

A–Z of nutritional supplements: dietary supplements, sports nutrition foods and ergogenic aids for health and performance—Part 20

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Accepted 9 March 2011

INTRODUCTORY REMARKS

As usual, the alphabet throws together a mixture of supplements with different levels of popularity and scientific support. Part 20 covers some rarely reported, studied and/or little used supplements in sport: glycine, histidine and inosine. The majority of human studies of supplementation with the essential amino acid histidine has involved clinical work. In terms of athletic performance, there is current interest in supplementation strategies to increase muscle content of the histidine-containing dipeptide (HCD), carnosine. Despite some interest in the use of a chicken breast extract (CBEX) described in this article, most of the focus in this area involves β -alanine supplementation (covered in part 5). There was some interest in inosine as an ergogenic aid in the 1990s but it appears not to have been studied since then. Meanwhile, there appears little role for glycine supplementation in sport although some interest in glycine-containing compounds is possible. β -Hydroxymethyl β -butyrate (HMB) is much more well known, with marketing usually targeting bodybuilders.

GLYCINE K Currell

Glycine is the smallest amino acid; it is non-essential and can be synthesised from serine. Glycine is present in most proteins and is particularly highly concentrated in collagen. Consequently, one of the highest food sources of glycine is gelatin. Glycine is also one of the three amino acid components of glutathione, which is a key component of the body's defences against oxidative stress; however, it is thought that glycine availability is not the limiting step in glutathione synthesis. Glycine ingestion increases plasma concentrations of insulin in a similar way to other amino acids.¹ Glycine is also an inhibitory neurotransmitter.

There is little research on supplementation with glycine. Research has looked at its potential role in decreasing inflammation.² Sport specific research has focused on combining glycine with other nutrients. Glycine-propionyl-L-carnitine (GPLC) has been shown to influence exercise performance,³ decrease oxidative stress⁴ and potentially increase vasodilation through increases in plasma nitrate.⁴ At present, there is insufficient evidence to suggest the use of glycine as a supplement to enhance sporting performance. However, further research on the effectiveness of GPLC is warranted.

HISTIDINE-CONTAINING DIPEPTIDES

W Derave and I Everaert

Carnosine (β -alanyl-L-histidine) and its methylated analogues anserine (β -alanyl-N₁-methylhistidine) and balenine (β -alanyl-N₃-methylhistidine) are HCDs present abundantly in mammalian skeletal muscles. Carnosine is the only HCD found in human skeletal muscles, whereas all three HCDs are present in the omnivorous human diet. In an attempt to understand the role of carnosine in human muscle, Harris *et al*⁵ searched for a carnosine loading protocol. They showed that β -alanine supplementation (4–6 g/day) for several weeks (4–10 weeks) resulted in elevated muscle carnosine levels (up to 80%). β -Alanine seems to be without adverse effects if the dose of 10 mg/kg body weight per 2-h interval, which can lead to paraesthesia, is not exceeded.⁵ Hill *et al*⁶ showed that carnosine loading leads to better performance during high-intensity exercise (cycling at 110% of W_{\max} to exhaustion). With the availability of more recent studies, it becomes evident that mostly high-intensity efforts that last several minutes experience a positive influence of β -alanine supplementation. Indeed, β -alanine was not ergogenic for repeated sprint performance (10×5 s sprint),⁷ while both a simulated 2000-m rowing race (± 6 min)⁸ and the sprint at the end of 2-h simulated cycling race⁹ were improved by β -alanine. It is plausible that high-intensity performance is affected in long-term vegetarians, as they are characterised with lower muscle carnosine levels (–26%). The ergogenic mechanism of β -alanine may reside in the attenuation of acidosis through the proton-buffering capacity of carnosine, whereas other physiological properties of carnosine (antioxidant, calcium sensitisation) cannot be excluded at present.¹⁰

Besides β -alanine supplementation, CBEX is also used, mainly in Japan, to elevate muscle carnosine stores. CBEX, obtained via hot water extraction of chicken breast, is a rich source of HCD, like anserine (1.4 g/100 ml) and carnosine (0.6 g/100 ml). An increase in the muscle carnosine content is likely to occur as a result of chronic CBEX supplementation. Long-term CBEX supplementation enhanced the time to exhaustion at the last spurt of a relatively high-intensity endurance performance.¹¹ Suzuki *et al*¹² showed that the acute supplementation with CBEX (0.4 g carnosine+1.1 g anserine) 30 min before 10×5 s repeated sprints, decreased the bicarbonate buffering in blood but did not affect performance. The effect of acute supplementation

with HCD on blood buffering and high-intensity exercise performance needs further investigation.

In conclusion, an increment in muscle carnosine levels, either by chronic β -alanine or CBEX supplementation, seems to be ergogenic mainly in high-intensity exercise lasting several minutes.

INOSINE

L McNaughton

Inosine is a nucleoside formed when hypoxanthine is attached to a ribose ring (also known as a ribofuranose) via a β -N₉-glycosidic bond. Inosine plays a role in several metabolic functions including increasing red blood cell concentrations of 2,3-diphosphoglycerate (2,3-DPG), which is involved in oxygen transport.¹³ It may also potentiate the action of endogenously formed adenosine and inhibit its uptake and clearance. It has been proposed to enhance exercise performance via the effects on 2,3-DPG or by an increase in ATP concentrations.¹⁴

Little scientific investigation has been conducted on inosine as an ergogenic aid and few peer-reviewed papers could be found. The available studies involving trained individuals investigated chronic intakes of large doses of inosine (eg, 5–10 000 mg/day), but these protocols did not provide an ergogenic effect for endurance^{15 16} or sprint activities.¹⁷ It is suggested that high-dose inosine, a uric acid precursor, combined with high urinary excretion, could be detrimental and result in kidney stones or acute renal failure.¹⁷ In summary, there appears to be little support for the use of inosine as an ergogenic aid though it is still used in some over-the-counter fitness products. There are continuing clinical trials that may indicate a future therapeutic effect as an antioxidant for exercise.

HYDROXYMETHYL BUTYRATE

G Slater

HMB is a metabolite of the essential branched chain amino acid leucine, via α -ketoisocaproate, the transamination product of leucine. Approximately 2–10% of leucine oxidation proceeds to HMB. Much initial research on HMB focused on animals, assessing effects on immune function, morbidity and mortality, colostral milk fat content, growth rates, safety and toxicity. Despite unconvincing results in animal research, HMB supplementation was used in humans in the mid-1990s on the presumption that it might enhance gains in muscle size and strength while reducing muscle damage and soreness associated with resistance training,¹⁸ and possibly also enhance aerobic capacity.

Supplementation with either 1.5 or 3.0 g/day of HMB had a favourable impact on indirect indices of muscle protein breakdown and muscle damage, with concomitant trends for enhanced strength and skeletal muscle hypertrophy.¹⁸ Consequently, the popularity of HMB supplementation increased dramatically, becoming one of the top supplements used by athletes in the late 1990s.¹⁹ More recently, interest in HMB supplementation among athletes has probably declined. Despite this, HMB research reports within the sports environment continue to emerge. There are several recent HMB reviews,^{20 21} with results of resistance training research from 2001 to 2007 consolidated into two meta-analyses.^{22 23} Nissen and Sharp²² concluded that HMB supplementation augmented lean mass and strength gains associated with resistance training, although the magnitude of effect was trivial (0.28% increase in lean mass gain per week). Rowlands and Thomson²³ identified similar small benefits from HMB supplementation

in untrained males but effects were trivial for strength and non-existent for body composition in trained lifters.

This disparity in responsiveness to HMB supplementation relative to resistance training status might be expected, given the suppression in skeletal muscle protein breakdown as a consequence of resistance training adaptations.²⁴ Furthermore, if HMB does enhance net protein balance following resistance training as a consequence of reducing protein degradation, any effect on adaptations is likely to be blunted compared with interventions that enhance protein synthesis as the protein synthetic response is many times more sensitive to nutrition interventions than degradation.²⁵ An exception may be in clinical conditions such as cancer in which skeletal muscle atrophy results from an elevation in skeletal muscle protein breakdown.²⁶

Short-term HMB supplementation appears to be safe, with daily doses equivalent to approximately 6 g/day (76 mg/kg) having no impact on indices of hepatic, renal or immune function.²⁰

Based on current available reports, the potential for HMB supplementation to enhance strength training adaptations appears to be small in previously untrained individuals and negligible in resistance-trained athletes. Given that the protein synthetic response is much more sensitive to nutrition interventions than protein breakdown, the resistance-trained athlete is advised to focus on proven strategies such as post-exercise ingestion of high biological value proteins rich in leucine to maximise adaptation to the resistance training stimulus.

CONCLUDING COMMENTS

While there is probably little reason to study (or take) glycine, histidine or inosine supplements, some investigation of other compounds containing these molecules may be warranted. In the case of histidine, there is good reason to try to enhance muscle storage of the HCD, carnosine, but the most common and effective supplement to achieve this is β -alanine rather than histidine or carnosine per se. Finally, there is evidence that supplementation with HMB offers some assistance in reducing the breakdown of muscle protein. However, the best application of this appears to be in clinical situations involving high levels of catabolism, such as cancer, rather than in athletic populations since strategies to increase muscle size and strength in resistance-trained groups are more effectively targeted at increasing protein synthesis.

Competing interests None

Provenance and peer review Commissioned; not externally peer reviewed.

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Br J Sports Med 2011 45: 530-532

doi: 10.1136/bjsports-2011-090020

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