Super Anti-Oxidizing Dietary Supplement

The world's first soft capsule turmeric supplement organically produced with Kangen Water®.

Enagic™ proudly cultivates the highest grade of turmeric and produces their Ukon™ in their facility in Okinawa Japan. Japan is well known for having one of the healthiest and longest living people on the planet, but did you know that Okinawa has the highest number of living centennials on Earth? Okinawa is also famous for it’s sub tropical climate which makes it ideal for growing the highest grade of turmeric. In fact, numerous turmeric varieties and strains from around the globe have been accumulated in the Okinawa islands to preserve, conserve and improve for use.

For over 4000 years, turmeric (Curcuma longa) has been used to treat a variety of conditions. Turmeric has been used in both Ayurvedic and Chinese medicine as an anti-inflammatory, to treat digestive and liver problems, skin disease and wounds. Today, turmeric is being researched and studied for it’s benefits to human health and well-being. Studies conducted by University of Maryland Medical Center, University of Texas, Medical University Graz in Austria and countless others show that turmeric and it’s biologically active compound Curcumin, may help fight infections and some cancers, reduce inflammation, and treat digestive problems, and a simple Google search of Turmeric reveals over 15 million sites describing the powerful benefits of its use.

GreenMedInfo.com founder Sayer Ji, says it best in his recent article 500 Reasons Turmeric May Be The World’s Most Important Herb: “Indeed, turmeric turns the entire drug-based medical model on its head. Instead of causing more side effects than therapeutic ones it has several hundred potential side benefits.”
Curcumin has been shown to exhibit antioxidant, anti-inflammatory, antiviral, antibacterial, anti fungal, and anticancer activities and thus has a potential against various malignant diseases, diabetes, allergies, arthritis, Alzheimer’s disease and other chronic illnesses – *Advanced Experimental Medical Biology*

The U.S. [National Institutes of Health](#) currently has registered 71 clinical trials completed or underway to study use of dietary curcumin for a variety of clinical disorders (dated September 2012). This increase in research and studies has prompted a wave of popularity with the naturally growing plant and Enagic™ has paved the way to harnessing the amazing attributes of turmeric in the revolutionary dietary supplement, Kangen Ukon™.

**The bottom line is that the therapeutic advantages of turmeric and curcumin are almost too numerous to list - Dr. Andrew Weil, Founder and director of the Arizona Center for Integrative Medicine**

Kangen Ukon™ is Enagic’s second premier product line, since its revolutionary Kangen Water™ machines were introduced decades ago. Their mission of promoting proactive health through products which “bring the body back to origin” expands into the dietary supplement field through Kangen Ukon™.

### Why is Kangen Ukon™ Special?

Enagic™ has obtained a patent for the innovative process behind the creation of Kangen Ukon™. Turmeric plants needs temperatures between 20 °C and 30 °C (68 °F and 86 °F) and a considerable amount of annual rainfall to thrive and it just so happens that one of the most prestigious areas in the world to grow turmeric happens to be right in Enagic’s back yard, Okinawa.
The Yanbaru region of Okinawa is where Enagic™ organically grows and harvests their turmeric exclusively used for Kangen Ukon™. The warm, wet, hilly regions of Yanbaru provide an optimal environment for providing the healthiest turmeric for their Ukon™ products. **Ukon™ turmeric is completely free of harmful chemicals** used in lower-quality, conventional turmeric farming.

Once harvested, the Okinawa turmeric is cleansed and sanitized by Strong Kangen Water and Strong Acidic Water at the Enagic Ukon™ Factory. It is the only supplement every produced combining Kangen Water, Turmeric and additive free spring ukon™ oils.

The 100% plant-based softgel Kangen Ukon™ capsule is made complete with antioxidant ingredients such as olive oil, perilla oil, flaxseed and tocotrienol. In addition, carrageenan, a seaweed derivative, is used as an ingredient for the coating of the capsule.

**Once produced, each capsule is individually enclosed to stay preserved and to prevent oxidation unlike bottled supplements which oxidize quickly once opened.**

Enagic’s continuous research on the body, health, water and powerful attributes of antioxidants has all culminated in the creation of Kangen Ukon™. Their attention to detail has delivered one of the most unique dietary supplements in the industry.

**The increase in popularity of Turmeric combined with the powerful marketing system of the Kangen Ukon™ Program, makes this a prime time to introduce Kangen Ukon™ to the world.** Contact the distributor who brought you to this website and **Join the Kangen Ukon™ Program NOW!**
Anticancer potential of curcumin: preclinical and clinical studies.

Aggarwal BB, Kumar A, Bharti AC.

Source

Cytokine Research Section, Department of Bioimmunotherapy, University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Boulevard, Box 143, Houston, TX, USA. aggarwal@mdanderson.org

Abstract

Curcumin (diferuloylmethane) is a polyphenol derived from the plant Curcuma longa, commonly called turmeric. Extensive research over the last 50 years has indicated this polyphenol can both prevent and treat cancer. The anticancer potential of curcumin stems from its ability to suppress proliferation of a wide variety of tumor cells, down-regulate transcription factors NF-kappa B, AP-1 and Egr-1; down-regulate the expression of COX2, LOX, NOS, MMP-9, uPA, TNF, chemokines, cell surface adhesion molecules and cyclin D1; down-regulate growth factor receptors (such as EGFR and HER2); and inhibit the activity of c-Jun N-terminal kinase, protein tyrosine kinases and protein serine/threonine kinases. In several systems, curcumin has been described as a potent antioxidant and anti-inflammatory agent. Evidence has also been presented to suggest that curcumin can suppress tumor initiation, promotion and metastasis. Pharmacologically, curcumin has been found to be safe. Human clinical trials indicated no dose-limiting toxicity when administered at doses up to 10 g/day. All of these studies suggest that curcumin has enormous potential in the prevention and therapy of cancer. The current review describes in detail the data supporting these studies.
Curcumin as an anti-cancer agent: review of the gap between basic and clinical applications.

Bar-Sela G, Epelbaum R, Schaffer M.

Source
Department of Oncology and Radiation Therapy, Rambam Health Care Campus, Haifa, Israel.

Abstract
Curcumin, commonly called diferuloyl methane, is a hydrophobic polyphenol derived from rhizome (turmeric) of the herb Curcuma longa. Extensive research over the last half century has revealed important functions of curcumin. In vitro and in vivo research has shown various activities, such as anti-inflammatory, cytokines release, antioxidant, immunomodulatory, enhancing of the apoptotic process, and anti-angiogenic properties. Curcumin has also been shown to be a mediator of chemo-resistance and radio-resistance. The anti-cancer effect has been seen in a few clinical trials, mainly as a native chemoprevention agent in colon and pancreatic cancer, cervical neoplasia and Barrets metaplasia. Some clinical studies with healthy volunteers revealed a low bioavailability of curcumin, casting doubt on the use of curcumin only as food additive. Our clinical experience with curcumin, along with the anti-metabolite gemcitabine in the treatment of patients with advanced pancreatic carcinoma, produced an objective response in less than 10% of patients, with a minor effect on survival. However, the safety of this combination was proved. Curcumin's potent anti-proliferative activity interacting with several intracellular signal transduction pathways may potentiate the anti-tumor effect of gemcitabine. The preclinical data lead to various, but still scarce, clinical studies (some on-going) that demonstrated the possible efficacy of this treatment as a chemopreventive or chemotherapeutic agent. This review will focus on the clinical evidence, including our experience with curcumin as a chemopreventive and therapeutic agent and the in vitro background results.
Four in the morning, four more at night. That's eight big mustard-yellow capsules every day. They contain nothing but turmeric, a spice. But for Jerry, they are medicine. He loves the stuff — says it changed his life.

Now this sort of thing is not uncommon; I'd guess 20% to 30% of my patients are into some type of supplements or "nutriceuticals." But Jerry stands out. He's a conservative, older guy from that generation of men who were most definitely not "in touch with" their bodies. He's practical, worldly, wise and skeptical. He's not interested in any other remedies or practices. (Monogamy in the supplement world is a true rarity, and it commands respect there too.) He has, in fact, gotten so many friends and acquaintances to use the stuff that it's sold out of the stores where he buys it.

(See pictures of spiritual healing around the world.)

But what got me interested in Jerry's turmeric wasn't his testimonials or even his personality — it was seeing him bounce back from surgery.

Jerry had two bad hips; the joints didn't form quite right as he grew up. They degenerated and started to hurt as he entered his 60s. When he first started coming to me, I gave him the usual anti-inflammatory medications we use
for arthritis pain. He had no side effects, but he wasn't helped much either, so he stopped the pills and lived with the pain. Then he found turmeric.

(See pictures of Cleveland's smarter approach to health care.)

Soon enough, there was no pain at all. And his lower back and hands, which ached before, were also now pain-free. So I was curious last year, when at age 73 he came in and told me he was ready for a hip replacement. "It's just so stiff" is all he would say. He certainly had the limp, the trouble with stairs and the slow rise from a chair that you see in folks with hip arthritis. His X-ray showed bone-on-bone erosion and plenty of spurring; his examination showed the profound loss of motion you would also expect. Everything said "just do a hip replacement" — except for that one cardinal feature: pain.

(See how to prevent illness at any age.)

He denied it. Even when I did the twisting maneuver we use to see if it's the hip that hurts, there was no wince, no ouch. I had never done the operation for anyone without pain. I explained this. And reasonable though he was, he still wanted a new hip, "to get rid of the stiffness."

Some kind of denial is going on here, was all I could think. I made sure he knew full well what the surgery would entail. He still wanted it. So I did the operation. "Can I keep up with the turmeric in the hospital?" he asked. I saw no reason why not. That's when I actually saw the big yellow capsules on his bedside table. And when I first gave them any serious thought.

Now, alternative-medicine doctors and orthopedic surgeons are miles apart on what eating plants can actually fix. Scurvy, night-blindness, constipation and, of course, hunger are the problems they tell us in medical school that plants can cure. Psychosomatic factors are said to underlie all the other "benefits." But I looked and found two well-done scientific papers studying the effects of turmeric on a group of patients who I thought should be far less likely to be affected by psychosomatic factors. Because they were rats.

(See the most common hospital mishaps.)

At the University of Arizona, researchers led by endocrinologist Janet Funk injected a bacterial substance known to cause joint inflammation (which is what arthritis ultimately is) into the bellies of the rodents. If the researchers gave them turmeric first (also by injection into the abdomen), there was far less joint swelling produced. A specific active ingredient of the turmeric worked better still. A rigorous protocol and pictures of the rats' normal and swollen joints convinced me there was a real effect. Further experiments by the group even showed how turmeric turns down inflammation, by blocking production of the protein that turns on the gene that tells tiny blood vessels to grow.

Read more: http://www.time.com/time/health/article/0,8599,1910028,00.html#ixzz2Joi13Pbh
UCLA Newsroom > All Stories > News Releases
Chemical in spice turmeric kickstarts cancer-killing mechanisms in human saliva

By Kim Irwin September 14, 2011

Turmeric root

Curcumin, the main component in the spice turmeric, suppresses a cell signaling pathway that drives the growth of head and neck cancer, according to a pilot study using human saliva by researchers at UCLA's Jonsson Comprehensive Cancer Center.

The inhibition of the pathway also correlated with reduced expression of a number of pro-inflammatory cytokines, or signaling molecules, in the saliva that promote cancer growth, said senior study author Dr. Marilene Wang, a professor of head and neck surgery and a Jonsson Cancer Center researcher.

"This study shows that curcumin can work in the mouths of patients with head and neck malignancies and reduce activities that promote cancer growth," Wang said. "And it not only affected the cancer by inhibiting a critical cell signaling pathway, it also affected the saliva itself by reducing pro-inflammatory cytokines within the saliva."

The study appears Sept. 15 in Clinical Cancer Research, a peer-reviewed journal of the American Association of Cancer Research.

Turmeric is a naturally occurring spice widely used in South Asian and Middle Eastern cooking and has long been known to have medicinal properties, attributed to its anti-inflammatory effects. Previous studies have shown it can suppress the growth of certain cancers. In India, women for years have used turmeric as an anti-aging agent rubbed into the skin, as a palliative for menstrual cramps and as a poultice on the skin to promote wound healing.

A 2005 study by Wang and her team first showed that curcumin suppressed the growth of head and neck cancer, first in cells and then in mouse models. In the animal studies, the curcumin was applied directly to the tumors in paste form.
In a 2010 study, also done in cells and in mouse models, the research team found that the curcumin suppressed head and neck cancer growth by regulating cell cycling, said Eri Srivatsan, an adjunct professor of surgery and Jonsson Cancer Center researcher who, along with Wang, has been studying curcumin and its anti-cancer properties for seven years. Srivatsan is a co-author of the current study.

Curcumin has been found to bind to and prevent an enzyme known as IKK, an inhibitor of kappa β kinase, from activating nuclear factor kappa β (NFKβ), a transcription factor that promotes cancer growth.

In this study, 21 patients with head and neck cancers gave samples of their saliva before and after chewing two curcumin tablets totaling 1,000 milligrams. One hour later, an additional sample of saliva was taken and proteins were extracted and IKKβ kinase activity measured. Thirteen subjects with tooth decay and five healthy subjects were used as controls, Wang said.

Eating the curcumin, Wang said, puts the chemical in contact not only with the cancer but also with the saliva, and the study found that the curcumin reduced the level of cancer-enhancing cytokines. An independent lab in Maryland was sent blind samples and confirmed the results: The pro-inflammatory cytokines in the saliva that help feed the cancer were reduced in patients who had chewed the curcumin, and the cell signaling pathway driving cancer growth was inhibited.

"The curcumin had a significant inhibitory effect, blocking two different drivers of head and neck cancer growth," Wang said. "We believe curcumin could be combined with other treatments, such as chemotherapy and radiation, to treat head and neck cancer. It also could perhaps be given to patients at high risk for developing head and neck cancers — smokers, those who chew tobacco and people with the HPV virus — as well as to patients with previous oral cancers to fight recurrence."

The curcumin was well tolerated by the patients and resulted in no toxic effects. The biggest problem was that their mouths and teeth turned bright yellow.

"Curcumin inhibited IKKβ kinase activity in the saliva of head and neck cancer patients, and this inhibition correlated with reduced expression of a number of cytokines," the study states. "IKKβ kinase could be a useful biomarker for detecting the effects of curcumin in head and neck cancer."

To be effective in fighting cancer, the curcumin must be used in supplement form. Although turmeric is used in cooking, the amount of curcumin needed to produce a clinical response is much larger. Expecting a positive effect through eating foods spiced with turmeric is not realistic, Wang said.

The next step for Wang and her team is to treat patients with curcumin for longer periods of time to see if the inhibitory effects can be increased. They plan to treat cancer patients scheduled for surgery for a few weeks prior to their procedure. They'll take a biopsy before the curcumin is started and then at the time of surgery and analyze the tissue to look for differences.

"There's potential here for the development of curcumin as an adjuvant treatment for cancer," Wang said. "It's not toxic, it's well tolerated, cheap and easily obtained in any health food store. While this is a promising pilot study, it's important to expand our work to more patients to confirm our findings."
Finding ways to better treat head and neck cancers is vital, as patients often require disfiguring surgery, frequently losing parts of their tongue or mouth. They also experience many side effects, including difficulty swallowing and dry mouth and have the potential for developing another oral cancer later.

The study was funded by Veterans Affairs Greater Los Angeles Health System, the West Los Angeles Surgical Education Research Center, the UCLA Academic Senate, the National Institutes of Health, and the Veterans Administration.

**UCLA's Jonsson Comprehensive Cancer Center** has more than 240 researchers and clinicians engaged in disease research, prevention, detection, control, treatment and education. One of the nation's largest comprehensive cancer centers, the Jonsson Center is dedicated to promoting research and translating basic science into leading-edge clinical studies. In July 2011, the center was named among the top 10 cancer centers nationwide by U.S. News & World Report, a ranking it has held for 10 of the last 12 years.
New Hybrid Drug Derived from Common Spice, May Protect, Rebuild Brain Cells After Stroke

Study from Cedars-Sinai Medical Center presented at American Heart Association International Stroke Conference

LOS ANGELES (Feb. 9, 2011) – Whether or not you’re fond of Indian, Southeast Asian and Middle Eastern food, stroke researchers at Cedars-Sinai Medical Center think you may become a fan of one of their key spices.

The scientists created a new molecule from curcumin, a chemical component of the golden-colored spice turmeric, and found in laboratory experiments that it affects mechanisms that protect and help regenerate brain cells after stroke. Research scientist Paul A. Lapchak, Ph.D., director of Translational Research in the Department of Neurology at Cedars-Sinai Medical Center, will present these findings at the American Heart Association International Stroke Conference in Los Angeles on Wednesday, Feb. 9, at 6:15 p.m. PST.

Only one drug is now approved for ischemic stroke, which occurs when a clot blocks blood flow to the brain. Commonly called a “clot-busting drug,” tissue plasminogen activator (tPA) is injected intravenously to dissolve clots and reinstate blood flow. If blood and oxygen are restored in time, consequences of the stroke, such as speech, memory, movement and other impairments, may be reduced.

The new curcumin-hybrid compound—CNB-001—does not attack clots but instead repairs stroke damage at the molecular level that feed and support the all-important brain cells, neurons.

Curcumin has been studied for its potential to treat brain injury and disease, and while the substance itself looks promising, it has several drawbacks, especially as an emergency stroke treatment, which must be quick to be effective: It is not well absorbed in the body, fails to reach its target in high concentrations, becomes depleted quickly, and is blocked from entering the brain by a natural protective mechanism called the blood-brain barrier.

“CNB-001 has many of the same benefits of curcumin but appears to be a better choice of compound for acute stroke because it crosses the blood-brain barrier, is quickly distributed in the brain, and moderates several critical mechanisms involved in neuronal survival,” Lapchak says, adding that he and his colleagues expect the new drug to move to human clinical trials soon.

When brain tissue is deprived of blood and oxygen, a cascading series of interrelated events triggers at the molecular level, breaking down the normal electrical and chemical “signaling pathways” responsible for nourishing and supporting neurons. The environment quickly becomes toxic, killing brain cells and destroying their support structures.

Theoretically, interrupting these harmful events and restoring normal pathway function could prevent cell death and the memory and behavioral deficits that result, but it will take a cocktail of drugs or a drug capable of targeting many mechanisms to correct the many pathways damaged by stroke, Lapchak says. CNB-001 protects brain cells from damage by repairing four major pathways. One mechanism also plays a major role in the growth and survival of neurons.

The drug reduced stroke-caused “motor deficits”—problems of muscle and movement control—in this laboratory study. It was effective when administered up to an hour after stroke, which correlates with about three hours in humans, the same time frame for which tPA is currently approved.
Lapchak and colleagues at the Salk Institute for Biological Studies used the same laboratory rabbit model to mimic human stroke that earlier researchers had employed before the clot-busting drug tPA entered clinical trials. Patrick D. Lyden, M.D., chairman of Cedars-Sinai’s Department of Neurology, helped lead a major trial that resulted in the Food and Drug Administration’s 1996 approval of tPA, still considered the stroke treatment gold standard.

Those who cook Indian, Thai, Malay and Persian dishes know turmeric well for its zesty flavor, use in curries and for the rich color it imparts to food. Turmeric also has a long history of use in Ayurvedic and Chinese traditional medicine.

Grants from the National Institute of Neurological Disorders and Stroke, part of the National Institutes of Health, supported the CNB-001 study (NS060685 to PAL).

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Citation: American Heart Association International Stroke Conference Wednesday, Feb. 9 at 6:15 p.m

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**National Cancer Institute**

*at the National Institutes of Health*

**NCI Drug Dictionary**

**curcumin**

A phytopolyphenol pigment isolated from the plant Curcuma longa, commonly known as turmeric, with a variety of pharmacologic properties. Curcumin blocks the formation of reactive-oxygen species, possesses anti-inflammatory properties as a result of inhibition of cyclooxygenases (COX) and other enzymes involved in inflammation; and disrupts cell signal transduction by various mechanisms including inhibition of protein kinase C. These effects may play a role in the agent's observed antineoplastic properties, which include inhibition of tumor cell proliferation and suppression of chemically induced carcinogenesis and tumor growth in animal models of cancer. Check for [active clinical trials](#) or [closed clinical trials](#) using this agent. ([NCI Thesaurus](#))

**Synonyms:**

- C.I. Natural Yellow 3
- Diferuloylmethane
- Turmeric Yellow

**Abbreviation:**

CU
Code name: C.I. 75300
Chemical structure: (E,E)-1,7-Bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione
Press Releases

Compound derived from curry spice is neuroprotective against stroke and traumatic brain injury

December 14, 2010

LA JOLLA, CA—A synthetic derivative of the curry spice turmeric, made by scientists at the Salk Institute for Biological Studies, dramatically improves the behavioral and molecular deficits seen in animal models of ischemic stroke and traumatic brain injury (TBI). Two new studies suggest that the novel compound may have clinical promise for these conditions, which currently lack good therapies.

Ischemic stroke is the leading cause of disability and the third leading cause of death of older people in the United States, while TBI is the leading cause of death and disability in both civilians and military personnel under the age of 45; in particular, it is the major cause of disability in veterans returning from Iraq and Afghanistan. In both conditions, those who survive frequently have serious behavioral and memory deficits. The only FDA-approved treatment for stroke is tissue plasminogen activator (TPA), which is effective only in about 20 percent of cases. There is no clinically documented treatment for TBI.

In earlier studies, David R. Schubert, Ph.D., and Pamela Maher, Ph.D., in the Salk Cellular Neurobiology Laboratory had developed a series of new compounds using a novel drug discovery paradigm that starts with natural products derived from plants; it then calls for selecting synthetic derivatives that show efficacy in multiple assays testing protection against various aspects of the nerve cell damage and death that occur in brain injuries and in age-associated neurodegenerative diseases. One compound, called CNB-001, which was derived from curcumin, the active ingredient in the spice turmeric, proved highly neuroprotective in all of the assays; it also enhanced memory in normal animals.
Derivatives of curcumin, the main active ingredient in the popular Indian spice turmeric, are neuroprotective against stroke and traumatic brain injury.

Photo by Badagnani (CC License)

While the Salk group has a great deal of expertise in age-associated neurological diseases such as Alzheimer's, they do not run animal models of TBI and stroke. "To test the prediction that drugs from our new drug discovery scheme will work in multiple models of CNS disease and trauma," Schubert explains, "we undertook a series of experiments to assay the drugs in collaboration with researchers at Cedars-Sinai and UCLA, who are leaders in the fields of stroke and TBI, respectively, and appreciate the potential for therapeutics based on natural products and their derivatives."

Employing the same animal model of stroke that was used to develop TPA, Paul Lapchak, Ph.D., of the Department of Neurology at the Burns and Allen Research Institute at Cedars-Sinai Medical Center in Los Angeles, collaborated with Schubert's team in a study that showed that CNB-001 was at least as effective as TPA in preventing the behavioral deficits caused by stroke. The study, published in the Dec. 2, 2010 edition of the Journal of Neurochemistry, also demonstrated that unlike TPA, which reduces clotting in the blood vessels of the brain, the Salk compound has a direct protective effect on nerve cells within the brain. Maher has found that it maintains specific cell signaling pathways required for nerve cell survival.

Similarly, in a study to be published in early 2011 in Neurorehabilitation and Neural Repair, Fernando Gomez-Pinilla, Ph.D., and his colleagues in the Department of Physiological Science and Division of Neurosurgery at the University of California, Los Angeles used a rodent model of TBI to demonstrate that CNB-001 dramatically reversed the behavioral deficits in both locomotion and memory that accompany the brain injury. As with stroke, CNB-001 was again found to maintain the critical signaling pathways required for nerve cell survival, as well as the connections between nerve cells that are lost with the injury.

The results of these two studies, which used two distinct models of brain injury, indicate that the Salk compound has clinical potential in conditions where there is currently no effective treatment.

"Existing drug therapies for complex neurological conditions such as stroke and Alzheimer's disease target only one aspect of the condition, while in fact many different factors contribute to the pathology," observes Schubert. "In the drug discovery program our lab uses at Salk, drug candidates must show efficacy in tissue culture models..."
of several aspects of the condition before they are introduced into animal models. We believe that this approach is making an important difference in the discovery of effective drugs."

In related work, Maher used the same drug discovery paradigm to identify a compound that is effective in animal models of Huntington's disease. "Although these brain disorders appear very different, they share common changes in the nerve cells, which suggests that compounds that prevent these changes will be effective in multiple disorders," she notes.

In addition to Schubert and Gomez-Pinilla, Aiguo Wu, Ph.D., and Zhe Ying of the UCLA Department of Physiological Science contributed to the TBI study.

Both studies were supported by the National Institutes of Health; Gomez-Pinilla's study received additional funding from the Craig Neilsen Foundation.

About the Salk Institute for Biological Studies?
The Salk Institute for Biological Studies is one of the world's preeminent basic research institutions, where internationally renowned faculty probe fundamental life science questions in a unique, collaborative, and creative environment. Focused both on discovery and on mentoring future generations of researchers, Salk scientists make groundbreaking contributions to our understanding of cancer, aging, Alzheimer's, diabetes, and infectious diseases by studying neuroscience, genetics, cell and plant biology, and related disciplines.

Faculty achievements have been recognized with numerous honors, including Nobel Prizes and memberships in the National Academy of Sciences. Founded in 1960 by polio vaccine pioneer Jonas Salk, M.D., the Institute is an independent nonprofit organization and architectural landmark.

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10010 North Torrey Pines Road, La Jolla, CA 92037 | 858.453.4100
New clinical trial supports benefits of turmeric extract to people with osteoarthritis

A new clinical trial supports the benefits to people with osteoarthritis who used a unique extract of turmeric. Scientists in Italy have studied the pain-relief, increased flexibility, and other effects of a special, patented extract of the roots of turmeric, the flavorful spice that has been used for centuries as a traditional remedy. Turmeric formulations have shown a wide range of safety and significant scientific and clinical benefits in recent animal research and human clinical trials.

The characteristic yellow color of turmeric, which is found in many yellow mustards and yellow curry preparations, derives from compounds known collectively as curcuminoids, whose most abundant member is curcumin. Curcumin is difficult to absorb into the human bloodstream from the gastrointestinal tract when consumed orally.

Researchers in Italy selected 50 patients with X-ray diagnosed osteoarthritis in either one or both knees to evaluate if the special turmeric formulation called Meriva® could provide more benefits to their standard medical therapy. In this trial, the patients were split into two groups: the first one received standard medical treatment as determined by patients' physicians, while patients in the second group added the special curcumin extract to their standard medical treatment.

After 90 days, the following benefits were observed: Compared to the controls, patients in the Meriva group experienced a 58 percent decrease in their overall pain, stiffness and physical functionality as measured by the widely used medical scoring method developed by Western Ontario and McMaster Universities (WOMAC). In addition, the Social and Emotional Index (SEI) score resulted in a greater than 300 percent improvement in Meriva patients compared to patients not taking the curcumin extract. Blood tests indicated that in patients having elevated levels of C-reactive protein (CRP), a 16-fold decrease of this inflammation marker was observed in the Meriva group. Finally, the subjects using Meriva were able to reduce their reliance on standard painkillers (NSAIDs, non-steroidal anti-inflammatory drugs) by 63 percent compared to patients on conventional medical therapy alone.

Taken together, these data show that Meriva turmeric extract improves the clinical benefit of a standard NSAIDs-based treatment of osteoarthritis, making it possible for patients to decrease their medication load and increase its efficacy.

Consistent with data from other human studies on various types of turmeric extracts, Meriva demonstrated a high degree of safety without producing any serious adverse side effects.

"This is great news for people who suffer from osteoarthritis and the physicians who treat them," said Mark Blumenthal, Founder and Executive Director of the nonprofit American Botanical Council, an independent herbal medicine research and education organization in Austin, Texas.
"Turmeric has long been known to have anti-inflammatory and pain-relieving properties and this trial, on this special turmeric extract, is another important step towards validating the curcumin in turmeric as an increasingly popular herbal dietary supplement. When one considers the overall safety of turmeric extract and curcumin, especially compared to some of the pharmaceutical drugs which have had to be removed from the market due to serious safety concerns, the growing clinical evidence for the use of turmeric extract is compelling," he added.

The authors of this trial write that "curcumin is one of the most extensively investigated products of natural origin. Its broad spectrum of bioactivity and low oral toxicity have expanded its use to several clinical conditions. Many potential beneficial properties of the natural product [i.e. curcumin] have not produced effective clinical results because curcumin shows a poor water solubility and stability, a low and unpredictable oral absorption, and a quick metabolism." Researchers believe that these problems have hampered the clinical development of curcumin as a pharmaceutical product and as a dietary supplement. Meriva has exhibited high levels of oral bioavailability in a previous comparative animal pharmacokinetic study.

The Meriva curcumin extract used in this clinical trial is a special patented combination of curcumin with soybean-derived phosphatidylcholine (1:2 ratio). Produced and distributed by Indena SpA of Milan, Italy, the world's largest manufacturer of standardized botanical extracts for the food, dietary supplement, pharmaceutical and cosmetic industries. Meriva has recently been introduced into the market as a dietary supplement ingredient marketed in the USA and Europe. In this clinical study, Meriva capsules prepared by Thorne Research Inc. (Dover, Idaho, USA) were used at a dosage of 1 gram Meriva curcumin complex per day (standardized to contain 18-22 percent curcuminoids, and corresponding to 200 mg curcumin per day).

SOURCE American Botanical Council
Turmeric

Other common name(s): jiang huang, haridra, Indian saffron

Scientific/medical name(s): *Curcuma longa, Curcuma domestica*

Description

Turmeric is a spice grown in India and other tropical regions of Asia. It has a long history of use in herbal remedies, particularly in China, India, and Indonesia. The root and rootstock, or rhizome, of the plant contain the active ingredient, curcumin. Curcumin is not related to cumin, which is a spice made from the seeds of a different plant.

Overview

Turmeric is a common food flavoring and coloring in Asian cooking. Animal and laboratory studies have found that curcumin, an antioxidant that is an active ingredient in turmeric, demonstrated some anticancer effects. However, clinical research is needed to determine curcumin's role in cancer prevention and treatment in humans. Several types of cancer cells are inhibited by curcumin in the laboratory, and curcumin slows the spread of some cancers in some animal studies.

Curcumin is being studied to find out whether it helps other diseases such as arthritis, Alzheimer’s disease, and stomach ulcers. It is also being studied to see whether it can help lower “bad cholesterol” and improve outcome in kidney transplants. A few early studies have been done in humans, but more human research is still needed to find out if curcumin can be effective in these uses.

How is it promoted for use?

Some researchers believe turmeric may prevent and slow the growth of a number of types of cancer, particularly tumors of the esophagus, mouth, intestines, stomach, breast, and skin. One researcher reported that curcumin, the active ingredient in turmeric, inhibited the formation of cancer-causing enzymes in rodents.

Turmeric is promoted mainly as an anti-inflammatory herbal remedy and is said to produce fewer side effects than commonly used pain relievers. Some practitioners prescribe turmeric to relieve inflammation caused by arthritis, muscle sprains, swelling, and pain caused by injuries or surgical incisions. It is also promoted as a treatment for rheumatism and as an antiseptic for cleaning wounds. Some proponents claim turmeric interferes with the actions of some viruses, including hepatitis and HIV.
Supporters also claim that turmeric protects against liver diseases, stimulates the gallbladder and circulatory systems, reduces cholesterol levels, dissolves blood clots, helps stop external and internal bleeding, and relieves painful menstruation and angina, chest pains that often occur with heart disease. It is also used as a remedy for digestive problems such as irritable bowel syndrome, colitis, Crohn’s disease, and illnesses caused by toxins from parasites and bacteria.

What does it involve?

Turmeric root is on the Commission E (Germany’s regulatory agency for herbs) list of approved herbs, and it is available in powdered form as a spice in most grocery stores. It can also be made into a tea or purchased as a tincture, capsule, or tablet. Ointments or pastes made from turmeric can be applied to the skin. Although there is no standardized dose for turmeric, some practitioners recommend taking a teaspoon with each meal. The dried root of turmeric normally contains from 3% to 5% curcumin. Today, many sellers market supplements that claim to be standardized to contain 95% curcumin compounds.

What is the history behind it?

The use of turmeric was described in traditional Chinese and Indian medicine as early as the seventh century AD. In various Asian folk medicine traditions, turmeric has been used to treat a long list of conditions, including diarrhea, fever, bronchitis, colds, parasitic worms, leprosy, and bladder and kidney inflammations. Herbalists have applied turmeric salve to bruises, leech bites, festering eye infections, mouth inflammations, skin conditions, and infected wounds. Some people inhale smoke from burning turmeric to relieve chronic coughs. Turmeric mixed with hot water and sugar is considered by some herbalists to be a remedy for colds.

In India and Malaysia, there is a custom of making turmeric paste to apply directly onto the skin, a practice now under study for the possibility that it may prevent skin cancer. The bright red forehead mark worn by some Hindu women is created by mixing turmeric with lime juice. Chefs frequently add turmeric to their creations because of its rich flavor and deep yellow-orange color. The seasoning is an important ingredient in Indian curries. It is also used to add color to foods such as butter, margarine, cheese, and mustard; to tint cotton, silk, paper, wood, and cosmetics; as a food preservative; and to make pickles.

What is the evidence?

Curcumin, an active ingredient in turmeric, is an antioxidant. Antioxidants are compounds that can protect the body’s cells from damage caused by activated oxygen molecules known as free radicals. Laboratory studies have also shown that curcumin interferes with several important molecular pathways involved in cancer development, growth, and spread.

Recently, curcumin has received a great deal more attention in studies than turmeric as a whole herb. Researchers are studying curcumin to learn whether it is an effective anti-inflammatory agent and whether it holds any promise for cancer prevention or treatment. A number of studies of curcumin have shown promising results. Curcumin can kill cancer cells in laboratory dishes and also reduces growth of surviving cells. Curcumin also has been found to reduce development of several forms of cancer in laboratory animals and to shrink animal tumors.
Human studies of curcumin in cancer prevention and treatment are in the very early stages. One study of 15 patients with colorectal cancer was done to find out how much curcumin they could safely take, and whether they could take a dose large enough to be detected in the blood. The patients were able to take 3.6 grams of curcumin without noting ill effects. At this high dose, some curcumin and its products were found in the blood. Lower doses may work for the stomach and intestine. Even though it does not absorb well into the body, it has been shown to absorb into the colon lining and into any cancerous tissue in the colon. The researchers recommended that the high dose be used when curcumin is tested for effects outside the intestine. Other small studies have found people were able to take up to 10 grams per day for a period of a few weeks without noting problems. Some researchers are currently working on ways to increase absorption of curcumin by combining it with other substances. Further clinical trials are needed to find out what role, if any, turmeric and curcumin may play in the prevention or treatment of cancer.

Curcumin is being studied to see whether it helps other diseases as well. One small study of curcumin and another antioxidant called quercetin was done in adults who had kidney transplants. Those who took the combination in high dosages had fewer transplant rejections than those who received lower doses or placebo. More studies are needed to find out whether this holds true. Curcumin may also promote the emptying of the gallbladder, but again, more studies are needed.

Early studies showed promise that curcumin could correct the problem of cystic fibrosis, but later studies have been inconsistent and often showed no effect. Curcumin also seemed to help prevent stomach ulcers in rodents, although there are not good studies in humans to recommend it for this use.

Early research has suggested that curcumin may help lower "bad" cholesterol, reduce inflammation, and help with arthritis symptoms, although more reliable human studies are still needed. Tests of curcumin in HIV disease have been mixed and have generally not shown it to be helpful. In studies of mice, curcumin appeared to help with blocking the plaques and proteins that cause problems in the brain during Alzheimer’s disease.

Although laboratory and animal tests look very promising, careful study is needed to find out whether curcumin will be useful for treating these conditions in humans. It is important to remember that extracted compounds such as curcumin are not the same as the whole herb, and study results would not be likely to show the same effects.

Are there any possible problems or complications?

This product is sold as a dietary supplement in the United States. Unlike companies that produce drugs (which must provide the FDA with results of detailed testing showing their product is safe and effective before the drug is approved for sale), the companies that make supplements do not have to show evidence of safety or health benefits to the FDA before selling their products. Supplement products without any reliable scientific evidence of health benefits may still be sold as long as the companies selling them do not claim the supplements can prevent, treat, or cure any specific disease. Some such products may not contain the amount of the herb or substance that is written on the label, and some may include other substances (contaminants). Though the FDA has written new rules to improve the quality of manufacturing processes for dietary supplements and the accurate listing of supplement ingredients, these rules do not take full effect until 2010. And, the new rules do not address the safety of supplement ingredients or their effects on health when proper manufacturing techniques are used. Most such supplements have not been tested to find out if they interact with medicines, foods, or other herbs and supplements. Even though some reports of interactions and harmful effects may be published, full studies of
interactions and effects are not often available. Because of these limitations, any information on ill effects and interactions below should be considered incomplete.

When used as a spice in foods, turmeric is considered safe. More research is needed to establish the safety of turmeric when used in herbal remedies. Little is known about the potential risks of taking the larger amounts used to treat illnesses. Taking large amounts by mouth may result in stomach pain, gas, indigestion, and nausea. Skin rash and stomach ulcers have been reported after long-term use, and allergic reactions are possible. People who are allergic to ginger or yellow food colorings are more likely to be allergic to turmeric.

A recent safety study in humans suggested that curcumin changes metabolism of oxalate, a substance that can form kidney stones. The researchers urged caution in use of this supplement by people with other conditions that make them susceptible to kidney stones.

People taking blood-thinning medications, drugs that suppress the immune system, or non-steroidal pain relievers (such as ibuprofen) should avoid turmeric because of the risk of harmful drug interactions. In animal and laboratory studies, turmeric made certain anti-cancer drugs less effective. Antioxidant supplements can interfere with the effectiveness of chemotherapy or radiation treatment. Patients who are in cancer treatment should talk to their doctor before taking vitamins, minerals, or other supplements.

In addition, other potential interactions between turmeric and other drugs and herbs should be considered. Always tell your doctor and pharmacist about any herbs or supplements you are taking.

People with bleeding disorders, obstructions of the bile duct, or a history of ulcers also should avoid turmeric. Women who are pregnant or breast-feeding should not use this herb. The amount of turmeric found in foods is thought to be safe for those who are not allergic to it. Applying turmeric to the skin for long periods of time can cause a yellow discoloration of the skin that may be difficult to remove.

Relying on this type of treatment alone and avoiding or delaying conventional medical care for cancer may have serious health consequences.

Additional resources

More information from your American Cancer Society

The following information on complementary and alternative therapies may also be helpful to you. These materials may be found on our Web site (www.cancer.org) or ordered from our toll-free number (1-800-ACS-2345).

Guidelines for Using Complementary and Alternative Therapies

Dietary Supplements: How to Know What Is Safe

The ACS Operational Statement on Complementary and Alternative Methods of Cancer Management

Complementary and Alternative Methods for Cancer Management
Placebo Effect

Learning About New Ways to Treat Cancer

Learning About New Ways to Prevent Cancer

References


Note: This information may not cover all possible claims, uses, actions, precautions, side effects or interactions. It is not intended as medical advice, and should not be relied upon as a substitute for consultation with your doctor, who is familiar with your medical situation.

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The effect of curcumin (turmeric) on Alzheimer's disease: An overview

Shrikant Mishra and Kalpana Palanivelu

This article has been cited by other articles in PMC.

Abstract

This paper discusses the effects of curcumin on patients with Alzheimer's disease (AD). Curcumin (Turmeric), an ancient Indian herb used in curry powder, has been extensively studied in modern medicine and Indian systems of medicine for the treatment of various medical conditions, including cystic fibrosis, haemorrhoids, gastric ulcer, colon cancer, breast cancer, atherosclerosis, liver diseases and arthritis. It has been used in various types of treatments for dementia and traumatic brain injury. Curcumin also has a potential role in the prevention and treatment of AD. Curcumin as an antioxidant, anti-inflammatory and lipophilic action improves the cognitive functions in patients with AD. A growing body of evidence indicates that oxidative stress, free radicals, beta amyloid, cerebral deregulation caused by bio-metal toxicity and abnormal inflammatory reactions contribute to the key event in Alzheimer's disease pathology. Due to various effects of curcumin, such as decreased Beta-amyloid plaques, delayed degradation of neurons, metal-chelation, anti-inflammatory, antioxidant and decreased microglia formation, the overall memory in patients with AD has improved. This paper reviews the various mechanisms of actions of curcumin in AD and pathology.

Keywords: Alternative approach to Alzheimer's, beta amyloid plaques, curcumin, curcumin and dementia, epidemiology, turmeric

Introduction
Alzheimer's disease

Alzheimer's disease (AD) is a progressive neurodegenerative disease. It is characterized by progressive cognitive deterioration together with declining activities of daily living and behavioral changes. It is the most common type of pre-senile and senile dementia. According to the World Health Organization (WHO), 5% of men and 6% of woman of above the age of 60 years are affected with Alzheimer's type dementia worldwide.[1] In India, the total prevalence of dementia per 1000 people is 33.6%, of which AD constitutes approximately 54% and vascular dementia constitutes approximately 39%. AD affects approximately 4.5 million people in the United States or approximately 10% of the population over the age of 65, and this number is projected to reach four times by 2050. The frequency increases to 50% by the age of 80 years. Every year more than $100 billion is spent for health care in the U.S. to treat AD in primary care settings alone.

Neuropathology of AD:

The neuropathological process consists of neuronal loss and atrophy, principally in the temporoparietal and frontal cortex, with an inflammatory response to the deposition of amyloid plaques and an abnormal cluster of protein fragments and tangled bundles of fibres (neurofibrillary tangles). Neurotic plaques are relatively insoluble dense cores of 5-10 nm thick amyloid fibrils with a pallor staining “halo” surrounded by dystrophic neuritis, reactive astrocytes and activated microglia. There is an increased presence of monocytes/macrophages in the cerebral vessel wall and reactive or activated microglial cells in the adjacent parenchyma.[2,3] The main protein component of amyloid in AD is the 39-42 amino acid (beta) amyloid peptide (A-beta) [Figure 1].

![Figure 1](image1)

Neuritic plaques are one of the characteristic structural abnormalities found in the brains of Alzheimer patients

Curcumin

Curcumin (Curcuma longa - Haldi) is the source of the spice Turmeric [Figure 2] and is used in curries and other spicy dishes from India, Asia and the Middle East. Similar to many other herbal remedies, people first used curcumin as a food and later discovered that it also had impressive medicinal qualities. It has been used extensively in Ayurveda (Indian system of Medicine) for centuries as a pain relieving, anti-inflammatory agent to relieve pain and inflammation in the skin and muscles. It has also proven to have anti-cancer properties.[4,5] Curcumin holds a high place in Ayurvedic medicine as a “cleanser of the body,” and today, science is finding a growing list of diseased conditions that can be healed by the active ingredients of turmeric.[6]
(2a) Turmeric, (2b) Turmeric plant, (2c) Keto and enol form of curcumin

The Plant

Botanical name: Curcuma longa; Family: Zingiberaceae, the ginger family. Turmeric is a sterile plant and does not produce any seeds [Figure 2]. The plant grows up to 3-5 ft tall and has dull yellow flowers. The underground rhizomes or roots of the plant are used for medicinal and food preparation. The rhizome is an underground stem that is thick and fleshy ringed with the bases of old leaves. Rhizomes are boiled and then dried and ground to make the distinctive bright yellow spice, turmeric.

Turmeric History:

Probably originating from India, turmeric has been used in India for at least 2500 years. It is most common in southern Asia and particularly in India. Turmeric was probably cultivated at first as a dye and later on it was used as cosmetic and as an auspicious and aromatic food substance. It possesses antiseptic, anti-inflammatory detoxifying properties as well as carminative properties. Turmeric has a long history of medicinal use in South Asia and was widely used in Ayurvedic, Siddha and Unani systems. It is thought to be a hybrid selection and vegetative propagation of wild turmeric (Curcuma aromatica), which is native to India, Sri Lanka and the eastern Himalayas and some other closely related species.

Curcumin and Alzheimer's Disease

Worldwide, there are over 1000 published animal and human studies, both in vivo and in vitro in which the effects of curcumin on various diseases have been examined. Studies include epidemiological, basic and clinical research on AD.

Bio Chemical properties

Epidemiological Studies
Various studies and research results indicate a lower incidence and prevalence of AD in India. The prevalence of AD among adults aged 70-79 years in India is 4.4 times less than that of adults aged 70-79 years in the United States. Researchers investigated the association between the curry consumption and cognitive level in 1010 Asians between 60 and 93 years of age. The study found that those who occasionally ate curry (less than once a month) and often (more than once a month) performed better on a standard test (MMSE) of cognitive function than those who ate curry never or rarely.

Mechanism of action of curcumin on Alzheimer's disease:

The process through which AD degrades the nerve cells is believed to involve certain properties: inflammation, oxidative damage and most notably, the formation of beta-amyloid plaques, metal toxicity. There have been several studies on effects of curcumin on AD. Outlined below are some of the studies and their conclusions.

**Effects of Curcumin on Macrophages**

A study conducted at UCLA found that curcumin may help the macrophages to clear the amyloid plaques found in Alzheimer's disease. Macrophages play an important role in the immune system. They help the body to fight against foreign proteins and then effectively clear them. Curcumin was treated with macrophages in blood taken from nine volunteers: six AD patients and three healthy controls. Beta amyloid was then introduced. The AD patients, whose macrophages were treated with curcumin, when compared with patients whose macrophages were not treated with curcumin, showed an improved uptake and ingestion of the plaques. Thus, curcumin may support the immune system to clear the amyloid protein.

**Curcumin on glial cells:**

Recent histological studies reveal the presence of activated microglia and reactive astrocytes around A-beta plaques in brains from patients with AD. The chronic activation of microglia secretes cytokines and some reactive substances that exacerbate A-beta pathology. So neuroglia is an important part in the pathogenesis of AD. Curcumin has a lipophilic property and can pass through all cell membranes and thus exerts its intracellular effects. Curcumin has anti-proliferative actions on microglia. A minimal dose of curcumin affects neuroglial proliferation and differentiation. Its inhibition of microglial proliferation and differentiation were studied and researched by the University of Southern California Los Angeles (UCLA). Researchers using doses of 4, 5, 10, 15, 20 microM concentration of curcumin in C-6 rat glioma 2B-clone cells, a mixed colony of both neuroglial cells in a six- day trial, showed that curcumin dose dependently stops the proliferation of neuroglial cells, by differentiate into a mature cell or undergo apoptosis. It inhibits neuroglial cells proliferation dose dependently (i.e.) higher the concentration, the greater the inhibition. It has shown to decrease the glutamine synthetase (GS)
assay, a marker enzyme for astrocytes. In the same study, curcumin was shown to increase CNP (2′3′- cyclic Nucleotide 3′-phosphohydrolase), a marker enzyme for oligodendrocytes. The overall effect of curcumin on neuroglial cells involves decreased astrocytes proliferation, improved myelogenesis and increased activity and differentiation of oligodendrocytes.

Go to:

**Curcumin as an Anti Inflammatory in Alzheimer's**

One of the important pathogenesis in Alzheimer's disease is the chronic inflammation of nerve cells. Several studies have demonstrated the associated inflammatory changes such as microgliosis, astrocytosis and the presence of pro-inflammatory substances that accompany the deposition of amyloid-β (Aβ) peptide. Patients with the prolonged use of certain nonsteroidal anti-inflammatory (NSAID) drugs such as ibuprofen have been shown to have a reduced risk of developing the symptoms of AD; however, the chronic use of NSAID can cause a toxic effect on the kidneys, liver and GI track. Curcumin has a potent anti-inflammatory effect. Through its various anti-inflammatory effects, it may have a role in the cure of AD. Curcumin inhibits Aβ-induced expression of Egr-1 protein and Egr-1 DNA-binding activity in THP-1 monocytic cells. Studies have shown the role of Egr-1 in amyloid peptide-induced cytochemokine gene expression in monocytes. By inhibition of Egr-1 DNA-binding activity by curcumin, it reduces the inflammation. The chemotaxis of monocytes, which can occur in response to chemokines from activated microglia and astrocytes in the brain, can be decreased by curcumin.[13,14]

Curcumin is found to inhibit cyclooxygenase (COX-2), phospholipases, transcription factor and enzymes involved in metabolizing the membrane phospholipids into prostaglandins. The reduction of the release of ROS by stimulated neutrophils, inhibition of AP-1 and NF-Kappa B inhibit the activation of the pro-inflammatory cytokines TNF (tumor necrosis factor)-alpha and IL (interleukin)-1 beta.[15,16] Overall, curcumin decreases the main chemical for inflammation and the transcription of inflammatory cytokines. Curcumin inhibits intracellular IL-12 p40/p70 and IL-12 p70 expression. The exposure to curcumin also impaired the production of pro-inflammatory cytokines (IL-1, IL-6 and TNF-). These studies indicate a potent inhibitor of pro-inflammatory cytokine production by curcumin and it may differ according to the nature of the target cells.

Go to:

**Curcumin as an Anti-oxidant**

Curcumin inhibits the activity of AP-1, a transcription factor involved in expression of amyloid, which is linked to AD. Curcuminoids are proven to have strong antioxidant action demonstrated by the inhibition of the formation and propagation of free radicals. It decreases the low-density lipoprotein oxidation and the free radicals that cause the deterioration of neurons, not only in AD but also in other neuron degenerative disorders such as Huntington's and Parkinson's disease.[16] In one study, curcuma oil (500 mg Kg(-1) i.p.) was given 15 min before 2 h middle cerebral artery occlusion, followed by 24 h reflow in rats. This significantly diminished the infarct volume, improved neurological deficit and counteracted oxidative stress.[17]

A study conducted at Nanjing Medical University (China) showed that a single injection of curcumin (1 and 2 mg/kg, i.v.) after focal cerebral ischemia/reperfusion in rats significantly diminished the infarct volume, improved neurological deficit, decreased mortality and reduced the water content in the brain.[18]
Curcumin has powerful antioxidant and anti-inflammatory properties; according to the scientists, these properties believe help ease Alzheimer's symptoms caused by oxidation and inflammation.[19] A study conducted at Jawaharlal Nehru University (India) demonstrated that the administration of curcumin significantly reduced lipid peroxidation and lipofuscin accumulation that is normally increased with aging.[20] It also increased the activity of superoxide dismutase, sodium-potassium ATPase that normally decreased with aging. In another study, curcumin has been shown to protect the cells from betaA (1-42) insult through antioxidant pathway.[21] Curcumin protects brain mitochondria against various oxidative stress. Pre-treatment with curcumin protects brain mitochondria against peroxynitrite (a product of the reaction of nitric oxide with superoxide) a potent and versatile oxidant that can attack a wide range of cells in vitro by direct detoxification and in vivo by the elevation of total cellular glutathione levels.[22]

Go to:

**Curcumin on Haemoxygenase Pathway**

Natural antioxidant curcumin has been identified as a potent inducer of hemoxygenase, a protein that provides efficient cytoprotection against various forms of oxidative stress. By promoting the inactivation of Nrf2-keap1 complex and increased binding to no-1ARE, curcumin induces hemoxygenase activity. The incubation of astrocytes with curcumin at a concentration that promoted hemoxygenase activity resulted in an early increase in reduced glutathione, followed by a significant elevation in oxidized glutathione content.[23–25] Glutathione is an important water-phase antioxidant and essential cofactor for antioxidant enzymes protecting the mitochondria against endogenous oxygen radicals. Its level reflects the free radical scavenging capacity of the body. GSH depletion leads to tissue damage due to lipid peroxidation and oxidative damage.

Go to:

**Beta-Amyloid Plaques**

The most prominent characteristic feature in AD is the presence of beta-amyloid plaques. These plaques are basically an accumulation of small fibers called beta amyloid fibrils. Because the deposition of beta-amyloid protein is a consistent pathological hallmark of brains affected by AD, the inhibition of A-beta generation, prevention of A-beta fibril formation, destabilization of pre-formed A-beta would be an attractive therapeutic strategy for the treatment of AD. The levels of beta-amyloid in AD mice that were given low doses of curcumin were decreased by around 40% in comparison to those that were not treated with curcumin. In addition, low doses of curcumin also caused a 43% decrease in the so-called “plaque burden” that these beta-amyloid have on the brains of AD mice. Surprisingly low doses of curcumin given over longer period were actually more effective than high doses in combating the neurodegenerative process of AD.[26] At higher concentration, curcumin binds to amyloid beta and blocks its self assembly. The key chemical features in amyloid beta are the presence of two aromatic end groups and any alterations in these groups has profound effect on its activity.

Because of the lipophilic nature of curcumin, it crosses the blood brain barrier and binds to plaques. Curcumin was a better A-beta 40 aggregation inhibitor and it destabilizes the A-beta polymer. In in vitro studies, curcumin inhibits aggregation as well as disaggregates to form fibrillar A-beta 40. A Japanese study showed that using fluorescence spectroscopic analysis with thioflavin T and electron microscopic studies, curcumin destabilizes the fA-beta(1-40) and fA-beta(1-42) as well as their extension.[27] Curcumin-derived isoxazoles and pyrazoles bind
to the amyloid beta peptide (Abeta) and inhibit amyloid precursor protein (APP) metabolism.[28] Curcumin given to APPswe/PS1dE9 mice for 7 days crosses the blood-brain barrier as demonstrated by multi-photon microscopy and reduces the existing senile plaques.[29] In another study, curcumin has been shown to increase the phagocytosis of amyloid-beta, effectively clearing them from the brains of patients with AD.[30]

Go to:

Metal Chelation

Studies showed that metals can induce A-beta aggregation and toxicity and are concentrated on Alzheimer's brain. Chelators' desferroxamine and cliquinol have exhibited anti-Alzheimer's effects. A study at Capital University Beijing demonstrated the toxicity of copper on neurons. A greater amount of H_2O_2 was released when copper (2)-A(beta)-40 complexes were added to the xanthene oxidase system. Copper was bound to A(beta)1-40 and was observed by electron paramagnetic resonance spectroscopy. In addition, copper chelators could cause a structural transition of A(beta). There was an increase on beta sheet as well as alpha-helix when copper was introduced.[31] Another study reveals that copper and zinc bind A-beta inducing aggregation and give rise to reactive oxygen species. There was a conformational change from beta sheet to alpha helix followed by peptide oligomerization and membrane penetration, when copper (or) zinc is added to A-beta in a negatively charged lipid environment.[32] Brain iron deregulation and its association with amyloid precursor protein plaque formation are implicated in the pathology of AD.[33]

Curcumin, by interaction with heavy metals such as cadmium and lead, prevents neurotoxicity caused by these metals. The intraperitoneal injection of lead acetate in rats in the presence of curcumin was studied microscopically. The results show lead-induced damage to neurons was significantly reduced in rats injected with curcumin.[34] A study at Chinese University of Hong Kong showed that by using spectrophotometry, the curcumin effectively binds to copper, zinc and iron. In addition, curcumin binds more effectively with redox-active metals such as iron and copper than the redox-inactive zinc. It is suggested that curcumin suppresses inflammatory damage by preventing metal induction of NF-kappa.[35,36]

Go to:

Cholesterol Lowering Effect

High-fat diets and increased blood cholesterol are linked to increased amyloid plaques by the intracellular accumulation of cholestryl esters.[37] Researchers believe that by inhibiting cholesterol formation and decreasing serum peroxides, curcumin might exert beneficial effects on AD.[38]

Safety

Oral bioavailability:

Curcumin has poor bioavailability. Because curcumin readily conjugated in the intestine and liver to form curcumin glucuronides.[39] In a clinical trial conducted in Taiwan, serum curcumin concentrations peaked one to two hours after an oral dose. Peak serum concentrations were 0.5, 0.6 and 1.8 micromoles/L at doses of 4, 6 and 8 g/day respectively.[40] It is also measured in urine at a dose of 3.6 g/day. Absorption is poor following ingestion
in mice and rats. 38% to 75% of an ingested dose of curcumin is excreted in the feces. Absorption appears to be better with food. Curcumin crosses the blood brain barrier and is detected in CSF.

**Side Effect**

No apparent side effects have been reported thus far. GI upset, chest tightness, skin rashes, swollen skin are said to occur with high dose. A few cases of allergic contact dermatitis from curcumin have been reported.[41]

The chronic use of curcumin can cause liver toxicity. For this reason, turmeric products should probably be avoided by individuals with liver disease, heavy drinkers and those who take prescription medications that are metabolized by liver. Curcumin was found to be pharmacologically safe in human clinical trials with doses up to 10 g/day. A phase 1 human trial with 25 subjects using up to 8000 mg of curcumin per day for three months found no toxicity from curcumin.[42]

**Interaction**

Curcumin is said to interact with certain drugs such as blood thinning agents, NSAIDs, reserpin. Co-supplementation with 20 mg of piperine (extracted from black pepper) significantly increase the bioavailability of curcumin by 2000%.[43]

**Contraindication**

Curcumin is not recommended for persons with biliary tract obstruction because it stimulates bile secretion. It is also not recommended for people with gallstones, obstructive jaundice and acute biliary colic. Curcumin supplementation of 20-40 mg have been reported to increase gallbladder contractions in healthy people.[44,45]

**Go to:**

**Human**

Epidemiological studies have shown that prevalence of AD is 4.4 lower amongst Indian Asians as compared to people of western origin.[9] Dementia incidence in western countries ($P < 0.21$) and East Asian countries were lower than that of Europe ($P < 0.0004$).[49]
Experimental studies: Statistical significance

*Clinical Vivo:* Blood from six patients with AD and three healthy controls was taken and the macrophage cells were isolated. After treatment of macrophages with curcuminoids, Aβ uptake by macrophages of three of the six AD patients was found to have significantly increased ($P < 0.001$ to 0.081).\[11\]

Five animal and two human studies showed statistically significant $P$ values.

**Conclusion**

Based on the main findings detailed above, curcumin will lead to a promising treatment for Alzheimer's disease. The clinically studied chemical properties of curcumin and its various effects on AD shows the possibility to do further research and develop better drugs based on curcumin for treating AD. The recent review paper of John Ringman also supports some of the abovementioned properties of curcumin in AD;\[50\] however, large-scale human studies are required to identify the prophylactic and therapeutic effect of curcumin.

Several unanswered questions remain: What is the one main chemical property of curcumin that can be exploited in treating AD? What is the role of curcumin in other neurological disorders such as Parkinson's, Huntington's and other dementias? How does curcumin interact with neuronal plaques? Is it effective only as a food additive? Would it be effective when used alone or with other anti inflammatory drugs?

**Footnotes**

**Source of Support:** Nil

**Conflict of Interest:** Nil

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Turmeric

Scientific Name
Curcuma longa, Curcuma domestica

Common Name
Indian saffron, curcumin, jiang huang

Clinical Summary

Turmeric is a plant that is native to South Asia but is cultivated in tropical areas around the world. The rhizome is used as a spice in regional cuisines, and as coloring agent in food and cosmetics for its yellow-orange color. It is also used in traditional medicine for circulation and digestion. The extract is marketed as a dietary supplement to improve memory, for arthritis, and for cancer prevention. The active constituents are turmerone oil and water-soluble curcuminoids, mainly curcumin which is the focus of most research. In vitro studies suggest that curcumin, the principal bioactive ingredient of turmeric, acts as a weak phytoestrogen, and exhibits neuroprotective, choleretic, anti-inflammatory, immunomodulatory, anti-proliferative, and chemopreventive effects. Curcumin, its analogs, and liposomal formulations have also produced chemosensitizing and radiosensitizing effects.

Turmeric and its active constituents have been investigated for their therapeutic activities in humans. Data from an epidemiological study suggest improved cognitive performance in elderly Asians who consume turmeric in the form of curry powder; however, no benefits from curcumin supplementation were detected in patients with...
Alzheimer’s disease (15). Turmeric may help alleviate symptoms of irritable bowel syndrome (16) as well as quiescent ulcerative colitis (17). Turmeric extract was found to be safe and equally effective as a non-steroidal anti-inflammatory drug for the treatment of osteoarthritis of the knee (18). Whether curcumin supplementation may increase cholesterol levels is unclear, as study results are mixed (19) (20).

In patients with colorectal cancer, oral curcumin administered during the pre-surgery waiting period improved cachexia and the general health of patients (21). In a phase II trial of oral curcumin in patients with advanced pancreatic cancer, no treatment-related toxic effects were observed and clinically relevant biological activity was seen in two patients despite limited absorption (22). In early phase studies, a combination of curcumin and docetaxel was shown to be safe (23). Curcumin with gemcitabine was also found to be safe and feasible for further study (24) (25), but a high-dose of curcumin must be used to achieve systemic effect (23) (25).

Curcumin is known to interfere with cytochrome P450 enzymes (26) (27) and may interact with chemotherapy drugs like cyclophosphamide and doxorubicin (28). It also has estrogenic activity (1) but the effects on breast cancer patients remain unclear. Overall, the development of turmeric for clinical use needs further investigation due to its inherent poor absorption, rapid metabolism, complex mechanistic profile, and largely preclinical data.
Disclaimer

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Turmeric
Overview:

Turmeric (Curcuma longa) has been used for 4,000 years to treat a variety of conditions. Studies show that turmeric may help fight infections and some cancers, reduce inflammation, and treat digestive problems, and it has gotten a lot of press lately.

But remember several facts when you hear news reports about turmeric. First, many studies have taken place in test tubes and animals, and turmeric may not work as well in humans. Second, some studies have used an injectable form of curcumin, the active substance in turmeric. Finally, some of the studies show conflicting evidence.

Turmeric is widely used in cooking and gives Indian curry its flavor and yellow color. It is also used in mustard and to color butter and cheese. Turmeric has been used in both Ayurvedic and Chinese medicine as an anti-inflammatory, to treat digestive and liver problems, skin diseases, and wounds.

Curcumin is also a powerful antioxidant. Antioxidants scavenge molecules in the body known as free radicals, which damage cell membranes, tamper with DNA, and even cause cell death. Antioxidants can fight free radicals and may reduce or even help prevent some of the damage they cause.

In addition, curcumin lowers the levels of two enzymes in the body that cause inflammation. It also stops platelets from clumping together to form blood clots.

Research suggests that turmeric may be helpful for the following conditions:

**Indigestion or Dyspepsia**

Curcumin stimulates the gallbladder to produce bile, which some people think may help improve digestion. The German Commission E, which determines which herbs can be safely prescribed in Germany, has approved turmeric for digestive problems. And one double-blind, placebo-controlled study found that turmeric reduced symptoms of bloating and gas in people suffering from indigestion.

**Ulcerative colitis**

Turmeric may help people with ulcerative colitis stay in remission. Ulcerative colitis is a chronic disease of the digestive tract where symptoms tend to come and go. In one double-blind, placebo-controlled study, people whose ulcerative colitis was in remission took either curcumin or placebo, along with conventional medical treatment, for 6 months. Those who took curcumin had a relapse rate much lower than those who took placebo.

**Stomach Ulcers**

Turmeric does not seem to help treat stomach ulcers. In fact, there is some evidence that it may increase stomach acid, making existing ulcers worse. (See “Precautions” section.)

**Osteoarthritis**
Because of its ability to reduce inflammation, researchers have wondered if turmeric may help relieve osteoarthritis pain. One study found that people using an Ayurvedic formula of herbs and minerals with turmeric, winter cherry (*Withinia somnifera*), boswellia (*Boswellia serrata*), and zinc had less pain and disability. But it's impossible to know whether it was turmeric or one of the other supplements -- or all of them together -- that was responsible.

**Heart Disease**

Early studies suggested that turmeric may help prevent atherosclerosis, the buildup of plaque that can block arteries and lead to heart attack or stroke. In animal studies, an extract of turmeric lowered cholesterol levels and kept LDL "bad" cholesterol from building up in blood vessels. Because it stops platelets from clumping together, turmeric may also prevent blood clots from building up along the walls of arteries. But a double-blind, placebo-controlled study found that taking curcumin, the active ingredient in turmeric, at a dose of up to 4 g per day did not improve cholesterol levels.

**Cancer**

There has been a great deal of research on turmeric's anti-cancer properties, but results are still very early. Evidence from test tube and animal studies suggests that curcumin may help prevent or treat several types of cancers, including prostate, breast, skin, and colon cancer. Its preventive effects may be because it is a strong antioxidant, protecting cells from damage. More research is needed. Cancer should be treated with conventional medications. Don’t use alternative therapies alone to treat cancer. If you choose to use complementary therapies along with your cancer treatment, make sure you tell all your doctors.

**Bacterial and Viral Infections**

Test tube and animal studies suggest turmeric may kill bacteria and viruses. But researchers don't know whether it would work in people.

**Uveitis**

A preliminary study suggests curcumin may help treat uveitis, an inflammation of the eye's iris. In one study of 32 people with chronic anterior uveitis, curcumin was effective as corticosteroids, the type of medication usually prescribed. More research is needed.

Source: [http://www.umm.edu/altmed/articles/turmeric-000277.htm#ixzz2Jon9lpqa](http://www.umm.edu/altmed/articles/turmeric-000277.htm#ixzz2Jon9lpqa)

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