the safety and efficacy of turmeric against human diseases, with numerous other studies underway. The most common human diseases in which turmeric has shown efficacy in human subjects by clinical trials are lupus nephritis, cancer, diabetes, irritable bowel syndrome (IBS), acne, and fibrosis. Turmeric has now become so popular that it is used in beverages, cosmetics, food preparations, and numerous health-care items (Fig. 2). In the sections to follow, we provide evidence for the biological activities of turmeric from both preclinical and clinical studies. The common chemical entities identified from turmeric are also discussed.

2 Chemical composition of turmeric

Turmeric is chemically diverse in composition. The qualitative and quantitative compositions of turmeric vary often with varieties, locations, sources, and cultivation conditions. To date, around 235 compounds, primarily phenolic compounds and terpenoids, have been identified from this spice (Fig. 3) [21]. Of these compounds, 22 are diarylheptanoids and diarylpentanoids, 8 phenylpropene and other phenolic compounds, 68 monoterpenes, 109 sesquiterpenes, 5 diterpenes, 3 triterpenoids, 4 sterols, 2 alkaloids, and 14 other compounds. The curcuminoids belonging to the group of diarylheptanoids are the major bioactive ingredients of turmeric. The most common curcuminoid present in turmeric is curcumin, which has been consumed for medicinal purposes for thousands of years. Commercial curcumin is usually a mixture of three curcuminoids: curcumin (71.5%), demethoxycurcumin (19.4%), and bisdemethoxycurcumin (9.1%) [22]. Three diarylpentanoids with a five-carbon chain between two phenyl groups have also been identified from turmeric. Calebin-A, vanillic acid, and vanillin are other phenylpropene and phenolic compounds identified from turmeric. The essential oils from leaves and flowers are usually dominated by monoterpenes. The most common monoterpenes present in turmeric are *p*-cymene, β-phellandrene, terpinolene (terpenoline), *p*-cymen-8-ol, cineole, and myrcene. Dried turmeric rhizomes usually yield 1.5–5% essential oils, which are dominated by sesquiterpenes and are responsible for its aromatic taste and smell. The most common sesquiterpenes identified from turmeric are α-turmerone, β-turmerone, turmeronol A, and turmeronol B [23]. The chemical structure of some other compounds identified from turmeric is shown in Fig. 3.

3 Preclinical studies with turmeric

Extensive research from both in vitro and animal models over the past several years has indicated the activities of turmeric against numerous ailments. In this section, we provide evidence from in vitro and animal models for the biological activities of turmeric.

3.1 Cell-based studies

3.1.1 Antimicrobial activity

Turmeric has been shown to inhibit the growth of numerous microorganisms including bacteria, viruses, and fungi (Table 1). For instance, turmeric was shown to inhibit the growth of *Helicobacter pylori*, which is associated with the development of gastric and colon cancers [24]. The minimum inhibitory concentration required to inhibit *H. pylori* growth was in the range of 6.25–50 μg/mL [24]. In a few cases, turmeric has been shown to act as a preservative by retarding microbial growth [25]. At a 5% concentration, turmeric

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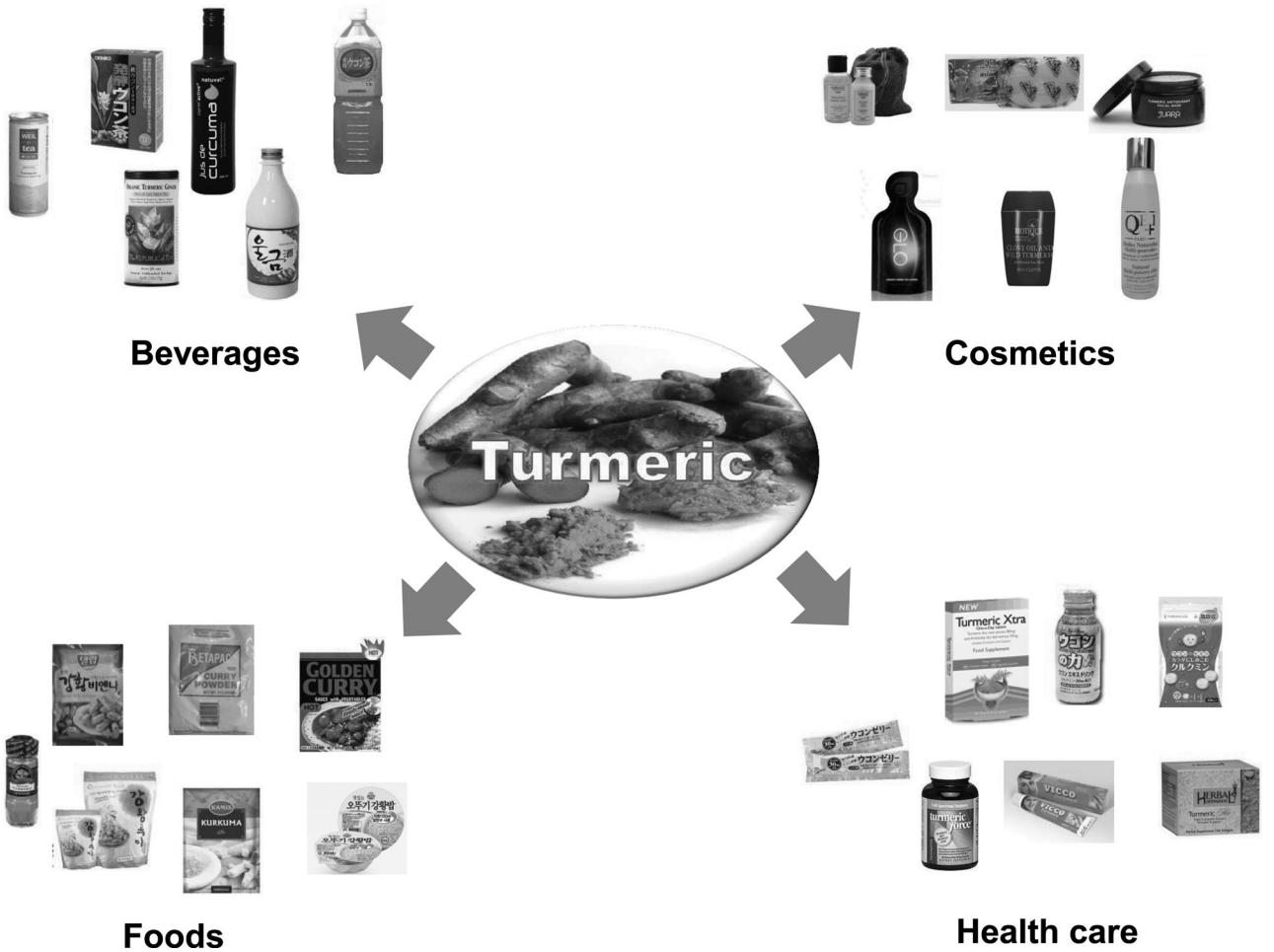

Figure 2. Common turmeric-based products. Turmeric-based preparations include but are not limited to beverages, cosmetics, food preparations, and health-care items.

exhibited antimicrobial activity against histamine-producing bacteria [26]. Turmeric extract has also shown activity against food-borne pathogens [27, 28]. The bactericidal activities of turmeric against *Escherichia coli* BL-21 strain were reported by another study [29].

Turmeric possesses antiviral activity. In one study, the spice inhibited hepatitis B virus replication in liver cells by enhancing the level of p53 protein [30]. Turmeric exhibits antifungal activity against numerous strains of fungus [31, 32]. This spice can also inhibit the production of aflatoxin [33].

3.1.2 Insecticidal and larvicidal activity

Turmeric is known to have insecticidal and larvicidal activities. For instance, turmeric possesses insecticidal activity against the maize weevil (*Sitophilus zeamais*) and the red flour beetle (*Tribolium castaneum*) in one study [34]. In another study, turmeric extract demonstrated larvicidal activity against the dengue vector *Aedes aegypti*, the yellow fever mosquito [35]. The concentration of turmeric required to kill 50% of the population (LC_{50}) was 115.6 ppm, and early instar larvae were more susceptible to the extract than the late instar larvae and pupae [35]. The larvicidal activity of turmeric against *Anopheles stephensi* and *Culex quinquefasciatus* mosquito larvae was demonstrated by another study [36]. Turmeric exhibits toxicity against red spider mites as well [37].

3.1.3 Antioxidant activity

Turmeric acts as a free radical scavenger in a number of in vitro studies (Table 1). In one study, ethanol extracts of turmeric were found to contain high antioxidant activities compared with aqueous extracts [38]. In a renal cell line, turmeric exhibited protection against oxidative stress induced by hydrogen peroxide [39]. The antioxidant activity of turmeric is supported by results from other in vitro assays as well

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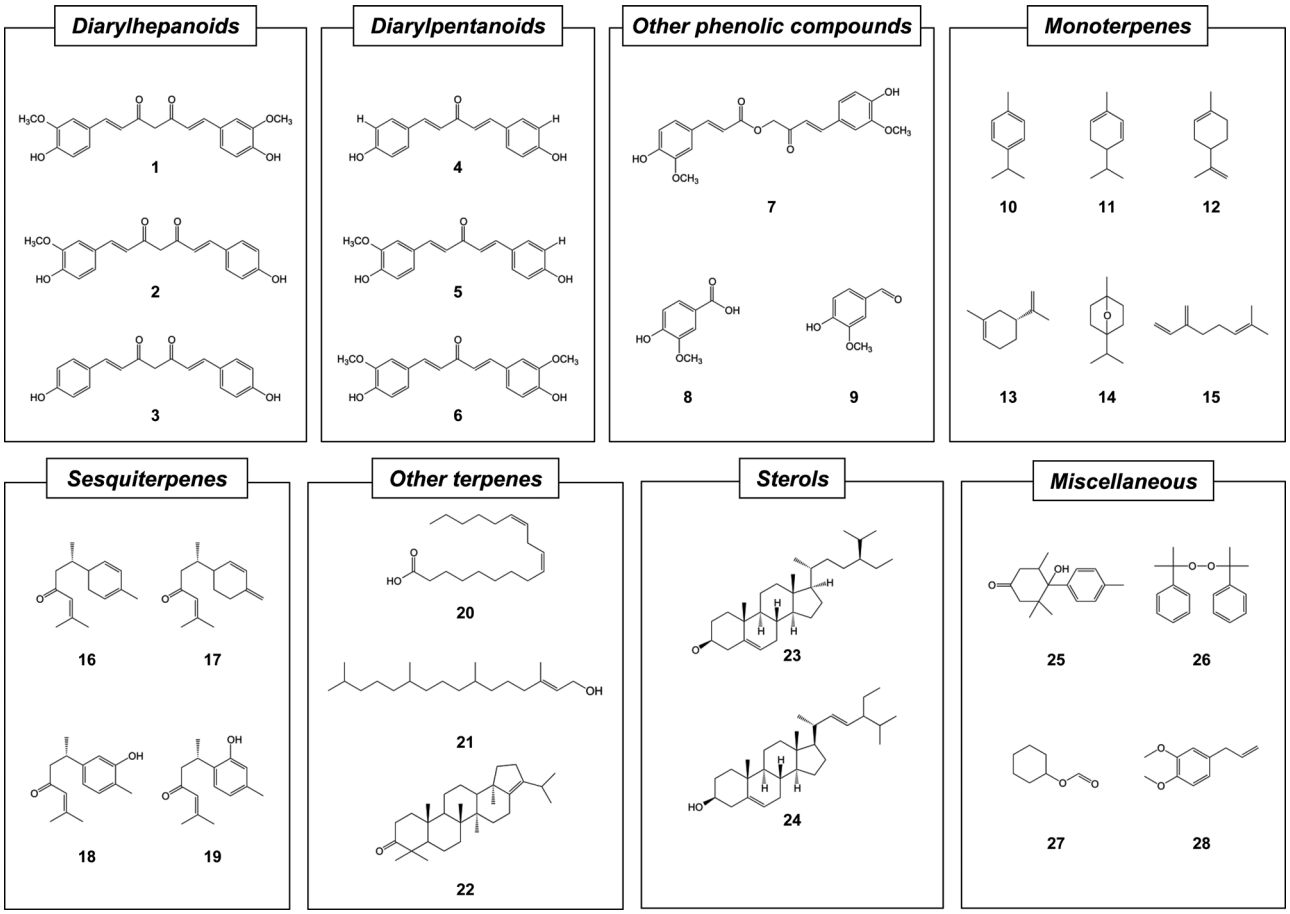

Figure 3. Molecular structure of common constituents of turmeric. (1) curcumin; (2) demethoxycurcumin; (3) bisdemethoxycurcumin; (4) 1,5-bis(4-hydroxyphenyl)-penta-(1*E*,4*E*)-1,4-dien-3-one; (5) 1-(4-hydroxy-3-methoxyphenyl)-5-(4-hydroxyphenyl)-1,4-pentadiene-3-one; (6) 1,5-bis(4-hydroxy-3-methoxyphenyl)-penta-(1*E*,4*E*)-1,4-dien-3-one; (7) calebin-A; (8) vanillic acid; (9) vanillin; (10) p-cymene; (11) β-phellandrene; (12) terpinolene; (13) p-cymen-8-ol; (14) cineole; (15) myrcene; (16) α-turmerone; (17) β-turmerone; (18) turmeronol A; (19) turmeronol B; (20) linoleic acid; (21) phytol; (22) hopenone I; (23) stigmasterol; (24) β-sitosterol; (25) curcuma-J; (26) dicumyl peroxide; (27) cyclohexylformate; (28) methyleugenol.

[40, 41]. In a hypercholesterolemic zebrafish model, turmeric extract exhibits hypolipidemic and antioxidant activities [42].

3.1.4 Antimutagenic activity

Turmeric has been shown to inhibit mutagenicity induced by chemical mutagens. One study investigated the protective effects of an aqueous turmeric extract as well as a curcumin-free turmeric extract against chemical-induced mutagenicity in bacterial strains. Both the aqueous extract and the curcumin-free extract exhibited antimutagenicity activities against bacteria [43]. In another study, turmeric as a component of one formulation had antimutagenic activity against various environmental mutagens such as sodium azide, 4-nitro-O-phenylenediamine, 2-acetamidofluorene, and benzo[a]pyrene in vitro [44]. In another in vitro study, the antimutagenic activity of turmeric was shown to be due to its ability to inhibit the formation of heterocyclic amines [45].

3.1.5 Growth inhibitory effects

Studies over the past several years have indicated the growth inhibitory effects of turmeric against numerous cancer cells. For instance, turmeric inhibited the growth of Chinese hamster ovary cells at a concentration of 0.4 mg/mL [46]. One study investigated the cytotoxic effects of turmeric force (TF), a supercritical and hydroethanolic extract of turmeric, alone and in combination with gemcitabine in two pancreatic carcinoma cell lines (BxPC3 and Panc-1) [19]. TF was highly cytotoxic to the BxPC3 and Panc-1 cell lines, with IC_{50} values of 1.0 and 1.22 μg/mL, respectively, and had cytotoxicity superior to that of curcumin. The combination of gemcitabine and TF was synergistic, with IC_{90} levels achieved in both

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Table 1. Biological activities of turmeric as shown in in vitro studies

Cell type	Dose, duration	Overall conclusion [Reference]
Anti-microbial		
H. pylori	6.25–50 μg/mL	Inhibited the bacterial growth [24]
Microorganisms	1.5% (v/v), 30 min	Retarded the microbial growth, delayed the chemical changes, and extended the shelf life of rainbow trout [25]
Bacteria	5%	Exhibited activity against histamine-producing bacteria [26]
Pathogen	0.004–2% (w/v), 24 h	Exhibited activity against food-borne pathogens [27, 28]
**E. coli* BL-21	50 mg/L, 24 h	Exhibited bactericidal activity [29]
HBV	200–500 mg/L, 9 d	Suppressed HBV replication in liver cells by enhancing the level of p53 protein [30]
Fungus	33 μg/mL	Exhibited activity against *Trichophyton longifusus* [32]
Fungus	1–1.5% (v/v), 21 d	Inhibited *Aspergillus flavus* growth and aflatoxin production [33]
Insecticidal and larvicidal		
Insect	18–24 μg/mg insect, 7 d	Exhibited activity against *Sitophilus zeamais* and *Tribolium castaneum* [34]
Larvae	115.6 ppm	Exhibited activity against the dengue vector *Aedes aegypti* [35]
Larvae	0.1–0.5%, 24–72 h	Exhibited activity against *Anopheles stephensi* and *Culex quinquefasciatus* mosquito larvae [36]
Spider mites	5–25 g/L	Exhibited toxicity against red spider mites [37]
Anti-oxidant		
In vitro assay	–	Ethanol extracts exhibited high anti-oxidant activities compared with aqueous extracts [38]
Renal cells	100 μg/mL, 3 h	Protected renal cells against oxidative stress induced by H_2O_2 [39]
In vitro assay	–	Exhibited anti-oxidant activity in in vitro assays [40, 41]
Zebrafish	10 μg/mL	Suppressed the incidence of atherosclerosis, exhibited hypolipidemic and anti-oxidant activities [42]
Anti-mutagenic		
S. typhimurium	25–200 μg /plate	Exhibited anti-mutagenicity against chemical-induced mutagenesis in bacteria [43]
S. typhimurium	2 mg/plate	Exhibited anti-mutagenicity to sodium azide, NPD, 2-AAF, and benzo[a]pyrene in vitro [44]
In vitro assay	0.2%	Reduced the formation of heterocyclic amines in vitro [45]
S. typhimurium	1–50 μg/plate	Exhibited anti-mutagenicity against IQ and 4-NQO mutagens [127]
Growth inhibitory effects		
CHO	0.4 mg/mL, 30 min	Inhibited the cell growth [46]
Pancreatic cancer cells	1–1.22 μg/mL, 72 h	Inhibited the growth and enhanced the gemcitabine effects in association with an inhibitory effect on NF-κB and STAT3 activities [19]
Colorectal, pancreatic, breast cancer cells	25 μg/mL, 24–48 h	Exhibited better potential than curcumin and inhibited the growth [18]
Leukemia cells	>50 μg/mL, 24 h	Exhibited cytotoxicity and inhibited production of LPS-induced TNF-α and PGE2 production [47]
Lymphoma cells	10 μg /mL, 48 h	Exhibited potent anti-growth activities [48]
Cancer cells	8.1–47.1 μg /mL, 48 h	Exhibited potent cytotoxic effects against cancer cells but exerted no damage on non-cancer cell line (MRC-5) [49]
Hepatocellular carcinoma	–	Inhibited proliferation and reduced PGE_2 release induced by oxidative stimulus [50]
Leukemia, lymphoma, myeloma cells	–	Down-regulated SIRT1 expression [51]
Colon cancer cells	50–500 μg /mL, 72 h	Induced apoptosis accompanied by caspase activation and G2/M cell cycle arrest [128]
Colon cancer cells	50 mg/mL, 72 h	Inhibited the expression of VEGF induced by As (III) [129]
Radioprotection		
Bacteria	20 μL/mL	Protected against gamma-radiation–induced inactivation of bacterial strains [52]
E. coli	–	Protected against X-ray–induced DNA damage [53]
Other activities		
Lymphocytes	–	Exhibited chemoprotective activity against benzo[a]pyrene-induced chromosomal damage [54]
HEK 293	10 μg/mL, 24 h	Recovered the cells from cisplatin-induced nephrotoxicity [55]
Keratinocyte cells	6.7 μg/mL, 48 h	Exhibited anti-psoriatic activity and down-regulated the expression of CSF-1, IL-8, NF-κB1, and NF-κB2 [56]

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Table 1. Continued

Cell type	Dose, duration	Overall conclusion [Reference]
Pancreatic tissue	–	Stimulated insulin secretion under basal and hyperglycemic conditions [57]
In vitro assay	0.16 μg/mL	Inhibited human pancreatic amylase activity [58]
PBMCs	100–800 μg/mL, 72 h	Exhibited immuno-stimulatory activity in human PBMCs [59]
In vitro assay	5 μg/mL	Inhibited Aβ fibril aggregation in a cell-free assay [130]

2-AAF, 2-Acetamidofluorene; Aβ, beta amyloid; CHO, Chinese hamster ovary; CSF, colony stimulating factor; *E. coli, Escherichia coli*; HBV, hepatitis B virus; *H. pylori, Helicobacter pylori*; IC_{50}, the half maximal inhibitory concentration; IL, interleukin; IQ, 2-amino-3-methylimidazo (4,5-f) quinoline; LPS, lipopolysaccharide; NF-κB, nuclear factor kappa B; NPD, 4-nitro-O-phenylenediamine; 4-NQO, 4-nitroquinoline-N-oxide; PGE_2, prostaglandin E_2; STAT3, signal transducer and activator of transcription 3; *S. typhimurium; Salmonella typhimurium*; TNF, tumor necrosis factor; TPA, 12-*O*-tetradecanoylphorbol-13-acetate; VEGF, vascular endothelial growth factor.
*studies with nano-particles.

pancreatic cancer cell lines at lower concentrations than for either agent alone. The synergistic effect was associated with an increased inhibitory effect of the combination on nucler factor-kappaB (NF-κB) and signal transducers and activators of transcription 3 (STAT3) activities as compared with single agent [19]. That TF has better potential than curcumin in inhibiting the growth of numerous types of cancer cells was recently reported by us [18]. In another study, organic extracts of turmeric exhibited cytotoxicity and inhibited production of lipopolysaccharide induced tumor necrosis factor-α (TNF-α) and prostaglandin E_2 (PGE_2) in human leukemia cells [47]. Turmeric inhibits promotion of lymphoma cells induced by 12-*O*-tetradecanoylphorbol-13-acetate (TPA) [48]. Another study evaluated the crude methanol and fractionated extracts (hexane and ethyl acetate) of turmeric for their cytotoxic potential against breast, nasopharyngeal, lung, cervical, and colon cancer cells and one noncancer human fibroblast cell line (MRC-5) [49]. The extract exhibited potent cytotoxic effects against cancer cells but caused no damage in MRC-5 [49]. In another study, turmeric inhibited the proliferation of human hepatocellular carcinoma cells that correlated with a reduction in PGE_2 production [50]. SIRT1, a protein involved in longevity and diverse metabolic diseases including cancer, was shown to be down-regulated by turmeric extract in numerous cancer types including leukemia, lymphoma, and myeloma [51]. Some of the other cancer types in which turmeric has shown antigrowth activities are listed in Table 1.

3.1.6 Radioprotector

In a few cases, turmeric offers protection against damage induced by radiation. For instance, one study investigated the effect of an aqueous extract of turmeric on the sensitivity of *E. coli*, *Bacillus megaterium*, and *B. pumilus* spores to gamma radiation [52]. The extracts offered protection to these organisms against inactivation by gamma radiation. The spice was also found to reduce the degradation of plasmid pUC18 DNA induced by radiation [52]. In another study, turmeric protected against X-ray-induced DNA damage of *E. coli* cells [53].

3.1.7 Other activities

In addition to the activities discussed above, turmeric exhibits numerous other activities by in vitro studies. For instance, in one study turmeric exhibited chemoprotective activity against benzo[a]pyrene-induced chromosomal damage in human lymphocytes [54]. In another study, cisplatin-induced nephrotoxicity in HEK 293 cells was recovered by turmeric treatment [55]. Psoriasis is a chronic inflammatory skin disorder characterized by rapid proliferation of keratinocytes and incomplete keratinization. The ethanolic extract from turmeric was shown to possess antipsoriatic activity in a keratinocyte cell line [56]. At the molecular level, the extract decreased the expression of colony stimulating factor (CSF)-1, interleukin (IL)-8, NF-κB1, and NF-κB2. The authors of this study suggested that turmeric might exert antipsoriatic activity by controlling the expression of NF-κB signaling biomarkers [56]. Within in vitro tissue culture conditions, turmeric possesses insulin-releasing actions [57]. Turmeric also inhibits human pancreatic amylase activity [58] and exhibits immune-stimulatory activities in human peripheral blood mononuclear cells [59].

3.2 Animal-based studies

3.2.1 Anti-inflammatory activity

Inflammation, in particular chronic inflammation, has been associated with numerous human chronic diseases, including cardiovascular, pulmonary, autoimmune, and degenerative diseases, cancer, and diabetes [60]. Research over the past several years using animal models has indicated that turmeric can act as an anti-inflammatory agent by modulating the expression of inflammatory molecules. For instance, turmeric was shown to possess anti-inflammatory activity during both N-nitrosodimethylamine administration and *Opisthorchis viverrini* infection in hamsters [61]. Turmeric exhibited its activity by reducing the aggregation of inflammatory cells surrounding the hepatic bile ducts, which correlated with a decrease in serum alanine transaminase level [61]. Acute pancreatitis is one of the more prominent

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inflammatory diseases and is characterized by interstitial edema, vacuolization, inflammation, and acinar cell necrosis [62–65]. One study evaluated the effects of *C. longa* against cerulein-induced acute pancreatitis and pancreatitis-associated lung injury in mice [66]. The oral administration of *C. longa* significantly ameliorated the severity of pancreatitis and pancreatitis-associated lung injury, as shown by a reduction in pancreatic edema, neutrophil infiltration, vacuolization, necrosis, serum amylase, lipase and cytokine levels, reduced mRNA expression of multiple inflammatory mediators such as IL-1β and IL-6 and TNF-α, and an induction in heme oxygenase (HO)-1 expression [66]. Turmeric also possesses anti-inflammatory activities against dimethylbenzene-induced ear vasodilation in mice, as well as the carrageenan-induced paw edema in a rat model [67]. In a rat model, turmeric exhibited protective effects against D-galactosamine-induced hepatitis in rats [68].

3.2.2 Anticancer activity

Turmeric has been most widely investigated for its anticancer activity. The most common cancer types in which turmeric has shown potential are those of the liver, breast, mouth, and stomach (Table 2). In a mouse model of hepatocellular carcinoma, lyophilized turmeric was shown to possess beneficial effects on the early and late stages of liver pathogenesis, and it prevented and delayed liver carcinogenesis [69]. In another mouse model, dietary turmeric significantly inhibited the tumor burden and tumor incidence induced by benzo[a]pyrene in the forestomach [70]. One study concluded that curcumin-free turmeric extract has the potential to reduce the incidence and multiplicity of forestomach tumors induced by benzo[a]pyrene in female Swiss mice [43]. Deshpande et al. also showed that turmeric has potential in reducing benzo[a]pyrene-induced forestomach papillomas in mice [16].

The anticancer activity of turmeric has been shown in rat models as well. One study investigated the modulatory effects of turmeric on nitrosodiethylamine (NDEA)-induced hepatocarcinogenesis in rats [71]. Female wistar rats were administered NDEA (200 ppm) through drinking water (5 days per week) for 4 weeks. Control and NDEA-treated rats received 0.2–5% turmeric diets before (2 weeks), during (4 weeks), and after NDEA exposure (10 weeks). NDEA-treated rats receiving 1 or 5% turmeric before, during, and after carcinogen exposure showed a significant decrease in the number of gamma glutamyl transpeptidase (GGT)-positive foci and in the incidence of NDEA-induced focal dysplasia and hepatocellular carcinomas. These studies suggested that turmeric has chemopreventive activities against NDEA-induced hepatocarcinogenesis in rats [71]. Some other studies using rat models have also shown the potential of turmeric against liver carcinogenesis [72, 73]. Another study investigated the modulating effects of turmeric and curcumin-free aqueous turmeric extract on the initiation or postinitiation phases of DMBA-induced mammary tumorigenesis in female Sprague-Dawley rats [17]. Dietary administration of turmeric (0.05–1%) 2 weeks before and 2 weeks after the DMBA treatment was associated with a significant suppression of DMBA-induced mammary tumorigenesis, as shown by a reduction in tumor multiplicity, tumor burden, and tumor incidence. However, simultaneous administration of the curcumin-free aqueous turmeric extract as the sole source of drinking water during the initiation phase did not suppress DMBA-induced mammary tumorigenesis [17].

Turmeric also exhibits activity against oral carcinogenesis in a hamster model [74]. The mechanism of turmeric-mediated chemoprevention in DMBA-induced hamster buccal pouch carcinogenesis at 2, 4, 6, 10, and 12 weeks was investigated. Dietary turmeric (1%) led to a decrease in DMBA-induced tumor burden and multiplicity and enhanced the latency period in parallel with its modulatory effects on oncogene products and various cellular responses during hamster buccal pouch tumorigenesis. DMBA-induced expressions of the ras oncogene product p21 and its downstream target, the mitogen-activated protein kinases, were significantly decreased by turmeric during hamster buccal pouch carcinogenesis. Turmeric also diminished the DMBA-induced mRNA expression of proto-oncogenes (c-jun, c-fos) and NF-κB [74]. The tumor retardation effects of turmeric against DMBA-induced buccal pouch tumors in Syrian golden hamsters has also been investigated [75]. Turmeric (10%) was either applied locally as paint or administered in the diet (1%) along with local application (10%) three times a week for 14 weeks. Tumor number and tumor burden were significantly lower in the animals that received turmeric in the diet. The study demonstrated the chemopreventive potential of turmeric against oral precancerous lesions [75].

3.2.3 Activity against neurodegenerative diseases

The most common neurodegenerative diseases in which turmeric has shown potential are Parkinson's disease, Alzheimer's disease, and arthritis. Multiple pathways including oxidative stress and mitochondrial damage have been implicated in neurodegeneration during Parkinson's disease. One study evaluated the neuroprotective property of turmeric against 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-mediated neurodegeneration in a mouse model [76] and found that chronic dietary consumption of turmeric protected the mouse brain against neurotoxic insults induced by MPTP [76]. Beta amyloid (Aβ) aggregation and tau phosphorylation are characteristic features of Alzheimer's disease. In a transgenic mouse model overexpressing Aβ protein, administration of HSS-888 (5 mg/day for 6 months), a standardized turmeric extract, significantly reduced Aβ aggregation, tau phosphorylation, and plaque burden [77].

Arthritis is a chronic inflammatory and destructive joint disease that affects 1% of the adult population worldwide [78, 79]. In a rat model in which arthritis was induced by collagen treatment, oral administration of turmeric extract (30, 60,

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Table 2. Biological activities of turmeric as shown in in vivo studies

Animal model	Dose, duration	Overall conclusion [Reference]
Anti-inflammatory		
Hamster	~0.25% cur, 1–2 months	Reduced the aggregation of inflammatory cells that was correlated with a decrease in sALT level [61]
Mouse	0.05–1 g/kg, 7 d	Ameliorated cerulein-induced acute pancreatitis and pancreatitis-associated lung injury [66]
Mouse	85–340 mg/kg, 7 d	Decreased DMB-induced ear vasodilatation, inhibited carrageenan-induced paw edema [67]*
Rat	1%, 15 d	Exhibited protective effects against D-galactosamine–induced hepatitis [68]
Rat	85–340 mg/kg, 7 d	Upregulated the level of IL-1β and reduced PGE_2 production [67]
Anti-cancer		
Mouse	50 mg/kg/d, 2–4 weeks	Exhibited beneficial effects on the early and late stages of liver pathogenesis, prevented and delayed liver carcinogenesis [69]
Mouse	–	Inhibited the tumor burden and tumor incidence induced by benzo[a]pyrene in forestomach [70]
Mouse	3 mg/d, 8 weeks	Reduced the incidence and multiplicity of forestomach tumors induced by benzo[a]pyrene [43]
Mouse	0.01–5%, 8 weeks	Inhibited benzo[a]pyrene-induced forestomach papillomas [16]
Mouse	100–200 mg/kg, 4 weeks	Suppressed melanoma growth and lung metastasis in association with a downregulation in the expression of MMPs [131]
Rat	0.2– 5% (w/w), 16 weeks	Exhibited chemopreventive activity against NDEA-induced hepatocarcinogenesis [71]
Rat	5%	Delayed the initiation of hepatocarcinogenesis induced by diethylnitrosamine [72]
Rat	0.05%, 20 weeks	Reduced the number of γ-glutamyl transpeptidase-positive foci (precursor of hepatocellular neoplasm) induced by aflatoxin B1 [73]
Rat	0.05–1%, 4 weeks	Exhibited activity against DMBA-induced mammary tumorigenesis [17]
Hamster	1%, 2–12 weeks	Exhibited chemopreventive activity against DMBA-induced HBP carcinogenesis [74]
Hamster	1–10%, 14 weeks	Lowered the tumor number and burden induced by DMBA in buccal pouch [75]
Hamster	2–5%	Inhibited the tumor burden and tumor incidence induced by MAMN [70]
Neurodegenerative diseases		
Mouse	1.65–3.3 g/kg, 3 months	Protected the brain against neurotoxic insults induced by MPTP in a PD model [76]
Mouse	5 mg/d, 6 months	Reduced the Aβ aggregation, tau phosphorylation, and plaque burden in an AD model [77]
Rat	110 mg/ml/kg, 4 weeks	Prevented the degenerative changes in the bones and joints of collagen-induced arthritic rats [80]
Rat	23–46 mg/kg, 2 weeks	Inhibited joint inflammation and periarticular joint destruction; prevented NF-κB activation and NF-κB-regulated genes including chemokines, COX-2, and RANKL [81]
Rat	56 mg /kg/d, 4 weeks	Inhibited joint swelling; however, increased the morbidity and mortality [132]
Rat	200 mg/kg, 4 weeks	Suppressed the incidence and severity of arthritis, modulated the production of inflammatory molecules, and activated anti-oxidant defense system [133]
Anti-depressant		
Mouse	25–100 mg/kg, 3 weeks	Attenuated swim stress-induced decreases in serotonin, 5-hydroxyindoleacetic acid, noradrenaline and dopamine, as well as increases in serotonin turnover [82]
Mouse	140–560 mg/kg, 2 weeks	Exhibited an inhibitory effect on MAO A activity in the brain [83]
Aging		
Mouse	0.6–2g/kg/d, 19 weeks	Exhibited anti-aging activity against UVB-induced skin changes that was likely mediated through inhibition of MMP2 expression [84]
Anti-diabetic		
Mouse	0.2–1 g/100 g diet, 4 weeks	Exhibited activity against type 2 diabetes [85]
Rat	200 mg/kg, 4 weeks	Alleviated hyperglycemia, dyslipidemia, atherogenic indices, and cellular toxicity in STZ-nicotinamide treated rats [86]
Rat	0.5%, 8 weeks	Prevented the development of cataracts in diabetic rats induced by STZ [87]

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Table 2. Continued.

Animal model	Dose, duration	Overall conclusion [Reference]
Rat	1 g/kg, 3 weeks	Reduced blood sugar, glycosylated hemoglobin, oxidative stress, and SDH activity in an alloxan-induced diabetes mellitus model [88]
Rat	0.5%, 8 weeks	Inhibited diabetes-induced oxidative stress without effecting hyperglycemic status [134]
Wound healing		
Rat	1% (w/w), 1 week	Accelerated normal and impaired diabetic wound healing [89]
Rabbit	15% (w/w), 2 weeks	Accelerated healing of experimentally created circular wounds [90]
Protection from chemical insults		
Mouse	1 g/kg, 5 d	Exhibited potential against DMBA-induced genotoxicity and oxidative stress [91]
Mouse	1–5%, 8 weeks	Exhibited protection against liver oxidative damage and genotoxicity induced by lead acetate [92]
Mouse	50 mg/kg	Recovered the weight loss, abrogated the elevations of serum urea, glucose, triglyceride level, and AAT activity, and prevented the perturbation of sBCHE activity induced by sodium arsenite [93]
Rat	5%, 2 weeks	Exhibited protection against CCl_4-induced liver damage [95]
Rat	100 mg/kg, 2 weeks	Exhibited protection against CCl_4-induced hepatotoxicity in association with an increase in the activities of anti-oxidants, phase II detoxification enzymes, and Nrf2 [96]
Rat	200 mg/kg, 30 d	Suppressed cardiac, hepatic, and renal toxicities induced by doxorubicin [97]
Atherosclerosis		
Rabbit	–	Decreased the susceptibility of liver microsomes and mitochondria to lipid peroxidation [100]
Rabbit	1.66–3.2 mg/kg, 7 weeks	Inhibited LDL oxidation and exhibited hypocholesterolemic effects [101]
Rabbit	1.66 mg/kg, 1 month	Inhibited erythrocyte and liver microsome membrane oxidation [102]
Other activities		
Rat	10–50 mg/kg, 2 months	Enhanced the learning ability and spatial memory, and modulated the central serotoninergic system activity [103]
Rat	500 mg/kg, 3 d	Exhibited protection against intravascular thrombosis [104]
Rat	100–300 mg/kg, 4 weeks	Decreased total plasma cholesterol and LDL cholesterol, and increased HDL cholesterol in rats fed a high-cholesterol diet [105]
Ovine	6.7–20 μg/mL, 22 h	Enhance apoptosis in neutrophils by downregulating cell survival proteins; upregulated IL-8 production, and reduced the risk of infections caused by impaired neutrophil functions [106]

AAT, alanine aminotransferase; Aβ, beta amyloid; AD, Alzheimer's disease; sALT, serum alanine transaminase; sBCHE, serum butyryl cholinesterase; CCl_4, carbon tetrachloride; COX-2, cyclooxygenase-2; Cur, curcumin; DMB, dimethylbenzene; DMBA, 7,12-dimethylbenz(a)anthracene; HBP, hamsterbuccalpouch; HDL, high-density lipoprotein; IL, interleukin; LDL, low-density lipoprotein; MAMN, methyl-(acetoxymethyl)-nitrosamine; MAO A, monoamine oxidase A; MMP, matrix metalloproteinase;
MPTP, 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine; NDEA, nitrosodiethylamine; NF-κB, nuclear factor kappa-B; Nrf2, NF-E2-related factor 2; PD, parkinson's disease; PGE_2, prostaglandin E_2; RANKL, receptor activator of nuclear factor kappa-B ligand. SDH, sorbitol dehydrogenase; STZ, streptozotocin; UVB, ultraviolet B.
* given in combination.

and 110 mg/mL/kg body weight) was shown to arrest the degenerative changes in the bones and joints of the rats [80]. The antiarthritic efficacy and mechanism of action of turmeric using a rat model of rheumatoid arthritis were determined in one study [81]. Turmeric extract was administered intraperitoneally to female Lewis rats prior to or after the onset of streptococcal cell wall-induced arthritis. The extract profoundly inhibited joint inflammation and periarticular joint destruction in a dose-dependent manner. The extract also prevented local activation of NF-κB and the expression of NF-κB-regulated genes including chemokines, cyclooxygenase-2, and receptor activator of nuclear factor kappa-B ligand (RANKL). Consistent with these findings, inflammatory cell influx, PGE_2 levels, and periarticular osteoclast formation were also inhibited by turmeric treatment [81].

3.2.4 Antidepressant activity

Depression is a mental disorder that affects a person's mood, thoughts, feelings, behavior, and overall health. The major disadvantage of currently available antidepressants is a plethora of associated side effects; hence novel approaches are being tried to find more efficacious and safer

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treatments. One study was undertaken to determine the behavioral, neurochemical, and neuroendocrine effects of ethanolic extract from *C. longa* using the forced swimming test in male mice [82]. The extract reduced the duration of immobility of mice when it was orally administered for 21 days. The extract markedly attenuated swim stress-induced decreases in serotonin, 5-hydroxy indoleacetic acid, noradrenaline, and dopamine concentrations. The extract also significantly reversed the swim stress-induced increases in serum corticotropin-releasing factor and cortisol levels. The authors of this study concluded that the antidepressant activities of the *C. longa* extract are mediated through regulations of the neurochemical and neuroendocrine systems [82]. In another study, the antidepressant activity of *C. longa* was mediated in part through monoamine oxidase A inhibition in the mouse brain [83].

3.2.5 Antiaging activity

The most common symptoms of aging skin are changes in skin thickness, elasticity, pigmentation, and wrinkling. One study examined the potential of turmeric as an antiaging agent against long-term, low-dose ultraviolet B (UVB) irradiation in melanin-possessing hairless mice [84]. The extract (at 300 or 1000 mg/kg, twice daily) prevented an increase in skin thickness and a reduction in skin elasticity induced by chronic UVB exposure. The extract also prevented the formation of wrinkles and melanin as well as increases in the diameter and length of skin blood vessels and in the expression of matrix metalloproteinase (MMP)-2. Inhibition in MMP-2 expression by turmeric was proposed to contribute to the prevention of UVB-induced skin aging in mice [84].

3.2.6 Antidiabetic activity

Turmeric has shown potential against diabetes in numerous animal models. For instance, in a genetically modified diabetic mouse model (KK-Ay), turmeric showed promise for the prevention and/or amelioration of type 2 diabetes [85]. Another study examined the modulatory effects of turmeric against diabetes and oxidative stress induced by streptozotocin (STZ) and nicotinamide in rats [86]. Diabetic rats orally received either distilled water (as vehicle) or 200 mg/kg body weight of turmeric rhizome powder suspension. Turmeric significantly alleviated (80–97%) the signs of diabetes (hyperglycemia and dyslipidemia) and elevations in atherogenic indices and cellular toxicity in STZ-nicotinamide-induced diabetic rats by increasing the production of insulin, enhancing the antioxidant defense system, and decreasing lipid peroxidation [86]. Turmeric (at 0.5% in the diet for 8 weeks) was also effective against the development of cataracts in diabetic rats [87]. Another study evaluated the efficacy of turmeric against alloxan-induced diabetes mellitus in a rat model [88]. Administration of turmeric to these diabetic rats was associated with a reduction in blood sugar and glycosylated hemoglobin levels. Turmeric supplementation also reduced the levels of oxidative stress in the rats. The activity of sorbitol dehydrogenase, which catalyzes the conversion of sorbitol to fructose, was also lowered significantly upon treatment with turmeric. The study revealed the effectiveness of turmeric in attenuating diabetes mellitus-related changes in this rat model [88].

3.2.7 Wound healing

Turmeric as a component of a polyherbal preparation has been shown to increase the cellular proliferation and collagen synthesis at wound sites in normal rats [89]. The turmeric formulation also increased the DNA, total protein, hydroxyproline, and hexosamine contents at the wound site [89]. The efficacy of a fresh turmeric paste to heal wounds has also been demonstrated in a rabbit model [90].

3.2.8 Protection from chemical insults

Turmeric has been shown to protect the normal cells, tissues, and organs against the damage caused by external insults. For instance, the spice exhibited effectiveness against DMBA-induced genotoxicity and oxidative stress in mice [91]. Turmeric has also been shown to protect against liver oxidative damage and genotoxicity induced by lead acetate in mice [92] and to reduce arsenic toxicity in mice [93].

Fluoride is toxic to neuronal development, and its excessive intake during pregnancy can cause adverse effects on neonatal development. One study demonstrated the efficacy of *C. longa* against fluoride toxicity in rat pups [94]. Turmeric also showed protective effects against carbon tetrachloride-induced liver damage in rats, as indicated by decreased serum concentrations of bilirubin, cholesterol, aspartate amino transferase, alanine amino transferase, and alkaline phosphatase [95]. In another study, the protective effects of turmeric against carbon tetrachloride-induced hepatotoxicity in rats were associated with an increase in the activities of antioxidants and phase II detoxifying enzymes and occurred through the activation of NF-E2-related factor 2 (Nrf2) [96]. Turmeric has also been shown to suppress the cardiac, hepatic, and renal toxicities induced by doxorubicin in a rat model [97].

3.2.9 Antiatherosclerotic activity

Atherosclerosis is characterized by oxidative damage that affects lipoproteins, the walls of blood vessels, and subcellular membranes. The oxidation of LDL also plays an important role in the development of atherosclerosis [98, 99]. In one study, *C. longa* extract decreased the susceptibility of liver microsomes and mitochondria to lipid peroxidation in atherosclerotic rabbits [100]. In another study, oral administration of a turmeric extract inhibited LDL oxidation and had hypocholesterolemic effects in atherosclerotic rabbits [101].

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Oral administration of turmeric extract has also been shown to inhibit erythrocyte and liver microsome membrane oxidation in rabbits fed an atherogenic diet [102].

3.2.10 Other activities

In addition to the activities indicated above, turmeric acts as a memory enhancer [103]. This spice can also act as an antiplatelet agent [104]. Whether turmeric has the potential to improve hepatic conditions was investigated in one study using a rat model [105]. Turmeric supplementation in rats fed a high-cholesterol diet was associated with decreases in total plasma cholesterol and LDL cholesterol and an increase in HDL cholesterol. Several other variables associated with hypercholesterolemia were improved by turmeric supplementation [105]. Turmeric reduces the risk of infections caused by impaired neutrophil functions in an ovine model [106].

4 Human studies

Turmeric has been tested in human subjects, with about a dozen trials completed to date. Most of these studies have indicated the safety and efficacy of turmeric. The most promising effects of turmeric have been observed against inflammatory conditions, cancer, diabetes, IBS, acne, and fibrosis (Table 3). Although turmeric has shown therapeutic efficacy against many human ailments, one of the major problems with turmeric is the poor bioavailability of its constituents. The poor bioavailability of curcumin, the major constituent of turmeric appears to be primarily due to poor absorption, rapid metabolism, and rapid systemic elimination [107]. One study demonstrated that *Curcuma* extract can be administered safely to patients with colorectal cancer at doses of up to 2.2 g daily, equivalent to 180 mg of curcumin [108]. However, curcumin was found to have low oral bioavailability due to intestinal metabolism. Numerous efforts are being pursued to improve curcumin's bioavailability. Adjuvants that can block the metabolic pathway of curcumin have been most extensively used to increase the bioavailability of this polyphenol [109]. Other promising approaches to increase the bioavailability of curcumin include use of nanoparticles [110], liposomes [111], micelles [112], phospholipid complexes [113], and structural analogues [114, 115].

One study conducted in India, compared the effects of experimental local-drug delivery system containing 2% whole turmeric (gel form) as an adjunct to scaling and root planing (SRP) with the effects observed using SRP alone [116]. Thirty patients with chronic localized or generalized periodontitis with pocket depth of 5–7 mm were selected for the study. Control sites received SRP alone, while experimental sites received SRP plus 2% whole turmeric gel for 7 days. Both groups demonstrated statistically significant reductions in the biomarkers of periodontitis. However, a greater reduction was seen in the parameters in the experimental group in comparison to the control group. The authors of this study concluded that whole turmeric gel can be effectively used as an adjunct to SRP and that whole turmeric is more effective than SRP alone in the treatment of periodontitis [116]. However, a long-term study comprising larger number of subjects are needed to further confirm the efficacy of whole turmeric.

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. A randomized and placebo-controlled study investigated the effects of oral turmeric supplementation on 24 patients with relapsing or refractory biopsy-proven lupus nephritis [117]. Each patient in the trial group received one capsule containing 500 mg of turmeric with each meal for 3 months; control patients received capsules containing starch that were identical in color and size to the turmeric capsules. A significant decrease in proteinuria was observed in the trial group compared with the control group. Also, systolic blood pressure and hematuria were significantly lower in the trial group after turmeric supplementation. The authors of this study concluded that 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 an safe adjuvant therapy for such patients [117]. However, long-term trials with larger number of patients are needed to further clarify these effects of turmeric.

Turmeric has also exhibited anticancer activity in human subjects. Increased levels of nitric oxide (NO) have been reported in different leukemia, including chronic myeloid leukemia (CML). One study evaluated the effects of turmeric powder in reducing NO levels in 50 CML patients [118]. The CML patients were divided randomly into two groups of 25 patients each. In group 1, patients were given imatinib (400 mg twice a day), while in group 2, patients were given imatinib (400 mg twice a day) along with turmeric powder (5 g three times/day dissolved in 150 mL of milk) for 6 weeks. Nitric oxide levels were estimated in these patients before and after receiving therapy. Nitric oxide levels were found to be significantly decreased in both the groups, although the decrease was more prominent in group 2. These results suggest that turmeric powder can act as an adjuvant to imatinib in decreasing the NO levels and may be useful in the treatment of CML [118]. However, large-scale study is required to further confirm the efficacy of turmeric in CML patients. The ethanol extract of turmeric was found to produce remarkable symptomatic relief in patients with external cancerous lesions in another study [119]. Although the effects of turmeric continued for several months, adverse reaction was noted in only one of the 62 patients evaluated [119]. One study evaluated the effects of turmeric in patients with peptic ulcers [120]. Forty-five patients (24 men and 21 women, between 16 and 60 years of age) were included in the study. Of these, 25 patients (18 men and 7 women) underwent endoscopy for their ulcers located in the duodenal bulb and gastric. Turmeric-filled capsules (300 mg each) were given orally at a dose of two capsules five times daily, one half to an hour before meals.

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Table 3. Biological activities of turmeric as shown in human studies

Type	No. of patients	Dose, duration	Overall conclusion [Reference]
Anti-inflammation			
Efficacy	30	2%, 7 days	Reduced the inflammation in patients with chronic localized or generalized periodontitis [116]
Lupus nephritis			
Randomized, placebo-controlled	24	500 mg/day, 3 months	Decreased proteinuria, hematuria, and systolic blood pressure in patients with relapsing or refractory lupus nephritis [117]
Anticancer			
Efficacy	50	15 g/day, 6 weeks	Significantly reduced NO level in CML patients when given alone or in combination with imatinib [118]
Efficacy	62	–	Produced remarkable symptomatic relief in patients with external cancerous lesions [119]
Phase II	45	3 g/day, 4 weeks	Reduced the ulcer size in patients with peptic ulcer [120]
Antidiabetic			
Randomized, double-blind	40	1.5 g/day, 2 months	Attenuated proteinuria, TGF-β, and IL-8 in patients with overt type 2 diabetic nephropathy [121]
Crossover	14	6 g, 15–120 min	Increased postprandial serum insulin levels, insignificant effect on plasma glucose levels and the glycemic index [122]
Irritable bowel syndrome			
Randomized, partially blinded	500	72–144 mg/day, 8 weeks	Improved the symptoms of IBS and reduced the prevalence of disease [123]
Randomized, crossover	8	0.5 g	Increased the bowel motility and activated the hydrogen-producing bacterial flora in the colon [124]
Antimutagenic			
Efficacy	16	1.5 g/day, 30 day	Significantly reduced the urinary excretion of mutagens in smokers [125]
Protection from fibrosis			
Efficacy	58	3 g/day, 3 months	Offered protection against benzo[a]pyrene-induced increases in micronuclei in circulating lymphocytes of healthy subjects; decreased the number of micronucleated cells in patients with submucous fibrosis [126]

CML, chronic myelogenous leukemia; IBS, irritable bowel syndrome; IL-8, interleukin-8; NO, nitric oxide; TGF, transforming growth factor.

The result after 4 weeks of treatment showed that ulcers were absent in 12 patients (48%). Eighteen patients had no ulcers after 8 weeks of treatment and 19 did not have ulcers after 12 weeks of treatment. The remaining 20 cases were not found to have ulcers and some did not undergo endoscopy. These 20 persons appeared to have erosions, gastritis, and dyspepsia, and turmeric capsules were given to these persons for 4 weeks. The abdominal pain and discomfort satisfactorily subsided in the first and second weeks. The study concluded that turmeric has the capacity to heal peptic ulcers [120]. However, further studies with larger number of patients are required to confirm the claims of the study.

End-stage renal disease due to type 2 diabetic nephropathy is a very common condition that is associated with high global levels of mortality and morbidity. Both proteinuria and transforming growth factor (TGF)-β may contribute to the development of end-stage renal disease in patients with diabetic nephropathy. One study investigated the effects of turmeric on serum and urinary TGF-β, IL-8, and TNF-α, as well as proteinuria, in patients with overt type 2 diabetic nephropathy [121]. The study consisted of 40 patients with overt type 2 diabetic nephropathy that were randomly assigned to either the trial group ($n = 20$) or the control group ($n = 20$). Each patient in the trial group received one capsule (containing 500 mg of turmeric, three times a day) with each meal for 2 months; the control group received placebo capsules containing starch for the same 2 months. Serum concentrations of TGF-β and IL-8 and urinary protein excretion and IL-8

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decreased significantly compared with the presupplementation values. No adverse effects related to turmeric supplementation were observed during the trial. The authors of this study concluded that short-term turmeric supplementation can attenuate proteinuria, TGF-β, and IL-8 in patients with overt type 2 diabetic nephropathy and can be administered as a safe adjuvant therapy for these patients [121]. However, long-term trials with larger number of patients are needed to clarify the effects of turmeric on renal function. Another study examined the effects of *C. longa* on postprandial plasma glucose and insulin levels and the glycemic index in healthy subjects [122]. Fourteen healthy subjects were assessed in a crossover trial. The study found that the ingestion of *C. longa* increased postprandial serum insulin levels but had no effect on plasma glucose levels or the glycemic index in these healthy subjects. The study concluded that *C. longa* might have an effect on insulin secretion [122].

A partially blinded, randomized, two-dose, pilot study assessed the effects of turmeric extract on symptoms of IBS [123]. Five hundred volunteers participated in the study. The volunteers were given one (72 mg) or two tablets (144 mg) of a standardized turmeric extract daily for 8 weeks. IBS prevalence decreased significantly in both the one- and two-tablet groups, and approximately two-thirds of all subjects reported an improvement in symptoms after treatment. The study concluded that turmeric might help reduce the symptoms of IBS [123]. However, placebo-controlled trials are warranted to confirm these findings. Another study conducted with eight healthy subjects reported that turmeric has the potential to increase bowel motility and to activate hydrogen-producing bacterial flora in the colon [124].

One study assessed the antimutagenic effects of turmeric in 16 chronic smokers [125]. Turmeric, given in doses of 1.5 g/day for 30 days, significantly reduced the urinary excretion of mutagens in smokers. In contrast, in six nonsmokers who served as control, there was no change in the urinary excretion of mutagens after 30 days. Turmeric had no significant effect on serum aspartate amino transferase and alanine amino transferase, blood glucose, creatinine, or the lipid profile. These results indicated that dietary turmeric is an effective antimutagen and that it may be useful in chemoprevention [125]. However, randomized placebo-controlled studies are required to confirm these findings. Turmeric extract also offers protection against benzo[a]pyrene-induced increases in micronuclei in circulating lymphocytes of healthy subjects [126]. In patients with submucous fibrosis, turmeric extract decreased the number of micronucleated cells both in exfoliated oral mucosal cells and in circulating lymphocytes [126].

In addition to the studies discussed in the above sections, numerous ongoing trials are evaluating the efficacy of turmeric in humans (http://www.clinicaltrials.gov). For instance, a phase II clinical trial from France was aimed to determine the efficacy and the tolerance on 15 days of a turmeric extract (Arantal®) in patients with osteoarthritis of the Knee (Gonarthrosis). The purpose of another phase I study was to assess the safety of advancing doses of curcuminoids administered orally for 14 consecutive days in adults with cystic fibrosis homozygous for ΔF508 CFTR. Whether antioxidant spices including turmeric can reduce cardiovascular risks was investigated in another randomized controlled trial from USA. These studies are completed; however, results are yet to be published.

5 Conclusions

Turmeric is a golden spice derived from the rhizome of the plant *C. longa*. Turmeric has long been used as a spice, flavoring agent, and colorant. Traditionally, the spice has been used to treat numerous human ailments. Turmeric is a rich source of numerous biologically active constituents such as polyphenols, sesquiterpenes, diterpenes, triterpenoids, sterols, and alkaloids. Modern science has delineated the molecular basis for the pharmacological properties of turmeric against human diseases, and some clinical trials have unequivocally demonstrated the safety and efficacy of turmeric in human subjects. The absence of any significant toxicity associated with this spice has made it superior to other medications. The existing human studies, in addition to in vitro and in vivo animal studies, provide a logical basis for further investigation of this spice for the prevention and treatment of human diseases.

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