

FUNCTIONAL INGREDIENTS FOR THE ATHLETE AND BEYOND

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KEY POINTS

- Creatine's potential benefits for health go far beyond physical performance, yet more targeted education and further research in a variety of demographics are needed for a wider consumer group to fully appreciate and understand this to the point where they supplement daily.
- Dairy ingredients that have traditionally been used for other benefits, such as higher-quality infant formulas, show promise for enhanced
 health and wellbeing, both in athletic and general populations. These include lactoferrin, alpha-lactalbumin, milk-fat globule membrane and
 phospholipid-rich whey protein. Whey protein is naturally composed of several fractions, the proportion of which can be adjusted to promote
 different health benefits.
- Lactoferrin is a whey protein fraction renowned for its role in immune-related properties. It also shows promise in maintaining optimal iron status in females.
- Alpha-lactalbumin, a whey protein fraction naturally rich in tryptophan, may help promote sleep, overnight recovery, improve cognitive
 performance and promote muscle protein synthesis.
- Milk fat globule membrane and other phospholipid-rich whey proteins provide the muscle-promoting benefits of whey protein, alongside
 phospholipids for cognitive performance and management of stress and anxiety.

INTRODUCTION

Both athletes and the general population are taking a more holistic approach to their well-being, turning to food and supplements to improve and optimize their physical and mental health and performance. This has led to growing interest in functional ingredients with varying levels of scientific substantiation for both safety and efficacy.

Bioactive compounds including creatine, lactoferrin, alpha-lactalbumin, and phospholipid-rich whey protein are gaining traction, scientific substantiation and consumer recognition. While not necessarily new ingredients *per se*, these compounds show promise in areas outside of their traditional use. All the nutrients discussed in this article can be found either mainly or exclusively in animal- sourced foods. However, the level is significantly less than that found in either supplements or food products enriched with these ingredients. This Sports Science Exchange (SSE) article examines the potential benefits for athletes and the wider population seeking enhanced immune function, improved mental well-being, better sleep and overall cognitive and physical performance. Filling gaps in the scientific literature, overcoming application challenges in formulating products with effective doses, consumer education and product availability are key to fully realizing the benefits of these ingredients for the athlete and beyond.

FUNCTIONAL INGREDIENTS

Creatine

Creatine supplementation has long been recognized for its potential to promote physical performance, particularly increasing power and speed, decreasing fatigue and promoting lean body mass (Rawson,

2018). However, the benefits are now known to surpass just those related to physical performance and anthropometry. Emerging evidence points to improvements in brain health as an underappreciated benefit of creatine supplementation across different populations. From women, who may have lower endogenous creatine stores, to vegans with reduced intakes, patients recovering from traumatic brain injury, to depression and anxiety, creatine is emerging as a potential go-to option for a wide demographic (Candow et al, 2023; Gutiérrez-Hellín et al, 2024; Smith-Ryan et al, 2021). However, it is still relatively underutilized and underappreciated outside of the athletic world.

Creatine products are still synonymous with sport, in terms of the claims being made and the brands selling them. For example, claims related to power are on almost half of creatine products, while cognition and brain claims stand at 16% and 13%, respectively (Nutrition Integrated, 2024). Indeed, most brands selling creatine are those within the sports nutrition arena, with the majority also having whey protein powders and pre-workouts in their range.

The most common product formulations reflect the history of creatine, as well as its limitations and instability in liquid applications. Three quarters of products in the US are ready-to-mix (RTM) powders, with 16% capsules and tablets, followed by the emerging gummy format at 7% (Nutrition Integrated, 2024). Most RTM powders are unflavored (93%), highlighting that creatine consumers are using it for nutrition benefits more than as a flavored beverage for enjoyment.

When it comes to the type of creatine used, creatine monohydrate is still the clear leader, even though other creatine formats are available.

1

This reflects the significant scientific substantiation on creatine monohydrate, its wide availability, safety, consumer familiarity and favorable price point. Creatine hydrochloride is a distant second in terms of usage in products with a significant number of other creatine formats used to a much lesser degree.

Kreider et al. (2022) reviewed the evidence behind the bioavailability, efficacy, safety and regulatory status of creatine monohydrate and several other types of creatine. There are other formats that have a growing body of evidence in their favor. However, many forms on the market are still lacking strong scientific backing, particularly to support their use over creatine monohydrate. Creatine monohydrate was highlighted as having strong evidence behind it, with some evidence for the following forms:

- Creatine salts:
 - Creatine Citrate
 - Creatine Pyruvate
- Magnesium Creatine Chelate
- Creatine Ethyl Ester
- Creatine HCI
- Creatine Nitrate
- Buffered Creatine Monohydrate

Most products suggest the standard 3-5 g/serving, with products in the US trending towards 5 g and Europe averaging 3 g/serving. This is likely reflective of the regulatory environment in Europe, which permits authorized health claims on creatine products with a 3 g serving.

To reach a wider group of consumers, some brands are positioning creatine products to tie in with other trends in the nutrition space and tout other benefits, either with or without additional bioactive ingredients. This includes promoting brain health and cognitive function, supporting hormonal balance, enhancing strength and promoting recovery.

To help athletes and the general population navigate the product landscape, they need to understand the benefits or risks of any of the co-formulated ingredients and choose the product that is optimal for themselves.

Whey Beyond Protein

Whey protein, long celebrated for its superior nutritional and functional properties, is a complex mixture of various protein fractions, each with distinct structural and biological characteristics, including its makeup of amino acids. While these fractions come together to provide a high-quality source of protein and bioactive components, utilizing technology to alter the proportion of these fractions may promote different health and technical benefits. The main protein fractions in sweet whey (the byproduct from cheese production) include beta-lactoglobulin, alphalactalbumin, glycomacropeptide (GMP), immunoglobulins, lactoferrin and more (Layman et al., 2018; unpublished observations) (Figure 1).

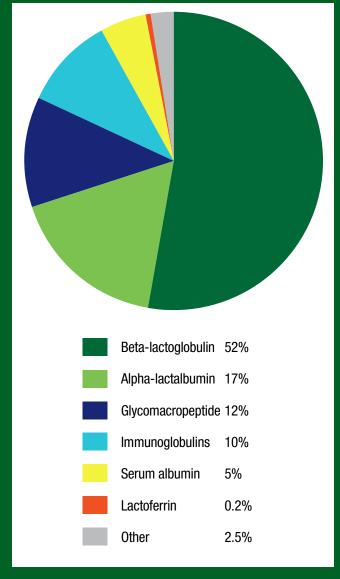


Figure 1: Proteins fractions in sweet whey (approx. %).

Lactoferrin

Lactoferrin is an iron-binding glycoprotein naturally present in mammalian milk, as well as body secretions such as tears, saliva and nasal fluid (Dix & Wright, 2018). The level in bovine whey protein is low (<0.5% for sweet whey protein, ~1.5% for milk whey protein). However, when utilizing technology such as ion exchange, this unique fraction can be isolated up to 95% purity.

Lactoferrin is perhaps best known for its role as the immune system's first line of defense. It exhibits broad-spectrum antimicrobial activity due to its ability to sequester iron, thus starving microbes of this vital element. Both *in vitro* and *in vivo* studies have highlighted the ability of lactoferrin to positively impact symptom severity and duration of illness, with mounting evidence for its use as a prophylactic and therapeutic agent (Zimecki et al., 2021). However, the potential benefits of lactoferrin extend beyond just those related to immunity, as highlighted in Figure 2 (Kowalczyk et al., 2022).

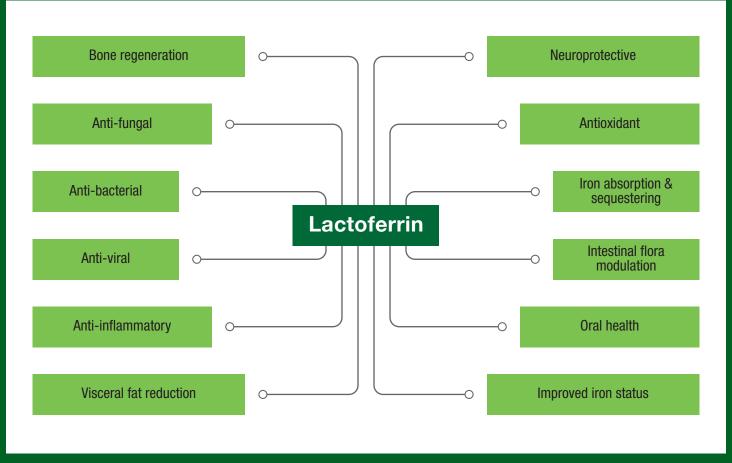


Figure 2: Overview of the potential health benefits of lactoferrin.

Immunity. Due to its antiviral properties, lactoferrin has been investigated in several trials for its potential to mitigate COVID-19 infections and reduce recovery time in COVID-19 patients (Rosa et al., 2023), Campione et al. (2021) investigated the effects of bovine lactoferrin on COVID-19 patients with mild-to-moderate symptoms. Thirty-two patients received 1 g bovine lactoferrin in oral format and 32 mg intranasally/day, while another group received standard pharmaceutical treatment (n=32) and a third group received no treatment (n=28). Those in the bovine lactoferrin group obtained a negative polymerase chain reaction (PCR) test significantly faster than both the standard pharmaceutical treatment group and untreated COVID-19 patients (14 vs. 27 vs. 33 days, respectively). The bovine lactoferrin group also reported faster recovery from symptoms compared to the other groups. Lactoferrin has also been proposed as a potential therapeutic agent due to its ability to protect against insultinduced oxidative stress and the subsequent "cytokine storm" found in more severe COVID-19 patients (Zimecki et al., 2021).

Bovine lactoferrin may favorably impact both incidence and the severity of symptoms of colds. Daily supplementation with 400 mg bovine lactoferrin plus 200 mg immunoglobin G (lgG) was found to significantly reduce the total number of colds over a 90-day period compared to placebo (48 vs 112, respectively) (Vitetta et al., 2013). This trend

continued even when accounting for medication (Vitetta et al., 2013). The treatment group (n = 47) also reported fewer cold-related symptoms compared to the placebo group (n = 43) (Vitetta et al., 2013).

These findings were similar in another study which investigated the effect of daily supplementation with 200 mg bovine lactoferrin, 600 mg bovine lactoferrin or placebo on prevalence and duration of infectious disease in otherwise healthy adults (Oda et al, 2020). The duration (days) of total infectious disease was reported to be significantly shorter in both 200 mg (2.0) and 600 mg (2.0) bovine lactoferrin groups compared to placebo (3.0). Meanwhile, the duration of summer colds was significantly shorter with 600 mg bovine lactoferrin compared to placebo (2.0 vs 3.0).

There are several proposed mechanisms for lactoferrin's antibacterial and antiviral properties, including direct binding to the virus or bacteria, release of antibacterial peptides during digestion, iron chelation, direct binding to the target cells leading to reduced viral attachment and expression of antiviral cytokines and chemokines (Hong et al., 2024).

Iron status. Athletes, especially female endurance athletes, face a higher risk of impaired iron status due to increased iron losses from both menstruation and the physiological demands of endurance

exercise (Alauntye et al., 2015). While iron supplements are often used to improve dietary intake, this can come with some unwanted side effects, such as gastrointestinal discomfort. The ability of lactoferrin to improve iron status has been tested in various female populations (Christofi et al., 2024).

Sixteen athletes were split into two groups: one taking both lactoferrin and iron (450 mg and 1.5 mg, respectively), and a control group taking only iron (1.5 mg), over 8 weeks (Koikawa et al., 2008). The control group experienced significant decreases in ferritin, serum iron and red blood cell counts, while the lactoferrin group maintained stable hematological markers. Additionally, the lactoferrin group had a higher red blood cell count and lower post-run blood lactate levels compared to the control group.

Other studies in female populations have highlighted the ability of lactoferrin to improve iron status during pregnancy, while avoiding or reducing gastrointestinal side effects (Lepanto et al., 2018; Nappi et al., 2009; Paesano et al., 2006).

Bone health. Lactoferrin may be beneficial to several aspects of bone health. It has been reported to promote bone growth by stimulating osteoblast proliferation, differentiation and survival, while inhibiting osteoclast formation (Cornish & Naot, 2010). One in vivo study in an animal model investigated the effects of bovine lactoferrin on bone regeneration during distraction osteogenesis (Li et al., 2015). Lactoferrin was found to significantly enhance bone formation, mineral density and mechanical strength at both early and late stages of healing. The treatment also improved biochemical markers of bone formation and reduced bone resorption.

Application. Lactoferrin is mainly available in the form of capsules, due to convenience, precise dosing and easy availability, with some RTM powders and lactoferrin gummies also available. While lactoferrin may become denatured with significant heat treatment (making ready-to-drink applications less common), the heat required to produce gummies was reported to have no impact on bioactivity of lactoferrin gummies (Wotring et al., 2022). Daily dosing of 200-600 mg, up to 1000 mg during times of illness, is reflective of the scientific literature for most benefits.

Alpha-lactalbumin

Also known as alpha, alpha-lac or lactalbumin, alpha-lactalbumin (ALAC) is one of the main protein fractions naturally occurring in milk. ALAC is the most prominent protein fraction in human milk and the second most prominent fraction in bovine milk. It is higher in tryptophan than other whey protein fractions, making it one of the highest natural dietary sources of this essential amino acid, as well as having a naturally higher level of cysteine than the other fractions (Layman et al., 2018) (Figure 1).

While standard whey protein provides roughly 15-22% of protein as ALAC, sophisticated processing methods, including membrane filtration, can increase the proportion of ALAC in whey to 30-95% purity, depending on the ingredient.

Sleep and Cognitive Performance. Tryptophan is an essential amino acid that serves as the precursor for serotonin and melatonin, both key neurotransmitters that help regulate mood, sleep, cognition and emotional well-being (Yousef et al., 2024). Ingestion of ALAC can increase the plasma tryptophan to large neutral amino acids (LNAA) ratio, enhancing tryptophan transport across the blood-brain barrier (Markus et al., 2005). Several studies have investigated the effects of evening consumption of ALAC on measures of sleep, with some studies in athletic populations (Barnard et al., 2024).

In a recent double-blind crossover study, 19 trained individuals with sleep difficulties consumed 40 g of ALAC or control (isocaloric collagen) before sleep (Barnard et al., 2025a). Supplements were taken 2 hr before bedtime for three nights in a controlled setting. Researchers tracked sleep architecture, blood tryptophan, mood and cognitive performance. The ALAC treatment significantly increased plasma tryptophan levels, boosted non-REM Stage 2 sleep and reduced REM sleep. ALAC also improved the next-morning reaction times in tasks involving attention, speed and orientation.

This echoed the results of a previous study conducted in female athletes (Miles et al., 2021). In a crossover study with 16 female athletes, ALAC supplementation after evening competition increased Stage 2 non-REM sleep and improved recovery compared to control (standard whey protein) or placebo (water). Performance in the Yo-Yo Intermittent Recovery Test was enhanced 24 hr post-exercise compared to placebo and control.

In another study of 18 female rugby players, nightly ALAC intake reduced sleep onset latency during bye and away game weeks (Gratwicke et al., 2023). Sleep improvements were not seen in the placebo group, suggesting ALAC may support faster sleep onset during competitive seasons.

However, seven days of ALAC supplementation did not improve sleep or physical performance compared to a control group in a study involving 24 trained athletes with mild to moderate sleep difficulties. These findings suggest that ALAC may be more effective for athletic populations with more severe sleep disturbances (Barnard et al., 2025b).

Physical Performance and Muscle Building. ALAC provides a high level of essential and branched chain amino acids that whey is renowned for, particularly leucine (Gorissen et al., 2018) making it an optimal choice for athletes of all levels wanting to support muscle growth and recovery. The impact of ALAC on measures of physical performance and muscle synthesis have been reported in a few studies.

Qin et al. (2019) investigated the effects of pre-exercise ingestion of ALAC versus whey protein isolate (CW), both combined with carbohydrate, on endurance performance, muscle pain and mood in 11 trained male runners. Participants consumed either the ALAC or CW beverage 2 hr prior to completing a self-paced 21-km run. Various physiological and psychological measures were assessed 2 hr before exercise, immediately before and immediately after exercise. While there was no significant difference in 21-km performance times between the two trials, ALAC

ingestion led to significantly higher-pressure pain threshold compared to CW, both before and after exercise, indicating reduced muscle sensitivity. Additionally, ALAC significantly reduced perceived fatigue and salivary cortisol levels after exercise compared to CW.

When compared to collagen peptides, ALAC supplementation led to significantly greater increases in myofibrillar and sarcoplasmic protein synthesis during short-term intensified aerobic training in endurance-trained individuals (Oikawa et al., 2020). Despite equal protein intake, the concentration of essential and branched chain amino acids in ALAC enhanced post-exercise muscle remodeling, highlighting the importance of protein quality in supporting training adaptations. Although most protein products marketed for overnight recovery utilize casein as the main protein source due to its slower absorption kinetics and wide scientific substantiation, whey protein consumed pre-sleep has been shown to be equally effective for increasing both mitochondrial and myofibrillar protein synthesis rates during overnight recovery from endurance exercise (Trommelen et al., 2023).

Application. While the science on the benefits of ALAC in both athletic and general population is growing, product options on the market utilizing higher purity ALAC ingredients are currently limited. This is projected to change due to the ever-growing recognition of whey protein's benefits from a wider consumer base, as well as increased desire from consumers for products to promote sleep without the use of melatonin. The recommended dose for ALAC to promote sleep and overnight recovery is 20-60 g (Barnard et al., 2024), which can be easily achieved in RTM format. Alpha-lactalbumin is the second most abundant whey protein fraction in bovine milk and therefore can be obtained by drinking fluid milk. However, the quantity is significantly less, accounting for only 3.5% of total protein in milk (Layman et al., 2018).

Phospholipid-Rich Whey Protein and Milk Fat Globule Membrane

The fat globules in milk are surrounded by a complex membrane called the milk fat globule membrane (MFGM). It is rich in several bioactive components including IgG, lactoferrin, sialic acid and lipids, like phosphatidyl serine, phosphatidyl choline, sphingomyelin and gangliosides (Figure 3). Phospholipids (PLs) are an integral part of the nervous system and are key for maintaining membrane integrity, neuronal membrane health and signaling capacity (Slykerman et al., 2024). They have been implicated in cognitive health with aging, as well as cognitive performance and psychological response to stress. Phosphatidyl choline also provides a dietary source of the essential nutrient, choline. Meanwhile, IgG and lactoferrin are renowned for their immune-related properties.

Cognitive Performance, Stress, and Anxiety. Stress management and cognitive performance are key across populations, with consumers looking to manage stress and anxiety through holistic means (Young et al., 2024). Dairy phospholipids are emerging in scientific literature as potential agents to satisfy this need.

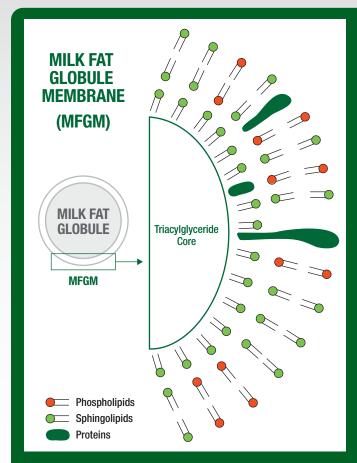


Figure 3: Schematic of milk fat globule membrane (MFGM).

Davies et al. (2023) found that twelve weeks supplementation with either 600 or 1200 mg of MFGM in healthy adults led to significantly lower stress scores at both six and twelve weeks compared to placebo. There was also a trend towards reduced anxiety by week twelve. Psychological assessments also indicated improved mood and sleep quality, suggesting MFGM may support emotional resilience and general mental well-being in healthy adults.

These results were echoed in an open-label pilot study, over four weeks of daily supplementation with 20 g phospholipid-rich whey protein (providing 1.4 g milk PLs and 13 g whey protein) in adults with intermittent anxiety (Ormond et al., 2024, unpublished results). Participants reported significant reductions in anxiety related to primary and secondary stressors, as well as lower overall anxiety severity. Sleep also improved, with easier sleep onset and greater alertness upon waking. One limitation with this study is that there was no control group for comparison.

Meanwhile, six weeks of bovine milk-derived PLs supplementation (2.7 g/day) in 54 high-perfectionist men showed that PL intake improved cognitive performance under stress, specifically reaction time during an attention-switching task and increased mid-stress energetic arousal (Boyle et al., 2019). The control group in this study consumed macronutrient-matched control, minus the PLs. While PLs did not reduce cortisol levels, they were linked to a trend toward reduced anticipatory stress and higher blood pressure responses.

When examining the specific PLs, phosphatidyl serine, a widely available supplement, has been reported to improve cognitive function tests in adults aged 50-69 compared to placebo, highlighting its potential for aging athletes and general population alike (Kato-Kataoka et al., 2010).

Application. The ingredients providing these unique components are generally labelled as whey protein phospholipid concentrate (WPPC), MFGM or phospholipid-rich whey protein. They normally provide a high level of whey protein, with the protein fractions in the standard ratio complimented by a higher level of fat containing the bioactive components mentioned here. While this area continues to build on the scientific side, products containing these ingredients are also starting to emerge. The high-quality whey protein, PLs, IgG and other bioactive components found in these ingredients are naturally occurring, therefore can be found in food sources of dairy proteins, such as full fat milk. However, as with the other ingredients, it is present at significantly lower levels than that found in the concentrate.

SUMMARY

Functional ingredients like creatine and dairy-derived lactoferrin, alphalactalbumin, and phospholipid-rich whey protein, such as MFGM, are gaining recognition for their benefits beyond their traditional uses. Backed by growing scientific evidence, these components support immune function, sleep, cognitive performance, mood and recovery appealing to both athletes and the wider wellness-focused population. While research and product development continue to evolve, these ingredients show strong potential to meet rising demand for holistic, functional nutrition solutions. Helping consumers understand where to find these ingredients and the optimal dose is key to embracing their benefits. These components can be found naturally occurring in foods such as meat and dairy products. However, the levels in typically consumed amounts of food sources are lower, sometimes significantly, than those used in the research shown to have a benefit. Thus addition of food products or supplements that utilize these ingredients may be warranted.

PRACTICAL APPLICATION

- Educate both athletes and general consumers on the benefits
 of creatine beyond physical performance and physique. Help
 them to navigate and select the correct creatine product,
 particularly for those that have additional claims or are
 blended with other ingredients.
- Creatine monohydrate still has the greatest level of scientific substantiation on its benefits, is widely available globally, safe and functions well in standard applications, such as RTM products. Many other formats do exist with varying levels of support.
- Lactoferrin in doses of 200-600 mg per day may have a broad array of benefits, including immune support, bone health and optimizing iron status without gastrointestinal challenges of iron supplementation.

- Alpha-lactalbumin provides the high essential and branched chain amino acid composition whey is renowned for, but with a higher level of tryptophan. Dosing 20-40 g pre sleep may help improve muscle protein synthesis overnight, promote a more restful night's sleep and increase morning performance.
- Phospholipid-rich whey protein, including MFGM, offers
 a high-quality whey protein with a guaranteed level of
 naturally occurring phospholipids, which may improve stress
 management, cognitive performance and support cognitive
 health with aging. Doses of 600 mg 2.7 g phospholipids
 have been shown to be effective in healthy adults and those
 with intermittent anxiety.

The views expressed are those of the authors and do not necessarily reflect the position or policy of PepsiCo, Inc.

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