

## MINI-REVIEW

## Dietary Turmeric Potentially Reduces the Risk of Cancer

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## Abstract

Turmeric, a plant rhizome that is often dried, ground and used as a cooking spice, has also been used medicinally for several thousand years. Curcumin, the phytochemical that gives turmeric its golden color, is responsible for most of the therapeutic effects of turmeric. In recent years curcumin has been studied for its effects on chronic diseases such as diabetes, Alzheimer's, and cancer. Though many researchers are investigating turmeric/curcumin in cancer therapy, there is little epidemiologic information on the effects of turmeric consumption. With limited availability of pharmacologic interventions in many areas of the world, use of turmeric in the diet may help to alleviate some of the disease burden through prevention. Here we provide a brief overview of turmeric consumption in different parts of the world, cancer rates in those regions, possible biochemical mechanisms by which turmeric acts and practical recommendations based on the information available.

**Keywords:** Curcumin – turmeric – diet - cancer chemoprevention – cancer in India – anticancer

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## Introduction

Turmeric is a plant rhizome that has been used as both a cooking spice and medicine for over 6000 years. Native to South and Southeast Asia, turmeric (*Curcuma longa*) is found in traditional dishes in India, Nepal, Pakistan, Bangladesh, China, Malaysia, Indonesia, Taiwan, Haiti, Jamaica, and El Salvador (Krishnaswamy, 2006). Turmeric contains a low molecular weight polyphenol called curcumin (diferuloylmethane), which has been studied extensively in modern medical research. *Curcuma longa* is the most studied of over 120 known species of curcuma; curcuminoids have been isolated from only a handful of these (Aggarwal et al., 2007). Curcumin has been shown to be a potent anti-inflammatory, antioxidant, antimutagenic, anti-atherosclerotic, antimicrobial, anti-rheumatic, chemopreventive, and hepatoprotective chemical (Chattopadhyay, 2004, Krishnaswamy, 2008). It is currently being investigated as a potential therapeutic mediator in several types of cancer, diabetes, Alzheimer's, HIV, cardiovascular disease, osteoporosis, and stroke recovery ([www.clinicaltrials.gov](http://www.clinicaltrials.gov)). Although purified curcumin is being examined in several disease pathways, evidence on the dietary effects of turmeric is limited.

## Turmeric Consumption

Turmeric is widely used as a cooking spice in India. It is also used topically for skin conditions and wounds and as a health tonic. The low rates of most cancer types in India (Nandakumar et al., 2005, Rostogi et al., 2008)

may be partially due to the effects of turmeric intake, but this has not been studied. Because Indians account for one-sixth of the world's population, and have some of the highest spice consumption in the world, epidemiologic studies in this country have great potential for improving our understanding of the relationship between diet and cancer.

There are very few studies that show the amount of turmeric consumption in the world. One such study shows the amount of turmeric consumed daily in India. Consumption varies between urban and rural populations, and between high- and low-income households. Diet surveys in India, using accurate measurement by weight, show the use of turmeric averages around 0.24 g/person/day among high-income households, and around 0.49 g/person/day among low-income households. In rural areas of India, consumption is around 0.73 g/person/day (Krishnaswamy, 2006). An estimation for turmeric consumption by some adults in India puts it as high as 4 g/person/day, which would supply approximately 80-200 mg of curcumin (Tapsell et al., 2006). It is used in both the fresh, root form and in the dried, ground form. Another study shows that in Nepal, the consumption rate of turmeric is between 0.5 and 1.5 g/person/day (Eigner and Scholz, 1999). It is traditionally combined with ghee, black pepper, and other spices in the typical dal recipe in Nepal, and in curries and other dishes in India (Eigner and Scholz, 1999, Krishnaswamy, 2006.). Today it is also used as a colorant and preservative in foods around the world, but information on dietary turmeric consumption in other countries is not available.

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## Cancer Incidence

Overall cancer rates are much lower in India than in western countries. In a report comparing cancer incidence rates among Indians residing in India, the US, the UK, and Singapore, and whites in the US, overall cancer rates were shown to be the lowest among Indians in India and Singapore, and highest among whites in the US. Cancer rates for Indians residing in the US and UK were intermediate (Rostogi et al., 2008). Cancers shown to have the lowest rate in India include esophagus, colorectal, liver, pancreas, lung, breast, uterine, ovary, prostate, bladder, kidney, renal, brain, non-Hodgkin lymphoma, and leukemia. Overall cancer rates in males were three times higher for whites in the US than for Indians in India and Singapore, and 50 – 75% higher for Indians in the US and UK. Prostate cancer rates were most notably different, with the rates in US whites being 20 times higher than in India. Overall cancer rates for women were also lowest in India, and more than 180% higher in US whites (Rostogi et al., 2008). Certain cancers were found to be more prevalent in Indians. The incidence of stomach cancer in males and females was highest among Indians in Singapore. The incidence of cancers of the mouth, pharynx, gall bladder, cervix, and male larynx were highest in India (Rostogi et al., 2008).

A cancer atlas of India, produced from data collected in 2001-2002, shows regional variations in different types of cancer. Data was collected via pathology laboratories in order to provide a more complete picture of cancer incidence in both urban and rural areas. Cancers of the mouth and tongue are especially prevalent in the southern states, while nasopharynx cancer is particularly high in the northern states. In the northern states there is a high incidence of gall bladder cancer whereas female thyroid cancers are highly prevalent in the northeastern states and along the southwest coast. Stomach and lung cancer rates are highest in the northeast state of Mizoram, though the overall rate of these cancers is low in India compared to other countries. Cervical and penile cancers are highly prevalent in the southern state of Tamil Nadu (Nandakumar et al., 2005).

## Lifestyle Factors

Several lifestyle factors may help to account for both the high and low rates of cancer seen in India. Cancers of the mouth, tongue, and pharynx may be attributable to the use of tobacco by both men and women. The different rates of these cancers according to region may be explained by the different types of tobacco used as well as the form in which they are consumed (Nandakumar et al., 2005). The high rate of nasopharyngeal cancer seen in the northeast may be due to a high rate of Epstein-Barr virus and consumption of smoked meats and fermented foods. The increased incidence of gall bladder cancer in the northeast coincides with an increased rate of gallstones in the same area. Interestingly, the rate of gall bladder cancer is also elevated in Indian migrants living in the UK, originating chiefly from the northern states. This suggests a possible genetic component. The high rates

of thyroid cancer in women in the northeast and along the southwest coast might have different contributing factors (Nandakumar et al., 2005). A study in 2002 showed that two-thirds of school children in the northeast state of Tripura had low levels of iodine (Chandra and Ray, 2002). This area also has a high incidence of endemic goiter. Conversely, the populations along the coast eat a diet high in iodine-rich seafood. An inadequate or excessive intake of iodine in these areas may contribute to the increased rates of thyroid cancer, though a clear relationship between iodine intake and thyroid cancer has not been established (Knobel and Madeiros-Neto, 2007). The increased rates of cervical and penile cancers found in southern India may be due to a high rate of human papilloma virus (HPV) infection in this population (Franceschi et al., 2005).

## Dietary Factors

Several dietary factors may contribute to the low overall rate of cancer in India. Among them are a relatively low intake of meat, a mostly plant-based diet, and a high intake of spices and seasonings with anticancer properties.

Diets high in red and processed meats have been associated with an elevated risk of colorectal, lung, and possibly stomach, breast, esophageal and liver cancers (Gonzalez, 2006, Cross et al., 2007, Lam et al., 2009, Cross et al. 2010). According to a 2006 poll, called The Hindu-CNN-IBN State of the Nation Survey, 31% of Indians are vegetarians (lacto-vegetarians or vegans), and an additional 9% are ovo-lacto-vegetarians (Yadav and Kumar, 2006). Though 60% of the population described themselves as non-vegetarians in this poll, a separate report claims that only 30% of the population in India eats meat regularly and those who do eat meat regularly only eat it once or twice a week (USDA Foreign Agricultural Service: Passage to India, available at: <http://www.fas.usda.gov/>). In comparison, only 3.2% of the US population follows a vegan, lacto-vegetarian, or ovo-lacto-vegetarian diet. India is the largest producer of fruits and second-largest producer of vegetables in the world. Only 2-4% of fruits and vegetables are processed and packaged, while the rest are sold as and consumed as fresh products. Grains and pulses also make up a large part of the Indian diet, pulses being the main source of protein for vegetarians (USDA Foreign Agricultural Service: Passage to India, available at: <http://www.fas.usda.gov/>).

A wide variety of spices and herbs are used in Indian cooking. The most commonly used spices are ginger, chilli powder, tamarind, coriander, turmeric, cumin, curry leaves, and garam masala, a spice mixture containing cardamom, black pepper, cumin, coriander, cinnamon, and cloves (Ferrucci et al., 2010). Additional ingredients that are widely used are onion, garlic, asafoetida, allspice, fennel, fenugreek, mustard seeds, nutmeg, and poppy seeds (Krishnaswamy, 2008, Ferrucci et al., 2010). Many of these ingredients have proven benefits to human health. They contain phytochemicals and other compounds that protect against inflammation, oxidative stress, genetic mutations, and various stages of cancer development (Bachmeier et al., 2008).

## Potential Mechanisms of Action

Several mechanisms of action have been elucidated in studies of the anticancer potential of curcumin. It has been shown to have antioxidant, anti-inflammatory, anti-angiogenic, chemosensitizing, and apoptotic activity.

Reactive oxygen species (ROS) are highly reactive free radicals that cause damage and toxicity to cells. Curcumin protects biomembranes against peroxidative damage by scavenging reactive free radicals (Aggarwal et al., 2007).

Inflammation is implicated in most modern disease processes including tumor development and metastasis (Mantovani et al., 2008). Curcumin acts as an anti-inflammatory agent by inhibiting cyclooxygenase-2 (COX-2), lipoxygenase (LOX), inducible nitric oxide synthase (iNOS), and nuclear factor- $\kappa$ B (NF $\kappa$ B) (Aggarwal et al., 2007, Bachmeier et al., 2008).

Angiogenesis is crucial for tumor growth and metastasis. It provides a blood supply to the tumor and a route for proliferating to new areas in the body. Curcumin has been shown to be a direct inhibitor of angiogenesis by inhibiting endothelial cell migration and invasion. Curcumin also indirectly inhibits angiogenesis by inhibition of vascular endothelial growth factor (VEGF), COX-2, and NF $\kappa$ B (Aggarwal et al., 2007).

Resistance to chemotherapeutic drugs is the main reason chemotherapy fails in cancer treatment. So-called cancer stem cells have been postulated to be those cells responsible for chemoresistance. Curcumin has been shown to increase the cellular accumulation of chemotherapy drugs in breast cancer treatment (Kawasaki et al., 2008). It enhances both chemo- and radio-sensitization in cisplatin-resistant ovarian cancer cells by reducing the expression of pro-survival proteins (Yallapu et al., 2010). It also inhibits genes involved in multidrug resistance such as P-glycoprotein and multidrug resistance-associated protein (MRP1) (Aggarwal et al., 2007).

Apoptosis, or programmed cell death, is disabled in cancer cells, allowing them to proliferate unchecked. Curcumin has been shown in several studies to induce apoptosis in vitro, in human cells lines such as leukemia cells, gastric and colon cancer cells, and breast cancer cells (Kuo et al., 1996, Moragoda et al., 2001, Choudhuri et al., 2002).

## Animal Studies

Curcumin has shown promising results in animal studies of cancer prevention and treatment. In a study using a mouse model of hepatocellular carcinoma (HCC), a diet consisting of 0.2% curcumin was administered starting four days before injection with N-diethylnitrosamine and continuing until death. At 42 weeks post-injection, the curcumin-fed mice showed a 62% reduction in incidence of HCC, and an 81% decrease in the number of tumors found compared to controls (Chuang et al., 2000). Mahmoud and colleagues, using a mouse model of familial adenomatous polyposis, reported a 64% decrease in tumor number in mice fed a 0.1% curcumin-containing diet compared to controls (Mahmoud et al., 2000). In another

study using a mouse model of colon carcinogenesis, tetrahydrocurcumin, an active metabolite of curcumin, significantly reduced preneoplastic aberrant crypt foci development after treatment with 1,2-dimethylhydrazene dihydrochloride to initiate tumors, compared with controls (Kim et al., 1998).

## Human Studies

Human studies of curcumin in cancer treatment have shown little toxicity and encouraging results. A phase I clinical trial studied the effect of 500 to 8000 mg/day of curcumin in 25 high-risk patients in 5 groups including oral leukoplakia, recently resected bladder cancer, cervical intraepithelial neoplasm, arsenic Bowen's disease of the skin, and intestinal metaplasia. No toxicity was noted in the study, and histological improvement was seen in the precancerous lesions in at least one patient from each group. Only two patients in the study developed blatant malignancies by the end of the 3-month treatment (Cheng et al., 2001). In another study, 25 patients with adenocarcinoma of the pancreas were administered 8000 mg/day of curcumin for eight weeks. No chemotherapy or radiation therapy was given during the study. No toxic effects were noted, and two patients in the study experienced tumor regression (Dhillon et al., 2008). In another small study, 1125 mg/day of curcumin was administered to patients with idiopathic inflammatory orbital pseudotumors for 6 to 22 months. No toxic effects were noted in the study. Four of the five patients completely recovered and the fifth improved but experienced partial restriction of eye movement (Lal et al., 2000).

## Concerns

A few concerns exist about the use of turmeric and curcumin, both as a potential therapeutic agent and dietary ingredient. These include the low bioavailability of curcumin and possible tumor promotion.

The low bioavailability of curcumin has been noted in several studies (Ireson et al., 2002, Garcea et al. 2004, Lao et al., 2009). Two small studies have shown that piperine, an alkaloid from black pepper and long pepper, may increase the bioavailability of curcumin. Shoba and colleagues report that the addition of 20 mg piperine to a 2 g dose of curcumin increased bioavailability by 2000% (Shoba et al., 1998). In another study, Anand et al. report that administration of 5 mg piperine resulted in doubling the absorption of the 2 g dose of curcumin over controls (Anand et al., 2007).

Curcumin is thus far considered to be nontoxic and having a protective effect on tumor development. However, a mouse study by Dance-Barnes and colleagues resulted in tumor promotion by curcumin. A dietary curcumin dose of 2000 p.p.m. was administered to transgenic mice expressing a doxycycline (DOX)-inducible lung cancer allele for nine months. Curcumin significantly increased tumor multiplicity and disease progression, similar to treatment with butylated hydroxytoluene, a known lung tumor promoter, compared to controls (Dance-Barnes et

al., 2009). In an in vitro study, curcumin was found to disrupt the function of p53, a known tumor suppressor, in colon cancer cells (Moos et al., 2004).

## Conclusion

Information on the consumption of turmeric in the world is limited. There is no proven correlation between dietary turmeric and decreased cancer risk, but based on the available information from studies on curcumin and cancer rates in Indians it is feasible. However, it is nearly impossible to account for several confounding factors of lifestyle, genetics, and other dietary components that may cloud the picture. Curcumin may act on several factors in inflammatory, tumorigenic, angiogenic, and apoptotic pathways, but more targeted studies are needed.

In the aforementioned studies, doses of 1125 to 8000 mg of curcumin per day were shown to have an effect on cancer progression. While most clinical studies have used purified curcumin, a limited number of studies have used turmeric as the study agent. For example, in one study, a dose of 1.5 grams of turmeric per day caused a significant reduction in the amount of mutagens excreted in the urine of smokers (Polasa et al, 1992). An analysis of turmeric powders sold in the United States showed that they contain 0.58 – 3.14% curcumin by weight (Tayem et al., 2006). The same study revealed that curry powders contained 0.05 to 0.58% curcumin by weight. Therefore, to achieve an analogous dose of curcumin in the diet, one would need to consume between 35.8 and 194 grams of turmeric, or roughly 16 to 88.2 teaspoons, per day. This is not realistic for most people; however, it is possible that as little as 1.5 grams of turmeric per day has biological activity, which is much more easily achieved.

Practical recommendations for obtaining curcumin in the diet might be to add turmeric to sweet dishes containing cinnamon and ginger, as turmeric blends nicely with these spices; to increase the consumption of dishes made with curry powder, a spice blend that contains turmeric as an ingredient; or to consume turmeric milk, a traditional Indian elixir made with milk, turmeric powder, and a little sugar, if needed to make it more palatable.

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