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## REPORT

A REPORT ON CURCUMIN'S  
ANTI-CANCER EFFECTS

by Terri Mitchell

Imagine a natural substance so smart it can tell the difference between a cancer cell and a normal cell; so powerful it can stop chemicals in their tracks; and so strong it can enable DNA to walk away from lethal doses of radiation virtually unscathed. Curcumin has powers against cancer so beneficial that drug companies are rushing to make drug versions. Curcumin is all this and more.

*Curcuma longa* is a ginger-like plant that grows in tropical regions. The roots contain a bright yellow substance (turmeric) that contains curcumin and other curcuminoids. Turmeric has been used in Ayurvedic and Chinese medicine for centuries. But it's only within the past few years that the extraordinary actions of curcumin against cancer have been scientifically documented. Among its many benefits, curcumin has at least a dozen separate ways of interfering with cancer.

## Curcumin blocks estrogen mimicking chemicals

One of the things that sets curcumin apart from most other anti-cancer supplements (I3C being an exception), is that this phenolic can actually block chemicals from getting inside cells. Importantly, curcumin can interfere with pesticides that mimic estrogen. These include DDT and dioxin, two extremely toxic chemicals that contaminate America's water and food. (Dioxin is so toxic that a few ounces of it could wipe out the entire population of New York City). Curcumin has the unique ability to fit through a cellular doorway known as the aryl hydrocarbon receptor. This is a feat it shares with estrogen and estrogen-mimicking chemicals. Because it can compete for the same doorway, curcumin has the power to block access to the cell and protect against estrogen mimickers.

Like estrogen, estrogen-mimicking chemicals promote the growth of breast cancer. In a study on human breast cancer cells, curcumin reversed growth caused by 17 $\beta$ -estradiol by 98%. DDT's growth-enhancing effects on breast cancer were blocked about 75% by curcumin.

Two other estrogen mimickers were tested for their ability to enhance breast cancer. Chlordane and endosulfane together make breast cancer cells grow about as much as 17 $\beta$ -estradiol. Curcumin can reverse that growth about 90%. Adding the soy phytochemical, genistein, causes a 100% growth arrest.

Curcumin's ability to block other chemicals have been documented. It has been tested against paraquat (weed killer), nitrosamines (in cooked meat and "lunch" meats) and carbon tetrachloride (a solvent in varnish and other products). In all cases, curcumin is able to block the chemical's effect. The beneficial effects are evident in a study where mice were treated with diethylnitrosamine. All mice treated with this chemical would usually develop liver cancer. However, when treated with curcumin, the percentage of animals developing cancer went from 100% to 38%, and the number of tumors dropped by 81%.

Drug companies rush to make synthetic versions

Banned Pesticide  
Could Be In Your Food

Chlordane is a pesticide composed of over 50 different chemicals. A chlorine chemical that mimics estrogen, chlordane was banned in the U.S. over 50 years ago. Nonetheless, it continued to be manufactured in the U.S. and shipped to Mexico where it was sprayed on food crops exported back to the U.S. According to the Agency for Toxic Substances and Disease Registry, almost every human on earth has chlordane in their fat. There is no way to get it out of the body. Losing weight simply concentrates the chemical in the remaining fat.

Besides being sprayed on America's corn, millions of tons of chlordane were put into the ground around house foundations to kill termites before it was banned. The half life of chlordane in soil is 22 years (which means it doesn't degrade for at least 40 years). That means that if you plant a vegetable garden next to your house, you might end up with a big dose of chlordane on your dinner plate.

One of the hottest areas of oncology drug development is in the area of kinase inhibitors. Kinases are the equivalent of phone lines into cancer cells. There are over 2000 known protein kinases, or phone lines. These lines run from the outside of a cell into the DNA command center. They carry messages. Cut these lines, and you can effectively stop the growth of some types of cancer cells.

Curcumin effectively blocks some of the lines. In cells treated with curcumin, certain "grow" signals are blocked from reaching the cell.

The most well-studied growth factor blocked by curcumin is nuclear factor-k B. NF-kB is activated by chemical messengers known as cytokines. Cytokines help the immune system, but they also activate signals that tell cells to multiply, grow. By interfering with those signals, curcumin effectively stops the growth of cancer cells by kinase pathways. It has been demonstrated, for example, that curcumin can prevent the bug that causes ulcers (*Helicobacter pylori*) from causing cancer. *H. pylori* increases levels of a cytokine (IL-8) that activates NF-kB. Curcumin blocks the process.

Drug companies are rushing to patent chemicals that do what curcumin does-inhibit kinases. AstraZeneca has gotten one off the ground called "Iressa". Iressa inhibits protein kinase C (PKC), a kinase that plays a significant role in cancer. PKC transmits signals from the "epidermal growth factor (EGF) receptor." Cutting off signal transmission through EGF significantly slows the growth of any cancer that uses this factor to grow-glioma, breast, prostate, skin and lung cancers.

Curcumin has long been known for its ability to prevent skin cancer. In 1993, researchers in Taiwan reported that curcumin inhibits PKC. The next year it was reported that curcumin blocks EGF signals up to 90% and stops growth.

It turns out that the structure of curcumin enables it to inhibit multiple kinases. This ability is shared with other phytochemicals including silymarin, apigenin and hypericin. While drug companies rush to try to recreate safe, patentable, chemical versions of this structure, curcumin sits ready and available for use. Blocking kinases, however, is only one of curcumin's anti-cancer effects.

Inflammation: Curcumin suppresses LOX and COX

Squamous cell carcinoma can affect the bronchial tubes, mouth or skin. When researchers at the University of Missouri treated oral squamous cell carcinoma cells with curcumin, it caused significant growth inhibition.

Curcumin is also notably effective against colon cancer. Inflammation appears to play a significant role in promoting this type of cancer. Curcumin has long been known for its anti-inflammatory action. More recently, it has been shown that curcumin inhibits cyclooxygenase (COX) and lipoxygenase (LOX), two enzymes that promote inflammation. Inflammation is in the limelight these days because of the discovery that people who take nonsteroidal anti-inflammatory drugs (NSAIDs), including aspirin, have stunning protection against colon cancer. Inflammation, it turns out, plays significant and diverse roles in the initiation and promotion of cancer. Oxidative stress helps activate PKC, for example. Part of curcumin's ability to block PKC signals is due to its powerful antioxidant activity.

Curcumin possesses several other anti-cancer benefits that make it useful for cancer prevention. One of its most recognized features is its antioxidant action. Turmeric is a spice that contains curcumin. It has traditionally been used as a food preservative for a good reason: it keeps food from going rancid-oxidizing. And just as it keeps oxygen from turning meat rancid, it protects our own bodies from damaging free radicals. Free radicals promote cancer by damaging DNA and activating genes.

Radiation damages DNA partially through free radicals. In a recent study, it was demonstrated that under laboratory conditions, curcumin could protect bacteria from a lethal dose of radiation almost perfectly. Bacterial DNA emerged virtually intact.

Curcumin kills cancer cells

Researchers in Connecticut testing random samples of U.S. produce found chlordane in vegetables grown on soil that hadn't been treated with chlordane for 20 years. So they decided to do an experiment. They grew vegetables on soil previously treated with chlordane to see what would happen. The soil they used was under the lawn of their own institution that had been sprayed with chlordane in 1960 to see how well it worked.

In May, 2000, they published their findings in the *Journal of Agricultural and Food Chemistry* (the journal of the American Chemical Society). All 12 vegetables they grew on soil sprayed decades earlier contained chlordane. Potatoes, carrots and beets absorbed chlordane systemically-it was in the flesh. Zucchini acted like a sponge for it. It also ended up in beans, eggplant, lettuce, dandelion and spinach.

After the findings were made public, the lead author, Dr. Mary Jane Incorvia Mattina was quoted as saying, "The main recommendation is to wash the foods you are going to eat, and not to plant near a house foundation that could have been treated with chlordane. If you take these precautions, you shouldn't have any cause for concern." When asked by us how one washes chlordane out of a vegetable, she admitted that it's impossible.

Mexico was still importing 45 tons of chlordane from the U.S. in 1997, when it instituted a program to gradually quit using the pesticide (it also plans to phase out DDT by the year 2007). The only official use of chlordane in Mexico (which grows vegetables for the U.S. market) is for killing termites in urban areas.

Curcumin can stop cancer in its earliest stages, long before it's detectable. It works at the level of the cell. One of the things it does is to tell damaged cells to self-destruct so they won't keep multiplying. The process is called "apoptosis" and it's the body's way of destroying abnormal cells that can become cancerous. Cancer cells can circumvent the process, but curcumin can override them and send "self-destruct" signals to many different types of cancer cells. Curcumin does not induce apoptosis of healthy cells, only cancerous ones. It identifies cancer cells by their abnormal chemistry. Unfortunately, it doesn't work in all types of cancer, but Indian researchers may have figured out why. Their findings, published in the Journal of Biological Chemistry, may lead to ways of making most types of cancer susceptible to curcumin's effects.

Before apoptosis is induced, curcumin stops cancer cells from multiplying. In cancer research, this is known as "interrupting the cell cycle." The cell cycle can be interrupted at several different points. This is the rationale behind using various chemotherapy treatments in one person. One drug stops the cells when they are in one stage of growth; another stops them at another stage. Using a variety of drugs that stop growth at different stages increases the chances of killing all the cancer cells. Curcumin arrests the growth of cancer cells in the G2 stage.

Other phytochemicals stop the cell cycle at other stages. Genistein, a soy phytochemical, arrests growth at G2, like curcumin. But epigallocatechin-3-gallate (EGCG) from green tea, arrests cancer cell growth at the G1 phase. Combining EGCG with curcumin increases the odds of killing more cells. Researchers at Sloan-Kettering Cancer Center have suggested that EGCG and curcumin be used together for cancer prevention.

#### Curcumin enhances immunity

Curcumin can also help the body fight off cancer should some cells escape apoptosis. When researchers looked at the lining of the intestine after ingestion of curcumin, they found that CD4+ T-helper and B type immune cells were greater in number. In addition to this localized immune stimulation, curcumin also enhances immunity in general. Researchers in India have documented increased antibodies and more immune action in mice given curcumin.

#### Curcumin stops angiogenesis

All of the above actions of curcumin stop cancer before it has a chance to become detectable. If cancer grows to the point that it is a detectable tumor, curcumin can still have an effect.

Certain enzymes enable tumors to create a blood supply for themselves. Known as "angiogenesis," this phenomenon allows tumors to invade surrounding tissue and spread. Working with blood vessels of the eye (where angiogenesis creates big problems for vision), researchers at Tufts University were able to inhibit blood vessel formation by using curcuminoids. Curcumin blocks AP-1, which enhances angiogenesis.

Curcumin may also inhibit angiogenesis by chelating metals used by enzymes that promote the growth of blood vessels. Some of the enzymes that promote angiogenesis are known as "metalloproteinases." Metalloproteinases require metals to work. Curcumin chelates iron and probably copper-both of which help metalloproteinases create new blood vessels for tumors. In a study on a highly invasive form of human liver cancer, curcumin inhibited metastasis 70% by suppressing metalloproteinase-9. Curcumin appears to be very protective against liver cancer. In a more recent study, the incidence of liver cancer was slashed 62%, with the number of tumors decreasing by 81% in mice given curcumin four days before a carcinogenic chemical.

### Curcumin, Free Radicals and Methylation

Methylation of DNA is critical for maintaining a cancer-free state. More specifically, certain patterns of methylated and non-methylated DNA keep cancer genes turned off, and tumor suppressor genes turned on. Dr. Khing Lertratanangkoon has done research showing that chemicals which deplete glutathione in the liver, cause DNA methylation disruption. In other words, maintaining glutathione is important for maintaining DNA methylation.

Glutathione is the liver's natural antioxidant. Chemicals (which are all processed by the liver) deplete glutathione. Curcumin protects glutathione in the presence of chemicals (including alcohol).

Dr. Lertratanangkoon has shown that a glutathione-depleting chemical can disrupt DNA methylation. But if curcumin is given at the same time, both methylation and glutathione are maintained. Bottom line: curcumin may also save DNA methylation patterns, another anti-cancer benefit.





Curcumin possesses several other anti-cancer benefits that make it highly effective as a cancer preventive agent against almost any type of cancer. One of its most talked-about features is its antioxidant action.

glutathione because these nutrients might interfere with curcumin's PKC inhibiting effects in actively growing cancer. Since thiol compounds are critically important anti-aging nutrients, cancer patients may consider avoiding or reducing thiol nutrients for a three to six month period while consuming high doses of curcumin (along with soy, green tea extracts, I3C and other nutrients that have shown specific anti-cancer effects). A comprehensive report on suggested nutrient dosing schedules for cancer patients will be published in a future edition of this magazine.

The cancer preventive effects of curcumin are powerful and proven. Curcumin interferes with the ability of estrogen-mimicking and other chemicals to do damage (a trait it shares with I3C). It is a powerful antioxidant that can alter gene expression, stop the cell cycle, and induce the self-destruction of cancer cells without affecting healthy ones. By blocking signals known as kinases, curcumin interrupts signals that enable cancer cells to grow. In addition, curcumin enhances immunity and blocks the invasion and metastases of tumors. Curcumin significantly reduces the risk of cancer after chemical exposure, and appears especially beneficial against colon and liver cancers. The actions of curcumin have been the subject of presentations at major meetings on cancer research, and the object of study by researchers at the most prestigious universities in the world. If curcumin were a drug, it would be hailed as one of the best all-around cancer drugs ever invented. As it is, it's a phytochemical with impeccable credentials, thousands of years of use behind it, and a very small price tag. No wonder a host of drug companies want to imitate it.

Note: There is still not a scientific consensus on how those with active cancer may best take advantage of the multiple potential benefits of curcumin. Most cancer patients have been taking 1800 to 3600 mg a day of curcumin. Life Extension has recommended that curcumin not be combined with the chemotherapy drug Camptosar (irinotecan) because of one animal study that indicated a possible adverse effect. Since curcumin has not been adequately tested with other chemotherapy drugs, it might be safe to wait until chemotherapy is completed before initiating curcumin. Cancer patients using curcumin may want to avoid high doses of "thiol" nutrients such as cysteine, lipoic acid, SAmE and

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