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REVIEW

Unveiling the Therapeutic Wonders of Curcumin: A Comprehensive Review of Its Impact on Human Health

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Abstract
Curcumin, a vital culinary spice, is the biphenolic active compound of turmeric and has a rich history of use in ancient therapeutic medicine. It has long been used for hundreds of years to treat various ailments such as cancer and neurodegenerative diseases. This review will show an overview of the plant of curcuma and the history of curcumin. In addition, its chemical composition will be discussed to clarify the chemical component essential for its biological activity. Recently, the biological activities of curcumin have been inve stigated. The studies mainly focused on their antitumor, antioxidant, anti-inflammatory, hepatoprotective, neuroprotective, and cardioprotective impacts. This review aims to provide a discussion about curcumin use and its effect on human health and disease prevention.
Keywords: Curcumin, Traditional Medicine, Chemical Composition, Biological and Therapeutic Properties

INTRODUCTION

Curcumin originates from the turmeric plant (*Curcuma Longa*), which is a sacred spice in India, where it has had an important place in social, culinary, and medicinal tradition. Turmeric is one of the main components of traditional Indian medicine, Ayurvedic medicine, which is probably the oldest medicinal tradition of humanity. In Chinese medicine, turmeric is used to treat abdominal pain. In the East, it was traditionally used for its anti-inflammatory action [1]. The therapeutic effects of curcumin have been confirmed by scientific studies, including antioxidant properties, anti-inflammatory, anticarcinogenic, anti-microbial, thrombolytic, cardiovascular (protection against myocardial infarction), hypoglycemic, and anti-arthritic [2,3]. Turmeric's antioxidant properties are associated with its composition of phenolic compounds, grouped under the name of curcuminoids, the main one being curcumin [4].

In this review, the essential impact of curcumin and its medicinal uses will be presented. First, a brief description of the curcuma plant, curcumin's history, and its chemical composition will be provided. In the second part, curcumin, the active compound derived from turmeric, possesses a range of biological properties that contribute to its potential therapeutic effects.

Description of Curcuma plant:

Curcuma longa L. is a species of perennial, rhizomatous, herbaceous plants of the genus Curcuma (family Zingiberaceae) native to south or southeast Asia. **(Figure 1).**

The main ovoid-shaped rhizomes provide round turmeric, and the secondary ones provide long turmeric. Thick, scaly, and wrinkled by desiccation, these rhizomes are orange yellow in section and brownish gray on the surface. An aromatic odor is released after sectioning the rhizome [5]. Its leaves, very long, oblong to elliptical, sheathing, have a powerful axial vein and parallel secondary veins. Within the leaves rises the inflorescence consisting of a cylindrical spike up to 20 cm long. **(Figure 2).**

It is composed of dark green and sterile imbricated bracts, in the axils of which white or yellowish flowers are born, one for each bract. Only the upper bracts, pink, are more beautiful [6].

The flowers have a short, tubular calyx with unequal teeth, a tubular corolla at its base, then divided into

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3 unequal yellow lobes and stamens, including only one fertile, bifid, the anther presenting a large, curved spur at the base. Turmeric is valued for its medical properties. Turmeric root has an active compound such as curcumin, which gives the plant antioxidant, anti-inflammatory, and anti-cancer properties [7].

Figure 1. Curcuma Plant [2]

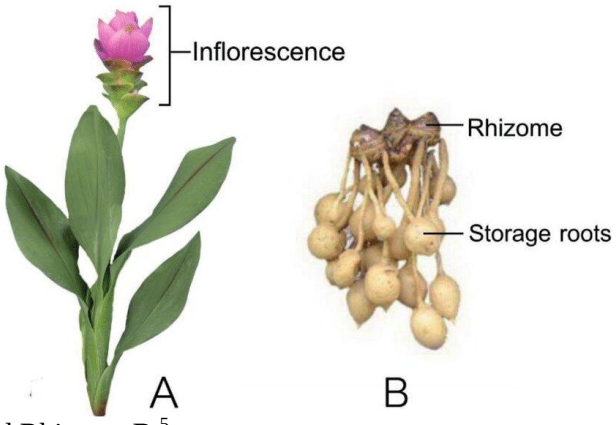

Figure 2. Inflorescence A - and Rhizome B [5]

HISTORY

Turmeric has been cultivated through the centuries in India. Although it was already appreciated there more than 3000 years ago, it is still very present in many Hindu mixtures, such as the masala mixture. It is also still used in rituals to symbolize the sun. It was introduced to Europe in the Middle Ages by Ottoman merchants, where it was widely used as a cheap saffron [8]. In the 18th century, turmeric, under its name Terra merita or Indian saffron, was imported to Europe by the great naval powers (Holland, the United Kingdom, Portugal, and France). If it is used as a spice, it is also used for its medicinal properties. Turmeric is a plant derived from the ginger family that has been used for centuries in Asia. Due to its antioxidant properties, it has long been used as a natural food preservative.

Turmeric powder is the main ingredient in curry, which gives it its intense yellow color. India, where it is believed to have originated, accounts for 90% of the world's turmeric production. It is also produced in other Asian countries such as China, Thailand, Cambodia, and Malaysia [8].

Using of curcumin in traditional medicine:

Curcuma Longa is a plant that grows wild in the forests of Southern Asia, including Indonesia, India, Indochina, nearby Asian countries, and some Pacific Islands. All of these areas have medicinal uses and traditional culinary practices going back to prehistory. In the Indian Ayurveda system of herbal medicine, turmeric is known as warming and strengthening for the entire body[9]. Traditional uses in India include improving intestinal flora, improving digestion, eliminating worms, cleansing the liver and gallbladder, relieving gas, normalizing menstruation, warming, and promoting proper metabolism, correcting both deficiencies and excesses, local application on cuts, sprains, burns, and bruises, providing soothing action in cough and asthma, acting as an antibacterial and anti-fungus, and in any condition of debility or weakness.

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The ancient Hawaiians used curcuma for many things, including ear infections and gastrointestinal ulcers, the prevention and treatment of sinus infections (it is very astringent and appears to pull mucus out). Turmeric is consumed as food, both in its raw and cooked forms, across Asia.

Another traditional use of turmeric is as a dye for cloth and a food colorant—in both cases a cheaper alternative to saffron. It was and is used in religious ceremonies—often representing purity, life, and prosperity. The rhizome is the part of the plant that is most largely used. It can be prepared in different ways and is reputed to alleviate coughs and asthma[10,11].

Chemical composition of curcumin:

Curcumin, or diferuloyl-methane, is the main pigment of turmeric (Curcuma longa), also called Indian saffron. It is a polyphenolic pigment (curcumoid) that gives a yellow color [12]. **(Figure 3).**

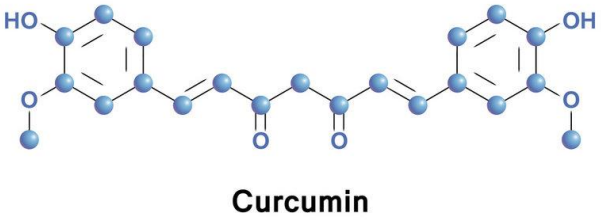

Figure 3: Turmeric and Chemical Structure of Curcumin [12]

The rhizomes can produce 2 to 7% essential oil, which is orange-red and slightly fluorescent. Its main constituents are a sesquiterpene, zingiberene (25%), and its ketone derivatives: turmerone (35%) and ar-turmerone (dehydroturmerone) (12%). **(Figure 4).**

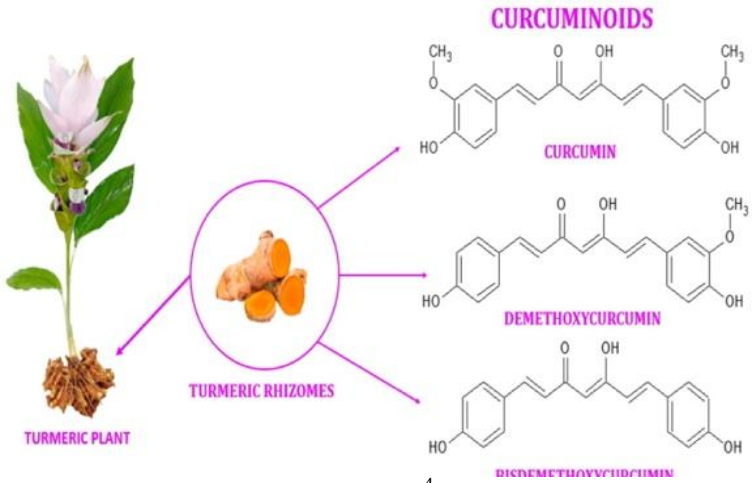

Figure 4: Curcuminoids Found in the Rhizomes of Turmeric [4]

Turmeric is mainly composed of carbohydrates, almost 65%. The carbohydrates present are simple sugars, such as fructose, glucose, and sucrose. There are approximately 10% lipids in turmeric. These include an omega-9, linoleic acid, an omega-6, and steroids (cholesterol, campesterol, and stigmasterol) [13].

A little less than 5% of turmeric powder is composed of minerals, such as calcium, magnesium, potassium, iron, or zinc. Some traces (<1%) of vitamins are found in turmeric, such as vitamins B1, B2, B3, B9, C, and E [13].

BIOLOGICAL AND THERAPEUTIC PROPERTIES OF CURCUMIN

Anti-inflammatory effect:

Inflammation is a cascade of chemical reactions following an attack on the body, which causes swelling (edema), heat (increased local blood circulation), and pain. Regardless of the type of inflammation, it is always comfortable to alleviate the pain. However, taking conventional anti-inflammatories such as NSAIDs (non-steroidal anti-inflammatory drugs), such as ibuprofen, aspirin, etc., leads to numerous side effects linked to the mechanism of action of these synthetic molecules:

digestive disorders, kidney problems, musculoskeletal changes, skin disorders, etc. [14,15].
Turmeric is particularly known for fighting inflammation. More than 6 studies have shown an anti-inflammatory effect of turmeric without toxic effects. The anti-inflammatory effect of curcumin is induced by its ability to stop the production of pro-inflammatory mediators. Indeed, curcumin acts directly on the enzymes responsible for producing inflammatory molecules, also called cyclooxygenase (Cox-2) and 5-lipoxygenase (Lox-5)[16]. Curcumin thus inhibits the production of prostaglandins, leukotrienes, thromboxanes, and cytokines. Osteoarthritis is a common complication among older individuals, and many treatments aim to reduce symptoms using anti-inflammatories. The need for new therapeutic approaches has led to the development of anti-arthritic drugs (e.g., Chondrosulf®, Art 50®), which are not without risks and can cause undesirable effects. Curcumin is considered an alternative to these treatments. In the first clinical study on the effectiveness of curcumin as an anti-rheumatic drug, researchers compared its anti-rheumatic power to that of phenylbutazone in 18 people. Each person received a daily dose of either 1200 mg of curcumin or 300 mg of phenylbutazone for 2 weeks. Curcumin was well tolerated at this dose and exerted activity comparable to phenylbutazone. Curcumin has also been shown to suppress inflammation by many different mechanisms and acts as a potential anti-inflammatory agent [17].

Anti-cancer effect:

Curcumin has shown considerable anticancer effects against several different types of cancer, including breast cancer, prostate cancer, colon cancer, bone cancer, melanoma, etc **(Figure 5).**

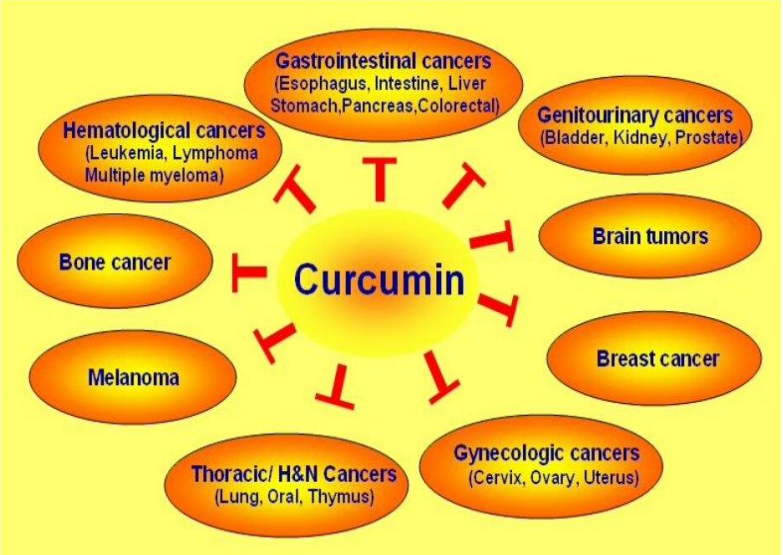

Figure 5: Anti-Cancer Effects of Curcumin[2]

Using highly advanced X-ray crystallography methods, a Chinese American research team demonstrated that active component in turmeric, curcumin, blocks the activity of an enzyme essential for tumor growth.
Preclinical studies performed indicate that curcumin's anticancer action is due to its ability to inhibit several key enzymes involved in tumor progression, including various tyrosine kinases that are already targeted by chemotherapy drugs, as well as certain oncogenes like Her2, another major target of chemotherapy [18].
To clarify curcumin's mechanism, the scientists have studied its inhibitory effect on a very broad range of kinases, a family of ATP-binding enzymes that are known to play crucial roles in tumor growth. They observed that very low concentrations of curcumin (picomoles per milliliter) led to the specific inhibition of an enzyme called dual-specificity tyrosine-regulated kinase 2 (DYRK2).
By blocking the activity of DYRK2, curcumin therefore promotes an accumulation of abnormal proteins, which ultimately cause the death of the cancer cell by intoxicating it. This is particularly true in the case of certain types of cancer that rely heavily on the presence of a functional proteasome, such as triple-negative breast cancer and multiple myeloma. This action of curcumin could even explain certain spectacular results that have been obtained during clinical trials [19].

In terms of cancer prevention, the positive action of curcumin on very advanced cancers, which no longer respond to chemotherapy in several cases, strongly suggests that this action will be even more effective against tumors in their early stages, which are indeed much more sensitive to the presence of anticancer agents. For this reason, regular consumption of turmeric can prevent cancer: Due to its anti-inflammatory action and its multiple anti-cancer properties, curcumin creates an inhospitable environment for microtumors that develop spontaneously during our lives, depriving the resources necessary for their progression into mature cancer [20].

Neuro-protective effect:

Many neurodegenerative illnesses of aging involve the accumulation of protein aggregates, inflammation, and oxidative damage. Curcumin has multiple characteristics for a neuroprotective drug, including antioxidant, anti-protein-aggregate activities, and anti-inflammatory.

Because of its oral safety, pluripotency, long history of use, and low cost, curcumin has high potential for the prevention of multiple neurological conditions for which current therapeutics are suboptimal. Examples reviewed include Parkinson's, Huntington's, Alzheimer's, head trauma, stroke, and aging [21].

i) Antioxidant properties:

The antioxidant property of curcumin prevents the alteration caused by exposure to fatal factors such as drugs, alcohol, heavy metals, and radiation. Because it is a hydrogen donor and a good free radical scavenger.

Curcumin is not very toxic and has limited bioavailability. Protects DNA from oxidative damage due to its ability to capture free radical [22].

ii) Neurotransmitter modulation:

Curcumin modulates the level of various neurotransmitters such as norepinephrine, serotonin, and dopamine in the brain. Norepinephrine is a neurotransmitter involved in emotions, sleeping, learning, and dreaming. Dopamine is involved in emotion, pleasure, and regulating locomotion, while serotonin plays an essential role in neurovegetative functions of the body, such as sleep, appetite, memory and learning, mood, behavior (including sexual behavior), cardiovascular functions, endocrine regulation, and muscle contraction [23].

iii) Amyloid-beta plaque disruption:

Alzheimer's disease promotes a regression in thinking, memory, learning, and organizing skills over time.

An abnormal accumulation of proteins in brain causes Alzheimer's disease. The build-up of these proteins, tau protein and amyloid protein, causes the death of brain cells. Scientists believe that amyloid protein accumulates in brain cells, forming larger masses called plaques.

Recent research on curcumin and amyloid-β has revealed that curcumin prevents amyloid-β aggregation, reaches brain cells, and protects neurons from multiple toxic insults of aging and amyloid-β in humans [24].

Cardioprotective effects:

Cardiovascular diseases (CVDs), disorders of the heart and blood vessels, are the most common cause of death worldwide and a major health problem worldwide. Individuals at risk for CVDs may present weight issues, high blood pressure, and lipid levels or altered glucose. Great progress in research has been made to study the pathogenesis mechanism of CVDs, but the mortality and morbidity of CVDs are still very high. For this reason, there is urgently a need for drugs to prevent and treat these diseases. Compared to traditional drugs, natural drugs have many benefits, such as low long-term toxicity, fewer side effects, and variable bioavailability [25].

Some studies have shown that pleiotropic effects of curcumin in CVDs propose that it is a promising drug candidate.

Specifically, curcumin can significantly inhibit foam cell formation, mitigate vascular endothelial dysfunction, reduce vascular smooth muscle cells (VSMCs) proliferation, protect cardiomyocyte injury after hypoxia and ischemia, inhibit myocardial hypertrophy and fibrosis, and reduce drug-induced myocardial injury [26].

On the other hand, endothelial progenitor cells (EPCs) have an important role in wound healing. Clinical studies have shown that curcumin promoted angiogenesis and migration and reversed the number of aging EPCs by up-regulation of angiotensin I (Ang I) and vascular endothelial growth factor (VEGF)-A4.

Finally, curcumin has a positive and protective effect on CVDs. It is important to note that curcumin is an alternative or complementary medicine, not a replacement for the main treatment, and should be used under the guidance of a doctor [27].

CONCLUSION

We have seen that the major active ingredient in turmeric, curcumin, acts on many targets and has the potential to treat various diseases. The exact

mechanisms by which curcumin produces its therapeutic effects have not yet been fully elucidated, but they are likely mediated through its its antioxidant and anti-inflammatory activity. Indeed, curcumin curcumin has been shown to offer protection against cancer, cardiovascular diseases, Alzheimer's disease, cystic fibrosis, pancreatitis, rheumatoid arthritis, and numerous other pathologies. However, at present, data regarding turmeric and curcumin are mostly based on laboratory studies on animals. Its effectiveness in humans remains to be proven. This will require years of research, as the the number of pathologies that this molecule can potentially treat is considerable. Thus, larger clinical trials are needed to fully evaluate its potential in terms of optimal dose, route of administration, and target diseases. In addition, all the studies performed have focused on the medical applications of curcumin, but none have been developed as a drug. One of the main obstacles to its use is its low bioavailability. For this reason, to benefit well from all its advantages, it is recommended for daily use to combine it with a fatty substance and pepper. A teaspoon of turmeric powder per day in the diet is sufficient to achieve a preventive effect. A lot of research has also been launched to improve its bioavailability. Turmeric, through its ancestral use in cooking as a spice and then in traditional medicine, has proven its safety and its health benefits.

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