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Anti – Inflammatory Properties of Curcumin

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ABSTRACT

Turmeric has been used for centuries as a spice, color, and medicine. Turmeric, as an herb, has the ability to fight a variety of diseases. Turmeric, an old herbal remedy and nutritive spice, contains curcumin, the most active polyphenolic component. Curcumin is a natural extract.

Key words:-Inflammation, nanoparticles, bioavailability, chronic inflammation.

INTRODUCTION

Turmeric is the spice responsible for the yellow color in curry. It has been used as a spice and medicinal herb in India for thousands of years. Turmeric used in herbal and traditional medicine to treat rheumatoid arthritis, chronic anterior uveitis, conjunctivitis, skin cancer, small pox, chicken pox, wound healing, urinary tract infections, and liver ailments, as well as to boost overall energy, dispel worms, regulate menstruation, dissolve gallstones, cleanse wounds, and even for various digestive disorders, among other things [4]. Turmeric was traditionally known as "Indian saffron" because of its vivid yellow-orange hue, and it has been used as a condiment [32]. Traditional Indian and Chinese medicines have used turmeric for the treatment of a diversity of diseases [9]. Turmeric (also known as Arab globe Curcuma, Haridra in Sanskrit, Chinese yellow ginger Jianghuang, Japanese Kyoo, or Ukon [33])

Turmeric powder has an earthy, mustard-like aroma and a warm, bitter, black pepper-like taste[5]. It is a perennial, rhizomatous, herbaceous plant native to the Indian subcontinent and Southeast Asia that thrives at temperatures ranging from 20 to 30 degrees Celsius (68 to 86 degrees Fahrenheit) and has a high annual rainfall [5]. Recently, science has begun to support Trusted Source's traditional statements that turmeric contains chemicals with therapeutic benefits. These chemicals are referred to as curcuminoids. The most significant is curcumin [1]. Turmeric contains 2% to 9% curcuminoids[23]. Curcumin is a vibrant yellow chemical produced by the Curcuma longa plant. It is the primary curcumin found in turmeric, a member of the Zingiberaceae ginger family.

It's sold as a herbal supplement, cosmetic ingredient, food flavoring, and food coloring[2]. Curcumin is a diarylheptanoid, a type of phenolic pigment that gives turmeric its yellow color [2]. Turmeric has traditionally been used to treat a variety of ailments, and it is especially popular in Southeast Asia, China, and India[3]. Despite its lengthy history in Ayurvedic treatment, where it is also known as haridra[5].

Turmeric is generally known in North India as "haldi," a name derived from the Sanskrit word haridra, and in the south as "manjal," a word that appears frequently in ancient Tamil literature. Turmeric gets its name from the Latin term terra merita, which refers to the color of ground turmeric, which resembles a mineral pigment. It is known as Terre merite in French and "yellow root" in many other languages. Its name is derived from the Latin word curcuma in numerous civilizations. Turmeric has at least 53 different names in Sanskrit, gauri (to make fair), gharshani (to rub), haldi (that draws attention to its bright color), haridra (loved to hari), harita (greenish), hemaragi (which shows golden color), hemaragini (gives the golden color), hridayavilasini (charming), jayanti (one that wins over diseases) etc [6]. In Northern India, mothers are given a tonic to drink twice a day after giving birth. This mixture consists of fresh turmeric paste, powdered dry ginger roots, and honey in a glass of hot milk. In order to promote healing of any lacerations from the birth canal, a poultice made of turmeric is applied to the perineum. While roasted turmeric is an antidysenteric for kids, powdered turmeric is used with boiling milk to treat coughing and other respiratory issues. In addition, dental conditions, stomach problems such dyspepsia and acidity, indigestion, gas, ulcers, and hallucinations are treated with this ancient medicine[7]. Kalyanavaleha, a semisolid treatment for hoarseness and speech impairment, is a mixture of curcuma longa, nine Indian Ayurvedic excipients, and cow's milk clarified butter[10].



Figure: 1 Turmeric [49].

Curcumin

Synonym

Curcuma aromatica, Curcuma domestica, Curcumae longa.

Natural source

Curcumin is found primarily in roots and rhizomes of the turmeric plant (Curcuma longa[36].

Geographical source

Curcumin is a product of Curcuma longa, a rhizomatous herbaceous perennial plant belonging to the ginger family Zingiberaceae, which is native to tropical South Asia[2,5].

2- Effects of curcumin:-

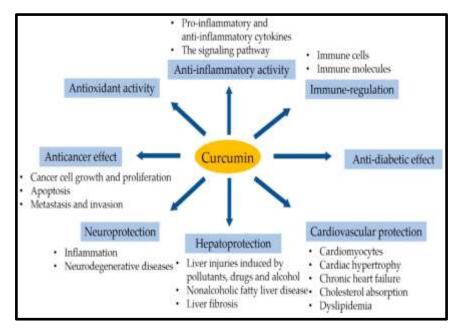


Figure:2[34]Effects of curcumin

3-Pharmacokinetics properties of Curcumin:

Curcumin's oral absorption is limited due to factors like low water solubility, poor intestinal permeability, alkaline pH instability, and fast metabolism. Its bioavailability is low in the intestines, spleen, liver, and kidneys, and negligible in the brain. Curcumin is extensively metabolized through conjugation

and reduction mechanisms[8,11,13,14,21]. The major curcumin in vivo metabolites are tetrahydrocurcumin, dihydrocurcumin, and curcumin glucuronides [14]. There are several strategies to increase curcumin bioavailability[15], some of them are as follows:

1-Mix with black pepper:-

According to studies, combining the piperine in black pepper with the curcumin in turmeric can boost curcumin absorption by up to 2,000%[16].Black pepper contains piperine, an alkaloid.Black pepper (Piper nigrum L.) is a widely used spice known as the "King of Spices"[18]. Belongs to the Piperaceae family [19]. There are two major possibilities regarding how this works.

First, piperine helps curcumin move through the intestinal wall and into the bloodstream, secondly it may block the liver's breakdown of curcumin, resulting in greater blood levels [15].

2-By complexation with phosphatidyl choline:-

Curcumin bioavailability can be improved by complexing it with phosphatidyl choline, as demonstrated by solubility, melting point, differential scanning calorimetry, thin layer chromatography, and infrared spectroscopy[20,21].

3-Curcumin nanoparticles:-

Curcumin nanoparticles, produced using high-pressure homogenization, significantly enhance bioavailability and concentration in plasma and brain, with a six-fold greater AUC and residence length in mice compared to normal curcumin[22,27].

Properties of curcumin

Chemical and physical properties of curcumin	Curcumin
Molecular formula	C21H20O6
Molecular weight	368.35g/mole
Melting point	183°C
Colour	Yellow
Solubility in water	Low
Reaction under base	Bright color
Reaction under acid	Bright yellow color
Monoisotopic mass	368.125977 Da (24)

Table:1 chemical and physical properties of curcumin [12].

4-Chemistry of curcumin

It is a polyphenolic molecule containing two aromatic rings, one hydroxy and one methoxy substituent on each . A seven-carbon chain with two – unsaturated carbonyl groups (tautomerizable) connects the rings[25].

Figure:3 structure of curcumin

Curcumin, a polyphenolic compound in turmeric, has antioxidant, anti-inflammatory, and anticancer properties. It's a beta-diketone molecule with keto-enol tautomerism, primarily found in keto form in neutral and acidic solutions[25,28]. Turmeric's chemical composition consist of 70% carbohydrates, 13% moisture, 6% protein, 6% essential oils (such as borneol, cineol, phellandrene, and sesquiterpenes), 5% fat, 3% minerals (such as potassium, calcium, phosphorus, iron, and sodium), 3-5 percent curcuminoids, and trace amounts of vitamins (B1, B2, C, and niacin)[29].

Constituent and composition of turmeric:-

Constituent	Composition
Curcuminoids	1-6%
Volatile oil	3-7%
Fiber	2-7%
Mineral matter	3-7%
Protein	6-8%
Fat	5-10%
Moisture	6-13%
Carbohydrates	60-70%

Table:2 Constituents of turmeric [26].

4-Extraction of curcumin

Curcumin, derived from Curcuma longa, can be extracted through solvent, maceration, Soxhlet, microwave, ultrasonic wave, enzyme, and supercritical liquid methods. It was first isolated in 1815 and purified in 1842. Its structure was discovered in 1910 and synthesized in 1913. The oxidation process that is triggered by light and heat can degrade curcuminoids and oleoresin from Curcuma longa. Currently, curcuminoid and oleoresin extraction procedures favor strategies that allow for easy control of heating[30,31,33].

Soxhlet extraction:-

Franz Ritter von Soxhlet, a German chemist, designed the Soxhlet extractor for lipid extraction in 1879. This apparatus is now also utilized to extract bioactive chemicals from natural sources[34]. Turmeric rhizomes were dried in an oven at 105 degrees Celsius for three hours. Dried rhizomes were triturated in a mortar and filtered through a mesh 80 screen to yield a uniform powder with a particle size of 0.18 mm. To prevent moisture absorption, the turmeric powder was stored in the refrigerator. As the reference process, the Soxhlet extraction was carried out as follows: 15 g of ground turmeric powder was weighed and loaded into the Soxhlet apparatus, which was gradually filled with acetone as the extraction solvent. The extraction experiment lasted 8 hours at 60 °C. Following the extraction, the acetone was removed from the extract using a rotary evaporator (Stuart RE300) under vacuum at 35°C. The residue (oleoresin) was dried and weighed before being dissolved in 10 mL methanol for HPLC analysis of curcumin concentration. Because of its strong solubilization capacity, acetone was utilized as the extraction solvent in all studies[35].

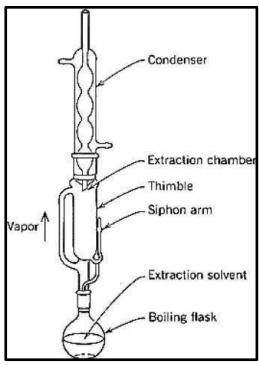


Figure :4 Soxhlet apparatus [48]

Microwave assisted extraction of curcumin:-

In order to extract curcumin with the use of a microwave, 0.5 g of powdered turmeric was weighed, diluted in 10 ml of acetone, and placed within a microwave chamber (a household Samsung microwave). Acetone which was used as extraction solvent has good dissipation factor which can be heated up to high extent and dissipate the microwave energy. The extraction process was conducted using a range of microwave operating powers (100-450 W) and irradiation periods (0.5-3 min). Because a longer irradiation period and higher power caused the solvent to boil, the samples were treated to intermittent microwave irradiation in an extraction time of up to three minutes. Subsequently, the solvent was extracted using a 0.45 µm filter and vacuum-evaporated, with the leftover residue being weighed and diluted in 10 milliliters of methanol for HPLC examination[35].

Ultrasound-assisted extraction of curcumin:-

Curcumin was extracted using an ultrasonic bath (Elmasonic S 10 H, Elma Schmibauer GmbH, Germany) with a 0.8-liter tank capacity. 90 W of bath power and a frequency of 37 kHz were used. 0.5 g of turmeric powder were dissolved in 10 ml of acetone and placed in an ultrasonic bath for the extraction experiment. The extraction was carried out between 10 and 40 minutes at varying temperatures between 25 and 40 °C. To stop solvent loss during the studies, parafilm was placed over the Erlenmeyer containing the sample. After passing the extract through a $0.45 \mu m$ filter, the solvent was vacuum-evaporated. To find the residue's curcumin concentration, it was weighed as oleoresin and dissolved in 10 milliliters of methanol for HPLC analysis[35].

Anti inflammatory action of curcumin:-

Inflammation

Inflammation is one of the body's natural defense mechanisms. The immune system uses this method to identify and eliminate harmful and alien stimuli, which kicks off the healing process. Inflammation is a complex, widespread physiological and pathological process. Visual aspects of inflammation include swelling, redness, heat, discomfort, and loss of function; the first four were discovered by Caelus, a Roman scientist. Typically, inflammation is the body's adaptive response to maintain homeostasis in the face of harmful stimuli and conditions (such as infection and tissue damage. Numerous reasons can cause inflammation, including blood clots, immune system failure, cancer, infection, chemical exposure, physical trauma, and neurological diseases such as depression or Alzheimer's. In particular, inflammation can result from several illnesses caused by bacteria, fungi, viruses, and protozoa. Chronic or frequent inflammation can help tumors grow and trigger autoimmune illnesses [37,38,39,47].

There are two types of inflammation:

•Acute inflammation: Acute inflammation, beneficial to the host, occurs during the acute phase of the inflammatory response, involving immune system migration and soluble mediators, and may repair damage and initiate healing. During the acute phase of the inflammatory response, immune system cells migrate to the site of injury in a highly organized series of events aided by soluble mediators such as cytokines, chemokines, and acute-phase proteins. Depending on the severity of the injury, this acute phase may be sufficient to resolve the damage and commence healing processes[40].

•Chronic inflammation: it includes tissue damage and fibrosis, may be caused by persistent inflammation, which might result from an inappropriate reaction to self-molecules or from prolonged stimulation. Chronic inflammation has been associated to a variety of conditions, including arthritis, asthma, atherosclerosis, autoimmune diseases, diabetes, cancer, and age-related problems[40].

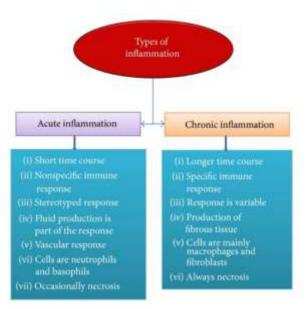


Figure:5 types of Inflammation [41].

Causes of Inflammation:

Many different things can cause inflammations. These are the most common:

- •Pathogens (germs) like bacteria, viruses or fungi.
- •External injuries like scrapes or damage through foreign objects (for example a thorn in your finger).
- •Effects of chemicals or radiation[43].

Symptoms of Inflammation:

There are five symptoms that may be signs of an acute inflammation:

- •Redness
- •Heat
- Swelling
- •Pain[43].

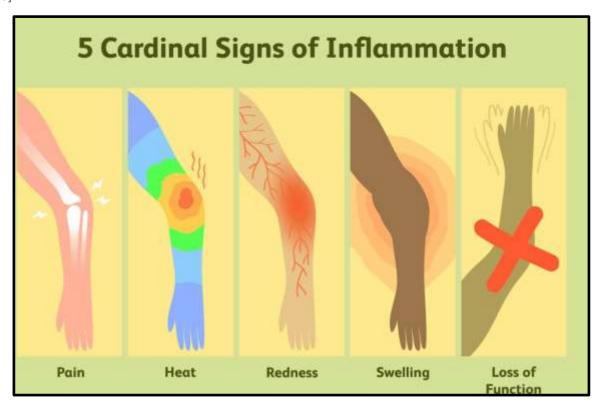


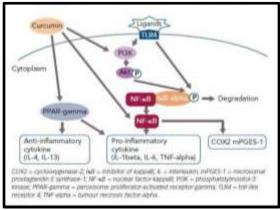
Figure:6 signs of Inflammation[50].

Mechanism of Inflammation:

Inflammation is a biological immune system response. Infectious and non-infectious substances, as well as cell injury, activate inflammatory cells and activate inflammatory signaling pathways, the most prevalent of which are the NF-B, MAPK, and JAK-STAT pathways. Inflammation is the immune system's response to harmful stimuli, such as pathogens, damaged cells, toxic compounds, or irradiation, and acts by removing injurious stimuli and initiating the healing process. The mammalian immune system has evolved a number of features that allow it to defend against microbial invasion as well as guard against trauma and neoplasia. It is also capable of removing denatured proteins and cells. The immune system is made up of identifiable tissues like the thymus, bone marrow, and spleen, as well as billions of motile cells that constantly monitor and protect the host. At the tissue level, inflammation is characterized by redness, swelling, heat, pain, and loss of tissue function, which result from local immune, vascular and inflammatory cell responses to infection or injury. Important microcirculatory events that occur during the inflammatory process include vascular permeability changes, leukocyte recruitment and accumulation, and inflammatory mediator release [42,44].

Anti- inflammatory mechanism of curcumin :-

Turmeric is a popular spice in India and has been used to cure inflammatory illnesses in Ayurveda. Turmeric is mostly used as an anti-inflammatory in western herbalism[45]. Numerous physiological properties of curcumin are demonstrated, such as its anti-inflammatory, antioxidant, and anticancer properties. It inhibits signaling pathways that include myeloid differentiation protein 2-Toll-like receptor 4 co-receptor pathways and nuclear factor kappa-B (NF-kappaB). It also activates peroxisome proliferator-activated receptor-gamma (PPAR-gamma) and inhibits the production of proinflammatory cytokines that include interleukin (IL)-1 beta and tumour necrosis factor-alpha (TNF-alpha)[46]. Many chronic diseases are related with oxidative stress, and its pathological circumstances are inextricably linked to inflammation; both are generated by one another. Inflammatory cells are also known to release a large number of reactive substances at their site, resulting in oxidative stress. This demonstrates a connection between inflammation and oxidative stress[47]. A number of reactive substances can initiate an intracellular signaling cascade that boosts pro-inflammatory gene expression. Inflammation has been identified as a stage of disease progression in many chronic diseases such as asthma, allergy, cancer, metabolic syndrome, multiple sclerosis, epilepsy, cardiovascular diseases, Parkinson's disease, cerebral injury, arthritis, psoriasis, diabetes, depression, obesity, and Acquired Immune Deficiency Syndrome (AIDS)[47].(TNF-) tumor necrosis factor is the primary inflammatory mediator in many disorders, and it is regulated by nuclear factor (NF)-B. TNF- is the most influential NF-B activator, and NF-B regulates its expression as well. Most cytokines activate NF-



B, TNF-, disease-causing viruses; mechanical, chemical, physical, and mental stress; curcumin prevents NF-B activation by responding to distinct inflammatory stimuli; curcumin has been demonstrated to reduce inflammation by separate pathways[47].

Figure:4 Anti inflammatory action of curcumin [46].

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44-MECHANISMS OF INFLAMMATION AND LEUKOCYTE ACTIVATION

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46-Anti-inflammatory Action of Curcumin and Its Use in the Treatment of Lifestyle-related Diseases

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