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CURCUMIN: A PHYTOMEDICINE IN MODERN HEALTHCARE

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ABSTRACT
Turmeric (Curcuma longa) are known to contain curcumin, a lipophilic polyphenol from the curcuminoid group. Curcumin has been used for generations in traditional medicine, due to antioxidant, anti-inflammatory, hepatoprotective, cardio-protective, antimicrobial, nephroprotective, immunomodulatory, hypoglycemic, anti-rheumatic, anti-cancer, and anti-fibrotic properties. Therefore, this study aimed to determine pharmacological activity potential of curcumin using selected test parameters. The results showed that curcumin had antioxidant and anti-inflammatory effects. These effects contributed to various mechanisms of action in numerous diseases, including cardiovascular, anti-cancer, arthritis, brain injury, Alzheimer's, digestive disorders, anti-aging, and hepatoprotection. Several external factors that influenced test results included curcumin dosage, duration of administration, and pain- or disease-inducing ingredients. In long-term therapy with certain drugs, the administration of curcumin could be considered at the right dose to avoid dangerous side effects.
KEYWORDS: *Curcuma Longa L., Curcuma, Turmeric, Spice, Curcuminoids, Pharmacological Effects, Biotechnological Applications;*

INTRODUCTION

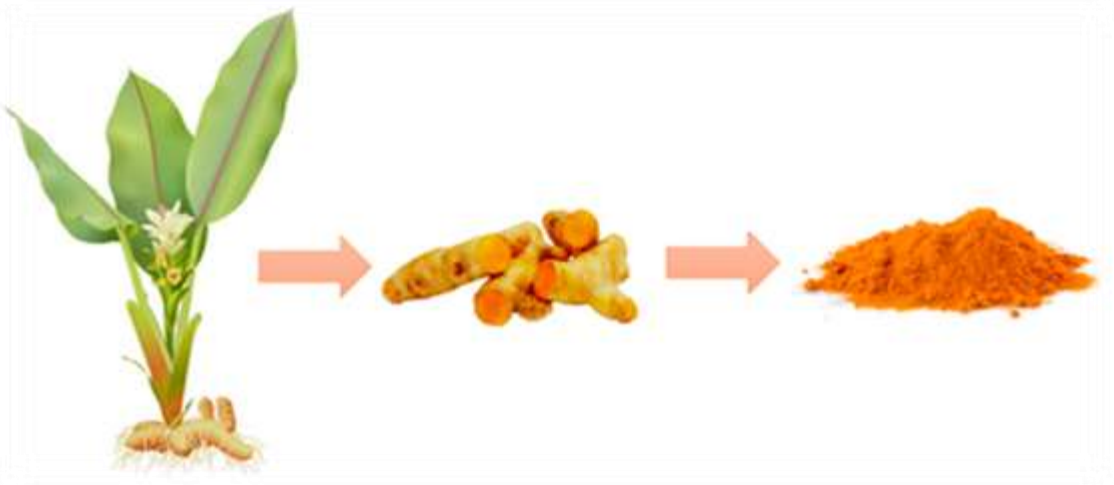
- The main ingredient of the *Curcuma longa* is the rhizome, a low-molecular-weight lipophilic molecule that can pass through the cellular membrane easily. By its chemical structure, it belongs to the group of polyphenols. Because of its intensive yellow color, it is used as a natural food coloring agent.
- The simple molecular structure and arrangement of functional groups are suitable for examining the relationship between the structure and its activity. The ability of curcumin to interact with different proteins facilitates selective modulation of multiple cellular signal pathways associated with various chronic diseases. The transcription factors, mediators of inflammation and enzymes such as protein kinase, reductase, and histone acetyltransferase are important molecules for curcumin binding.
- Curcumin is a powerful epigenetic regulator in many diseases, such as neurological disorders, inflammatory diseases, diabetes, and different types of cancer. Furthermore, it modulates various proteasomal pathways and reduces glycogen metabolism through selective inhibition of phosphorylase kinase enzyme.
- The studies have shown that curcumin exhibits anti-inflammatory, hypoglycemic, antioxidant, antimicrobial, antiviral, anticancer, neuroprotective, and many other effects. However, the main obstacle to the effective manifestation of the pharmacological activity of curcumin is its poor aqueous solubility and low bioavailability.
- The main factors contributing to the low bioavailability of curcumin in the blood plasma and tissues are its poor absorption, fast metabolism, and rapid systemic elimination. The enhancement of the solubility and bioavailability of this promising molecule is crucial for potential clinical application. Different approaches in developing curcumin formulations can improve its physicochemical characteristics and enable safe and efficient use. For that purpose, formulations including nanoparticles, liposomes, micelles, phospholipid complexes, hydrogels, etc., have been described in the reference sources.
- The aim of this paper is to analyze the factors influencing the bioavailability of curcumin, as well as to review pharmacological activities of curcumin and strategies in order to enhance its bioavailability.

PHYSICO-CHEMICAL PROPERTIES OF CURCUMIN

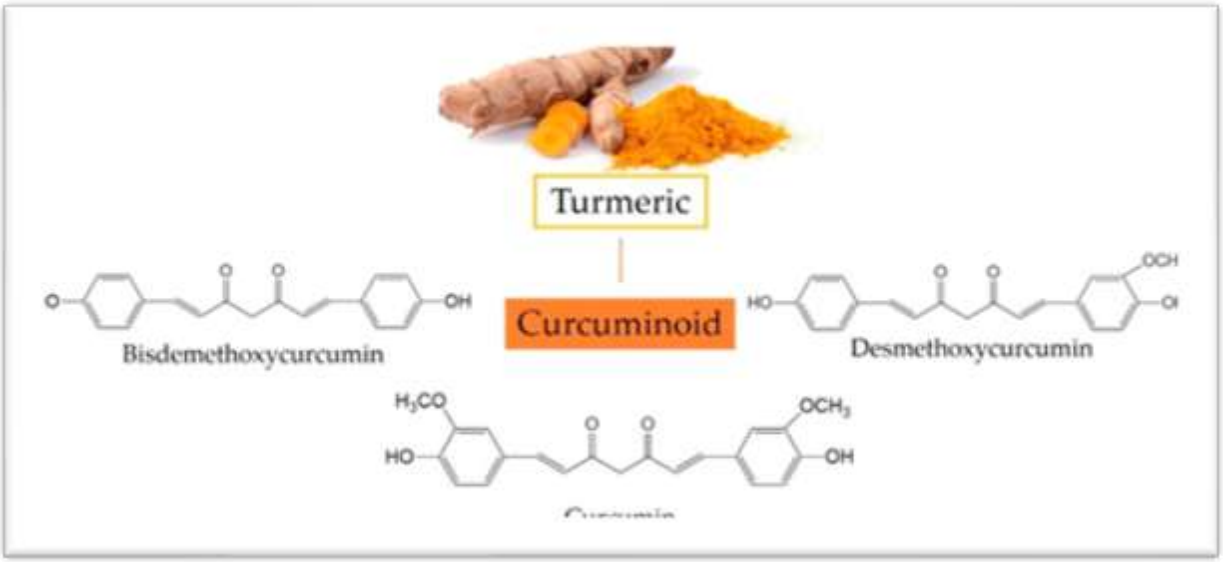
To present the chemical properties of curcumin, the key characteristics, including its color (fresh sample and prepared sample) taste, odor, miscibility and solubility, pH, specific gravity, refractive index and iodine value;

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S/No.	Characteristics	Value in sample of *C. longa* L
1.	Colour of Fresh Sample	Pale Brown
2.	Colour of Prepared Sample	Yellow
3.	Taste	Spicy Bitter
4.	Odour	Aromatic
5.	Miscibility and Solubility	Insoluble in water but miscible in Chloroform
6.	pH (at 29 °C)	6.95
7.	Specific Gravity	1.45
8.	Refractive Index (at 20 °C)	1.44
9.	Iodine Value	51.39



CHEMICAL STRUCTURE OF CURCUMIN



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EXTRACTION AND STANDARDIZATION OF CURCUMIN

Historically, curcuminoids have been extracted using methods such as conventional solid–liquid extraction, sonication, Soxhlet extraction, and similar processes. But during these conventional extraction processes, curcuminoids are degraded by exposure to light, elevated temperatures, and oxygen. Traditional extraction methods can be replaced by pressurized liquid extraction (PLE), which is more effective and often uses less solvent. PLE may be utilized to speed up extraction and retain the solvent in the compressed liquid zone throughout the pressures between 3.5 and 35 MPa and temperatures that lie between 313 and 473 K. In order to address various difficulties, novel extraction methods have been designed. These methods include MAE, UAE, EAE, and PLE. These state-of-the-art techniques demonstrate the potential to extract curcumin from plant sources and are considered ecologically friendly green technology.

Conventional Methods for Extraction of Curcumin

- The ideas behind sample extraction have existed since the beginning of human history. Throughout these ages, key natural chemicals from medicinal and other economically important plants were routinely subjected to percolation through soaking.
- In fact, to speed up the mass transfer of the target compounds into the organic phase, the necessary products were sometimes leached with the proper solvent while being heated and/or stirred. Up until the invention of the Soxhlet extractor at the end of the 17th century, maceration and its associated problems, such as ineffective extraction and excessive time consumption, remained common.
- In fact, a German scientist named Franz Ritter von Soxhlet (January 12, 1848-May 5, 1926) created extraction equipment in 1879 that is now known as the Soxhlet extractor. For the solid–liquid extraction of bioactive chemicals from plants, the Soxhlet extraction method is considered the gold standard and the method of reference. Several publications have reported the utilization of a Soxhlet extractor to extract curcumin from plants
- Soxhlet extraction, and solid–liquid extraction, they discovered that Curcumin extracted using the Soxhlet method had a greater yield than either the solid–liquid extraction method or the UAE. In contrast to the UAE, Soxhlet extraction was conducted at a considerably greater temperature for a much longer period of time. The effectiveness of Soxhlet extraction has been improved by the development of microwave, automated, ultrasound, high-pressure assisted, and other forms of Soxhlet extraction.
- Solid–liquid extraction, usually referred to as “maceration” or “soaking”, is a routinely used and well-known technique for solvent extraction of solid materials. Curcumin has been extracted from plants using a wide variety of solvents, such as nonpolar organic solvents and mixtures of organic solvents and water. The solvents used for the extraction of curcumin from *C. longa* L by Popuri and Pagala comprise acetone, ethyl acetone, ethanol, methanol, and isopropanol.
- The outcomes demonstrated that ethanol extraction at 30 °C for 1 h with a sample-to-solid ratio of 8:1 generated the highest yield. In accordance with it, ethanol was the most favored organic solvent for extracting curcumin. Additionally, the solvent mixture’s ethanol content is a significant factor in the extraction efficiency.

STANDARDIZATION OF CURCUMIN

Standardization of curcumin involves using analytical techniques like HPLC or UV Vis spectrophotometry to accurately quantify the amount of curcumin in an extract or product, ensuring a consistent and predictable level of the active compound. This process typically includes preparing a standard curcumin solution, creating a calibration curve by measuring its absorbance or peak area at different known concentrations, and then comparing the analytical signal of the sample to the calibration curve to determine its curcumin content.

✓ **Analytical methods for standardization**

Reliable and validated analytical methods are used for the identification, separation, and quantification of curcuminoids to ensure product quality.

1. **High-performance liquid chromatography (HPLC)**

HPLC is considered the gold standard for analyzing curcuminoids due to its high accuracy and ability to quantify each curcuminoid individually.

- **Process:** A mobile phase (often a mixture of solvents like methanol, acetonitrile, and water) is passed through a C18 column. The curcuminoids are separated based on their different interactions with the column, resulting in distinct peaks on a chromatogram.
- **Detection:** A UV-Vis detector set to a specific wavelength, typically around 420–425 nm, is used to detect the separated curcuminoids. A validated method would ensure high accuracy and precision, according to guidelines like those from the International Conference on Harmonization (ICH).
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2. **High-Performance Thin-Layer Chromatography (HPTLC)**
This is a simpler, faster, and more cost-effective chromatographic method than HPLC, suitable for routine analysis of curcumin.
- **Process:** Samples and standards are spotted onto a pre-coated silica gel plate. The plate is placed in a mobile phase (e.g., chloroform-methanol) that moves up the plate, separating the compounds.
- **Detection:** The separated bands can be visualized and quantified using a densitometer at a specific wavelength, such as 427 nm. The method is validated according to ICH guidelines for parameters like linearity, precision, and accuracy.

3. **UV-Visible (UV-Vis) Spectrophotometry**
This technique can be used for the quantitative estimation of total curcuminoid content but cannot differentiate between the individual curcuminoids.
- **Process:** A curcumin extract is dissolved in a solvent like methanol or ethanol, and its absorbance is measured using a spectrophotometer, typically at a maximum wavelength of 424 nm.
- **Application:** While fast and economical, it is generally used for total curcuminoids, whereas HPLC or HPTLC is necessary for quantifying the individual component.

➢ PHARMACOLOGICAL ACTIVITIES OF CURCUMIN:

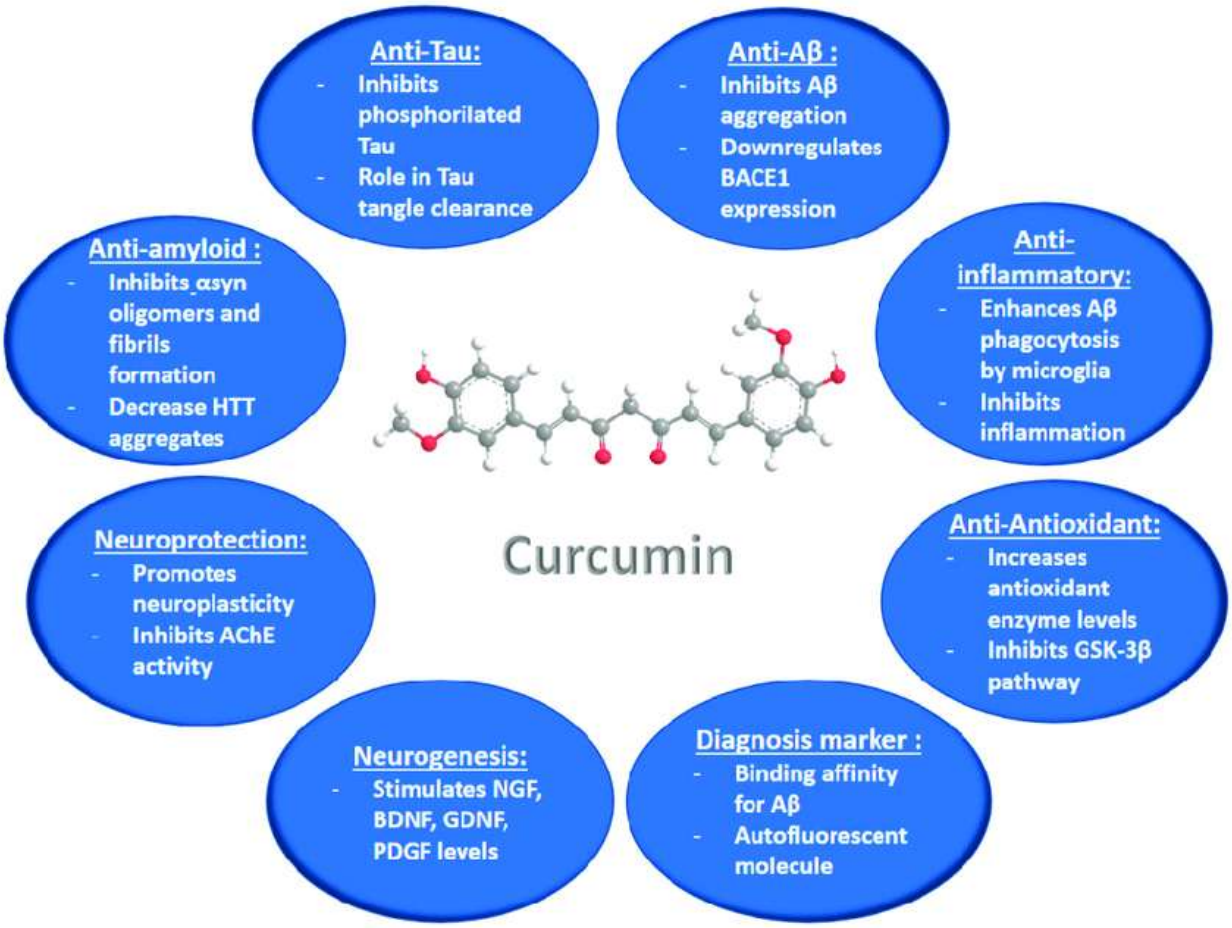
- **Anti-Inflammatory**
Curcumin effectively reduces inflammation by suppressing signaling pathways and lowering histamine levels.
- **Antioxidant**
It acts as a scavenger of reactive oxygen species, preventing lipid peroxidation and DNA damage.
- **Anti-Cancer**
Curcumin shows promise in cancer prevention (chemo preventive) and treatment (chemotherapeutic), inhibiting cell proliferation and growth.
- **Antimicrobial**
It exhibits antibacterial, antifungal, and antiviral properties, including activity against viruses like the Coronavirus.
- **Wound Healing**
Curcumin promotes wound healing and can be used in formulations to treat hypertrophic scarring.
- **Antimalarial and Antiparasitic**
Studies have shown curcumin to have significant effects against malaria parasites and other parasitic infections.
- **Lipid Regulation:**
Curcumin has been found to regulate lipid levels, which is beneficial for cardiovascular health.

MECHANISM OF ACTION

Curcumin's mechanism of action is complex, involving anti-inflammatory, antioxidant, and anticancer properties by targeting various signaling pathways and molecules in the body. It inhibits key transcription factors like NF-κB and modulates inflammatory cytokines, growth factors, and enzymes such as COX-2 and MMP-9. Curcumin also promotes antioxidant defenses, influences cell survival proteins, and interacts with cellular pathways involved in cell proliferation and apoptosis, contributing to its potential therapeutic benefits in various diseases.

The mechanism of action of curcumin regulating the inflammation, neuroprotection, neurogenesis, and various diseases regulated bellow the flow chart.

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CLINICAL APPLICATION IN MODERN HEALTHCARE

1. **Anti-Inflammatory & Pain Management**

Clinical Applications

- Arthritis (Rheumatoid & Osteoarthritis)
- Multiple randomized controlled trials (RCTs) have shown that curcumin can reduce joint pain and improve function in osteoarthritis patients.
- It acts through inhibition of NF-κB, COX-2, and inflammatory cytokines (e.g., TNF-α, IL-1β).
- In some studies, curcumin's efficacy was comparable to NSAIDs like diclofenac but with fewer gastrointestinal side effects.
- Postoperative and chronic pain
- Curcumin supplements have been used as adjunct therapy to reduce post-surgical pain and inflammation.

2. **Cardiometabolic Health**

Clinical Applications

- **Hyperlipidemia & Atherosclerosis**
- Curcumin supplementation can **lower LDL, total cholesterol, and triglycerides**, and increase HDL levels in some populations.
- It improves **endothelial function** and may reduce arterial stiffness, benefiting cardiovascular health.
- **Diabetes Mellitus (Type 2)**
- Curcumin improves **insulin sensitivity**, lowers fasting glucose, and reduces HbA1c levels.
- It may protect pancreatic β-cells and reduce diabetic complications through antioxidant mechanisms.

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3. **Antimicrobial & Wound Healing**
Clinical Applications

- **Topical applications** of curcumin (gels, creams) promote **wound healing** through collagen deposition, angiogenesis, and reduced infection.
- Demonstrates **broad-spectrum antibacterial, antiviral, and antifungal** activity, especially against resistant strains (e.g., MRSA), though mainly as adjunctive therapy.
- Curcumin-containing mouthwashes and gels are being used in **periodontal disease** management due to anti-plaque and anti-inflammatory effects.

4. **Gastrointestinal Disorders**
Clinical Applications

- **Inflammatory Bowel Disease (IBD)**
- Curcumin has been shown to **induce and maintain remission** in ulcerative colitis and reduce inflammation in Crohn's disease.
- Acts through downregulation of inflammatory cytokines and NF-κB pathways.

Dyspepsia & Peptic Ulcer Disease

- Curcumin improves **functional dyspepsia symptoms** and supports mucosal healing, though it should be used cautiously in patients with gallbladder disease.

5. **Dermatological Uses**
Clinical Applications

- Topical curcumin is effective in **psoriasis, eczema, acne**, and wound care due to anti-inflammatory and antimicrobial properties.
- It may help **lighten hyperpigmentation** and protect against photoaging

Limitations and Challenges of Curcumin:

Despite its wide range of therapeutic potentials, curcumin faces several significant limitations and challenges that hinder its clinical application.

✓ **Poor Bioavailability**
Curcumin exhibits **low absorption**, **rapid metabolism**, and **quick systemic elimination**, resulting in minimal bioavailability when taken orally. Its poor water solubility and instability in physiological pH further reduce its effectiveness in systemic circulation

✓ **Chemical Instability**
Curcumin is unstable in alkaline conditions and undergoes rapid degradation, which leads to a loss of pharmacological activity before reaching target tissues

✓ **Absence of Standardized Formulations and Dosage**
There is currently **no universally accepted dosage or standardized formulation** of curcumin for clinical use. Different studies use varied doses, formulations, and treatment durations, making it difficult to compare results or establish clinical guidelines

✓ **Limited Clinical Evidence**
Most evidence supporting curcumin's efficacy comes from **in vitro** and **animal studies**. Large-scale, well-controlled human clinical trials are still limited, and more rigorous research is needed to confirm its therapeutic benefits in humans

✓ **Formulation and Cost Barriers**
Efforts to overcome bioavailability issues—such as the development of liposomal, nanoparticle, or phospholipid-based formulations—increase the cost and complexity of manufacturing (Prasad et al., 2014). This makes curcumin-based therapies less accessible in low-resource settings.

✓ **Potential Side Effects and Drug Interactions**
Although generally considered safe, high doses of curcumin may cause gastrointestinal disturbances. It can also interact with drugs such as anticoagulants, antidiabetics, and chemotherapy agents, posing safety concerns in certain populations

✓ **Regulatory and Quality Control Issues**
Curcumin products are often classified as **dietary supplements or herbal products**, leading to variations in purity, potency, and quality due to lack of strict pharmaceutical regulation.

The main limitations of curcumin are its poor bioavailability due to poor absorption, rapid metabolism, and quick elimination, along with instability in the body. Challenges also include potential allergy or skin irritation and, in high doses of the turmeric powder itself, a risk of kidney stone formation from its high oxalate content. Furthermore, commercial turmeric powders can be adulterated with fillers, questionable colorants, or even lead.

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FUTURE PESPECTIVES OF CURCUMIN

Curcumin, the principal bioactive compound of *Curcuma longa* (turmeric), has attracted significant scientific interest due to its anti-inflammatory, antioxidant, antimicrobial, and anticancer properties. However, its clinical application is still limited due to issues like poor bioavailability and rapid metabolism. Future research is focused on overcoming these limitations and exploring novel therapeutic potentials.

1. **Future Curcumin Derivatives and Analogues**
   research is exploring the synthesis of curcumin analogues with higher stability and potency. Structural modifications can enhance its biological activity and improve its pharmacological properties.
2. **Clinical Trials and Standardization**
   Although numerous preclinical studies support curcumin's therapeutic benefits, large-scale, randomized clinical trials are still limited. Future perspectives involve conducting standardized, multi-center trials to establish clinical efficacy, optimal dosage, and safety profiles for various diseases.
3. **Curcumin in Combination Therapies**
   Combining curcumin with conventional drugs may enhance therapeutic efficacy and reduce side effects. Future research is expected to focus on synergistic effects with chemotherapeutic agents, antibiotics, and anti-inflammatory drugs.
4. **Use in Personalized and Preventive Medicine:**
   With advances in genomics and precision medicine, curcumin may play a role in individualized treatment plans, especially for chronic diseases such as cancer, cardiovascular diseases, and neurodegenerative disorders. Preventive applications through nutraceuticals and functional foods are also expected to grow.

CONCLUSION

- Curcumin, the principal bioactive compound of turmeric (*Curcuma longa*), has emerged as a promising therapeutic agent in modern healthcare due to its wide range of pharmacological properties, including anti-inflammatory, antioxidant, antimicrobial, anticancer, and neuroprotective effects. Numerous preclinical and clinical studies highlight its potential in preventing and managing chronic diseases such as cancer, cardiovascular disorders, neurodegenerative conditions, diabetes, and inflammatory diseases.
- Despite its therapeutic promise, the clinical application of curcumin faces major challenges such as poor bioavailability, rapid metabolism, and limited systemic absorption. To overcome these barriers, modern research focuses on novel formulations like nanoparticles, liposomes, phospholipid complexes, and structural analogues to enhance its stability and efficacy.
- Overall, curcumin represents a bridge between traditional medicine and modern therapeutic strategies. With continued research, improved formulations, and well-designed clinical trials, curcumin holds great potential to become an effective adjunct or alternative therapy in contemporary healthcare systems.

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