first endurance

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HALO™

RESEARCH

CURCUMINOIDS & OMEGA-3 SUPERBA2™ KRILL OIL

JOINT HEALTH
MUSCULE-SKELETAL SUPPORT
BRAIN & CARDIO HEALTH
CURCUMIN & SUPERBA2™ OMEGA-3

- Alleviates joint discomfort during & following exercise*
- Regulates exercise-induced inflammation and soreness*
- Proprietary HALO blend optimizes uptake & effectiveness*
- Supports cognitive brain functions & immune system health*

Use Directions: Take two capsules daily. Consider a second serving following extreme exercise.

SUPPLEMENT FACTS

30 servings per container.

Serving size	**2 Capsules**
Amount Per Serving	**% Daily Value**
Choline (as phosphatidyl choline) 25 mg	5%
HALO Proprietary Blend [Krill Oil as Superba2™,** Turmeric Extract (*Curcuma longa*)(rhizome)(95% curcuminoids)] 800 mg	*

*Daily Value not established

Other Ingredients: MCT oil, hypromellose, vanillin, silica.

** Superba2™ is a registered trademark of Aker BioMarine.

Allergens: Shellfish (Krill)

STORE IN A COOL, DRY PLACE
KEEP OUT OF REACH OF CHILDREN

No artificial flavors or sweeteners
MADE IN THE USA

HALO[1]: OMEGA-3[2] & CURCUMINOID[3] COMBINATION FOR YOUR MOVING PARTS – A WORMHOLE FOR FASTER RESULTS

Instead of trying to go faster than the speed of light, we found a wormhole.

Sooner or later, all long-term endurance athletes face the issue of how to keep exercise performance at its peak. Fueling and hydration should not be hindrances to peak performance anymore. What else could go wrong? Your moving parts – joints and bones. Musculoskeletal systems (connective tissues) have not been given the same nutritional attention as muscular functions. Connective tissue dysfunction is common and normal for long-distance exercisers, but seldom specifically addressed by a focused dietary supplement approach. We have changed that lack by introducing HALO, a very specific and unique omega-3/curcuminoid combination new to endurance athletes.

Almost everyone, including high-performance athletes, are not getting enough omega-3s for optimal health. Few are using curcuminoids regularly, and even if so, the current products available have not delivered on curcumin's promise as shown clearly by a massive amount of in vitro and animal study results not being matched by human studies. Until now.

Controlled human clinical studies show benefits for musculoskeletal tissues during long-term endurance exercises for both omega-3s and curcumin/curcuminoids. Overall, the results are agreed upon as statistically significant, but a closer look sees that the magnitude of change could be improved – results are smaller than what real-life exercising individuals want and need. Something is better than nothing in this case, but we want more – we want definite, reproducible and noticeable improvements in feeling better, and being better, too. Insiders in the fields of omega-3s and curcumin know that each nutrient has not been optimized for delivery to tissues in bioactive forms. There is a room for improvement to achieve real-life benefits.

HALO has changed that delivery roadblock by utilizing a unique, patent-pending, proprietary blend of krill oil and curcuminoids combined in a way to efficiently deliver each nutrient where they belong and work the best – your cell membranes. By realizing and applying basic biology and biochemistry facts, HALO has leaped ahead of prevailing practices to solve the issues that suppress delivery and activity of both omega-3 fatty acids and curcuminoids. We went with how human bodies work, not how to force more compounds

[1] HALO™ is a registered trademark of First Endurance. In this document, the all-caps word "HALO" refers to HALO™ trademarked product and has been removed from common usage in this document in order to improve readability.
[2] Omega-3 and omega-3s will be used throughout this Research Packet to describe long-chain, polyunsaturated omega-3 fatty acids, aka n3-PUFAs, primarily EPA (eicosapentaenoic acid, C20:5 n3) and DHA (docosahexaenoic acid, C22:6 n3).
[3] Curcumin is the major curcuminoid in turmeric roots and dietary supplements. Some products use relatively pure (95%) curcumin only (natural or synthetic), and some use all three curcuminoids naturally present in turmeric. Sadly, even the scientific literature has degenerated into calling curcuminoids "curcumin" or "curcumins" – be aware that curcuminoids are more than curcumin, but sometimes are called "curcumin." Curcumin is becoming a generic term, which is imprecise for differentiating what exactly is in a product, or used in a research article. We feel there is a beneficial difference to using the complete set of curcuminoids, which mirrors the thousands of years of human use of turmeric root powders in foods (mostly as a component of curry). Curcumin alone does not match the human dietary usage of curcuminoids as in turmeric.

into the body against how our bodies work. Instead of trying to go faster than the speed of light, we found a wormhole.

HALO – MOST EFFICIENT OMEGA-3 & CURCUMINOID DELIVERY

Omega-3s from the usual source -- oily triglyceride molecules from seafood, softgels or capsules -- take a long, metabolically-bumpy, winding road to get where they exert their health benefits in cell membrane phospholipids. Omega-3 oils do not dissolve in watery liquids, and need to be deconstructed and then restructured by digestion into new oily triglycerides shuttling around your body in protein-coated luggage bags (lipoproteins). Next, omega-3 triglycerides need to enter cells via a complicated and tightly controlled series of signals, receptors and transporters, where they can be stored (poorly) inside cells as fat, or undergo yet more deconstruction into omega-3 fatty acids to be burnt as fuel or reconstructed into new membrane phospholipids. During all these processes, omega-3 fats need constant antioxidant protection to keep from going rancid (oxidized). Omega-3s naturally attract oxidative free radicals like magnets because of their multiple double bonds, an inescapable fact. Rancid omega-3s are anti-omega3s – a little-known fact. Because oil and water do not mix, these processes need to take place surrounded by specialized proteins, meaning a rather cumbersome utilization process, especially compared to sugars and proteins.

HALO uses cut-to-the-chase Superba2™ krill oil, which protects its membrane-ready omega-3 phospholipids by enough fat and self-contained antioxidants to efficiently bypass the usual fat processing mosh pit, sending its omega-3s by cell-to-cell handoffs (diffusion) of membrane identical, plug-n-play phosphatidylcholine. Because phospholipids (aka lecithins) can mix with water and fat.

Curcuminoids are fat-soluble and insoluble in water and aqueous solutions (like your cells and blood). Combining curcuminoids with Superba2™ krill oil allows the omega-3 phospholipids and triglyceride fats in krill oil to entrap and protect curcuminoids from aqueous solutions by their mutual molecular attractions. By using hard, vegetarian LiquidCaps and the right blend of MCT[4] oil, HALO's patent-pending blend allows curcuminoids to bypass and escape their usual metabolic disintegration/removal processes and go with the omega-3 phospholipids via normal fat and phospholipid transport systems – straight to cell membranes, where they both can exert their benefits. HALO prevents curcuminoids from having their usual DNF outcome (poor absorption and delivery to cells), and brings them with active omega-3 phospholipids to the finish line.

HALO COMBINATION ADVANTAGES

HALO's uniqueness also means a lower dose of each nutrient per serving is sufficient to maximize delivery and effects. Only two easy-to-swallow capsules are needed daily, and can be ingested at any time of the day, and both together or one at different times with or without a meal – that's dosing flexibility.

[4] MCT = Medium Chain Triglycerides, an oil derived from coconut and/or palm sources containing predominantly saturated fatty acid chain lengths of 6, 8 & 10 carbons length (C8:0, C10:0, C12:0), making them liquid at room temperature. MCTs are transported and metabolized differently than other fatty acids, mostly bypassing the lipoprotein system, and getting metabolized by the liver.

We want taking HALO to be a pleasant experience too. By using krill oil in LiquidCaps, the typical burping-up-dead-codfish smell from fish oil capsules is a thing of the past. The proprietary blend means that curcuminoids bypass the liver (called first-pass bypass), which reduces alteration of curcuminoids as well as increased bile output associated with water-soluble or dry powder curcumin materials (this is one way how your body gets rid of curcuminoids).

By using the same ratios of all the curcuminoids present in turmeric roots, HALO matches the health properties found with turmeric intakes. Similarly, HALO's proprietary blend surpasses the usual use of turmeric in curry to protect curcuminoids, enabling higher doses than found in curry diets.

WHY HALO?
EXERCISE & MUSCULOSKELETAL DISCOMFORT

Exercise is a normal, willful stress. If you exercise, you know pain. Pain from exercise is normal, both during and afterwards. Muscular pain from exertion means you are succeeding as you exceed your oxygen supply, your fuel supply and eventually your biomechanical limits. Musculoskeletal pain from long-term endurance exercise is also normal – you are using and perhaps overusing your muscles, joints, bones and nerves. Discomfort and soreness from exercise are a given.

Recovery is also a given, and tied to discomfort levels. You want to keep your exercise-associated discomfort manageable without reducing performance, so you can recover more easily and keep training and racing – even improve performance too at the same time. Fortunately, there is reproduible human clinical evidence to show how two particular nutrients – omega-3 fatty acids and curcuminoids – can individually reduce exercise-associated soreness and joint discomfort. Even better, First Endurance has succeeded in developing a patent-pending combination of the two nutrients that brings out the best of each nutrient, particularly important for curcuminoids. Because just throwing two ingredients in a pill is not easy as it looks, we have spent years perfecting how to get both nutrients into your cell membranes, not just your gut and liver. Get ready to be amazed.

(**Citations for Exercise & Musculoskeletal Discomfort**: Aderem 2015; Almekinders 2019; Baumert 2016; Boling 2009; Cheng 2020; Cheung 2003; Clark 2008; Close 2019; Cosca 2007; DiFiori 2014; Fatouros 2016; Flakoll 2004; Francis 2019; Graven-Nielsen 2014; Harty 2019; Hashiwaki 2014; Heiss 2019; Hotfiel 2018, 2019; Kakouris 2021; Knechtle 2018; Lehmann 1993; Ma 2019; Myer 2010; Owens 2019, Paulsen 2012; Peake 2005; Rodenburg 1993; Saxton 2003; Scheer 2021; Schoenfeld 2012; Smith-Ryan 2020; Sousa 2020; Tee 2007; Turner 2010; Vickers 2001; Vilella 2020; Witvrouw 2014; Zdzieblik 2017, 2021)

> "In longer ultra-marathons, ~50–60% of the participants experience musculoskeletal problems." (Knechtle 2018, Abstract)

YOU DESERVE A HALO

At First Endurance, part of our mission is to adapt nutritional strategies to provide peak performance. Protecting musculoskeletal integrity and improving post-exercise recovery is an integral part of our

mission. We are introducing a protective, nutritional HALO for your overall musculoskeletal system health. HALO provides two much-needed classes of nutrients that are notoriously low in typical diets: omega-3 fatty acids and polyphenols. But even better is that we have cracked the code for your body to utilize the benefits of omega-3s and curcuminoids. It's all about tissue and cell uptakes of each nutrient – getting the max amount of each nutrient to where they can work the best for your body. Typical omega-3 and curcumin sources still leave much to be desired for getting into your cells, and often do not fulfill the promise that research has shown these two nutrients can accomplish for you.

After years of focusing on absorption, bioavailability and tissue uptake of nutrients, we have found a way to combine these two important nutrients together in a way that maximizes their benefits. **It's all about getting the right amounts of omega-3 phospholipids and bioactive, free curcumin *into your cell membranes*, where they exert their benefits**. Your HALO.

Performing better and being healthier *is* an option now!

HALO BENEFITS

-Comforts achy joints from exercise-induced stress*
-Lessens DOMS (Delayed Onset Muscle Soreness) & EIMD (Exercise-Induced Muscle Damage)*
-Reduces normal, exercise-induced inflammation*
-Enhances muscle and joint recovery (Repair, Refurbish, Recover)*
-Neutralizes free radicals without reducing the oxidative trigger for muscle recovery*
-Antioxidants play an important role in keeping joints healthy and comfortable*
-Supports a healthy immune system*
-Helps maintain and protect a healthy heart and circulatory system*
-Maintains brain functions (alertness, cerebral blood flow, cognition, concentration, eicosanoid synthesis, executive functions, focus, glucose uptake, learning, membrane fluidity, memory, mood, motor skills, myelin sheath turnover, neurogenesis, neuroprotection, reaction time, processing speed, vision, gray matter volume).*

*

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

QUOTATIONS FROM LITERATURE – Musculoskeletal Discomfort

> "Iliotibial band syndrome (ITBS) is the second most common running injury [1]."
> Aderem 2015, p. 1

> "Ultra-endurance sports are associated with prolonged physical exercise both during training and competition. Musculoskeletal injuries are common as a result of the repetitive physical stresses."
> Almekinders 2019, p. 25

"People who engage in unaccustomed, strenuous physical exercise can experience stiff or sore muscles, a feeling that is usually apparent for 24–72 h after exercise. This phenomenon is known as delayed onset muscle soreness."
Baumert 2016, p.2

"The prevalence of overreaching and OTS [OverTraining Syndrome] is difficult to establish as specific diagnostics are absent, but studies report that ~30% of both young athletes (< 18 years) and elite athletes (> 18 years old) have experienced overreaching/OTS at least once [6–9]. However a prevalence of as high as ~60% in male and female elite runners have been described [10]."
Cheng 2020, p. 1

"Delayed onset muscle soreness (DOMS) is a familiar experience for the elite or novice athlete. Symptoms can range from muscle tenderness to severe debilitating pain.
Cheung 2003, Abstract

"Common overuse injuries in runners and other endurance athletes include patellofemoral pain syndrome, iliotibial band friction syndrome, medial tibial stress syndrome, Achilles tendinopathy, plantar fasciitis, and lower extremity stress fractures."
Cosca 2007, p. 237

"Given this trend toward early and multifaceted training, frequent competition, and single sport specialization, it is no surprise that overuse injuries and burnout are common."
DiFiori 2014, p. 6

"EIMD and its associated inflammatory response is of paramount importance for athletes' performance for two basic reasons: 1) the rate of deterioration and recovery of performance and discomfort (DOMS) after an athletic activity is largely dependent on the magnitude of EIMD-induced inflammatory response and 2) it affects the frequency of training stimuli, that is, the time needed for optimal recovery in between practices, official events, and/or an event and a practice.
Fatouros 2016, p. 180

"Exercise-induced muscle damage (EIMD) is typically caused by unaccustomed exercise and results in pain, soreness, inflammation, and reduced muscle function. These negative outcomes may cause discomfort and impair subsequent athletic performance..."
Harty 2019, Abstract

"Clinical signs include impaired muscular force capacities, painful restriction of movement, stiffness, swelling, and altered biomechanics in adjacent joints."
Heiss 2019, Abstract

"In longer ultra-marathons, ~50–60% of the participants experience musculoskeletal problems."
Knechtle 2018, Abstract

"The main consequence of EIMD for the athlete is the loss of skeletal muscle function and soreness."
Owens 2019, Abstract

" 'Extreme' exercise protocols, encompassing unaccustomed maximal eccentric exercise across a large range of motion, generally inflict severe muscle damage, inflammation and prolonged recovery (> 1 week)."
Paulsen 2012, Abstract

"The main findings of our review were that MSKI [musculoskeletal injuries] were mostly overuse injuries, predominantly affecting the lower limbs with different injury patterns and diagnosis between different types of UER [ultra-endurance running] activities."
Scheer 2021, p. 12

"Damage can be specific to just a few macromolecules of tissue or result in large tears in the sarcolemma, basal lamina, and supportive connective tissue, and inducing injury to contractile elements and the cytoskeleton."
Schoenfeld 2012, Abstract

"Injuries are a normal and expected part of exercise participation."
Smith-Ryan 2020, Abstract

"Patellofemoral pain (PFP) is often seen in physically active individuals and may account for 25-40% of all knee problems seen in a sports injury clinic. ... Alarmingly, a high number of individuals with PFP have recurrent or chronic pain."
Witvrouw 2014, p. 411

HALO ACTIVES – OMEGA-3s & CURCUMINOIDS

HALO has two very active nutrients – phospholipid omega-3 fatty acids EPA/DHA[5] from phosphatidylcholine and curcuminoids. Each has its own story about affecting health. We'll take a look at each nutrient by itself, and then learn why we put them together the way we did. That makes all the difference!

HALO OMEGA-3s

HALO KRILL OIL– MOST EFFICIENT OMEGA-3s

[5] EPA is eicosapentaenoic acid, DHA is docosahexaenoic acid, the two most important omega-3 fatty acids.

HALO contains Superba2™ Krill Oil, the most efficient way to nutritionally deposit omega-3 fatty acids EPA & DHA into your cell membranes, where they exert their benefits. And that's what omega-3s are all about!

Krill (*Euphasia superba*) are small shrimp-like creatures that are a major global biomass, highly sustainable, and loaded with omega-3 fatty acids and astaxanthin (a powerful carotenoid antioxidant which makes krill and krill oil red in color). Krill oil omega-3s are about half triglyceride oil and half phospholipids. Krill oil phospholipid omega-3s are identical to your omega-3 cell membrane phospholipids, and can go directly into cells. That's why less krill oil is needed than fish/algal oil to supply cell membranes with what they crave. Fish oil takes the long route with a lot of metabolic fuss and risk of oxidative damage to supply DHA/EPA for cell membrane phospholipid synthesis. Think of krill oil as plug-and-play, cut-to-the-chase, activated omega-3s.

Omega-3 fatty acids DHA and EPA from krill oil efficiently populate cell membranes where the DHA and EPA fatty acids are precursors for signaling molecules (eicosanoids, maresins, oxylipins, protectins, resolvins, etc.) that help maintain normal, healthy musculoskeletal tissue integrity and cardiovascular functions. Omega-3-rich brain membranes allow normal brain functions (attention, cognition, focus, executive functions, memory, mood control) to operate at peak efficiency, responding to your body's need to perform.

The omega-3 oil portion of krill oil helps to stabilize the phospholipids in the bottle and body, and also help push the omega-3 phospholipids to reach membranes once swallowed, since oil and water do not mix, but phospholipids and water do. The omega-3 oil portion of krill oil also helps attract curcumin (which is fat-soluble, but not water soluble itself), which allows for the curcuminoid/omega-3 phospholipid interactions in HALO. This escort of curcuminoids by oil & phospholipids helps free curcuminoids get into cell membranes, where they work together with omega-3 phospholipids to promote healing and recovery signaling.

MEMBRANE-IDENTICAL PHOSPHOLIPID EPA/DHA

Omega-3 fatty acids are well-known to be vital, if not essential, for good health, and that spills over into exercise and physical performance. But oil and water don't mix. Simply increasing fish or fish oil intake is not the best way to get omega-3 fatty acids EPA and DHA into your cells. We found a better way to get EPA/DHA in the right form into the right place (your cell membranes) efficiently, tolerably and conveniently – Superba2™ krill oil. Krill oil is rich in phospholipid omega-3s, and the majority of that is called sn1-palmitate-sn2-docosahexaenoate phosphatidycholine – the same molecule in your cell membranes that supplies bioactivity from omega-3s. It's like drawing the Advance to Go (Collect $200) card when playing Monopoly! You get two benefits at once! Read on the for details.

OMEGA-3 FATTY ACIDS BACKGROUND

There has been quite a large amount of research on omega-3s. In fact, omega-3s are the fifth-most studied molecule (nutrient or drug), with over 40,000 studies reported, trailing only penicillin, vitamin D, aspirin

and prednisone. Omega-3s are that important, but also still underappreciated. We aim to fix that. With HALO.

Normal diets have a low amount of omega-3s. Unless you are a native North American Inuit or Eskimo (with genetic adaptations), your body does not store omega-3s as body fat or "burn" omega-3s for energy, but when in membrane phospholipids, they make your cells function better. How? In two different ways.

HOW OMEGA-3 FATTY ACIDS WORK IN MEMBRANES: REASON #1 – FLUIDITY
Omega-3 membrane phospholipids account for fluidity of membranes, a forgotten attribute needed for all cells, but especially for brain and nerve cells to function optimally. There is a sweet-spot amount of how much of your membrane is comprised of omega-3 phospholipids – too little and your membranes slow down transporting things in and out of your cells. Your membranes are less efficient because they cannot cluster linked functions in areas called lipid rafts.

On the other hand, if your membranes are too fluid, they also disrupt lipid rafts, leading to similar problems as insufficient omega-3s. Also, since omega-3s readily attract oxidative free radicals, having too much can increase overall oxidative processes, damaging membrane phospholipids and associated glycoproteins, receptors, embedded proteins, further disrupting cell membrane function. The nature of free radicals also passes on oxidative damage to internal cell structures, including DNA, which further decreases cell efficiency and sets the stage for long-term issues. This is one reason to avoid large amounts of omega-3s in your diet and supplements – more is not necessarily better. This is possibly a reason why some omega-3 human studies show poor results – they missed the sweet spot of membrane fluidity and reached the trash dump of wasting energy on removal of excess omega-3s.

HOW OMEGA-3 FATTY ACIDS WORK IN MEMBRANES: REASON #2 – SPMs
But another equally or perhaps more important role of omega-3 fatty acids is as precursors to signaling molecules (eicosanoids and SPMs – Special Pro-resolving Mediators) that maintain a healthy status quo by resolving and promoting normal recovery processes.

Important! These signals are made from EPA and DHA omega-3 fatty acids in membrane phospholipids, specifically phosphatidylcholine phospholipids, by specific enzymes activated by stresses. These omega-3 phospholipid signals are commands for physical healing. Not having enough EPA/DHA membrane phospholipids is not having enough balance to recover quickly and fully.

SPMs have short lifespans – seconds at most, and are continuously made and destroyed quickly so your cells can react quickly to their surroundings. This means you want a steady supply of dietary precursors (omega-3s) to replace the steady losses. Since omega-3s are not stored much, this means a steady daily intake of omega-3s is healthy.

But there's more to the story. Our bodies have figured out that opposing cellular and tissue functions can be performed by using two slightly different molecules as precursors for SPMs/eicosanoids – omega-3s and omega-6s. Like an on/off switch. For example, sometimes you want more inflammation, sometimes you want less. Or you want less blood flow, or more. Your cells can do either by tapping into the right cell

membrane phospholipids to make the right SPMs/eicosanoids for the job at hand. You need both types of omegas to repair cells and recover from damage.

Omega-3 fatty acid-derived signals counteract and balance the signaling mediators produced by Omega-6 fatty acids (like arachidonic acid). Omega-6 fatty acids, like omega-3s, are also incorporated into membrane phospholipids and contribute to membrane fluidity, and are part of an initial response to cellular damage, which also promotes discomfort, inflammation and immune overstimulation. Omega-6s jump-start responses to stress by being very offensive. That's perfectly normal and fine to start responding this way, until omega-6s keep getting activated by cell damage or stress, and/or there are not enough omega-3s around to balance the omega-6 effects. The omega-6 signaling molecules are also a signal for omega-3 signals to follow.

But if there is a preponderance of omega-6 membrane phospholipids over omega-3 membrane phospholipids, the balance is tilted to more offensive responses, pushing back the reparative, normative responses from omega-3s. The entire recovery period is slowed or even halted when there are too many omega-6s vs. too little omega-3s.

WORLDWIDE, COMMON OMEGA-3 DEFICIENCY – ATHLETES TOO

This is exactly what our current diets do – emphasize omega-6 fats over omega-3s. When excessive, Omega-6 signals delay recovery and prevent feeling better. It's this balancing act by Omega-3 signals that help you recover from exercise and other stressors. These actions also involve your circulatory and immune system cells, partners in restoring your exercised muscles back to their best behavior.

There is an omega-3 fatty acid deficiency problem worldwide. Even the World Health Organization (WHO) agrees. Simply put, less than 5% of humans on planet Earth ingest the 500 mg per day of omega-3 fatty acids from their diet recommended by authoritative health and nutrition groups. And most of the omega-3s that people ingest from diets (80-90%) is plant omega-3s (alpha-linolenic acid or ALA),[6] not the much more useful DHA/EPA omega-3s found predominantly in animal food sources, especially oily fish and fish oil supplements (vegan algal DHA sources are also available nowadays). And those plant ALA omega-3s are in oily triglyceride form, which need a labyrinthic and low-throughput conversion route to become omega-3 membrane EPA/DHA phospholipids in your body. So…why not just give EPA/DHA omega-3 phospholipids?

Athletes mirror the poor *intakes* and *status* of omega-3 fatty acids exhibited by the world's population. Most athletes in the US and Europe have an Omega-3 Index (O3I – a test of how much EPA/DHA you have in your cells) around 4% -- a long way to go to achieve optimal omega-3 effects of >8% O3I. In short, everyone, including athletes, can benefit from consuming more omega-3 fatty acids. But it takes 1000-4000 mg of fish/algal oil EPA/DHA supplements daily for weeks or months to reach an O3I of 8 or more.

[6] The primary plant omega-3 fatty acid is Alpha-Linolenic Acid (ALA, C18:3 n3), a shorter precursor of EPA/DHA that we humans slowly convert in small amounts into EPA and DHA. Without additional dietary EPA/DHA intake, cell levels of EPA/DHA are not optimal. ALA sources are certain plant seeds and oils, most of which also contain omega-6 fatty acids, further reducing the omega-3 impact of ALA. Even more important, ALA cannot substitute for EPA/DHA in making eicosanoids and SPMs.

Krill oil is more efficient, and can do the same faster at 300-1000 mg daily. Because Superba2™ Krill Oil has a high amount of well-protected, membrane-specific EPA/DHA phospholipids, it delivers those phospholipids to your cell membranes directly. Unlike fish/algal oil triglycerides, the omega-3 phospholipids in krill oil are identical to those in human cell membranes. Unlike oily omega-3 sources (plant, fish or algal oils), Superba2™ Krill Oil can fill membranes with omega-3 phosphatidylcholine at lower doses than omega-3 oil supplements. Instead of needing 20+ steps to get a fish oil DHA into a membrane omega-3 phospholipid molecule, krill oil's omega-3 phospholipids need just a few self-facilitated transport steps – much more efficient, direct and easier.

Even better, Superba2™ Krill Oil comes with its own antioxidant protection built-in – astaxanthin. The red color of krill oil is from astaxanthin a carotenoid family member, similar to beta carotene, lutein, lycopene and zeazanthins. Astaxanthin is a more powerful and safer antioxidant than its carotenoid family members, and some even call it the most potent antioxidant (we will not go that far – they are all important). Astaxanthin is especially good at preventing omega-3s from free radical, oxidative damage, so you have less anti-omega-3s to worry about. One more way krill oil is more efficient than other omega-3 sources.

The amount of astaxanthin in krill oil is relatively small, and at higher daily doses can provide additional body-wide antioxidant protections, but we're happy with it protecting krill oil and membrane phospholipid omega-3s.

OMEGA-3s & EXERCISE PERFORMANCE

Longer endurance exercise volume can decrease body levels of omega-3, blunting exercise performance, mental prowess, tissue repair and muscle/joint/bone integrity. Fortunately, taking omega-3 supplements (EPA/DHA) improves various measures of endurance exercise capacity, muscle energetics and sometimes performance itself. And this evidence is based on fish oil supplementation, without using krill oil. Results might be even better if krill oil was used.

OMEGA-3s & OVEREXERTION – DOMS/EIMD[7]

Recovery from muscle-damaging exercise is usually improved by DHA/EPA supplements – less muscle soreness and/or less markers of tissue damage. Although most human studies showing benefits were from eccentric-exercise or resistance training, others were from endurance exercise or long-duration events. A few studies did not find improvements in resolution of DOMS/EIMD, although one unwittingly used an active agent (lecithin, a choline-containing phospholipid) as the placebo. The bottom line is that when someone exercises past their tolerance, they may get DOMS/EIMD, and supplementing with omega-3s EPA/DHA can lessen the effects (pain, discomfort, soreness, loss of function, structural damage) by a noticeable amount and speed up return to normalcy by days.

OMEGA-3s & HEALTHY JOINTS

[7] DOMS = Delayed-Onset Muscle Soreness; EIMD = Exercise-Induced Muscle Damage

Along with long-term endurance exercise comes achy joints. Backs, hips, knees, ankles, shoulders – you name it, just about any joint can have normal, occasional discomfort from usage. And having more Omega-3s in your body can help with joint comfort. How? Since Omega-3s are the source of universal signals to keep your body healthy and aid recovery under physical stress, all systems are affected, including muscles, bones and joints. For example, people with knee joint discomfort had more discomfort if their Omega-3s were lower (as indicated by the Omega-6/Omega-3 ratio in diet, blood and cells). A strong link between more DHA and more endorphins, the brain's natural pain-killer, was found by a recent review of normal, everyday joint discomfort. Reviews of Omega-3s and joints found that higher DHA/EPA intakes and better status showed more comfortable joints in persons with everyday joint discomfort from movement.

KRILL OIL & YOUR MUSCULOSKELETAL SYSTEM – HUMAN STUDIES

By itself, krill oil has been applied to musculoskeletal health, including joint comfort. Overall, the results show that krill oil soothes achy joints and sends soothing signals to your connective tissues. Keep in mind these results are with krill oil only, without any curcuminoids involved.

One study gave 1000 mg krill oil (240 mg DHA/EPA) or 2000 mg of DHA/EPA as ethyl esters oil (1700 mg DHA/EPA) for four weeks each in a crossover design in mildly overweight subjects. Each subject took each treatment after washout periods in a random order. Even though the omega-3 oil gave seven times as much DHA/EPA than the dose of krill oil, the hsCRP levels (a measure of cellular stress) were reduced significantly more (three times more) by krill oil. This study showed the increased efficiency of krill oil over higher doses of oily omega-3s for cell membrane signaling effects that interact with your connective tissues and immune system cells. Another study gave 300 mg of krill oil daily for 14 days to persons with joint discomfort. Again, hsCRP levels were significantly reduced, and joint comfort improved. This study showed the ability of krill oil to work relatively quickly to saturate cell membranes with phospholipid DHA/EPA to contribute to signaling joint tissues to improve their health. In another study, a higher dose of krill oil (2000 mg daily, with 309 mg DHA/EPA) was able to decrease an endocannabinoid (2-AG) signal in obese subjects in four weeks, whereas an equivalent dose of DHA/EPA from menhaden (fish) oil had no effect. Again, krill oil was more efficient than fish oil for improving signals that are pro-healing and calming.

Advantages of Krill Oil Over Fish Oil

1. Cell-membrane-identical phospholipid EPA/DHA forms (not found in fish oils);
2. Built-in antioxidant protection from naturally-occurring astaxanthin (freshness);
3. Preservative-free;
4. No stomach upset or burpback;
5. Miscible in water (body fluids);
6. Rapid stomach emptying;
7. Easily absorbed;
8. Less digestion & metabolism required for use by the body;
9. Efficient delivery and integration of EPA/DHA into cell membranes;
10. Supplies choline, a newly recognized essential nutrient;
11. Raises omega-3 levels in cells;

12. Efficiently affects the endocannabinoid system;
13. Sustainable & eco-friendly;
14. No environmental contaminant concerns (by-catch, mercury, heavy metals, pollutants);
15. No heat during processing keeps molecular integrity of oil;
16. No ill effects on the food chain by a large margin than fishing;

Advantages of Superba2™ Krill Oil Over Other Krill Oils

1. Aker BioMarine has led eco-friendly harvesting methods;
2. Aker BioMarine initiated krill fishing companies joining the Association of Responsible Krill (ARK) Fishing Companies, in conjunction with the World Wildlife Fund to make sure krill is harvested responsibly and subject to independent oversight;
3. Aker BioMarine is certified by the 3rd-party Marine Stewardship Council and Friends of the Sea as sustainable since 2010;
4. Aker BioMarine funds marine conservation and sustainability efforts, including working with World Wildlife Fund-Norway;
5. Devoted ships to harvest & immediately process oil onboard to preserve freshness;
6. Patented Eco-Harvesting® technology to reduce by-catch (harvesting krill is safe for other marine creatures);
7. Aker BioMarine's krill oil is 100% traceable to exactly where it came from;
8. Traceability informs regulatory agencies and consumers that regulations and limits are upheld;
9. Superba2™ has an ever-increasing number of human studies to support its actions and advantages;
10. Most human studies on krill oil used Superba krill oil;
11. Best-documented bioactivity.

For more information, visit the link to Aker BioMarine's Superba2™ website:

https://www.superbakrill.com

(**Citations for HALO Omega-3s – Phospholipids & Background**: AHA 2017; Bennenberg 2010; Berdeaux 2010; Bradbury 2011; Calder 2009, 2020; Chapkin 2008a, 2008b; Chen 2016; Chianese 2018; Colletti 2021; Danaei 2009; Daniells 2015; Deelen 2019; Del Gobbo 2016; Derbyshire 2018; Dolecek 1992; Einvik 2010; Fats of Life 2020; Gammone 2018; Harasymowicz 2019; Hishikawa 2017; Hu 2019; Janssen 2014; Joint WHO/FAO 2003; Kwantes 2015; Laye 2018; Lentjes 2017; Levy 2010; Li 2020; Mas 2012; Mozaffarian 2013; Murru 2013; Muskiet 2004; ODS 2020; Pocobelli 2010; Qi 2002; Serhan 2002; Shearer 2010; Sommer 2011, Souza 2020; Trikalinos 2012; Ulven 2011, 2015; Vannice 2014; Xie 2019

(**Citations for HALO Omega-3s – Deficiencies**: Anzalone 2019; Bradbury 2011; Chen 2016; Chianese 2018; Danaei 2009; Davinelli 2019; Derbyshire 2019; Dobnic 2017; Fenton 2016; Gollasch 2019; Grant 2016; Harris 2016, 2017, 2021a, 2021b; Hingley 2017; Hu 2019; Joint WHO/FAO 2003; Liu 2013; Mielgo-Ayuso 2020; Mozaffarian 2013; Oliver 2019; Pocobelli 2010; Qi 2002; Ritz 2020; Stark 2016; Trikalinos 2012; Vannice 2014; von Schacky 2014; Walker 2019; Wilson 2016; Yates 2009

(**Citations for HALO Omega-3s – Performance & DOMS**: Alkhedhairi 2022; Avila-Grande2020; Bermon 2017; Black 2018; Buckley 2009; Capo 2014, 2015,2016; Cheung 2003; Chianese 2018; Colletti 2021; Corder 2016; Cornish 2022; Da Boit 2015, 2017; Derbyshire 2018; DiLorenzo 2014; Fats of Life 2020; Gammone 2018; Georges 2018; Gerling 2014, 2019; Gravina 2017; Gray 2014; Guzman 2011; Harty 2019; Hashiwaki 2014; Heileson 2020; Heiss 2019; Herbst 2014; Hill 2007; Hingley 2017; Hotfiel 2018, 2019; Houghton 2012; Hunter 2019; Jackson 2012; Jakeman 2017; Jannas-Vela 2017; Jeromson 2015; Jouris 2011; Kawabata 2014; Kunz 2022; Kwantes 2015; Lembke 2014; Lenn 2002; Lewis 2015, 2020; Lv 2020; Macartney 2014; Martorell 2014, 2015; McAnulty 2011; McGlory 2019a, 2019b; Mickleborough 2013, 2015; Mielgo-Ayuso 2020; Miotto 2019; Nikolaidis 2004; Ninio 2008; Ochi 2017, 2018, 2019; Owens 2019; Paulsen 2012; Peoples 2008; Phillips 2003; Philpott 2018, 2019; Poprzecki 2009; Prego-Dominguez

2016; Ramos-Campo 2020; Rodacki 2012; Rossato 2020; Santos 2017; Schoenfeld 2012; Shei 2014; Simopoulos 2007, 2008; Sinnott 2013; Skarpanska-Stejnborn 2010; Smith 2015; Smith-Ryan 2020; Sousa 2020; Tartibian 2009, 2010, 2011; Tinsley 2017; Tiryaki-Sonmez 2011; Tokuyama 2011; Tsuchiya 2016, 2019, 2021; VanDusseldorp 2020; Viljoen 2019; Visconti 2021; Walser 2008; Wilson 2016; Xin 2021; Yoshino 2016; Zebrowska 2015

(**Citations for HALO Omega-3s –Healthy Joints**: Baker 2012; Colletti 2021; Deutsch 2007; Galan-Arriero 2017; Goldberg 2007; Harasymowicz 2019; Henrotin 2011; Kuszewski 2020 1; Kwantes 2015; Laslett 2020, 2021; Maroon 2006; Roe 2005; Sandford 2018; Sibille 2018; Smith-Ryan 2020; Stonehouse 2022; Suzuki 2016; Tokuyama 2011; Vitetta 2022

(**Citations for HALO Omega-3s – Krill Oil (Superba2™)**: Banni 2011; Bjorndal 2018; Cicero 2016; Colletti 2021; Da Boit 2015; Daniells 2015; Deutsch 2007; Konagai 2013; Krafft 2022; Kwantes 2015; Le Grandois 2019; Murru 2013; Rokke 2010; Skarpanska-Stejnborn 2010; Storsve 2020; Suzuki 2016; Ulven 2011, 2015; Winther 2011; Xie 2019

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

HALO CURCUMINOIDS

CURCUMINOIDS BACKGROUND

The other major active in HALO is actually three closely-related compounds – curcumin, demethoxycurcumin (DMC) and bisdemethoxycurcumin (BDMC). Together they are termed curcuminoids, and are naturally found in turmeric (*Curcuma longa*) roots and rhizomes. Turmeric root powder is about 2-5% curcuminoids, and has a pungent, spicy, bitter taste. We use an ethanol-water extract of turmeric roots to achieve 95% curcuminoids potency – no harsh solvents.

Curcuminoids are polyphenols, a common class of compounds in plant foods with biological activities. Turmeric curcuminoids are typically ~60-70% curcumin, with lesser amounts of DMC (20-27%) and BDMC (10-15%). Thus, 1000 mg of 95% curcuminoids has 570-665 mg of curcumin, 190-257 mg DMC and 95-143 mg BDMC. DMC and BDMC have one or two methoxy groups on the ring ends deleted, for those who are counting. Both DMC and BDMC show equivalent or greater actions as curcumin, are present in turmeric and thus, 95% curcuminoids are more than comparable to 95% or 100% curcumin for biological actions. We prefer to use the natural forms and ratios of curcuminoids as found in turmeric root, rather than isolate curcumin by itself, which is more commonly used.[8]

Curcuminoids are brightly colored, yellow-orange compounds, commonly used as natural colors for food and fabrics, although their color fades with time. Turmeric root has long been a staple of Asian Indian food, mostly as a substantial component of curry spice blends. Turmeric root and curry spices can be found in almost every grocery store.

[8] For more information on curcuminoids, see the links below for each molecule at PubChem: https://pubchem.ncbi.nlm.nih.gov/compound/969516 (curcumin); https://pubchem.ncbi.nlm.nih.gov/compound/Demethoxycurcumin; https://pubchem.ncbi.nlm.nih.gov/compound/Bisdemethoxycurcumin .

Unlike omega-3s, curcuminoids are not essential nutrients, are not found in humans on a curcuminoid-free diet, and human bodies cannot make curcuminoids. Humans do not have curcuminoid deficiencies, but they do have better health with curcuminoids intake. These are accessory nutrients – they add to and protect the health you already have.

(**Citations for Curcuminoids Background**: Ahmed 2014; Anonymous 2010; Asher 2013; Bejar 2018; Blumenthal 2021; Bresciani 2020; Committee Herbal Medicine Products 2009; Coyner 1987; Erscheinungsdatum Bundesanzeiger 1990; Govindarajan 1980; Gupta 2013; Hatamipour 2019; Kalaycioglu 2017; Khajehdehi 2012; Krishnamurthy 1976; Li 2011; Natural Standard 2011; Ng 2006, 2012; Padmanaban 2018; Pawar 2014; Sharifi-Rad 2020; Shishodia 2005; Snow 1995; Srimal 1997; Tayyem 2006; Thamlikitkul 1989)

HOW IS HALO DIFFERENT FROM OTHER CURCUMIN PRODUCTS?

HALO is the only liquid form of curcuminoids in krill oil, using mutually attractive molecular traits of each to protect and enhance the biological actions of each. Unlike most curcumin products, HALO does not try increase water solubility of curcumin or omega-3s, and instead, shunts curcuminoids and membrane-ready omega-3 phospholipids (not triglycerides) together directly into normal fat absorption pathways, where they reach cell membranes by simple diffusion, a normal delivery process already known for phospholipids, as well as several other targeted pathways.

Curcumin products range from simple turmeric root powder aka turmeric spice (2-6% curcuminoids) to dry powder extracts enriched for curcuminoids or curcumin (from 5% to 99% curcuminoids), synthetic curcumin (95-99%) to turmeric root oleoresins (turmeric root oil) to dozens of combinations of any these sources with black pepper, cyclodextrin carbohydrates, detergents, emulsifiers, fibers, gelation, micronization, nanocomplexing, oils, phytosomes, solid fats, and even solid phospholipids. Traditional Asian Indian cooking uses turmeric in curry spice or as itself typically blended with oil or fat before adding foodstuffs.

There are currently available curcumin products using soy lecithin (solid phospholipid mixtures including phosphatidylcholine), such as Longvida® and Meriva® with other ingredients. None of these contain omega-3 phospholipids, and cannot have the molecular interactions of curcuminoids and omega-3 fatty acids found in HALO. Yours truly spearheaded the combination of krill oil with curcumin in softgels years ago, but this composition has shown serious manufacturing issues. HALO in LiquiCaps takes advantage of the attraction between krill oil and curcuminoids to bypass those issues and more easily deliver curcumin and omega-3 fatty acids to cell membranes, where they belong.

First of all, in vitro and animal studies on curcumin absorption are mostly irrelevant to humans. In vitro studies pour gigantic amounts of curcumin along with solvents or detergents to force curcumin into cells – this is not representative at all for you or I swallowing curcuminoids. Unfortunately, most claims of curcumin's reputation as a wonder supplement are based on in vitro studies. Foolishness. Animal studies have clearly shown they are different from humans in their uptake – their guts are different enough to allow more curcumin into the bloodstream and tissues than humans can do. Also, massive doses are used, doses that were shown to have no absorption or effects in human studies. Again, little relevance to humans, and insufficient for supporting product claims in humans.

HALO's raison d'etre was to solve the significant biological challenges of delivering bioactive, unmetabolized (free) curcuminoids to cell membranes of people. Heretofore, the story of curcumin absorption, uptake and bioavailability is a sordid story of great expectations smothering scientific validity. In brief, technical deficits, reporting biases, conflicts of interest, misrepresentation, deceit and fraud concerning curcuminoid bioavailability have ended up confusing both researchers and the public alike. Claims about curcuminoids absorption have degenerated into an Emperor's New Clothes Falderal, with a few exceptions. For an insight into these important issues, the reader is referred to articles describing the scientific issues about curcuminoid absorption, uptake and bioavailability in humans (Douglass 2015; Stohs 2018, 2019 293, 9417, 2020, 2021).

Even so, the bioavailability brouhaha is not a finished story. Human clinical studies for over half a century with all types of curcumin have found evidence of efficacy in many conditions, offering strong support for real-life results seen from HALO. A bottom line is that some curcumin is better than none, but more free curcumin is ideal.

(**Citations for How Is HALO Different From Other Curcumin Products?**: Douglass 2015; Stohs 2018, 2019 293, 9417, 2020, 2021)

CURCUMINOIDS & EXERCISE PERFORMANCE

Can taking curcumin supplements help me to bike, climb, perform, row, run, ski or swim faster, longer, stronger? This question has surprisingly not been studied enough to give a firm answer. Only two reports describing one recent human study actually examined the ability of untrained persons to exercise better, looking into fatigue thresholds and times to exhaustion (TTE) from cycle ergometry to exhaustion performed at day 0 and after 28 days of supplementation with no exercise in between (Goh 2020; Herrick 2020). These reports did find small but statistically significant improvements in right leg vastus lateralis muscle neuromuscular fatigue threshold (PWCFT – a measurement of peak work capacity), and ventilatory threshold (VT) average values. TTE, Ratings of Perceived Exertion (RPE), Respiratory Exchange Ratio (RER) and VO_2peak were not different between placebo and curcumin groups. These results suggest that curcumin might be able to reduce neuromuscular fatigue during cycling exercise to exhaustion. This study design is poorly relevant to long-term endurance exercise, but does give a hint of curcumin doing something good for muscular fatigue during exhaustive cycling. Whether or not these findings can translate to improved performance times remains to be seen. But simply putting an "enhanced-absorption" curcumin into a pill and taking it is not a sure-fire way to go.

Usually, we do not like to rely on animal studies, but this one gives another hint for success from curcumin. A mouse study did find significant improvements in swim-to-the-death and uphill treadmill times, along with improvements in lower lactate and muscular damage markers from increasing doses of curcumin, but the amounts were not reported (Huang 2015). A strength of this study, not seen in human studies, is a dose-response curve for efficacy. Since we know animals absorb more free curcuminoids than humans, this study is not directly relevant to humans but shows a potential for human efficacy of curcuminoids for exercise performance ... **IF** bioactive, free curcumin can get absorbed into cell membranes.

Other human studies have looked at physiological parameters during exercise in many types of settings with or without exercise, many of which were in untrained/sedentary persons, obese/diabetic persons, inactive elderly persons or doing resistance training, not representative of long-term endurance athletes. Most, but not all, of these studies found improvements of antioxidant capacity, elder fitness, blood vessel (endothelial) function, normal inflammatory responses to exercise, lipid profiles, and premenstrual mood. These findings were reinforced by reviews that also included studies on DOMS/EIMD discussed below (Campbell 2021; Suhett 2021). Despite differing curcumin doses, differing preparations, study designs, exercise modalities, acute vs. chronic administration, durations of exercise and curcumin administration, and different outcomes measured, in general there were positive effects of curcumin supplementation, more so when combined with exercise, suggesting a general effect on health and well-being.

In summary, administration of curcumin to exercising humans who are not long-term endurance athletes leads to some relevant improvements in markers of exercise stress and in markers of overall health. But we already know how to maintain and improve long-duration, intense endurance exercise without curcuminoids. Stay tuned for even better reasons to use curcumin than mere performance.

(**Citations for Curcuminoids & Exercise Performance**: Akazawa 2012; Amirkhani 2017; Avansar 2017; Bankowksi 2022; Campbell 2021; Changal 2020; Cheragh-Birandi 2020; Choi 2019; Fakhri 2019; Falgiano 2018; Franceschi 2016; Goh 2020; Herrick 2020; Huang 2015; Oliver 2016; Osali 2020; Santos-Parker 2017; Sedaghat 2018; Sugawara 2012; Suhett 2021; Takahashi 2013; Zoodfekr 2017)

CURCUMINOIDS & OVEREXERTION, MUSCLE SORENESS, DOMS/EIMD[9], & RECOVERY

As indicated in the Omega-3 section, when someone exercises past their tolerance, they may get DOMS/EIMD, causing exercise-induced pain, discomfort, soreness, loss of function, structural damage and delayed return to normalcy. Fortunately, research on effects of supplemental curcumin on muscle soreness after exercise has exploded in the past few years, offering a wealth of data and interpretation to support using curcumin to reduce post-exercise muscle soreness, and aid recovery.

With a huge spread of experimental conditions as seen with curcumin and DOMS/EIMD studies, determining if curcumin can benefit long-term, endurance exercise recovery is complicated. And there's another issue if curcumin and/or omega-3s work too well – the specter of slowing or preventing the damaging signals too well that also initiate repair processes. Underlying the effects of any compound with significant anti-inflammatory and antioxidant activity (legendary for curcumin and omega-3s) is inhibiting or slowing normal repair processes, delaying recovery. While this mechanism has not been specifically studied for curcumin, various studies have expressed findings that curcumin is not able to decrease reparative processes.

Strong evidence that long-term use of enhanced-absorption curcumin provides benefits for joint structure comes from a recent study of 50 people around 60 years of age (Nakagawa 2022). These persons had painful, end-stage, degenerative knee joints and were treated by mosaicplasty – a procedure that takes plugs of cartilage with bone from healthy joint areas and puts them into a damaged area, effectively seeding the

[9] DOMS = Delayed-Onset Muscle Soreness; EIMD = Exercise-Induced Muscle Damage

damaged cartilage with healthy parts that jump-start cartilage repair. Note that cartilage repair is very slow and some wrongly think it cannot repair – it can, but needs help. The subjects were given placebo or curcumin for a year, and then their knee cartilage was looked at again by arthroscopy with an ultrasound probe of mechanical properties (stiffness), along with MRI imaging. Folks, this is an extremely advanced method of treating bad knees, and the intra-articular imaging is what-you-see-is-what-you-get evidence. The usual questionnaires for joint pain and movement were given every three months out to a year. A stable blood level of total curcumin for a year was found for the curcumin group, and zero for the placebo group. After a year, there was no difference between groups for the questionnaire measures for pain, movement, daily living activities. This null result was likely due to three factors: 1) both groups benefited from the implantation of cartilage plugs, as would be expected; 2) both groups used analgesics as needed (which was not tracked), as most other human joint studies do; and 3) cartilage turnover half-life is two years, meaning the observations were too early to give a fair assessment of efficacy. Like taking a cake out of the oven halfway through baking time, cartilage needs enough time to see and feel a true end result – many human studies have this design and, perhaps wrongly, concluded an intervention 'did not work.' Don't blame the oven for lame results. The MRI imaging was not different between the groups. So far so bad. But the intra-articular tests of cartilage structure were improved in the curcumin group better than the placebo group – surface roughness and cartilage stiffness were improved more in the curcumin group – this is chondroprotection. Given the worst-case scenario of knee joint damage along with the multiyear time for cartilage to repair, the result of using only curcumin causing improvements in actual cartilage structure are impressive. One wonders if using other nutritional means to protect cartilage (such as omega-3 fatty acids) would lead to a faster course of repair.

This means that using the right amount of curcumin should not hamper recovery, adaption to training, maintenance of muscle mass or maintenance of muscle metabolic capacity. In other words, it appears that curcumin cannot degrade long-term exercise performance...if not taken in excess.

CURCUMIN, ENDURANCE EXERCISE AND DOMS/EIMD

Let's start with the most pertinent studies of curcumin on long-term endurance exercise.

One study gave a low dose of curcumin (10 mg) along with 140 mg of Boswellia extract daily in an enhanced-absorption, phytosome form (Fitomuscle®) to 47 male master cyclists (~46 years old) for 12 weeks (Chilelli 2016). All were long-time, long-term endurance cyclists (~200 km/week). They were all put on a Mediterranean Diet to reduce dietary influences on biomarkers of inflammation and glycation (sugars, especially fructose, wrongly attaching to proteins). After 12 weeks, the curcumin/Boswellia group showed significant reductions in advanced glycation endproducts (AGEs) from baseline and from the control group, as well as a large reduction in MDA (malondialdehyde) blood levels, showing a strong, protective antioxidant effect. Inflammatory markers were lower in the curcumin/Boswellia group, but the large individual variations prevented statistical significance from being found. These results showed that a combination of anti-inflammatory herbals, including a low dose of curcumin, had antioxidant and anti-inflammatory actions in chronically exercising male cyclists when taken for an extended time. Based on many other human studies, Boswellia extract is likely the major driver of results for this study, rather than curcumin itself. Importantly, long-term use (3 months) was successful – something rarely studied.

Another combination product with 500 mg each of curcumin (as Longvida®, an enhanced absorption curcumin) and a proprietary pomegranate extract was taken daily for 26 days then doubled for three days before a half-marathon race in eight subjects training for a half-marathon (15 miles/week, 3 women, 5 men) (Tanner 2020 1). 10 similar subjects were the control group, but not supplemented. Compared to control subjects, supplemented subjects showed differences in nine inflammatory proteins and 39 mRNA expressions in whole blood that together are potentially beneficial for improving exercise recovery. Similarly, an open-label pilot field study on 15 men and women training for a half-marathon used curcumin/pomegranate with the same dosing schedule but with 500 mg methylsulfonylmethane (MSM) added (Tanner 2020 AT6137). Inflammatory protein and mRNA changes conducive to accelerated muscle recovery after a half-marathon were found. These two studies identified biomarkers to further investigate DOMS/EIMD in larger human studies, but did not measure or report muscle soreness. Nevertheless, this curcumin combination effected beneficial changes in muscle biomarkers that bolsters findings of less soreness and better muscle recovery from endurance exercise as seen in other curcumin studies.

Twenty-eight men were given 1500 mg curcumin or placebo daily for four weeks, immediately before and immediately after a half-marathon race (Faria 2020). Markers of muscle damage were measured at baseline, immediately before, immediately after, and two, 24, and 48 hours after the half-marathon race. Increased IL-10 and less myoglobin, compared to placebo, were found, although CK, LDH, ALT, AST, IL-6 were not different between groups. These results found some amelioration of muscle damage biomarkers from an endurance running race.

A crossover study of 11 recreational male athletes cycled for two hours at 95% lactate threshold to elicit an inflammatory response (increased IL-6, IL1-RA) (Sciberras 2015). Compared to a control (no supplementation) and placebo trials, curcumin administration (500 mg daily for three days and 500 mg just before exercise trial as Meriva®, an enhanced absorption curcumin) led to trends ($p = 0.06, 0.18$) for reducing inflammatory cytokines immediately after and one hour after exercise. Authors concluded that the results would have been statistically significant if 26 subjects would have been studied. Laboratory aerobic exercise at fixed intensity does not fully mimic long-term endurance race conditions, something we see over and over with human studies.

In a much-overlooked area of exercise – gut health during exercise – 500 mg curcumin (as Meriva®) or placebo was given for three days to eight recreationally active persons (2 women, 6 men) in a crossover study (Szymanski 2018). Non-heat acclimated subjects ran for one hour at 65% VO_2max in a Darwin chamber (37 degrees C / 25% humidity) and blood was drawn for intestinal health and inflammatory markers pre, post, one hour and four hours after exercise. GI barrier damage was seen by this exercise, but was significantly reduced by curcumin, as were heart rate, cytokine biomarker responses, body temperature and the Physiological Strain Index (measure of heatstroke risk). Authors indicated that curcumin should help with reducing heat stress during exercise before acclimation sets in (about two weeks of training). Another corollary to this study is that GI absorptive function was likely maintained, which would facilitate uptake of carbs, electrolytes and water during long-duration exercise. This mechanism alone suggests that curcumin can maintain exercise performance in long-term exercise events when using carb/electrolyte drinks.

An enhanced-absorption curcumin using gum ghatti at a dose of 90 mg curcumin daily was given for seven days to untrained, active, healthy males who then underwent a max-effort 14km run (Roohi 2017). Total Antioxidant Capacity was increased by curcumin before exercise and for immediately after the run, but not 24 and 48 hours later. Minor improvements in MDA and glutathione (GSH) levels were also noted for the curcumin group after exercise. This study showed that antioxidant effects of curcumin were not in the range that would impair recovery or adaptation, and that relatively low doses of curcumin accumulated and reached a steady-state with efficacy. This means that taking curcumin daily is more important than when curcumin is ingested.

An enhanced absorption curcumin (500 mg of curcumin as Cureit™) or placebo (15 subjects per group) was taken daily for 12 weeks and then downhill treadmill running (10% grade for 45 minutes) was used to induce leg DOMS (Amalraj 2020). Muscle soreness was significantly reduced by curcumin, and lower levels of muscle damage markers (creatine kinase, CK) and increased VO_2max as a measure of recovery were found.

Another study used downhill treadmill running (10% grade for 45 minutes at 66% VO_2max) in 23 recreationally active men and women given 2000 mg curcumin + 20 mg piperine or placebo for eight days before the run, and daily for four days thereafter (Cardaci 2020). Although there was no difference between groups for DOMS, markers of protein ubiquitination were reduced by curcumin. These events would reduce muscle protein breakdown during rest and after damaging exercise, improving functional muscle recovery.

The standard downhill treadmill running protocol as outlined above by Amalraj and Cardaci was also used for another curcumin DOMS human study (Drobnic 2014). Twenty men doing at least four hours per week of regular aerobic exercise were given placebo or curcumin (400 mg daily as Meriva®, an enhanced absorption curcumin) for two days before and after downhill running to elicit DOMS. Muscle soreness was significantly reduced by curcumin, as were serum biomarkers of muscle damage and systemic inflammation. In addition, MRI of thigh areas showed curcumin reduced muscular injury by half in 4 of 6 areas imaged. Antioxidant tests were not different between groups, and muscle biopsies showed similar findings of muscle inflammation and sarcolemmal disruption. The authors stated that a larger subject number would have found statistical significance for more functional and biochemical parameters.

Three different reports (Jager 2017, 2019; Oliver 2017) used the same 63 moderately trained subjects (32 women, 31 men) to determine the effect of curcuminoids (as CurcuWIN®, an enhanced absorption curcumin) on DOMS/EIMD after downhill running. These subjects were also used in the curcumin blood flow study by Oliver mentioned above (Oliver 2016). Two doses of curcuminoids (50 and 200 mg) were compared to placebo for eight weeks, followed by the one-hour downhill running trial and follow-up for three days. Downhill running produced muscle damage and decreased power and torque. Both curcuminoid doses reduced CK levels compared to placebo, but changes in three plasma cytokine biomarkers (IL-6, IL-10, TNF-alpha) were not significant among groups. Thigh pain was reduced in the 200 mg curcuminoids group compared to placebo and 50 mg groups in the first report (Jager 2017), but not the second report (Jager 2019), which had four additional subjects. Peak extension torque values were not

reduced in the 200 mg curcuminoids group, but remained decreased in the placebo and 50 mg curcuminoid groups. Other measurements of strength were not different among the groups. Overall, curcuminoids improved some measures of muscle soreness and recovery, but not all. Attenuation of performance decrements suggests better recovery after curcumin.

Using 14 trained men in a simulated dual stress challenge (mental stress testing during aerobic cycling exercise for 35 minutes at 65% VO_2max) with a crossover design found that taking 1569 mg enhanced absorption curcuminoids (CurcuFresh®) for three days prior to testing and just before testing did not affect antioxidant actions, but there was no change in oxidative stress from the challenge (McAlister 2020). In other words, the exercise and mental stress were not enough to change oxidative stress, and thus, there was nothing for curcumin to change. This study emphasizes that long-term endurance exercise is different from laboratory exercise testing, and results from lab testing need to be considered in light of not causing real stress to prevent false negative interpretations.

CURCUMIN & RESISTANCE/HIGH INTENSITY INTERVAL TRAINING

Although resistance training (weightlifting), High-Intensity Interval Training (HIIT) and other short-term, exhaustive exercises are not the same kind of exercise as long-duration endurance, they too can be intense, fatiguing and lead to DOMS/EIMD. Since the biological mechanisms for DOMS/EIMD responses are similar, effects from shorter-term, intense exercises should be applicable to intense, long-duration endurance exercise resulting in DOMS/EIMD.

Sixteen studies found varying degrees of reducing oxidative damage, normal exercise-induced anti-inflammatory biomarkers, and muscle/joint soreness. These mostly positive results were seen in several types of agony-inducing exercise, from single muscle-joint combo (biceps flexes) to whole body (drop jumps). Short-term, damaging exercise results support similar outcomes in endurance studies for ameliorating damaging endurance exercises.

WRAP-UP FOR CURCUMIN AND DOMS/EIMD

Overall, supplementing various product forms of curcumin or curcuminoids before, during and after exercise to muscle soreness (characterized as DOMS/EIMD), whether from aerobic or anaerobic exercises, led to less muscle soreness, less loss of muscular strength or performance, faster recovery, and often reduced biomarkers of muscle damage, systemic inflammation and oxidation in normal, healthy persons. And we all know that recovering faster means better training and better performance.

13/17 Studies found significant reductions in muscle soreness after damaging exercise – both less peak pain and less pain duration. 22/26 Studies found some kind of anti-inflammatory effect after damaging exercise. 4/5 Studies found antioxidant effects after damaging exercise. 12/12 Studies found other effects that lead to faster recovery from damaging exercise.

Seven recent reviews / meta-analyses have echoed these findings after reviewing subsets of the studies presented herein (Beba 2022; Campbell 2021, Doma 2020; Fang 2021; Fernandez-Lazaro 2020; McFarlin

2019; Hewlings 2017; Yoon 2020). Reviews also included results from in vitro and animal studies that further support human study findings.

It is important to keep in mind that these studies used unaltered, dry, powdered curcumin/curcuminoids, or absorption-enhanced curcumin preparations that show little, if any absorption of free curcumin into bloodstream and tissues. Durations were also short – days instead of months. These factors mean that the benefits observed are a floor of effect for curcuminoid supplementation – logically, anything with better uptake or duration of free curcuminoids should exhibit better results, especially for DOMS/EIMD. See the comment from McFarlin 2019, below.

Here are excerpts from each review concerning curcumin and muscle soreness:

> Beba 2022:
> "Curcumin supplementation may improve some aspects of DMOS, including muscle damage, muscle soreness, inflammation, muscle strength, and joint flexibility."
>
> Campbell 2021:
> "Various curcumin-based interventions have improved self-perceived measures of pain and tenderness, reduced evidence of muscle damage, ameliorated inflammatory markers, increased markers of antioxidant capacity, diminished markers of oxidative stress, reduced markers of AGEs, and attenuated loss in mean power of single-leg sprints."
>
> Doma 2020:
> "Accordingly, selected root plants minimised the level of several biomarkers of muscle damage, inflammation and muscle soreness during periods of exercise-induced muscle damage."
>
> Fang 2021:
> "The current evidence revealed a [sic] efficacy of curcumin in reducing CK serum levels and muscle soreness index among adults. Therefore, curcumin may be known as a priority EIMD recovery agent in interventions."
>
> Fernandez-Lazaro 2020:
> "In summary, the administration of curcumin at a dose between 150-1500 mg/day before and during exercise, and up until 72 h' post-exercise, improved performance by reducing EIMD and modulating the inflammation caused by physical activity."
>
> Hamidie 2017:
> "Based on our previous experiments we conclude that indeed curcumin treatment have [sic] ability to increase performance through regulated mitochondria biogenesis on skeletal muscle."
>
> Hewlings 2017:

"It may also help in the management of exercise-induced inflammation and muscle soreness, thus enhancing recovery and subsequent performance in active people."

McFarlin 2019:
"To date most exercise studies have used curcumin acutely to impact short-term recovery. Given these effects, it is reasonable to speculate that curcumin might be a beneficial addition to a long-term training program."

Sorrenti 2020:
"In conclusion, curcumin can be considered an effective natural remedy to modulate oxidative stress and inflammation, improving athletic performance."

Suhett 2021:
"In conclusion, the evidences presented indicate that curcumin supplementation in human beings is likely safe and beneficial for sport and physical activity, due to the reduction of inflammation and oxidative stress, reduction of pain and muscle damage, improved muscle recovery, sport performance, psychological and physiological responses (thermal and cardiovascular) during training, as well as the GI function."

Yoon 2020:
"Although conflicting results regarding the effects of curcumin supplementation on DOMS exist in literature, it may be considered as a method of nutritional intervention for reducing post-exercise DOMS."

LESSONS LEARNED FROM CURCUMIN & DOMS/EIMD

A clear dose-response was not seen for curcumin, as most doses showed significant effects from 26-6000 mg per day. One study showed a medium dose (400 mg) was more favorable than lower or higher doses, suggesting that there is a U-shape (or inverted U-shape) dose-response curve of curcumin and DOMS/EIMD effects. In other words, there is a sweet spot or zone dose where curcumin can help muscle recovery from strenuous, damaging exercise. This zone probably depends on the type of curcumin preparation.

The use of many, various enhanced-absorption curcumin materials seemed to show equivalent results to higher amounts of unaltered curcumin/curcuminoid materials, indicating these materials were delivering curcumin to areas of the body in amounts sufficient to elicit whole body and localized exercised muscle benefits.

Better results were seen when curcumin products were given consistently before (longer than 1-2 weeks), during and after exercise (usually 4 days). These findings argue for daily, long-term, consistent use of curcumin for best results, which also mirrors the long-term benefits seen for dietary turmeric/curcumin intakes and other human studies on non-sporting conditions.

Importantly, curcumin did not squelch oxidation or post-exercise inflammation completely, which can be taken as not impeding the body's normal process of adaptation to and recovery from intense exercise which some antioxidants or corticosteroids/NSAIDs in high doses have illustrated.

Thus, taking curcumin in a manner that improves uptake can reduce normal muscle pain and soreness from any type of soreness-inducing, strenuous, intense exercise.

(**Citations for Curcuminoids & DOMS, EIMD, Overexertion, Post-Exercise, Recovery**: Amalraj 2020; Bankowski 2022; Basham 2018, 2020; Campbell 2021; Cardaci 2020; Chilelli 2016; Davis 2019; Delecroix 2017; Doma 2020; Fang 2021; Faria 2020; Fernandez-Lazaro 2020; Hamidie 2017; Hewlings 2017; Hillman 2021; Jager 2017, 2019; Jones 2009; Mallard 2020; McAlister 2020; McFarlin 2016, 2019; Nicol 2015; Oliver 2017; Roohi 2016; Samadi 2019; Schwarz 2020; Sciberras 2015; Szymanski 2018; Tanabe 2015, 2019 524, 2019 82; Tanner 2020 1, 2020 AT6137; Udani 2009; Wang 2019; Yoon 2020)

CURCUMINOIDS, EXERCISE & JOINT HEALTH

So much focus on exercise and sports is on muscle performance that the nuts and bolts of how you actually perform are taken for granted, until you feel normal discomfort or loss of function in your joints after strenuous exercise. This is like looking at the motor of a race car and ignoring the wheels/suspension/body.

During long-term exercise, your connective tissues, especially the ones that connect your muscles to your bones to propel you, are also under mechanical and physical stresses. Given their nature and poor blood supply compared to muscles, it is no surprise that DOMS/EIMD also adversely affects your joints. We think of joints as locations, like knee or ankle, but when they are sore from overexertion, there are multiple tissues involved – tendons, ligaments, cartilage, synovial (joint) linings, bursa, periosteum and bone (not to mention your GI tract). And don't forget that each muscle has connective tissues inside of itself – basal lamina, epimysium, endomysium, sheaths – that shape and hold your muscles, nerves and blood vessels in working order. Immune system cells, blood vessels and nerves are always hanging in and around connective tissues too.

Sooner or later, a normal outcome of long-term exercise will be overuse to joints and connective tissues. Unlike muscles, joint tissues are locked into their shape, have fewer cells, and some are inside articular joints where there are no blood or lymphatic vessels, which are around (not inside) articular joints in the synovial lining and adjacent bone. Partly because joints are moving parts that have physical stresses coursing through them, Nature has figured out it is easier to make them extremely tough, but without a lot of flimsy, fragile nerves, blood and lymphatic vessels that would constantly break, causing loss of joint function….and loss of movement! Obviously, movement was selected for in human evolution, even though there are compromises.

Non-muscle musculoskeletal tissues are called connective tissues for a reason – they literally connect muscles with bones. They do have robust maintenance and repair processes constantly ongoing, but they also are compromised because of what they are. Any structural changes, especially on a microscopic scale, take much longer to normalize in connective tissues. For example, bones are continuously replacing and rebuilding themselves, with a half-life of one year. That means every two years or so you mostly have a new skeleton. Tendons and ligaments that are actively used take 1-2 years for their normal maintenance half-life, or longer if structural damage is constant (like overuse). Some of these tissues have a much slower

replacement half-life, but have less stress placed on them. But the Tortoise Race award goes to cartilage tissue – a half-life of two years! Because of lack of blood supply inside cartilaginous joints, water, nutrients and signaling molecules need to diffuse from far distant locations (from a cartilage cell's perspective).

Point is that connective tissues take the hits from exercise/movement physical forces and are tough enough to withstand a lot of that kind of physical, mechanical stress. But they also have a harder time patching up any normal, exercise-induced microdamage. Eventually, your connective tissues become your weakest link and your performance may suffer if they lose too much function. The best way to deal with normal, exercised-induced connective tissue wear and tear is prevention. Give your connective tissues what they need to fend off stress from physical forces. We have already seen how omega-3 fatty acids (delivered efficiently by Superba2™ krill oil in HALO) can maintain and support connective tissues. Your joints have other allies, including curcuminoids, which simultaneously help muscles and joints during exercise.

(**Citations for Exercise & Joints/Musculoskeletal Health**: Aderem 2015; Almekinders 2019; Andersen 2013; Anderson 2020; Ansari 2017; Benca 2020; Bertelsen 2017; Bessa 2008; Bishop 1999; Bogusiak 2018; Burns 2003; Cheron 2017; Clarsen 2010; Dakin 2014; Gosling 2008; Haeberle 2018; Hinder 2019; Hollander 2021; Kluitenberg 2015; Knechtle 2018; Knez 2006; Kronisch 2002; Lopes 2012; Maffulli 1998; Maselli 2020; McHardy 2006; Melody 1999; Mousavi 2021; Nelson 2011; O'Toole 1989; Pfeiffer 1995; Pradas 2021; Riley 2008; Saragiotto 2014; Scheer 2021; Smith 2018; Smith-Ryan 2020; Spiesz 2015; Spiker 2012; Stoop 2019; Walter 1989; Winter 2020; Wu 2021; Yanturali 2015; Zech 2021; Zingg 2013)

CURCUMINOIDS & YOUR MUSCULOSKELETAL SYSTEM – HUMAN STUDIES

A normal outcome of long-term exercise will be (sooner or later) overuse of joints and connective tissues. Now that we have seen curcuminoids can lessen the impact of musculoskeletal discomfort and normal inflammatory processes in muscles, after long-duration exercise, does the same hold true for connective tissues?

The answer is it's a very good bet. Your whole body sees curcuminoids like your muscles do, including extra-articular joint tissues (those that have blood supply and are not actually inside a joint). And since the attenuation of normal inflammatory processes after intense, muscle-damaging exercise has been shown in muscles, other musculoskeletal tissues should follow the same trends. Signaling molecules reach deep into tissues regardless of blood supply As seen in non-exercise studies of joint health, curcumin certainly supports and maintains healthy joints.

There are many controlled human studies on intra-articular joint conditions, which manifest joint discomfort by nerves on the outside of joints (there being no nerves inside articular joints like knees, hips, shoulders, elbows or ankles). There are also controlled studies and reviews on the positive effects of curcumins on everyday sources of joint discomfort in healthy persons (including the studies illustrated above for DOMS/EIMD), even in short time periods (one hour). Long-term administration (months) of curcumins maintained the effects. Because of laws regulating dietary supplements and foods, we are not allowed to discuss these additional lines of evidence in detail, even the ones applicable to exercise injuries. Let's just say what's good for your muscles is good for your joints!

(Citations for Curcuminoids & Joints/Musculoskeletal System: Akuri 2017; Amalraj 2017; Appelboom 2014; Atabaki 2020; Badria 2004; Bannuru 2018; Basu 2021; Beba 2022; Belcaro 2010 55, 2010 337; Bucci 1994; Calderon-Perez 2021; Chainani-Wu 2003; Chandran 2012; Cheragh-Birandi 2020; Chin 2016; Dai 2021; Daily 2016; Deodhar 1980; Di Pierro 2013; EFSA 2017; Gupte

2019; Hashemzadeh 2020; Henrotin 2010, 2011, 2014, 2015, 2019; Hsaio 2021; Jahromi 2021; Jurenka 2009; Karlapudi 2018; Kertia 2012; Khalife 2011; Khanna 2020; Kizhakkedath 2013; Kulkarni 1991; Kuszewski 2020 1; Kuptniratsaikul 2009, 2014; Lopresti 2021; Madhu 2013; Mobasheri 2012; Nakagawa 2014, 2020, 2022; Onakpoya 2017; Panahi 2014, 2015, 2016; Panda 2018; Peng 2021; Pinsornsak 2012; Riva 2017 1006; Riva 2017 1684; Ross 2016; Rudrappa 2020; Sahebkar 2016; Satoskar 1986; Shadnoush 2020; Shehzad 2012; Shep 2019, 2020; Shokri-Mashhadi 2021; Singhal 2021; Srivastava 2016; Sterzi 2016; Thanawala 2021; Thomas 2021; Uddin 2021; Wang 2020; Wu 2019; Yang 2019; Zeng 2021)

HALO CHOLINE

ANOTHER ESSENTIAL NUTRIENT WITH DEFICIENT INTAKE

Superba2™ krill oil naturally contains choline as phosphatidylcholine, enough to contribute a useful amount of choline to daily diets. This is important, as choline has been known to be an essential nutrient since 1998 by the Institute of Medicine (Wallace 2018). Finally, the latest changes to food and dietary supplement labels by the USFDA (effective now) have officially anointed choline as an essential nutrient with a Daily Value (DV) to be listed with other essential vitamins and minerals such as niacin (watch for choline in updated versions of MultiV and MultiV-PRO). That means that anything over 2% of the DV in a serving of a product must be listed on Supplement Facts labels. Choline's DV is 550 mg, based on the amount needed for 97.5% of the population to have an intake that prevents deficiency signs (liver damage, at first). HALO delivers 25 mg of choline (5% DV) from phosphatidylcholine, found in cell membranes and your bloodstream.

Choline is found in our diets and in our cells as water-soluble salts and in phospholipids (such as phosphatidylcholine), soluble in water and oil. Richest dietary sources are phosphatidylcholines found in egg yolks, organ meats, soy, nuts and seeds. Like omega-3s, total choline intakes in the US are woefully low, with adults averaging 270 mg daily intakes, about half the DV. Small amounts of choline can be made in human brains, but never enough to fully prevent deficiency symptoms elsewhere. Thus, any additional choline in the diet is important and useful.

Choline is a simple but powerful little molecule. It has three methyl groups on a nitrogen itself stuck on the end of ethanol. It's all about the methyl groups, also known as one-carbon units. Turns out that one little carbon unit can do hidden big science to keep you running (literally and figuratively). Both choline salts and phosphatidylcholines exert a wide spectrum of important, essential functions to maintain health, but in vastly different ways. They are interconvertible in our cells, but how well this works is dependent on your genetics and epigenetics.

Choline has three major roles in human bodies: 1) in phospholipids for unique cell membrane structure and functions including bioactive EPA/DHA; 2) as a methyl (one carbon unit) donor to assist folate/B12 functions, synthesize many other metabolites, and to tag DNA with methyl groups at specific sites to control gene expression (epigenetics) – a vastly underrated function of choline; and 3) as a precursor for other important intermediary metabolites such as creatine, acetylcholine (a major excitatory neurotransmitter), alpha-glycerophosphocholine (GPC), betaine, bile salts (taurocholate, for one), CDP-choline (cytidine-5'-diphosphocholine), and many others. Most of these have been studied and shown to have benefits for different aspects of human health and exercise themselves, usually in large doses. Choline touches everything.

CHOLINE AND EXERCISE

The study of choline and exercise performance is a reflection of the confusion over which form, how much, and what it does in the body that has plagued acceptance of choline as an essential nutrient until very recently. Before 2000, blood free-choline levels were shown to decrease by 10-40% after long-duration, intense exercise, such as marathons. Lesser intensity or times of exercise did not decrease blood levels. Since free choline is the precursor to make acetylcholine, the major excitatory neurotransmitter that nerves use to contract muscles, any decrease was a concern that performance would suffer. In trying to find out if choline would improve or maintain exercise performance, both lecithin and choline salts were used at doses of around 2 grams of choline just before long-term running or cycling exercises. Improvements in heart rate, heart rate recovery post-exercise, and blood lactate levels were found, and some performance times were better, some not or not measured. Better results (including cutting off five minutes from a 20-mile run) were found when blood choline levels would be decreased but were maintained with choline supplementation. In several studies, no performance improvements were found from supplemental choline when blood choline levels would not be decreased by the exercise, even if blood choline levels were increased over the placebo groups. In other words, you want to maintain blood choline levels to prevent performance deficits – boosting choline blood levels over normal does not help. Supplemental choline can do that.

A different kind of performance study on visuomotor skills from a crossover study found that compared to placebo, choline (two grams choline bitartrate) an hour before the skill task showed better target hits and reaction times plus decreased pupil sizes – a marker of cognition and augmentation of cholinergic functions (Naber 2015). These findings have relevance to long-duration skill sports such as baseball, basketball, cricket, race car driving, soccer, tennis and other sports dependent on eye-hand coordination.

CHOLINE & EXERCISE SUMMARY

Long story short: research on choline is like a glass half full, or half empty. One can find evidence for both performance improvements (with conditions) and incorrect, sweeping conclusions that choline does not improve exercise performance (a clear case of by selection bias – seeing what you want to see, not seeing what you do not want to see and not seeing the whole tamale/big picture). Conditions for success are long-duration, strenuous exercise of two hours or longer to show benefits from choline supplementation. Given that most exercisers will be properly hydrated, fueled and not losing electrolytes, rather than top up blood choline levels immediately before exercise, it makes more sense to efficiently build up cell membrane choline levels with phosphatidylcholine from krill oil consistently ingested – with additional benefits from the omega-3 fatty acids.

(**Citations for Choline & Exercise**: Atzler 1935; Bjorndal 2018; Bucci 1993; Buchman 1999, 2000; Conlay 1986, 1992; de la Huerga 1951, 1952; Deuster 2002; Ernst 1960; Ganz 2017; Hirsch 1978; Hoeg 2020; Jager 2007; Martinez 2016; Mies 1958; Modinger 2019; Naber 2015; Newsom 2016; Penry 2008; Sandage 1992; Spector 1995; Staton 1951; Storsve 2020; von Allworden 1993, 1995; Wallace 2018; Warber 2000; Wurtman 1977)

COMBINATIONS OF OMEGA-3s & CURCUMINOIDS & CHOLINE FOR EXERCISE

Since choline, curcumin and omega-3s have been shown individually to benefit muscle and joint health for exercising (and non-exercising) persons, it makes sense to try them together. However, to date, there are no reports of curcumin mixed or taken together with krill oil found in the scientific literature of exercising persons. There are a few reports of a single human study that combined an enhanced-absorption curcumin (Longvida®) with a DHA-rich fish oil given together in separate pills or given individually (or a placebo) twice daily for 4-16 weeks in mostly older subjects that were sedentary and overweight/obese (Kuszewski 2020 625, 2902, 3190). These studies focused on cardiovascular and mental tests, and showed some benefits from each, but nothing extra from the combination. These studies are quite different from HALO with respect to how the curcumin and omega-3s were given, and did not have exercise stress – thus they do not have direct relevance to long-term endurance exercisers who want peak performance, recovery and musculoskeletal comfort. Interestingly, curcumin affected different tests than fish oil, showing room for an additive or synergistic effect if each could be delivered to cell membranes more efficiently.

(**Citations for Combinations of Omega-3s & Curcuminoids for Exercise**: Kuszewski 2020 625, 2902, 3190)

HALO™ SUMMARY

In summary, HALO has been carefully designed and manufactured in a unique, proprietary, patent-pending blend to deliver bioactive omega-3 fatty acids with protected curcuminoids to cell membranes, a unique breakthrough in delivery of these beneficial agents to your cells. In our beta-testing of HALO with trusted sources, we have found results that have surpassed the scientific literature findings of both omega-3s and curcumin, reinforcing the "feelability" of HALO for normal, everyday musculoskeletal aches and pains. Your locomotive system now has a protective HALO to maintain and support peak exercise performance.

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

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HALO ACTIVES – OMEGA-3 FATTY ACIDS & KRILL OIL (Superba2™) – EXERCISE & MUSCULOSKELETAL HEALTH

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HALO ACTIVES – CURCUMINOIDS – EXERCISE & MUSCULOSKELETAL HEALTH

(**Citations for Curcuminoids Background | Curcuminoids & Exercise Performance | Curcuminoids & DOMS, EIMD, Overexertion, Post-Exercise, Recovery | Curcuminoids & Joints/Musculoskeletal System**)

(**Citations for Curcuminoids Background**: Ahmed 2014; Anonymous 2010; Asher 2013; Bejar 2018; Blumenthal 2021; Bresciani 2020; Committee Herbal Medicine Products 2009; Coyner 1987; Erscheinungsdatum Bundesanzeiger 1990; Govindarajan 1980; Gupta 2013; Hatamipour 2019; Kalaycioglu 2017; Khajehdehi 2012; Krishnamurthy 1976; Li 2011; Natural Standard 2011; Ng 2006, 2012; Padmanaban 2018; Pawar 2014; Sharifi-Rad 2020; Shishodia 2005; Snow 1995; Srimal 1997; Tayyem 2006; Thamlikitkul 1989)

(**Citations for How Is HALO Different From Other Curcumin Products?**: Douglass 2015; Stohs 2017, 2019 293, 9417, 2020, 2021)

(**Citations for Curcuminoids & Exercise Performance**: Akazawa 2012; Amirkhani 2017; Bankowski 2022; Campbell 2021; Cheragh-Birandi 2020; Choi 2019; Fakhri 2019; Falgiano 2018; Franceschi 2016; Goh 2020; Herrick 2020; Huang 2015; Oliver 2016; Osali 2020; Santos-Parker 2017; Sedaghat 2018; Sugawara 2012; Suhett 2021; Takahashi 2013; Zoodfekr 2017)

(**Citations for Curcuminoids & DOMS, EIMD, Overexertion, Post-Exercise, Recovery**: Amalraj 2020; Bankowski 2022; Basham 2018, 2020; Campbell 2021; Cardaci 2020; Chilelli 2016; Davis 2019; Delecroix 2017; Doma 2020; Fang 2021; Faria 2020; Fernandez-Lazaro 2020; Hamidie 2017; Hewlings 2017; Hillman 2021; Jager 2017, 2019; Jones 2009; Mallard 2020; McAlister 2020; McFarlin 2016, 2019; Nicol 2015; Oliver 2017; Roohi 2016; Samadi 2019; Schwarz 2020; Sciberras 2015; Szymanski 2018; Tanabe 2015, 2019 524, 2019 82; Tanner 2020 1, 2020 AT6137; Udani 2009; Wang 2019; Yoon 2020)

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COMBINATIONS OF OMEGA-3s & CURCUMINOIDS

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