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Scientist Bharat Aggarwal Pays Homage to India's Haldi

By Francis C. Assisi

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15 October 2005 -- The figures on breast cancer are telling.

About 211,240 women in the United States will be diagnosed with invasive breast cancer in 2005, and approximately 40,410 women will die from the disease this year.

So scientists have taken up the challenge to confront the beast. This week, cancer expert Bharat Bhushan Aggarwal, one of the world's most highly cited cancer researcher, has done it again.

From The University of Texas M. D. Anderson Cancer Center, Aggarwal and colleagues report on their latest study showing that Curcumin, the main ingredient of turmeric, inhibits the spread of breast cancer and improves the effectiveness of current remedies. They believe that it could lead to a new way of treating people in the advanced stages of the disease.

The study, published in the Oct. 15 issue of the journal Clinical Cancer Research, reports that the spice appears to shut down a protein active in the spread of breast cancer.

The non-toxic, natural curcumin repelled progression of the disease to the lungs and also appeared to reverse a "side-effect" of a commonly prescribed chemotherapy whose prolonged use may actually help to spread the disease.

Curcumin breaks down the dose, making the therapy less toxic, but the drug stays just as powerful in fighting cancer.

Researchers studied 60 mice with breast cancer. Among a control group who were not treated, 96 per cent went on to develop visible signs of lung cancer, while treatment with the chemotherapy drug Taxol "modestly reduced" the incidence.

But those given curcumin alone or curcumin plus Taxol had far fewer signs of the disease.

"We are excited about the results of the study and the possible implications for taking the findings into the clinic in the next several years," says Bharat Aggarwal, Ph.D., professor of cancer medicine in M. D. Anderson's Department of Experimental Therapeutics. "At this time, advanced breast cancer is a difficult foe to fight with few proven treatments available after surgery, chemotherapy and radiation therapy."

Taxol is currently used as the front-line chemotherapeutic agent in breast cancers, but because the drug frequently induces drug resistance after prolonged use, it is not effective in treating metastatic breast cancer, says Aggarwal.

RESEARCH RESULTS

The researchers studied 60 mice with breast cancer, which were randomly assigned to one of four groups: control group, Taxol only, curcumin only and the combination of Taxol and curcumin. After the tumors grew to 10 mm (about the size of a pea), they were surgically removed, and the mice were fed a powdered curcumin diet.

Macroscopic lung metastasis, or metastasis that is visible to the naked eye, was seen in 96 percent

of the mice in the control group. Treatment using Taxol alone only "modestly reduced" the incidence of metastases, while the group using curcumin alone and curcumin plus Taxol "significantly reduced" both the incidence and numbers of visible lung metastases.

Microscopic metastasis, or metastasis that is visible only when using a microscope, was found in the lungs of 28 percent of mice treated with the combination of curcumin and Taxol, and there was no macroscopic disease present. The micrometastases present consisted of only a few cells, suggesting that the combination inhibited the growth of breast cancer tumor cells that were in the lung before the tumors were removed.

In a previous study published in the Aug. 15 issue of the journal Cancer, M. D. Anderson researchers found that when the nuclear factor-kappa B (NF-kB) (a powerful protein known to promote the inflammatory response necessary to cause breast cancer to spread) is shut down, cancer strains are unable to grow and cells are pushed to commit suicide.

The mechanism in this curcumin study works the same way. Taxol activated the NF-kB in breast cancer cells, while curcumin stopped this activation by blocking the protein known as "IKK" that switched on the NF-kB, demonstrating how curcumin and Taxol work against one another. Taxol produced the inflammatory response, triggering metastasis, and curcumin suppressed it, causing cell death.

Extracted from the roots of the curcuma longa plant, curcumin is a member of the ginger family. While it is not used in conventional medicine, it is widely prescribed in Indian medicine as a potent remedy for liver disorders, rheumatism, diabetic wounds, runny nose, cough and sinusitis. Traditional Chinese medicine uses curcumin as a treatment for diseases associated with abdominal pain, and it is used in ancient Hindu medicine as a treatment for sprains and swelling.

The study was funded by the United States Department of Defense. Co-authors include Shishir Shishodia, Ph.D.; Yasunari Takada, Ph.D.; Sanjeev Banerjee, Ph.D.; Robert A. Newman, Ph.D.; Carlos Bueso-Ramos, M.D., Ph.D.; and Janet E. Price, Ph.D.

CLINICAL TRIALS

At least a dozen clinical trials on humans are under way in the United States, Israel and England to test the safety and dosages of turmeric's main ingredient, curcumin. It's a hot topic in health journals, too, cited 967 times since 2000 in articles reported on PubMed, the National Library of Medicine's research service.

So far, of the 250 studies conducted worldwide in 2005, Aggarwal has published 6 studies on curcumin.

Low rates among Indians for colorectal, prostate and lung cancers as well as coronary heart disease and Alzheimer's first drew Western researchers to curcumin. While genetics might have explained the low incidences, the rise in rates among Indians whose parents had moved to Western countries suggested a dietary cause. Subsequent lab tests on diseased cells and in mice strengthened claims for curcumin.

It's been demonstrated in animals to protect the liver, inhibit tumors, reduce inflammation and fight some infections. Curcumin has both antioxidant and anti-inflammatory properties, according to researchers, and may help lower cholesterol.

Microscopic evidence of lung cancer was found in just 28 per cent of mice given both and there were no visible signs of the disease at all.

Dr Mark Matfield, scientific consultant for the St Andrews-based Association for International Cancer Research in Scotland, said: "We have known for some time that curcumin has anti-cancer effects, but this study has really advanced our understanding of exactly how this works. The finding that curcumin can decrease the spread of cancer when it is treated with Taxol is really interesting and potentially very important.

"However, as the authors of this study pointed out, these are only preliminary findings. The crucial next stage is to confirm these findings in patients suffering from lung cancer."

Dr Julie Sharp, senior cancer information officer at Cancer Research UK, said: "A number of laboratory studies have suggested that curcumin could be used to treat and even prevent some types of cancer. But, as yet there is no evidence confirming this in humans. These findings will

need to be followed up with clinical trials in humans."

Nevertheless, in presentations to fellow South Asians, Dr Aggarwal has been encouraging the lavish use of turmeric in daily food preparations.

OTHER USES OF CURCUMIN

While turmeric has a long history of use by herbalists, most studies to date have been conducted in the laboratory or in animals and it is not clear that these results apply to people. Nevertheless, research suggests that turmeric may be helpful for the following conditions.

Digestive Disorders

(stomach upset, gas, abdominal cramps): The German Commission E (an authoritative body that determined which herbs could be safely prescribed in that country and for which purpose[s]) approved turmeric for a variety of digestive disorders. Curcumin, for example, one of the active ingredients in turmeric, induces the flow of bile, which helps break down fats. In an animal study, extracts of turmeric root reduced secretion of acid from the stomach and protected against injuries such as inflammation along the stomach (gastritis) or intestinal walls and ulcers from certain medications, stress, or alcohol. Further studies are needed to know to what extent these protective effects apply to people as well.

Osteoarthritis

Because of its ability to reduce inflammation, turmeric may help relieve the symptoms of osteoarthritis. A study of people using an Ayurvedic formula of herbs and minerals containing turmeric as well as Withinia somnifera (winter cherry), Boswellia serrata (Boswellia), and zinc significantly reduced pain and disability. While encouraging for the value of this Ayurvedic combination therapy to help with osteoarthritis, it is difficult to know how much of this success is from turmeric alone, one of the other individual herbs, or the combination of herbs working in tandem.

Atherosclerosis

Early studies suggest that turmeric may prove helpful in preventing the build up of atherosclerosis (blockage of arteries that can eventually cause a heart attack or stroke) in one of two ways. First, in animal studies an extract of turmeric lowered cholesterol levels and inhibited the oxidation of LDL ("bad") cholesterol. Oxidized LDL deposits in the walls of blood vessels and contributes to the formation of atherosclerotic plaque. Turmeric may also prevent platelet build up along the walls of an injured blood vessel. Platelets collecting at the site of a damaged blood vessel cause blood clots to form and blockage of the artery as well. Studies of the use of turmeric to prevent or treat heart disease in people would be interesting in terms of determining if these mechanisms discovered in animals apply to people at risk for this condition.

Cancer

There has been a substantial amount of research on turmeric's anti-cancer potential. Evidence from laboratory and animal studies suggests that curcumin has potential in the treatment of various forms of cancer, including prostate, breast, skin, and colon. Human studies will be necessary before it is known to what extent these results may apply to people.

Roundworms and Intestinal worms

Laboratory studies suggest that curcuminoids, the active components of turmeric, may reduce the destructive activity of parasites or roundworms.

Liver Disease Animal studies provide evidence that turmeric can protect the liver from a number of damaging substances such as carbon tetrachloride and acetominophen (also called paracetamol, this medication, used commonly for headache and pain, can cause liver damage if taken in large quantities or in someone who drinks alcohol regularly.) Turmeric accomplishes this, in part, by helping to clear such toxins from the body and by protecting the liver from damage.

Bacterial Infection

Turmeric's volatile oil functions as an external antibiotic, preventing bacterial infection in wounds.

Wounds

In animal studies, turmeric applied to wounds hastens the healing process.

Mosquito Repellent

A mixture of the volatile oils of turmeric, citronella, and hairy basil, with the addition of vanillin (an extract of vanilla bean that is generally used for flavoring or perfumes), may be an alternative to D.E.E.T., one of the most common chemical repellents commercially available.

Eye Disorder

One study of 32 people with uveitis (inflammation of the uvea, the middle layer of the eye between the sclera [white outer coat of the eye] and the retina [the back of the eye]) suggests that curcumin may prove to be as effective as corticosteroids, the type of medication generally prescribed for this eye disorder. The uvea contains many of the blood vessels that nourish the eye. Inflammation of this area, therefore, can affect the cornea, the retina, the sclera, and other important parts of the eye. More research is needed to best understand whether curcumin may help treat this eye inflammation.

LATEST RESEARCH IN INDIA

In tandem with Aggarwal's findings, scientists at the Bose Institute (Kokata) are also reporting that the true therapeutic benefit of the use of natural products, especially acceptable dietary components such as curcumin, has opened new horizons in cancer prevention and treatment.

In their report 'Amelioration of immune cell number depletion and potentiation of depressed detoxification system of tumor-bearing mice by curcumin,' S.Pal and colleagues from the Bose Institute say, "The ability of curcumin to regress tumor as well as to protect the host from tumor-induced immunosuppression and toxicity strongly supports the candidacy of curcumin as a potential agent for the dietary therapy of cancer."

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