

Curcumin and Beyond: A Review of Turmeric's Pharmacological Benefits

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ABSTRACT

Turmeric (*Curcuma longa*), a rhizomatous herbaceous plant, has been widely studied for its therapeutic properties, largely attributed to its active constituent, curcumin. This review consolidates current findings on the pharmacological effects of turmeric and its bioactive components, including anti-inflammatory, antioxidant, antimicrobial, anticancer, and neuroprotective properties. Emphasis is placed on curcumin's molecular mechanisms of action, bioavailability challenges, and the potential of turmeric beyond curcumin—highlighting other constituents like turmerones. The review also explores clinical applications and future research directions in enhancing turmeric's therapeutic efficacy.

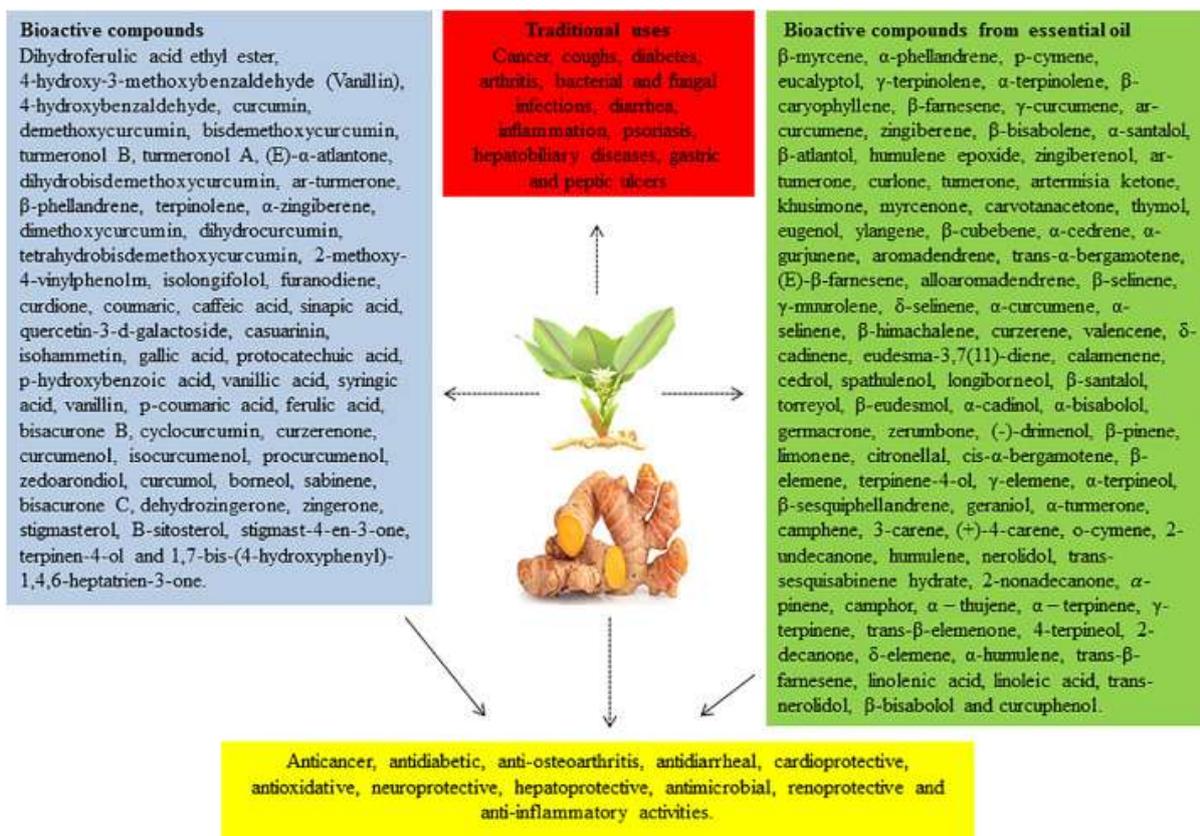
KEYWORDS: Turmeric, *Curcuma longa*, Curcumin, Turmerones, Pharmacological effects, Anti-inflammatory, Antioxidant, Anticancer, Neuroprotection, Bioavailability, Herbal medicine, Phytochemicals, Clinical trials.

I. INTRODUCTION

Worldwide, medicinal plants and their active components have been utilized in traditional and modern medicine to address, control, and prevent a wide range of illnesses in both humans and animals. It has been reported that approximately 80% of the world's population relies on medicinal plants and their bioactive compounds (bioactive compounds) for their primary healthcare needs (1, 2, 3). It is intriguing that the inclination

towards medicinal plants over conventional medicines may be attributed to the effectiveness of their bioactive components, as well as other factors such as accessibility, affordability, availability, and their reputation for being less toxic (3, 4, 5). Many scientists from various regions have been interested in medicinal plants and their biologically active ingredients because of these modern possibilities, which has led to testing as natural therapeutically active ingredients in the creation of new drugs and drug products (6, 7). Furthermore, traditional medicine examined the use of medicinal plants for the treatment of serious chronic diseases such as cancer, diabetes, and hypertension (3, 8, 9). One of the well-known herbs used is *Curcuma Longa*, which has been found to be medically effective in treating many human complaints.

Curcuma longa, a rhizome plant commonly known as turmeric, is a member of the Zingiberaceae family (10). India is widespread in China, Sri Lanka, West and East Africa, and other tropical countries. In China, people call it Lake and or jianghuang. Chinese traditional medicine (TCM) is used to cure, prevent and treat many diseases, including psoriasis, familiar liver diseases, cancer, cough, diabetes, arthritis, diarrhea, inflammation, skin problems, stomach ulcers, stomach ulcers, and more (10, 11). It has a major impact on the color, taste and nature of food, while simultaneously promoting blood circulation, eliminating stagnation and reducing depression (12).



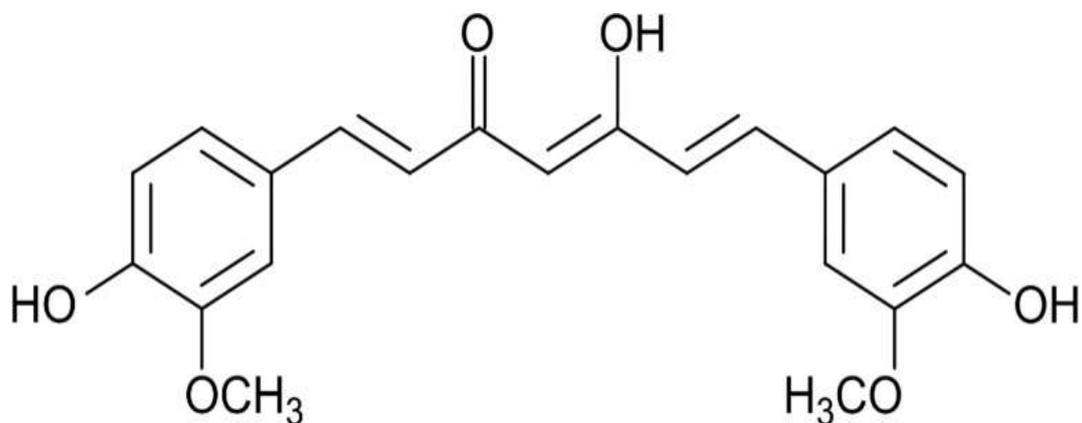
Moreover, a number of studies have demonstrated the many pharmacological activities of *C. longa* and its bioactive compounds, including antioxidant (13), hepato-protective (14), anti-osteoarthritis (15), anti-inflammatory (16), anti-cancer (17), anti-arthritic (18), neuro-protective (19), anti-diabetic (20), anti-diarrheal activity (21), anti-microbial (22), anti-atherosclerotic, antidepressant, anti-aging, wound healing, and memory-enhancing properties (10, 23). More than 300 physiologically active substances, including polyphenols, sesquiterpenes, diterpenes, triterpenoids, sterols, and alkaloids, are found in turmeric, which supports its use in traditional medicine (Fig. 1). Curcuminoids are a type of phenolic chemicals that give turmeric its characteristic yellow color (24). Turmeric contains 2–9% curcuminoids, depending on where it came from and how fertile the soil was in the area where it was grown (25).

Curcumin (77%), desmethoxycurcumin (17%), bis-desmethoxycurcumin (3%) and cyclocurcumin (a minor ingredient) are the four

primary curcuminoids (25, 26). In patients with type-2 diabetes mellitus and metabolic syndrome, curcumin, an active phytochemical found in turmeric, has demonstrated promise in successfully lowering cholesterol levels. Because it can lower C-reactive protein levels, it is also considered cardioprotective (27). Elemene, a substance derived from turmeric, has been authorized for the treatment of cancer in China (23).

Curcumin: A Historical Perspective

The *Curcuma* species has a long history that stretches back 5,000 years to Ayurvedic medicine and 2,000 years to Atharvedic medicine. Curcumin, which was initially isolated in 1815 (Vogel and Pelletier, 1815) and the pure crystalline component published in 1870 (Daube, 1870) (28), is the most active of the curcuminoids discovered in *C. longa*. Polish scientists originally postulated the curcumin structure in 1910 (Figure 1) (Miłobędzka et al., 1910) (29).



Chemical structure of curcumin

Although 1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione is commonly referred to as curcumin, the molecule is also called "curcumin I." Curcumin, to put it briefly, is a diferuloylmethane with the chemical formula $C_{21}H_{20}O_6$, a crystalline yellow-orange color, a molecular weight of 368.39 g/mol, and a melting temperature of 183°C. Chemically, it demonstrates keto-enol tautomerism, meaning that while its more stable enol form predominates in solid states and alkaline solutions, its main keto form is found in neutral and acidic solutions (Anand et al., 2007) (30). Curcumin II [demethoxycurcumin, 1-(4-hydroxy-3-methoxyphenyl)-7-(4-hydroxyphenyl)-1,6-heptadiene-3,5-dione] and curcumin III [bisdemethoxycurcumin, 1,7-bis(4-hydroxyphenyl)-1,6-heptadiene-3,5-dione] are two more substances that are referred to be curcumin (Buckingham, 2018) (31).

It's interesting to note that everyone refers to this natural polyphenol as the "wonder drug of life" (Gera et al., 2017) (32). Turmeric was utilized in traditional Far Eastern medicine to treat wound healing, liver and digestive system issues, and inflammatory disorders of numerous organs. The first studies on the health advantages of curcumin were conducted in the 1970s. Di Mario et al. (2007) (33), Adhvaryu et al. (2008) (34), Chandran and Goel (2012) (35), Yanpanitch et al. (2015) (36), Gera et al. (2017) (32), and Salehi et al. (2019a) (37) have all demonstrated the numerous therapeutic potentialities of curcumin. However, because to its limited bioavailability, turmeric is rarely used in medical clinics and is still not commercially regarded as a medicinal drug (Gera et al., 2017) (32).

When curcumin is taken orally, its hydrophobic properties cause the gastrointestinal

(GI) system to absorb it slowly. However, curcumin, which is classified as a Generally Recognized As Safe (GRAS) substance with a steady metabolism and minimal toxicity, appears to offer a promising potential for the medicinal development of turmeric (Nelson et al., 2017) (38). Curcumin's coloring properties for industrial uses are also noteworthy (Joshi et al., 2009; Buckingham, 2018) (39, 40).

In this regard, the review focuses on curcumin's uses in food and biotechnology, as well as in promoting health and preventing disease. The bioavailability, bioefficacy, safety, adverse effects, and quality aspects of curcumin are also discussed. Additionally, special attention is paid to curcumin's many uses, optimizing culinary appeal, agro-industrial processes to counteract its instability and low bioavailability, health issues, and future clinical use techniques.

PHARMACOLOGICAL ACTION

Studies have demonstrated that turmeric has a wide spectrum of pharmacological efficacy with few side effects, whether it is taken as a powder, extract, or an isolated component. Methoxy groups on the phenyl ring, phenolic, and 1, 3-diketone systems are important contributors to curcumin's wide range of pharmacological actions. In both local and foreign markets, there are numerous products containing curcumins or turmeric to treat a variety of illnesses. In contrast to other phyto-antioxidants, curcumin is a potent natural ingredient that is safe and nontoxic (Table 2). This is the cause of curcumin's diverse biological effects. For many years, Chinese and Indian medicine have used turmeric as an anti-inflammatory drug.

Plant Species	Biological Activities	Turmeric Extract
Curcuma longa	Antioxidant Activity	Ethanollic Extract
		Methanolic Extract
		n-butanol extract
		Aqueous Extract
		Fat-Soluble Extract
		Antibacterial Activity
	Aqueous Extract	
	Methanolic Extract	
	Ethyl Acetate Extract	
	Chloroform Extract	
	Antifungal Activity	
		Chloroform Extract
Ethanollic Extract		
Aqueous Extract		
Ethyl Acetate Extract		
Anti-inflammatory		Oil-Free Aqueous Extract
	Ethanollic Extract	
	Hexane Extract	
	Ethyl Acetate Extract	
	Supercritical carbon dioxide extract	
	Volatile Oil	
Anti-Cancerous Activity		Petroleum Ether Extract
		Ethanollic Extract
		n-hexane Extract
Immunomodulatory Activity		Ethanollic Extract
Antiviral Activity		Methanolic Extract

Antioxidant activity

Its main ingredient, turmeric, is frequently regarded as the strongest antioxidant available. Water and fat-soluble preparations of turmeric and its curcumin component have antioxidant activity comparable to that of vitamins C and E. The main reason for turmeric's hepatoprotective properties is its ability to lower the generation of pro-inflammatory cytokines. By reducing the oxygen level of cells, curcumin shields the body's cells from harm caused by free radicals. Pure curcumin is more effective than demethoxycurcumin and bisdemethoxycurcumin at scavenging superoxide anion. It lowers the risk of high blood pressure, macular degeneration, cataracts, glaucoma, heart disease, and high cholesterol (41).

The phenolic and flavonoid content of Ryudai gold (RD) turmeric is substantial, and it has a strong scavenging effect. [Reference 6] Raising the extraction temperature to the proper level increases the concentration of curcuminoid, which increases antioxidant activity. 90°C is maintained for 60 minutes to provide potent antioxidant qualities. Both the antioxidant activity and the amount of curcuminoids were reduced by the extreme heat treatment. [Source 7] Turmeric extract is shielded from hydrogen peroxide-induced peroxidation of lipids and red blood cells. Oxidative damage is avoided and toxic metabolite binding to DNA is reduced. Curcumin, a pro-oxidant, is a potent bioprotectant that has many

therapeutic applications when transition metal ions (Cu and Fe) are present (42).

Superoxide anion, hydroxyl radical, singlet oxygen, peroxy nitrite, and nitric oxide are among the ROS that this treatment effectively neutralizes. [Source 8] Compared to powder, turmeric peels have a higher phenolic content. Ginger peels exhibit a high phenolic content when mixed with it. Peels have a higher antioxidant activity than the commercial powder version as a result. There are several well-preserved phytochemicals with antioxidant qualities in its peels. [Source 9] significant quantities of polyphenols, flavonoids, and ascorbic acid are found in Chittagong's muraethanolic extract of Bangladeshi turmeric, while significant yields are found in chora extract. The ethanolic extract of Khulna's mura exhibits DPPH solid radical-scavenging activity, and the chora has a high FRAP (Ferric reducing antioxidant power) factor (43).

In order to prevent damage from free radicals, it is concluded that the ethanol extract of turmeric has a stronger antioxidant effect than the aqueous extract. [Source 10] Numerous long-term health problems, such as cancer, cataracts, inflammatory and cardiovascular diseases, and more, are associated with damage from free radicals. Through their ability to scavenge radicals, block their formation, or speed up their breakdown, antioxidants shield tissues from harm caused by free radicals. Because they influence the formation of FR or transform into free radicals, drugs may be dangerous. Additionally, contaminants, chemicals, herbicides, etc., in food might cause FR. A new study suggests that synthetic antioxidants might be bad for people's health. Antioxidant-acting natural compounds have become more popular in recent years (44).

Incorporating modern technologies, collaborative research, and traditional health beliefs into contemporary approaches greatly benefits those without access to costly Western medical systems. The inhibitory and antioxidant effects of TEL (turmeric extract loaded nanoliposomes) have been significantly greater than those of free turmeric extract. It has contributed to the development of food-functional nanocarriers. [Source 11] Curry leaf, lemongrass, turmeric, and torch ginger have the highest levels of DPPH and FRAP in tumors. The phenolic components of turmeric, torch ginger, and lemon herb are extracted using 80% acetone as a solvent. [Source 12] Turmeric oil is a viable and environmentally

friendly method for removing silver nanoparticles (45).

Antimicrobial activity

Antimicrobial Activity: When tested for microbial susceptibility, an ethanolic extract of turmeric (*Curcuma longa*) was found to be effective against all tested bacteria, with the lowest inhibition zone observed against *Staphylococcus epidermis* and the highest inhibition zone against *Shigella flexneri*. Numerous phytochemicals, including tannins, alkaloids, phenols, steroids, flavonoids, phlorotannin, cardiac glycosides, terpenoids, triterpenes, saponin, and others, can account for turmeric's antibacterial properties. [Reference 23] Both the sulfur-functionalized carbon dots (S-CD) and the carbon dots made from turmeric (S-CD) exhibited strong antioxidant activity (46).

Reactive oxygen production was higher in the sulfur-functionalized CD than in the non-functionalized CD, indicating the antibacterial activity of the S-superior CD. The CD demonstrated a more potent antibacterial impact on Gram-positive (*L. monocytogenes*) bacteria (*E. coli*) than on Gram-negative bacteria. Sulfur functionalization has demonstrated enhanced functioning in curcumin-derived CD, which has great promise for usage in biomedical and food packaging applications. Thus, there is no need to worry about toxicity when using turmeric-based multifunctional CD materials in food packaging and biomedical applications. [Source 24] (47).

Salmonella typhi, *Staphylococcus aureus*, *Escherichia coli*, and *Candida albicans* were evaluated with ethanol turmeric extract, N-hexane, water, and chloroform. Turmeric extract in water reduced *Salmonella typhi* and *Escherichia coli* infections. Methanol extracts regulated the growth of additional microorganisms while water extracts inhibited the growth of *Staphylococcus aureus* and *Escherichia coli*. [Source 25] *Staphylococcus aureus* inhibitory activity was enhanced by turmeric aqueous extracts. Turmeric, *Mucor sp.*, and anti-stolonifer ethanol extracts were found to have anti-pyroid properties. The parts might have antimicrobial and preservation properties (48).

The antibacterial efficacy of light-activated hydrogel coatings was unaffected by the incubation temperature. In order to avoid *Listeria innocuous* sausage cross-contamination, curcumin-loaded hydrogels and UV-A light have been demonstrated to be an effective source for antimicrobial coating. Foods that have an edible

antimicrobial microbial coating have a longer shelf life and a lower risk of foodborne illness. [Reference 27] It has been demonstrated that three curcuminoids—curcumin, bisdemethoxycurcumin (BDC), and demethoxycurcumin (DMC)—have antifungal and antibacterial properties against *Aspergillus niger* and *Candida albicans*, as well as against bacteria like *Bacillus subtilis* and *Staphylococcus aureus*. Conventional medicine has employed the antimicrobial drugs fluconazole and kanamycin to treat a variety of bacteria and fungi. [Citations 28 and 29] (49).

Anti-inflammatory activity

The inflammatory response-related enzymes COX-I and COX-II, as well as the ROS-producing enzymes cyclooxygenase and lipoxygenase, are inhibited by turmeric. Since AgNPs' effects were demonstrated to be stronger than those of traditional diclofenac sodium, it was determined that turmeric oil mediated by silver nanoparticles might be used as an anti-inflammatory medication. [Source 70] Compared to unfermented turmeric, turmeric fermented with *Lactobacillus fermentum* has a larger quantity of curcumin. Cell survival is enhanced by the turmeric that *L. fermentum* has fermented. Fermented turmeric's anti-inflammatory properties resulted from its suppression of the c-Jun N-terminal kinase (JNK) signal pathway. Without changing cytotoxicity, curcumin concentration increases during the fermentation of lactic acid bacteria (50).

Because curcumin and turmeric essential oils work together to protect against DSS-induced colitis, they have a stronger anti-inflammatory effect than curcumin alone. ETO-curcumin helps initiate anti-inflammatory cytokines like IL-10, IL-11, and FOXP3 in the colon. [Source 75] 91% protection is offered by curcuma-modified molecular weight pectin, a protective inhibitor of pro-inflammatory mediators like IL-8, TNF- α , and NF-Lisboa. The expression of IL-10, Galectin-3, H + K+-ATPase, oxidative, and gastro-protective mediators (IgA, mucin, NOx, prostaglandin E2, and zinc) are all modulated and suppressed by MTrPP. [Source 76] Nigeria. The essential oil of ginger and turmeric rhizomes prevents the hippocampus and prefrontal cortex from using acetylcholinesterase (AChE) or adenosine deaminase (ADA) to inhibit cytokines and inflammatory biomarkers like IL-6 (51).

When taken orally, *C. longa* hot water extract (WEC) guards against ethanol-induced liver

damage. Hepatic oxidation and inflammation are decreased by the WEC component bisacurone. Liver damage caused by ethanol may be treated with oxidative stress and inflammatory cytokines. [Source 80] Ginkgo and turmeric's roots, gums, and leaves contain secondary metabolites (alkaloid, polyphenolic compounds, and phenolic acid) that make them more potent anti-inflammatory medications than common ones like aspirin and diclofenac sodium. [Source 81] The key ingredient in turmeric, curcumin (CUR), has a number of disadvantages, including as restricted absorption, rapid metabolite excretion, and poor water solubility. CUR exhibits superior anti-inflammatory activity as nanoparticle and NLC formulations improve their stability (52).

Anti-cancerous activity

Turmeric's main polyphenol, curcumin, has a variety of biological effects. It operates as an anti-cancer medication by altering molecular targets that help cell signaling activities. It suppresses apoptosis, transformation, and proliferation. Curcuminoids and their derivatives have the potential to greatly enhance curcumin's anti-cancer effects. [Reference 85] The three active curcuminoids that are produced from turmeric are bisdemethoxycurcumin, demethoxycurcumin, and curcumin. These curcuminoids inhibit the growth and potentiality of human lung cancer A549, colon cancer HT29, and glioma cell lines T98G. Lung cancer cell lines' viability and proliferation are decreased by single curcuminoids. When combined with cisplatin, the crude extract more effectively decreases the viability of A549 lung cancer cells than when either substance is used alone (53).

The Gemini surfactant–curcumin (Gemini–Cur) nanoparticle stops the development of cancer cells by causing apoptosis. Gemini–Cur effectively reduces the expression of Bcl-2 in breast cancer cells while upregulating the expression of p16INK4a, p14ARF, and Bax. Gemini surfactants boost curcumin's distribution, which strengthens its anti-cancer effects. A powerful anti-cancer agent is a nanomaterial known as Gemini–Cur. [Source 95] The dietary polyphenols turmeric curcumin and black long pepper piperine are active and have anti-cancer effects on a variety of malignancies, including colorectal cancer (CRC). Curcumin's medicinal effect is aided by piperine. Both the free and emulsion versions of HCT116 cell growth were not significantly impacted by piperine therapy.

CurcuEmulsomes resulted in an increase in Caspase 3 levels (54).

In vitro and in vivo, curcumin has shown strong anti-cancer properties against a number of different types of cancer, including colorectal, pancreatic, prostate, breast, and head and neck cancer. Additionally, numerous clinical studies with human participants have demonstrated its efficacy and safety in cancer patients, either by itself or in combination with other anti-cancer medications. Curcumin is believed to have a multifaceted anti-cancer action by disrupting specific cellular pathways and promoting or suppressing the synthesis of different types of cytokines, enzymes, or growth factors, including MAPK, EGF, NF κ B, PKD1, COX-2, STAT3, TNF- α , and I κ B β (55).

Immunomodulatory activity

Turmeric extract contains bioactive monosaccharides, curcuminoids, and antioxidants that are phenolic and flavonoid. TE shows better resistance on artificial human intestinal and stomach juice. TE has prebiotic potential and inhibits the generation of IL-8 generated by LPS in the HT29-19A cell line. [Scitation 100] In comparison to albino mice fed a baseline diet, those fed an Aflatoxins-added diet gained weight, had decreased FER and spleen weight, and had higher blood MDA and IL-6 levels. Neither relative thymus weight nor food intake are impacted. Aflatoxin's pro-inflammatory properties are enhanced when turmeric is added (56).

Curcumin interfered with meat T cells IL-2, IL-12, IFN- γ and TNF-Q produce. At the same dose, lac cells are less susceptible to the inhibitory effects of curcumin. [Ref 105] Curcumin has been identified as a potent immunomodulatory agent over the past 20 years and affects the activation of B cells, T cells, neutrophils, macrophages, native killer cells and dendritic cells. Curcumin suppresses inflammatory cytokines such as chemokines, IL-1, IL-2, TNF, IL-6, IL-8, and IL-12 when activating the transcription factor NF-B. Small amounts of curcumin also help to produce more antibodies (57).

Administration of curcumin enhanced the continued performance of animals experiencing ischemia. 1. Based on histological analysis, curcumin treatment significantly reduced skeletal muscle damage and fibrosis associated with ischemic injury. Mirrors for TNF, IL-1, and IL-6 were all reduced after curcumin treatment. This indicates reduced macrophage infiltration and

inflammatory response at the local level. Curcumin therapy inhibited the NF-B signal path. 1 .Curcumin is one of the LPS-induced NF-B activations in macrophages. Curcumin has been proven to reduce the severity of hind-limb injuries after ischemic surgery. This indicates potential use in pad therapy. 2. [Citation110] The immune-modulatory effect of *Aspergillus oryzae* fermented CI (FCL) was evaluated in 7 RAW264 cells (58).

Antiviral activity

Curcumin functions as an anti-infective agent against various viruses. These methods involve either direct disruption of viral replication machinery or modulation of viral replication-associated cellular NF-B and PI3K/Akt signaling pathways. This research discusses current findings, highlighting curcumin's antiviral effects and potential molecular mechanisms. [Citation114] Curcumin possesses antiviral, anti-inflammatory, antinociceptive, antipyretic, and antifatigue properties that help manage COVID-19 symptoms. It exhibits antioxidant, antiapoptotic, and antifibrotic features and inhibitory effects on NF-B, Toll-like receptors, inflammatory cytokines, bradykinin, and chemokines, among additional molecular processes. Based on scientific studies, curcumin might contribute to the treatment of COVID-19 (59).

Turmeric spices can block important proteins from SARS-Cov-2, and thus can be used as a therapeutic or protective agent against SARS-Cov-2 by inhibiting viral important proteins. The most effective inhibitors of viral primary proteases, spike glycoproteins, and RNA polymerases are 4, 23, and 6 links. Phytochemical analysis identified compounds as terpenes, saponins, alkaloids, flavonoids, tannins, cardiac glycosides, and cartilage softening chemicals. 2. curcuma longa has significant inhibitory activity and can develop effective antivirals against polio and measles viruses. [Citation118] (60).

Curcumin treatment did not involve HCV-NR RNA replication or assembly/release of viruses. 3. CO incubation with curcumin from COV successfully blocked invasion of all primary HCV genotypes. 3. Antiviral properties were recognised by other curcumin compounds, but not tetrahydrocurcumin. Curcumin reduces the fluidity of HCV cases, which causes reduced viral binding and fusion, as well as intercellular permeability. Kurkumapurcumin blocks the entry of HCV into primary human hepatocytes, regardless of

genotype, by altering membrane fluidity to prevent viral binding and fusion (61).

BIOAVAILABILITY AND DELIVER CHALLENGES

Bioavailability Challenges

- **Poor Aqueous Solubility:** Curcumin is lipophilic (fat-soluble) and has very low solubility in water, which hinders its absorption in the aqueous environment of the gastrointestinal tract (62).
- **Limited Absorption in the Gut:** Even when some curcumin dissolves, its absorption through the intestinal walls is poor. It can bind to enterocyte proteins, modifying its structure and further reducing absorption.
- **Rapid Metabolism:** Once absorbed, curcumin undergoes extensive and rapid metabolism in the intestine and liver. Enzymes like glucuronidase and sulfotransferase quickly convert curcumin into glucuronide and sulfate conjugates. These metabolites are often less biologically active and are readily eliminated (63).
- **Rapid Systemic Elimination:** The conjugated metabolites of curcumin are quickly excreted from the body through feces and urine, resulting in very low levels of free curcumin in the bloodstream and tissues, even after high oral doses.
- **Chemical Instability:** Curcumin is unstable at alkaline pH and can degrade rapidly in the physiological environment (64).
- **Reaching Therapeutic Concentrations:** Because of low bioavailability, it is difficult to achieve and maintain therapeutically relevant curcumin concentrations in target tissues with oral administration of unformulated turmeric or curcumin (65).
- **Maintaining Stability During Delivery:** Because of curcumin's vulnerability to degradation, it is difficult to ensure its chemical stability throughout the delivery process, from ingestion to reaching the target location.
- **Target Delivery:** For specialized therapeutic uses such as cancer treatment or neurological diseases, delivering curcumin to damaged tissues or cells while avoiding systemic exposure is a key challenge (66).
- **Formulation Complexity:** Creating effective formulations that increase bioavailability frequently requires complex processes and

materials, which might affect the cost and scalability of possible treatments (67).

- **Combining with Piperine:** Piperine, a component of black pepper, inhibits curcumin metabolizing enzymes, considerably boosting its bioavailability.
- **Nanoformulations:** Curcumin can be encapsulated in nanoparticles, liposomes, micelles, and nanoemulsions, which improves its solubility, absorption, and stability and may allow for targeted delivery (68).
- **Lipid-Based Carriers:** Lipid-based formulations can improve the solubility and absorption of curcumin.
- **Cyclodextrin Complexes:** Encapsulating curcumin within cyclodextrin molecules can increase its water solubility and stability (69).
- **Self-Microemulsifying Drug Delivery System (SMEDDS):** These formulations spontaneously generate microemulsions in the gastrointestinal tract, which improves curcumin solubilization and absorption.
- **Structural analogies:** Researchers are looking on synthetic curcumin equivalents that are more stable and bioavailable (70).

CLINICAL APPLICATIONS AND TRIALS

- **Anti-inflammatory:** prevents the synthesis of inflammatory chemicals.
- **Antioxidant:** Eliminates free radicals and reduces oxidative stress.
- **Anticancer:** Modulating pathways related to cancer formation and progression.
- **Antimicrobial:** Effective against certain bacteria, viruses, and fungus.
- **Neuro-protective:** Protects nerve cells from injury.
- **Cardio-protective:** promotes cardiovascular health.
- **Hypo-glycemic:** Lowers blood sugar levels.
- **Hypo-lipidemic:** lowers blood lipid levels (71).

Based on these characteristics, clinical studies have examined the effectiveness of turmeric and curcumin in addressing different conditions, including:

Inflammatory Conditions:

- **Arthritis:** Numerous studies have demonstrated curcumin's ability to alleviate pain and inflammation associated with osteoarthritis and rheumatoid arthritis.

- **Inflammatory Bowel Disease (IBD):** Research has investigated its effects on ulcerative colitis and Crohn's disease, with some results suggesting possible improvements in symptoms and inflammation (72).

Metabolic Disorders:

- **Type 2 Diabetes Mellitus (T2DM):** Curcumin has shown potential in enhancing blood glucose regulation, insulin sensitivity, and lipid profiles in individuals diagnosed with T2DM.
- **Metabolic Syndrome:** Studies indicate possible advantages in managing various aspects of metabolic syndrome (73).
- **Cancer:** A variety of preclinical investigations suggest that curcumin has potential anticancer properties. Clinical studies are examining its effectiveness in cancer prevention and as a complementary treatment for different cancers, such as colorectal, prostate, breast, and pancreatic cancer. Initial-phase trials have also looked into its ability to alleviate side effects related to cancer treatments.
- **Neurodegenerative Diseases:** Research is being conducted on curcumin's potential benefits for Alzheimer's disease and other neurodegenerative disorders because of its antioxidant and anti-inflammatory effects. Some studies have indicated that older adults receiving curcumin supplementation maintain stable cognitive function (74).
- **Cardiovascular Diseases:** Investigations are being carried out to assess the heart-protective benefits of curcumin, including its potential to enhance endothelial function and lower cardiovascular risk factors.
- **Skin Conditions:** Research on topical curcumin has examined its effectiveness for conditions such as psoriasis, eczema, and wound healing, revealing favorable outcomes attributed to its anti-inflammatory and antioxidant characteristics (75).
- **Infections:** Clinical trials are investigating the antimicrobial effects of curcumin for a range of infections.

Challenges and Considerations:

Despite encouraging preclinical and certain clinical results, several obstacles remain:

- **Bioavailability:** Curcumin has low oral bioavailability owing to inadequate absorption, rapid metabolism, and swift elimination from

the body. Numerous clinical studies use enhanced formulations (such as piperine, nanoparticles, liposomes) to boost absorption.

- **Standardization:** The composition of turmeric extracts and curcumin products can differ, impacting the uniformity of results (76).
- **Dosage and Duration:** The ideal dosages and treatment lengths for various conditions are still being studied.
- **Study Design:** Some clinical trials face challenges related to sample size, design, and endpoints.
- **Regulatory Environment:** Herbal supplements like turmeric operate under a different regulatory framework in comparison to pharmaceutical drugs (77).

II. CONCLUSION

Turmeric, derived from the *Curcuma longa* plant, has been used for centuries in traditional medicine to treat various health conditions. Its active compound, curcumin, has potent anti-inflammatory, antioxidant, and antimicrobial properties, making it a potential therapeutic agent for several diseases. Research has shown that curcumin can modulate multiple cellular pathways, suppressing inflammatory cytokines and enzymes, and exhibiting anticancer, neuroprotective, and cardiovascular-protective effects. Clinical trials have explored curcumin's efficacy in managing conditions such as arthritis, inflammatory bowel disease, metabolic disorders, cancer, neurodegenerative diseases, and skin conditions. While results are promising, challenges remain, including curcumin's poor bioavailability due to limited solubility, rapid metabolism, and swift elimination. To overcome these challenges, researchers have developed various formulations, such as nanoparticles, liposomes, and cyclodextrin complexes, to enhance curcumin's absorption and stability. Despite these advancements, standardization of turmeric extracts and curcumin products remains a concern, and optimal dosages and treatment durations for various conditions are still being investigated. Regulatory frameworks for herbal supplements also differ from those for pharmaceuticals, impacting the development of curcumin-based therapies. Turmeric and curcumin have shown significant potential in preventing and treating various diseases, but further research is needed to overcome bioavailability and formulation challenges, standardize products, and establish optimal dosing regimens. With continued investigation and development, curcumin may

become a valuable adjunct therapy for a range of health conditions.

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