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Turmeric – A Spice of Panacea

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Abstract

Turmeric (Curcuma longa L.) is a yellow spice, native to the Indian subcontinent which has been used traditionally for its therapeutical values since time immemorial. It is used as a dietary spice and for the treatment of various illnesses such as biliary disorders, anorexia, cough, diabetic wounds, hepatic disorders, rheumatism, and sinusitis. Curcumin, is the active component of turmeric which was reported to have a wide spectrum of biological functions which include its anti-inflammatory, antioxidant, anticarcinogenic, antimutagenic, anticoagulant, antifertility, antidiabetic and antimicrobial activities. Curcumin is remarkably non-toxic and exhibits limited bioavailability. Curcumin exhibits great promise as a therapeutic agent, and is currently in human clinical trials for a variety of conditions, including multiple myeloma, pancreatic cancer, myelodysplastic syndromes, colon cancer, psoriasis and Alzheimer's disease.

Keywords: Turmeric, Curcumin, Anti-Inflammatory, Antioxidant, Anti Microbial, Bioactive.

Introduction

Turmeric is a vibrant yellow spice, derived from the rhizome of the plant *Curcuma longa* L. It is a perennial herb that belongs to the family Zingiberaceae (ginger). The plant grows to a height of three to five feet; it has oblong, pointed leaves and bears funnel-shaped yellow flowers. It bears ovate, pyriform or oblong rhizomes, which are often branched and brownish-yellow in colour. It is thought to be indigenous to the Indian subcontinent. It is grown and harvested commercially in India, China, and many regions of tropical south Asia and needs temperatures between 20 °C and 30 °C and a considerable amount of annual rainfall to thrive (**Hatcher *et al*, 2008**). India is the largest producer and dominates the international trade. Erode, a city in the South Indian state of Tamil Nadu, is the world's largest producer and most important trading center of turmeric in Asia. For these reasons, Erode in history is also known as "Yellow City" or "Turmeric City". Sangli, a town in the southern part of the Indian western state of Maharashtra, is the second largest and most important trading center for turmeric in Asia. India produces 600,000 tons of turmeric annually which is 75% of world production of 800,000 tons. Other producers in Asia include Bangladesh, Pakistan, Sri Lanka, Taiwan, China, Myanmar and Indonesia. It is also cultivated in the Caribbean and in Central and South America, with Jamaica, Haiti and Peru being the most important producing countries (**Nitesh Kumar and Sunil Kumar Sakhya, 2013**). The wild turmeric is called *C. aromatica* and the domestic species is called *C. longa*. The alternative botanical names of *Curcuma longa* is *Curcuma rotunda* and *Amomum curcuma* (**Ishita Chattopadhayay *et al*, 2004**). *Curcuma longa* is classified by Linnaeus as follows (**National Plant Database**):

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Table 1. Scientific classification of *Curcuma longa L.*

Kingdom	Plantae-Plants
Subkingdom	Tracheobionta - Vascular plants
Superdivision	Spermatophyta - Seed plants
Division	Magnoliophyta - Flowering plants
Class	Liliopsida – Monocotyledons
Subclass	Zingiberidae
Order	Zingiberales
Family	Zingiberaceae - Ginger family
Genus	*Curcuma L.*
Species	*Curcuma longa L.*

Traditional Uses

The rhizome, the portion of the plant used medicinally, is usually boiled, cleaned, and dried, yielding a yellow powder. Dried *Curcuma longa* is the source of the spice turmeric, the ingredient that gives curry powder its characteristic yellow color. Turmeric is used extensively in foods for its flavor and color; it is a medicinal plant extensively used in Ayurveda, Unani and Siddha system of medicine as home remedy for various

diseases (**Eigner and Scholz, 1999**). Turmeric is consumed in the countries of its origin for a variety of uses, including as a dietary spice, a dietary pigment, and an Indian folk medicine for the treatment of various illnesses. It is used in the textile and pharmaceutical industries and in Hindu religious ceremonies in one form or another. Current traditional Indian medicine uses it for biliary disorders, anorexia, cough, diabetic wounds, hepatic disorders, rheumatism, and sinusitis. The old Hindu texts have described it as an aromatic stimulant and carminative. Powder of turmeric mixed with slaked lime is a household remedy for the treatment of sprains and swelling caused by injury, applied locally over the affected area. In some parts of India, the powder is taken orally for the treatment of sore throat. This nonnutritive phytochemical is pharmacologically safe, considering that it has been consumed as a dietary spice (**Anil Kumar *et al,* 2011**).

Turmeric in Global Scenario

Turmeric came into the global limelight when the controversial patent "Use of Turmeric in Wound Healing" was awarded, in 1995, to the University of Mississippi Medical Center, USA. Indian Council of Scientific and Industrial Research (CSIR) aggressively contested this award of the patent. It was argued by them that turmeric has been an integral part of the traditional Indian medicinal system over several centuries, and therefore, is deemed to be 'prior art', hence is in the public domain. Subsequently, after protracted technical/legal battle USPTO decreed that turmeric is an Indian discovery and revoked the patent (**BioMed analysis**).

Composition of Turmeric

Turmeric contains protein (6.3%), fat (5.1%), minerals (3.5%), carbohydrates (69.4%) and moisture (13.1%). The essential oil (5.8%) obtained by steam distillation of rhizomes has a-phellandrene (1%), sabinene (0.6%), cineol (1%), borneol (0.5%), zingiberene (25%), sesquiterpines (53%) and curcumin (diferuloylmethane) (3-4%). Turmeric contains volatile as well as nonvolatile compounds. Volatile compounds are turmerone, zingiberone, curloneand ar-turmerone, nonvolatile compounds include the curcuminoids.

The significance of turmeric in medicine has changed considerably since the discovery of the anti-oxidant properties of naturally occurring phenolic compounds. Curcuminoids is refered to a group of phenolics present in turmeric, which are chemically related to its principal ingredient, curcumin. Curcumin (diferuloylmethane) (3–4%) is responsible for the yellow colour, and comprises curcumin I (94%), curcumin II (6%) and curcumin III (0.3%). Demethoxy and bisdemethoxy derivatives of curcumin have also been isolated. Curcumin was first isolated by Vogel and Pelletier (1815) and its chemical structure was determined by Roughley and Whiting (1973).` Commercially available curcumin contains approximately 77% curcumin, 17% demethoxycurcumin, and 3% bisdemethoxycurcumin (**Ishita Chattopadhayay *et al,* 2004**). The IUPAC name of curcumin is (1,7-bis (4-hydroxy-3-methyoxy-phenyl)hepta-1,6-diene-3,5-dione) and its chemical structure is depicted in Figure 1 (Merck Index).

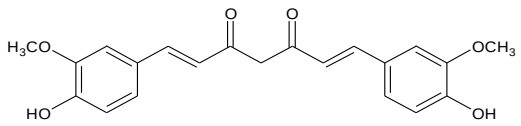

Figure 1. Structure of Curcumin (diferuloylmethane)

Chemical Constituents of Curcumin

The three principal colouring components of curcumin that are present in various proportions are all dicinnamoylmethane derivatives:

1) 1,7-Bis-(4-hydroxy-3-methoxyphenyl)-hepta-1,6-diene-3,5-dione = diferuloylmethane

(Chemical formula: $C_{21}H_{20}O_6$: C.A.S. number: 458-37-7, Formula weight: 368)

2) 1-(4-Hydroxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)-hepta-1,6-diene-3,5-dione = p-hydroxycinnamoylferuloylmethane

(Chemical formula: $C_{20}H_{18}O_5$: C.A.S. number: 33171-16-3, Formula weight: 338)

3) 1,7-Bis-(4-hydroxyphenyl)-hepta-1,6-diene-3,5-dione=p,p-dihidroxydicinnamoylmethane

(Chemical formula: $C_{19}H_{16}O_4$: C.A.S. number: 33171-05-0, Formula weight: 308) (Merck Index)

Besides these major constituents, minor amounts of oils and resins naturally occurring in turmeric may be present in curcumin. The predominant constituents of these oils and resins appear to be sesquiterpene ketones and alcohols: α-turmeron, β-turmeron, curlon, zingiberen, ar-turmeron, turmenorol A, turmeronol B etc. (**Ohshiro and Kuroyanagi, 1990**).

Physio-Chemical Properties of Curcumin

Curcumin is an oil-soluble pigment, practically insoluble in water at acidic and neutral pH, and soluble in alkali. It has a melting point at 176–177°C. It forms a reddish-brown salt with alkali and is soluble in ethanol, alkali, ketone, acetic acid and chloroform (**Ishita Chattopadhayay *et al,* 2004**).

Analogues and Derivatives of Curcumin

The curcumin analogues are classified into three groups: analogues from turmeric, analogues from Mother Nature and synthetic analogues.

Natural Analogues from Turmeric

It includes curcumin, demethoxycurcumin

(DMC) and bisdemethoxycurcumin (BDMC) collectively called curcuminoids. Of the three curcuminoids, curcumin is the most abundant one in turmeric, followed by DMC and BDMC (**Preetha Anand *et al,* 2008**). A lesser known curcuminoid from turmeric is cyclocurcumin, first isolated and characterized by **Kiuchi *et al.,*** (1993).

Natural Analogues Made by Mother Nature

The curcumin molecule is unique that it has a greater number of molecular targets than any other molecule so far reported. In order to define a drug profile of such a molecule, it is necessary that, along with its synthetic analogues, its naturally occurring analogues should also be analyzed. Such natural analogues include ferulic acid, cinnamic acid, caffeic acid, chlorogenic acid, capsaicin, gingerol, paradol, zingerone, eugenol, dibenzoylmethane, dehydrozingerone, cassumin and yakuchinone (**Kim et al., 2005, Keum et al., 2002, Mahady et al., 2003**).

Synthetic Analogues Made by Man

Synthetic analogues are obtained by modifying the basic structure of curcumin to access related compounds by chemical synthesis. It may be classified into 3 broad groups namely, "curcumin derivatives", "curcumin analogues" and "metal complexes of curcumin". Compounds that retain the basic structural features of curcumin are designated as "curcumin derivatives". "Curcumin analogues" encompass all other compounds with some preceived or claimed structural analogue to curcumin. The third group is metal complexes of curcumin and its analogues (**Preetha Anand *et al,* 2008**).

Pharmacological Properties

Anti - Inflammatory Effects

It was reported that curcumin is a highly pleiotropic molecule capable of interacting with numerous molecular targets involved in inflammation. Curcumin can differentially block inflammatory enzymes involved in inflammation and extracellular matrix degradation at both the mRNA and protein levels (**Tunstall *et al.,* 2006 and Sharma *et al.,* 2006**). It modulates the inflammatory response by down-regulating the activity of cycloxygenase-2 (COX-2), lipoxygenase and inducible nitric oxide synthase (iNOS) enzymes (**Jurenka, 2009**). It inhibits the production of the inflammatory cytokines, tumor necrosis factor–alpha (TNF-α), interleukin-1 (IL-1), IL-2, IL-6, IL-8, IL-12, monocyte chemoattractant protein (MCP) and migration inhibitory protein (**Goel *et al.,* 2008**).

Because of its ability to modulate immune cells and immune cell cytokines, curcumin has been shown to affect several autoimmune diseases. Inflammation is a critical feature of most autoimmune diseases. Several reports suggest that curcumin has potential against alzheimer's disease, multiple sclerosis, inflammatory bowel disease, rheumatoid arthritis, renal ischemia, scleroderma and asthma (**Jagetia & Aggarwal, 2007, Zhang *et al.,* 2006, Natarajan and Bright, 2002, Holt *et al.,* 2005, Funk *et al.,* 2006, Jackson *et al.,* 2006, Shahed *et al.,* 2001, Tourkina *et al.,* 2004, Ram *et al.,* 2003, Kohli *et al,* 2005**).

Anti – Oxidant Effects

Curcumin exhibits potential antioxidant activity. It acts as a scavenger of oxygen free radicals. It can protect haemoglobin from oxidation. *In-vitro*, curcumin can significantly inhibit the generation of reactive oxygen species (ROS) like superoxide anions, H_2O_2 and nitrite radical generation by activated macrophages, which play an important role in inflammation. Curcumin also lowers the production of ROS *in-vivo*. Its derivatives, demethoxycurcumin and bis-demethoxycurcumin also have antioxidant effect (**Ishita Chattopadhayay *et al,* 2004**).

Curcumin exerts powerful inhibitory effect against H_2O_2 induced damage in human keratinocytes and fibroblasts (**Phan *et al,* 2001**). An *in-vitro* study measuring the effect of curcumin on endothelial heme oxygenase-1, an inducible stress protein, was conducted utilizing bovine aortic endothelial cells. Incubation (18 hours) with curcumin resulted in enhanced cellular resistance to oxidative damage (**Mortellini *et al.,* 2000**). Another *in-vitro* study demonstrated that low concentrations of curcumin incubated with activated macrophages resulted in a decrease in mRNA levels and nitric oxide synthase activity. This study demonstrates curcumin's antioxidant role in down-regulating nitric oxide formation, a key element in inflammation and possibly in the process of carcinogenesis (**Brouet and Ohshima, 1995**).

Anti – Cancer Effects

Curcumin has been shown to exhibit therapeutic potential against variety of different cancers including leukemia and lymphoma; gastrointestinal cancers, genitourinary cancers, breast cancer, ovarian cancer, head and neck squamous cell carcinoma, lung cancer, melanoma, neurological cancers and sarcoma (**Preetha Anand *et al,* 2008**). Breast cancer is the most common and frequently diagnosed cancer at a median age of 61 years in women. Several reports have described the anticarcinogenic activity of curcumin in a variety of breast cancer cell lines. Curcumin has potential over gastrointestinal cancers such as oesophageal cancer, gastric cancer, intestinal cancer, hepatic cancer, pancreatic cancer and colorectal cancer (**Tunstall *et al.,* 2006, Cao *et al,* 2007, Anand *et al,* 2007, Ajaikumar *et al,* 2009**). Numerous reports indicate that curcumin has activity against genitourinary cancers such as bladder cancer, kidney cancer and prostate cancer (**Kamat *et al.,* 2007, Jung *et al,* 2005, Shankar *et al.,* 2007**). Curcumin has been shown to have synergistic and remedial properties in hematologic cancers which include leukemia, lymphoma and multiple myeloma (**Chen *et* al., 2007, Gururajan *et al.,* 2007**).

Anti – Microbial Effects

Curcumin exhibits antiviral, antibacterial, antifungal and anti – protozoan activities on both *in-vitro* and *in-vivo* models (**Ishita Chattopadhayay *et al*, 2004, Rasmussen, 2000**). There are several reports indicating that curcumin may have potential against AIDS. These effects are mediated through suppression of replication of human immunodeficiency virus (HIV) by inhibition of HIV long term repeat and HIV protease (**Ganesh and Aggarwal, 2007**). Indium curcumin and indium diacetylcurcumin was reported to have antibacterial activity against *Staphylococcus aureus, S. epidermidis, Pseudomonas aeruginosa* and *E.coli* (**Merline et al., 2014**). Curcumin also prevents the growth of *Helicobacter pylori* strains both *in-vitro* and *in-vivo* (**Ronita *et al*., 2009**). Curcumin has also been found to have moderate activity against *Plasmodium falciparum*, *Leishmania major* and *Trepanosoma spp* organisms (**Cui *et al*., 2007, Changtam *et al*., 2010**).

Curcumin in Human Clinical Trials

Curcumin is under active investigation for its clinical benefit, although clinical trials are still in relatively early phases. Early trials emphasized safety pharmacokinetics. While continuing to assess these aspects of curcumin's activity, current trials are also exploring efficacy (**Hatchera, 2008**).

Conclusion

Curcumin is now available in pure form, which shows a wide spectrum of biological activities. It would be easier to develop new drugs from this compound after extensive studies on its mechanism of action and pharmacological effects. Recent years have seen an increased enthusiasm in treating various diseases with natural products. Curcumin is a non-toxic, highly promising natural antioxidant compound having a wide spectrum of biological functions. It is expected that curcumin may find application as a novel drug in the near future to control various diseases.

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