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REVIEW ARTICLE

Multiple health benefits of curcumin and its therapeutic potential

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Abstract
Turmeric, or *Curcuma longa* as it is formally named, is a multifunctional plant with numerous names. It was dubbed "the golden spice" and "Indian saffron" not only for its magnificent yellow color, but also for its culinary use. Turmeric has been utilized in traditional medicine since the dawn of mankind. Curcumin, demethoxycurcumin, and bisdemethoxycurcumin, which are all curcuminoids, make up turmeric. Although there have been significant advancements in cancer treatment, cancer death and incidence rates remain high. As a result, there is an increasing interest in discovering more effective and less hazardous cancer treatments. Curcumin is being researched for its anti-inflammatory, anti-cancer, anti-metabolic syndrome, neuroprotective, and antibacterial properties. Turmeric has long been used as a home remedy for coughs, sore throats, and other respiratory problems. As a result, turmeric and its compounds have the potential to be used in modern medicine to cure a variety of diseases. In this current review, we highlighted therapeutic potential of curcumin and its multiple health benefits on various diseases.

Keywords Neuroprotective activity · Antimicrobial properties · *Curcuma longa* · Therapeutic potential · Health benefits · Anti-cancer

Introduction

Turmeric has piqued the interest of the medical and scientific communities, as well as the culinary community. Turmeric (*Curcuma longa*) is a ginger-related perennial herbaceous rhizomatous plant (Karthika et al. 2021a, b; Priyadarsini 2014). However, turmeric is a spice popular in the Middle East and Asia for flavoring food and as a component of traditional medicines due to its health benefits. It has been discovered in nutraceuticals, beverages, and processed foods in recent years. Turmeric (Zingiberaceae family) is derived from the rhizome of *Curcuma longa L.* (Fig. 1). Curcumin, demethoxycurcumin, and bisdemethoxycurcumin are some of the bioactive components found in turmeric (Fig. 2), with curcumin being the most common. Curcumin, also known as diferuloylmethane, is a yellow pigment found in 60 to 70% of crude turmeric extracts and is the curcuminoid that has received the most investigation. Turmeric also includes fiber, proteins, resins, and volatile oils like turmerone, atlantone, and Zingiberene, all of which have potential pharmacological effects (Shep et al. 2019). A range of possible health

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Fig. 1 Rhizome of *Curcuma longa* L

advantages have been demonstrated in a preclinical study, including treatment for heart disease, arthritis, Alzheimer's disease, gastrointestinal problems, and the metabolic syndrome (Xu et al. 2018). Anti-cancer agents have been extracted from a variety of plants, including *Curcuma longa*, *Erythroxylum previllei*, *Cephalotaxus* species, *Betula alba*, *Catharanthus roseus*, and *Taxus brevifolia*, in addition to chemically synthesized anti-cancer drugs (M. Kabir et al. 2021). Curcumin has been shown to be effective in the treatment of a variety of chronic diseases, including neurodegenerative disorders, obesity, liver disease, metabolic syndrome, arthritis, inflammation, and cancers (El-Sayed et al. 2021; Sharma et al. 2021). Curcumin's antioxidant properties, as well as its anti-inflammatory properties, make it an effective chemosensitizer and chemotherapeutic agent for the treatment and management of colon cancer and other diseases (Karthika et al. 2021b). Curcumin can affect a wide range of cancer-fighting molecules, including transcription factors, which play a key role in growth factors, DNA replication, and cytokines, which play a key role in apoptotic protein and cell signaling (Bhattacharya et al. 2021c).

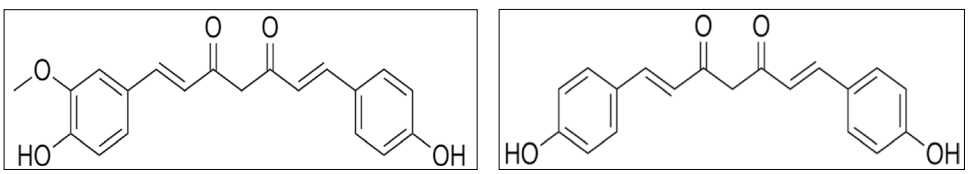
Asian countries have utilized *Curcuma longa* for centuries as a medical plant because of its anti-cancer properties (Allegra et al. 2017), antioxidant, anti-inflammatory (Wang et al. 2021), anti-mutogenic, and antibacterial qualities (Mahady et al. 2002; Roy et al. 2021b). Because curcumin is poorly soluble in water and has poor intestinal absorption, as well as fast metabolic breakdown in humans, its systemic distribution and bioavailability have been severely limited (Nelson et al. 2017). This is because black pepper contains piperine, a bioavailability booster, which increases curcumin absorption by 2000% (Gorgani et al. 2017; Sahu and Nema 2021). To achieve quantifiable concentrations of curcumin in the bloodstream, human volunteers were required to consume gram doses of curcumin powder (Dei Cas and Ghidoni 2019). In addition to capsules, pills, and ointments, there are energy drinks, soaps, and cosmetics that contain curcumin (Gupta et al. 2013). To name a few, curcumin can be added to micelles, micro-emulsion and liposomal lipid nanoparticles, and other lipid and biopolymer particles (Sanidad et al. 2019; Yao et al. 2014). They have also made turmeric essential oils encapsulated with curcuminoids and turmerone, which increases intestinal permeability (Purpura et al. 2018). These new formulations have been shown to improve oral bioavailability in human subjects (Purpura et al. 2018), and certain techniques have shown comparative efficacies (Asher et al. 2017; Purpura et al. 2018).

Curcumin, a polyphenol, targets a variety of signaling pathways and also has cellular action, indicating that it has many health benefits (Gupta et al. 2013). It has been shown to help in the management of inflammatory (Aggarwal et al. 2009), metabolic syndrome (Noce et al. 2021; Tagde et al. 2021c), pain (Paultre et al. 2021), and inflammatory and degenerative eye conditions (Allegri et al. 2010; Mazzolani and Togni 2013). This is in addition to the fact that it is beneficial to the kidneys (Trujillo et al. 2013). Curcumin is well recognized and utilized in a variety of ways around the world for its possible advantages to health. Curcumin-containing turmeric is used in curries in India, tea in Japan, cosmetics in Thailand, as a colorant in China, and drinks in Korea (Abd El-Hack et al. 2021).

In this current review, we highlighted therapeutic potential of curcumin and its multiple health benefits on various diseases.

Nutritional and chemical composition of *Curcumin longa*

Turmeric is a strong source of carbs and fiber, and it also contains some protein and fat, although it is devoid of cholesterol entirely. As a natural food product, it is believed to



Demethoxycurcumin Bisdemethoxycurcumin

Fig. 2 Structure of demethoxycurcumin, and bisdemethoxycurcumin

be nutrient-dense because of its high pyridoxine, vitamin C, and potassium content, as well as calcium, magnesium, and phosphorus content. Turmeric's nutritional profile is summarized in Table 1 (Pradeep et al. 1993). All the molecules that make up turmeric have a wide spectrum of bioactive properties. Turmeric has been implicated in roughly 326 biological processes in all (Anderson et al. 2000). Curcumin, bisdemethoxycurcumin, and demethoxycurcumin are the most investigated curcuminoid polyphenols.

Table 1 Nutritional profile of turmeric

Ingredients	Quantity (g) per 100 g
Water	6
Sodium	0.03
Riboflavin	0.00019
Protein	8.5
Potassium	0.2
Phosphorus	0.026
Niacin	0.0048
Iron	47.9
Fat	8.9
Carbohydrate	69.9
Calcium	0.2
Ash	6.8
Ascorbic acid	0.05

Multiple pharmacological properties of curcumin

Anti-cancer agent

Cancer is responsible for approximately one-fifth of all deaths worldwide (Karthika et al., 2021a, b; Rahman et al. 2021a, b; Mazumdar et al. 2016) . Oncologists are studying curcumin's anti-cancer properties alone or in combination with standard chemotherapeutics (Batra et al. 2019). Oncology researchers have been examining curcumin's anti-cancer properties for some time now, and they have seen significant improvements in cases of gastrointestinal, breast, and lung cancer (Shah et al. 2020; Hashem et al. 2021). Therefore, sulfone is found in curcumin aptamers, which inhibits tumor growth in the prostate, colon, lung, and pancreas in humans (Sahoo et al. 2021). Curcumin also inhibits carcinogenesis by altering tumor development and angiogenesis in in vitro and in vivo trials (Rubagotti et al. 2017). Curcumin's several mechanisms of action are depicted in Fig. 3. Apoptotic signals are generated through both intrinsic and extrinsic pathways. The intrinsic pathway has been discovered to suppress the expressions of B-cell lymphoma extra-large and B-cell lymphoma 2 (Bcl-2) by inducing the mitochondrial membrane (Karthika et al. 2021b; Tagde et al. 2021b). Colorectal cancer chemotherapy currently relies on the use of cytotoxic drugs like 5-fluorouracil, oxaliplatin, and irinotecan. When curcumin and 5-fluorouracil are given through the DNA mismatch repair mechanism, effective status is demonstrated

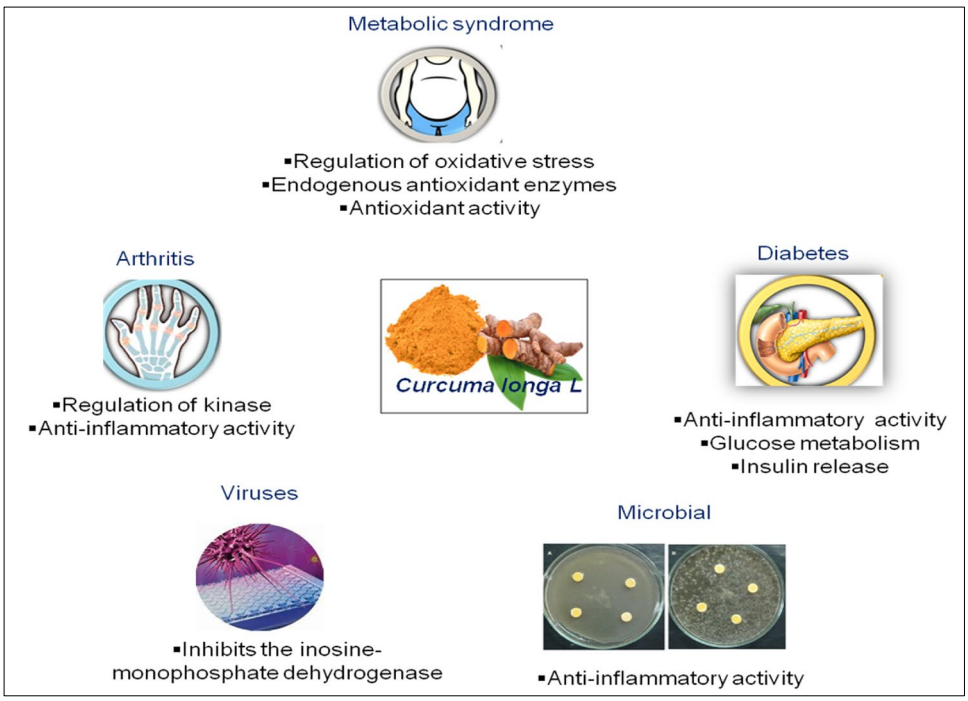


Fig. 3 Multiple mechanisms action of curcumin

(Karthika et al. 2021b; Sethy et al. 2021). However, curcumin has the ability to disrupt the mitochondrial membrane potential balance, which can lead to increased Bcl-xL suppression (Balasubramanian et al. 2007; Herrera-Calderon et al. 2020). After treatment with curcumin, it was confirmed that autophagy may play a role in programmed cell death type II and may effectively inhibit the growth of malignant glioma cells (Aoki et al. 2007). In vitro studies have shown that curcumin and its derivatives can effectively induce apoptosis in a variety of cell lines by downregulating or suppressing intracellular transcription factors (Adeola et al. 2021; Chopra et al. 2021a; Tagde et al. 2021d). Curcumin has been shown to induce apoptosis in colon cancer cells in vitro. Curcumin's ability to induce apoptosis in cancer cells while causing no toxicity in healthy cells is remarkable. Induction of p53, generation of reactive oxygen species, and activation of apoptotic proteins like BAX that can downregulate anti-apoptotic genes Bcl-2 and BclxL are all part of the proapoptotic mechanism (Bhattacharya et al. 2021b; Heo et al. 2018).

Curcumin was found to be well tolerated and safe in the clinical trials I and II. According to the clinical trial III report, they were able to tolerate a dose of 12 g/mg of curcumin without experiencing any side effects. The clinical trial report on the effect of curcumin in colorectal cancer is given in the Table 2.

Anti-inflammatory

Oxidative stress has been connected to a number of chronic diseases, and its pathogenic mechanisms are comparable to those of inflammation in the sense that one can readily cause the other (Shams ul Hassan et al. 2021). In reality, at the site of inflammation, inflammatory cells produce a range of reactive species, resulting in oxidative stress, establishing the relationship between inflammation and oxidative stress (Rahman et al. 2020; Rahman et al. 2021b). A number of reactive oxygen/nitrogen species can also activate an intracellular signaling cascade that increases the production of pro-inflammatory genes. A range of chronic diseases and syndromes have been associated with inflammation (Chopra et al. 2021b; Fatima et al. 2022; Goyal et al. 2022). Alzheimer's disease, Parkinson's disease, multiple sclerosis, epilepsy, brain injury, cardiovascular disease, metabolic syndrome, cancer, diabetes, obesity, depression, exhaustion, and acquired immune deficiency syndrome are all examples of these conditions (Fadriquela et al. 2021; Grewal et al. 2021; Hewlings & Kalman 2017; Karthika et al. 2022). Curcumin, as an anti-inflammatory drug, has the ability to inhibit NF-B activation (Darvesh et al. 2012; Kaur et al. 2021; Rong et al. 2021; Tagde et al. 2021a).

Curcumin, as a potential anti-inflammatory agent, has also been shown to reduce inflammation through a variety of other mechanisms that are beyond the scope of this review. Furthermore, it has been shown to inhibit pro-inflammatory cytokine release at the same level as dexamethasone (an FDA-approved drug for the treatment of sepsis) while having fewer side effects, whereas dexamethasone has been linked to adverse effects such as hypertension in the elderly and stunted growth in children when used for longer periods of time (Nahar et al. 2015). Nanocurmin has thus emerged as a viable drug for the treatment of inflammatory disease due to its ability to regulate inflammatory pathways.

Anti-oxidant activity

A important purpose for curcumin is to reduce oxidative damage (Chopra et al. 2021a; Hossain et al. 2020). There have been a few studies that show that antioxidants like superoxide dismutase (SOD) can boost serum activity (Bajgai et al. 2022; Kabir et al. 2022; Sahoo et al. 2021). Purified

Table 2 The results of a clinical trial involving curcumin and colorectal cancer

Type of study	Year	Subjects	Results	References
Absorbance of colorectal cancer	2013	26 patients, 2.35 g once a day for 14 days	Curcuminoids were discovered in 28 of the 35 colon biopsy samples	Irving et al. (2013)
General health of patients	2011	126 patients received a daily dose of 1.08 g of curcumin for 10–30 days	Colorectal cancer is improved	He et al. (2011)
Antioxidant properties are predicted using in vivo studies	2005	12 patients in the UK were given a daily dose of 450–1800 mg	DNA adducts were reduced	Garcea et al. (2005)
Report on a patient with sporadic polyposis	2017	54 polyps in a 57-year-old man. The research took 3.5 months to complete	During endoscopy surveillance, the number of polyps was reduced	Alfonso-Moreno et al. (2017)
Phase I safety study	2015	A single dose of liposomal curcumin (10–400 mg) was given to 50 men and women	High doses of schistocytes appeared in the best-tolerated dose of 120 mg/m^2	Storka et al. (2015)

curcuminoid reinforcement had a substantial influence on all oxidative stress markers investigated, such as SOD and catalase plasma behavior, as well as glutathione peroxidase (GSH) serum levels, according to some randomized controlled data (Damiri et al. 2022; Sahoo et al. 2021). SOD and catalase are oxidative neutralization proteins that can be inhibited by it (Sahoo et al. 2021). However, it can also stop ROS-producing enzymes like lipoxygenase/cyclooxygenase and xanthine hydroperoxidase/oxidase from multiplying (Priyadarsini et al. 2003) (Shams ul Hassan et al. 2021). Curcumin, being a lipophilic molecule, is an excellent scavenger of peroxyl radicals, making it an antioxidant that, like vitamin E, breaks the chain of oxidative damage (Meng et al. 2021). A study's ethical approval code must be stated for any animal or human interventional research or other investigations that require ethical approval.

The injection of nanocurcumin and lead, as well as a reduction in ROS, restored the reduced and oxidized glutathione levels. The chelation activity of nanocurcumin and its increased bioavailability were most likely responsible for the removal of lead from soft tissues and blood. The literature examined the protective properties of nanocurcumin and curcumin against lung harm caused by paraquat exposure in a similar way (Chopra et al. 2021a). Reference looked explored the antioxidant activity of curcumin nanocrystals in Wistar rats to see if they may protect them from the circulatory harmful effects. According to the study's findings, curcumin nanocrystals at a dose of 40 mg were more effective in lowering lipid peroxidation and boosting antioxidant activities and detoxifying enzymes such as superoxide dismutase, catalase, and glutathione peroxidase. These findings show that nanocurcumin is a powerful antioxidant capable of protecting the body from a variety of pollutants (Rajasekar and nanotechnology 2015). Diabetic mice given nanocurcumin for 20 days demonstrated an increase in antioxidants as well as a reduction in OS. According to the findings, curcumin nanoparticles were more effective at reducing OS. One of the studies examined the regulating impact of nanocurcumin against tartrazine-induced damage on the antioxidant state of rats in another investigation (El-Desoky et al. 2020).

Activity to prevent obesity, cardiovascular disease, and liver toxicity

There are encouraging evidences that curcumin can increase the lipid and fat content of persons who have been preservative-free. These studies look at how curcumin oral preparations affect lipid profiles, basal metabolic rate, and glucose levels in obese patients. There were only substantial changes in triglyceride levels after 30 days of curcumin administration (Wise et al. 1998). The study looked at body mass index and weight loss in people with non-alcoholic fatty liver diseases (Perumal Samy et al. 2010). Turmeric supplementation for 4 weeks in obese women with systemic inflammation did not significantly alter oxidative stress or inflammatory markers, nor did it have a significant impact on the metabolic profile (Chereddy et al. 2013; Panchatcharam et al. 2006). Because ethanol's oxidation produces apoptosis and cell injury-initiating products, its metabolism-related toxic effects can cause morphological changes and clinical disorders in the liver (e.g., acetaldehyde and ROS). These products may cause fatty liver, hepatic inflammation, alcoholic hepatitis (necrosis), and progressive alcoholic cirrhosis (fibrosis) (Bhattacharya et al. 2021a). Despite curcumin's potential as an anti-inflammatory and antifibrotic agent against liver damage, male C57BL/6 mice showed some concentration-dependent negative effects. Curcumin appears to have two effects on alcoholic liver injury, according to these findings. Curcumin's hepatoprotective effect was observed at 0.1 mM, whereas a 1-mM dose resulted in an acceleration of liver injury and cellular edema (Farzaei et al. 2018).

Metabolic syndrome

Curcuminoids have also been shown to reduce plasma triglycerides and cholesterol levels via influencing gene expression and the activity of lipoprotein metabolism enzymes (Panahi et al. 2015; Sahebkar 2014). In a randomized, double-blind, placebo-controlled study employing a parallel group design, 117 patients with MetS were given 1 g of curcumin with 10 mg of piperine to increase absorption or placebo + 10 mg of piperine for 8 weeks (Kuptniratsaikul et al. 2014). Other variables, such as serum lipids and glucose levels, as well as baseline blood cytokine concentrations, remained statistically significant after controlling for potential confounders, with the exception of IL-6. According to the findings of this investigation, curcumin supplementation lowers blood levels of pro-inflammatory cytokines in MetS patients (Kuptniratsaikul et al. 2014). Inflammatory cytokines were also investigated in the study stated above. Curcumin treatment reduced mean serum levels of interleukin-1 ($p = 0.042$), interleukin-4 ($p = 0.008$), and vascular endothelial growth factor (VEGF) ($p = 0.01$). On the other hand, there were no significant variations in the levels of IL-2, IL-6, IL-8, IL-10, interferon gamma (IFN), epidermal growth factor (EGF), and MCP-1. According to the researchers, the findings demonstrate that curcumin may have immunomodulatory effects via altering the levels of IL-1, IL-4, and VEGF in circulation (Ganjali et al. 2014). Recent research has discovered that curcuminoids alter gene encoding and enzymatic expression in lipid metabolism, resulting in decreased plasma triglycerides and cholesterol levels as well as an increase in high cholesterol lipoproteins (Mohammadi et al. 2013; Naeini et al. 2019). Turmeric powder or curcuminoid extracts had a favorable

effect on glucose and insulin management, as well as blood lipid profiles, according to Supplemental Digital Content 2 (http://links2.lww.com/NT/A28). Only six clinical studies had been discovered before to 2009. New administration approaches have increased curcumin bioavailability. In the last 10 years, over 50 reports of trials examining the effects of various forms and doses of oral turmeric and curcuminoids in healthy people and people with T2DM and MetS have been published. The findings of these research are summarized in Table 3.

Anti-viral activity

Curcumin has been shown to have broad-spectrum antimicrobial activity, including antibacterial, antiviral, antifungal, and antimalarial properties in several studies. Due to its extended antimicrobial activity and safety property even at high doses (12 g/day) as assessed by clinical trials in humans, curcumin was used as a structural sample to design new antimicrobial agents with modified and increased antimicrobial activities through the synthesis of various derivatives related to curcumin (Zorofchian Moghadamtousi et al. 2014). Curcumin includes graphene oxide, which has a synergistic antiviral impact when used together to treat resveratrol infection. In addition, resveratrol infects newborns' lower respiratory tracts, causing serious lung disease. Curcumin also has an antiviral action that is dose-dependent (Dourado et al. 2021). Curcumin inhibits the inosine-monophosphate dehydrogenase (IMPDH) enzyme in a non-competitive or competitive way. Curcumin is involved in viral entrance and other stages of the life cycle, rather than viral RNA replication. IMPDH should be inhibited to become possible antiviral, anti-proliferative, and antiparasitic properties of curcumin (Faixová et al. 2021).

Depression and anxiety

Depression manifests itself in two ways: anxiety and depression. A lot of clinical studies have looked into the effect of curcumin taken orally on mental disorders. Curcumin was given orally at doses ranging from 500 to 1000 mg on a regular basis in these investigations, either alone (Sahebkar et al. 2013), with BioPerine (Rahmani et al. 2016), or even in conjunction with standard antipsychotics such escitalopram, venlafaxine, or fluoxetine. The only trial not included was one in which curcumin treatment reduced anxiety but not despair, possibly due to the shorter administration time (30 days vs. 5–8 weeks in other studies) (Nieman et al. 2012). Other hypotheses have emerged in recent decades as the monoamine depletion theory has dominated depression pathophysiology. One of them suggests that inflammation is important in the pathophysiology of depression. The similarities between "sickness behavior" and depression symptoms such as anorexia, decreased locomotor activity, and cognitive disturbances that can be found in both conditions prompted this hypothesis, and some studies have found that these depression symptoms are positively correlated with C-reactive protein levels (CRP) (Fried et al. 2020).

Anti-asthma and anti-diabetic

Curcumin alleviated coughing, rhinorrhea, and cold symptoms by reducing nasal air flow resistance. It also reduces intercellular grip molecules and lowers IL-4, IL-8, and tumor necrosis factor alpha (TNF- α), while raising IL-10 levels. Curcumin reduced allergic airplane irritations via the nasal channel in allergic asthma mice while maintaining structural reliability (Fu et al. 2015). Curcumin's antioxidant capabilities are linked to its improved anti-diabetic properties (Slavova-Kazakova et al. 2021). Curcumin was investigated to see if it could reduce superoxide production and the

Table 3 Clinical trials on the effects of *Curcuma longa* on glucose/insulin regulation and serum lipid profiles

Subjects	Treatment protocol	Outcomes for each form of curcuminoids (comparing C vs baseline or controls)	References
T2DM	Dose range 66 to 6 g/day Treatment lengths 10 days to 6 months	Powdered turmeric or C-fraction: inconsistent or no effect on BG, BP, BMI, HbA1c, IR, serum lipids, blood oxidative stress markers; ↓serum cytokines	Singletary (2020)
Prediabetes, hypercholesterolemia	Dose range 180 to 2 g/day Treatment lengths 4 weeks to 9 months	Powdered turmeric or C-fraction: (↓BG, ↓HbA1c, ↓IR, ↓newly diagnosed diabetics, ↑adiponectin measured from only 1 study)	Ferguson et al. (2018, 2019); Singletary (2020)
MetS	Dose range 400 mg/day to 2.4 g/day Treatment lengths 1–12 months	C-fraction + piperine: (↓TG, ↓TC, ↓Lp(a), ↓BG, ↓CRP,↓MDA, ↓leptin, ↓cytokines; ↑adiponectin, ↓SOD	Singletary (2020)
Healthy adults	Dose range 500 mg/day to 2.8 g/day Treatment lengths 4–12 weeks	Powdered turmeric or C-fraction: inconsistent or no effect on serum lipids, BG, blood oxidative stress markers	Santos-Parker et al. (2017); Thota et al. (2018)

reserve of vascular protein kinase C in the development of diabetes-induced endothelial dysfunction. Prior research has shown that curcumin has the ability to quickly slake reactive oxygen species, which can cause oxidative damage (Ishaq et al. 2021). Curcumin's particular protective characteristics are thought to be influenced by this property. By installing and activating antioxidant/cytoprotective enzymes like heme oxygenase-1, curcumin can protect cells from oxidative stress. The defense mechanisms of HO-1 in diabetes may provide some new therapy options for the emergence of HO-1 in the management of diabetic diseases (Siegel et al. 2014; Zhang et al. 2016).

Antimicrobial effects

Turmeric is an antibacterial substance that can be used to treat potentially fatal bacterial infections (Mythri and Srinivas Bharath 2012). Applying turmeric oil decreases fungal growth and the development of aflatoxins B1 and G1 by a significant amount (Silvestro et al. 2021). Curcumin is a potent antioxidant; however, its poor water solubility limits its application. The nano-curcumin destroys the bacteria's cell wall, resulting in their death (Motawi et al. 2020). To prevent or control *Acinetobacter baumannii* infections, a combination of epigallocatechin gallate (EGCG) and turmeric could be used in medicine (Motawi et al. 2020). *Acanthamoeba castellanii* is difficult to eradicate because the amoeba encysts are resistant to anti-amoebic medications. On *Acanthamoeba castellanii* cysts, the amoebicidal activity of ethanol extracts of plant varieties such as daffodil, groundnut, and turmeric was tested. Turmeric mouthwash can also help to prevent plaque and gingivitis. Additionally, turmeric mouthwash has been shown to significantly reduce total bacteria count (Wang et al. 2010). In addition, curcumin also has a dose-dependent inhibitory effect on infectivity and cell proliferation. It inhibits *Vibrio vulnificus* proliferation, which reduces *Vibrio vulnificus* cytotoxicity in HeLa cells. Curcumin prevents host cell rounding and actin aggregation via preventing bacterial adhesion and RTX toxin binding to host cells (Doggui et al. 2012). Curcumin has also been shown to have a wide variety of antiviral action (Doggui et al. 2012). In the fight against human immunodeficiency viruses (HIVs), a number of studies have been undertaken on its various processes. Curcumin has been discovered to inhibit HIV-1 integrase activity (Kulkarni et al. 2012). In addition, this polyphenol and its analogues have the ability to prevent viral genes from infecting and reproducing. They block the action of HIV protease and HIV-related kinases (e.g., tyrosine kinase). Curcumin also works well with biopharmaceuticals. Curcumin inhibits apurinic/apyrimidinic endonuclease-1's redox activity, which is noteworthy. As a result, a large number of genes and pathways are influenced. Curcumin has been found to slow the reproduction of the Kaposi's sarcoma-associated herpesvirus, hence controlling the pathologic processes that follow (e.g., angiogenesis) (Keshavarzi et al. 2019; Talebi et al. 2021). Turmeric plant organic components have also been found to have anti-influenza potential, according to researchers (Roy et al. 2021a). It can stop the influenza A virus (IAV) from adhering to surfaces and replicating (Betts et al. 2014).

Arthritis

Rheumatoid arthritis is an inflammatory condition in which synovial fibroblasts proliferate over time. Anti-inflammatory and anti-arthritic effects have been discovered in curcumin (Sumeet et al. 2018). Patients with active RA were given curcumin in real time and compared to a diclofenac sodium control group. Curcumin-treated patients had the greatest overall improvement in rheumatoid arthritis, and these values were significantly higher than those treated with diclofenac sodium (El-Sayed et al. 2012; Waghmare et al. 2011). Curcumin was found to be a safer and healthier alternative to diclofenac sodium (Waghmare et al. 2011). The antioxidant, anti-inflammatory, anti-proliferative, and immune-suppressive properties of curcumin have been linked to rheumatoid arthritis symptom alleviation (Alsamydai & Jaber 2018).

Supplementary Digital Content 1, available at http://links.lww.com/NT/A27, offers information on 21 clinical trials that looked at the effects of turmeric powder or curcumin-containing supplements on arthritis symptoms and signs. The findings of these studies are summarized in Table 4. The bulk of these studies focused on patients with osteoarthritis of the knee, and the majority of the participants were women (75%). The vast majority of patients were from the Middle East and Asia.

Anti-obesity

Curcumin improves the lipid and fat content of pre-served persons, which leads to the conclusion that it is effective in the treatment of obesity. They first look at how curcumin oral preparations affect lipid profile parameters, basal metabolic rate, and glucose levels in obese adults. After 30 days of curcumin administration, only triglyceride concentrations showed substantial changes, while other parameters remained unchanged (Banez et al. 2020). BMI and body weight reduction were also reported in the study that looked at such factors in NAFLD patients (Perumal Samy et al. 2010). The findings also revealed that a 4-week turmeric supplementation of 2.8 g/day had no effect on oxidative stress or inflammatory parameters in obese systemic inflammation females, nor does it induce a significant change in

Table 4 *Curcuma longa* for arthritis: a summary of clinical trials

Treatment composition	Treatment protocol	Outcomes (comparing C vs baseline or controls)	References
C-fraction + piperine	Dose range 500 mg/day–1.5 g/day Treatment length 6 weeks	↓Pain, ↓stiffness, ↓use of NSAIDs, ↓MDA	Panahi et al. (2016); Rahimnia et al. 2015)
Nanoparticles of C-fraction	Dose range 180 mg/day–2.1 g/day Treatment lengths 4–8 weeks	↓Pain, ↓use of NSAIDs, ↑walking ability	Nakagawa et al. (2014); Shin et al. (2017)
Powdered turmeric or C-fraction	Dose range 90 mg/day to 1.2 g/day Treatment lengths 2–16 weeks	C + NSAID vs NSAID: inconsistent improvement	Kuptniratsaikul et al. (2014); Srivastava et al. (2016)
Reconstituted mix of C-fraction + non-curcumin constituents of turmeric	Dose range 500 mg/day–1.5 g/day Treatment lengths 1–3 months	C vs NSAID: similar efficacy	Amalraj et al. (2017); Shep et al. (2019)

NSAID nonsteroidal anti-inflammatory drugs, *MDA* malondialdehyde

metabolic profile (Chereddy et al. 2013; Panchatcharam et al. 2006).

Curcumin's safety and toxicity, or side effects

Turmeric has been studied in vitro, in animal models, and in clinical trials for its safety. The organism is not toxic, according to a thorough investigation into the matter. Curcumin can inhibit the growth of probiotics and has antiproliferative effects in healthy cells, according to studies on cultured cells. Even so, there is very little evidence of genotoxicity and mutagenicity. Curcumin can be used orally in humans with no adverse effects. In a small number of cases, gagging, tongue redness, atrial fibrillation, and gastrointestinal issues (flatulence, diarrhea, nausea, and constipation) have all been reported. Because intravenous curcumin has a higher biocompatibility than oral curcumin, it should be taken at a lower dose (Soleimani et al. 2018). Oral curcumin at a dose of around 1000 mg/kg body mass caused a small reduction in weight gain in F2 generation chicks, according to one study (Alhalmi et al. 2021). Nanomaterials made from dipeptide curcumin are far too safe. A dipeptide is formed by the amino acids alpha, beta-dehydrophenylalanine, and methionine, which are all easily soluble in nature (Subramani et al. 2017). Animals showed no signs of acute toxicity. After a single oral dose, the pharmacokinetic parameters of a curcumin preparation were assessed in healthy human volunteers. Curcumin has been linked to some negative side effects (at 10 and 12 g) (Akter et al. 2021a, b, c; Vareed et al. 2008). These side effects were classified as non-serious because they corresponded to WHO toxicity grade 1. Curcumin is regarded as safe to use, according to this study. In a phase I clinical trial, 25 patients with a high risk of cancer or pre-malignant lesions were given various curcumin doses (500 mg, 1, 2, 4, 8, and 12 g/day). Curcumin was taken for 3 months orally. Even at doses of 8 g curcumin per day, Cheng et al. (2001) found no toxic effects. In humans, Sharma et al. (2007) found that 1.5 g of turmeric powder per day (approximately 150 mg of curcumin, the average consumption in India) had no negative effects (Sharma et al. 2007). Furthermore, Lal et al. (2000) found that 1.125 mg of curcumin per day had no adverse effects in humans (Lal et al. 2000). The treated patients, however, found doses greater than 8 g/day intolerable. Furthermore, when applied intravenously, curcumin-loaded blood serum albumin nanoparticles demonstrated minimal toxicity in HCT116 tumor xenograft models (Hong et al. 2021). Rabbits in the curcumin nanosuspension group had a lower risk of local irritation, phlebitis, and erythrocyte hemolysis than rabbits in the curcumin solution group, according to a new intravenous curcumin experiment (Gao et al. 2011).

Conclusions

For its multiple health benefits, curcumin has attracted a lot of research. These benefits appear to be mediated via anti-oxidant and anti-inflammatory pathways. We came to the conclusion that natural ingredients can be prominent in the field of different disease cure based on their reports and findings. Curcumin has anti-inflammatory, antioxidant, neuroprotective, and anti-cancer properties, as well as a variety of molecular targets. Curcumin is poorly absorbed and rapidly eliminated and metabolized when given orally to human volunteers, according to research. Curcumin may aid in the treatment of oxidative and inflammatory conditions, metabolic syndrome, arthritis, anxiety, and hyperlipidemia, according to research. It may also aid in the management of exercise-induced inflammation and muscle soreness, allowing active people to recover faster and perform better.

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Declarations

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