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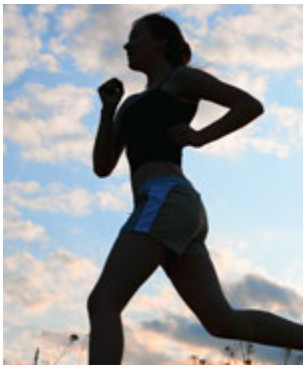
Report

# Safely Manage Joint Inflammation: Curcumin

By Susan Evans



The standard of care for the arthritic patient is prescription drugs with a long list of side effects.1-3 These drugs do nothing to stop the bone and joint destruction caused by osteoarthritis or rheumatoid arthritis.4,5 Beyond that, the patient must learn to live with their crippling pain and limited mobility.

Fortunately, help is readily available. A highly specialized complex of curcumin known as BCM-95® fights the joint-damaging effects of arthritis by attacking multiple inflammatory targets at once.

A team of internationally recognized scientists has published an impressive clinical trial of this superior-absorbing curcumin complex that most Life Extension® members have used for the past several years. The study subjects were rheumatoid arthritis patients who suffered from sky-high levels of inflammation that affected not only their joints but other vital tissues as well.5

In this 2012 study, curcumin beat out the standard arthritis drug diclofenac on most measures of effectiveness.5 Curcumin was free of any of the side effects that so often accompany drug therapy.

The study also showed this superior-absorbing curcumin directly attacked the source of the problem—inflammation— rathe than simply masking pain and other symptoms.5

## Applying Curcumin's Multitargeted Benefits To Arthritis

Curcumin is derived from the bright yellow Indian spice turmeric and has been used by traditional medicine for almost four thousand years.6 Curcumin is well-established in the medical literature as a powerful anti-inflammatory ingredient.5 Unlike pharmaceuticals, curcumin acts through multiple pathways and on numerous targets to limit the inflammatory response that underlies both rheumatoid and osteoarthritis (See table 1 at bottom of this page).6

Scientists now universally recognize that multi-targeted therapies like curcumin are vastly superior to the typical single-targeted mechanisms of conventional drug treatments.6,7 Curcumin is a potent antioxidant, and also boosts natural antioxidant systems inside your cells.8 Curcumin can also enhance other natural detoxifying machinery in your liver.8 By slowing naturally occurring cell death in joint tissue, curcumin can help preserve supple, youthful joints.9-12

But where curcumin really shines is in directly suppressing the inflammation that underlies not only rheumatoid arthritis, but also most of the chronic diseases of aging that afflict all of us sooner or later.13 One recent report showed that curcumin can reduce all of the inflammation-promoting molecular targets for which the FDA currently approves single-targeted (and often dangerous) pharmaceuticals.7

Curcumin's ability to safely quash inflammation in such a broad-spectrum manner makes it a compelling topic among anti-aging researchers. It is being studied for its potential benefits in a number of inflammation based diseases such as Alzheimer's, cardiovascular disease, cancer, multiple sclerosis, and diabetes.5,13 To explore curcumin's therapeutic potential for rheumatoid arthritis, one of the most inflammatory diseases known, a distinguished team of international researchers decided to examine the benefits of curcumin. Based in the US at Baylor University Medical Center and in India at the Nirmala Medical Centre, the team's members represent some of the most advanced thinkers in the field.

**TABLE 1: MULTIPLE MOLECULAR TARGETS BLOCKED BY CURCUMIN7,40**

| **Molecular Target Inhibited by Curcumin** | **Pathologic Effect** |
|---|---|
| Tumor Necrosis Factor (TNF) | Destroys joint cartilage and other tissues |
| Vascular Endothelial Growth Factor (VEGF) | Promotes excessive blood vessel growth in inflamed joints and in cancers |
| Human Epidermal Growth Factor (EGF) | Promotes growth and activity of cells involved in joint destruction in rheumatoid arthritis32 and in many cancers |
| Estrogen Receptors | Promote growth of many breast cancers; also decrease effectiveness of drugs used in rheumatoid arthritis33 |
| Nuclear factor-kappa B (NF-kB) | Potent inducer of the inflammatory cascade by activating the genes responsible for producing inflammatory compounds |
| Curcumin suppresses activity of at least 5 categories of molecular signals that promote inflammation and joint destruction in rheumatoid arthritis, and are implicated in many cancers. | |

# Curcumin's Effectiveness Against Rheumatoid Arthritis

The researchers enrolled 45 people with active rheumatoid arthritis during a flare-up of the disease.5 That strategy allowed the researchers to test curcumin's effects at the peak of the inflammatory response. Each of the 45 patients was randomly assigned to one of three study groups. **Group 1** was the curcumin-only group. Each patient in this group received **500 mg/day** of the superior-absorbing curcumin .5,14,15 **Group 2** received the curcumin formulation in addition to **50 mg/day** of the non-steroidal anti-inflammatory drug diclofenac sodium. **Group 3** received only diclofenac. All patients took their assigned drug regimen for 8 weeks.

Throughout the study, the patients were evaluated using a standard rheumatoid arthritis disease activity score.5 In addition, blood tests were done at the beginning and the end of the treatment period, to determine the patients' overall degree of inflammatory responses. Patients also assessed their own pain levels on a 0-10 scale. Finally, the researchers tracked the number of patients who achieved improvements of **20%**, **50%**, or **70%** in tenderness or swollen joints by the end of the study.

The results were compelling, and demonstrated the practical advantages of curcumin over the standard drug treatment.

**Curcumin-treated patients hurt less.** All patients in the study experienced significant improvements in their disease activity scores by the end of the study.5 Patients in the curcumin-only group showed *improvement* of **44.5%**; improvement was **44.4%** in the curcumin plus diclofenac group, and **42.1%** in the diclofenac-only group. (Patients' self-measured pain scores showed a greater difference in favor of the curcumin-only group, which had a mean **60%** reduction in pain scores; the curcumin-plus-diclofenac group's mean reduction was **56%**; and that of the diclofenac-only group was **50%**.)

**Curcumin-treated patients' joints were less swollen and tender.** The curcumin-only group had the largest number of patients experiencing **20%**, **50%**, or **70%** reductions in overall joint swelling and tenderness (**93%**, **73%**, and **33%**, respectively).5 **Curcumin-induced measurable changes on blood tests of inflammation.** These impressive improvements in joint pain and swelling were matched by changes in blood markers of inflammation. For scientists, these improvements in the patients' blood markers of inflammation are exciting proof that curcumin is hitting its multiple targets and quelling the inflammatory process.

For example, the curcumin-only and curcumin-plus-diclofenac groups saw reductions of **11.2** and **13.3%** in the **erythrocyte sedimentation rate** test, a measure of inflammation; the diclofenac-only group had just an **8.3%** reduction. Still more dramatic results were seen on the more sensitive **C-reactive-protein** (CRP) measurement that is capable of detecting systemic inflammation; the curcumin-only group had a **52%** reduction in CRP, the curcumin-plus-diclofenac group had a **26.9%** CRP reduction, and the diclofenac-only group had a **1.5%** increase in CRP.5 **Curcumin-treated patients had no side effects.** While patients in the groups receiving diclofenac experienced drug-related adverse events, those in the curcumin-only group had none at all.

In summary, this study was the first to demonstrate that curcumin is superior to a standard anti-inflammatory drug for use in rheumatoid arthritis. It also showed that adding the standard drug did little to enhance the effect of curcumin acting alone; indeed, on many of the study's measures, curcumin alone outperformed the drug/curcumin combination.5 Let's now look at the special characteristics of the curcumin formulation that was used in this study. Those characteristics not only explain this study's success, but they also open the door to similar improvements in other inflammatory diseases for which curcumin holds promise.

**WHAT YOU NEED TO KNOW: CONTROL JOINT INFLAMMATION WITH CURCUMIN**

- Rheumatoid arthritis, a highly inflammatory condition, is the second most-common form of arthritis.
- Standard treatments for rheumatoid arthritis do little to change the underlying inflammatory causes of the disease; instead, they simply mask the symptoms while joint destruction continues.
- The more effective "biological agents" available today are not only costly but potentially dangerous in their wide array of side effects.
- Curcumin, a natural spice-derived nutraceutical, has shown promise in reducing inflammation in a host of conditions, but its usefulness has been limited by its low bioavailability in humans.
- A new form of curcumin, BCM-95®, has been developed with nearly 7 times the bioavailability of standard curcumin; it also remains at active levels in the blood for nearly twice as long.
- A clinical trial of BCM-95® in patients with active rheumatoid arthritis demonstrated superiority on most measures to a standard anti-inflammatory drug.
- Curcumin, and BCM-95® in particular, may hold hope for sufferers of osteoarthritis as well and may also be active in preventing other inflammatory conditions such as cancer and the consequences of obesity.

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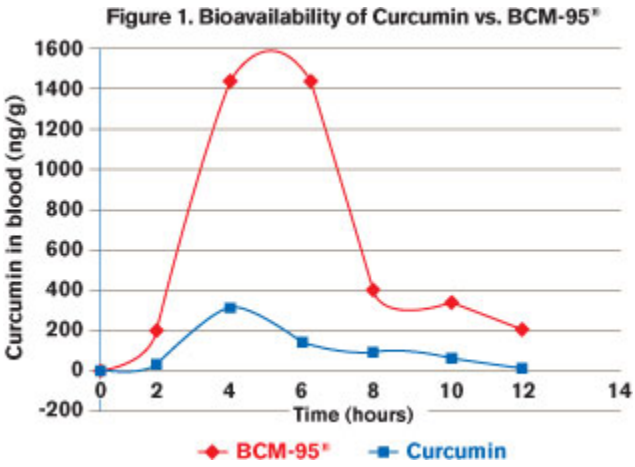
# Enhanced Bioavailability




Despite its clear ability to reduce markers of inflammation in laboratory studies, development of curcumin as a human nutraceutical has been hampered by one major obstacle. Curcumin in its natural state is not well absorbed from the human intestinal tract. In addition, it appears to be rapidly broken down both in the intestine and after absorption into the bloodstream.14,16,17

That has meant the need to deliver very large doses of the supplement, doses so large that in some cases people have balked at the size and number of capsules required to achieve a good effect.14,18,19 Doses as high as **12,000 mg** (that's **12 grams**, more than a third of an ounce) have been used in efforts to get significant amounts of curcumin into the bloodstream.18 At such high doses, even curcumin can produce uncomfortable symptoms such as abdominal fullness and bloating, though no true toxicity has been demonstrated.19

To improve effectiveness and reduce the dose size required, researchers in the rheumatoid arthritis study made use of a specialized curcumin complex that has increased bioavailability. Bioavailability is a measure of how much of a given dose of a drug or nutrient makes it into the bloodstream for delivery to target tissues.

Researchers showed in 2008 that curcumin's bioavailability could be enhanced through a very simple expedient process.14 Curcumin is first extracted from the turmeric root. Next, it is highly purified, and then reconstituted with certain other components of the original turmeric plant. Those constituents are thought to increase intestinal absorption and also reduce natural breakdown of curcumin in the body. The reconstituted curcumin mixture used by most Life Extension members today is called BCM-95®.14

**WHAT IS RHEUMATOID ARTHRITIS?**

Although many people use the term "arthritis" to refer to any condition involving painful, achy, swollen joints, there are actually several different forms of the disease. The most common form of arthritis is osteoarthritis, formerly known as "degenerative arthritis." While less common than osteoarthritis, rheumatoid arthritis still affects some 1.5 million US adults.36 Rheumatoid arthritis is more than twice as prevalent among women as among men.37

Rheumatoid arthritis is an inflammatory disease that most obviously affects the joints, but its impact is seen in tissues and organ systems throughout the body. Inflammation centers on the membranes lining the affected joints, causing them to swell, limiting their movement, and causing pain. Over time, those inflamed membranes erode the cartilage that normally cushions the joint, and eventually they even erode away the bone itself. That can deform the joint and further impair movement.

Symptoms of rheumatoid arthritis are pain, swelling, and redness of the joints. It can begin at any age (unlike osteoarthritis, which doesn't occur until at least mid-life). There is as yet no known cure for rheumatoid arthritis.37

Recent science is showing that osteoarthritis has a major inflammatory component as well, contrary to our long-held beliefs.38 That's good news for the millions of sufferers of osteoarthritis, because curcumin's powerful and multi-targeted suppression of inflammation may offer relief for them as well as for those with rheumatoid disease.

Clinical studies of BCM-95® in human volunteers have shown that its bioavailability is nearly **seven times** greater than that of a standard extract of curcumin.14,15 BCM-95® was also more than **six times** as bioavailable as a leading mixture of

curcumin with two other natural products, lecithin and piperine.14 BCM-95® is not only better absorbed than standard curcumin, it achieves significant blood levels and remains in the blood longer (See figure 1 above).15 This means that your body can reap the beneficial effects of curcumin for considerably longer. This advantage applies not only to rheumatoid arthritis, but to other conditions for which curcumin may be indicated.

## Curcumin and Osteoarthritis

**Osteoarthritis**, long thought to be a purely "degenerative" disease, is now recognized to have multiple inflammatory components. Scientists are rapidly exploring curcumin's potential role in suppressing those inflammatory processes.

One of the key features of osteoarthritis is the breakdown of the slippery cartilage that lines joints, lubricating them and cushioning them from the impact of constant use.12 That cartilage breakdown is triggered by multiple pro-inflammatory signaling molecules, many of which are secreted from the membranes that line the joint.10

Studies now show that curcumin can protect this vital lubricating cartilage in several ways. Curcumin directly counteracts the effect of those inflammatory molecules, especially within cartilage cells themselves.12 In the joint-lining membranes, curcumin suppresses the growth of the inflammatory cells that are responsible for cartilage destruction.20 And curcumin even inhibits the "cartilage-eating" enzymes that carry out the destructive process itself.21,22

**HIGHLY BIOAVAILABLE CURCUMIN FIGHTS FAT-RELATED INFLAMMATION**

The availability of the highly bioavailable form of curcumin, BCM-95®, is making possible new progress in old diseases. BCM-95® was recently shown in an animal study to reduce the amount of inflammation associated with obesity, a major cause of accelerated aging, diabetes, and other chronic diseases.24,39 In that study BCM-95® also reduced levels of one particular inflammatory molecule, IL-2 that is associated with loss of brain cells in Alzheimer's disease.39 These early reports illustrate the tremendous potential associated with the dramatic enhancement in bioavailability of curcumin in tissues throughout the body.

A pair of human studies showed that joint pain was reduced and joint function was improved, in patients taking a commercial curcumin complex that was formulated to improve absorption.23 Those studies, like the one detailed above, also demonstrated improvements in blood tests measuring inflammation.

**CURCUMIN FIGHTS CANCER**

Curcumin is taking center stage in the fight against cancer. To date, curcumin has been shown in human clinical trials to prevent or mitigate cancers of the gastrointestinal tract (such as colorectal and esophageal cancers), the breast, prostate, liver, cervix, and skin, as well as a form of leukemia, chronic lymphocytic leukemia, common in older adults.41-44 Promising results are also being published in studies of curcumin and pancreatic cancer, one of the deadliest cancers that afflict humans.45-48 Most of these trials have been early stage studies, with small numbers of subjects, but their preliminary results are encouraging.

Animal and basic lab science studies are shedding increasingly clear light on just how curcumin exerts its anticancer activities. Here's what we know:

**Curcumin prevents DNA damage.** Damage to your DNA is inevitably the first step in cancer development. Damaged or "mutated" DNA can trigger unbridled growth of cells that lack normal restraints, leading to a full-blown tumor. Studies show that curcumin can reduce the rate of cancer-inducing DNA damage.49,50 In one human study, colon cancer patients supplemented with curcumin (up to **3.6 g/day** for 7 days) had a **58%** reduction in DNA damage in their intestinal tissue.51

**Curcumin ramps up liver detoxifying enzymes.** Many cancer-causing chemicals enter your body each day; your body relies on sophisticated detoxification systems, mostly in the liver, to render those toxins harmless. Curcumin

powerfully increases production of those enzymes, boosting your body's ability to rid itself of dangerous tumor-inducing substances.49

**Curcumin quenches the fires of inflammation.** Inflammatory processes throughout your body promote cancer development. Curcumin acts at multiple molecular targets to shut down chronic inflammation and reduce production of the chemical cytokines that promote it, directly reducing your risk of developing a tumor.49,52,53 When a group of colon cancer victims took curcumin (**3.6 g/day** for four months), their blood levels of inflammatory cytokines dropped by up to **62%**.49

**Curcumin promotes cancer cell suicide.** Normal cells are equipped with a "self-destruct" program that causes them to die if they begin to reproduce too fast or become damaged in ways that could harm your body. Cancer cells disable that program early in their progression, allowing their explosive replication. Curcumin switches the self-destruct program back on, causing abnormal cells to quickly bow out.54-56

**Curcumin breaks the link between obesity and cancer.** The risk of almost all cancers is increased in obesity. That's in part because of raised insulin levels seen in obese people and those with type 2 diabetes (insulin is a growth factor that promotes cancer development).17 By reducing insulin resistance, curcumin helps lower your insulin levels and reduce your cancer risk.57, 58

**Curcumin suppresses molecules cancers need to sustain their growth and invade your tissues.** As tumors grow, they stimulate formation of new blood vessels to support their voracious appetites for nutrients and oxygen. They over-produce molecules that help them "stick" to adjacent tissue and invade it. Finally, they make enzymes that literally "melt" the protein glue that holds normal tissues together, allowing them to spread to far away parts of the body through metastasis. Curcumin acts to suppress production of many of these cancer-promoting chemicals.59

**Curcumin stops pre-malignant tissue from progressing.** Cancers in some organs, such as the intestine and cervix, develop slowly enough that we can detect areas of abnormality before they turn malignant. Removing them, however, requires invasive procedures that don't always catch every lesion and that bring with them some risk of their own. Human studies show that curcumin supplementation triggers improvement in precancerous lesions of the bladder, mouth, stomach, and cervix.41,60 Curcumin supplementation reduced the number and size of precancerous intestinal polyps by **60%** and **51%**, respectively, in people at high risk for colon cancer.61

**TABLE 2: ARTHRITIS DRUGS, THEIR EFFECTS, AND SIDE-EFFECTS**

| Drug Category | Used In | Intended Effect | Side Effects |
|---|---|---|---|
| Non-Steroidal Anti-inflammatory Drugs (NSAIDs, e.g., ibuprofen, diclofenac) | Osteoarthritis and Rheumatoid Arthritis | Relieve joint pain and inflammation | Gastrointestinal bleeding, liver toxicity, allergic reactions5,25 |
| Glucocorticoids (steroids given orally or by injection into the joint) | Osteoarthritis and Rheumatoid Arthritis | Relieve inflammation | Gastrointestinal bleeding, high blood pressure, osteoporosis, immune suppression, weight gain, loss of insulin sensitivity26 |
| "Conventional" Disease-Modifying Anti-Rheumatic Drugs (DMARDs, e.g., methotrexate, leflunomide, sulfasalazine,) | Rheumatoid Arthritis | Slow disease progression | Immune suppression, increased infection risk, may interfere with responses to vaccination27 |

| | | | |
|---|---|---|---|
| "Biologic" DMARDs (e.g., infliximab, etanercept) | Rheumatoid Arthritis | Block or reduce production of inflammatory mediators | Increased risk of infection,28-30 injection site reactions,28,29 may interfere with responses to vaccination,27 disturbed lipid profile31 |

## Summary

Inflammation lies at the heart of virtually all diseases associated with aging. In fact, people with inflammatory conditions experience accelerated aging that affects every tissue and organ in their bodies.

Rheumatoid arthritis is one of the most aggressive and destructive of the inflammatory conditions that afflict humans, and it is one that has proven resistant to all but the most dangerous forms of standard medical treatment.

Curcumin has held out great hope for management of all kinds of inflammatory diseases, but its benefits have been hampered by its poor absorption and availability to inflamed tissues. A superior-absorbing curcumin formulation( BCM-95®) has up to **7 times** the bioavailability of commercial products.

A clinical trial of BCM-95® among sufferers of active rheumatoid arthritis demonstrated not only that the formula was safe, but also that the effectiveness of only **500 mg** a day exceeded that of a standard anti-inflammatory drug.5

Additional new studies suggest that this curcumin formula can reduce obesity-associated inflammation as well.24 Together, these findings suggest that highly bioavailable curcumin represents an entirely new chapter in the management of some of humankind's most feared diseases.

If you have any questions on the scientific content of this article, please call a **Life Extension**® Health Advisor at 1-866-864-3027.

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