Examine.com

Research Digest

Exclusive Sneak Peek

Issue 7 ◆ May 2015

Click here to purchase ERD

Spicing up your workout

Curcumin supplementation likely attenuates delayed onset muscle soreness (DOMS)

Introduction

Curcumin is probably best known as a component of the herb turmeric. Turmeric contains 2–5% curcuminoids such as curcumin and its related compounds, methoxy-curcumin and bisdemethoxycurcumin. Curcuminoids are phenolic compounds that give turmeric (and curry) its yellow color, and have been in use as a remedy in Indian Ayurvedic and Chinese medicine for several millennia. In recent years, biomedical research has shown that curcuminoids elicit multiple biological effects that are relevant to human health, including anti-inflammatory, analgesic, anti-cancer, antidepressive, and antidiabetic properties.

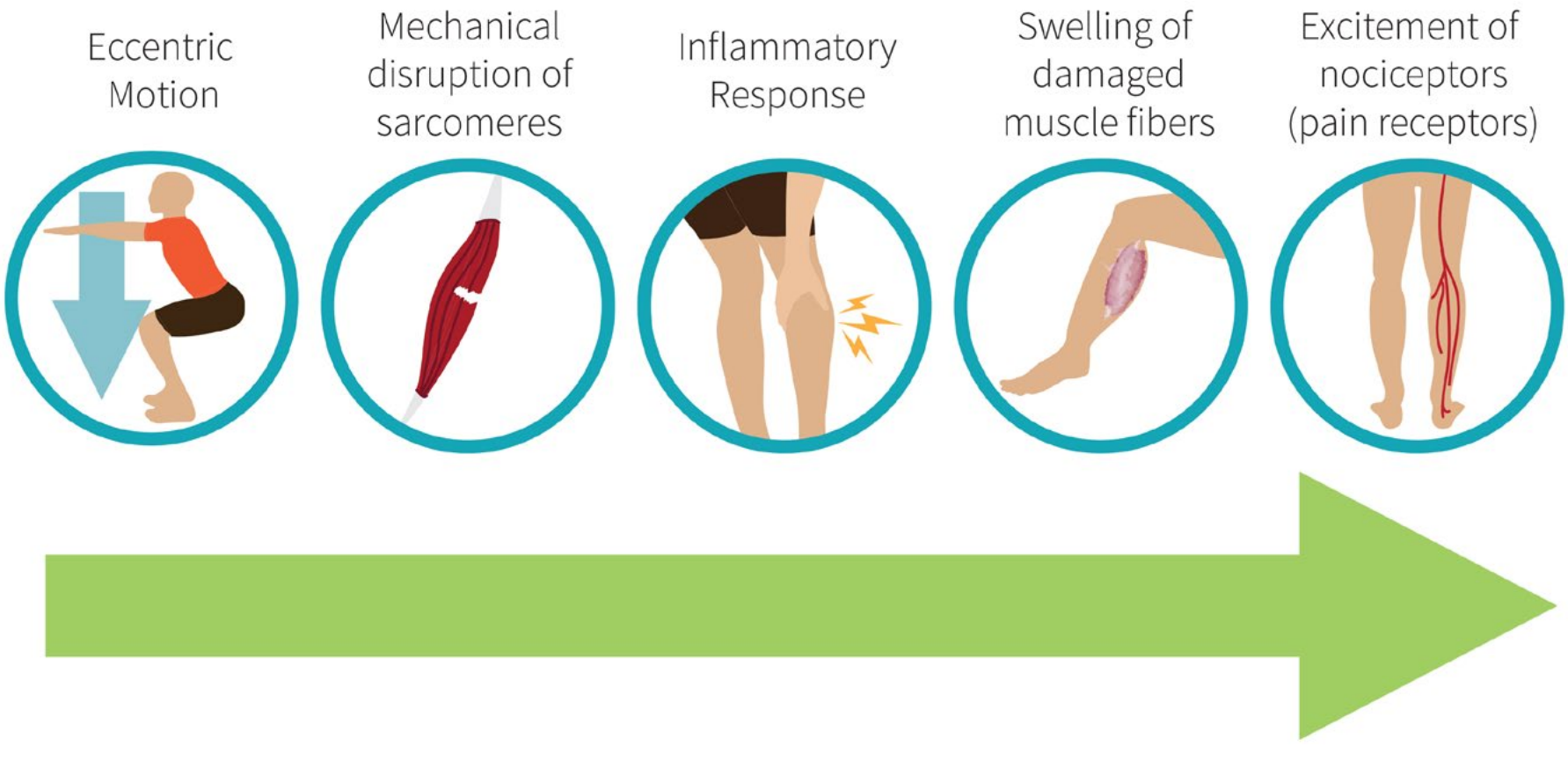
A search for "curcumin clinical trial" in Pubmed yields no fewer than 273 hits, underscoring the scientific interest in the biological activity of this chemical. Doing the same kind of search for cinnamon or even resveratrol yields less than half that number, which shows that interest in curcumin is strong within the research community.

Scientific interest in curcuminoids started in the 1980s, when studies showed that the administration of curcuminoids decreased the physiological markers of inflammation and improved morning stiffness, walking time, and swelling in patients with rheumatoid arthritis while also reducing postoperative pain. Recent research has also shown some of the mechanisms through which they work. For example, curcuminoids have been shown to increase expression and activity of peroxisome proliferator-activated receptor gamma (PPAR-gamma), which mediates anti-inflammatory and glucose uptake processes. Curcuminoids are also potent antioxidants, a property which may protect DNA from oxidation damage. Also, they inhibit activation of nuclear factor kappa B (NFkappaB), which further contributes to their anti-inflammatory effects. Furthermore, they inhibit nitric oxide (NO) production through inhibition of inducible and endothelial nitric oxide synthase (iNOS and eNOS), which may also mediate anti-inflammatory effects.

It is very well known that unaccustomed physical activity results in sore muscles, affectionately referred to as delayed onset muscle soreness (DOMS) amongst gym goers. Exercise performed in a way to which you are not accustomed, in terms of load or intensity, range of motion, or degree of muscular fatigue, will result in some muscle damage. The majority of this damage is induced during the eccentric phase of movement, e.g., when "yielding" to gravity and descending in squats. The muscle damage is characterized physiologically by soreness, tenderness, reduced strength, reduced stretch tolerance, swelling, and increases in plasma creatine kinase (CK) and sometimes even plasma myoglobin. All of these biomarkers normally peak 1–2 days after the inducing exercise bout and usually last no more than 3–5 days.

This pattern underscores that the muscle damage phenomenon is not just a mechanical tearing damage, but a progressive biochemical phenomenon. The general process is depicted in Figure 1. At a cellular level, these effects are usually explained by membrane disruption of muscle fibers and subsequent invasion of neutrophils, monocytes, and natural killer (NK) cells secreting cytokines, resulting in pain sensation, localized edema, and increased temperature. However, it should be noted that this process is very complex and in reality, it's poorly understood.

Figure 1: The development of DOMS



> “[...] only one leg was trained while the subjects took curcumin and the other one was trained without taking it, acting as a control.”

Thus, the purpose of the current study was to examine if and to what extent a curcumin supplement prevented the muscle damage and soreness induced by a heavy eccentric exercise bout.

Exercised-induced muscle damage involves some inflammatory processes that may contribute to DOMS. Since curcumin is known to have anti-inflammatory properties, the effect of curcumin on DOMS was investigated.

Who and what was studied?

Prior to enrollment, the study organizers performed a power analysis that showed that 19 subjects were needed to detect minimal meaningful differences in pain scores in the study. 19 subjects were initially included, but two withdrew before starting because they were unable to comply with the study commitment. This left a sample of 17 adult men who were healthy, nonobese, and recreationally active, but not doing lower-body resistance training.

Subjects in the study were instructed to do leg workouts, with or without a curcumin supplement. To control for differences between individual responses and to allow the subjects to be their own controls, a design was used in which only one leg was trained while the subjects took curcumin and the other one was trained without taking it, acting as a control. Also, to compensate for any possible differences between dominant and nondominant legs, the leg to be trained first and the training session in which the subject would receive the curcumin supplement or the placebo was randomly selected for each subject. The subjects were also blinded to the nature of the supplement.

The experiment was set up so that there would be two separate training sessions, one for each leg. In one bout, the subjects would ingest capsules containing the curcumin supplement and in the other they would ingest placebo capsules. The supplementation protocol consisted of taking five capsules (containing curcumin or placebo) twice daily for 2.5 days before and after each exercise bout, with a 14-day washout period in between the exercise bouts, allowing the curcumin to clear the subjects’ bodies.

The curcumin supplement was actually a blend of curcuminoids—29mg of bisdemethoxycurcumin, 62.7mg of demethoxycurcumin, and 964mg of curcumin, totalling about 1060mg of curcuminoids per capsule. The placebo was an inert plant cellulose compound. The curcumin supplement and the placebo were put in identical opaque capsules, preventing the subjects from identifying them by color, smell, or taste.

Because eccentric exercise is known to stimulate more muscle damage than concentric exercise, the exercise protocol was seven sets of 10 repetitions of “eccentric leg presses.” During the eccentric (or “yielding”) phase, the weight would be supported only by the “test leg” from full extension down to 90 degrees, while during the concentric (or actual lifting) phase, both legs would be used to press up the weight. Before the test workouts, the highest weight the

subjects could lift for one repetition with one leg (their "1 repetition maximum," 1RM) was determined. For the test workout, they would do 120% of that weight for five sets of 10 repetitions followed by another two sets of 10 repetitions at 100% of their 1RM. All subjects completed this protocol.

The subjects did a testing panel before each exercise bout (baseline), immediately after the bout (post) and again 24 and 48 hours later. The testing panel looked at muscle pain both during exercise and passively, muscle tenderness and swelling, jump performance, and biochemical markers of muscle damage and inflammation including CK, interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α).

The data were analyzed using a technique called magnitude-based inferences, which replaces the very binary yes/no statistical significance paradigm with a more gradual description of the likelihood of observed between-group differences being significant treatment effects.

Seventeen healthy men participated in a crossover study where they were randomized to exercise one leg using eccentric leg presses while taking either 2.5g turmeric or placebo twice a day for 2.5 days before and after the exercise bout. Muscle pain, tenderness, and swelling were measured along with performance on a single-leg jump test and biochemical markers for inflammation and muscle damage. After waiting 14 days, the other leg was exercised in a similar manner while switching placebo for turmeric or vice versa.

What were the findings?

First of all, all 17 subjects completed the study, so there were no issues with compliance. Furthermore, the increases in muscle soreness and plasma CK across both groups in the study confirmed that the exercise protocol was adequate to cause muscle damage.

As seen in Figure 2, curcumin reduced exercise-induced pain in single-leg squats, single-leg vertical jumps, gluteal stretch, and walking downstairs, with moderate-to-large (0.6-2.0) effect sizes at the 48-hour time point and for all of those except walking downstairs for the 24-hour time point; effect sizes ranged from moderate (0.6-1.2) to very large (>2.0) and probabilities of "likely" (>75%).

Curcumin improved first-jump performance from immediately post-exercise to 24 hours and 48 hours post-exercise, relative to the placebo group (by 15.4% and 15.8%, respectively), whereas the difference between the curcumin and placebo group were trivial during second and third jumps.

The cutoffs used for these magnitude-based inferences

The researchers assigned cutoffs for the differences observed, and labeled them with qualitative terms for magnitude and probability. They reported both the probability and magnitude of the effects using these qualitative terms.

Effect sizes were reported as: "trivial", 0.0–0.2; "small", 0.2–0.6; "moderate", 0.6–1.2; "large", 1.2–2.0; and "very large", >2.0

Probabilities were reported as "almost certainly not" <0.5%; "very unlikely", <5%; "unlikely", <25%; <75%, "possibly", <75%; "likely" >75%; "very likely">95% and "almost certain", >99.5

Thus a statistical effect (i.e. between-group difference) could be described as an "unlikely" "moderate" effect, if there was <25% probability of an effect of 0.6-1.2 effect sizes.

Curcumin likely (>75%) had a small lowering effect on serum CK 24 and 48 hours post-exercise, relative to placebo. While curcumin did not affect TNF-α, it influenced IL-6 levels in a rather peculiar manner: It induced a small increase in the IL-6 levels relative to placebo immediately post-exercise and 48 hours post-exercise, and decreased it 24 hours post-exercise (all with probabilities of "likely").

Finally, there was no effect of curcumin on swelling or tenderness. However, this could be a signal-to-noise issue, as the study was designed with statistical power for detecting differences in pain, not in swelling or tenderness. If the variation in these measures were higher than for pain, which the authors hint at, this could mean that the study is simply underpowered to detect differences in these measures.

Curcumin decreased most measures of pain relative to placebo, and improved first-jump performance in a 3-jump test. There were also minor effects on biochemical markers of inflammation and muscle damage.

What does the study really tell us?

From a technical point of view, the study is very well executed, with a proper a priori sample size calculation, blinding, a strong study setup, and sound statistical methods and reporting.

As far as the biology goes, the study shows (not surprisingly) that curcuminoids do in fact inhibit part of the muscle damage induced by unaccustomed exercise, in terms of subjective markers, such as pain; pseudo-objective markers, such as jumping performance (pseudo-objective, because it also depends on pain); and objective markers, such as serum CK. This has been shown before in animal studies with eccentric exercise.

One finding that stands out is the effect of curcumin on IL-6. It appears as if it increases the exercise-induced effects on IL-6 acutely and at 48 hours post-exercise, but inhibits it at 24 hours post-exercise. IL-6 can be considered a good guy as well as a bad guy, depending upon circumstances—the acute exercise-induced increase in IL-6 has been proposed as an effector of some of the beneficial metabolic effects of exercise (here and here), while chronically elevated IL-6 is generally considered catabolic to muscle and is associated with a range of morbidities and mortality in the elderly. So, it's possible that curcumin potentiates the acute beneficial metabolic effects of exercise through IL-6.

This study extends findings about curcumin's effects on eccentric exercise in animals. The pattern of curcumin's effects on IL-6 may indicate a somewhat novel finding in humans.

Figure 2: Improvements in leg pain from taking curcumin

OUTCOME		LIKELIHOOD 24 HRS	LIKELIHOOD 48 HRS
SINGLE LEG SQUAT		VERY LIKELY	VERY LIKELY
WALK DOWNSTAIRS		NONE	VERY LIKELY
STRETCH QUADS		NONE	NONE
STRETCH GLUTES		LIKELY	MOST LIKELY
SINGLE LEG VERTICAL JUMP		VERY LIKELY	LIKELY

The big picture

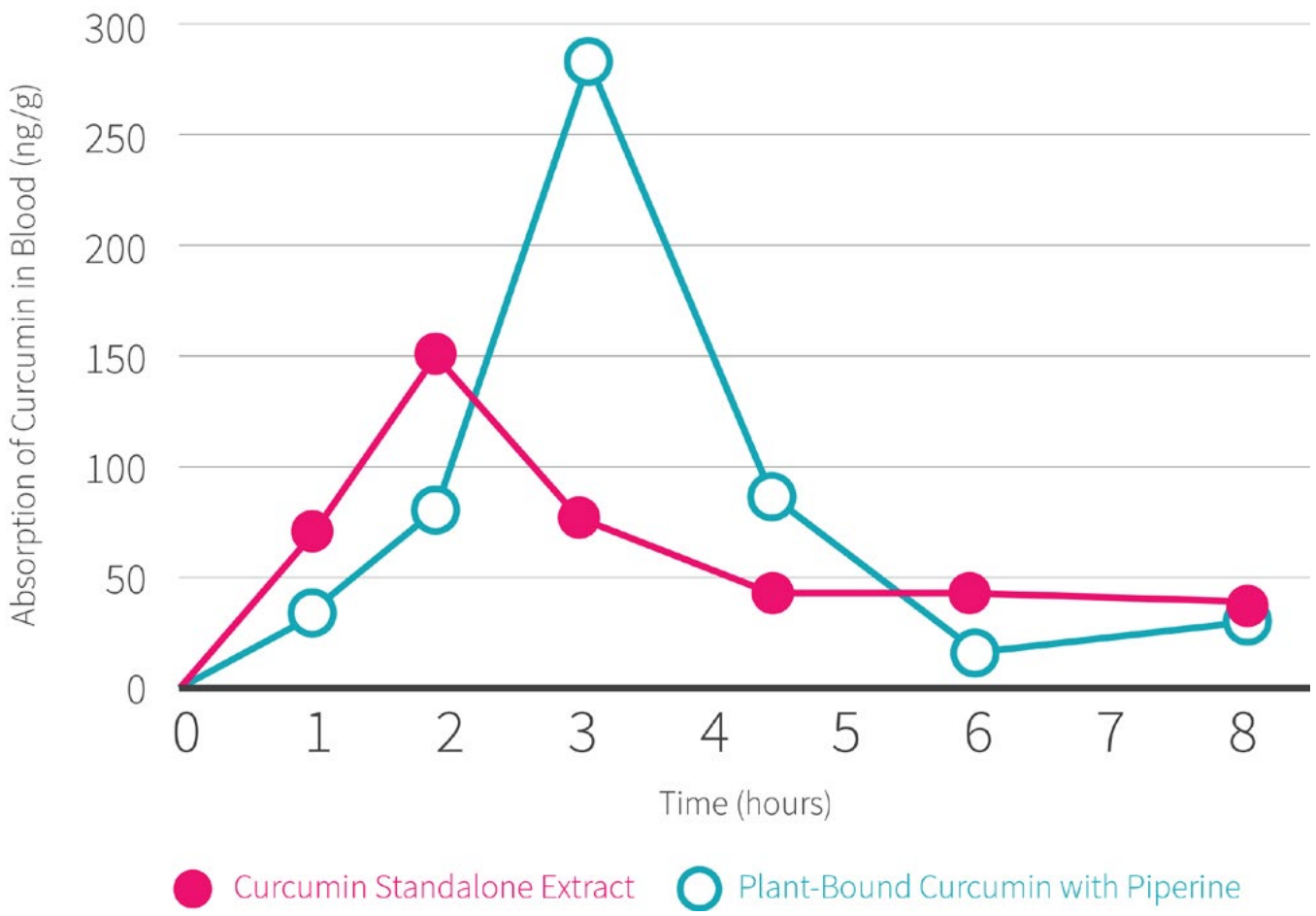
A large number of studies have looked into ways to inhibit DOMS with a variety of anti-inflammatory and analgesic compounds, but it turns out that the inflammation in muscle damage is somehow tied to the remodelling of muscle. In some cases, and maybe most of them, inhibiting soreness of muscle damage may also partially inhibit the adaptation, i.e., hypertrophy. As there are no longitudinal human resistance or endurance training studies with curcumin administration, we cannot know if the inhibition of muscle damage provided by curcumin also inhibits the adaptation that we sweat so much to achieve, making it hard to draw any conclusions from the effects.

In reality, of course, muscle damage is not that big of a problem for regular trainees, because muscles develop a resistance to damage through what is known as the "repeated bout effect", which is described in the FAQ section. So if exercise intensity is increased gradually, as it typically should be, severe muscle soreness will hardly ever be encountered. The only people to whom this could be interesting for performance reasons would be individuals who are subjected to physical workloads to which they cannot realistically be accustomed. This could be the case for ultra-endurance athletes, who may be working continually for 3, 4, or 5 days in row in competitions, an amount of work for which it is impossible to be 100% conditioned.

It could also be relevant for athletes in competitions with tightly packed events or military personnel, as they sometimes have to maintain muscle function during sustained physical activity with little chance of rest. There's no room for muscle soreness, when on long-distance recon mission. For these individuals, reducing soreness and muscle damage is as relevant as sustained performance is important, even in the light of possible impaired adaptation.

Lastly, this trial may actually have underestimated the potential effect of curcumin on DOMS, as additives that increase absorption (such as piperine, show in Figure 3) were not used.

Figure 3: Absorption of curcumin with and without piperine (in rats)



Source: Shoba et al., Planta Med. 1998

This study provides evidence that curcumin may be useful for pain and some aspects of performance in the short-term. Longer-term studies are needed to ascertain the effects of chronic curcumin consumption on muscle growth.

Frequently asked questions

Is muscle damage bad?

No, muscle damage is not inherently bad. But it's not inherently good, either. With resistance training, protein synthesis is elevated only for approximately two days after training. When muscles are sore for four or five days, it does not mean that muscle growth is occurring throughout this period as muscle protein synthesis has been repeatedly shown to increase for only 48 hours. Rather, it keeps you from training again and thereby providing the muscle with a new stimulus. If anything, muscle damage or DOMS is a marker of how accustomed you are to a given stimulus. And this "accustomedness" dissipates with time. Alas, the best way to get sore from a workout is to do it infrequently.

What is the relevance of such an extreme eccentric exercise muscle damage model?

One could ask if having untrained subjects do 7 set of 10 repetitions of maximal eccentric contractions is even related to exercise. Truth be told, it's not. The stimulus is intended to create a degree of muscle damage and must therefore be grossly unaccustomed, unlike what would be considered a typical exercise prescription. Muscle damage models are used to research basic behaviors in muscle biology, particularly membrane disruption and activation of the resident muscle stem cells, the satellite cells, and the training and training-induced response should not be considered "training" *per se*.

What is the "repeated bout effect"?

Muscle damage only occurs with unaccustomed exercise. So when the muscle gets used to a given stimulus, muscle damage and DOMS no longer manifest. In fact, it has been shown that a single bout of exercise can provide some degree of protection against another bout completed nine months later, without any exercise in the interim. Exactly what mediates this protective effect of exercise is poorly understood.

What should I know?

Unaccustomed exercise, particularly high-force eccentric exercise, is known to induced muscle damage and soreness, known as DOMS. In this study, subjects went through an exercise protocol designed to induce muscle damage in order to test if curcumin supplementation would reduce the degree of muscle damage, strength deficit and soreness caused by the exercise. The study showed that curcumin administration reduced exercise-induced soreness and prevented some aspects of exercise-induced strength deficits. ◆

> "No, muscle damage is not inherently bad. But it's not inherently good, either."