

Turmeric curcuminoid polyphenolics as antioxidant and anticarcinogenic agents

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Abstract

In this review content, it has been described the botanical and the chemical properties of turmeric (*Curcuma longa*), and its curcuminoid polyphenolic structures and antioxidant and anticarcinogenic influences on various cell proliferation and apoptosis. Besides it was emphasized the innovative anticarcinogen complex as boron-curcumin, and the safety evaluation with turmeric curcumin and the dose and toxicity in consuming for animals and human.

Keywords: Turmeric, *Curcuma longa*, Antioxidant, Anticarcinogenic.

Introduction

Turmeric (*Curcuma longa*) is extensively consumed as a spice, food preservative, colouring food and agent and it is cultivated in India, South East Asia and China and other countries (Figure 1). Turmeric is a medicinal plant extensively used in Ayurveda, Unani and Siddha medicine as home remedy for various diseases (1). Dried turmeric powder is also utilized in sub-continental cooking and is the main ingredient in all forms of “curry” preparations. The wild turmeric is called *C. aromatica* and the domestic species is called *C. longa*. Turmeric has been described as *C. longa* by Linnaeus and its taxonomic profile is as follows (1)

Class	Liliopsida
Subclass	Commelinids
Order	Zingiberales
Family	Zingiberaceae
Genus	<i>Curcuma</i>
Species	<i>Curcuma longa</i>

Curcuma longa, a perennial herb and member of the Zingiberaceae (ginger) family, grows to a height of 3-5 feet with a tropical climate. It has oblong, pointed leaves and funnel-shaped yellow flowers (2) (Figure 1). Dried turmeric plant is the source of the spice, the ingredient that gives curry powder and has characteristic yellow-orange color (Figure 1).

It has stated that turmeric spice is an antioxidant, anticarcinogenic and has hepatoprotective, anti-inflammatory, and antimicrobial properties. Besides, its utilizing in cardiovascular disease and gastrointestinal disorders. Current review has focused on turmeric’s phenolic antioxidants as anticarcinogen agents



Figure 1: Turmeric (*Curcuma longa*) plant (left) and turmeric root and powder (right) (Anonim,2019)

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Bioactive Constituents of Turmeric and Main Component Curcumin

Turmeric spice includes 6.3% of total protein, 5.1% of total fat, 69.4% of carbohydrate and 13.1% of moisture. The main bioactive component of turmeric is curcumin (diferuloylmethane) as 3-4% and remain is essential oils including α -phellandrene (1%), sabinene (0.6%), cineol (1%), borneol (0.5%), zingiberene (25%) and sesquiterpenes (53%) in the structure (3). Curcumin is responsible for the yellow color and comprises three derivative containing curcumin I (94%), curcumin II (6%), and curcumin III (0.3%) (3). The melting point of curcumin is 176-177 °C and turns to reddish-brown salt with alkali agents. Turmeric is soluble in ethanol, acetic acid, ketone and chloroform. Figure 2 shows the chemical composition of curcumin and its keto-enol structure (3,4).

Curcumin can exist in at least two tautomeric forms, keto and enol. It is stated that the enol form is more energetically stable in the solid phase and in solution (Figure 2).

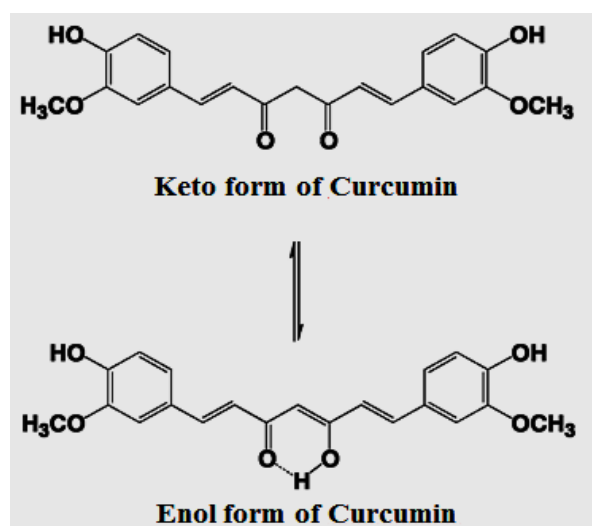


Figure 2. The Chemical Structure of Curcumin (4)

The chemical structures of curcumin derivatives as curcumin I, curcumin II demethoxycurcumin, and curcumin III bis-demethoxycurcumin are given in Figure 3. Curcumin is the principal curcuminoid of spice turmeric, is a member of the ginger family (Zingiberaceae) and the other two curcuminoids are demethoxycurcumin and bis-desmethoxycurcumin (Figure 3).

The curcuminoids are polyphenols and are responsible for the yellow-orange color of turmeric. Turmeric powder is yellow pigmented and has numerous curcuminoids that include curcumin (77%), demethoxycurcumin (17%), and bisdemethoxycurcumin (3%). Curcumin is a polyphenol (1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione).

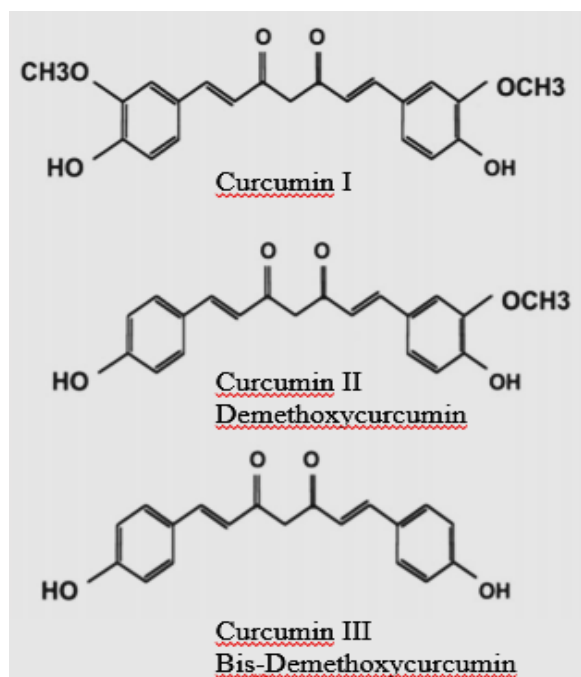


Figure 3. Curcumin Derivatives in Turmeric (5)

Health Effects of Curcumin

Curcumin is brightly yellow coloured and may be used as a food colouring. As a food additive, its E number is E100. In ayurvedic medicine, it has been used for various disorders including asthma, bronchial hyperactivity, coryza, cough, sinusitis, allergy, anorexia, and hepatic diseases (6).

It has been reported that many positive health on anti-infectious (7), anti-oxidant (8), anti-inflammatory (9,10), hepatoprotective (11), cardio protective (12), thrombosuppressive (13), anti-arthritic symptoms (14). It has been reported that curcumin suppresses the type II diabetes symptoms, reduces blood cholesterol, prevents LDL oxidation, inhibits platelet aggregation, suppresses thrombosis and myocardial infarction, suppresses rheumatoid arthritis and multiple sclerosis symptoms and Alzheimer (15). It has been most importantly determined that curcumin has chemo preventive, and anti-carcinogenic properties (16).

Antioxidant Effects of Curcumin

Through a variety of assay systems *in vitro* and *in vivo* researches shown that curcumin and related compounds have great antioxidative activities. It is stated that, not only the phenolic hydroxyl (OH) groups of curcumin are most important in its antioxidative property but also the OH groups in the curcumin derivative bis (3,4-dihydroxycinnamoyl)-methane and also possible role of β -diketone moiety in the curcumin structure (17-24). According to studies, the presence of an ortho alkoxy group seems to potentiate the antioxidant activity, as does an additional hydroxy group as in bis (3,4-dihydroxy)cinnamoyl methane (24). It is reported that water-soluble and fat-soluble extracts of turmeric and its curcumin component exhibit strong antioxidant activity, comparable to ascorbic acid (vitamin C) (25).

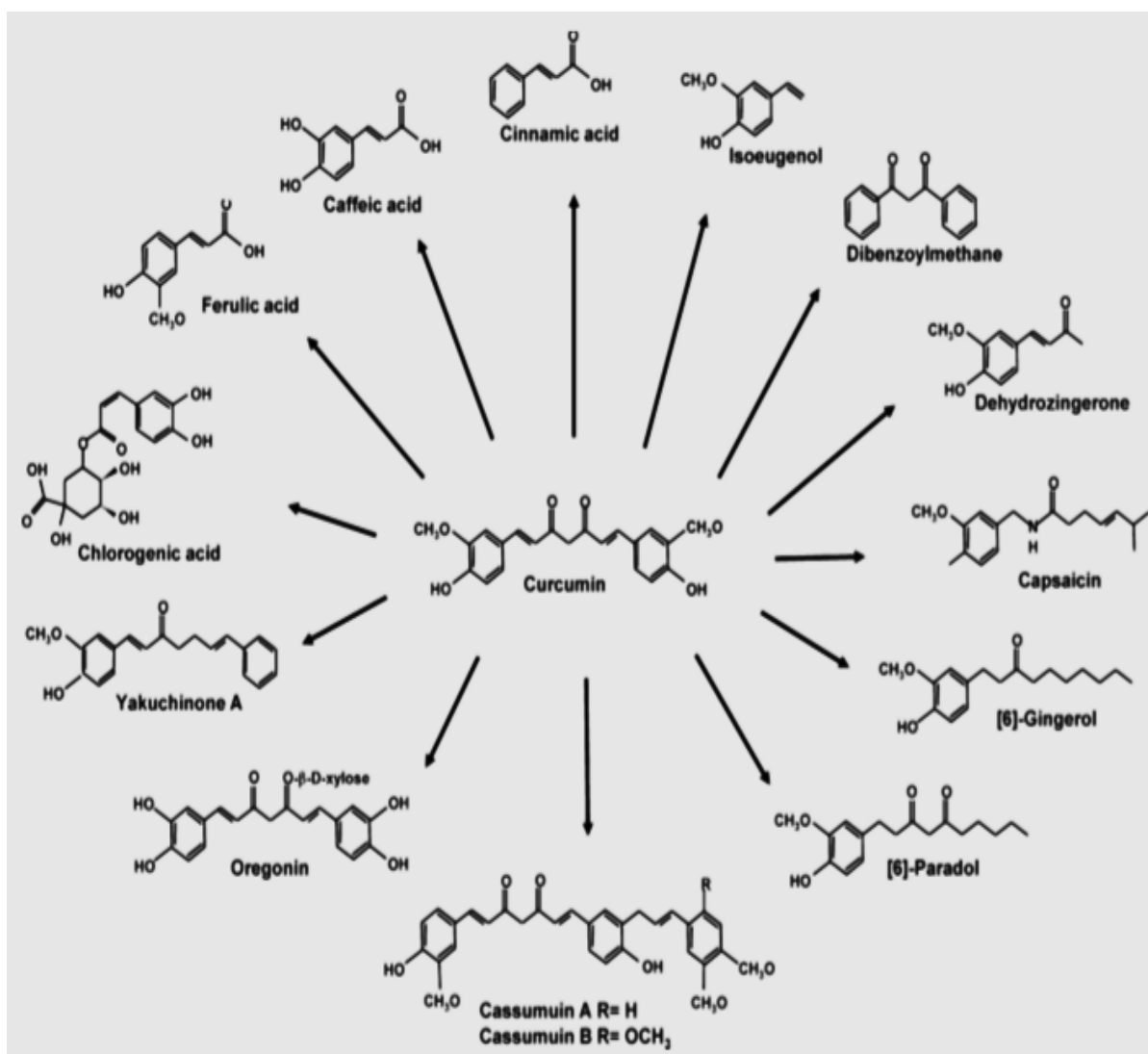


Figure 3. Curcumin analogues from mother structure (19)

Figure 3 shows a number of naturally occurring bioactive compounds having some structural similarity to the curcumin molecule, or at least having a pharmacophore including one aryl function with 3,4 substitution, either a methoxylated phenol or catechol (Figure 3). These compounds include ferulic acid, cinnamic acid, caffeic acid, chlorogenic acid, capsaicin, gingerol, paradol, zingerone, eugenols) or in two aromatic rings (e.g., oregonin, nitric oxide synthase--iNOS inhibitor, dehydroguaietic acid, yakuchinones, cassumunins). The same chromophore is responsible for both the antioxidant and prooxidant properties of curcumin and its analogues that may be owing to the its radical-generating or hydrogen bond donor-acceptor properties.

Anticarcinogenic effects of curcumin

The extensive studies suggested that curcumin has the great potential in the prevention and treatment of cancer. *In vitro* and *in vivo* preclinical and clinical studies shown that curcumin has positive effects in the cancer treatment (15)

Curcumin has been shown to promote apoptosis in certain cancer cell lines and to inhibit telomerase activity, an important factor in tumorigenesis. One possible mechanism for the induction of tumor cell death is through the generation of reactive oxygen intermediates.

The oleoresin of turmeric which obtained after the extraction of curcumin has antimutagenic properties, thought to be mediated through its antioxidant action (16). In this chemopreventive effect, the anti-inflammatory properties of curcumin are also important and it is stated due the suppression of prostaglandin synthesis.

Curcumin polyphenolic substance has antiproliferative effects (5). It is reported that curcumin suppresses the proliferation of a wide variety of cancer tumor cells containing breast carcinoma, colon carcinoma, renal cell carcinoma, hepatocellular carcinoma, T cell leukaemia, B cell lymphoma, melanoma and prostate carcinoma, acute myelogenous leukaemia, basal cell carcinoma (5).

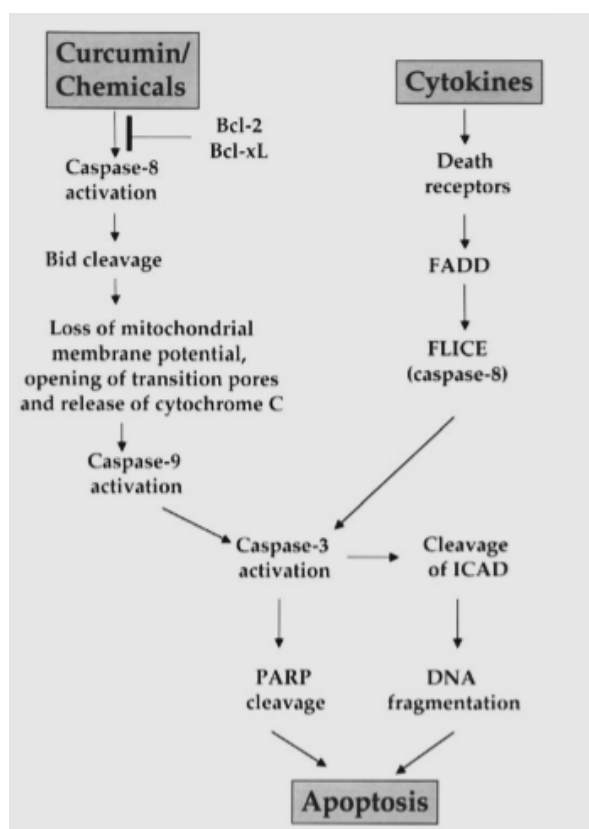


Figure 4. Curcumin Analogues from Mother Structure (5)

Besides, curcumin also inhibits the cell proliferation induced by growth factors such as IL-2-induced proliferation of PBMC, PDGF-induced proliferation of VSMC and PHA-induced proliferation of PBMC were inhibited by treatment with curcumin (26). It is stated that the suppression of cell proliferation by curcumin usually occurs through its effects on the cell cycle (27). Figure 4 shows the mechanism of apoptosis with curcumin. Moreover the suppression of proliferation, curcumin induces apoptosis in wide spectrum of cells. In this point, the apoptosis could be either mitochondria-dependent or mitochondria-independent as shown in Figure 4. It is also reported that curcumin induces apoptotic cell death by DNA-damage in human cancer cell lines, TK-10, MCF-7 and UACC-62 by acting as topoisomerase II poison (28).

Boron-Curcumin Complex

It is stated that curcumin can be used for boron quantification in the so-called curcumin method. It reacts with boric acid and gives a red coloured compound, known as rosocyanine (29). Rosocyanine is formed as 2:1 complex from curcumin and boric acid in acidic solutions. The boron complexes formed with rosocyanine are dioxaborines (1,3,2-dioxaborine). Curcumin possesses a 1,3-diketone structure and can therefore be considered as a chelating agent.

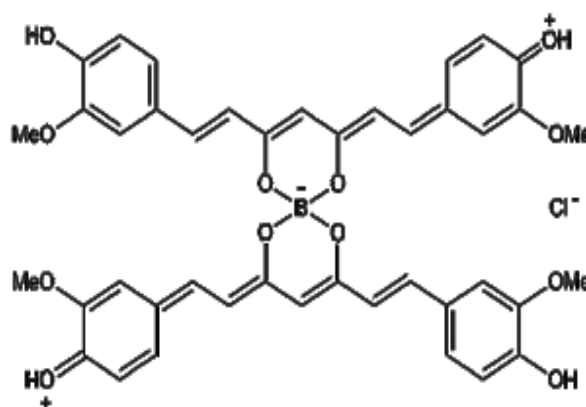


Figure 5. Curcumin-Boron Complex (Rosocyanine) (29)

It has been put forward that innovative synthetic strategies lead to soluble and crystallisable metal curcumin complexes (29). Also, it was described that the special emphasis is placed on the highly promising and exciting medicinal applications of metal curcumin complexes, with the three most important areas being anticancer activity and selective cytotoxicity, anti-Alzheimer's disease activity, and antioxidative/neuroprotective effects (29).

Safety evaluation with turmeric and curcumin

Based on the detailed studies, it has been stated that the safety evaluation of the rhizomes of turmeric and its alcohol extract, curcumin was performed. However, the utilization of very high doses (100 mg/kg body weight) resulted in ulcerogenic situation in animals, as evidenced by one rat study (30)

It has been reported that no pathological, behavioural abnormalities or lethality (31) and also no adverse effects were observed on growth and the level of erythrocytes, leucocytes, blood constituents such as haemoglobin, total serum protein, alkaline phosphatase, etc. in male and female Wistar rats, guinea pigs and monkeys of both sexes which were fed with turmeric at a dose of 300 mg/kg body weight (32).

Although various studies shown that no significant toxicity has been reported following either acute or chronic administration of turmeric extracts at standard doses, it was reported the average intake of turmeric by Asians varies from 0.5-1.5 g/day/person, which produces no toxic symptoms (33). Human clinical trials also indicate that curcumin has no toxicity when administered at doses of 1-8 g/day (34) and 10 g/day (35). It was also shown that there is no evidence that dietary consumption of turmeric as a spice adversely affects pregnancy or lactation, the safety of curcumin supplements in pregnancy and lactation has not been established.

Conflict of interests: We declare that we have no conflict of interests.

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