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COVER STORY

The Spice of Life
Unlocking the power of curcumin

Imagine if the key to disease prevention was as close as your kitchen shelf. It's not the product of someone's imagination, but the product of years of medical research. Scientists are beginning to take notice of a well-known spice as a potent new preventive therapy against disease, especially cancer.

by John C. Martin

Cancer takes the lives of more than 1,500 people a day—over 5 million since 1990—and is the second leading cause of death in the United States.(1)

While those statistics are staggering, the medical community is maintaining its focus on mechanisms behind the disease and discovering new, potentially effective methods of treating it. A similar emphasis is placed on prevention, as more and more scientists attempt to uncover the mystery behind 'carcinogenesis,' particularly at the genetic level.

What is drawing the attention of medical oncologists and researchers these days is a substance known as curcumin, a naturally occurring yellow pigment found in the spice tumeric, which is part of the ginger plant family. Tumeric is widely consumed in its countries of origin not only as a spice, but as a medicine for the treatment of a variety of illnesses. It was long ago used as an anti-inflammatory among Indian practitioners.(2)

Today, curcumin is showing a much broader potential. Not only does the extract work as an antioxidant and anti-inflammatory, but a series of studies in the past four years, focusing on cancer at the cellular level, reveals some exciting findings. For one thing, research is discovering that curcumin is a powerful carcinogenic inhibitor, slowing cancerous cell proliferation by inducing apoptosis, a pre-programmed set of processes within a cell that results in its death.

Curcumin targets cancer proliferation

In two recent studies, scientists at New York's Columbia University researched curcumin's therapeutic potential against prostate cancer. In one case last year, the scientists discovered that curcumin had a powerful ability to induce apoptosis and inhibit prostate cell proliferation in vitro by interfering with the cells' protein signaling pathways that typically begin the growth process.(3) Just recently, the researchers extended those findings to determine if they could achieve similar results in an animal model.(4) In their latest study, the researchers found that prostate cancer cells that had been injected subcutaneously into mice, which had been fed a diet of 2% curcumin for six weeks, were unable to develop extensively and underwent significant apoptosis. "Curcumin could be a potentially therapeutic anti-cancer agent, as it significantly inhibits prostate cancer growth… and has the potential to prevent the progression of this cancer to its hormone refractory state," the study authors concluded.

Yet prostate cancer is not curcumin's only target. Other cancer investigations have drawn similarly powerful conclusions about this intriguing substance.

Curcumin as an antioxidant

Curcumin, the extract found in a common household spice, is common no longer. It's been drawing more and more attention among medical experts the last several years for its antioxidant and anti-inflammatory qualities.

When the body responds to a physical injury, a series of changes occurs through which free radicals are released. These free radicals, or "oxidants," protect the body from foreign invasion, such as infection. However, in the process of killing invading bacteria, oxidants can

A study this past spring at Wayne State University investigated the effect of curcumin on certain gastrointestinal and colon cancers in the lab.(5) Several immunoblot analyses demonstrated that curcumin blocked cell proliferation and induced apoptosis in both gastrointestinal and colon cancer cell lines.

A Chinese study published five years earlier found apoptosis is the result when curcumin is introduced to certain skin, colon, kidney and liver cancer cells, either in cultures or in mouse embryo fibroblasts—large, flat oval cells found in connective tissue and inherent in the formation of fibers.(6)

Other studies using rodents found curcumin is effective in reducing skin inflammation, inhibiting formation of edemas—an abnormal accumulation of cellular fluid, resulting in swelling—and inhibiting skin tumors when the substance is applied topically(7) or orally in concentrations of either 0.2% or 1%.(8)

Curcumin has had similar effects on other types of cancer. When Polish researchers last year assessed the potency of the extract on lymphoid cells—those found in tissues comprising the lymph nodes— apoptosis resulted, although apoptotic symptoms were uniquely different in the various cells tested, the scientists reported. (9)

Treating eye disorders

Curcumin is apparently more than your typical kitchen spice. It's the substance that gives ginger its yellowish color, and it has been implicated in the treatment of certain eye diseases and conditions. One of those is known as chronic anterior uveitis (CAU), an inflammatory condition of the vascular layer of the eye, particularly the area comprising the iris. In one small study, curcumin was given orally to 32 chronic anterior uveitis patients who were divided into two groups. The first group received curcumin alone, whereas the second group received a combination of curcumin and antitubercular treatment. Amazingly, all of the patients treated with curcumin alone improved, compared to a response rate of 86% among those receiving the combination therapy. The researchers concluded that curcumin was just as effective as corticosteroid therapy, the only available standard treatment for chronic anterior uveitis at present, adding that "the lack of side effects with curcumin is its greatest advantage compared with corticosteroids."

Similar research using rats and rabbits found that curcumin effectively inhibited chemically induced cataract formation, even at very low dietary levels. The same study also found, for the first time, that this type of induced cataract may be accompanied by apoptosis of epithelial cells in the eye and that curcumin may lessen the apoptotic effect.

To determine just how effective curcumin might be as an anticarcinogenic agent, it was compared to other compounds and plant extracts in fighting human oral squamous carcinoma.(10) Cell lines were grown in vitro for 72 hours, then the number of cells were counted to determine proliferation and growth. The researchers found that curcumin was "considerably more potent" compared to plant phenolics genistein and quercetin in inhibiting this type of cancer. Only cisplatin, a platinum-based substance also tested in the study, was found to be more effective.

Still more research focused on the effect of curcumin on the development of pulmonary fibrosis by testing a group of rodents.(11) Scientists in India induced the lung disorder in rats, while giving them dosages of curcumin both 10 days prior and then daily throughout the experiment. Remarkably, curcumin demonstrated its powerful anti-inflammatory and anti-fibrotic effect in each rat studied.

Even breast cancer apparently cannot avoid the power of this extract, which inhibits the growth of breast tumors that result from exposure to environmental estrogenslike chemicals and pesticides, when used in combination with isoflavonoids. Scientists found the curcumin combination inhibited the growth of estrogen receptor-positive cancer cells in a test tube up to 95%.(12)

also harm our cells. Such oxidants can include superoxide, hydrogen peroxide, hydroxyl radicals and lipid peroxides. Over time, as our cells continue to be affected by these free radicals, or oxidants, organs begin to degenerate. The result can be such diseases and conditions as chronic inflammation, heart disease, aging acceleration and chaotic cell growth leading to cancer.

The body does have built-in defense mechanisms to protect itself from free radical damage, but eventually, aging and disease deplete the body's ability to keep oxidants at bay. Studies show that curcumin can inhibit, or possibly even reverse this process by scavenging or neutralizing free radicals and breaking their subsequent oxidative chain reaction.

Research as early as 1995 has shown that a diet that includes curcumin can restrict this oxidative stress. Scientists in India found curcumin inhibited lipid peroxidation, superoxides and hydroxyl radical.

Two more recent studies were published last year. In the first analysis, scientists found that prolonged exposure by curcumin to endothelial cells of the bovine aorta resulted in "enhanced cellular resistance to oxidative damage."

Doctors in a separate investigation discovered that curcumin suppressed oxidative stress induced by trichloroethylene in mouse liver. The researchers concluded that curcumin's benefit seems to be derived from its ability to inhibit increases in cellular levels of peroxisome, a component associated with oxygen utilization in cells.

The oxidation of LDL, the "bad" cholesterol, plays an important role in the development of atherosclerosis. Based on that knowledge, medical researchers have also examined the effect of curcumin on LDL oxidation and plasma lipid levels. In one investigation, doctors in Spain fed 18 rabbits a high cholesterol diet to induce atherosclerosis. The rabbits were divided into three groups; one group was given 1.66 milligrams of curcumin per kilogram of body weight, the second group was given 3.2 mg, and a third group was designated as a control. After seven weeks, the investigators found that the group fed the

In one of the earliest studies examining curcumin as a potential cataract therapy, researchers fed two groups of rats diets that included corn oil, or a combination of curcumin and corn oil for 14 days. Afterward, their lenses were removed and examined for the presence of lipid peroxidation. The scientists discovered that “the lenses from curcumin-treated rats were much more resistant to… induced opacification than were lenses from control animals.”

Awasthi S et al. Curcumin protects against 4-hydroxy-2-trans-nonenal-induced cataract formation in rat lenses. Am J Clin Nutr 1996 Nov;64(5):761-6.

Lal B et al. Efficacy of curcumin in the management of chronic anterior uveitis. Phytother Res 1999 Jun;13(4):318-22.

Pandya U et al. Dietary curcumin prevents ocular toxicity of naphthalene in rats. Toxicol Lett 2000 Jun 5;115(3):195-204.

The how’s and why’s

What exactly is the mechanism behind curcumin’s ability to counteract such a wide array of cancer progression? For several years, medical research focusing on cancer causation has centered on the notion of angiogenesis, the natural blood vessel growth that accompanies metastases. The new blood vessels literally provide nutrition and sustenance to new and growing tumors throughout the body. That may be one basis, medical researchers contend, for curcumin’s efficacy. In 1998, Harvard researchers tested the substance for its ability to inhibit the growth of endothelial cells; those which line the interior of blood vessels, as well as the growth of new blood vessels in the corneas of mice.

“Curcumin effectively inhibited endothelial cell proliferation in a dose-dependent manner,” they wrote. “Curcumin and its derivatives [also] demonstrated significant inhibition of …corneal neovascularization in the mouse… These results indicate that curcumin had direct antiangiogenic activity in vitro and in vivo. The activity of curcumin in inhibiting carcinogenesis in diverse organs such as the skin and colon may be mediated in part through angiogenesis inhibition.”(13)

lower curcumin dosage decreased LDL’s susceptibility to lipid peroxidation, and both dosage groups had lower cholesterol levels.

Motterlini R, Foresti R, Bassi R, Green CJ. Curcumin, an antioxidant and anti-inflammatory agent, induces heme oxygenase-1 and protects endothelial cells against oxidative stress. Free Radic Biol Med 2000 Apr 15;28(8):1303-12.

Ramirez-Tortosa MC et al. Oral administration of a turmeric extract inhibits LDL oxidation and has hypocholesterolemic effects in rabbits with experimental atherosclerosis. Atherosclerosis. 1999 Dec;147(2):371-8.

Ruby AJ et al. Anti-tumour and antioxidant activity of natural curcuminoids. Cancer Lett 1995 July 20;94(1):79-83.

Watanabe S, Fukui T. Suppressive effect of curcumin on trichlorothylene-induced oxidative stress. J Nutr Sci Vitaminol 2000 Oct;46(5):230-4.

Other studies, such as one by Taiwanese scientists four years ago, examined the molecular mechanisms behind curcumin. They concluded, after studying curcumin’s effect on mouse fibroblast cells, that it directly suppresses the expression of nuclear oncogenes, the genetic mutation that launches the process of cancer cell growth, among other things.(14) Other studies have examined the possibility that the mechanisms behind curcumin may lie in its ability to block the activity of specific oxidants, and halt signal transduction pathways between cells during the initial tumor growth process.(15)

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Tapping curcumin's power

There appear to be other promising implications for this seemingly miraculous substance. Research has demonstrated curcumin's neuroprotective benefits following ethanol-induced brain injury by significantly reversing lipid peroxidation and promoting antioxidants in the brain.(16) Scientists have also been successful at suppressing chemically-induced inflammation and hyperplasia—abnormal cell growth that can be a precursor to cancer—in the liver, as demonstrated in rodents.(17)

Some of the newest studies are pointing to curcumin's potential as an inhibitor of viral progression in AIDS.(18) Researchers at the National Cancer Institute analyzed how curcumin inhibits the activity of integrase in the development of the human immunodeficiency virus (HIV). Integrase is the enzyme that inserts HIV's genes into a cell's normal DNA. Based on their observations, the government researchers suggested that new anti-AIDS strategies might have to be developed that point to curcumin as a potent inhibitor of integrase in the development of HIV.

Much earlier studies have examined other causes for curcumin's anti-HIV activity, such as its ability to inhibit the action of protease, another enzyme in the process of viral development.(19)

More recently, scientists have examined how curcumin blocks formation of the Epstein-Barr virus (EPV) associated with HIV. The virus can cause such diseases as infectious mononucleosis and nasopharyngeal carcinoma. In one study,(20) scientists discovered that treating EPV-infected lymphoid cells with curcumin augmented apoptosis, similar to what has been found in cancer research. "A further investigation of this effect may be useful in prevention and therapy of B-cell lymphoma in immunodeficient patients," the researchers wrote.

Doctors have even found that curcumin, among other common spices, can prevent bacteria such as E. coli from being destroyed by irradiation.(21) The findings, reached in a study from India, carry implications that curcumin and other spice extracts could be used to protect healthy tissue in people undergoing radiation therapy. It is believed that the spices used in the study—red chili powder, black pepper and turmeric—provided their protective effect by blocking the bacteria's DNA from radiation exposure. The researchers added that there is no cause for concern because irradiation doses typically used to process prepared foods are high enough to kill any E. coli.

Review

Study after study over the past five years has demonstrated the benefits of curcumin, a substance found in turmeric. Used as long as 6,000 years ago by Indians and other cultures as a treatment for a range of ailments, medical experts more recently are beginning to discover its untapped potential.

Accelerated healing

Medical science has found signs of curcumin's abilities to fight tumor

Muscle regeneration

Believe it or not, curcumin has something in it that repairs muscle better than anything presently known. Derived from the spice turmeric, curcumin speeds recovery without injections or side effects. Although the data is preliminary, it appears that when curcumin is taken orally, it has the ability to home in on injured muscle. Once there, it changes the biochemistry of baby muscle cells, causing them to grow faster and clump together quicker to create new tissue. According to the study, curcumin caused muscle cells to fuse together twice as fast as they ordinarily would.

It's not known exactly how curcumin works. Researchers do know, however, that curcumin suppresses a factor that influences growth factors. This factor, NF B (nuclear factor kappa B), plays a prominent role in immunity and cell growth. Immediately after muscle injury, the immune system dispatches cells to the area. Their job is to destroy old tissue and begin new construction. NF B is one of the lines of communication immune cells use to get things done. By influencing NF B, curcumin modulates the repair process.

The regeneration of muscle is a complex phenomenon. Curcumin works in part by changing the arrival time and status of chemical messengers known as cytokines. Cytokines appear at the scene early on, and they have a powerful effect on inflammation and cell growth. A cytokine known as IL-6 (interleukin-6), for example, makes muscle cells multiply. Another one called TNF (tumor necrosis factor) keeps cells from growing up, developing. By suppressing one, and enhancing the other, curcumin can speed things up.

The authors of the study believe that curcumin works by other mechanisms that probably involve growth factors, but this has not been proven yet. In other attempts to make muscles regenerate, researchers have tried injecting synthetic growth factors or transplanting myoblasts–all with limited

Wound treatment may be enhanced by curcumin, it turns out. In an experiment using groups of curcumin-treated and untreated rats and guinea pigs, researchers discovered “faster wound closure” in the treated animals compared to their untreated counterparts. Subsequent biopsies of the wounds showed redevelopment of epidermal cells, increased migration of various other cells to the wound site like myofibroblasts, fibroblasts and macrophages, and extensive re-growth of blood vessels.

As a follow-up to a study, scientists reached similar results among diabetic rodents who experienced impaired healing. The researchers found improved blood vessel formation, increased cell migration to the wound site, and higher levels of collagen, a fibrous protein found in connective tissue, bone and cartilage.

Sidhu GS et al. Enhancement of wound healing by curcumin in animals. Wound Repair Regen 1998 Mar-Apr;6(2):167-77.

Sidhu GS et al. Curcumin enhances wound healing in streptozotocin induced diabetic rats and genetically diabetic mice. Wound Repair Regen 1999 Sep-Oct;7(5):362-74.

formation and growth in cancer by inducing the programmed cell death known as apoptosis and inhibiting metastases. Curcumin has also been implicated as an anti-inflammatory, a scavenger of free radicals, a treatment for certain eye diseases and conditions like cataracts, an effective therapy against ethanol-induced brain damage, hyperplasia and as an inhibitor of the human immunodeficiency virus. Before much longer, it may be plausible to think curcumin could spark a medical revolution.

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success. Curcumin seems to be a much safer, more effective treatment–at least in the early stages. The effects of curcumin are felt early on–right after injury when the body first sends out the repair squads. So if you want to try curcumin for muscle regeneration, make sure you take it as soon as the injury occurs. The authors of the study predict that curcumin may be useful not only for accidental injuries or sports, but also to help repair surgical damage.

Thaloor D, et al. 1999. Systemic administration of the NF- B inhibitor curcumin stimulates muscle regeneration after traumatic injury. Am J Physiol 277(2 pt 1):C320-29.

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Curcumin and Cancer

Cancer cells are everything we would like healthy cells to be. They quickly adapt to toxic environments, they readily alter themselves to assure their continued survival, and they are immortal. All of these factors make cancer an extremely difficult disease to treat.

Chemotherapy drugs have a high rate of failure. That's because these drugs usually kill only specific types of cancer cells within a tumor, or the cancer cells mutate and become resistant to the chemotherapy.

An example of how cancer cells mutate to ensure their survival can be seen in the recently approved "miracle" drug Gleevec (STI-571). This drug produced striking benefits in the treatment of chronic myeloid leukemia and was quickly approved by the FDA. In a recent clinical trial, however, many patients relapsed as their cancer cells grew resistant. Doctors found that a protein in the cellular DNA targeted by STI-571 altered its shape, thus rendering the drug useless in killing these mutant cancer cells. The company that makes STI-571 is already developing strategies to overcome this resistance, but this case of a new drug quickly losing its effectiveness is an illustration of how easily cancer cells will mutate to avoid total eradication.

Oncologists are increasingly using combination chemotherapy regimens that consist of several cytotoxic drugs that work by different mechanisms of action. The objective is to obliterate as many different types of cancer cells within the tumor, or interfere with as many cancer cell survival factors as possible. Despite the use of these potent multi-drug cocktails, 552,000 Americans died of cancer last year.

Curcumin's potential anti-cancer benefits

Curcumin may be effective in helping to suppress the escape mechanisms cancer cells use to avoid eradication by conventional therapies. Curcumin has been shown to inhibit cancer cell propagation via the following mechanisms:

- Inhibiting the epidermal growth factor receptor site (EGFR), in a dose dependent response. Two thirds of all cancers over-express this receptor as a primary means for hyper-proliferation.

- Inhibiting induction of the basic fibroblast growth factor (bFGF). This is responsible for angiogenesis of endothelial cells. Curcumin's effect here again was a dose dependent response.

- Inhibiting expression of cyclooxygenase-2 (COX-2), the enzyme involved in the production of PGE2, a tumor promoting prostaglandin.

- Inhibiting a transcription factor in cancer cells known as nuclear factor kappa beta (NF-kB). Many cancers over-express NF-KB and use this as a growth vehicle to escape cell regulatory control.

- Increasing expression of nuclear p53 protein in human basal cell carcinomas, human hepatomas and leukemia cell lines. This increases apoptosis (cell death) in these cancers.

- Inhibiting induction of hepatocyte growth factor (HGF). Over-expression is involved in hepatcellular carcinoma.

Based on the multiple favorable mechanisms listed above, higher-dose curcumin would appear to be a useful supplement for cancer patients to take.

As far as curcumin being taken at the same time as chemotherapy drugs, there are contradictions in the scientific literature. Some studies indicate significant benefit, whereas other studies hint at reduced benefit or even potential toxicity.

Chemotherapy drugs are highly toxic in and of themselves. Whether high-dose curcumin is beneficial or detrimental depends on the type and dose of the chemotherapeutic drug used, the kind of cancer cell being attacked, and the dose of the curcumin. Until more definitive information is published, we prefer to err on the side of caution and recommend that chemotherapy patients wait four weeks after their last dose of chemo before taking high-doses of curcumin.

Life Extension believes the multiple mechanisms of curcumin's actions against cancer cells warrants aggressive further investigation. We will keep members fully informed of our findings, but at this time, we have to take a cautious stance and officially state that high-dose curcumin should not be taken with anti-cancer drugs.

Cancer patients are faced with many difficult treatment choices. With the exponential increase of new scientific information, conflicts will inevitably occur. Life Extension remains at the forefront in evaluating new scientific data to help members make informed choices.

Curcumin dosing

As far as prevention is concerned, the evidence is substantial that curcumin may be effective in protecting against cancer and a host of other diseases.

For disease prevention purposes, healthy people typically take 900 to 1800 mg of curcumin (with piperine added to enhance assimilation into the bloodstream) a day. Cancer patients often take two to three times this much curcumin-piperine for a six to twelve month period and then taper off the dose.

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