RESEARCH PAPER

Curcuma Longa L: An Ancient Herb with Modern Therapeutic Potential

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ABSTRACT

Curcuma longa is a popular medicinal herb with numerous ethnobotanical, pharmacological, and therapeutic uses. The plant exhibits strong antioxidant, antiviral, antifungal, antibacterial, and anti-inflammatory, antidiabetic, anticancer, hepatoprotective and cardioprotective properties and is rich in curcuminoids, volatile oils, and many secondary metabolites. Turmeric has been used for ages to treat inflammatory conditions, wound healing, digestive problems, skin conditions, and systemic infections in conventional medicinal systems including Traditional Chinese Medicine, Ayurveda, Siddha, and Unani. With the use of molecules like demethoxycurcumin, bisdemethoxycurcumin, Ar-turmerone, and other terpenoids, curcumin has been determined by contemporary phytochemical research to be the primary bioactive component responsible for its pharmacological effects. To increase curcuminoids output; a number of extraction methods have been refined including maceration, Soxhlet, Supercritical fluid extraction, microwave assistance, and ultrasound assistance. Curcumin's poor solubility and low bioavailability limit its therapeutic usage despite encouraging preclinical results. This has led to the development of improved formulations such nanoparticles, micelles, liposomes, and phytosomes (e.g., Meriva®, Longvida®, Theracurmin®, BCM-95®). It has a great safety profile at therapeutic levels and is beneficial for illnesses like cancer, arthritis, metabolic syndrome, inflammatory bowel disease, and cardiovascular problems, according to clinical trials. All things considered, Curcuma longa is a multipurpose medicinal plant with significant therapeutic potential that merits additional study to maximize its clinical relevance through better delivery methods and standardized formulations.

Keywords: Herb, Curcuma Longa L., Traditional uses, Phytochemistry, Pharmacological properties.

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INTRODUCTION

Nowadays, the use of therapeutic herbs is becoming more and more popular. The plants provide essential services that greatly contribute to ecosystems. Humans and other living things cannot exist as they should in the absence of plants [Singh JS et al. 2002]. Medicinal plants, which have been used for thousands of years in traditional medicine all throughout the world, are the source of the oldest kind of medication. Human cultures have transmitted actual data about their beneficial effects across time [Khan et al. 2014]. According to WHO definition, traditional medicine includes treatment approaches that have been used hundreds of years before modern medicine was developed and made widely available, and they are still in use today. Conventional medicine is the culmination of many generations of indigenous medical practitioners' therapeutic experiences. Ayurvedic preparations include organic matter, minerals and medicinal herbs, among other things. Only traditional medications that mainly employ medicinal plant extract's for therapeutic purposes and they are considered herbal remedies. Since over 5000 years ago, they have been utilized in literature from India, China, Egypt, Greece, Rome, and Syria. Charak Samhita, Atharvaveda, Sushruta Samhita, and the Rigveda are among the classical Indian texts. Thus, Herbal medicines and traditional cures come from the rich traditions of ancient civilizations and scientific legacy [Rastogi et al. 1990]. Curcuma longa demonstrates a wide variety of biological processes mainly due to its principle compound, curcumin. Many research shows that it possesses strong anti-inflammatory, antioxidant, antiviral, antibacterial, antidiabetic, and anticancer characteristics [Aggarwal, B. B. et al. 2009]. Its potent antioxidant capacity helps prevent oxidative stress by neutralizing free radicals related tissue damage [Hewlings et al. 2017].

Ethnobotanical Use

Numerous taxa of commercial, medical and cultural significance are found in the genus Curcuma L. with 150,000 hectares under cultivation and India is the world's top producer of turmeric [Sasikumar B et al. 2005]. Andhra Pradesh has the most area planted with turmeric; Kerala, Tamil Nadu, Orissa, Karnataka, and Maharashtra come next. Numerous species that are economically significant as food, colouring, medicinal, and condiments are found in the genus Curcuma L. [Skorniekova J et al. 2004]. It can be found all over south and southeast a few species in Asia making their way to the South Pacific, Australia, and China. Each has a minimum of 40 species; India and Thailand have the most variety. Myanmar, Bangladesh, Indonesia, and Vietnam come

next. The quantity of species that need to be identified is still up for debate because there hasn't been a thorough taxonomic revision. Current estimates range from roughly 503 to 80 species [Larsen K et al. 1998]. There is a lot of variety within and between species in the genus. It has recently gained attention as a potential source of drugs for a range of illnesses due to its curcumin, oleoresin, oil, and other complex chemical components. Both the perfume industry and aromatherapy use turmeric oil, in addition to its cultural, religious, and magical applications [Sopher D E et al. 1964]. According to ethnobotanical evidence, turmeric was first used in India in relation to worship of Sakthi or the adoration of the heavenly by the pre-Aryans, mother or goddess. Later, it was traded as a coloring agent and condiment [Smith R M et al.1981]. The genus inception and dissemination primarily occurred in the Indo-Malayan region, supporting the notion of its Indo-Malayan origin and center of variety [Harlan J R et al. 1975]. It is thought that turmeric originated in Southeast Asia, traveled to neighboring regions before moving to tropical East and West Africa, they lived in China, Japan, Indochina, and other South Pacific islands. It was only recently introduced to Central America and the Caribbean Islands. People in South East Asia and Indo-China who eat rice frequently use turmeric as a spice and condiment [Purseglove J W et al. 1981]. According to reports, the Western Ghats region is home to about eight species that produce tubers, sixteen non-tuberous species and one stolon-bearing species. As a result, it is regarded as the genus's top hotspot, on par with the northeastern part of India. As a result, the India's South Western Peninsula, which is a center of variety within the genus, may have been one of its original Asian habitats. In Orissa's Turmeric in the districts that are dominated by tribes of Koraput, Mayurbhanj, Ganjam, Gajapati, as well as Kandhamal is the primary cash crop. Orissa has farmed turmeric from ancient times. Growing turmeric is directly linked to the native tribes' traditional customs and religious ceremonies in Orissa. In order to increase the quantity and turmeric's quality, In the Kandhamal region of Orissa, Khonds used to perform strange, antiquated religious practices including human sacrifice. During the Kedu-jatra festival in March or April, a boy who was not Khond was kidnapped from the plains and imprisoned in the hamlet, where he was given all the delights of life before to the human sacrifice known as the Meria sacrifice (buffalo sacrifice) [Mally et al. 1908].

Traditional uses of Curcuma longa as medicine

Curcuma longa has a lengthy history of medicinal utilization in Ayurveda, Siddha, Unani, & Conventional Chinese Medicine due to its broad therapeutic activities, especially its traditional antioxidant and antimicrobial benefits. In Ayurveda, turmeric is frequently utilized to purify blood, lessen inflammation, heal wounds, and treat digestive issues like indigestion and bloating and liver disorders [Sharma. R., et al. 2020]. Traditionally, turmeric paste was applied to burns, wounds, and skin infections because it was believed to prevent microbial growth and speed wound healing, indicating early recognition of its antimicrobial potential. The yellow pigment, rich in curcuminoids, was also used in herbal preparations to counteract oxidative stress, reflecting its traditional role as an antioxidant tonic for improving immunity and strengthening overall health. In folk medicine, turmeric milk has been consumed for centuries to fight infections, soothe the throat, and promote internal healing, while traditional Chinese Medicine has made use of it to improve blood circulation, relieve pain, and manage inflammatory conditions [Li et al. 2019].

Botanical description

Grown as an annual crop, turmeric is an upright perennial herb. An upright aerial stem with leaves is the primary representation of the plant's above-ground anatomy. Each plant may have two to five aerial stems, or tillers. The inflorescence emerges through the aerial stem as a cylindrical, fleshy center spike that is 10 to 15 cm long. The spike's bracts subtend flowers. Their length is less than half the bracts are acute, indistinct, lanceolate, and adnate. The upper bracts are white, and the lower bracts are green. The axial of the bract bears one to four flowers that open one at a time. A spike produces about thirty blooms; the calyx is small, divided almost midway down on one side, and typically toothed. The corolla has a golden tip and is tubular, slender, and white. The bracts at the top and bottom are typically sterile. Turmeric seeds are fertile and exhibit seed set. Depending on the blooms fertilized, an inflorescence may have one or many sunken capsules that contain seeds [Nazeem et al. 1994]. Rhizomes are created at the foot of the aerial stem beneath the earth. Mother rhizomes, primary, secondary, and even tertiary fingers comprise these rhizomes, all of which combine to form a tight clump. Rhizomes are pale yellow, reddish yellow, or orange-brown in color and grow symbodically. Using a somatic chromosomal 63 is the number ($2n = 3x = 63$), C. longa is primarily triploid [Nair et al. 2009].

Origin and Classification

Curcuma longa, also referred to as turmeric, has 1400 species throughout 49 genera that are members of the Zingiberaceae family. The Indo-Malayan area is where the genus first appeared. The genus contains over 80 species worldwide [Ravindran et al. 2007]. C. longa is one of about 40 species that are native to India, demonstrating their Indian ancestry. Apart from C. longa, other minor sources of curcumin color include C. xanthorrhiza Roxb., C. malabarica Vel., etc. Based on numerical taxonomic analysis, Six taxonomic variations of C. longa were found by Velayudhan et al. (1999): The following varieties of C. longa are available: typica, atypica, camphora, spiralifolia, musacifolia, and platifolia. The majority of India is where C. longa was found is either typical or unusual [velayudhan k c et al 1999]. Curcuma longa, or turmeric, is a member of the the taxonomic group that follows: Clade: Angiosperms (flowering plants); Kingdom: Plantae (plants); Clade: Monocotyledons (monocotyledons); Order: Zingiberales; Family: Turmeric; Family: Zingiberaceae (ginger family) Curcuma longa is the species. According to this categorization, Turmeric is a member of the plant kingdom, more precisely to flowering plants that have a single cotyledon (monocots). It is further classified under the family Zingiberaceae and order Zingiberales, which also contain other noteworthy species like ginger [Vera-Ramirez L., et al. 2013].

Geographical distribution and habitat:

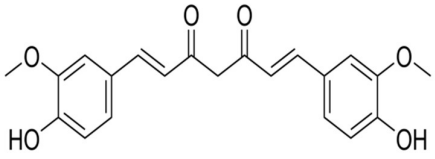
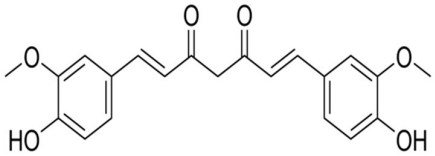
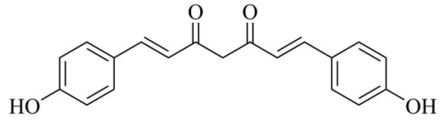
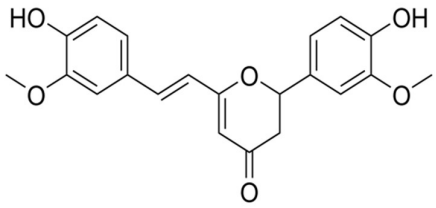
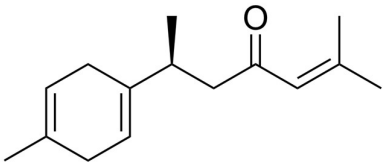
The herb Curcuma longa L. is perennial indigenous to tropical South and Southeast Asia. The Indian subcontinent, namely the states of Kerala, Karnataka and Tamil Nadu which are also significant hubs for commercial production, is generally thought to be its origin [Sahoo et al. 2022]. Due to its culinary, medical, and industrial value, turmeric is now grown in many tropical and subtropical nations, including Bangladesh, Sri Lanka, Thailand, Indonesia, and portions of Africa and the Caribbean [Sharma et al. 2021]. With around 80% of the world's supply, India continues to be the biggest producer. Thailand, Indonesia, and other nations with favorable climates come next [Sharifi-Rad, J., et al. 2020]. Despite the fact that C. longa is rarely seen in the wild, human cultivation has caused it to naturalize in several tropical areas outside of its original habitat. Traditional agricultural methods and trading channels are directly associated with its proliferation. Turmeric grows best in temperatures between 20°C and 30°C that are warm and humid. It also needs a lot of rainfall each year, typically between 1,500 and 3,000 mm. the rhizomes may be harmed by

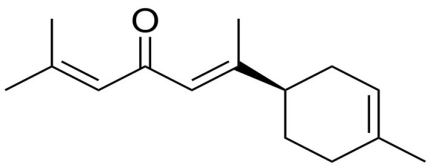
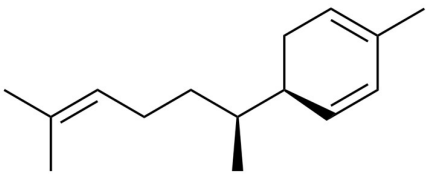
frost and extended flooding. Because turmeric is vegetatively grown by rhizomes, optimal rhizome development usually requires a dry season after a period of warm, humid weather. The plant grows best in full sunlight, though it can withstand some shade. It prefers Fertile, well-drained soils with a pH range: mildly acidic to neutral (6.0–7.5) [Wu, H., et al. 2024].

Phytochemistry

The medicinal herb Curcuma longa L. is rich in bioactive compounds. Phytochemical investigations of C. longa have revealed a range of secondary metabolites, including as curcuminoids, essential oils, alkaloids, flavonoids, terpenoids, phenolics, and glycosides [Sharifi-Rad, J., et al. 2020]. Curcuminoids (curcumin, demethoxycurcumin, and bisdemethoxycurcumin) which give turmeric its characteristic yellow color and many of its therapeutic properties, are the most studied phytochemicals [Wu, H., et al. 2024]. Table 1 displays the phytoconstituents' structures and IUPAC names.

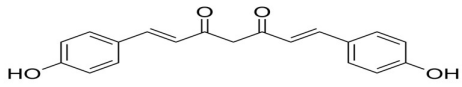
Table1: Phytoconstituents structures and their IUPAC name.

Sr. No	Name of Phytoconstituents	Structure	IUPAC Name
1.	**Curcuminoids**		
	Curcumin (Diferuloylmethane)		1,6-heptadiene-3,5-dione 1,7-bis(4-hydroxy-3-methoxyphenyl) (1E,6E)
	Demethoxycurcumin (DMC)		(1E,6E)-(4-hydroxy-3-methoxyphenyl)-7-(4-hydroxyphenyl)-Hepta-1,6-diene-3,5-dione
	Bisdemethoxycurcumin (BDMC)	 Bisdemethoxycurcumin (BDMC)	(1E,6E)-1, hexa-1,6-diene-3,5-dione 7-bis(4-hydroxyphenyl)
	The cyclocurcumin		3,4-dihydro-2H-pyran-4- [(E)-2-(4-hydroxy-3-methoxyphenyl)ethenyl] one-2-(4-hydroxy-3-methoxyphenyl)-6-[
2.	**Volatile oils**		
	Turmerone		(6S)-2-methyl-6-(4-)-hept-2-en-4-one methylcyclohexa-1,4-dien-1-yl).

	Atlantone		Hepta-[(1R)-4-] 2,5-dien-4-one (5E)-2-methyl-6-methylcyclohex-3-en-1-yl].
	Zingiberene		(5R)-2-methyl-5-[(2S)-6-methylhept-5-en-2-yl]cyclohexa-1,3-diene

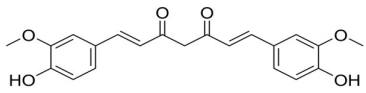
Curcuma species are abundant in carbs, proteins, terpenoids, alkaloids, flavonoids, tannins, saponins, phenols, and other nutrients. They are also a precursor to many vitamins, such as polyphenol, beta carotene, and vitamin C, as well as unsaturated fat and volatile oil. Numerous additional important phytochemicals, including Proteins, carbohydrates, amino acids, alkaloids, tannins, steroids, phenolic compounds, phytosterols, terpenoids, flavonoids, and glycosides, were also found in the turmeric leaf and rhizome [Khatun M et al. 2021]. Numerous experts have studied the chemical components of turmeric in great detail. Currently, over 235 compounds, mostly terpenoids and phenolic compounds, have been identified from turmeric. These include phenylpropene and other phenolic compounds, diarylheptanoids and diarylpentanoids, monoterpenes, sesquiterpenes, diterpenes, triterpenoids, sterols, and a few alkaloidal compounds. The leaves are excellent sources of minerals and nutrients. About 80% of curcuminoids are made up of the head curcumin, or curcumin [Sabale P et al. 2013]. Turmeric's yellow colour is caused by polyphenols called curcuminoids. The primary components of curcuminoids are 71.5% curcumin, 19.4% demethoxycurcumin, and 9.1% bisdemethoxycurcumin [Dairam A et al. 2007].

Bis-demethoxycurcuminR1 = HR2 = H



(1E,6E)-1,7-bis(4-hydroxyphenyl)hepta-1,6-diene-3,5-dione

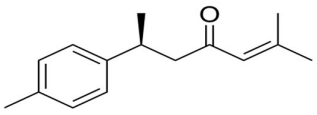
Demethoxycurcumin



(1E,6E)-1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione

A range of monoterpines, sesquiterpenes, and diterpines are found in the essential oil (5%) of turmeric. The main monoterpines are terpinolone, cineole, β-phellandrane, and p-cymene. Three significant sesquiterpenes are α-turmerone, β-turmerone, and Ar-turmerone [Ohshiro M et al. 1990].

Ar-turmerone



(6S)-2-methyl-6-(4-methylphenyl)hept-2-en-4-one

Medicinal 1.3% of leaves, 0.3% of flowers, and 4.3% of roots and rhizomes yield oil contain 3.8% vary by part [Ashraf K et al. 2017]. By lowering the chance of infection , phytochemicals are chemical substances contained in plants enhance a plant's inherent defenses and maintain its health. In addition to their protective qualities in plants, phytochemicals shield people against illnesses. Microbes, bacteria, fungi, and viruses have been suppressed by the extraction of secondary metabolites from plants [Rajkumari S et al. 2017]. AIDS patients have been treated using alkaloids, which are present in some plants. Curcumin and its analogues may therefore be promising as novel therapeutic options for HIV treatment. Flavonoids have antimicrobial and cell-supporting properties [Kumar N et al. 2013]. Because phenolic and flavonoid compounds have been shown to have a variety of common consequences, such as the counteraction of malignant growth and free radical scavenging, Turmeric's high phenolic and flavonoid content may be the reason for its usage as a microbe-free skin and skin ulcer treatment, as well as its moderate anticarcinogenic and antiviral properties [Verma RK et al. 2018]. Tannins inhibited the growth of many microorganisms, yeasts, and parasites. Terpenoids are a variety of phytochemicals, including non-aromatic and sweet-smelling ones, have been investigated as

potential antibacterial, antineoplastic and other therapeutic candidates. Saponins have the ability to harm agents that cause cancer. Saponins include both resistive modulatory effects and direct toxicity. Alkaloids are secondary metabolites with antibacterial properties [Mohebbati R et al. 2017]. Two of turmeric's constituents, flavonoids and curcumin, been connected to the plant's physiological and chemopreventive properties in several tumor bioassays, in which has been demonstrated to halt tumor cell development. Alkaloids that have been completely isolated and their synthetic In contemporary medicine, equivalents are commonly employed because to their antimicrobial, antispasmodic, and pain-killing qualities. The rhizome of C. longa, commonly known as turmeric, has long been utilized in Asian traditional medicine as well as spice or food ingredient. It is known as "Jianghuang" in conventional Chinese medicine and has been utilized extensively to treat cardiovascular illness, liver problems, and diabetic wounds [Chinese et al. 2010]. Turmeric's primary constituents, according to phytochemical analysis, are volatile oils and curcuminoids [Meng F.C. et al. 2018]. The main curcuminoids in turmeric are curcumin and two demethoxy derivatives with anti-inflammatory, anti-cancer, neuroprotective, Anti-Alzheimer's, and antioxidant qualities: demethoxycurcumin and bisdemethoxycurcumin [Shi L. et al. 2015]. Drug research has long focused on curcuminoids. Additionally, Turmeric's volatile oil is frequently utilized in health and beauty products because of its antibacterial, antifungal, and antiarthritic qualities [Gul P., et al. 2015]. Recent research has demonstrated the anti-cancer, anti-inflammatory, antiplatelet, anti-angiogenic, and neuropharmacological activities of turmerones, the active ingredients in turmeric oil [Yue G.G.L. et al. 2015].

Extraction methods

Curcumin can be obtained primarily through two methods: synthesis and plant extraction [Pabon et al. 2010]. It is said that the extraction process is crucial in determining the amount and quality of bioactive chemicals; therefore, it is crucial to select suitable and efficient techniques and run them under ideal circumstances. Crude curcumin extracts typically comprise a range of substances, such as sugar, essential oil, its derivatives bisdemethoxycurcumin and demethoxycurcumin or other small molecules [Horosanskaia et al. 2020]. The first and extraction is the most important process for getting curcumin from a plant material. A few basic objectives guided the development of all extraction techniques: (a) extracting certain chemicals from plant sources; (b) improving the extraction process's selectivity; (c) boosting efficiency of extraction; and (d) providing a dependable and replicable procedure [Zhang et al. 2019]. (table2)

Table 2: Different extraction methods are used to extract the curcuma longa.

S.No.	Extraction method	Solvent used	Extract type	Reference
1.	Maceration	Ethanol	Ethanolic	**[Paulucci et al. 2013]**
2.	Soxhlet	Ethanol	Ethanolic	**[Braga et al. 2003]**
3.	Microwave-assisted	Ethanol	Oil	**[Fernández-Marín et a. 2021]**
4.	Ultrasound-assisted	Ethanol	Ethanolic	**[Slaček et al. 2023]**
5.	Microwave-assisted	Deep eutectic solvent (ChCl-CA)	Curcuminoids	**[Patil et al. 2023]**
6.	Supercritical	Ethanol	Curcuminoids	**[Martinez-Correa et al. 2017]**
7.	Microwave-assisted	Ethanol	Curcuminoids	**[Singh, et al. 2022]**
8.	Ionic liquid	DPCARB (carbamate ionic	Curcumin	**[Sahne, et al. 2017]**

		liquid)		
9.	Deep Eutectic Solvent Extraction	**Choline chloride–propylene glycol deep eutectic solvent**	Curcumin	**[Le, et al. 2022]**
10.	Supercritical	CO_2	Curcuminoid-terpenoid	**[Widmann, et al. 2022]**
11.	MUAE (Microwave–Ultrasound-Assisted Extraction)	NADES (Choline chloride–Lactic acid)	Curcuminoid	**[Sahlan, et al. 2025]**
12.	UA-TPP	t-Butanol	Curcuminoids	**[Patil et al. 2020]**
13.	imultaneous extraction–nanoencapsulation	Ethanol	Curcuminoids	**[Santos, et al.2020]**
14.	Microemulsion (ME	Hydrophobic deep eutectic solvent (HDES)	Curcuma longa constituents (Curcuminoids & turmerones)	**[Supaweera et al. 2022]**
15.	Solvent extraction	Methanol/Water	Bioactive compounds (phenolics, flavonoids, curcuminoids)	**[Tonin et al.2021]**
16.	Microwave-assisted extraction (MAE) & Ultrasound-assisted extraction (UAE)	Ethanol–Water mixture	Phenolic antioxidants & Curcumin	**[Yaman et al. 2025]**
17.	Soxhlet extraction	Methanol	Curcumin (with phenolics & flavonoids)	**[Shukla, B., et al. 2024]**

Curcumin is frequently extracted from plants using traditional techniques including maceration, solvent extraction or soxhlet extraction [Paulucci, et al. 2013]. New extraction methods like As more effective

alternatives to traditional extraction, techniques such as enzyme-assisted extraction, super critical liquid extraction, ultrasound-assisted extraction, and microwave-assisted extraction have been developed. Often known as "maceration" or "soaking," solid-liquid extraction is A popular and extensively utilized technique for solvent extraction of solid materials. Numerous Curcumin has been extracted from plants using a variety of solvents, such as non-polar organic solvents and a mixture of organic solvents and water [Shirsath et al. 2017] conducted a comparison of the extraction solvents used to separate curcumin from Curcuma Longa L. (ethanol, methanol, acetone, isopropanol and ethyl acetone). The maximum yield (0.26 mg/10 g) was obtained when ethanol the process of extraction was done at an hour at 30 C with a 1:8 solid to solvent ratio, Sogi et al. (2010) found. As a result, the most popular organic solvent for extracting curcumin was ethanol [Popuri et al. 2013; Dutta et al. 2015]. Soxhlet extraction, developed in 1879 by German scientist Soxhlet, is currently regarded as the gold standard for the solid-liquid extraction of bioactive compounds from plants. Curcumin extraction from plants with a Soxhlet extractor has been documented in several publications [Luque de Castro et al. 2010]. For example, a comparison of the curcumin extraction yield from Soxhlet extraction, automated Soxhlet extraction, ultrasound-assisted the rate of Soxhlet extraction was greater of curcumin extraction than maceration extraction and UAE. Automated soxhlet extraction, ultrasound-assisted soxhlet extraction, high-pressure soxhlet extraction, and soxhlet extraction with microwave assistance has all been created to enhance soxhlet extraction performance and reduce or minimize the drawbacks of the traditional soxhlet extractor [Kurmudle, et al. 2011]. The components of plant cell walls are a number of intricate structured polysaccharides that provide cells stability and resistance to intracellular component extraction. The term enzyme-assisted extraction (EAE) refers to this procedure. Therefore, Enzymes with specific hydrolytic capabilities disassemble the plant cell wall matrix to gain access to the bioactive substances that are confined to the cellular walls as well as those found in the cytosolic areas. Amyloglocosidase, glucoamylase, and α-amylase are among the enzymes utilized in the EAE method to extract curcumin [Sahne et al. 2017; B Jyotirmayee et al. 2002]. This strategy is becoming increasingly popular due to its effectiveness, simplicity, sustainability, and environmental friendliness. Remember that temperature, time, pH, and enzyme concentration are some of the variables that affect the specificity and selectivity of enzymes. Using a single-factor method of assess the impact of various circumstances of the enzyme reaction on curcuminoid recovery, it was discovered that the yields of curcumin increased by 26.04% and 31.83% when α-amylase at 3% was utilized 2% glucoamylase was used at pH 4.5 with five hours of incubation, eight hours of extraction, and acetone as a solvent, and at pH 5.0 with five hours of incubation and eight hours of extraction [Ammon, et al. 1991].

Pharmacological Properties

Research has shown that turmeric possesses a broad range regarding pharmacological activity regardless of whether it is used in powder, extract, or isolated form, There aren't many negative effects. The methoxy group of curcumin on the 1, 3-diketone, phenolic, and phenyl ring systems is primarily responsible for its numerous impacts of pharmacology. There are numerous curcumin or goods enhanced with turmeric that are sold in both home and foreign markets for a range of conditions. Unlike Curcumin, like other phyto-antioxidants, is a potent, safe, and natural substance (Table 4). Curcumin has a wide spectrum of biological effects because of this. Turmeric has long been used as an anti-inflammatory in Chinese and Indian medicine. Oral curcumin is a great remedy for neurological conditions, diabetes, cancer, and digestive problems. In Ayurvedic tradition, curcuma longa is mainly used orally, but it can also be applied topically and breathed to treat wounds, boils, bruises, blisters, ulcers, eczema, insect bites, parasite infections, bleeding, and skin disorders like pemphigus and herpes zoster [WHO et al. 1999]. Curcumin can also be applied topically to reduce irritation and inflammation to minimize the symptoms of inflammatory skin conditions and allergies. Table 3 lists a variety of turmeric's pharmacological effects, some of which are discussed in the sections that follow.

Table 3: Turmeric extract exhibits a number of therapeutic qualities.

S. No.	Plant part used	Medicinal properties	Extract used	References
1.	Rhizome	Anti-inflammatory	Soxhlet (ethanolic)	**[Urošević.et.al. 2022]**

2.	Rhizome	Antioxidant	Ethanolic	**[Sabir.et.al. 2020]**
3.	Rhizome	Antioxidant	Ethanolic	**[Pan.et.al. 2020]**
4.	Rhizome	Antibacterial	Hydro distillation (for essential oil) and ethanolic distillation (for curcuminoids)	**[Naz.et.al. 2010]**
5.	Rhizome	Antioxidant, Antimicrobial, Anticancer	Methanolic	**[Ogbonna.et.al. 2021]**
6.	Rhizome	Antioxidant, Antimicrobial, Mutagen-protective	Essential oil (by vapor phase or hydro distillation)	**[Guerrini.et.al. 2023]**
7.	Leaves	Antioxidant, Antimicrobial, Iron-chelation, Cholinesterase inhibition	DES-based ultrasound assistance	**[Oliveira.et.al. 2021]**
8.	Rhizome	Cytotoxic, Antioxidant, Anti-inflammatory	Curcumin I, II, and III are curcuminoids.	**[Ramsewak.et.al. 2000]**
9.	Rhizome	Anti-inflammatory	COFAE, or oil-free aqueous extract	**[Bagad.et.al. 2013]**
10.	Rhizome	Cytotoxic, Antimicrobial, Antioxidant	Hydro distillation of essential oil	**[Camilo.et.al. 2020]**
11.	Rhizome	Antifungal	Alcoholic extract	**[Chen.et.al. 2018]**
12.	Rhizome	Antifungal	Aqueous extract (used in TiO_2 nanoparticle biosynthesis)	**[Jalill.et.al. 2016]**

Antioxidant properties

The potent antioxidant properties of turmeric and its main component, curcumin, are well known; the

activity of its fat-soluble and water-soluble extracts is similar to the effects of vitamins C and E [Akter et al. 2019]. Curcumin is believed to have an antioxidant capacity 2.75 times higher than vitamin C's and 1.6 times higher than vitamin E's because of its methoxy, phenolic, and diketone groups [S. Abrahams et al. 2019]. According to Jyotirmayee et al. (2022), pure curcumin has greater superoxide scavenging capabilities than demethoxycurcumin and bisdemethoxycurcumin. It effectively prevents oxidative damage and reduces cellular oxygen levels. Curcumin also lowers the possibility of hypertension, cardiovascular illness, cataracts, Glaucoma, retinal degeneration, and hypercholesterolemia. Ryudai Gold (RD) turmeric has potent antioxidant action due due to its high flavonoid and phenolic content [M. Ulamek-Koziol et al. 2020]. Curcumin enhances endogenous antioxidant systems and scavenges free radicals by increasing the production of glutathione (GSH) and superoxide dismutase (SOD) [Mortellini et al. 2000]. It boosts cellular resilience to oxidative stress and protects against hyperglycemia, excessive urination, and diabetes-related micro- and macrovascular issues [Chinenye, et al. 2011]. Because free radicals destroy proteins, lipids, and DNA, natural defense mechanisms including SOD, CAT, GSH, GPx, vitamin C, and vitamin E help prevent oxidative damage [Arshad, et al. 2017]. Curcumin contributes to its antioxidant properties by giving off hydrogen atoms from its phenolic groups [Samarghandian et al. 2017], also increases the expression and activity of MSRA, SOD, CAT, and GPx. Additionally, it removes ROS such H_2O_2, HO•, and ROO•, shielding the cytoplasm from oxidative damage [Haryuna, et al 2017].

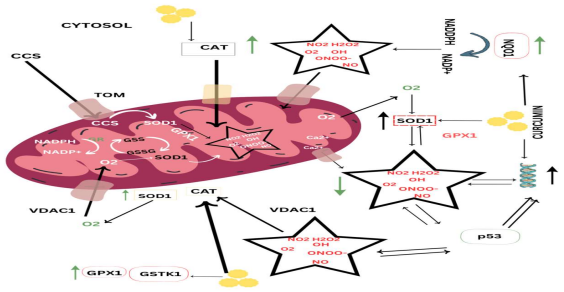


Figure 1: Curcumin's antioxidant action an illustration

of an antioxidant enzyme network that control production of ROS, or reactive oxygen species, which participate in several cellular processes. Among the antioxidant enzymes are HMOX1, GPX1, GSTK1, SOD1, CAT, and NQO1 are all upregulated by curcumin. The gatekeeper proteins like VDAC1 carry the ROS from the cytoplasm to the mitochondrion, where antioxidant enzymes scavenge them. HMOX1, heme oxygenaseGSTK1, glutathione-s-transferase kappa; GR, glutathione reductase; NO2, nitrogen dioxide; H2O2, hydrogen peroxide; OH, hydroxyl radical; O2, superoxide; NO, nitric oxide; TP53, cellular tumor antigen p53; VDAC1, voltage-dependent anion channel; and $ONOO^-$, peroxynitrite. Upregulation is represented by the green arrow and downregulation by the red arrow [Sureshbabu A et al.2023]

Antimicrobial Properties:

Turmeric's ethanolic extract proved effective against every tested bacterium when assessed for microbial susceptibility, with Staphylococcus epidermis exhibiting the least inhibition zone and Shigella flexnerri the most. Turmeric's antibacterial properties can be attributed to a variety numerous phytochemicals, including cardiac glycosides, terpenoids, triterpenes, phenols, alkaloids, flavonoids, phlorotannin, tannins, and more [Sureshbabu A et al.2023]. N-hexane, water, chloroform, and ethanol turmeric extract were evaluated against Escherichia coli, Staphylococcus aureus, Salmonella typhi, and Candida albicans. Salmonella typhi and Escherichia coli growth was water turmeric extract inhibits. While methanol extracts prevented the growth of other bacteria, water extract decreased the growth of Escherichia coli and Staphylococcus aureus [Oghenejobo et al. 2022]. Turmeric aqueous formulations show increased Staphylococcus aureus inhibitory action. It was discovered that Turmeric and Mucor sp. ethanolic extracts had anti-stolonifer and anti- pyroid qualities. The components might act as an antibiotic preservative [Roy et al. 2022]. It has been demonstrated that three curcuminoids are curcumin, bisdemethoxycurcumin, and demethoxycurcumin have antifungal and antibacterial properties against bacteria such as Bacillus subtilis and Staphylococcus aureus, as well as Aspergillus niger and Candida albicans. The antibacterial medications fluconazole and kanamycin have been used in conventional medicine to combat a range of bacteria and fungi [Pundir et al. 2010]. Turmeric oil contains two additional volatile sesquiterpenes and monoterpenes used in antimicrobial research: turmerone and zingiberene. Candida albicans, Staphylococcus aureus, Bacillus subtilis, and Cryptococcus neoformans demonstrated less antibacterial activity than Escherichia coli and Pseudomonas aeruginosa [Singh, R. P.; et al. 2012]. Aspergillus Niger, Staphylococcus aureus, and Candida albicans were all significantly inhibited by essential oil of turmeric. Turmerone, a vital source of antibacterial

activity, is the most significant part of Roma turmeric. This is an opportunity to treat eye infections with a lens made of turmeric rhizome oil [Ungphaiboon et al.2005]. Figure 2 shows the main antibacterial pathways that curcumin activates.

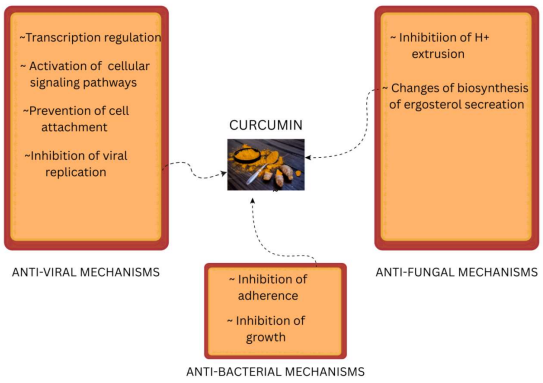


Figure 2: Antimicrobial mechanism of curcumin.

Antibacterial activity

Numerous studies have confirmed the broad-spectrum antimicrobial activities of curcumin, the main bioactive component of Curcuma longa, which has long been recognized for its potent antibacterial qualities. It was first discovered that compounds of curcumin have strong biological activity, including antiviral potential [Hussain et al. 2022], later studies verified its extensive antiviral, antifungal, and antibacterial properties. Curcumin inhibits both Gram-positive and Gram-negative bacteria by compromising the integrity of the bacterial membrane [Gupta, et al. 2012]. Formulations and extracts based on turmeric have demonstrated antibacterial properties against a number of pathogens, such as Vibrio cholerae, Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli, and Bacillus subtilis [Sasidharan NK et al. 2014], however, turmeric oil has shown efficacy against Staphylococcus aureus and Bacillus subtilis [S. Ungphaiboon et al. 2005]. Furthermore, compared to curcumin and diacetyl-curcumin, curcumin metal complexes like indium-curcumin exhibit even greater antibacterial activity with much lower MIC values, particularly against Staphylococcus aureus and Staphylococcus epidermidis [Negi, et al. 1999]. Since bacterial behavior and pathogenicity are also influenced by quorum-sensing mechanisms, the demonstrated ability of curcumin and its derivatives to interfere with bacterial survival suggests their potential relevance in targeting multiple microbial regulatory pathways [Tajbakhsh et al. 2008]. By producing and detecting signaling molecules, quorum sensing enables bacteria to monitor cell density and coordinate group behaviors, allowing them to act collectively within a population [L. A. et al. 2016]. Biofilm production, in which microbial cells embed themselves inside an extracellular polymeric matrix to build structures that are much more difficult to eliminate than planktonic cells, is one important QS-regulated function. Because of their slow microbial metabolism and the barrier that extracellular polymers create, biofilms can be up to 1000 times more resistant to antibiotics [Sharma et al. 2014]. Preventing the formation of biofilms is a crucial tactic for lowering persistent infections because they restrict the penetration of antibiotics and protect bacteria from immune responses. Treating bacteria linked to biofilms frequently necessitates higher antibiotic dosages [Selvam et al. 2019]. Curcumin suppresses the bacterial quorum sensing (QS) system, as seen in figure 3 below. Unlike many antibiotics that rely on single-target methods, curcumin exhibits a multimodal anti-infective potential by acting on numerous molecular pathways [A. E. Krausz et al.2015]. Curcumin can decrease biofilm biomass, prevent adhesion, and inhibit the synthesis of QS-dependent virulence factors by interfering with QS signaling. Additionally, research indicates that curcumin considerably lowers the bacterial load in periodontal and urinary tract infections and prevents biofilm formation in a number of pathogenic habitats [S. Izui et al. 135]. For instance, biofilm thickness dropped from 16 to 10 µm in E. coli and from 11 to 6.36 µm in Proteus mirabilis after curcumin therapy. By lowering cell density and restricting the formation of extracellular polymeric substances, a crucial QS-dependent component for biofilm maturation, curcuminoid-based nano-hybrids also demonstrate potent antibiofilm efficacy [Fulaz et al. 2019].

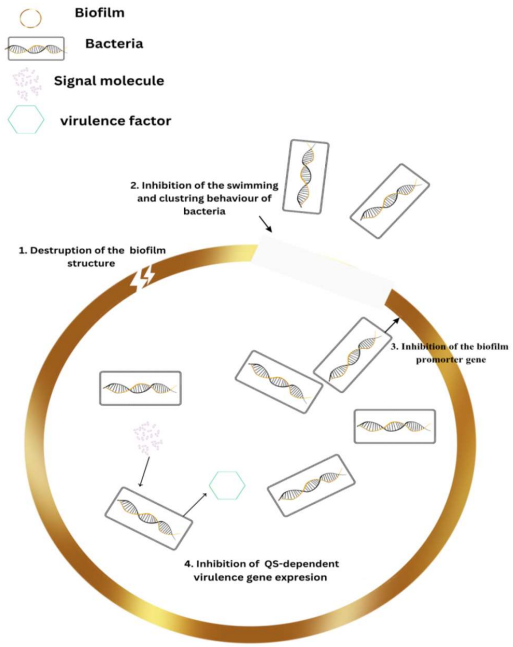


Figure3. Curcumin inhibits the bacterial quorum sensing (QS) system.

[Liu & Nizet, 2009; Wu & Seyedsayamdost, 2017] Microbial pathogenicity is further decreased by QS disruption. Curcumin has been demonstrated to disrupt the manufacture of QS-regulated pigments, peptides, and secondary metabolites including alkylquinolones, which are important in pathogenesis. Curcumin exhibits concentration-dependent anti-QS action by preventing pigment synthesis in QS-mediated pathways. Curcumin autoxidation is another mechanism that contributes to its antibacterial and antibiofilm capabilities. Curcumin spontaneously transforms into several reactive intermediates, including spiroepoxides and bicyclopentadiones [Morohoshi et al., 2007]. These oxidation products could increase curcumin's biological activity and provide an extra pathway for its antibacterial and antiviral properties-

Antiviral activity

Because curcumin can alter cellular signaling, inflammation, apoptotic pathways, and viral entry processes, it has broad antiviral efficacy against a variety of enveloped and non-enveloped viruses [Mathew, D. et al. 2018]. In Zika and Chikungunya viruses, it prevents early viral attachment and cell binding, prevents the entry of the bovine herpesvirus via changing the development of lipid rafts, It stops the hepatitis C virus's primary genotypes from infecting liver cells [Desai, S.J et al. 2018]. Additionally, curcumin prevents noroviruses from entering, and its antiviral properties are strengthened when photodynamically triggered with particular light wavelengths. By preventing viral attachment, it exhibits strong anti-Zika action [Yang et al. 2016]. It inhibits the viruses that cause chikungunya, vesicular stomatitis, and gastroenteritis by lowering viral fusion and absorption [Gao,Y et al. 2019]. By preventing internalization and decreasing replication, curcumin suppresses the viruses that cause pig reproductive and respiratory syndrome and viral hemorrhagic septicemia [Li, et al. 2020]. Tetrahydrocurcumin and curcumin analogs have potent anti-HIV actions by preventing viral integration and replication [Mirani et al. 2019]. Additionally, curcumin and its derivatives decrease infection in certain strains of the dengue virus by inhibiting its proteases [Balasubramanian et al. 2019]. By inhibiting hemagglutinin activity, interfering with viral signaling pathways, and enhancing survival in infected mice, curcumin suppresses the influenza-A virus [Rai et al. 2020]. Additional research demonstrates that curcumin derivatives have excellent structure–activity connections when it comes to blocking influenza neuraminidase [Han,S. et al. 2018]. Enterovirus-71 replication is considerably decreased by curcumin. Additionally, it demonstrates promise against The first and second strains of SARS-CoV by focusing on ACE-2 receptors, spike proteins, and viral proteases in docking experiments. Curcumin's wide range of antibacterial activity is further demonstrated by further antifungal activity in tissue culture [Maurya et al. 2020].

Anti-fungal activity

For a long time, extracts and compounds made from many natural resources, particularly plants, have been an effective way to stop rotting and fungal infections. Many researchers have been carried out to investigate curcumin and turmeric in relation to lowering fungal infections and spoiling because of the extensive traditional use of turmeric in food goods. Research on the use of turmeric powder in plant tissue culture revealed that turmeric at 0.8 and 1.0 g/L R. S. [Upendra et al. 2011] shown strong inhibitory efficacy against fungal contaminations. The ethanolic extract has been shown to turmeric possesses antifungal properties against Microsporumcanis and Trichophyton longifusus. According to [S. Ungphaiboon et al. 2005], with minimal inhibitory concentrations ranging from 128 to 256 g/mL, the methanol extract of turmeric demonstrated effectiveness of antifungals against Cryptococcus neoformans and Candida albicans. The

antifungal activities of C. longa hexane extract at 1000 mg/L were demonstrated to be effective against Rhizoctonia solani, Phytophthora infestans, and Erysiphe graminis. Furthermore, it was shown that 1000 mg/L of C. longa ethyl acetate extract inhibited R. solani, P. infestans, Puccinia recon dita, and Botrytis cinerea [M.-K. Kim et al. 2003]. Curcumin exhibited antifungal efficacy against P. infestans, R. solani, and Pu. Recondite at 500 mg/L. Fusarium solani and Helminthosporium oryzae, two phytophagous fungi, are susceptible to the antifungal effects of curcumin and turmeric oil. With IC50 values of 19.73 and 12.7 g/mL, [H. Chowdhury et al. 2008] respectively, turmeric oil showed the strongest antifungal efficacy against F. solani and H. oryzae. [M. Wuthi-udomlert et al. 2000] certain The crude methanol extract of C. longa inhibits clinical isolates of dermatophytes. 18-month-old and freshly distilled oil produced from the rhizome of C. longa demonstrated the greatest antifungal effectiveness against 29 clinical isolates of dermatophytes, with MIC values of 7.2 and 7.8 mg/mL, respectively.

Anti-inflammatory

Curcuma longa exhibits strong anti-inflammatory activity through the modulation of multiple cellular signaling pathways. Curcumin significantly reduces pro-inflammatory mediators, including MMP-1, MMP-3, IL-1β, and TNF-α by controlling the mTOR pathway, as shown in models of collagen-induced arthritis [Dai Q et al. 2018]. Enzyme inhibition is another reason for its anti-inflammatory properties and mediators involved in inflammation, including COX, LOX, phospholipases, leukotrienes, prostaglandins, nitric oxide, and hyaluronidase [Bundy R et al. 2004]. Curcumin prevents retinal pigment epithelial cell inflammation induced by high glucose by blocking the ROS/PI3K/AKT/mTOR signaling pathway, while also regulating the TLR4/MyD88/NF-κB axis to reduce osteoarthritis-related inflammation and tissue injury [Ran Z et al. 2019]. Essential oils derived from turmeric rhizomes rich in components such as ar-turmerone, α-turmerone, and β-turmerone have demonstrated notable anti-inflammatory properties [Zhang Y et al. 2019]. Among these, ar-turmerone inhibited STAT3 and NF-κB signaling pathways with potent IC_{50} values, showing strong activity in inflammatory cell models [Ibáñez MD et al. 2020]. Additionally, α-turmerone suppressed signaling mediated by HIF-1α by inhibiting erythropoietin promoter activation. Turmeronols A and B further reduced inflammatory mediator production by suppressing NF-κB signaling in activated microglial cells [Del Prete D et al. 2016]. Other turmeric-derived compounds, including bisabola-3,10-diene-2-one and 3-hydroxy-1,7-bis(4-hydroxyphenyl)-1,3-heptadiene-5-one, also demonstrated anti-inflammatory properties by preventing LPS-stimulated RAW264.7 cells with IC_{50} from producing nitric oxide values stronger than hydrocortisone Overall, both curcumin and turmeric essential oils act through multiple pathways mTOR/PI3K/Akt, TLR4/NF-κB, ROS-mediated cascades, and turmeric's long-standing use as a natural anti-inflammatory drug is validated by STAT3 inhibition, which suppresses important inflammatory mediators and enzymes [Saji R, et al. 2023]. Figure 4 below illustrates the anti-inflammatory action mechanism.

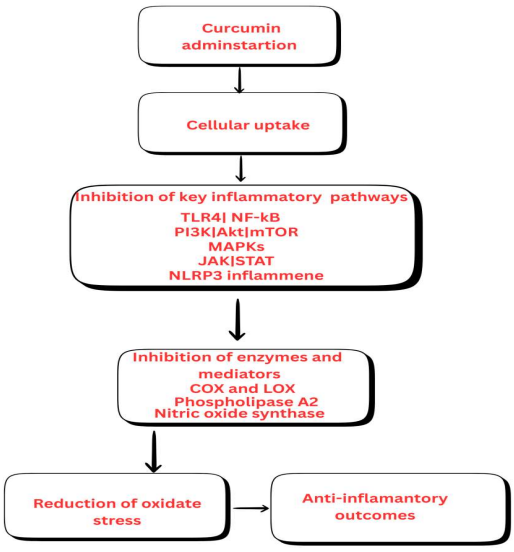


Figure 4: Anti-inflammatory action mechanism.

Antidiabetic Activity

In 2021, 529 million people worldwide suffered from diabetes; predictions indicate that number will rise to 1.31 billion by 2050 [Yuan T et al. 2017]. When it comes to glucose, turmeric extract works well with drugs used to treat diabetes. Additionally, it can prevent type-2 diabetes by lowering the body's resistance to insulin. Additionally, turmeric helps people with diabetes mellitus [Nasri et al. 2014]. In order to manage diabetes, turmeric is used to boost the liver's transformation of cholesterol into bile acids and reduce intestinal absorption of cholesterol. Both curcuminoids and sesquiterpenoids are present in the turmeric ethanolic extract, which has a greater hypoglycemic effect than either one alone. Turmeric has strong anti-diabetic effects via reducing

inflammation and oxidative stress [Marton et al. 2021]. By dramatically reducing blood levels of the three curcuminoids curcumin, demethoxycurcumin, and bisdemethoxycurcumin, as well as blood glucose, alanine aminotransferase, and aspartate amino transferase have demonstrated excellent anti-diabetic activity as well as improving the liver histopathology score [Islam et al. 2024]. Zhong and associates reduced glucose intolerance and insulin resistance, lipid buildup and intolerance to pyruvate in the liver of mice given a diet high in fat by modifying gut flora [Zhong et al. 2022]. Furthermore, curcumin treatment enhanced the expression of an enzyme in the liver that breaks down insulin and preserved the pancreatic islets' structural integrity [Lee et al. 2022]. Research has shown that curcumin at 15 μM inhibits the growth of adipocytes and kills preadipocytes. This process is associated with decreased increase of lipids in 3T3-L1 adipocytes, maintenance of β-catenin down-regulation produced by differentiation medium, and PPARγ and CCAAT enhancer binding protein down-regulation. Curcumin targeted white adipose tissue to regulate lipid metabolism and lower chronic inflammation, which is essential for treating obesity-related health issues, according to two more trials [Sahebkar et al. 2022]. Furthermore, in a mouse model of obesity caused by a high-fat diet, the cumin dietary intervention demonstrated potential in lowering metabolic illness in living things. This impact was mediated via controlling the functional polarization of macrophages in white adipose tissue and suppressing the expression of uncoupling protein 1 in brown adipose tissue [Rodrigues et al. 2019].

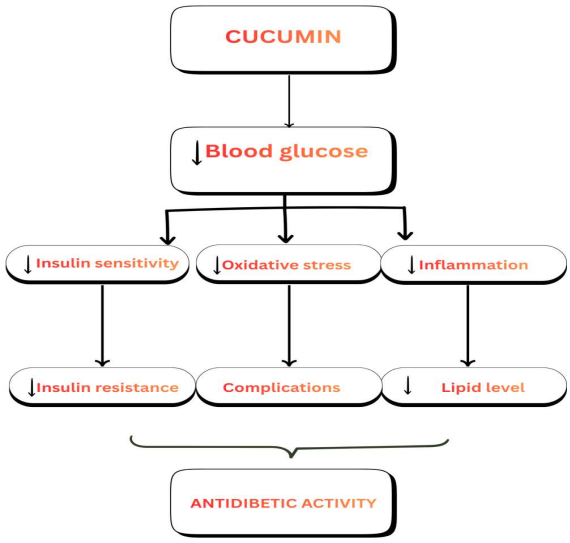


Figure 5. Mechanism of antidiabetic activity

Anticancer and Chemopreventive Activity

Turmeric's main polyphenol, curcumin, modulates several molecular pathways linked to cell signaling, proliferation, and death to produce powerful anti-cancer actions. Studies show that whole turmeric extract demonstrates stronger anticancer activity than isolated curcuminoids due to synergistic interactions among its components [Kukula-Koch et al. 2019]. Curcuma longa yielded a new bioactive fraction (NCCL) greater cancer-cell death than its isolated marker compound, indicating improved efficacy of combined phytochemicals. Non-curcuminoid compounds such as turmerones also possess significant anticancer properties, which are further enhanced through encapsulation technologies. Curcuminoid rich extracts prepared using green microwave-assisted extraction displayed higher anti-cancer activity against HeLa, HT-29, MCF-7, and A549 cells compared to pure curcuminoids [Lateh et al. 2019]. Combined curcuminoids (CUR, DMC, BDMC) demonstrated synergistic inhibitory effects in a 1:1:1 ratio and down-regulated cancer-related proteins in prostate cancer PC3 cells [Meng et al. 2021]. Structural modifications of curcumin, including dimethyl-curcumin and hispolon derivatives, enhance its anti-tumor potential by altering key functional groups. Extraction methods also influence curcuminoid yield and anti-cancer efficacy, with ethyl acetate extracts showing superior activity [Deserti, et al. 2018]. Curcumin's activity in hormone-refractory prostate cancer is increased by maspin expression, which enhances cancer-cell sensitivity to curcumin therapy. Standardized turmeric extract Turmesac® induces apoptosis and cell-cycle arrest more efficiently than reference chemotherapeutic agents [Firoz, et al. 2020]. Nano-formulations such as Gemini surfactant–curcumin nanoparticles significantly increase apoptotic gene expression and improve curcumin delivery. Emulsomes co-loaded with curcumin and piperine enhance caspase-3 activity and apoptotic markers in colorectal cancer cells [Bolat et al. 2020]. Fungal-chitosan nanoparticles loaded with curcumin further improve bioavailability and promote apoptosis in A549 and HCT-116 cells [Almutairi et al. 2020]. Curcumin and its analogues regulate multiple pathways related to invasion, cell death, and control of the genome, establishing it as an important multi-targeted anticancer molecule. Although curcumin-free turmeric shows lower in-vitro activity, it effectively inhibits colorectal tumor growth in vivo, suggesting that whole turmeric contains additional bioactive compounds contributing to its holistic anticancer effects [Zhai et al. 2020].

Cardiovascular diseases:

Lowering triglyceride and cholesterol levels, limiting platelet aggregation, and lessening the susceptibility of low density lipoprotein (LDL) to lipid peroxidation are some of turmeric's cardiovascular system-protective qualities [Srivastava R et al. 1989]. Turmeric extract was shown to reduce plasma cholesterol and triglyceride levels as well as LDL's vulnerability to lipid peroxidation. The impact of turmeric extract on cholesterol levels may result from the intestines' reduced absorption of cholesterol and the liver's increased conversion of cholesterol to bile acids. It is believed that components of C. longa decrease platelet aggregation by potentiating prostacyclin synthesis and inhibiting thromboxane generation [Lee et al. 2006]. Curcumin protects against oxidative damage caused during the development of atherosclerosis by mobilizing α-tocopherol from adipose tissue. Curcumin raises the transit of VLDL cholesterol in plasma, which raises α-tocopherol levels. It has been demonstrated that curcumin can release α-tocopherol from adipose tissue to protect the body from oxidative damage brought on by atherosclerosis. Furthermore, plasma may contain more LDL cholesterol, which would increase the amounts of α tocopherol. In general, the animals' fatty acids were less susceptible to oxidation in the vessel wall [Soni KB et al 1992]. For seven days, consuming 500 mg/d of curcumin orally was found to dramatically lower serum lipid peroxides (33%), raise HDL cholesterol (29%), and lower total serum cholesterol (12%) [Rahim-Mahdy et al. 2025].

Marketed formulations:

Rahim -Mahdy and Seifert's extensive investigation examined 125 turmeric supplements available in India, Germany, Australia, United Kingdom, and United States. Labels for packages for sIn April and May, supplements promoted on the pertinent websites were examined of 2022. And; the table 4 lists the product retrieval websites for each nation [Hegde et al. 2023].

Table 4: Retrieval of preparation-related information

Nation	Data retrieval website	The most recent product retrieval date
India	www.pharm easy. In	25.05.2022
	www.amazon.in	
	www.1mg.com	
	www.healthkart.com	
Germany	www.shop-apotheke.com	08.05.2022
	www.dm.de	
Australia	www.chemistwarehouse.com	28.05.2022
	www.barnesnaturals.com	
	www.pharmacyonline.com	
	www.pharmacy4less.com	
UK and USA	www.hollandandbarrett.com	UK- 29.05.2022 and USA- 09.05.2022
	www.amazon.com.uk	
	www.puritanspride.com.uk	
	www.superdrug.co.uk	
	www.wildnutrition.com	
	www.target.com	
	www.bioschwartz.com	

	www.walgreens.com	

A thorough analysis of There are 125 turmeric supplements available in Germany, India, Australia, the UK, and the US revealed a number of commercially available curcumin formulations intended to improve its bioavailability. Among these, Meriva®, a phosphatidylcholine–curcumin phytosome complex with roughly 18–22% curcuminoids, showed a 30-fold increase in bioavailability and clinical efficacy in lowering serum lipid and uric acid levels in patients with non-alcoholic fatty liver disease when given 1000 mg daily for eight weeks. 30% curcuminoids are present in Theracurmin®, a submicron colloidal dispersion, showed better systemic absorption and bioavailability that was around 42 times higher. In clinical trials with 60 patients receiving 400 mg daily for four weeks, Longvida®, a solid-lipid curcumin particle formulation with 20% curcuminoids, demonstrated significant cognitive advantages and over 100-fold increased bioavailability. Similarly, in 140 osteoarthritis patients treated with 500 mg daily for 28 days, BCM-95® (Curcugreen®), a standardized blend of curcuminoids and turmeric essential oil containing 95% curcuminoids, significantly reduced pain outcomes and increased bioavailability by almost seven times. In participants given 500 mg twice daily for 90 days, the CurQfen® formulation which is based on a curcumin-galactomannoside combination using soluble fenugreek fiber achieved up to 270-fold increased bioavailability and was found to be safe for regular intake. A single 500 mg oral dose of NovaSol®, a micellar curcumin system standardized to 95% curcuminoids, increased systemic exposure by 185 times, while CurcuWIN®, which combined curcumin with polymeric carriers using UltraSOL technology, demonstrated a 46-fold increase in absorption and significant anti-inflammatory activity. Finally, a standardized 95% curcuminoid mixture called C3 Complex® was used as a benchmark for comparison without improved bioavailability. Together, these commercially available formulations are Meriva®, Theracurmin®, Longvida®, BCM-95®/Curcugreen®, CurQfen®, NovaSol®, CurcuWIN®, and C3 Complex® represent important pharmaceutical advancements that improve curcumin's therapeutic efficacy and worldwide commercial presence by addressing its inherent problems of poor solubility, low absorption, and rapid metabolism through a variety of delivery methods [Velayudhan et al. 2012].

Table 5: Curcumin complexes' clinical applications

S.No.	**Complicated| complex**	**Contents**	**Curcuminoids**	**claimed increase in bioavailability**	**Based on Hegde et al. (2023), the generation**
1.	Meriva®	Curcumin-phosphatidylcholine phytosome	18–22%	30 × (Indena 2019)	2nd
2.	Theracurmin®	Submicron colloidal dispersion of curcumin	30%	According to Theravalues Corporation (n.d.), 42 ×	2nd

3.	Longvida®	Solid lipid curcumin particle (SLCP)	20%	> 100 × (Jamwal et al. 2018)	3rd
4.	BCM-95®/Curcugreen®	Curcuminoids with turmeric essential oil	95%	6.9 × (Antony et al. 2008))	1st
5.	CurQfen®	Curcumin-galactomannoside compound with soluble fenugreek fiber (fenugreek galactomannan)	40%	270 x (Akay Group, n.d.)	3rd
6.	The NovaSol®	Micellar curcumin	95%	Schiborr et al. (2014) state that 185 ×	2nd
7.	CurcuWin®	Cellulosic and natural polymer carriers combined with curcumin (water-dispersible UltraSOL) technology)	20%	46 ×	2nd
8.	C3 Complex®	Standardized curcuminoid mixture	95%	None	Point of reference

Patents

Turmeric has several therapeutic uses. In India, it has long been used as an antiseptic and to treat various types of wounds. This has been thoroughly documented and recorded. Nevertheless, two non-resident Indians, Drs. Hari Har P. Cohly and Suman K. Das of the A patent application was filed by the University of Mississipi Medical Center in Mississipi for "use of

turmeric in wound healing" to the US Patent Office in December 1993 despite the plant's widespread use as a folk remedy. In March 1995, the patent was approved. It stated that it was a revolutionary discovery to administer a sufficient quantity of turmeric orally and locally to improve the healing process of wounds. India's Scientific and Industrial Research Council, contested the claims in March 1995 and found This discovery was widely known in India at the time the patent was submitted, as evidenced by the 32 references, some of which date back more than a century. In October 1996, it formally requested that the patent be reexamined at the USPTO. After lengthy techno-legal debates, all six claims were categorically rejected in March 1997. It was decided that the medicinal properties of turmeric were not patented, and the patent was withdrawn for failing to meet the novelty criterion. The development has broad ramifications for the public domain preservation of traditional Indian knowledge, as stated by the CSIR's Director General at the time, Dr. R. A. Mashelkar. India has created a comprehensive approach to IPR conflicts by putting the Traditional Knowledge Digital Library, Plant Varieties Bill, and Geographical Indications Bill into effect.Turmeric has numerous uses and is intricately linked to Classical, folk, religious, cultural, and social art forms in addition to It's therapeutic, aesthetic, and ethnobotanical benefits for humans. The aforementioned narrative makes it clear that turmeric has several health benefits. It is an important plant that existed before many other cultivated crops. Further research on turmeric's value addition is therefore urgently needed, given its insecticidal, fungicidal, and medicinal properties [Hewlings, et al. 2017].

Clinical Studies and Therapeutic Potential

Because of its bioactive component curcumin, Curcuma longa, also referred to as turmeric, has been thoroughly investigated for its wide therapeutic potential. Curcumin is a prospective treatment for a number of chronic illnesses since clinical Studies have indicated that it possesses potent anti-inflammatory properties, antioxidant, antibacterial, anticancer, and neuroprotective properties [Gupta et al. 2013]. Curcumin has been shown to have positive effects on illnesses like arthritis, metabolic syndrome, anxiety, and hyperlipidemia in a number of randomized controlled trials. These regulation of inflammatory cytokines is primarily responsible for the effects, oxidative stress indicators, and lipid metabolism [Rahimi et al. 2016]. Furthermore, curcumin is a useful supplement to traditional treatments due to its natural origin and safety profile. To improve its therapeutic efficacy, a number of innovative formulations, including liposomes, phospholipid complexes, and nanoparticles, have been developed. However, its limited bioavailability continues to be a significant restriction. The therapeutic potential of Curcuma longa is a multifunctional medicinal herb used to treat human health is generally supported by the growing body of clinical evidence [Prasad et al. 2013].

Clinical Trials and Human Studies

The highly pleiotropic compound curcumin was first shown to possess antibacterial qualities in 1949. Since then, studies have shown that the polyphenol has antibacterial, anti-inflammatory, hypoglycemic, antioxidant, and wound-healing qualities [Aggarwal et al. 2009]. Numerous preclinical research conducted over the last thirty years have shown the potential of curcumin as a remedy for numerous health ailments. Curcumin is safe, tolerable, and nontoxic at large doses, according to human clinical research [Gupta SC et al. 2012]. In these clinical studies, curcumin has been administered either by themselves or in conjunction with Soy isoflavones, bioperine, sulfasalazine, mesalamine, prednisone, gemcitabine, piperine, doce taxel, and quercetin. Completed curcumin clinical trials: Clinical research across a wide range of diseases demonstrates the therapeutic potential of curcumin. In colorectal cancer patients, oral curcumin at doses of 0.036–0.18 g daily for decreased glutathione S-transferase activity after four months [Sharma et al. 2004], while intake of 0.45–3.6 g/day over the same duration significantly decreased PGE_2 production. A short 7-day regimen of 0.45–3.6 g/day led to a reduction in M1G levels, and administration of 1.44 g/day for six months resulted in decreased number and size of polyps without toxicity [Cruz-Correa et al. 2006]. In smokers, doses of 2–4 g/day for one month reduced ACF formation, and 1.08 g/day for 10-30 days of weight gain, lowered p53 expression and serum TNF-α [He ZY et al. 2011]. In 1.5 g daily for six weeks decreased lipid peroxidation and raised GSH levels in pancreatic cancer patients, whereas Although 8 g/day was well tolerated, there was only partial action and limited absorption in some cases. Combination therapy using gemcitabine with curcumin was not feasible at 8 g/day for four weeks, though 8 g daily alone remained secure and well-tolerated in another cohort [Kanai M et al. 2011]. In head and neck cancer, two curcumin Tablets lowered salivary IL-8 levels and IKKβ kinase activity. Patients with Crohn’s disease receiving 1.08 g daily for a month followed by 1.44 g/day for two months showed notable reduction in inflammatory and

CDAI scores markers [Holt PR et al. 2005]. Irritable bowel syndrome patients consuming 0.072–0.144 g/day of standardized turmeric extract for eight weeks experienced a notable reduction in symptom prevalence. Curcumin at 1 g/day for 6–12 weeks also reduced gastricm ulcer formation. In chronic bacterial prostatitis, when combined with other phytochemicals, prulifloxacin's therapeutic efficacy was increased by 0.2 g/day for two weeks [Cai T et al. 2008]. β-thalassemia patients taking Oxidative stress indicators improved after 12 months at 0.5 g/day [Kalpravidh et al.2010], while no antiviral benefit was observed in AIDS patients taking 2.5 g/day for eight weeks [James et al. 1996]. A diabetic subject achieved a reduction in blood sugar levels during fasting between 140 and 70 mg/dL [Srinivasan et al. 1972], and in a larger group, 0.6 g/day for eight weeks decreased oxidative and inflammatory indicators and enhanced endothelial function [Usharani et al. 2008]. Curcumin intake of 6 g for 15–120 minutes increased postprandial insulin with minimal impact on the glycemic index or plasma glucose [Wickenberg J et al. 2010], and chronic administration of 1.5 g/day for nine months improved β-cell function, increasing HOMA-β and adiponectin while lowering HOMA-IR and C-peptide [Chuengsamarn et al. 2012]. In renal-transplant patients, 480–960 mg daily for one month enhanced the results of early grafts [Shoskes et al. 2005]. Curcumin at 1 g/day for six months protected against antituberculosis-drug-induced hepatotoxicity [Adhvaryu et al. 2008]. For Helicobacter pylori infection, For a week, taking 0.06 g daily reduced serologic markers of stomach inflammation and alleviated dyspeptic symptoms [Di et al. 2007], though 0.12 g/day for four weeks did not improve eradication rates [Koosirirat et al. 2010]. Long-term intake of 1.125 g/day for 6–22 months promoted recovery from disease in affected individuals [Lal et al. 2000].

Challenges and limitations of current research: First, inadequate pharmacokinetics and bioavailability are a significant problem. Low water solubility, quick metabolism, poor absorption, and quick systemic elimination are the characteristics of curcumin. Even when preclinical research demonstrate encouraging results, these pharmacokinetic characteristics restrict the attainment of therapeutic plasma/tissue concentrations in humans [Arif, et al. 2020]. For instance, a pilot human study discovered that there was no dose-dependent rise in plasma curcumin levels or antioxidant capacity when the dosage of C. longa was increased from 1.5 g to 6.0 g [Uchio et al. 2021]. Second, there is variation in clinical trial quality, duration, dosages, and formulations. Comparisons are challenging since several studies use different extracts, curcumin adjuvant combinations such with piperine, or innovative delivery methods liposomes, nanoparticles. Furthermore, there are significant differences in trial inclusion criteria, endpoints, and outcome measures; for example, the osteoarthritis scoping review found that sample sizes and methodological quality precluded drawing firm conclusions [de et al. 2022]. Meta-analyses highlight the fact that many RCTs have small sample sizes, short durations, and considerable bias. Thirdly, time and sample size frequently insufficient. The potential to identify clinically significant effects and evaluate long-term safety or disease-modification is limited by the fact that many trials enroll comparatively few people and monitor them for brief periods of time. For instance, a meta-analysis on arthritis warned against interpreting the results due to the small number and poor quality of RCTs [Zeng et al. 2022]. Reviews of metabolic syndrome settings also mentioned brief therapies and small sample sizes. Fourth, it is important to recognize the possibility of bias and reporting constraints in current trials. Certain trials include sponsorship that could add bias, lack blinding, or use insufficient control groups [Marton et al. 2021]. The included RCTs showed a high risk of bias, a narrow language/database scope, and possible publication bias, according to the meta-analysis. Fifth, it is yet unclear how preclinical promise will translate into clinical relevance. Curcumin exhibits wide anti-inflammatory, antioxidant, and signaling-modulatory properties in lab models; however, the extent of these effects in humans, particularly in large-scale, well-controlled trials, is still unclear. Certain results seem encouraging, but rigorous large-scale trials frequently fail to substantiate [Fahira et al. 2019]. Precise therapeutic targeting is further complicated by curcumin's many routes and intricate mechanisms. Finally, there are important concerns with standardization, regulations, and reproducibility. The composition, curcuminoid level, and presence of additional plant components differ among botanical extracts. It is difficult to guarantee stability, uniformity, and strict quality control from batch to batch. The regulatory frameworks for botanical therapies are different from those for conventional pharmaceuticals, which could make it more difficult to translate them into regular clinical use [Pharmedico et al. 2024].

Safety, Toxicity, and Side Effects

Curcuma longa has long been used in traditional medicinal and dietary purposes and is generally considered safe for human ingestion. Curcumin, Turmeric's primary active component has been

demonstrated to in numerous clinical and toxicological investigations to have minimal toxicity and excellent tolerance when taken within therapeutic levels. Curcumin dosages up to 8–12 g daily are generally well tolerated without creating significant side effects, according to human research [Sharma et al. 2020]. There have occasionally been reports of mild and temporary gastrointestinal problems such nausea, flatulence, diarrhea, and stomach pain, mainly at larger doses or in sensitive people [Chainani-Wu et al. 2003]. Curcuma longa has a good safety margin, according to toxicological tests; at modest doses, animal trials have shown no discernible evidence of organ toxicity. However, extremely high curcumin concentrations may cause hepatotoxicity, changes in blood parameters, and changes in liver enzyme levels, underscoring the necessity of cautious dose regulation [Zheng et al. 2017]. Additionally, because curcumin is bioactive, it may affect the pharmacodynamics of a number of medications. It has been demonstrated to increase the risk of bleeding by intensifying the effects of anticoagulant and antiplatelet drugs like aspirin and warfarin [Basnet et al. 2011]. Similarly, if curcumin is not well controlled, it may increase the hypoglycemic action of antidiabetic medications, resulting in dangerously low blood glucose levels. Similarly, if curcumin is not well controlled, it may increase the hypoglycemic action of antidiabetic medications, resulting in dangerously low blood glucose levels [Sharma et al. 2020]. Curcumin's low solubility and bioavailability, which leads to quick metabolism and systemic removal, is another drawback of its use. In order to improve absorption and reduce toxicity, researchers have created innovative formulations such nanoparticles, liposomes, phospholipid complexes, and piperine co-administration [Anand et al. 2007]. Even though these developments increase safety and therapeutic efficacy, there is still a lack of long-term safety evidence on these formulations, which calls for more research. Additionally, because of curcumin's chelating qualities, excessive or extended usage of turmeric supplements may result in iron shortage or impede the absorption of iron [Jurenka et al. 2009].

Interactions with conventional medications

Substances used in the diagnosis, treatment, or prevention of disease are referred to as conventional drugs (https://www.dictionary.merriam-webster.com/drug). The majority of pharmaceuticals on the market today come from natural sources that have been chemically altered to increase their effectiveness and safety. Herbal medicines, on the other hand, are herbal remedies made from plant components or fractionated or refined extracts of plants utilized in their natural state and are typically supplied as supplements (https://www.who.int/medicines/areas/traditional/definitions/en/). Natural products are utilized as an alternative treatment or as a supplement to conventional medications; however, the likelihood of pharmacokinetic interactions increases when they are used concurrently with conventional medications [Siah, et al. 2016]. Curcuma longa L. rhizome, either fresh or dried, a a Zingiberaceae family member, is known as turmeric. It is an ancient medicinal herb that is mostly used to treat inflammatory, gastrointestinal, and cancerous illnesses. Pharmacokinetic alterations via CYP450 were the most evaluated pathways, followed by P-gp. Glutathione-S-transferase, uridine dinucleotide phosphate glucuronosyltransferase, and organic anion-transporting polypeptides were investigated less frequently [Prasad et al. 2011].

Interaction with P-glycoprotein: Multidrug resistance 1 (MDR1) genes encode P-glycoprotein (P-gp), an efflux pump from the ATP-binding cassette (ABC) super family that eliminates numerous medicines and other xenobiotics from the intracellular compartment [Aggarwal et al. 2003]. There are two ways to explain the significance of P gp: First, P-gp is in charge of the low levels of medicines in cells, including those used in chemotherapy, which diminishes their clinical effectiveness. Second, Certain P-gp inhibitors, such as grapefruit juice, can increase drug levels that cause toxicity and are P-gp substrates, particularly for medications with brief therapeutic windows [Choi et al. 2005]. The pharmacokinetics of concurrently administered medications may therefore be impacted by any chemical that modifies P-gp protein expression. The first study on curcumin's dose-dependent inhibitory effects in vitro action at doses of 25 and 100 μMonP-gpusing Rat hepatocyte primary cultures was reported in 1998 by Romiti et al. At doses ranging from 1 to 10 μM, curcumin dramatically reduced P-gp expression and MDR1 mRNA levels inside KB-V1 cells (cervical cells in humans resistant to multiple drugs) [Yu et al. 1999]. In Caco-2 cell lines, they found showed P-gp activity was decreased by curcumin and demethoxycurcumin, but not by Curcumin bisdemethoxy. C. longa extract (100 μM) in Caco-2 cells markedly boosted P-gp activity, but curcumin (30 μM) had the opposite effect, decreasing both P-gp activity and MDR1 mRNA expression [Ampasavate et al. 2010]. Another study found that curcumin and tetrahydrocurcumin, a metabolite of curcumin, increased MDR1 mRNA levels and P-gp function in Caco-2 cells overexpressing P-gp within an hour of

incubation. Demethoxycurcumin, bisdemethoxycurcumin, and 15 µM curcumin all showed inhibitory effects on P-gp Curcumin has the greatest impact in cell lines KB-V1, which are Cervical cancer cells in humans [Juan et al. 2013].

Interaction with drug-metabolizing enzymes and other transporters

Another ABC efflux pump component that causes medication resistance in a variety of cancer types is MRP1, or multidrug resistance protein 1. Evaluated the impact of Curcumin decreased MRP1 activity in Human embryonic kidney cells, or HEK293 at concentrations of 5–10 µM. Therefore, it may have an impact on the bioavailability and plasma levels of chemotherapeutic drugs when administered concurrently. The primary component of phase II drug metabolism, UDPG, or uridine dinucleotide phosphate glucuronosyltransferase, are in charge of glucuronidation processes that convert lipophilic medicines into more polar metabolites in order to prepare them for elimination [Chearwae et al. 2004]. Oral treatments with varying doses of curcumin (10–100 mg/kg) totally inhibited the glucuronidation of mycophenolic acid, a UDPG substrate, in isolated microsomes from the duodenal tissue of C57BL/6 mice. Furthermore, within the intestinal cell line LS180, 50 µM doses of curcumin demonstrated 80–98% inhibition of the glucuronidation of mycophenolic acid [King et al. 2000]. In a different investigation, LS180 treated with a variety of curcuminoids doses showed a 12.2±1.8 µM IC50 for acetaminophen glucuronidation inhibition. UDPG activity was likewise inhibited by purified curcumin, demethoxycurcumin, and bisdemethoxycurcumin, with IC50 values of 2.2±0.1, 13.9±2.3, and 9.8±1.4 µM, respectively [Basu et al. 2004]. On the other hand, Suresh and Srinivasan (2006) observed that Curcumin in food (0.2%) had neither either inhibitory or inductive effect on UDPG in Wistar rats. Sulfotransferase is another drug -degrading enzyme that transfers the "sulfo" the acceptor molecule's moiety, like a a xenobiotic [Volak, et al. 2008]. Acetaminophen was not sulfated in cell lines LS180 by any of the curcuminoids or curcuminoid that have been identified combinations. Curcumin was also shown to be the most potent inhibitor, with an IC50 of 2.6±0.4. Another enzyme involved in the phase II metabolism of xenobiotics is glutathione-s-transferase (GST), which catalyzes the conversion of reduced glutathione to electrophilic substrates in order to detoxify these compounds [Paul et al. 2012]. Curcumin inhibited several GST subtypes, including GSTA1-1, GSTM1-1, and GSTP1-1, with IC50 values of 18.8±0.77 µM, 0.3±0.10 µM, and 15.1±1.12 µM, respectively, according to Appiah-Opong et al. (2009) using human recombinant GSTs. Furthermore, curcumin inhibited the cytosolic GST enzymes in rats and humans by 4.2±0.23 and 50.5%, respectively [Townsend et al. 2003]. With IC50 values ranging from 0.04 µM to 5 µM, curcumin demonstrated an inhibitory impact on GSTP1-1, GSTA1-1, GSTA2-2, GSTM1-1, and GSTM2-2 in a different study on human recombinant GST enzymes [Appiah-Opong et al. 2009]. The bilayer of lipids in many membranes of cells contains a type of membrane-active transporters called organic anion transporting polypeptides. They are essential for the disposal of certain pharmacological drugs, and interference with them may have detrimental therapeutic consequences. Curcumin may impact other medicines' pharmacokinetics because it and OATPs, particularly OATP1B1 and OATP1B3, are substrates and inhibitors of its metabolites, curcumin-O-glucuronide and curcumin-O-sulfate [Zhou et al. 2017].

Curcumin's impact on the pharmacokinetics of traditional medications

Curcumin's interactions cardiovascular drugs, antidepressants, analgesics, antihistamines, chemotherapy medications, Anticoagulants, immunomodulators, and antibiotics are among the classes of conventional drugs that have been studied.

Antidepressants: 1. Buspirone: Sprague-Dawley rats were given 200 mg/kg of curcumin taken orally along using intravenous buspirone at a dose of 10 mg/kg to evaluate the ensuing pharmacokinetic alterations; however, buspirone pharmacokinetic parameters did not differ significantly [Sun et al. 2016].

Midazolam

The total area under the concentration-time curve (AUC) (3.8 fold, $p = 0.03$) and the AUC for midazolam (20 mg/kg) during the first four hours (2.6 fold, $p = 0.04$) increased in rats given 60 mg/kg of curcumin orally, while the maximum serum concentration (Cmax) stayed constant. The main reason for this effect was the downregulation of intestinal CYP3A4 iso form [Kim et al. 2015]. However, eight healthy participants in a randomized controlled study participants, a A two-day dose of curcumin (four grams of curcuminoids and twenty-four milligrams of piperine, four times a day) did not substantially alter the pharmacokinetics of three milligrams of midazolam per day. Due to the limited size of the sample (8 participants) and brief duration of follow-up, the outcomes of this human study can only

be applied to acute drug combinations; additional research on chronic effects is necessary[Zhang et al. 2007].

Antihistamines: Loratadine Rats' loratadine pharmacokinetics were dramatically altered by a single dosage of curcumin (0.5–8 mg/kg) resulting in increases of Cmax and total AUC of 34.2–61.5% and 39.4–66.7%, correspondingly ($p<0.05$). Improved gastric absorption from decreased P gp activity and a decrease in first pass metabolism from decreased intestinal and hepatic CYP3A4 activity could account for the higher oral bioavailability of loratadine. Short-term co-administration of curcumin and loratadine should be regarded as safe because loratadine is reported to be safe, well-tolerated, and free of major adverse effects; however, longer-term interactions should be further investigated [Li et al. 2011].

Anticoagulants: Warfarin: Following seven days of co-administration of warfarin and curcumin, the overall AUC increased by 1.6 times and the Cmax increased by 1.5 times ($p<0.05$). Additionally, there was a 57.14% decrease in warfarin clearance ($p<0.05$). A.C. Liu et al. (2013) asserted that the pharmacodynamic parameters of warfarin, such as anticoagulant activity, had not changed during the experiment, despite these pharmacokinetic changes. However, co-administration of curcumin with warfarin should be continuously monitored because warfarin has a limited therapeutic window and little variations in its serum level could result in bleeding and related problems [Leynadier et al. 2000].

Clopidogrel

Curcumin increased oral clopidogrel's overall AUC and Cmax in a rat model by 1.61 and 1.81 times, respectively ($p<0.05$). The aforementioned changes were only noticeable at 100 mg/kg of curcumin; no discernible changes were seen at lower dosages. While curcumin shown inhibitory effects on this isoform, Clopidogrel is a prodrug that CYP2C19 metabolism activates. However, P-gp decreases clopidogrel absorption; hence, curcumin's suppression of P-gp may be one of the ways that clopidogrel's pharmacokinetics are changed [Liu et al. 2013].

Future Perspectives and Research Gaps

Although Curcuma longa pharmacological qualities have been thoroughly investigated, the creation of gel formulations for topical treatments is still in its infancy and confronts a number of obstacles. The lack of well-designed clinical trials assessing the pharmacokinetics, safety, and effectiveness of Curcuma longa gel in humans is the main research gap. Although instructive, the majority of current research has been done on animal models or in vitro systems, which do not accurately reflect the intricate physiological reactions in human skin [Taubert et al. 2006]. Therefore, additional randomized controlled clinical trials are required to establish uniform dosage and application methods and validate the therapeutic claims. The absence of formulation standardization is another crucial problem. Different research have utilized different gelling agents, such as carbopol, HPMC, or chitosan, and different types of curcumin extracts, such as pure curcumin, ethanolic extracts, or essential oils of turmeric. This has resulted in varied results and made it challenging to compare data across investigations [Gupta et al. 2021]. To guarantee repeatability, effectiveness, and product stability, formulation factors like pH, viscosity, penetration enhancers, and curcumin content must be standardized. Curcumin's low bioavailability and poor solubility also make it difficult for the skin barrier to absorb it. Curcumin's solubility, stability, and penetration in topical applications have improved because to novel techniques such the utilization of nanocarriers, liposomes, nanoemulsions, and polymeric hydrogels [Jaiswal et al. 2020]. By extending curcumin's retention period and regulating its release at the target site, these innovative delivery methods may improve therapeutic efficacy. Furthermore, long-term stability and safety studies are required to comprehend the behaviour of Curcuma longa gel in various environmental settings and over extended periods of use. Assuring patient safety requires assessing possible skin irritation, allergenicity, and interactions with other topical drugs [Tortora et al. 2022]. Regulatory and commercialization issues, such as bioequivalency studies, standard quality control processes, and Good Manufacturing Practices for large-scale production, should also be covered in future study. The development of successful Curcuma longa gel formulations can be significantly advanced by incorporating interdisciplinary approaches that combine pharmaceutical technology, dermatological research, and material engineering. Additionally, researchers should concentrate on target-specific formulations with clinical validation, such as gels intended for wound healing, anti-inflammatory therapy, or cosmetic applications. Overall, filling in these research gaps will make it possible to successfully translate laboratory results into Curcuma longa gel products for therapeutic and cosmetic use that are safe, efficacious, and clinically proved [Hewlings et al. 2017].

Potential for developing new drugs from Curcuma longa

Curcuma longa has become a potent source of bioactive substances with enormous potential for the creation of novel medications. The plant's rhizome is home to a vast range of phytochemicals, the most significant of which are curcuminoids and volatile oils, which give the plant its numerous therapeutic advantages [Anand et al. 2007]. Curcumin, the primary curcuminoid, has been well studied for its anti-inflammatory, antioxidant, antibacterial, anticancer, hepatoprotective, and neuroprotective qualities. It is a very adaptable lead compound for drug design because it acts by modulating a number of cellular targets, such as cytokines (TNF-α, IL-6, IL-1β), enzymes (COX-2, LOX, iNOS), transcription factors (NF-κB, AP-1), and growth factors (VEGF, EGF) [Zhou et al. 2017]. Curcumin's potential as a multi-target therapeutic agent is highlighted by its capacity to simultaneously control many biochemical pathways, setting it apart from many single-target synthetic medicines. Curcumin is a promising prototype chemical in the realm of drug research and development. However, its quick systemic clearance, low bioavailability, and poor water solubility have hampered its therapeutic potential. Researchers have started creating curcumin analogs and other medication delivery methods to solve these shortcomings. For example, compared to natural curcumin, synthetic derivatives like EF24, GO-Y030, and CDF have demonstrated better stability, greater potency, and improved pharmacokinetic characteristics in preclinical animals [Choudhury et al. 2021]. Furthermore, curcumin's solubility, skin permeability, and systemic bioavailability have significantly improved thanks to nanotechnology-based delivery methods such nanoparticles, liposomes, micelles, and nanoemulsions. These advancements enable the development of curcumin-based nanomedicines for the treatment of cancer, wound healing, inflammatory illnesses, and neurological disorders including Alzheimer's. Other components of Curcuma longa, such as ar-turmerone, curdione, and germacrone, have beneficial pharmacological qualities in addition to curcumin. By encouraging neural stem cell proliferation and differentiation, ar-turmerone has demonstrated neuro-regenerative potential, indicating potential uses in neurodegenerative diseases [Rahmani et al. 2018]. Similar antibacterial and anticancer properties are shown by curdione and germacrone, which could result in the discovery of novel lead compounds for pharmaceutical development. Another encouraging feature is the synergistic interaction between curcuminoids and essential oils, since whole-extract formulations frequently show better therapeutic results than isolated substances. Future studies should concentrate on applying laboratory results to clinical settings. This entails carrying out thorough pharmacokinetic and pharmacodynamic investigations, refining structural analogs for improved receptor binding, and carrying out multi-center clinical trials to verify safety and efficacy. Furthermore, new derivatives from Curcuma longa with specific biological effects can be found more quickly thanks to computational technologies like molecular docking, QSAR modeling, and AI-based drug screening. To transform these natural substances into medicines that are therapeutically feasible, cooperation between phytochemists, pharmacologists, and medicinal chemists will be crucial. Curcuma longa has significant promise for the development of next-generation therapeutic agents that combine the safety of natural products with the accuracy of contemporary drug design, thanks to ongoing advancements in biotechnology and nano-medicine [Choudhury et al. 2021]..

CONCLUSION

Curcuma longa is a very useful medicinal plant with tremendous therapeutic potential because of its rich phytochemical profile, which includes essential oils and curcuminoids. Numerous studies demonstrate curcumin's potent Hepatoprotective, anti-inflammatory, anti-cancer, antibacterial, and antioxidant, cardioprotective, and neuroprotective properties. These impacts arise from its ability to regulate multiple biochemical pathways; making it a promising multi-target therapeutic candidate. Modern delivery technologies; including nanoparticles, liposomes, micelles, nano-emulsions, and solid-lipid carriers, have significantly enhanced its stability, absorption, and therapeutic effectiveness, despite the fact that its poor solubility and limited bioavailability are still significant drawbacks. Other components of Curcuma longa, such as germacrone, curdione, and ar-turmerone, exhibit significant pharmacological activity and could be used as lead molecules in the development of new drugs. More standardized formulations and carefully planned to confirm safety, effectiveness, and the optimal dosage, clinical trials are required in humans despite a wealth of pre-clinical evidence. It is anticipated that developments in biotechnology, computational drug design, and nano-medicine may hasten the conversion of molecules generated from Curcuma longa into potent, clinically proven medicinal treatments. All things considered, Curcuma longa continues to be a potent, safe, and adaptable natural resource with

enormous potential for future medication development and therapeutic uses.

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