
23 Curcumin Derived from Turmeric (*Curcuma longa*): a Spice for All Seasons

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23.1 INTRODUCTION

Curcuma longa or turmeric is a tropical plant native to southern and southeastern tropical Asia. A perennial herb belonging to the ginger family, turmeric measures up to 1 m high with a short stem and tufted leaves (Figure 23.1A). The parts used are the rhizomes. Perhaps the most active component in turmeric is curcumin, which may make up 2 to 5% of the total spice in turmeric (Figure 23.1B). Curcumin is a diferuloylmethane present in extracts of the plant. Curcuminoids are responsible for the yellow color of turmeric and curry powder. They are derived from turmeric by ethanol extraction. The pure orange-yellow, crystalline powder is insoluble in water. The structure of curcumin (C₂₁H₂₀O₆) was first described in 1815 by Vogel and Pellatier and in 1910 was shown to be diferuloylmethane by Lampe et al. [1]. Chemical synthesis in 1913 confirmed its identity [2].

Turmeric is widely 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 [3] 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 [4]. The old Hindu texts have described it as an aromatic stimulant and carminative [5]. 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, at doses up to 100 mg/day, for centuries [6]. Recent phase I

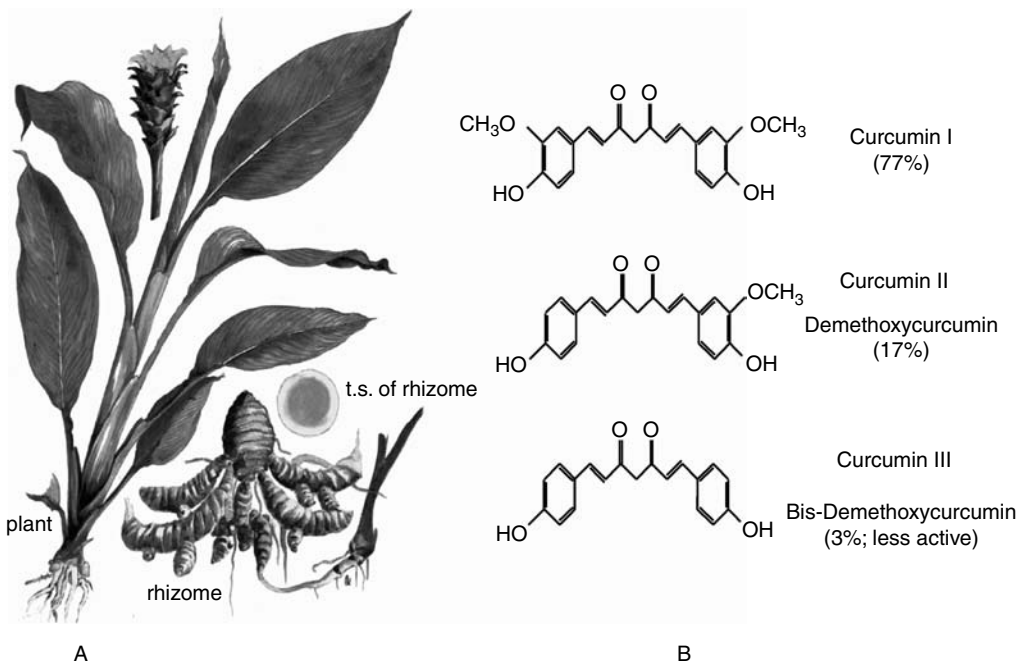


FIGURE 23.1 The plant *Curcuma longa* (panel A), from which curcumin is derived, and its structure (panel B).

clinical trials indicate that people can tolerate a dose as high as 8 g/day [7]. In the U.S., curcumin is used as a coloring agent in cheese, spices, mustard, cereals, pickles, potato flakes, soups, ice-creams, and yogurts (www.kalsec.com).

Curcumin is not water-soluble, but it is soluble in ethanol or in dimethylsulfoxide. The degradation kinetics of curcumin under various pH conditions and the stability of curcumin in physiological matrices have been established [8]. When curcumin was incubated in 0.1M phosphate buffer and serum-free medium (pH 7.2 at 37°C), about 90% decomposed within 30 min. A series of pH conditions ranging from 3 to 10 were tested, and the results showed that decomposition was pH-dependent and occurred faster at neutral-basic conditions. It is more stable in cell culture medium containing 10% fetal calf serum and in human blood. Less than 20% of curcumin decomposed within 1 h, and after incubation for 8 h, about 50% of curcumin still remained. Trans-6-(4'-hydroxy-3'-methoxyphenyl)-2,4-dioxo-5-hexenal was predicted to be the major degradation product, and vanillin, ferulic acid, and feruloyl methane were identified as minor degradation products. The amount of vanillin increased with incubation time.

Numerous studies have indicated that curcumin has antioxidant and anti-inflammatory properties. A Medline search revealed over 1000 publications describing various activities of this polyphenol. The following sections describe some of its major biological and clinical effects.

23.2 ANTICANCER PROPERTIES OF CURCUMIN

23.2.1 CURCUMIN INHIBITS TUMORIGENESIS

Numerous reports suggest that curcumin has chemopreventive and chemotherapeutic effects (Figure 23.2). Its anticancer potential in various systems was recently reviewed by our laboratory [9]. Curcumin blocks tumor initiation induced by benzo[a]pyrene and 7,12dimethylbenz[a]anthracene

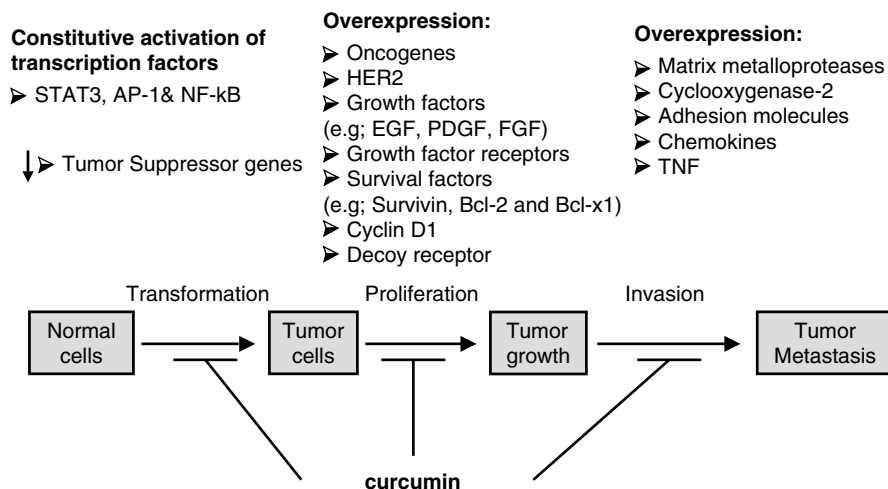


FIGURE 23.2 Various steps involved in tumorigenesis and metastasis and their suppression by curcumin.

[10], and it suppresses phorbol ester-induced tumor promotion [11, 12]. *In vivo*, curcumin was found to suppress carcinogenesis of the skin [12–15], the forestomach [16, 17], the colon [18–20], and the liver [21] in mice. Curcumin also suppresses mammary carcinogenesis [22–24].

23.2.2 CURCUMIN EXHIBITS ANTIPROLIFERATIVE EFFECTS AGAINST CANCER CELLS

Compounds that block or suppress the proliferation of tumor cells have potential as anticancer agents. Curcumin has been shown to inhibit the proliferation of a wide variety of tumor cells, including B-cell and T-cell leukemia [25–28], colon carcinoma [29], and epidermoid carcinoma cells [30]. It has also been shown to suppress the proliferation of various breast carcinoma cell lines in culture [31–33]. We showed that the growth of the breast tumor cell lines BT20, SKBR3, MCF-7, T47D, and ZR75-1 is completely inhibited by curcumin, as indicated by MTT dye uptake, [³H] thymidine incorporation, and clonogenic assay [31]. We also showed that curcumin can overcome Adriamycin resistance in MCF-7 cells [31]. Recently, we have shown that curcumin can activate caspase-8, which leads to cleavage of Bid, thus resulting in sequential release of mitochondrial cytochrome C and activation of caspase-9 and caspase-3 [34]. More recently, we have demonstrated that curcumin can suppress the proliferation of multiple myeloma cells [35]. Woo et al. [36] have demonstrated that curcumin can cause cell damage by inactivating the Akt-related cell survival pathway and release of cytochrome c, providing a new mechanism for curcumin-induced cytotoxicity.

Zheng et al. [37] explored the apoptosis-inducing effects of curcumin in human ovarian tumor A2780 cells. They found that curcumin could significantly inhibit the growth of ovarian cancer cells by inducing apoptosis through up-regulation of caspase-3 and down-regulation of expression of NF-κB. Studies have also been performed to examine the synergy of curcumin with other antiproliferative agents. Deeb et al. [38] investigated whether curcumin and TNF-related apoptosis-inducing ligand (TRAIL) cooperatively interact to promote death of LNCaP cells. At concentrations at which neither of the two agents alone produced significant cytotoxicity in LNCaP cells, cell death was markedly enhanced (two- to three-fold) if tumor cells were treated with curcumin and TRAIL together. The combined curcumin and TRAIL treatment increased the number of hypodiploid cells and induced DNA fragmentation in LNCaP cells. The combined treatment induced cleavage of procaspase-3, procaspase-8, and procaspase-9, truncation of BID, and release

Pro, and American Nutrition supply 500-mg capsules; Amerifit supplies 1700-mg capsules; and XKMS supplies 300-mg capsules. Curcumin combined with piperine (also bioperine derived from black pepper), which has a higher bioavailability than curcumin alone, is available from Life Extension in a formulation referred to as “super curcumin” [164].

23.9 CONCLUSION

From all these studies, it is clear that curcumin exhibits activities against cancer, cardiovascular diseases, and diabetes, the major ailments in the U.S. This drug has also shown therapeutic effects against Alzheimer’s disease, multiple sclerosis, cataract formation, HIV, and drug-induced nonspecific toxicity in the heart, lung, and kidney. Several of the studies establishing curcumin’s potential were carried out in animals. Further testing of curcumin in humans is required to confirm these observations. A clinical development plan for using curcumin to treat cancer was recently described by the NCI. Studies also show that in countries such as India where curcumin is consumed, the profile of cancer incidence is very different than those that do not (such as the U.S.; see Table 23.3).

TABLE 23.3
Comparison of Cancer Incidence in U.S. (Curcumin Non-Users) and India (Curcumin Users)

| Cancer | U.S. | | India | |
|---------------------------|-------|--------|-------|--------|
| | Cases | Deaths | Cases | Deaths |
| Breast | 660 | 160 | 79 | 41 |
| Prostate | 690 | 130 | 20 | 9 |
| Colon/rectum | 530 | 220 | 30 | 18 |
| Lung | 660 | 580 | 38 | 37 |
| Head and neck SCC | 140 | 44 | 153 | 103 |
| Liver | 41 | 44 | 12 | 13 |
| Pancreas | 108 | 103 | 8 | 8 |
| Stomach | 81 | 50 | 33 | 30 |
| Melanoma | 145 | 27 | 1.8 | 1 |
| Testis | 21 | 1 | 3 | 1 |
| Bladder | 202 | 43 | 15 | 11 |
| Kidney | 115 | 44 | 6 | 4 |
| Brain, nervous system | 65 | 47 | 19 | 14 |
| Thyroid | 55 | 5 | 12 | 3 |
| Endometrial cancers | 163 | 41 | 132 | 72 |
| Ovary | 76 | 50 | 20 | 12 |
| Multiple myeloma | 50 | 40 | 6 | 5 |
| Leukemia | 100 | 70 | 19 | 17 |
| Non-Hodgkin’s lymphoma | 180 | 90 | 17 | 15 |
| Hodgkin’s disease | 20 | 5 | 7 | 4 |

Showing cases per 1 million persons calculated on the basis of current consensus:
Endometrial cancers include Cervix uteri and Corpus uteri.

GLOBOCAN 2000: Cancer Incidence, Mortality and Prevalence Worldwide, Version 1.0.
IARC Cancer Base No. 5. Lyon, IARC Press, 2001.