



AIS SPORTS SUPPLEMENT FRAMEWORK

CURCUMIN (DIFERULOYLMETHANE)

What is it?

- > **Overview:** Curcumin is the most abundant phenolic compounds in turmeric, a spice commonly found in curry powders and sauces with a long history of use in cooking and in traditional Indian and Chinese systems of natural medicine.¹ More recently, curcumin has been investigated for medicinal properties, health, and possible sport recovery and performance benefits. Turmeric is “generally recognised as safe” by the US FDA, indicating that it can be a safe food additive. However, curcumin is an unstable compound and its bioavailability is very poor. As such, recent efforts have focused on developing curcumin formulations with greater bioavailability and systemic tissue distribution. Broadly, these formulations include lipid additions (turmeric oil and piperine), adsorption on matrices (lecithin), and curcumin size reduction to nano particles.²
- > **Curcumin has a number of potential health/ performance benefits**
 - In health, curcumin has been shown to aid in the management of oxidative stress and inflammatory conditions such as metabolic syndrome and arthritis.³
 - Curcumin has been found to have non-steroidal anti-inflammatory drug-like actions as evidenced by a largely dampened activity of markers of oxidant and inflammatory pathways (e.g. COX-2 and NF-κB signalling) in disease^{4,5}, although clear associations between pathway markers and muscle performance in athletes remain unclear.
 - Curcumin has been associated with reduced exercise-induced muscle damage (EIMD) and exercise-induced muscle soreness (EIMS), plus lowered delayed-onset muscle soreness (DOMS). As such, curcumin may be used in the treatment of pain and inflammation following exercise, reduction of oxidative stress following exercise, plus alleviation of muscle damage, improving muscle recovery, EIMS and DOMS.
 - Curcumin supplementation usually has no noticeable side effects. However, there are safety concerns when consumed in doses > 2g/day.
 - Effects of long-term supplementation on the magnitude-efficacy of the training response and adaptability are at the time of writing unknown, but warrant investigation.
- > **Mechanistic evidence and nature of benefits for athletes.**
 - Reduced pain following heavy muscular exercise loading is reported by way of lower DOMS or other muscle soreness scores in most⁶⁻¹⁰ but not all studies.¹¹
 - The reduction in DOMS is also associated with improved joint range of motion, suggesting reduced musculotendinous stiffness⁶. Curcumin also lowers the marker of muscle damage - creatine kinase (CK) - concentration within the blood, suggesting the reduced muscle soreness findings may be associated with attenuation of muscle cell damage. More conclusively, a recent meta-analysis found a significant effect of curcumin supplementation on reducing CK [weighted mean difference [WMD] = -48.5 IU.L⁻¹; 95% CI: -80.7, -16.4; p=0.003] and muscle soreness index [WMD = -0.5; 95% CI: -0.8, -0.2; p=0.001], leading to the author conclusion that “curcumin may be known as a priority EIMD recovery agent in interventions”.¹⁰
 - Reduced inflammation is inferred from a reduction in markers of systemic inflammatory modulatory pathways, models which were developed largely from *in vitro* research models within the (health) therapeutic use setting. Additionally, advanced glycation end-products (AGEs) produced from muscle-damaging eccentric exercise (e.g. jumping, resistance training, and hard running), are associated with reduced subsequent performance, although may not be mechanistically determinant but a side effect. Nevertheless, 3 months of curcumin plus *Boswellia serrata* (BSE) gum resin supplementation was shown to lower AGEs and lipid- peroxidation outcomes in athletes.¹² Six days of curcumin supplementation during a bout of EMID attenuated post-exercise concentration of the inflammatory cytokines IL8 and TNF-α, but not IL6 or IL10.¹¹ Meanwhile in a similar experimental model, curcumin increased IL6 concentrations at 0-h (31 %; 90%CI ±29 %) and 48-h (32 %; ±29 %) relative to baseline, but decreased IL-6 at 24-h relative to post-exercise [-20 %; ±18 %] ⁷. In contrast, Tanabe et al.¹³ reported no significant changes in IL6 and TNF-α.
 - Reduced oxidative stress markers post-exercise in the urine or blood support other *in vitro* models suggesting anti-oxidant effects. For example, curcumin can modulate the activation of T-cells, B-cells, NK cells, neutrophils, macrophages, and dendritic cells¹⁴, and at low doses, curcumin can also enhance antibody responses, suggesting it may modulate the immune system.¹⁵ However, in athletes, results are mixed and not all chronic (e.g. 28 d) supplementation studies show consistent effects on system oxidative stress or inflammatory markers.^{7,9}



> Effects on recovery and performance in athletes.

- A selection of well-designed and executed studies suggest worthwhile improvements in skeletal muscle function following a single bout of strenuous or damaging exercise; whether these largely laboratory-based surrogate muscle-function outcomes translate to real-world performance remains to be established.
- Nicol et al.⁷ supplemented athletes with a very high dose of curcumin stated as equivalent to 0.3 g/kg/d or apparently ~1060 mg twice daily (from 2.5 g curcumin), or control, for 2.5 days before and 2.5 days after severe EMID. Associated with moderate-large standardised reductions in pain perception during single-leg squat was a small increase in single-leg jump performance (15%; 90 %CL ± 12%) with curcumin supplementation.
- Tanabe et al.⁷ gave 14 healthy men 150 mg/d curcumin before and 12 h after maximal eccentric arm exercise. Maximal voluntary contraction torque decreased less and recovered faster (e.g. 4 days post-exercise: -31 ± 13 % vs. -15 ± 15 %) with curcumin compared with placebo.
- Delecroix et al.¹⁶ gave 10 elite rugby players 6 g curcumin + 60 mg piperine/d for 48 h before and following EIMD. Curcumin supplementation resulted in a moderate reduction in sprint mean power output [-1.1; 90%CI -1.9 to -0.9] at 24-h post exercise, but no other outcomes were clear. The lack of a consistent performance outcome and the addition of piperine (which may enhance bioavailability of curcumin up to 2000%), needs to be considered in the context of this study.
- Hillman et al.⁶ studied the effects of a 500 mg dose of curcumin supplementation twice daily for 10 days (6 days pre, day of and 3 days post exercise) on DOMS and muscle power following plyometric exercise in 22 men and women. Following 5 x 20 drop jumps on day 7, vertical jump test performance was reduced in placebo but maintained following curcumin supplementation (curcumin benefit +1.6 inches 90%CI 0.63 to 2.6).
- Several other studies were conducted, but used measures of performance that have poor reliability. For example, Jäger et al.¹⁷ supplemented two doses for 8 weeks but report mostly inconclusive results to muscle function, probably related to the use of isokinetic peak torque as the performance measure¹⁷, which has poor reliability.¹⁸
- Overall, there is building evidence to suggest a benefit to recovery of muscle performance in power or explosive activities from several days of curcumin supplementation at specified doses (500-2500 mg of curcumin twice daily). However, the evidence remains mixed, coupled with confounding effects from co-ingredients, and more high-quality studies in explosive, power and sprint, plus endurance models, are required before firm dose efficacy and performance-based conclusions can be formed.

What does it look like?

> Curcumin is a yellow powder most often available in capsule form.

- Examples of commercial curcumin in unmodified form are CurcuFresh⁹ and combined formulation.⁷
- Commercial products with adjunct ingredients to improve bioavailability include Meriva®, a Phytosome® delivery system⁸, CurcuWIN®, which contains other antioxidants.^{17, 19}

> Format and Bioavailability

- Unformulated curcumin has poor bioavailability due to poor absorption, rapid metabolism and elimination from the body.²⁰ In humans, when unformulated curcumin was administered, only low levels of curcumin were detected in the serum of one-third of the individuals given very high doses of curcumin (10,000-12,000 mg/day).²¹
- Nutraceutical companies have trialled formulating curcumin with adjuvants (e.g. piperine, turmeric oil, etc), nanoparticles, liposomes, micelles, nano-curcumin, and phospholipid complexes²⁰, some of which may also be bioactive making a clean inference to the bioaction of curcumin difficult. Processing may also provide curcumin metabolites which have a shorter half-life^{20, 22}. Some authors have used more bioavailable forms.^{8, 11, 19}
- Only two studies have used commercially available supplements^{7, 9}, which potentially require higher doses, but are cheaper for consumers. Currently, there is a lack of clarity on what products are most efficacious and more research and consumer data is required.
- Effective dose of curcuminoids (the bioactive fraction of total curcumin) is probably key to optimal bioactivity i.e. aiming for a total daily dose of at least 200 to 1000 mg per day. There is uncertainty on the safety of curcumin larger than 2g/day and no more than 8 g of total curcumin should be taken per day.²³
- Currently, the optimal dose of curcumin for post-exercise recovery is unknown. Previous studies have used 90 to 6000 mg/d doses, with 90 mg the lowest effective dose to show some impact on recovery markers²⁴. Clear benefits to subsequent performance were seen with 500 mg⁶ or 2.5 g⁷ of curcumin taken twice daily, for 10 or 5 days respectively.
- Effective dosage for an individual may also be influenced by training volume and intensity, as exercise load affects (generally increases) endogenous antioxidant response. The amount of exogenous antioxidant-rich foods within the normal diet (e.g. fruits and vegetables) can also increase the antioxidant response.

How and when do I use it?

- > Curcumin as a supplement will most frequently come in capsule form.
 - The scope of research to date covers a 2 day to 12-week supplementation period prior to a test bout of exercise and 24-72 h recovery regimen. The clearest evidence for efficacy is 2-5 day supplementation at a high dose (2 x 500-2500 mg of curcumin per day; or a dose of a hybrid product providing around 200-1000 mg of curcuminoids per dose) prior to exercise that the athlete is interested in recovering from.
- > Summary of some protocols of use from various Turmeric extracts summarised in²⁵:
 - 180 mg-5 g/day of curcumin
 - 180 mg/day of curcumin Theracurmin® (nano-curcumin)
 - 500 mg/day of Meriva® curcumin (with food-grade lecithin)
 - 6 g of Turmeric extract + 60 mg of piperine/day
 - 400 mg/day of Longvida® curcumin (offers a 7.5-hour half-life, compared to the 2-3 hour half-life of standard curcumin)

Are there any concerns or considerations?

Effective dose and co-ingredient risk

- > Optimal, threshold, and minimal effective dose and bioavailability of the native and advanced available compounds remain to established.
- > Advanced formulations often carry additive and adjunct compounds that may be bioactive. Sports dietitians and athletes should be cautious in regards to inadvertent doping.
- > Turmeric extracts contain active non-curcuminoid fractions of polysaccharides (turmerinosaccharides) and Turmeric oils. There is weak evidence for the efficacy of these products (Turmacin®) in improving pain threshold and range of motion in healthy participants.²⁶

Unknown effects of long-term use on training response

As with some other compounds that dampen the oxidative and pro-inflammatory response to exercise (e.g Vitamin E), the possibility of reducing the training-response signal for adaptation requires systematic investigation. Until this work is complete, coaches and athletes should be aware that the long-term effects of curcumin on training adaptation is unknown.

Where can I find more information?

Supplement safety information and batch tested product list

www.sportintegrity.gov.au/what-we-do/anti-doping/supplements-sport

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Athletes should be aware that the use of supplements may have doping implications. Athletes are reminded that they are responsible for all substances that enter their body under the 'strict liability' rules of the World Anti-Doping Code. Some supplements are riskier than others. The Sport Integrity Australia (SIA) app is a useful resource to help mitigate the risk of inadvertent doping by helping to identify supplements that have been batch-tested. The SIA App provides a list of more than 11,000 batch-tested products. We recommend that all athletes consult the educational resources of SIA regarding the risks associated with supplements and sports foods.. While batch-tested products have the lowest risk of a product containing prohibited substances, they cannot offer you a guarantee that they are not contaminated (www.sportintegrity.gov.au/what-we-do/supplements-sport).

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