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Review Article

Curcuma longa Linn. (Turmeric): Phytopharmaceutical Approach from Traditional Knowledge to Conventional Medicine

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Abstract

The traditional Indian system of medicine uses turmeric, scientifically known as *Curcuma longa* Linn. (*C. longa*). It is a great example of how traditional knowledge about plants has been combined with modern scientific research on medicines. For a long time, turmeric has been used in systems such as Ayurveda, Siddha, and Unani medicine. These systems have shown that turmeric has many health benefits, such as reducing inflammation, fighting free radicals, killing harmful bacteria, and even helping with cancer. The main phytoconstituent (active ingredient) in turmeric is curcumin, along with other compounds such as demethoxycurcumin, bisdemethoxycurcumin, and certain oils such as turmerones. These compounds work by targeting important processes in the body, such as inflammation and cell growth, through pathways like Activated B-Cells, Nuclear Factor kappa B (NF-κB), Mitogen-Activated Protein Kinase (MAPK), and Phosphoinositide 3-kinase (PI3K)/ Protein kinase-B (Akt). New technologies, like eco-friendly ways to extract curcumin, better ways to separate and standardize it, and advanced delivery methods like nanoparticles, have helped make curcumin more stable and easier for the body to use. Clinical studies have shown that turmeric can help with conditions like inflammation, metabolic issues, problems with the brain, and cancer. It is now used not just in traditional remedies but also in health foods, supplements, and conventional drugs. Looking ahead, there are opportunities to create new, better versions of curcumin, use Artificial Intelligence (AI) to design medicines, and make herbal mixtures that meet international safety standards.

Keywords: Curcumin, Nanotechnology, Bioavailability, Clinical validation, Nutraceuticals.

INTRODUCTION:

Turmeric has been an integral part of Indian traditional medicine systems, particularly Ayurveda, Siddha, and Unani systems, for thousands of years¹. Its use dates back over 4,000 years in the Indian subcontinent, where it was esteemed not only as a spice and coloring agent but also as a sacred herb with various potent pharmacological properties². Ancient texts describe turmeric as a remedy for various ailments, including respiratory disorders, liver diseases, skin conditions, and wound healing. Turmeric rhizome and powder were widely used in religious rituals and traditional functions, symbolizing purity, prosperity, and protection³. Over time, its application spread across Asia, the Middle East, and Africa through trade routes, earning it recognition as a versatile herbal medicine in several ancient cultures⁴. Turmeric's ethnomedicinal significance lies in its broad therapeutic spectrum, supported by centuries of traditional knowledge. Traditional medicine

practitioners used it as an anti-inflammatory, antimicrobial, and digestive tonic, and it formed the basis of many traditional remedies for pain, infection, and metabolic disorders. *C. longa*, the main bioactive compound, along with the other curcuminoids and volatile oils, was later shown to account for many of these pharmacological effects^{5,6}. These findings bridged the gap between ancient wisdom and modern scientific validation, positioning turmeric as a model plant for integrating ethnopharmacology with contemporary medicine⁷. In the modern global health context, turmeric has gained remarkable attention as a natural therapeutic agent and functional food ingredient. It is now incorporated into nutraceuticals, dietary supplements, and cosmetic formulations worldwide⁸. The increasing consumer demand for herbal and preventive healthcare solutions has further boosted turmeric's importance in the pharmaceutical and nutraceutical industries. Research has expanded its

scope beyond traditional uses, exploring its potential in the treatment of chronic inflammatory diseases, cancer, neurodegenerative disorders, and metabolic syndromes^{9,10}. Moreover, ongoing advancements in nanotechnology and formulation science aim to enhance curcumin's bioavailability and clinical efficacy, ensuring that the ancient wisdom surrounding turmeric continues to develop within the context of medicine¹¹. Thus, *C. longa* stands as a bridge between tradition and innovation, an example of how ancient practices, when scientifically standardized, can contribute meaningfully to present-day global healthcare practices¹².

BOTANICAL DESCRIPTION AND TAXONOMY:

C. longa is a herbaceous perennial plant belonging to the family *Zingiberaceae*. It grows from thick, branched, yellowish-orange rhizomes that possess a characteristic aromatic odor and slightly bitter taste. The plant typically reaches a height of about 60 cm to 100 cm and bears large, oblong lanceolate leaves that are bright green and arranged in two rows, forming a pseudo-stem¹³. The flower cluster is a dense spike composed of pale-yellow flowers surrounded by green or reddish specialized leaves. The flowers are zygomorphic and

bisexual, although fruit formation is rare, and when produced, it is a small capsule containing few seeds (Figure 1)¹⁴. The rhizome, which serves as the main medicinal and commercial part, is rich in curcuminoids and essential oils responsible for its color, aroma, and therapeutic properties¹⁵. Turmeric is widely distributed in tropical and subtropical regions of the world. It is believed to have originated in South and Southeast Asia, particularly in India, which remains the largest producer and exporter globally¹⁶. The plant is extensively cultivated across India, China, Indonesia, Sri Lanka, Thailand, and parts of Africa and Central America¹⁷. It thrives in warm, humid climates with well-drained, fertile soils and requires abundant rainfall for optimal growth. Cultivation of *C. longa* is primarily done through non-reproductive propagation using rhizome segments¹⁸. Planting usually occurs before the monsoon season, and the crop matures within 7 to 9 months¹⁹. Proper irrigation, weed control, and pest management practices are essential for achieving high yields and quality rhizomes²⁰. After harvesting, the rhizomes are cleaned, boiled, dried, and polished before being ground into the characteristic yellow powder used for medicinal, edible, and cosmetic purposes²¹.



Figure 1: (A) Plant and (B) Dried Rhizomes of *C. longa*

PHYTOCHEMICAL CONSTITUENTS:

C. longa is a rich source of various phytochemical constituents responsible for its broad pharmacological and therapeutic activity. The two major classes of bioactive compounds are curcuminoids and essential oils, which contribute to the plant's color, aroma, and biological activities²². In addition, turmeric contains various secondary metabolites such as alkaloids, flavonoids, tannins, saponins, and steroids that enhance its antioxidant, antimicrobial, anti-inflammatory, and anticancer properties²³. Curcuminoids are polyphenolic compounds primarily responsible for the yellow pigmentation of turmeric. The principal curcuminoids include curcumin (diferuloylmethane),

demethoxycurcumin, and bisdemethoxycurcumin. Among these, curcumin is the most abundant and biologically active, showing potent antioxidant, anti-inflammatory, and anticancer properties²⁴. The essential oil fraction of turmeric, which constitutes about 3% to 7% of the rhizome, is composed mainly of sesquiterpenes and monoterpenes. Major constituents such as ar-turmerone, α -turmerone, β -turmerone, and zingiberene are known for their antimicrobial, anti-inflammatory, and neuroprotective actions²⁵. In addition to these, several other bioactive secondary metabolites, including phenolic acids, sterols, sugars, and resins, contribute synergistically to the therapeutic profile of turmeric (Table 1)²⁶⁻²⁹

Table 1: Phytochemical Constituents of *C. longa* and their Pharmacological Activity

Category	Constituent	Chemical nature / Class	Pharmacological activity
Curcuminoids	Curcumin	Polyphenolic compound	Antioxidant, anti-inflammatory, anticancer
	Demethoxycurcumin	Polyphenolic compound	Antioxidant, hepatoprotective
	Bisdemethoxycurcumin	Polyphenolic compound	Anti-inflammatory, antitumor
Essential oils	ar-Turmerone	Sesquiterpene	Antimicrobial, neuroprotective
	α-Turmerone	Sesquiterpene	Anti-inflammatory, immune-modulatory, antifungal
	β-Turmerone	Sesquiterpene	Cytotoxic, antioxidant
	Zingiberene	Monoterpene	Antibacterial, flavor compound
Other secondary metabolites	Flavonoids	Polyphenolic compounds	Free radical scavenging, cardioprotective
	Tannins	Polyphenolic compounds	Astringent, antimicrobial
	Saponins	Glycosides	Immunostimulant, hypocholesterolemia
	Sterols (e.g., β-sitosterol)	Phytosterol	Anti-inflammatory, hypocholesterolemia
	Sugars and resins	Carbohydrate derivatives	Contribute to stability and texture

EXTRACTION AND STANDARDIZATION TECHNIQUES:

Extraction of phytoconstituents from *C. longa* is a fundamental step in developing standardized phytopharmaceutical formulations. Traditionally, methods such as solvent extraction, Soxhlet extraction, and hydrodistillation have been used to isolate curcuminoids and essential oils from turmeric rhizomes³⁰. These conventional techniques are simple and effective but often require longer extraction times, large volumes of organic solvents, and high temperatures that may degrade thermolabile constituents. Recently, the focus has shifted toward green and efficient extraction approaches that are environmentally sustainable and preserve phytochemical integrity³¹. Techniques such as supercritical fluid extraction (SFE), microwave-assisted extraction (MAE), ultrasound-assisted extraction (UAE), and pressurized liquid extraction (PLE) have shown superior yields and shorter processing times with minimal solvent use³². These modern methods enhance extraction efficiency while maintaining the chemical

stability of curcuminoids and essential oils, aligning with green chemistry principles and pharmaceutical quality requirements. The standardization of *C. longa* extracts is essential to ensure consistency, efficacy, and safety³³. Quality control parameters include macroscopic and microscopic evaluation, determination of moisture and ash content, and estimation of curcuminoid concentration using chromatographic techniques such as High-Performance Liquid Chromatography (HPLC), Thin-Layer Chromatography (TLC), and Gas Chromatography-Mass Spectrometry (GC-MS)³⁴. Spectroscopic methods like Ultraviolet visible (UV-Vis) and Fourier transform infrared (FTIR) spectroscopy are utilized to confirm bioactive compound identity and purity (Table 2)³⁵⁻⁴⁶. Additionally, microbial limit tests, heavy metal analysis, and physicochemical characterization are conducted as per pharmaceutical reference standards. Through precise isolation and systematic standardization, high-quality turmeric extracts with consistent pharmacological properties can be achieved for use in conventional medicine⁴⁷.

Table 2: Extraction and Standardization Techniques of *C. longa*

Category	Technique	Principle	Advantages	Limitations
Conventional methods	Solvent extraction	Uses solvents like ethanol, methanol, or acetone to dissolve curcuminoids and essential oils from the powdered rhizome	Simple, cost-effective, widely applicable	Time-consuming, high solvent use, thermal degradation possible
	Soxhlet extraction	Continuous hot solvent circulation extracts curcuminoids exhaustively from plant material	High yield, reproducible	Requires a long extraction time and high energy
	Hydrodistillation	Steam or water distillation separates essential oils from the rhizome	Suitable for volatile oils, an established process	High temperature may affect sensitive compounds
Green and modern extraction technologies	SFE	Utilizes supercritical carbon dioxide (CO ₂) for solvent-free extraction of curcuminoids and essential oils	High purity, no solvent residue, preserves thermolabile compounds	Expensive setup and maintenance
	MAE	Microwave energy disrupts plant cells, enhancing solvent penetration and release of phytochemicals	Rapid, energy efficient, minimal solvent	Not suitable for heat-sensitive solvents
	UAE	The cavitation effect of ultrasonic waves enhances mass transfer and solvent diffusion	Fast, low solvent use, preserves compound stability	Scale-up challenges in large production
	PLE	Uses high temperature and pressure to increase the solubility and diffusion rate of bioactive compounds	High yield, short time, eco-friendly	Requires specialized equipment
Quality control and standardization parameters	Macroscopic and microscopic evaluation	Morphological and histological identification of rhizome features	Confirms botanical authenticity	Preliminary identification only
	Physicochemical tests	Includes moisture content, ash value, and extractive value determination	Ensures purity and quality stability	Does not identify specific compounds
	Chromatographic techniques	Quantifies curcuminoids and essential oil constituents	Accurate, reproducible, regulatory compliant	Requires trained personnel and equipment
	Spectroscopic analysis	Identifies functional groups and confirms compound purity	Quick and non-destructive	Limited compound specificity
	Microbial and heavy metal analysis	Tests for contaminants and toxic elements	Ensures safety and regulatory compliance	Requires a specialized laboratory setup

PHARMACOLOGICAL ACTIVITIES:

C. longa shows a wide range of pharmacological activities primarily due to its bioactive constituent, curcumin. It has been widely studied for its anti-inflammatory, antioxidant, antimicrobial, and anticancer properties⁴⁸. Curcumin modulates key molecular targets, including transcriptional regulators, cytokines, enzymes, and growth factors, that contribute to its

therapeutic potential in various diseases. Additionally, *C. longa* shows hepatoprotective, neuroprotective, cardioprotective, and antidiabetic effects, making it a multifunctional agent in both preventive and supportive medicine (Figure 2)^{49,50}. Its diverse pharmacological properties have led to its inclusion in dietary supplements, nutraceuticals, and supportive therapies, highlighting its relevance in conventional medicine and holistic healthcare approaches (Table 3)⁵¹⁻⁶¹.

Pharmacological Activities of *Curcumin* (*Curcuma longa*)

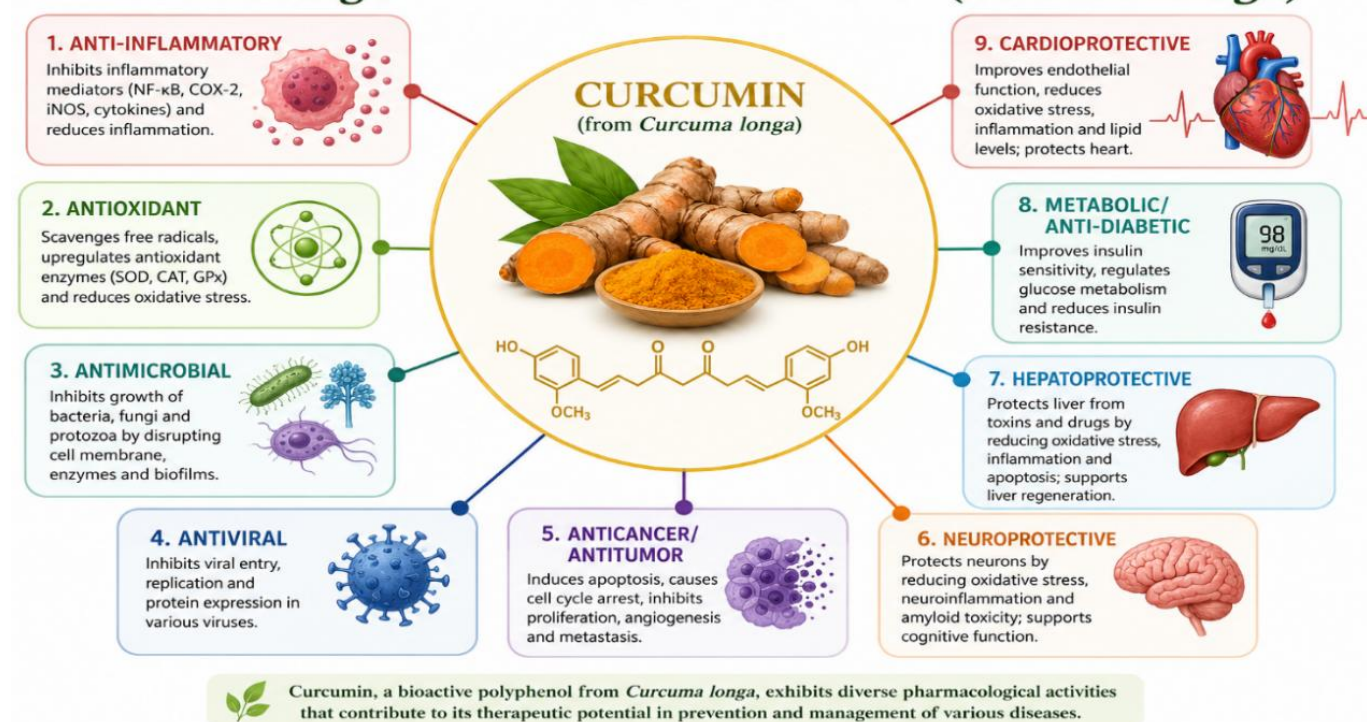


Figure 2: Curcumin exhibits diverse pharmacological activities with significant therapeutic potential

Table 3: Pharmacological Activities of *C. longa*

Pharmacological activity	Bioactive compounds	Mechanism of action	Therapeutic significance
Anti-inflammatory	Curcumin, Demethoxycurcumin, Bisdemethoxycurcumin	Inhibits cyclooxygenase-2 (COX-2), lipoxygenase (LOX), and inducible nitric oxide synthase (iNOS); tumor necrosis factor- α (TNF- α), interleukin-1 β (IL-1 β), and interleukin-6 (IL-6)	Management of arthritis, inflammatory disorders, and autoimmune diseases
Antioxidant	Curcuminoids, Phenolic compounds	Scavenges reactive oxygen species (ROS) and reactive nitrogen species (RNS); enhances superoxide dismutase (SOD), catalase, and glutathione peroxidase (GPx) activity	Prevention of oxidative stress, aging, and metabolic disorders
Antimicrobial	Curcumin, Turmerones, Essential oils	Disrupts microbial cell membranes, inhibits nucleic acid synthesis, and quorum sensing	Treats bacterial and fungal infections, wound healing, and skin infections
Antiviral	Curcumin, Essential oils	Inhibits viral replication, interferes with viral protein expression	Potential activity against influenza, hepatitis C virus (HCV), herpes simplex virus (HSV), and severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2)
Anticancer/ Antitumor	Curcumin	Induces apoptosis (caspase-3 activation), inhibits NF- κ B and signal transducer and activator of transcription-3 (STAT-3), suppresses angiogenesis, blocks epithelial-mesenchymal transition (EMT)	Breast, colon, lung, prostate, pancreatic cancer, used in adjuvant therapy in chemotherapy
Neuroprotective	Curcumin, Turmerones	Reduces neuroinflammation, oxidative stress, inhibits amyloid plaque formation, and modulates neurotransmitters	Used in Alzheimer's, Parkinson's, and Huntington's diseases
Hepatoprotective	Curcumin, Curcuminoids	Stabilizes hepatocyte membranes, enhances detoxifying enzymes, suppresses lipid peroxidation	Fatty liver disease, hepatitis, cirrhosis, toxin-induced liver damage
Metabolic/ Anti-	Curcumin	Enhances insulin sensitivity, reduces systemic inflammation, and regulates	Diabetes mellitus, insulin resistance,

diabetic		glucose metabolism	obesity
Cardioprotective	Curcumin, Turmerones	Inhibits platelet aggregation, improves endothelial function, and reduces oxidized low-density lipoprotein (LDL)	Hypertension, atherosclerosis, myocardial ischemia, dyslipidemia

Anti-inflammatory and Antioxidant Properties:

C. longa is broadly accepted for its potent anti-inflammatory and antioxidant activities, primarily associated with curcumin and related curcuminoids. Curcumin exerts its anti-inflammatory action by inhibiting key inflammatory mediators such as COX-2, LOX, and iNOS⁶². It also inhibits pro-inflammatory cytokines like TNF- α , IL-1 β , and IL-6. As a powerful antioxidant, curcumin neutralizes ROS and RNS, preventing oxidative damage to lipids, proteins, and Deoxyribonucleic Acid⁶³. It also enhances the activity of endogenous antioxidant enzymes such as SOD, catalase, and GPx. These combined effects make turmeric an effective natural agent in managing oxidative stress-related disorders, including arthritis, metabolic syndrome, and aging⁶⁴.

Antimicrobial and Antiviral Activities:

The essential oils and phenolic compounds in turmeric display marked antimicrobial activity against a broad spectrum of bacteria, fungi, and viruses. Curcumin and turmerones disrupt microbial cell membranes, inhibit quorum sensing (a cell-to-cell communication mechanism used by microorganisms), and interfere with nucleic acid synthesis, leading to microbial cell death⁶⁵. Research has shown effective antibacterial action against *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Bacillus subtilis*, as well as antifungal effects against *Candida albicans* and *Aspergillus niger*⁶⁶. Turmeric extracts also show antiviral properties, inhibiting viral replication of pathogens such as the influenza virus, HCV, HSV, and SARS-CoV-2⁶⁷. The combined antimicrobial and antiviral potential of *C. longa* supports its traditional use in wound healing, respiratory infections, and skin diseases⁶⁸.

Anticancer Potential:

Curcumin is one of the most widely studied natural compounds for its anticancer properties⁶⁹. It shows pleiotropic effects by targeting multiple cellular pathways involved in carcinogenesis, including cell proliferation, apoptosis, angiogenesis, and metastasis. Curcumin induces apoptosis in cancer cells through activation of caspase-3 and modulation of B-cell lymphoma-2 family proteins. It inhibits transcription factors like Nuclear Factor Kappa Light Chain Enhancer of NF- κ B and STAT-3, which regulate genes responsible for tumor growth and survival⁷⁰. Furthermore, curcumin interferes with angiogenic signaling (Vascular endothelial growth factor) and EMT, thereby suppressing tumor progression and metastasis⁷¹. In preclinical and clinical studies, curcumin has shown inhibitory effects against several cancers, including breast, colon, lung, prostate, and pancreatic cancer. Its synergistic action with conventional chemotherapeutic drugs improves efficacy and reduces drug resistance,

making it a potential supplementary therapy in cancer therapy⁷².

Neuroprotective and Hepatoprotective Effects:

The neuroprotective activities of *C. longa* are primarily mediated by curcumin's potential to attenuate oxidative stress, neuroinflammation, and amyloid plaque formation⁷³. It inhibits microglial activation and modulates neurotransmitter balance, thereby protecting neuronal health. Curcumin also crosses the blood-brain barrier, making it beneficial in the prevention and treatment of neurodegenerative disorders such as Alzheimer's, Parkinson's, and Huntington's diseases⁷⁴. Similarly, turmeric shows strong hepatoprotective effects against toxins and oxidative stress-induced hepatic injury. Curcumin stabilizes hepatocyte membranes, enhances detoxifying enzyme activity (like glutathione-S-transferase), and suppresses lipid peroxidation⁷⁵. It also suppresses inflammatory markers in the liver and promotes regeneration of hepatic tissue, thereby preventing conditions such as fatty liver disease, hepatitis, and cirrhosis⁷⁶.

Metabolic and Cardiovascular Benefits:

Curcumin shows considerable metabolic and cardioprotective effects, contributing to the management of diabetes, obesity, dyslipidemia, and hypertension. It improves insulin sensitivity by modulating insulin receptor signaling and reducing systemic inflammation. Turmeric also decreases blood glucose levels, triglycerides (TGs), and LDL cholesterol, while enhancing high-density lipoprotein (HDL) cholesterol levels⁷⁷. Cardioprotective actions are mediated through inhibition of platelet aggregation, improvement of endothelial function, and decrease of oxidized LDL-induced atherogenesis⁷⁸. Curcumin's antioxidant activities also prevent oxidative damage to cardiac tissue, reducing the risk of myocardial injury and ischemia. These diverse effects highlight turmeric's potential as a natural therapeutic agent in managing metabolic and cardiovascular disorders^{79,80}.

FORMULATION AND DELIVERY TECHNIQUES:

Despite its extensive pharmacological potential, curcumin, the principal bioactive compound of *C. longa*, suffers from poor water solubility, low gastrointestinal (GIT) absorption, rapid metabolism, and systemic elimination, which limit its therapeutic efficacy. To overcome these challenges, modern formulation and delivery strategies have been developed to increase bioavailability, stability, and targeted delivery⁸¹.

Nanocarriers and Bioavailability Enhancement Strategies:

Nanotechnology-based delivery systems have emerged as a novel strategy to improve curcumin's

pharmacokinetic (PK) profile. Various nanocarriers such as liposomes, solid lipid nanoparticles (SLNs), nanostructured lipid carriers, polymeric nanoparticles, micelles, and nanoemulsions have been employed to encapsulate curcumin^{82,83}. These systems increase solubility, protect the compound from metabolic degradation, and aid controlled and targeted release. For example, liposomal curcumin enhances cellular uptake and prolongs circulation time, whereas polymeric nanoparticles allow sustained release and improved tissue distribution⁸⁴. Nanoemulsions and micellar formulations improve oral bioavailability by enhancing solubilization in the GIT. Additionally, approaches such as combined administration with piperine, phospholipid complexes (phytosomes), and solid dispersions have shown significant improvement in curcumin absorption and systemic bioavailability⁸⁵.

Herbal Formulations and Combination Therapies:

Traditional and modern herbal formulations often combine turmeric with other medicinal plants to achieve synergistic therapeutic effects. Turmeric is incorporated in various forms such as powders,

capsules, tablets, tinctures, extracts, and nutraceutical formulations⁸⁶. Combination therapies utilize the synergistic pharmacological activities of curcumin and other plant bioactive compounds, enhancing efficacy while minimizing side effects and adverse effects. Examples include formulations of turmeric with ginger (*Zingiber officinale*) for anti-inflammatory activity, black pepper (*Piper nigrum*) for enhanced bioavailability, or boswellia (*Boswellia serrata*) for joint health⁸⁷. Polyherbal formulations are commonly used in nutraceuticals, dietary supplements, and functional foods to provide holistic benefits such as antioxidant support, anti-inflammatory effects, and metabolic regulation. Modern pharmaceutical technologies have also promoted the development of curcumin-loaded transdermal gels, topical ointments, and oral nanocapsules, expanding its therapeutic application in localized and systemic disorders (Table 4)⁸⁸⁻⁹⁵. By combining advanced delivery systems with traditional knowledge, turmeric-based formulations achieve improved bio-efficacy, patient compliance, and clinical relevance in conventional medicine⁹⁶.

Table 4: Herbal Formulations and Combination Therapies of *C. longa*

Formulation type	Combinations	Mechanism of action	Therapeutic significance
Powder/ Capsule	Turmeric rhizome powder	Easy oral administration, delivers curcuminoids	General health, antioxidant support, and anti-inflammatory effects
Extracts/ Standardized extracts	Curcumin-rich turmeric extract	Concentrated bioactive delivery	Anti-inflammatory, hepatoprotective, and metabolic regulation
Polyherbal capsule/ Tablet	Turmeric + Ginger	Synergistic anti-inflammatory and digestive support	Arthritis, joint pain, GIT disorders
	Turmeric + Black pepper	Piperine enhances curcumin bioavailability	Enhanced systemic absorption and efficacy
	Turmeric + Boswellia	Synergistic inhibition of inflammatory mediators	Osteoarthritis, rheumatoid arthritis, and joint health
Functional foods/ Beverages	Turmeric + Milk/ Honey	Nutritional supplementation and antioxidant effect	General wellness, immunity support
Topical formulations (Gels, ointments, creams)	Turmeric + Aloe vera/ Essential oils	Anti-inflammatory, wound healing, skin soothing	Skin disorders, minor burns, dermatitis
Nanocarrier-based formulations	Curcumin-loaded liposomes, nanoparticles, micelles	Controlled release, enhanced solubility, and absorption	Targeted therapy for cancer, neurodegenerative, and metabolic disorders
Ayurvedic/ Traditional formulations	Chyawanprash (Turmeric + multiple herbs)	Immunomodulation, rejuvenation	General health, antioxidant, and anti-aging benefits

CLINICAL STUDIES AND THERAPEUTIC APPLICATIONS:

C. longa has shifted from a traditional herbal remedy to a widely studied natural therapeutic agent in modern clinical practices. Its principal bioactive, curcumin, has been the focus of multiple clinical trials investigating its

efficacy in a variety of health conditions, confirming many of its traditional uses with scientific evidence⁹⁷.

Evidence Based Clinical Findings:

Clinical studies have highlighted the anti-inflammatory and antioxidant benefits of turmeric in several chronic diseases and conditions. Randomized controlled trials

(RCTs) in patients with osteoarthritis and rheumatoid arthritis have shown that curcumin supplementation significantly reduces joint pain, stiffness, and inflammatory markers, with comparable efficacy to non-steroidal anti-inflammatory drugs (NSAIDs) but with fewer side effects^{98,99}. In metabolic disorders, curcumin has shown promising effects on type 2 diabetes and dyslipidemia. Clinical trials report improvements in glycemic control, insulin sensitivity, TG levels, and HDL cholesterol, supporting its role as a supportive in managing metabolic syndrome¹⁰⁰. Turmeric has also been evaluated in neurodegenerative disorders. Clinical studies in geriatric populations suggest that curcumin

supplementation can improve cognitive function, attention, and mood, likely through its antioxidant, anti-inflammatory, and anti-amyloidogenic activities¹⁰¹. While larger long-term clinical trials are ongoing, preliminary results indicate neuroprotective activity^{102,103}. In the context of hepatic and GIT health, curcumin has been shown to reduce liver enzyme levels, improve fatty liver disease markers, and relieve dyspepsia. Furthermore, multiple clinical studies report turmeric's cardioprotective effects, including reduced LDL oxidation, improved endothelial function, and decreased systemic inflammation (Table 5)¹⁰⁴⁻¹¹⁰.

Table 5: Evidence Based Clinical Findings of *C. longa*

Therapeutic area	Clinical evidence	Mechanism of action	Study highlights
Anti-inflammatory activity	Multiple RCTs show curcumin reduces markers like C-Reactive Protein, TNF- α , and IL-6 in chronic inflammatory diseases such as rheumatoid arthritis and osteoarthritis	Inhibits NF- κ B activation, COX-2, and LOX pathways, and suppresses pro-inflammatory cytokine release	Daily doses of 500 to 2000 mg curcumin improved joint pain and swelling
Antioxidant effect	Clinical trials show increased serum antioxidant capacity and decreased oxidative stress biomarkers after curcumin supplementation	Scavenges ROS, enhances activities of antioxidant enzymes like SOD and catalase, and upregulates Nuclear Factor Erythroid-2 Related Factor-2 pathway	Curcumin supplementation (1g/day) improved oxidative stress indices in metabolic syndrome patients
Cardiovascular protection	Shown to improve endothelial function and lipid profile; reduces LDL, TGs, and total cholesterol	Enhances nitric oxide production, ROS, and systemic inflammation	Meta-analysis of 8 RCTs (2021) confirmed improvement in lipid metabolism and vascular function
Antidiabetic and metabolic regulation	Demonstrated significant reduction in fasting glucose, Hemoglobin A1c, and insulin resistance in diabetic and prediabetic subjects	Modulates the Activated Protein Kinase pathway and Peroxisome Proliferator Activated Receptor Gamma expression, improves β -cell function and insulin sensitivity	Curcumin prevented diabetes development in prediabetic individuals
Neuroprotective and cognitive effects	Improved memory, mood, and cognitive function in mild cognitive impairment and Alzheimer's patients	Reduces amyloid plaque formation, inhibits monoamine oxidase enzymes, and enhances Brain Derived Neurotrophic Factor levels	Small RCTs show that 400 to 800 mg/day curcumin improved attention and memory
Anticancer activity	Early phase clinical trials indicate suppression of tumor proliferation and improved patient tolerance when used adjunctively	Induces apoptosis, suppresses angiogenesis, and inhibits multiple oncogenic signaling pathways (e.g., PI3K/Akt, MAPK)	Curcumin has been shown to enhance chemotherapy efficacy and reduce side effects in colorectal and breast cancer studies
GIT and liver protection	Improved symptoms in irritable bowel syndrome, ulcerative colitis, and non-alcoholic fatty liver disease patients	Enhances bile secretion, modulates gut microbiota, and reduces hepatic oxidative stress	RCTs show curcumin improved bowel symptom scores and reduced Alanine Aminotransferase/Aspartate Aminotransferase levels in non-alcoholic fatty liver disease
Immunomodulatory effects	Strengthens immune defense and reduces autoimmune response markers	Regulates T-cell proliferation, antibody response, and cytokine balance (T-helper type 1/type 2 cells)	Studies show reduced infection rate and inflammatory cytokines after 8 weeks of supplementation

Role in Conventional Medicine and Nutraceuticals:

The clinical authentication of turmeric has facilitated its combination into conventional medicine, nutraceuticals, and functional foods. Turmeric-based dietary supplements, standardized extracts, and curcumin-enhanced formulations are now widely available globally¹¹¹. Its inclusion in functional foods, beverages, and health-promoting products targets general health, immune support, antioxidant protection, and chronic disease prevention¹¹². Modern formulation techniques, such as nanoencapsulation, liposomal curcumin, and phytosome complexes, have enhanced the bioavailability and treatment effectiveness of curcumin, enabling its use in systemic therapy. Moreover, turmeric is increasingly used as an adjuvant therapy in combination with conventional drugs for cancer, metabolic disorders, neurodegenerative diseases, and inflammatory conditions, improving efficacy while minimizing adverse effects¹¹³. Overall, clinical evidence positions *C. longa* as a multifunctional therapeutic agent, bridging the gap between traditional wisdom and modern evidence-based medicine. Its application in nutraceuticals and functional foods further underscores its role in preventive health, wellness promotion, and integrative therapy, making it a key natural compound in modern healthcare approaches¹¹⁴.

ONGOING CLINICAL TRIALS ON *C. LONGA* FORMULATIONS:

The table below presents 25 of the most recent and ongoing clinical trials investigating the therapeutic efficacy of *C. longa* (Table 6)¹¹⁵⁻¹³⁹. These studies highlight the growing global interest in turmeric-based formulations as potential therapeutic agents for inflammatory, metabolic, oncologic, cardiovascular, and dermatologic conditions^{140,141}. Recent advances in formulation science, such as liposomal curcumin, phytosome (lecithin-based) systems, curcumin piperine combinations, berberine curcumin blends, and standardized curcuminoid capsules, are designed to overcome curcumin's traditionally low bioavailability¹⁴². Clinical trials are currently evaluating these innovative formulations across different delivery routes, including oral, topical, and local (intra-anal) applications¹⁴³. The variety of sponsors, from academic hospitals to nutraceutical companies, shows an integration of pharmaceutical and dietary supplement research. Most trials are in Phase I or Phase II, focusing on bioavailability, safety, and anti-inflammatory efficacy, while several explore adjunctive roles in cancer therapy, diabetes, and cardiovascular disease¹⁴⁴. Together, these ongoing investigations signify a major translational initiative to validate *C. longa* as a scientifically based therapeutic supplement. The results of these studies will determine the clinical significance of turmeric-derived compounds in evidence-based medicine, potentially facilitating the way for standardized, bioavailable curcumin formulations in future pharmacotherapy¹⁴⁵.

Table 6: Ongoing Clinical Trials on Curcumin Based Formulations

Clinical trial no.	Formulation title	Phase	Status	Year
NCT06063486	Curcumin (C3 complex + Bioperine) to improve inflammatory response - oral supplement formulation	Phase II	Recruiting/ Active	2025
NCT07063056	Curcumin and Astaxanthin - supplement for lowering TGs and inflammation (oral nutraceutical)	Not drug phase (supplement RCT)	Not yet recruiting/ Registered 2025	2025
NCT06626230	Safety of Anal Curcumin - local/intra-anal curcumin delivery (dose-escalation)	Phase I	Not yet recruiting/ Registered 2025	2025
NCT05768919	Liposomal Curcumin in combination with radiotherapy - liposomal formulation	Phase I/ early	Recruiting/ Active	2024
NCT05753436	Curcumin's effect on diabetic patients with atherosclerotic complications - oral curcumin supplement	Not specified	Recruiting/ Active	2024 to 2025
NCT05596214	Curcumin + Berberine combination (oral nutraceutical) - metabolic/inflammatory endpoints	Not specified	Active/ Recruiting (recent registration)	2023 to 2024
NCT05542394	Dose ranging curcumin preparation - PK/ dose assessment (formulation under development)	Phase I/ dose-ranging	Active / Recruiting	2023 to 2024
NCT04896164	Curcumin to reduce mucositis in transplant patients - oral curcumin (anti-inflammatory)	Interventional (not classical drug phase)	Completed	2021 to 2023

NCT04687449	Oral curcumin in chronic obstructive pulmonary disease - capsule formulation for inflammation/ respiratory outcomes	Phase II	Completed	2021 to 2023
NCT04315350	Curcumin for hepatic insulin resistance / Non-Alcoholic Fatty Liver Disease (NAFLD) - oral curcumin formulation	Phase II/ interventional	Completed/ Active (2020 to 2022)	2020 to 2022
NCT04294836	Curcumin in advanced cervical cancer - topical/ adjunct or intralesional use	Interventional oncology (phase not classical)	Recruiting/ Active (updates through 2022)	2020 to 2022
NCT04109742	Curcumin for Pediatric NAFLD - oral formulation (capsule/ syrup)	Phase IIa (pediatric RCT)	Recruiting/ Active (posted 2019, updates later)	2019 to 2022
NCT03953261	Curcumin in Systemic Lupus Erythematosus - oral curcumin capsules (2 g/day)	Interventional (not specified phase)	Completed	2019 to 2021
NCT03935958	Curcumin in Kidney Transplant Recipients - oral curcumin supplement	Interventional	Completed	2019 to 2022
NCT03795792	Oral curcumin for metabolic syndrome - RCT (capsule formulation)	Interventional (randomized)	Completed	2018 to 2021
NCT03769766	Curcumin to prevent progression of low-risk localized prostate cancer - oral curcumin (C3 complex)	Phase II	Active/ Recruiting updates across years	2018 (updated in 2025)
NCT03621865	Comparative PK study of multiple turmeric extract formulations (bioavailability/ PK)	Phase I (PK)	Completed	2018 to 2019
NCT03223883	Curcumin effects on vascular function in chronic kidney disease - oral curcumin formulation (vascular endpoints)	Interventional (phase not classical)	Active/ Recruiting updates 2018 to 2024	2018 to 2024
NCT03065504	Turmeric-containing tablets effects on sebum/ skin endpoints - oral turmeric tablets	Interventional	Completed	2017 to 2019
NCT03066791	Turmeric and turmeric-containing tablets on sebum production - oral turmeric tablets	Interventional	Completed	2017 to 2019
NCT02598726	Curcumin + Piperine in ureteric stent pain - oral curcumin with piperine (bioenhancer)	Interventional	Completed	2016 to 2018
NCT01489592	Curcumin effect on iron metabolism in healthy volunteers - oral curcuma longa 6 g dosing	Phase I/ pharmacology	Completed	2012 to 2014
NCT06407609	Lecithin-based preparation containing <i>C. longa</i> and <i>Boswellia serrata</i> - microbiota and GIT endpoints (lecithin phytosome formulation)	Not specified (nutraceutical)	Recruiting/ Active (recent registration)	2023 to 2024
NCT07183215	Efficacy test of Curcuminoid Standardized Turmeric Capsules - osteoarthritis knee	Not a classical drug phase (herbal RCT)	Not yet recruiting/ Registered 2025	2025
NCT06177483	Bioavailability evaluation of CurQ+ curcumin formulation - PK/ bioavailability study	Phase I/ bioavailability	Completed (PK dates 2024)	2024 (PK completion)

CHALLENGES AND FUTURE DIRECTIONS:

Limitations in Pharmacokinetics and Stability:

Although the broad therapeutic potential of *C. longa* and its key active constituent curcumin is well recognized, major challenges remain in its pharmacokinetic properties¹⁴⁶. Curcumin shows poor aqueous solubility, low GIT absorption, rapid metabolism, and systemic elimination, leading to limited bioavailability. These limitations constrain its effective concentration in plasma and target tissues, thereby decreasing

therapeutic efficacy¹⁴⁷. Additionally, curcumin is chemically unstable, susceptible to degradation under alkaline or light-exposed conditions, which further challenges formulation development. To address these limitations, advanced strategies such as nanoparticle encapsulation, liposomal delivery, SLNs, micelles, and phospholipid complexes have been investigated¹⁴⁸. However, although promising preclinical results, translating these formulations to reproducible and regulatory-compliant products remains challenging due to variable reproducibility, cost, and safety validation¹⁴⁹.

Opportunities for Novel Drug Development:

The increasing understanding of curcumin's molecular mechanisms provides promising opportunities for novel drug discovery and development¹⁵⁰. Curcumin regulates multiple signaling pathways such as NF-κB, MAPK, and PI3K/Akt, making it a potential lead compound for multitarget therapy in chronic and inflammatory diseases, cancer, neurodegenerative disorders, and metabolic syndromes¹⁵¹. Advancements in structure-

activity relationship studies have led to the synthesis of curcumin analogs and derivatives with improved stability, solubility, and bioavailability¹⁵². Moreover, combination therapy approaches involving curcumin with standard drugs have shown synergistic effects, facilitated dose reduction, and minimized side effects¹⁵³. The incorporation of AI-driven drug discovery and nanotechnological delivery platforms further opens new aspects for targeted and precision medicine applications of *C. longa*-based formulations (Table 7)¹⁵⁴⁻¹⁶⁰.

Table 7: Opportunities for Novel Drug Development from *C. longa*

Opportunity area	Description	Approaches	Expected outcome
Multitarget therapeutic potential	Curcumin modulates multiple molecular pathways involved in inflammation, oxidative stress, and cancer	Targets NF-κB, MAPK, PI3K/Akt signaling pathways	Effective in chronic diseases like cancer, diabetes, and neurodegenerative disorders
Curcumin analog development	Structural modification to improve stability and bioavailability	Synthesis of analogs such as EF24, 3,4-difluorobenzylidene curcumin, and GO-Y030	Enhanced solubility, metabolic stability, and therapeutic potency
Nano formulations	Utilization of nanotechnology to overcome pharmacokinetic limitations	Curcumin-loaded nanoparticles, liposomes, micelles, SLNs	Improved absorption, sustained release, and targeted delivery
Combination therapy	Use of curcumin with conventional drugs for synergistic effects	Curcumin + paclitaxel, Curcumin + metformin	Reduced dosage requirement and minimized side effects
Bioenhancer combined administration	Use of natural bioenhancers to increase curcumin absorption	Piperine from <i>Piper nigrum</i> , quercetin, or resveratrol	Enhanced oral bioavailability and therapeutic concentration
Phytopharmaceutical development	Transformation of standardized extracts into regulated herbal drugs	Development of fixed-dose herbal formulations	Compliance with regulatory standards
AI and Computational Drug Design	Application of AI for curcumin analog screening and molecular docking	In-silico modeling for receptor interaction prediction	Accelerated lead optimization and targeted drug design
Controlled and Targeted delivery systems	Site-specific delivery to enhance efficacy and reduce systemic toxicity.	Curcumin-loaded transdermal patches, hydrogels, and implants	Controlled drug release and improved patient compliance
Synergistic herbal formulations	A combination of <i>C. longa</i> with other medicinal herbs.	Formulations with <i>Withania somnifera</i> or <i>Glycyrrhiza glabra</i>	Enhanced therapeutic spectrum and holistic efficacy
Personalized and Precision Medicine	Integration of pharmacogenomics with curcumin therapy	Individualized dosing based on genetic profiles	Optimized therapeutic response with minimal adverse effects

INTEGRATING TRADITIONAL KNOWLEDGE WITH EMERGING RESEARCH:

The traditional use of *C. longa* in Ayurveda, Siddha, and Traditional Chinese Medicine offers a rich database of ethnopharmacological evidence¹⁶¹. However, modern scientific validation of these practices remains limited. To bridge this gap, there is a strong need for holistic approaches combining traditional wisdom with advanced research methodologies¹⁶². This includes

standardization of herbal raw materials, use of validated biomarkers, and clinical trial designs that coordinate with regulatory guidelines. Collaborative research between traditional healers and pharmacologists can promote the development of evidence-based herbal formulations¹⁶³. Additionally, global harmonization of regulatory frameworks, including the WHO, Food and Drug Administration, and the European Medicines Agency guidelines for herbal medicines, will accelerate the acceptance of *C. longa*-derived products in the global

market¹⁶⁴. Ultimately, such incorporation will increase scientific authenticity, ensure patient safety, and promote long-term utilization of this ancient therapeutic source¹⁶⁵.

CONCLUSION:

C. longa, the golden herb of Ayurveda, embodies the successful integration of traditional wisdom and modern scientific advancement. From its ancient roots as a sacred and therapeutic spice in Indian traditional systems of medicine to its advanced role as a globally recognized phytopharmaceutical, turmeric has shown an exceptional range of biological and therapeutic activities. Clinical studies substantiate its efficacy in inflammatory, metabolic, cardiovascular, neurodegenerative, hepatic, and neoplastic disorders, confirming its potential as both a preventive and complementary therapeutic agent. However, challenges related to curcumin's low bioavailability, chemical lability, and pharmacokinetic limitations continue to restrict its full therapeutic application. The future of *C. longa* exists in multidisciplinary integration combining green chemistry extraction, nanocarrier delivery, and AI-assisted drug discovery to develop bioavailable derivatives and standardized formulations compliant with global regulatory standards. Equally important is the ethical incorporation of traditional knowledge with modern pharmacological validation to ensure sustainability, safety, and clinical reliability. Thus, *C. longa* stands as a model phytopharmaceutical that bridges ancient ethnomedicine and modern evidence-based therapeutics. Its journey from kitchen spice to clinical therapeutic agent showcases how traditional botanical knowledge, when explored through systematic scientific methodologies, can yield innovative strategies for global health and personalized medicine.

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