COMPREHENSIVE STUDY OF TURMERIC AND ITS MAIN COMPOUND CURCUMIN

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Abstract

Curcumin is a hydrophilic polyphenolic compound of turmeric rhizome (Curcuma longa) that has secured vast interest in scientific circles due to its health benefit potential. The present review is a critical synthesis of the literature on turmeric and curcumin, including their chemical properties, pharmacological activities, therapeutic applications, and such challenges as poor bioavailability. The Review Methodology consisted of a systematic search of peer-reviewed databases and journals that provided articles on turmeric, curcumin, and their effects on health, and included exclusively the articles that are recent (not older than about 5 years) and have high-quality clinical evidence. Findings and general at a glance point to the conclusion that curcumin is safe and well-tolerated in most cases with doses up to a few grams a day with an early suggestion of effective treatment as an adjunct in inflammatory diseases, oncology, and other treatment systems but the harder working meta-analyses have shown that many are not yet conclusively proven due to lack of methodological strength in these studies. These findings are critically assessed in the Discussion section as the paper points to the dichotomy existing between the attractive pharmacological profile of curcumin and barriers to its subsequent implementation in clinical settings. To sum up, curcumin is an interesting but complicated nutraceutical; it is a multi-targeted nutraceutical with numerous bioactivities, but its clinical effects require a solution to bioavailability factors, and efficacy needs to be demonstrated by properly designed trials. The future of research is on improved delivery systems to enhance the pharmacokinetics of curcumin and larger/quality studies to ascertain its therapeutic worth in different uses.

Keywords: *curcuma longa, curcuminoids, curcumin, Anti-cancer, Anti-asthmatic, osteoarthritis, Anti-inflammatory, Anti-oxidant, Chemoprotective, Cardioprotective*

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1. Introduction

1.1 History and Significance of Turmeric

Turmeric (*Curcuma longa* L.), commonly referred to as the "Golden Spice" or "Indian Saffron," is a perennial rhizomatous herb belonging to the family **Zingiberaceae**. It is indigenous to the Indian subcontinent and Southeast Asia, where it has been cultivated for more than 4,000 years for its medicinal, culinary, religious, and cultural significance. The dried rhizome of turmeric has historically been valued as a natural coloring agent, flavoring spice, food preservative, and therapeutic herb. Ancient Indian texts such as the *Atharva Veda*, *Charaka Samhita*, and *Sushruta Samhita* extensively describe the use of turmeric in treating wounds, skin disorders, digestive ailments, respiratory diseases, and inflammatory conditions. Owing to its sacred status in Hindu culture, turmeric has also been used in religious ceremonies, marriage rituals, and traditional festivals, symbolizing purity, prosperity, and good health (Prasad & Aggarwal, 2011; Hewlings & Kalman, 2017).

India is the world's largest producer, consumer, and exporter of turmeric, contributing approximately 80% of global production. The increasing recognition of turmeric's therapeutic value has transformed it into a commercially important medicinal plant with widespread applications in pharmaceuticals, nutraceuticals, cosmetics, and functional foods. Scientific investigations have revealed that the remarkable medicinal properties of turmeric are primarily attributed to its major polyphenolic constituent, **curcumin**, along with other curcuminoids and volatile oils. These bioactive compounds exhibit diverse pharmacological activities, including antioxidant, anti-inflammatory, antimicrobial, anticancer, hepatoprotective, cardioprotective, and neuroprotective effects. Consequently, turmeric has emerged as one of the most extensively researched medicinal plants worldwide, bridging the gap between traditional herbal medicine and evidence-based modern therapeutics (Gupta et al., 2013; Amalraj et al., 2017).

1.2 Traditional and Modern Medicinal Uses

Turmeric has occupied a central position in traditional healthcare systems, including Ayurveda, Siddha, Unani, and Traditional Chinese Medicine (TCM), for centuries. In Ayurveda, turmeric is classified as a *Rasayana* (rejuvenating agent) and is believed to balance the Kapha and Vata doshas due to its bitter (*Tikta*) and pungent (*Katu*) taste with hot potency (*Ushna Virya*). Traditionally, it has been employed for the treatment of wounds, burns, skin infections, arthritis, gastrointestinal disorders, liver diseases, diabetes, respiratory ailments, menstrual irregularities, and microbial infections. Turmeric paste has long been applied externally to promote wound healing and reduce inflammation, whereas turmeric

milk has been consumed to relieve sore throat, cough, common cold, and digestive discomfort (Chainani-Wu, 2003).

Modern scientific research has validated many of these traditional applications through extensive pharmacological and clinical investigations. Curcumin, the principal bioactive constituent of turmeric, has been shown to regulate numerous molecular targets involved in inflammation, oxidative stress, apoptosis, angiogenesis, and cellular proliferation. It modulates several important signaling pathways, including **NF-κB, MAPK, PI3K/Akt, JAK/STAT, and Nrf2,** thereby contributing to its broad therapeutic potential. Experimental and clinical studies have demonstrated that curcumin exhibits antioxidant, anti-inflammatory, antimicrobial, antiviral, anticancer, antidiabetic, cardioprotective, neuroprotective, hepatoprotective, nephroprotective, immunomodulatory, and wound-healing activities. Furthermore, advances in pharmaceutical sciences have facilitated the development of nanoformulations, liposomes, phytosomes, solid lipid nanoparticles, and other novel drug delivery systems to overcome the poor aqueous solubility and limited bioavailability of curcumin. As a result, turmeric has become an important component of functional foods, dietary supplements, cosmetic formulations, and complementary therapeutic products worldwide (Hewlings & Kalman, 2017; Kunnumakkara et al., 2017; Tomeh et al., 2019).

1.3 Objectives and Scope of the Review

Turmeric and its principal bioactive constituent, curcumin, have attracted considerable scientific attention because of their diverse pharmacological properties and extensive therapeutic potential. Although numerous studies have investigated various aspects of turmeric and curcumin, the available information remains scattered across botanical, phytochemical, pharmacological, pharmaceutical, and clinical literature. Therefore, a comprehensive review integrating these multidisciplinary findings is essential to provide a holistic understanding of their medicinal importance.

The primary objective of this review is to critically summarize the current knowledge regarding turmeric and curcumin by discussing their botanical characteristics, phytochemical composition, chemical properties, extraction methods, pharmacological activities, molecular mechanisms of action, pharmaceutical formulations, clinical applications, safety profile, and recent advances in drug delivery technologies. Additionally, this review highlights the major challenges associated with curcumin, particularly its poor bioavailability and stability, while discussing innovative strategies developed to enhance its therapeutic efficacy. By consolidating evidence from recent scientific studies, this review aims to serve as a valuable reference for researchers, clinicians, pharmaceutical scientists, and healthcare professionals

involved in the development and therapeutic application of turmeric-based products (Amalraj et al., 2017; Kunnumakkara et al., 2017).

2. Botanical Profile and Phytochemistry

2.1 Taxonomy and Botanical Description

Turmeric (*Curcuma longa* L.) is a perennial rhizomatous herb belonging to the family Zingiberaceae. It is one of the most economically important species of the genus *Curcuma* and has been cultivated for thousands of years for its medicinal and culinary value. The plant is characterized by a thick yellow-orange underground rhizome, which is the principal medicinal part. It grows up to 60-100 cm in height and possesses large lanceolate leaves with pale yellow flowers enclosed by green bracts. Propagation occurs mainly through rhizomes rather than seeds (Ravindran et al., 2007; Amalraj et al., 2017).

Table 1: Scientific Classification

Taxonomic Rank	**Classification**
Kingdom	Plantae
Family	Zingiberaceae
Genus	*Curcuma*
Species	*Curcuma longa* L.

2.2 Geographical Distribution and Cultivation

Turmeric is native to India and Southeast Asia and is widely cultivated in tropical and subtropical regions. India is the largest producer and exporter, accounting for nearly 80% of global production. The crop grows best in warm, humid climates with well-drained loamy soil (pH 5.5-7.5) and temperatures between 20-35°C. It is propagated using rhizome pieces and harvested after 7-9 months. Harvested rhizomes are boiled, dried, and polished before being processed into powder or used for curcumin extraction (Prasad & Aggarwal, 2011; Amalraj et al., 2017).

2.3 Phytochemical Constituents

Turmeric contains more than 235 bioactive compounds, including curcuminoids, essential oils, phenolics, flavonoids, terpenoids, proteins, carbohydrates, vitamins, and minerals. Among these, curcuminoids are the major active constituents responsible for most of the pharmacological activities, while essential oils contribute to its aroma and therapeutic properties (Li et al., 2011; Hewlings & Kalman, 2017).

2.4 Curcuminoids and Essential Oils

Curcuminoids constitute approximately **2-8%** of dried turmeric rhizomes and include:

- **Curcumin:** 70-80%
- **Demethoxycurcumin:** 15-20%
- **Bisdemethoxycurcumin:** 3-5%

Curcumin is the principal bioactive compound exhibiting antioxidant, anti-inflammatory, antimicrobial, anticancer, antidiabetic, and neuroprotective activities. Turmeric also contains 3-7% essential oils, mainly ar-turmerone, α-turmerone, β-turmerone, zingiberene, germacrone, and curlone, which contribute to its characteristic aroma and possess antimicrobial and anti-inflammatory properties (Kunnumakkara et al., 2017; Amalraj et al., 2017).

2.5 Nutritional Composition

Besides its medicinal constituents, turmeric is a rich source of carbohydrates, dietary fiber, proteins, vitamins, and minerals, making it a valuable functional food.

Table 2. Nutritional composition of dried turmeric powder (per 100 g)

Component	Amount
Energy	354 kcal
Carbohydrates	64.9 g
Protein	7.8 g
Fat	9.9 g
Dietary Fiber	21.1 g
Calcium	183 mg
Iron	41.4 mg
Magnesium	193 mg
Potassium	2525 mg
Vitamin C	25.9 mg

The nutritional value, together with its phytochemical richness, makes turmeric an important ingredient in functional foods, nutraceuticals, and pharmaceutical formulations (USDA FoodData Central, 2024; Hewlings & Kalman, 2017).

3. Curcumin: Chemistry and Pharmacokinetics

3.1 Chemical Structure and Properties

Curcumin (diferuloylmethane) is the principal bioactive polyphenolic compound isolated from the rhizomes of *Curcuma longa* L., accounting for approximately **70-80%** of total

curcuminoids. Its molecular formula is **$C_{21}H_{20}O_6$** with a molecular weight of **368.38 g/mol**. Structurally, curcumin consists of two aromatic phenolic rings connected by a seven-carbon α,β-unsaturated diketone linker, which exists in keto-enol tautomeric forms. Curcumin is a bright yellow crystalline powder, practically insoluble in water but readily soluble in organic solvents such as ethanol, methanol, acetone, and dimethyl sulfoxide (DMSO). The presence of hydroxyl and methoxy groups contributes to its strong antioxidant and free radical scavenging properties (Anand et al., 2007; Hewlings & Kalman, 2017).

3.2 Biosynthesis

Curcumin is synthesized in turmeric rhizomes through the phenylpropanoid pathway. The biosynthesis begins with the amino acid phenylalanine, which is converted into feruloyl-CoA through the action of phenylalanine ammonia-lyase (PAL) and other enzymes. Curcumin synthase (CURS) catalyzes the condensation of feruloyl-CoA with malonyl-CoA to produce curcumin. The biosynthesis is influenced by genetic factors, environmental conditions, and cultivation practices, which affect the final curcumin content in turmeric rhizomes (Katsuyama et al., 2009).

3.3 Absorption, Distribution, Metabolism, and Excretion (ADME)

Curcumin exhibits **poor oral absorption** due to its low aqueous solubility and limited intestinal permeability. Following absorption, it is widely distributed to tissues but is rapidly metabolized in the liver and intestinal mucosa to glucuronide and sulfate conjugates. It also undergoes reduction to tetrahydrocurcumin and hexahydrocurcumin, which retain certain biological activities. Most ingested curcumin is excreted through the feces, while only a small fraction is eliminated in urine. Rapid metabolism and elimination contribute to its low systemic availability after oral administration (Anand et al., 2007; Nelson et al., 2017).

3.4 Bioavailability and Stability

The clinical application of curcumin is limited by its **poor bioavailability**, resulting from low water solubility, poor intestinal absorption, rapid metabolism, and rapid systemic elimination. In addition, curcumin is chemically unstable under alkaline conditions and undergoes degradation upon exposure to light, heat, and oxygen. To overcome these limitations, several approaches such as co-administration with **piperine**, encapsulation in nanoparticles, liposomes, phytosomes, micelles, and solid lipid nanoparticles have been developed to enhance its stability, absorption, and therapeutic efficacy (Hewlings & Kalman, 2017; Kunnumakkara et al., 2017).

4. Conventional Extraction Methods

Extraction is a crucial step in obtaining curcumin from turmeric (*Curcuma longa* L.) rhizomes. Conventional extraction methods are widely used because of their simplicity, cost-effectiveness, and ability to produce satisfactory yields of curcuminoids. These methods primarily employ organic solvents such as ethanol, methanol, acetone, ethyl acetate, and hexane, selected based on the polarity of the target compounds. The most commonly used conventional extraction techniques include maceration, Soxhlet extraction, and reflux extraction (Li et al., 2011; Amalraj et al., 2017).

4.1 Maceration

Maceration is one of the simplest and oldest extraction techniques used for isolating curcumin from dried turmeric rhizomes. In this method, finely powdered turmeric is soaked in an appropriate solvent, such as ethanol or methanol, at room temperature for **24-72 hours** with occasional stirring. During this period, the solvent penetrates the plant cells and dissolves the curcuminoids. The extract is then filtered, and the solvent is removed using rotary evaporation to obtain a concentrated extract.

Advantages

- Simple and inexpensive.
- Requires minimal equipment.
- Suitable for heat-sensitive compounds.

Limitations

- Long extraction time.
- Higher solvent consumption.
- Lower extraction efficiency than other methods.

4.2 Soxhlet Extraction

Soxhlet extraction is the most commonly used conventional method for extracting curcumin due to its high extraction efficiency. In this technique, powdered turmeric is placed in a cellulose extraction thimble inside a Soxhlet apparatus. The extraction solvent is heated until it vaporizes, and the vapor condenses into the extraction chamber containing the sample. Once the chamber fills, the solvent carrying dissolved curcuminoids siphons back into the boiling flask. This cycle is repeated continuously for **4-8 hours**, allowing complete extraction of curcumin.

Among conventional techniques, Soxhlet extraction generally provides the **highest yield** because fresh solvent repeatedly comes into contact with the plant material.

Advantages

- High extraction efficiency.
- Better recovery of curcuminoids.
- Continuous extraction without replacing solvent.

Limitations

- Long extraction duration.
- High solvent and energy consumption.
- Possible degradation of heat-sensitive compounds due to prolonged heating.

4.3 Reflux Extraction

Reflux extraction is another widely employed conventional technique in which powdered turmeric is heated with an organic solvent under reflux conditions. The solvent is continuously boiled and condensed back into the extraction vessel, preventing solvent loss while maintaining a constant extraction temperature. The extraction generally requires **1-3 hours**, making it faster than maceration.

This method enhances the diffusion of curcuminoids into the solvent due to elevated temperature and continuous solvent circulation.

Advantages

- Faster extraction than maceration.
- Improved extraction efficiency.
- Reduced solvent loss through continuous condensation.

Limitations

- Heating may degrade thermolabile compounds.
- Lower extraction efficiency compared to Soxhlet in some cases.

Comparison of Conventional Extraction Methods

Method	**Principle**	**Extraction Time**	**Advantages**	**Limitations**
Maceration	Soaking powdered rhizomes in solvent at room temperature	24-72 h	Simple, economical, suitable for heat-sensitive compounds	Low yield, long extraction time
Soxhlet Extraction	Continuous hot solvent extraction through repeated reflux cycles	4-8 h	High extraction efficiency, maximum curcumin yield	High solvent and energy consumption, prolonged heating
Reflux	Heating sample with	1-3 h	Faster extraction,	Risk of degradation

Extraction	solvent under reflux		good recovery	of heat-sensitive compounds

Overall, Soxhlet extraction remains the preferred conventional method for laboratory-scale isolation of curcumin because of its high extraction efficiency, whereas maceration is suitable for preliminary extraction of thermolabile compounds, and reflux extraction provides a balance between extraction time and yield (Li et al., 2011; Amalraj et al., 2017).

5. Pharmacological Activities

Curcumin, the principal bioactive constituent of *Curcuma longa* L., possesses a wide range of pharmacological activities due to its ability to modulate multiple cellular signaling pathways, enzymes, cytokines, and transcription factors. Numerous **in vitro**, **in vivo**, and clinical studies have demonstrated its therapeutic potential in the prevention and management of inflammatory, metabolic, infectious, cardiovascular, neurological, and neoplastic diseases. The major pharmacological activities of curcumin are discussed below.

5.1 Antioxidant Activity

Curcumin exhibits potent antioxidant activity by scavenging reactive oxygen species (ROS) and reactive nitrogen species (RNS), thereby protecting cells from oxidative damage. It enhances endogenous antioxidant defense systems by increasing the activities of superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), while reducing lipid peroxidation and oxidative stress. These properties contribute to its protective role against aging, cardiovascular diseases, diabetes, and neurodegenerative disorders. Furthermore, curcumin activates the **Nrf2 signaling pathway**, which regulates the expression of several antioxidant enzymes and cytoprotective proteins. Through these mechanisms, curcumin helps maintain cellular redox balance and minimizes oxidative damage associated with chronic diseases and environmental stress (Menon & Sudheer, 2007).

5.2 Anti-inflammatory Activity

Curcumin exerts significant anti-inflammatory effects by suppressing the activation of nuclear factor-kappa B (NF-κB) and inhibiting the production of pro-inflammatory mediators such as tumor necrosis factor-alpha (TNF-α), interleukin-1β (IL-1β), interleukin-6 (IL-6), cyclooxygenase-2 (COX-2), and inducible nitric oxide synthase (iNOS). These mechanisms make curcumin effective in reducing inflammation associated with arthritis, inflammatory bowel disease, psoriasis, and other chronic inflammatory disorders. In addition, curcumin inhibits the activation of macrophages and other inflammatory cells, thereby limiting tissue injury. Its anti-inflammatory effects have been widely demonstrated in both experimental and

clinical studies, supporting its use as a complementary therapeutic agent (Aggarwal & Harikumar, 2009).

5.3 Antimicrobial Activity

Curcumin possesses broad-spectrum antimicrobial activity against various bacterial, fungal, viral, and parasitic pathogens. It inhibits microbial growth by disrupting cell membrane integrity, preventing biofilm formation, and interfering with nucleic acid and protein synthesis. Studies have demonstrated inhibitory effects against *Staphylococcus aureus*, *Escherichia coli*, *Candida albicans*, and several pathogenic viruses, indicating its potential as a natural antimicrobial agent. Curcumin also enhances the effectiveness of certain conventional antibiotics by reducing microbial resistance and inhibiting quorum sensing mechanisms. These properties make it a promising candidate for the development of novel antimicrobial formulations (Teow et al., 2016).

5.4 Anticancer Activity

Curcumin has attracted considerable attention as a potential anticancer agent due to its ability to inhibit tumor initiation, proliferation, angiogenesis, invasion, and metastasis. It induces apoptosis, arrests the cell cycle, and regulates multiple signaling pathways including PI3K/Akt, MAPK, Wnt/β-catenin, and NF-κB. Curcumin has demonstrated promising activity against breast, colorectal, lung, prostate, pancreatic, and liver cancers and may enhance the efficacy of conventional chemotherapy while minimizing adverse effects. Moreover, curcumin selectively targets cancer cells with minimal toxicity toward normal tissues, making it an attractive molecule for cancer prevention and adjunctive therapy (Kunnumakkara et al., 2017).

5.5 Antidiabetic Activity

Curcumin improves glucose homeostasis by enhancing insulin sensitivity, reducing insulin resistance, protecting pancreatic β-cells, and suppressing oxidative stress and inflammation. It has also been reported to improve lipid metabolism and reduce fasting blood glucose and glycated hemoglobin (HbA1c) levels in patients with type 2 diabetes mellitus. Additionally, curcumin inhibits the formation of advanced glycation end products (AGEs), which play a significant role in diabetic complications. These multifaceted effects contribute to improved metabolic control and reduced progression of diabetes-related complications (Marton et al., 2021).

5.6 Cardioprotective Activity

Curcumin exerts cardioprotective effects by reducing oxidative stress, inhibiting inflammatory responses, improving endothelial function, and regulating lipid metabolism. It

has been shown to reduce myocardial injury, improve cardiac function, and decrease the progression of atherosclerosis and hypertension through modulation of multiple molecular pathways. Curcumin also decreases low-density lipoprotein (LDL) oxidation and improves vascular function, thereby lowering the risk of cardiovascular diseases. Its antioxidant and anti-inflammatory actions collectively contribute to maintaining cardiovascular health (Alwi et al., 2021).

5.7 Neuroprotective Activity

Curcumin exhibits neuroprotective properties by reducing oxidative stress, suppressing neuroinflammation, and preventing amyloid-β plaque formation. It also inhibits tau protein aggregation and improves neuronal survival, making it a promising therapeutic agent for Alzheimer's disease, Parkinson's disease, and other neurodegenerative disorders. Owing to its ability to cross the blood-brain barrier, curcumin protects neuronal cells from oxidative injury and apoptosis. These effects may help preserve cognitive function and delay the progression of age-related neurological diseases (Goozee et al., 2016).

5.8 Hepatoprotective Activity

Curcumin protects hepatic tissue against chemical-, alcohol-, and drug-induced liver injury by reducing oxidative stress, inhibiting inflammatory cytokines, and enhancing antioxidant enzyme activity. It has shown beneficial effects in non-alcoholic fatty liver disease (NAFLD), hepatic fibrosis, and chronic liver inflammation. Furthermore, curcumin suppresses hepatic lipid accumulation and inhibits fibrogenic pathways, thereby improving liver function. These properties support its potential role in preventing and managing various liver disorders (Farzaei et al., 2018).

5.9 Wound Healing Activity

Curcumin accelerates wound healing by promoting fibroblast proliferation, collagen deposition, angiogenesis, and tissue remodeling. Its antimicrobial and anti-inflammatory properties further reduce wound infection and inflammation, thereby enhancing the healing process. Curcumin also stimulates re-epithelialization and increases the formation of granulation tissue, leading to faster wound closure. These characteristics have encouraged the incorporation of curcumin into hydrogels, nanofibers, films, and other advanced wound dressing systems (Akbik et al., 2014).

5.10 Immunomodulatory Activity

Curcumin regulates both innate and adaptive immune responses by modulating the activity of macrophages, T lymphocytes, B lymphocytes, dendritic cells, and natural killer cells. It also regulates cytokine production and immune signaling pathways, contributing to its therapeutic

potential in autoimmune and inflammatory diseases. Additionally, curcumin suppresses excessive immune activation while preserving normal immune function, thereby maintaining immune homeostasis. This dual action makes it useful in chronic inflammatory and immune-mediated disorders (Momtazi-Borojeni et al., 2018).

5.11 Gastroprotective Activity

Curcumin protects the gastrointestinal tract by reducing gastric acid secretion, inhibiting *Helicobacter pylori* growth, suppressing gastric inflammation, and enhancing mucosal defense mechanisms. These effects contribute to its protective role against gastric ulcers, gastritis, and inflammatory bowel diseases. It also promotes mucosal healing by reducing oxidative stress and inflammatory cytokine production within the gastrointestinal tract. Consequently, curcumin has shown promise as a complementary therapy for various digestive disorders (Jain et al., 2011).

5.12 Nephroprotective Activity

Curcumin demonstrates nephroprotective effects by reducing renal oxidative stress, inflammation, fibrosis, and apoptosis. It has shown protective activity against diabetic nephropathy, ischemia-reperfusion injury, and drug-induced nephrotoxicity. Curcumin also improves renal antioxidant enzyme activity and suppresses inflammatory mediators involved in kidney damage. These actions help preserve renal function and delay the progression of chronic kidney diseases (Soetikno et al., 2019).

5.13 Anti-obesity Activity

Curcumin inhibits adipocyte differentiation, suppresses lipid accumulation, and improves energy metabolism by regulating adipogenic transcription factors. It also reduces obesity-associated inflammation and improves insulin sensitivity, suggesting its potential role in obesity management. Furthermore, curcumin modulates lipid metabolism by regulating AMP-activated protein kinase (AMPK) signaling and reducing adipose tissue inflammation. These combined effects contribute to weight management and improved metabolic health (Ejaz et al., 2009).

5.14 Anti-aging Activity

Curcumin possesses anti-aging properties by reducing oxidative stress, preventing chronic inflammation, protecting mitochondrial function, and delaying cellular senescence. These effects contribute to healthy aging and may reduce the risk of age-related disorders. Curcumin also promotes cellular repair mechanisms and protects DNA from oxidative damage, thereby improving longevity and overall cellular health. Its multitargeted

mechanisms make it a promising natural compound for healthy aging interventions (Grabowska et al., 2016).

6. Molecular Mechanisms of Curcumin

Curcumin exerts its therapeutic effects through the modulation of multiple molecular targets and intracellular signaling pathways involved in inflammation, oxidative stress, cell proliferation, apoptosis, and gene regulation. Unlike conventional drugs that often act on a single target, curcumin is considered a multi-targeted phytochemical capable of interacting with transcription factors, protein kinases, enzymes, growth factors, cytokines, and cellular receptors. These interactions contribute to its antioxidant, anti-inflammatory, anticancer, cardioprotective, and neuroprotective properties (Aggarwal & Sung, 2009; Kunnumakkara et al., 2017).

6.1 Cell Signaling Pathways

Curcumin regulates several important cell signaling pathways involved in cell survival, proliferation, inflammation, and apoptosis. It suppresses the activation of nuclear factor-kappa B (NF-κB), mitogen-activated protein kinase (MAPK), phosphoinositide 3-kinase/protein kinase B (PI3K/Akt), Janus kinase/signal transducer and activator of transcription (JAK/STAT), and Wnt/β-catenin pathways. Simultaneously, curcumin activates the Nrf2/Keap1 pathway, enhancing cellular antioxidant defenses. Through modulation of these pathways, curcumin regulates gene transcription, inhibits abnormal cell proliferation, and protects cells against inflammatory and oxidative damage (Kunnumakkara et al., 2017; Giordano & Tommonaro, 2019).

6.2 Anti-inflammatory Mechanisms

The anti-inflammatory effects of curcumin are primarily mediated through inhibition of inflammatory transcription factors and cytokines. Curcumin suppresses NF-κB activation, thereby reducing the expression of inflammatory mediators including TNF-α, IL-1β, IL-6, COX-2, iNOS, and prostaglandin E_2 (PGE_2). It also inhibits the activity of lipoxygenase (LOX) and cyclooxygenase enzymes involved in arachidonic acid metabolism. Furthermore, curcumin decreases leukocyte infiltration and macrophage activation, thereby limiting tissue inflammation and preventing chronic inflammatory responses (Aggarwal & Harikumar, 2009; Jurenka, 2009).

6.3 Antioxidant Mechanisms

Curcumin protects cells from oxidative stress by directly scavenging free radicals and enhancing endogenous antioxidant defense systems. It activates the Nrf2 signaling pathway,

leading to increased expression of antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), and heme oxygenase-1 (HO-1). Additionally, curcumin inhibits lipid peroxidation, preserves mitochondrial function, and reduces oxidative damage to proteins, lipids, and DNA. These mechanisms contribute significantly to its protective effects against chronic diseases associated with oxidative stress (Menon & Sudheer, 2007; Scapagnini et al., 2011).

6.4 Regulation of Apoptosis and Gene Expression

Curcumin regulates apoptosis by modulating both intrinsic (mitochondrial) and extrinsic apoptotic pathways. It promotes the expression of pro-apoptotic proteins such as Bax, p53, caspase-3, caspase-8, and caspase-9, while suppressing anti-apoptotic proteins including Bcl-2 and Bcl-xL. In addition, curcumin regulates the expression of numerous genes involved in inflammation, cell cycle progression, angiogenesis, and metastasis by influencing transcription factors such as NF-κB, AP-1, STAT3, and β-catenin. Through these mechanisms, curcumin inhibits abnormal cell growth, induces programmed cell death, and suppresses tumor progression, making it a promising therapeutic agent for cancer and other chronic diseases (Shishodia, 2013; Kunnumakkara et al., 2017).

7. Challenges and Recent Advances

Despite its remarkable pharmacological potential, the clinical application of curcumin remains limited because of its poor physicochemical and pharmacokinetic properties. Extensive research has therefore focused on developing innovative delivery systems and formulation strategies to overcome these limitations and improve its therapeutic efficacy. Recent advances in nanotechnology and pharmaceutical sciences have significantly enhanced the bioavailability, stability, and targeted delivery of curcumin, expanding its potential for clinical applications (Anand et al., 2007; Hewlings & Kalman, 2017).

7.1 Poor Bioavailability

One of the major challenges associated with curcumin is its poor oral bioavailability, which significantly limits its therapeutic effectiveness. Curcumin exhibits low aqueous solubility, poor gastrointestinal absorption, rapid metabolism in the liver and intestine, and rapid systemic elimination, resulting in very low plasma concentrations after oral administration. In addition, curcumin undergoes extensive glucuronidation and sulfation, reducing the amount of free curcumin available for biological activity. These limitations have prompted extensive research into strategies that improve its absorption and systemic availability (Anand et al., 2007; Nelson et al., 2017).

7.2 Strategies to Improve Bioavailability

Several approaches have been developed to enhance the bioavailability of curcumin. Co-administration with piperine, a natural alkaloid from black pepper, inhibits hepatic glucuronidation and significantly increases curcumin absorption. Other strategies include phospholipid complexes, cyclodextrin inclusion complexes, polymer-based carriers, self-emulsifying drug delivery systems (SEDDS), and solid dispersions. These approaches improve solubility, intestinal permeability, and systemic circulation, thereby increasing the therapeutic efficacy of curcumin (Shoba et al., 1998; Prasad et al., 2014).

7.3 Nano-curcumin and Novel Formulations

Nanotechnology-based formulations have emerged as one of the most effective solutions for improving curcumin delivery. Nano-curcumin formulations, including polymeric nanoparticles, liposomes, phytosomes, nanoemulsions, micelles, solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), dendrimers, and hydrogels, provide enhanced solubility, prolonged circulation time, controlled drug release, and targeted tissue delivery. These formulations protect curcumin from degradation and improve its therapeutic performance in cancer, inflammatory disorders, neurodegenerative diseases, and wound healing. Several nano-curcumin formulations are currently undergoing clinical evaluation for various chronic diseases (Yallapu et al., 2012; Salehi et al., 2019).

7.4 Current Research Trends

Current research on curcumin focuses on developing advanced drug delivery systems and expanding its clinical applications. Recent studies are exploring stimuli-responsive nanoparticles, targeted drug delivery, co-delivery systems, 3D-printed pharmaceutical formulations, curcumin analogues, and combination therapies with conventional drugs to improve treatment outcomes. Additionally, researchers are investigating the role of curcumin in immunotherapy, precision medicine, regenerative medicine, and the management of chronic diseases such as Alzheimer's disease, cancer, diabetes, and cardiovascular disorders. Continued advancements in nanomedicine and molecular pharmacology are expected to further enhance the clinical translation of curcumin-based therapeutics (Kunnumakkara et al., 2024; Tomeh et al., 2019).

8. Future Perspectives

Curcumin continues to attract considerable attention because of its broad pharmacological activities and favorable safety profile. Although substantial progress has been made in understanding its therapeutic potential, several scientific and technological challenges remain. Future research should focus on improving curcumin's bioavailability, validating its

clinical efficacy through large-scale trials, and developing advanced delivery systems to facilitate its translation into routine clinical practice. Emerging technologies such as nanomedicine, precision therapeutics, and artificial intelligence are expected to further expand the scope of curcumin-based therapies (Kunnumakkara et al., 2017; Hewlings & Kalman, 2017).

8.1 Emerging Therapeutic Applications

Recent research suggests that curcumin has promising applications beyond conventional disease management. Ongoing studies are investigating its role in immunotherapy, regenerative medicine, tissue engineering, antimicrobial resistance, autoimmune diseases, metabolic disorders, neurodegenerative diseases, and cancer therapy. Curcumin is also being explored as an adjunct to chemotherapy, radiotherapy, and immunotherapy to improve therapeutic outcomes while reducing treatment-related adverse effects. Furthermore, advanced biomaterials incorporating curcumin are being developed for wound healing, bone regeneration, and targeted drug delivery, highlighting its expanding biomedical applications (Gupta et al., 2013; Salehi et al., 2019).

8.2 Personalized Medicine

Advances in pharmacogenomics and precision medicine have created new opportunities for the individualized use of curcumin. Future therapeutic strategies may involve tailoring curcumin formulations and dosage regimens according to a patient's genetic profile, disease characteristics, metabolic status, and treatment response. Personalized nanoformulations and targeted delivery systems have the potential to maximize therapeutic efficacy while minimizing adverse effects. The integration of biomarkers and genomic data may further facilitate the development of customized curcumin-based therapies for chronic diseases such as cancer, diabetes, and cardiovascular disorders (Nelson et al., 2017; Kunnumakkara et al., 2017).

9. Conclusion

Turmeric (*Curcuma longa* L.) has been recognized for centuries as an important medicinal plant with diverse therapeutic applications in traditional and modern medicine. Among its numerous bioactive constituents, curcumin is the principal compound responsible for most of the plant's pharmacological activities, including antioxidant, anti-inflammatory, antimicrobial, anticancer, antidiabetic, cardioprotective, neuroprotective, hepatoprotective, and wound-healing effects. These biological properties are mediated through the modulation of multiple molecular targets and signaling pathways, making curcumin a promising multitarget therapeutic agent.

Despite its remarkable pharmacological potential, the clinical application of curcumin is limited by poor aqueous solubility, low bioavailability, rapid metabolism, and limited systemic absorption. Recent advances in pharmaceutical technologies, particularly nanoformulations, lipid-based carriers, phytosomes, and polymeric delivery systems, have significantly improved its stability, bioavailability, and therapeutic efficacy. Furthermore, increasing evidence from preclinical and clinical studies supports the potential use of curcumin in the prevention and management of chronic diseases such as cancer, diabetes, cardiovascular disorders, neurodegenerative diseases, and inflammatory conditions.

Overall, curcumin remains one of the most promising natural bioactive compounds, with considerable potential for the development of safe, effective, and innovative therapeutic interventions.

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11. Conflict of Interest

The authors declare that there are no conflicts of interest regarding the publication of this review.

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