INSIDER’s Take

• Specialty carbohydrates and even a mineral-laden ingredient are innovating energy management for sports.

• A number of anti-inflammatory botanicals are offering new ways for active consumers to manage post-exercise soreness and muscle damage.

• Immune function has become a popular post-exercise focus in sports nutrition, and this is an area where probiotics and special plant compounds are grabbing attention.

The sports nutrition market is no stranger to innovation. Its historical client base has been on a nonstop quest to find the latest and greatest supplement to help more quickly build muscle and fuel workouts. These days, innovative ingredients are targeting various finer aspects of sports nutrition, such as the many aspects of recovery. The sports market has been seeing more ingredients promising to address inflammation, oxidative stress, nutrient depletion, blood flow and immune function.

In many cases, the emergence of innovative ingredients is driven by new consumer demands. The sports market has experienced a surge in new consumers from outside of the traditional core sports nutrition user pool of bodybuilders and world-class athletes. One way these new consumers have impacted the sports market is by demanding protein alternatives to dairy-based proteins.

To traditional tribes in various parts of the world, insects are not innovative ingredients, but to the somewhat civilized sports nutrition industry, insect protein is an innovative way to offer a full range of amino acids in a complete protein package. Cricket protein checks off a lot of the du jour boxes for non-core sports nutrition consumers: sustainable, environmentally friendly, paleo and nutrient-dense. As for the “yuck” factor, high-quality cricket powder does not have a strong flavor or color, and crickets are in the same animal family as lobsters and shrimp, which were also once considered too yucky to consume.

While whey protein still reigns supreme in sports nutrition, with solid results in research trials and at the retail cash register, plant proteins offer innovative ways for sports nutrition companies to forgo or supplement animal-based proteins. Pea, hemp, chia, quinoa and even algae are increasingly popular sources of vegan proteins. There is not a lot of research on plant proteins in sports nutrition, but the studies are forthcoming.
A 2015 publication of research led by the National Institute for Health and Medical Research in France, compared the effects of oral supplementation of pea protein (as NUTRALYS®, from Roquette) with whey protein and placebo on biceps muscle thickness (MT), finding similar MT increases between pea and whey proteins, indicating the plant version could be a viable alternative to the dairy staple.\(^1\)

Pea protein is especially rich in the amino acids lysine, arginine and the branched chain amino acids (BCAAs) leucine, isoleucine and valine. It is easy to digest and does not have some of the tricky whey compounds such as lactose and casein.

Citrulline, a non-essential amino acid, has become increasingly popular in combination with malate for helping to address fatigue and muscle weakness. One study on muscle energetics found citrulline malate supplementation in adult males undergoing an exercise-recovery protocol significantly reduced fatigue and increased the rates of post-exercise phosphocreatine recovery and oxidative production of ATP (adenosine triphosphate, the “energy molecule”).\(^2\)

Muscle fatigue is also inhibited by carnosine, a dipeptide of the amino acids beta alanine and histidine. The beta alanine prevents the histidine from linking up with other proteins. Histidine is a physico-chemical buffer of hydrogen ions that can accumulate in muscles as byproducts of energy production from glucose. High levels of hydrogen ions can cause muscle fatigue.

Supplementation with beta alanine increases skeletal muscle concentrations of carnosine and high intensity exercise capacity, according to 2007 research on CarnoSyn®, from NAI International.\(^3\) Research results published in 2009 further showed CarnoSyn supplementation in endurance cyclists enhanced sprint performance at the end of a simulated race.\(^4\) CarnoSyn supplementation in track-and-field athletes also slightly inhibited fatigue during repeated bouts of sprinting.\(^5\)

**Energy and Hydration**

One necessity common in both core and non-core sports nutrition users is energy or fuel. Both groups of consumers have embraced various stimulants to provide a pep in their step, but true energy comes from the production and breakdown of inside cell mitochondria. Several ingredients—such as ribose, coenzyme Q10, carnitine and creatine—that directly support ATP production have been on the market for quite a while.

An innovative ingredient made from peat and apples (elevATP™, from Futureceuticals) focuses on promoting ATP levels in red blood cells, major carriers of this energy molecule. Trace minerals from ancient peat are responsible for increasing ATP—minerals are cofactors in enzymatic reactions that produce ATP—while the polyphenols from apples offer antioxidant properties to balance out the reactive oxygen species (ROS) that can result from these enzymatic cycles.

Preliminary research published in 2013 showed elevATP acutely increased blood ATP levels without increasing ROS.\(^6\) Follow-up research published in 2014 confirmed the results on blood ATP levels and also found the increased ATP was likely from mitochondria-containing blood cells such as platelets and white blood cells, not from red blood cells such as erythrocytes, which do not have mitochondria and rely on glycolysis to increase ATP.\(^7\) They noted elevATP did not appear to
increase extracellular ATP such as in plasma. However, they did report a single dose of elevATP (150 mg) increased intramuscular ATP, which suggests the ingredient may impact ATP levels in other tissues.

In practical application, research published in 2015 demonstrated that elevATP supplementation (150 mg once daily) in healthy, male weightlifters improved body composition after eight weeks of resistance training. The researchers noted supplementation increased muscle cross-sectional area (CSA) and MT, without affecting body fat or weight. There were also no adverse effects on vital signs or blood markers. They noted while further research is needed to pinpoint the mechanisms of action, elevATP may be a better alternative than oral ATP supplementation, which has been shown to suffer poor bioavailability.

A 2016 publication looked at a blend of elevATP (150 mg), B vitamins (38 mg) and a combination of caffeine anhydrous and pterostilbene-bound caffeine (180 mg) in a study involving resistance-trained subjects and 12 weeks of weight training. Compared to placebo, the combination supplement showed greater increases in both CSA and MT without affecting blood pressure, heart rate and various markers of safety. There was also an improvement in fat mass and body fat percentage in the supplement group, compared to those taking placebo, a result attributed to the formula’s extended-release caffeine.

Energy production in the body is fueled by glucose and fats. Carbohydrates are the primary dietary energy macronutrient, as they directly replenish glucose stores. Some innovative specialty carbs have emerged as optimal sources of such fueling.

Highly branched cyclic dextrin (HBCD) may be a better carb alternative to glucose and similar carbs, and the key may be the molecular weights of the carbs and how they affect digestion. Researchers from Kyoto University in Japan found when low molecular weight carbs such as glucose are used in a sports drink, the osmotic pressure increases, which slows down gastric empty time. However, HBCD (as CLUSTER DEXTRAN®, from Glico), which has a higher molecular weight, did not increase osmotic pressure. Researchers noted a sports beverage containing HBCD can handle additional vitamins, minerals and organic acids without affecting gastric emptying time.

A patented polyglucoside extracted from barley starch (as Vitargo S2®, from Genr8) is designed to more quickly restore glycogen (glucose is stored as glycogen) and also offers a high molecular weight. Thus, the unique carb’s S2’s low osmolality allows it to replenish glycogen levels quicker than glucose without slowing down gastric emptying compared to glucose, according to research from the Karolinska Institute at the University College of Physical Education and Sports, Stockholm, Sweden. Study results published in 2008 further showed that athletes taking the Vitargo S2 predecessor Vitargo (from Swecarb AB) immediately following intense cycling sessions experienced 20 percent higher work output for a subsequent intense workout two hours later, compared to those taking a low-molecular weight glucose supplement.

Sports drinks replenish not only carbs for energy, but also several crucial nutrients, including electrolytes. L-alanine and L-glutamine are non-essential and conditionally essential amino acids, respectively, and both are involved in the production and storage of glucose. L-alanylglutamine (as
Sustamine®, from Kyowa Hakko) is a dipeptide that may offer improved bioavailability over other forms of these aminos, according to Kyowa Hakko.

Animal research published in 2015 found both low- (0.1 g/kg) and high-dose (0.5 g/kg) Sustamine helped limit post-workout protein degradation, by acting on signaling proteins, including nuclear factor kappa-B (NF-kB) and AMP-activated protein kinase (AMPK) that promote phosphorylation.13 Human research also published in 2015 demonstrated endurance-trained men taking low and high doses of Sustamine (300 mg and 500 mg) added to a sports drink experienced increased time to exhaustion compared to those taking either a regular sports drink or no hydration.14 Further, both doses increased plasma glutamine levels within 45 minutes of ingestion, and the high levels remained 60 minutes at 60 minutes post ingestion in the high dose group.

Recovery: Inflammation, Muscle Dynamics and Immune Function

Exercise can trigger inflammation response in both the muscles and joints. Inflammatory signaling molecules called cytokines acting systemically and in muscle tissue can impact muscle damage and regeneration. The goal here is management, avoiding a prolonged inflammatory state that can lead to more extensive tissue damage and scarring.

Several anti-inflammatory ingredients have been making ground in the sports market for specific benefits to muscles and, in some cases, joints.

Compounds in tart cherry (Prunus cerasus L.) target both inflammation and oxidative stress in exercise recovery. A study published in 2014 looked at these benefits in trained cyclists taking Montmorency tart cherry concentrate (as CherryActive, from CherryActive Ltd.) and discovered lower levels of lipid hydroperoxides (an oxidative stress marker) and high-sensitivity C-reactive protein (CRP, an inflammatory marker) in the supplemented group, compared to those taking placebo.15 The researchers concluded the reduced inflammation and oxidative stress was due to anthocyanins that increased expression of endogenous glutathione-related antioxidant enzymes, which inhibited lipid peroxidation.

Further benefit to recovery was reported in a 2015 placebo-controlled study that found a short-term dose of freeze-dried tart cherry powder supplement (as CherryPURE®, from Shoreline Fruit) helped speed recovery from muscle soreness, limit strength declines and decrease markers of muscle catabolism in resistance-trained adults.16 A follow-up study on CherryPURE was published in 2016 and demonstrated endurance-trained runners and triathletes taking the tart cherry supplement before, during and after a race had 13 percent faster half-marathon finish times and tested lower for markers of muscle catabolism, inflammation and oxidative stress, compared to the placebo group.17 The researchers also noted perception of muscle soreness was lower in the supplement group, compared to placebo.

A pair of botanicals steeped in traditional medicine of India (Ayurveda) offers anti-inflammatory properties that have proven useful in sports.

Ashwagandha (Withania somnifera) has both antioxidant and anti-inflammatory benefits. Recent research found the botanical acts on key cytokines, including tumor necrosis factor-alpha (TNFa)
and Nf-kB, to limit expression of pro-inflammatory chemokine genes (CCL2 and CCL5).\textsuperscript{18} Aswagandha’s direct effect on exercise physiology has also been studied.

A 2012 research publication reported elite cyclists who consumed ashwagandha extract (from Dabur India Ltd.) showed a 13 percent increase in oxygen uptake (VO2max), a measure of aerobic capacity, compared to the placebo group.\textsuperscript{19} The researchers credited the benefit to increased red blood cell and hemoglobin counts, which improve oxygen transport to muscles. Then in 2015, a study report detailed how young male subjects with little weightlifting experience who took 300 mg twice daily of ashwagandha root extract capsules (as KSM-66, from Ixoreal BioMed) had greater increases in muscle strength on bench presses and leg-extension exercises, and significantly greater increases in muscle size (arms and chest), compared to the placebo group.\textsuperscript{20} The ashwagandha group also showed a greater reduction in exercise-induced muscle damage, based on the marker creatine kinase, as well as greater increases in testosterone and decreases of body fat.

Curcumin, an active compound from turmeric (Curcuma longa), has been increasingly popular in the greater dietary supplement marketplace, partly for its anti-inflammatory actions. Like its Ayurveda cousin, curcumin impacts inflammation and oxidative stress by affecting TNFα and Nf-kB.\textsuperscript{21} Several recently reported studies have shown benefits to muscles. Human research published in 2015 found oral curcumin decreased inflammation and increased muscle regeneration.\textsuperscript{22} The researchers noted curcumin decreased leg pain associated with delayed-onset muscle soreness (DOMS) following exercise, as evidenced by performance metrics, lower blood CK levels and higher blood levels of interleukin-6 (IL-6), an anti-inflammatory cytokine.

Additional animal research on curcumin in exercise focused on the botanical’s ability to help muscle tissue grow new mitochondria. The muscles have the highest amount of mitochondria in the body, which helps provide the ATP needed to fuel contractions and growth. Endurance training is known to prompt muscles to clear out damaged mitochondria and promote mitochondrial biogenesis, the growth of new mitochondria by replicating existing mitochondria in the muscle tissue cells. Research published in 2015 detailed how curcumin treatment in combination with endurance training can accelerate mitochondrial biogenesis in muscles by increasing levels of cAMP (cyclic adenosine monophosphate).\textsuperscript{23}

Human data on curcumin and muscle health has shown similar benefits. In a 2015 publication involving young men who were healthy, but not regular weightlifters, those who took a water-stable form of curcumin (Theracurmin®, from Theravales) one hour before and 12 hours after exercise had slightly decreased peak CK activity, compared to placebo, and smaller maximal voluntary contraction (MVC) loss, which resulted in less muscle damage.\textsuperscript{24} Then a 2016 placebo-controlled study report showed oral curcumin supplementation (as Longvida®, from Verdure Sciences) in healthy university students, who had not resistance trained in the six months prior, inhibited increases in pro-inflammatory cytokines CK, TNFα and IL-8 for up to four days of recovery from exercise-induced muscle damage (EIMD).\textsuperscript{25} However, there were no differences between the groups on anti-inflammatory IL-6 levels and subjective muscle soreness.
Lemon verbena (Aloysia triphylla and Lippia citrodora) has also exhibited anti-inflammatory benefits, in addition to antioxidant actions. In 2011, Spanish researchers reported a proprietary lemon verbena extract (as PLX®, from Monteloeder) taken by healthy males after 90 minutes of eccentric exercise protected against oxidative damage and reduced markers of muscular damage, without blocking cellular adaptation to exercise.\textsuperscript{26} The same researchers published results in 2012 showing PLX supplementation in university students helped reduce oxidative stress markers during 21 days of aerobic exercise.\textsuperscript{27} Specifically, PLX activated glutathione-reductase in erythrocytes and lymphocytes and reduced levels of malondialdehyde and protein carbonyls in plasma.

Omega-3s are also masters at inflammation management, as long-chain omega-3s docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) are directly involved in the inflammatory cascade, in which they produce anti-inflammatory cytokines and compete with pro-inflammatory fatty acids for key enzymes. However, omega-3 fatty acids also offer a source of fuel for ATP production—the use of fats for energy fuels endurance exercise—and increase cardiovascular contributions to exercise.

Research has shown omega-3 supplementation limits post-exercise inflammation and muscle damage, and curbs muscle pain by significantly reducing blood levels of lactate and CRP.\textsuperscript{28,29} In a 2015 study, men who took a patented lipid and omega-3 blend derived from New Zealand green-lipped mussel (as PCSO-524®, from Pharmalink) for 26 days prior and 96 hours following muscle-damaging exercise had significantly lower inflammatory markers, resulting in less pain and loss of both strength and range of motion (ROM), compared to those taking placebo.\textsuperscript{30} A 2015 study involving elite cyclists found an association between omega-3 supplementation and both improved blood flow (i.e., flow mediated dilation, or FMD) and increased VO2 max, compared to placebo.\textsuperscript{31} The researchers tied these benefits to increased nitric oxide (NO) from omega-3 supplementation.

**Blood Flow and Nitrates**

The increased blood flow and VO2maxare top benefits for sports nutrition, but muscle efficiency improvement leading to performance benefits are also attributable to nitrates, which are commonly ingested via green leafy vegetables and beetroot (Beta vulgaris).

Arginine is a precursor to NO. In 2015, research on an inositol-stabilized arginine silicate (as Nitrosigine®, from Nutrition 21) demonstrated blood arginine levels increase within 30 minutes of a single dose (500 mg), and NO levels significantly rise over a period of at least 14 days post use.\textsuperscript{32} Another 2015 study showed healthy adults taking the supplement prior to an intense exercise increased muscle pump (swelling) and decreased biomarkers of muscle damage throughout recovery.\textsuperscript{33} Improved blood flow from Nitrosigine supplementation may also enhance cognitive performance, including focus and mental clarity.\textsuperscript{34}

Studies on beetroot help address muscle hypoxia, the limiting of oxygen availability in muscles during exercise that can reduce muscle function. Researchers reported in a 2014 publication how healthy subjects taking nitrate-rich beetroot before both moderate- and hypoxic-intensity exercise experienced faster oxygen uptake than those taking control supplements.\textsuperscript{35} They noted tolerance to hypoxic exercise was improved in the beetroot group.
A 2011 study in male club-level cyclists found taking a half liter of beetroot juice prior to time trial rides (4km and 16 km) increased mean power output and performance, compared to control juice. Subsequent research on beetroot juice in time-trialing cyclists found similar benefits and noted a post-drink increase in plasma NO. However, other studies have found no such effect from acute beetroot juice supplementation in either cyclists or runners.

Spinach has also emerged as a viable nitrate source for sports nutrition. Preliminary research on red spinach (Amaranthus dubius) being conducted at Auburn University, Alabama, has found recreationally trained adults taking the high-nitrate red spinach extract (as OXYSTORM™, from PLT) showed improved ventilator threshold (when ventilation increases faster than VO2). Part of the research still ongoing is looking at the extract’s effect on exercise performance.

**Immune Function**

Intense exercise can lower immune function. Upper respiratory tract infections (URTIs) are a common result, so the sports world is increasingly paying attention to innovative ingredients researched for benefits to immune health and URTIs specifically.

One innovative immune health ingredient with research relevant to and conducted directly on athletes is a mixture of beta-glucans derived from baker’s yeast (Saccharomyces cerevisiae). In a 2012 study, healthy adult subjects taking a yeast-derived beta-glucan (as Wellmune®, from Biothera) experienced fewer days of URTI symptoms, compared to the control group, and the supplement group appeared to have improved breathing ability. Specifically on athletes, a 2013 study found Wellmune supplementation in recreationally active men and women before a cycling exercise support blood leukocytes (white immune cells) and increased key cytokines—IL-2, IL-4, IL-5 and interferon-gamma (IFN-γ)—important to mucosal immune function. A subsequent 2013 publication further investigated suppressed mucosal immunity from strenuous exercise, finding Wellmune supplementation in runners was associated with a 37 percent decrease in the number of cold/flu symptom days following a marathon run, compared to placebo, and increased salivary immunoglobulin A (IgA), a marker of mucosal immunity.

Mucosal lining in the gut see tons of antigens (foreign body triggering an immune response) every day, and the microbiota of the gut help protect the mucosa by competing with antigens and secreting potent antimicrobial peptides (AMPs), among other mechanisms still being explored.

For sports nutrition consumers, probiotics may help with gastrointestinal problems associated with high-intensity exercise and improve immune management. Animal research has suggested probiotic supplementation (Lactobacillus plantarum) can even increase muscle mass via an anti-inflammatory action and enhance exercise performance by limiting plasma lactate, ammonia, CK and serum glucose levels.

In 2012, researchers published results on a multi-species probiotic (as Ecologic®Performance, from Winclove b.v)—Bifidobacterium bifidum W23, Bifidobacterium lactis W51, Enterococcus faecium W54, Lactobacillus acidophilus W22, Lactobacillus brevis W63 and Lactococcus lactic W58—detailing beneficial effects on gut barrier function and various immune-modulating compounds. They reported endurance-trained athletes (triathletes, runners and cyclists) taking the probiotic
supplement post-exercise for 14 weeks tested for reduced zonulin—increased levels of the protein zonulin cause leaks in the gut barrier—as well decreased carbonyl proteins (marker of protein oxidation) and decreased TNFa.

One innovative probiotic ingredient, GanedenBC30, from Ganeden Biotech, is spore-forming and protected by a hard outer shell; the probiotic germinates once safely inside the small intestines. Research on GanedenBC30 has highlighted the probiotic’s immunomodulating abilities, such as supporting frontline immune cells (mononuclear phagocytes) and managing inflammatory compounds in the gut.\textsuperscript{47,48}

As a bonus to athletes, research on GanedenBC30 in an in vitro model of the stomach and small intestines revealed the probiotic improves the digestion of carbohydrates (fructose and lactose) and proteins/ams acids.\textsuperscript{49} Specifically, the supplement improved absorption of leucine by 23 percent, isoleucine by 20 percent, valine by 7 percent, glutamine by 116 percent, ornithine by 100 percent, tryptophan by 100 percent and citrulline by 128 percent.

Research will continue to surface on these innovative ingredients, and new innovative ingredients will continue to test the sports nutrition market. After all, sports nutrition consumers are always looking for something new, something novel, something to improve exercise even if only slightly. Whether such innovation means the latest performance enhancer and recovery aid, or trendier sourcing cred—including sustainable, environmental and organic—sports nutrition consumers will eagerly give innovative ingredients a try, especially if backed by good science and research.

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