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REPORT

Novel Turmeric Compound Delivers Much More Curcumin to the Blood

By Dale Kiefer



Life Extension readers have long been aware of the vast array of health benefits conferred by the curry spice turmeric, which is the source of curcumin. Scientific researchers around the world are investigating applications for curcumin that include fighting cancer, arthritis, diabetes, cardiovascular disease, osteoporosis, and reversing the pathological processes underlying Alzheimer's disease, among other conditions.¹⁻¹³

Curcumin has long been known to have poor bioavailability, requiring high doses to achieve desired blood levels. A novel curcumin absorption system has been developed that delivers up to seven times more pharmacologically bioactive curcumin to the blood compared with commercial curcumin products.

This revolutionary development will radically change the extent to which people may obtain additional health benefits from this revered herb.

A wealth of data shows that curcumin and its related chemicals (collectively known as curcuminoids) help to prevent and fight a wide range of diseases—from cancer to cardiovascular disease—through a variety of mechanisms.^{1,5,7-19} These include powerful anti-inflammatory, antioxidant, chemopreventive (cancer-preventive), and antineoplastic (cancer-fighting) properties.

Perhaps one of curcumin's most important activities in the human body is its ability to inhibit activation of the transcription factor, nuclear factor-kappa B (NF- κ B),⁴⁻⁶ a potent inducer of chronic inflammation. NF- κ B is a protein that acts as a sort of switch, turning on inflammation by activating genes involved in the production of inflammatory compounds. As NF- κ B activation has been implicated in all the stages of carcinogenesis, this transcription factor is a potential target in cancer chemoprevention and is the subject of intensive research.

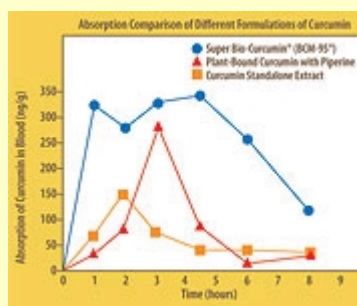
THE CURCUMIN REVOLUTION: GREATLY ENHANCED BIOAVAILABILITY

Despite its impressive array of benefits, the effectiveness of oral supplementation with curcumin has been limited by poor absorption into the bloodstream through the digestive tract. In the past, a few formulators worked around this problem by adding a derivative of black pepper, piperine, which enhanced the absorption of ingredients such as curcumin.²⁰ Scientists have long sought a more bioavailable form of curcumin to provide even greater pharmaceutical potencies to maximize curcumin's efficacy.

Life Extension has reviewed numerous curcumin products that showed varying degrees of enhanced absorption. One published clinical study caught our attention. In it, a novel manufacturing technology was able to dramatically increase blood plasma curcumin to levels not previously seen through supplementation. While only 50-60% of pure curcumin administered to animals is typically absorbed, this new technology increased the absorption of curcumin to a remarkable 96%.²¹ This impressive rise in bioavailability was achieved without the addition of piperine.

Impressed with these data and seeking to verify these findings, Life Extension then ran an objective comparison trial on human volunteers to determine if this novel curcumin could really deliver significantly greater concentrations of curcumin to the

ABSORPTION COMPARISON OF DIFFERENT FORMULATIONS OF CURCUMIN



ABSORPTION OF SUPER BIO-CURCUMIN IN RATS COMPARED WITH CONVENTIONAL CURCUMIN⁶¹

bloodstream and for a longer sustained time period.²² The findings from Life Extension's independent study basically mirrored those in the first study. As a result, we identified a curcumin formula that provides better bioavailability than was ever thought possible. Known as BCM-95®, this "next generation" formulation is far more readily absorbed than other currently or previously available curcumin products. In fact, both studies delivered close to seven times more curcumin than was previously available from a standard supplement.

Life Extension's study of this new formulation was designed to document the "pharmacokinetics," or absorption, circulation, and metabolism of curcumin and curcuminoids in human subjects. The study compared BCM-95® with two other curcumin products: a plant-bound curcumin formulation with piperine and a purified 95% curcumin standalone extract (which is what most supplement companies sell today). Eleven volunteers were recruited. They were divided into three groups. Subjects received BCM-95®, plant-bound curcumin extract with piperine, or ordinary curcumin extract. Blood was drawn at baseline and again six times over the following eight hours. After a two-week washout period, subjects were switched (crossed over) to an alternate formulation; BCM-95® subjects were given ordinary "control" curcumin, while subjects originally given either of the two "control" curcumin formulations were given BCM-95®.

NEW FORMULATION INCREASES BLOOD LEVELS MORE, SOONER, LONGER

Subjects' plasma samples were subsequently assayed to determine curcumin concentrations. The results clearly showed that BCM-95® was rapidly absorbed from the digestive system, allowing more of turmeric's powerful disease-fighting chemicals to circulate throughout the bloodstream, while delivering the full punch of curcumin's properties as never before. In fact, curcumin reached a peak within one hour in the bloodstreams of subjects who took BCM-95®. After a brief dip at about two hours' post-dose, curcumin reached a second, still higher peak again at 4.5 hours, and then gradually declined. By eight hours' post-dose, curcumin was still detectable in subjects' blood.²²

In contrast, ordinary standalone curcumin took two hours to reach peak concentration, and then rapidly declined. By 4.5 hours' post-dose, when BCM-95® curcumin was just hitting its stride, curcumin from this control formulation had virtually disappeared from subjects' bloodstreams. Even at its peak, this control curcumin formulation reached only about half the concentration of curcumin from BCM-95®. Likewise, the BCM-95® showed superior absorption compared with the plant-bound curcumin with piperine formula. Thus, BCM-95® not only delivers more curcumin to the bloodstream, sooner, but it sticks around nearly twice as long, too. This is an extremely important advantage, which should result in greatly enhanced benefits.

How did the inventors of this patent-pending curcumin achieve this breakthrough? Rather than focusing on further purification of curcumin and curcuminoids derived from turmeric (usually marketed as "95% curcumin/curcuminoids"), the formulators went back to the "roots," so to speak, reincorporating many of the components of raw turmeric root—which are normally removed during the extraction process—and greatly enhancing the bioavailability of active constituents in the process. In essence, this revolutionary reformulation relies on the inherent synergy of the turmeric rhizome's natural components to dramatically enhance bioavailability.

As a result, BCM-95® is six-to seven times more bioavailable than ordinary 95% extract. Just one 400 mg dose of this new bioavailability-enhanced turmeric extract is equivalent to taking 2,772 mg of standard "95%" curcumin extract or 2,548 mg of

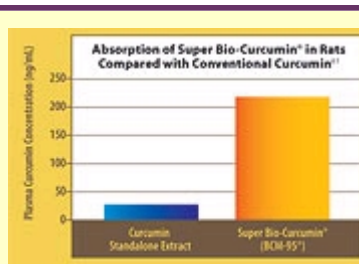


Chart 1. Bioavailability in rats fed with BCM-95® is 7.8 times higher than conventional curcumin.

ABSORPTION OF SUPER BIO-CURCUMIN IN HUMANS COMPARED WITH CONVENTIONAL CURCUMIN²²

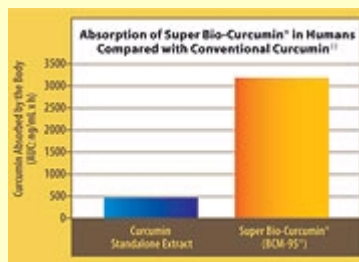


Chart 2. Super Bio-Curcumin® (BCM-95®) showed 6.9 times greater bioavailability (absorption and sustainability over 8 hours) in humans compared with conventional curcumin (as measured by the area under the curve [AUC] in a plot of blood levels against time, that is, the total amount of curcumin absorbed by the body over 8 hours).

ABSORPTION OF SUPER BIO-CURCUMIN IN HUMANS COMPARED WITH PLANT-BOUND CURCUMIN WITH PIPERINE²²

plant-bound curcumin extract with piperine. In the Life Extension human trial, BCM-95® delivered 6.93 times more curcumin to the bloodstream than the ordinary standalone curcumin product and 6.37 times more curcumin to the bloodstream than the plant-bound curcumin extract with piperine.²²

Life Extension's results confirmed the findings shown previously for BCM-95®.

CURCUMIN'S MANY BENEFITS

Curcumin's benefits are so diverse that they affect virtually every organ system in the body. It's no accident that the National Institutes of Health has funded numerous studies investigating curcumin, which include diverse applications such as treatment of cystic fibrosis, the feasibility of controlling the autoimmune disease, scleroderma, and various cancer chemoprevention trials.²³ Meanwhile, pharmaceutical companies around the world are actively working to derive patentable molecules based on curcumin, which they hope to market, at great profit, as anticancer treatments.²⁴

Among other activities, curcumin has demonstrated antibacterial, antifungal, antiviral, anti-inflammatory and antioxidant capabilities.¹⁸ It's even showing great promise in the fight against the most common genetic disorder in Caucasians, cystic fibrosis.¹⁴ To this list, add powerful anticancer protection, cardiovascular protection, and protection against neurodegenerative disorders, such as Alzheimer's and Parkinson's diseases.^{8,16,25-29} Additionally, curcumin shows promise as a potential treatment for multiple sclerosis,⁷ and may protect against cataracts³⁰ as well as reverse some of the damage associated with the high blood sugar levels that characterize diabetes.³¹ Curcumin also shows great promise as a treatment for skin disorders such as psoriasis, and in the treatment of wounds.^{9, 32}



POWERFUL CANCER PROTECTION

Scientists usually go out of their way to avoid hyperbole when describing the subjects of their inquiries, but curcumin's amazing properties evidently tempt even the most staid researcher to throw caution to the wind. "Curcumin appears to possess all the desirable features of a desk-designed, multipurpose drug," wrote one research team, recently.³³ Other investigators focused on promising anticancer activity. "Curcumin... has emerged as one of the most powerful chemopreventive and anticancer agents," wrote Indian researchers last year. "Its biological effects range from antioxidant [and] anti-inflammatory to inhibition of angiogenesis, and [it] is also shown to possess specific antitumoral activity."²⁷ Although

anticancer drugs weaken the immune system, curcumin actually enhances it, ^{12,34-43} acting as an "immunorestorator."³⁴ It's little wonder, then, that cancer prevention and treatment has emerged as one of the most avidly researched aspects of curcumin's potential benefits.

Writing in *Cancer Letters*, American scientists noted recently, "Pre-clinical studies in a variety of cancer cell lines including breast, cervical, colon, gastric, hepatic, leukemia, oral epithelial, ovarian, pancreatic, and prostate have consistently shown that curcumin possesses anticancer activity in vitro and in pre-clinical animal models."⁴⁴ Other investigators wrote: "Carcinogenesis encompasses three closely associated stages: initiation, progression, and promotion. [Curcumin] has been shown to possess anti-inflammatory, antioxidant, and antitumor properties. [It] has also been shown to be beneficial in all three stages of carcinogenesis."⁴³

SPECIFIC ANTICANCER MECHANISM DISCOVERED

In mid-2007, scientists at the University of Alabama at Birmingham published a report in the journal *Cancer Research*, detailing at least one of perhaps many mechanisms by which curcumin functions as an anticancer agent. The investigators grew prostate cancer cells in the laboratory, and exposed them to varying concentrations of curcumin. The curcumin reduced the cells' production of a protein known as MDM2, which is associated with the formation of malignant tumors. Simultaneously, curcumin prompted the cells to produce another protein associated with the promotion of programmed cell death (apoptosis).²⁷ Like NF-kB, an inducer of inflammation, MDM2 has been suggested as a novel target for human cancer therapy.

To test curcumin's effects in a live model, the scientists grafted human prostate cancer cells onto special mice, which subsequently developed tumors. The mice were then fed either curcumin or a placebo, five days a week, for four weeks. Afterwards, curcumin-fed mice were further divided into three test groups. One group continued to receive curcumin alone, while

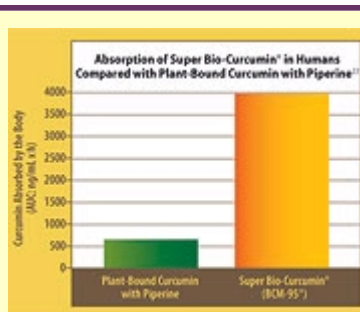


Chart 3. Super Bio-Curcumin® (BCM-95®) showed 6.3 times greater bioavailability (absorption and sustainability over 8 hours) in humans compared to plant-bound curcumin with piperine (as measured by the area under the curve [AUC] in a plot of blood levels against time, that is, the total amount of curcumin absorbed by the body over 8 hours).

another received curcumin plus the cancer chemotherapy drug, gemcitabine. The final group received curcumin plus radiation treatment.

“Curcumin inhibited growth of [human-to-mouse prostate cancer grafts] and enhanced the antitumor effects of gemcitabine and radiation. In these tumors, curcumin reduced the expression of MDM2,” wrote the researchers. This suppression, or “down-regulation” of MDM2 expression was declared to be a newly discovered mechanism by which curcumin exerts its anticancer activity. MDM2 down-regulation by curcumin “may be essential for its chemopreventive and chemotherapeutic effects,” the scientists concluded.²⁷

It’s interesting to note that epidemiological studies show the incidence of prostate cancer among men in India to be among the lowest in the world. One recent study estimated that the annual prostate cancer incidence rate in India ranges from 5.0 to 9.1 per 100,000/year. In contrast, among whites in the United States, the incidence rate is 110.4 per 100,000/year—more than ten times higher compared with men from India. The rate for African Americans is even higher.⁴⁵ Perhaps not coincidentally, Indian men’s consistent intake of turmeric, in the form of curry, is among the highest in the world. The average intake of turmeric in the Indian population is 2-2.5 g/day, providing 60-200 mg curcumin.



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PANCREATIC CANCER

Curcumin has also been shown to enhance the efficacy of the chemotherapy agent, gemcitabine, in the treatment of pancreatic cancer. Although it is currently the best treatment for this aggressive cancer, gemcitabine often loses its effectiveness as cancer cells develop resistance to the drug. Scientists from the University of Texas M.D. Anderson Cancer Center showed recently that curcumin prevents the development of this resistance, in both cultured pancreatic cancer cells and in living animal models of the disease. "Overall, our results suggest that curcumin potentiates the antitumor effects of gemcitabine in pancreatic cancer by suppressing proliferation, angiogenesis, NF- κ B, and NF- κ B-regulated gene products," concluded the scientists.⁴⁶

COLON AND BREAST CANCERS

Curcumin's efficacy against colon cancer has received great attention, primarily because curcumin's bioavailability has been less of an issue, given that the colon is exposed to curcumin as it passes through the digestive tract.¹⁷ Its excellent tolerability and safety have been demonstrated in five Phase I clinical trials in colon cancer, and Phase II trials are currently enrolling patients.⁴⁴ British investigators showed recently that curcumin interferes with the proliferation of various types of colon cancer, and that it enhances the efficacy of an existing chemotherapeutic agent, oxaliplatin.⁴⁷

Curcumin's potential role in the fight against breast cancer is nothing short of remarkable. Italian researchers reported recently that curcumin is effective against a common variety of breast cancer cells and a mutant line of cells that has developed resistance to common chemotherapy drugs. "Through analyses of the effects on cell proliferation, cycling and death, we have observed that the antitumor activity of curcumin... is at least equal in the [multi-drug-resistant breast cancer] cell line compared to the [ordinary breast cancer cell line]," wrote researchers.⁴⁸ This efficacy also held true for a type of multi-drug-resistant leukemia cell.

The Italians' research indicates that curcumin seems capable of adapting its anticancer activity according to need. "Remarkably," wrote the scientists, "[curcumin and one of its derivatives] appeared to modify their molecular effects according to the diverse gene expression patterns existing in the [multidrug-resistant and ordinary breast cancer cell line]. Clearly, the structure and properties of curcumin can form the basis for the development of antitumor compounds...⁴⁸

NOVEL CURCUMIN FORMULATION: WHAT YOU NEED TO KNOW

- One of today's most promising natural disease-fighting agents is curcumin. Derived from the curry spice turmeric, curcumin has been used for millennia to target disease and promote good health.
- Most commercially available preparations of curcumin have very poor bioavailability, impairing their ability to confer life-sustaining properties.
- Scientists have recently discovered a novel curcumin preparation with exceptional bioavailability. In a human study, this advanced curcumin preparation—termed BCM-95®—delivered up to seven times more curcumin to the bloodstream than a standard curcumin product. This increased bioavailability should greatly enhance curcumin's benefits.
- Curcumin promotes health by diverse mechanisms. Scientists have documented curcumin's anti-inflammatory, antioxidant, anti-microbial, neuroprotective, cancer-fighting, and immune-enhancing abilities.
- Studies suggest that curcumin may help prevent or fight prostate, pancreatic, breast, and colon cancers.
- Curcumin may help protect the brain against the devastating consequences of stroke and exposure to toxic heavy metals.
- Individuals who consume more curcumin-rich curry are less likely to experience cognitive decline, suggesting curcumin could help protect the nervous system against aging. In laboratory and animal models, curcumin shows promise in preventing the pathological changes seen in the brains of Alzheimer's disease sufferers.



Among curcumin's many benefits, protection from neurological damage ranks high on many researchers' lists. "Curcumin has at least 10 known neuroprotective actions and many of these might be realized in [living subjects]... wrote American scientists recently, in *Advances in Experimental Medicine and Biology*. "Dietary curcumin is a strong candidate," they added, "for use in the prevention or treatment of major disabling age-related neurodegenerative diseases like Alzheimer's, Parkinson's, and stroke."¹⁶

These scientists are not alone in their assessment of curcumin's potential for protection against dreaded diseases such as Alzheimer's. Numerous researchers are investigating curcumin's protective activities in the brain. For example, Chinese scientists reported in early 2007 that curcumin protects the brains of laboratory animals from a type of injury that often follows stroke. Known as ischemia/reperfusion injury, this damage to brain tissue is believed to occur due to stroke-related deficits in the blood-brain barrier. A single injection of curcumin dramatically reduced ischemia-reperfusion damage, neurological deficits, and death, among animals with experimentally induced stroke.⁴⁹



As another example, South African investigators wondered if curcumin could protect rats' brains from lead poisoning. One way lead damages brain tissue is by inducing lipid peroxidation.⁵⁰ Brain tissue is largely composed of lipids, so it's especially vulnerable to this type of damage. By adding curcumin to test animals' diets, lead toxicity was significantly reduced, possibly by raising concentrations of the antioxidant glutathione.⁵¹ Previously, Indian researchers reported that curcumin raised concentrations of glutathione and two potent antioxidant enzymes, superoxide dismutase and catalase, in the brains of lead-poisoned rats, significantly attenuating lead-induced damage.⁵²

Other researchers report that curcumin may chelate, or bind to, toxic heavy metals, such as lead and cadmium, greatly reducing their toxicity to neurological tissues.⁵³

Furthermore, scientists have reported that curcumin protects brain tissue against oxidative stress by promoting production of a protective enzyme, heme oxygenase-1 (HO-1). "In the [central nervous system]," wrote the researchers, "HO-1 has been reported to operate as a fundamental defensive mechanism for neurons exposed to an oxidant challenge."⁵⁴ Traumatic injury to the brain also results in oxidative stress, often affecting cognition and "synaptic plasticity," which is believed to play a crucial role in healthy learning and memory. In animal experiments, US researchers showed, "Supplementation of curcumin in the diet dramatically reduced oxidative damage and... counteracted the cognitive impairment caused by [traumatic brain injury]."⁵⁵

COGNITIVE DECLINE AND DEMENTIA

Even in the absence of injury or toxicity, loss of cognitive function is a hallmark of aging. Memory loss is believed to begin by age 50, and, by age 80, it's predicted that nearly half of all individuals will advance to some form of dementia.⁵⁶

Wondering if curcumin might protect aging brains from cognitive decline, Asian scientists conducted an epidemiological study of curry consumption and cognitive function among the elderly. They found that men and women who consumed turmeric-laced curry "occasionally," "often," or "very often," had significantly better scores on a standardized test of mental status than subjects who "never or rarely" consumed curry. The investigators described these findings as "tentative evidence of better cognitive performance from curry consumption in nondemented elderly Asians... ²⁵

ALZHEIMER'S DISEASE PROTECTION

Curcumin may offer protection against the most common cause of dementia: Alzheimer's disease. Alzheimer's disease is characterized by the accumulation of a malformed protein, amyloid-beta. Ordinarily, immune cells known as macrophages identify these defective proteins, engulf them, and destroy them. But for reasons that are not entirely clear, macrophages fail to perform this crucial function in Alzheimer's disease.⁵⁷ Using animal models of Alzheimer's, scientists have shown that curcumin can enhance clearance of amyloid-beta, while reducing fibrils, which are also associated with Alzheimer's pathology. Curcumin's ability to cross the blood-brain barrier and directly bind to plaques may be important in its anti-amyloid activity.⁵⁸



Los Angeles-based researchers tested the anti-amyloid activity of human macrophages taken from Alzheimer's disease patients. After incubation with curcumin in the laboratory, uptake of amyloid-beta by macrophages from half of the patients significantly increased. The researchers concluded that this modification of the innate immune system by curcumin, "might be a safe approach to immune clearance of [abnormal amyloid-beta accumulation] in Alzheimer's disease brain."⁵⁹ These data appear to indicate that curcumin is protective against the development of Alzheimer's disease, and that it may even help reverse the disease process, once begun.

SAFETY AND DOSING

Given that turmeric is a food that has been safely consumed for millennia, curcumin would appear to be the perfect dietary supplement.³ In fact, "Curcumin has an outstanding safety profile and a number of [multifunctional] actions... wrote US researchers recently.¹⁶ Phase I clinical trials, using massive doses of curcumin (up to 8 g/day for four months) in human volunteers, "did not result in discernible toxicities... ¹⁷

Of course, not everyone finds curry palatable, especially on a routine basis. But virtually anyone can swallow a simple daily supplement. Most commercial products provide 300-500 mg per pill, standardized to 95% curcumin. Reported adverse reactions have been limited to mild gastrointestinal distress, which may be minimized by consuming curcumin with food.⁶⁰

CONCLUSION

In this overview, we've seen that curcumin has served mankind for thousands of years, and we've noted some of the potent benefits scientists continue to discover. The advent of a revolutionary delivery system promises to make these benefits available to anyone willing to take the proactive step of supplementing the diet with just one or two capsules of enhanced-bioavailable curcumin each day.

If you have any questions about the scientific content of this article, please call one of our Health Advisors at 1-800-226-2370.

Note: BCM-95® is a registered trademark of Dolcas-Biotech, LLC.

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