

Nutritional Strategies to Promote Muscle Hypertrophy

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Abstract

The use of nutritional supplements in sport is widespread, and few serious athletes do not, at some stage in their career succumb to the temptation to experiment with one or more nutritional supplements. Supplementation is particularly prevalent among strength and power athletes, where an increase in muscle mass can benefit performance. Protein supplements have not been shown to be effective except in those rare cases where the dietary protein intake is inadequate. Individual amino acids, especially ornithine, arginine and glutamine are also commonly used, but this is not supported by documented evidence. A variety of mineral supplements, including chromium, boron and vanadium, as well as more exotic compounds such as hydroxymethylbutyrate (HMB) are also used by strength athletes, but again there are no well controlled studies to provide evidence of a beneficial effect. Creatine is perhaps the most widely used supplement in sport at the moment. Supplementation can increase muscle creatine phosphate levels, and, although not all published studies show positive results, there is much evidence that strength can be improved and muscle mass increased by supplementation.

Key words: creatine, muscle hypertrophy, nutrition supplements, protein.

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A very wide range of supplements are currently on sale to athletes, and a large fraction of the total number are promoted as having beneficial effects on muscle growth and repair. Although there is some experimental evidence to support the use of some of these products, the claims made for others are not supported by experimental evidence. Food supplements are not subject to regulation in the same way as drugs, and the consumer is often confused. This review will briefly discuss some of the evidence relating to nutritional interventions that may influence the growth and development of skeletal muscle.

In sports that require strength and power a high lean body mass, and especially a high muscle mass, confers a definite advantage. Supplement use is widespread among athletes in strength sports, and a wide variety of supplements are used. A few of the supplements that are more commonly used by athletes are described briefly below, but this list is by no means comprehensive.

Protein and Amino Acids

The idea that athletes need a high protein diet is intuitively attractive, and indeed there is evidence that the requirement for protein is increased by physical activity, [18]. Muscles consist largely of protein, and their involvement is fundamental to performance in all sports.

It is also readily apparent that regular exercise has a number of highly specific effects on the body's protein metabolism. Strength training results in increases in muscle mass, indicating an increased formation of actin and myosin, and it is tempting to assume that this process is dependent on protein availability. Endurance training has little effect on muscle mass, but does increase the muscle content of mitochondrial proteins, especially those involved in oxidative metabolism. Hard exercise also results in an increased level of muscle damage, usually at the microscopic level, and there is clearly a role for protein in the repair and recovery processes.

The changes that comprise that adaptive response are selective, and are specific to the training stimulus: they are also dependent on the availability of an adequate intake of protein in the diet. The case for a high protein diet for athletes thus seems to be well founded and is widely believed to be true. In a survey of American college athletes, 98% believed that a high protein diet would improve performance. There is, however, compelling evidence that protein supplementation is not necessary for the athlete. The dietary protein requirements of the general population have been the subject of extensive investigation. It is now generally accepted that

Nutritional strategies to promote muscle hypertrophy

a daily requirement of about 0.6 grams of protein per kilogram body weight per day will meet the needs of most of the population, provided that a variety of different protein sources make up the diet, and provided also that the energy intake of the diet is adequate to meet the energy expenditure [17]. To allow for individual variability and variations in the quality of ingested proteins, the Recommended Daily Allowance for protein is set at about 0.8 g/kg in most countries.

The contribution of protein oxidation to energy production during exercise decreases to about 5% of the total energy requirement, compared with about 10-15% (i.e. the normal fraction of protein in the diet) at rest, but the absolute rate of protein degradation is increased during exercise because of the high energy turnover [4]. This leads to an increase in the minimum daily protein requirement, but this will be met if a normal mixed diet adequate to meet the increased energy expenditure is consumed. Deficiencies in protein intake are more likely in the sedentary individual, especially when energy intake is restricted in order to control body weight, than in the athlete training hard who consumes sufficient energy to meet the demand. In spite of this clear relationship between total energy intake and the adequacy of dietary protein intake, however, many athletes ingest large quantities of protein-containing foods and expensive protein supplements. Daily protein intakes of up to 400 grams are not unknown in some sports, and in the diet of body builders, protein typically accounts for more than 20% of total energy intake, and occasionally as much as 40% [1]. Disposal of the excess nitrogen is theoretically a problem if renal function is compromised, but there does not appear to be any evidence that excessive protein intake among athletes is in any way damaging to health [17].

Although the recommended protein intake for athletes has been set at about 1.2-1.7 g/kg/d, [17] protein may account for a lower than normal percentage of total energy intake on account of the increased total energy intake. In endurance athletes, and especially in marathon runners, it is not uncommon to find that protein accounts for less than 10%, and sometimes even less than 8%, of total energy intake. Even lower values - perhaps even less than 5% of total energy intake - may be able to provide sufficient protein when the total intake is very high. It seems clear, therefore, that supplementation with protein is not necessary for athletes, except perhaps in the rare situations where energy intake is restricted. Even then, restriction of energy intake will severely limit the duration and intensity of exercise that can be performed and there is unlikely to be a need for a higher intake of protein than will be supplied by the diet.

Sales of whole protein powders account for a major part of the nutritional supplement sales to athletes, but a number of individual amino acids are also popular. Ar-

ginine and ornithine are reported to stimulate growth hormone release and to promote growth of lean tissue when taken during a period of strength training (see [3] for a review of these studies). There is some published evidence to support this, but any increase in growth hormone secretion is small compared with that which results from about of high intensity exercise. A number of other amino acids (including histidine, lysine, methionine and phenylalanine), are sold as anabolic agents, but [3] concluded after a review of the literature that there is little reason to believe that amino-acid supplements will promote gains in muscle mass.

Not with standing the lack of experimental data to support their beliefs, most strength trained athletes believe that a high protein diet can improve the rate of gain of muscle mass. Science ignores this accumulated wisdom at its peril, and it is possible that there may be effects that remain to be identified. It is clear that a prolonged period of training will cause substantial changes in the structural and functional characteristics of skeletal muscle and other tissues. Although major changes in muscle function are not apparent in response to single exercise bouts, small cumulative changes must take place between training sessions. There is good evidence of adaptive changes in muscle structure and function taking place in response to only a few exercise sessions [10]. These changes are different from those that are commonly observed to occur after a single exercise bout, when the observed responses are largely catabolic in nature and evidence themselves as muscle damage and soreness [2]. Nonetheless, there must be adaptive changes involving synthesis of new proteins in response to each training stimulus. It is likely that the methods currently available are simply inadequate to measure these changes with any degree of reliability.

In the recovery period, muscle glycogen synthesis is a priority, but synthesis of new proteins should perhaps be seen as being of equal or even greater importance. Because little attention has been paid to this area, it is not at present apparent what factors may be manipulated to influence these processes. The hormonal environment is one obvious factor that may be important, and nutritional status can influence the circulating concentration of a number of hormones that have anabolic properties, the most obvious example being insulin. It is, however, increasingly recognised that cell volume is an important regulator of metabolic processes [31, 16] and there may be opportunities to manipulate this to promote tissue synthesis. During and after exercise there may be large changes in cell volume, secondary to osmotic pressure changes caused by metabolic activity, hydrostatic pressure changes, or by sweat loss.

Alterations in cell volume induced by changes in osmolality are well known to alter the rate of glycogen synthesis in skeletal muscle [19]. Amino acid transport

into muscles is also affected by changes in cell volume induced by manipulation of the trans-membrane osmotic gradient: skeletal muscle uptake of glutamine is stimulated by cell swelling and inhibited by cell shrinkage [20]. The intracellular glutamine concentration appears to play an important role in a number of processes, including protein and glycogen synthesis [28], but the effect of ingestion of glutamine on these aspects of post-exercise recovery is not known at this time.

The full significance of these findings for the post-exercise recovery process and the roles they play in adaptation to a training program remain to be established. Manipulation of fluid and electrolyte balance and the ingestion of a variety of osmotically active substances or their precursors offers potential for optimising the effectiveness of a training regimen.

Creatine

Creatine has been used by many successful athletes, particularly in track and field athletics, but also now in many, if not most, other sports. Some indication of the extent of its use is gained from the fact that the estimated sales of creatine to athletes in the United States alone in 1997 amounted to over 300,000 kg. This represents a remarkable growth, as its use first became popular in sport after the 1992 Olympic Games in Barcelona. What distinguishes creatine from other ergogenic aids is that it seems to be effective in improving performance. More significantly, perhaps, its use is not prohibited by the governing bodies of sport, and there appear to be no harmful side effects even when very large doses are taken, at least in the quantities that are necessary to produce an ergogenic effect.

Creatine is an amino acid (methylguanidine-acetic acid) which occurs naturally in the diet, being present in meat: 1 kg of fresh steak contains about 5 g of creatine. The normal daily intake is less than 1 gram [14], but the estimated daily requirement for the average individual is about 2 grams [32]. The body has a limited capacity to synthesise creatine in the liver, kidney and pancreas and in other tissues, but the primary site of synthesis in man is the kidney. This supplies the amount required in excess of the dietary intake, and is also the only way in which vegetarians can meet their requirement. Synthesis occurs from amino acid precursors (arginine and glycine), but the synthetic pathway is suppressed when the dietary creatine intake is high.

Studies of resting human skeletal muscle have shown the CP concentration to be about 75 mmol/kg dry weight and the free creatine concentration to be about 50 mmol/kg [13]. There is, however, quite a large range of values reported in the literature, and it seems clear that there is considerable inter-individual variability. A number of factors may account for this, including differences in the composition of the preceding diet. The muscle fibre composition may also be of some impor-

tance: the CP content is higher in ST fibres than in FT fibres in women, although in men the difference was not statistically significant [27]. There is some evidence that the muscle total creatine content is higher in women than in men.

The first study to systematically investigate the effects of supplementation of large amounts of creatine was that of Harris et al [12]. In a comprehensive study, they showed that ingestion of small amounts of creatine (1 g or less) had a negligible effect on the circulating creatine concentration, whereas feeding higher doses (5 g) resulted in an approximately 15-fold increase. Repeated feeding of 5 g doses every 2 h maintained the plasma concentration at about 1 mmol/l over an 8 hour period. Repeated feeding of creatine (5 g four times per day) over a period of 4-5 days resulted in a marked increase in the total creatine content of the quadriceps femoris muscle. An increase in muscle creatine content was apparent within two days of starting this regimen, and the increase was greatest in those with a low initial level: in some cases an increase of 50% was observed. Approximately 20% of the increase in total muscle creatine content is accounted for by creatine phosphate.

It seems clear that there is an upper limit to the creatine and CP levels that can be achieved in muscle, and this is not unexpected. There was some evidence, from a model where one leg was exercised during a period of creatine supplementation while the other leg was rested, that exercise enhanced the effect of creatine supplementation on the muscle creatine content. There was no effect of creatine supplementation on the ATP content of the muscle, and no adverse side effects were noted, even when 30 g/day were taken for 7 days. In contrast to these reported effects of creatine supplementation on muscle creatine and CP content of human skeletal muscle, there seems to be little effect in the rat [25], and care may be necessary in the translation of data from animal models to the human situation.

Creatine and Muscle Strength

Although there have been numerous investigations into the effects of creatine supplementation on the ability to generate high levels of muscle power, few studies have looked for possible effects on muscle strength. This seems surprising in view of the importance of a high force generating capacity for the development of power. In an early study, subjects performed 5 sets of 30 maximal voluntary isokinetic contractions before and after supplementation with creatine or placebo [11]. No effect was seen in the placebo group, and an increase in muscle peak torque production was seen in the creatine group only in the later stages of some of the sets. No effect of creatine supplementation on peak torque was seen, but this experimental model might not allow subjects to generate maximum forces because of the large number of contractions to be performed.

Nutritional strategies to promote muscle hypertrophy

More recently, five days of creatine supplementation was shown to be effective in increasing maximum voluntary isometric strength of the knee extensor muscles in individuals engaged in a strength training program [21]. This gain was maintained in a subsequent test after a period during which a placebo was administered. In a second group of subjects, the treatment order was reversed: no gain in strength was seen after the first period of placebo administration, but an increase was observed in the third test, after the creatine supplementation period. Isometric endurance capacity at various fractions of MVC was also increased after creatine supplementation but was not affected by the placebo treatment.

In a group of previously untrained young women, the effects of a 10 week program of strength training were enhanced by daily supplementation with creatine relative to the effects observed with placebo treatment [29]. Similarly, it was found that a 7-day supplementation period increased performance in strength related tasks in young men undertaking a strength training program [30].

More information is clearly required as none of these studies was able to provide a mechanism for the observed effects, though all three studies reported an increase in body mass with creatine supplementation. It does, however, appear that short term supplementation with creatine can increase the force generating capacity of skeletal muscle.

Creatine and Body Mass

Many studies and much anecdotal report support the suggestion that acute supplementation with creatine is associated with a prompt gain in body mass. This typically seems to amount to about 1-2 kg over a supplementation period of 4-5 days, but may be more than this. In reviewing those studies where changes in body mass were reported: 11 studies where body mass increases occurred and 3 where no change in mass were found [3].

Because of the rapid increases in body mass, it must be assumed that this is mostly accounted for by water retention. Increasing the creatine content of muscle by 80-100 mmol/kg will increase intracellular osmolality, leading to water retention. A reduction in urinary output during supplementation was found, tending to confirm this suggestion [15]. The increased intramuscular osmolality due to creatine itself, however is not likely to be sufficient to account for all of this water retention. It has been suggested that co-ingestion of creatine and carbohydrate, which results in high circulating insulin levels [8, 9], may stimulate glycogen synthesis, which will further increase the water content of muscle. Evidence from an animal model, however, does not show an effect of creatine on glycogen resynthesis in muscle or liver after exercise-induced glycogen depletion [26].

There is some preliminary evidence for a stimulation of protein synthesis in response to creatine supplementation [34], but further experimentation is required. It seems unlikely that major effects on muscle protein content can be achieved within 4-5 days. It must be conceded, however, that the reported gains in muscle strength within the same time scale are difficult to explain.

b-Hydroxy b-Methyl Butyrate (HMB)

b-hydroxy b-methylbutyrate is a metabolite of leucine, and is also present in small amounts in some foods. There appears to be only one study published in a peer-reviewed journal in which the effects of HMB administration to humans has been investigated [24]. This paper presented the results of two supplementation studies which showed that subjects ingesting 1.5 or 3 g of HMB per day for 3-7 weeks experienced greater gains in strength and in lean body mass compared with control groups. Although it is not easy to find any fault with this study, it would be premature to conclude on the basis of this report that there is an advantage to be gained from HMB supplementation. Nonetheless, it is sold in large amounts in sports nutrition stores.

Chromium Picolinate

Chromium is an essential trace element which has a number of functions in the body, and has been reported to potentiate the effects of insulin [22]. Because of the anabolic effects of insulin, it might be expected that amino acid incorporation into muscle protein would be stimulated, enhancing the adaptive response to training. There is also some evidence to suggest an increased urinary chromium loss after exercise, further supporting the idea that athletes in training may have higher requirements than sedentary individuals. Chromium is widely used as a supplement by strength athletes, and is usually sold as a conjugate of picolinic acid: this form is reported to enhance chromium uptake [5].

Supplementation of the diet with chromium picolinate was reported to enhance the adaptive response to a strength training program, with an increase in lean body mass [5]. No direct measures of muscle mass were made, however, and the results of this study must be viewed with caution. A number of subsequent studies, mostly using more appropriate methodology, have failed to reproduce these results, with no effect on lean tissue accretion or on muscle performance being seen [3, 33]. Nonetheless, chromium supplementation remains popular.

Vanadium

Vanadium is also sold as a promoter of the action of insulin, and there is a limited amount of data from animal studies to support this. There has been little attempt to investigate possible anabolic actions in humans, but

one study has looked at the effects of oral supplementation with vanadyl sulphate on body composition and strength in weight-trained subjects [6]. There was no effect of a 12 week supplementation period at a daily dose of 0.5 mg/kg on any of the measured variables. It has to be concluded on the basis of the available information that an anabolic effect for vanadium supplementation has not been established.

Boron

Boron has been claimed to increase circulating testosterone levels [23], and this has clear potential for promoting growth. The experimental evidence, however, is not strong, and is derived from a single study on postmenopausal women. More recent studies have not shown evidence of a positive effect of boron supplementation in amounts of 2.5 mg/day over a 7-week period in male bodybuilders engaged in a strenuous training program [7]. Boron supplementation had no effect on the gain in lean body mass or in strength that occurred during the study period, and also had no effect on the circulating testosterone level. The balance of available evidence, therefore, does not support a role for boron supplements in promoting muscle hypertrophy.

No mention has been made of supplements such as iron or calcium or of the varied vitamin preparations which are widely used by the general public. The evidence suggests that the use of these supplements is perhaps more prevalent in athletes than in the general population, but the perceived benefits are similar. Iron, of course, is important to the athlete because of the importance of haemoglobin in oxygen transport, and while anaemia is not more prevalent in athletes than in the general population the consequences may be more apparent. Nonetheless, the same principles apply, and supplementation is not warranted unless a specific deficiency is known to exist.

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References

- [1]Burke LM, Inge K: Protein requirements for training and "bulking up", in Burke LM, Deakin V (ed): *Clinical sports nutrition*. Sydney, McGraw Hill, 1994, pp 124-150.
- [2]Clarkson PM: Eccentric exercise and muscle damage. *Int J Sports Med* 1997; 18, S3: 14-17.
- [3]Clarkson PM: Nutritional supplements for weight gain. *Sports Science Exchange* 1998; 11: 1-10.
- [4]Dohm GL: Protein as a fuel for endurance exercise. *Ex Sport Sci Rev* 1986; 14: 143-173.
- [5]Evans GW: The effect of chromium picolinate on insulin controlled parameters in humans. *Int J Biosoc Med Res* 1989; 11: 163-180.
- [6]Fawcett JP, SJ Farquhar, RJ Walker, Thou T, Lowe G, Goulding A: The effect oral vanadyl sulfate on body composition and performance in weight-training athletes. *Int J Sport Nutr* 1996; 6: 382-390.
- [7]Ferrando AA, NR Green: The effects of boron supplementation on lean body mass, plasma testosterone levels, and strength in male bodybuilders. *Int J Sport Nutr* 1993; 3: 140-149.
- [8]Green AL, Simpson EJ, Littlewood JJ, Macdonald IA, Greenhaff PL: Carbohydrate ingestion augments creatine retention during creatine feeding in humans. *Acta Physiol Scand* 1996a; 158: 195-202.
- [9]Green AL, Hultman E, Macdonald IA, Sewell DA, Greenhaff PL: Carbohydrate ingestion augments skeletal muscle creatine accumulation during creatine supplementation in humans. *Am J Physiol* 1996b; 271: E821-E826.
- [10]Green HJ, Jones S, Ball-Burnett ME, Smith D, Livesey J, Farrance BW: Early muscular and metabolic adaptations to prolonged exercise training in man. *J Appl Physiol* 1991; 70: 2032-2038.
- [11]Greenhaff PL, Casey A, Short AH, Harris RC, Soderlund K, Hultman E: Influence of oral creatine supplementation on muscle torque during repeated bouts of maximal voluntary exercise in man. *Clin Sci* 1993; 84: 565-571.
- [12]Harris RC, Soderlund K, Hultman E: Elevation of creatine in resting and exercised muscle of normal subjects by creatine supplementation. *Clin Sci* 1992; 83: 367-374.
- [13]Harris RC, Hultman E, Nordesjo LO: Glycogen, glycolytic intermediates and high-energy phosphates determined in biopsy samples of musculus quadriceps femoris of man at rest. *Scand J Clin Lab Invest* 1974; 33: 109-120.
- [14]Heymsfield SB, Arteaga C, McManus C, Smith J, Moffitt S: Measurement of muscle mass in humans. *Am J Clin Nutr* 1983; 37: 478-494.
- [15]Hultman E, Soderlund K, Timmons JA, Cederblad G, Greenhaff PL: Muscle creatine loading in men. *J Appl Physiol* 1996; 81: 232-237.
- [16]Lang F, Busch GL, Volkl K: The diversity of volume regulatory mechanisms. *Cell Physiol Biochem* 1998; 8: 1-45.
- [17]Lemon PWR: Effect of exercise on protein requirements. *J Sports Sci* 1991; 9 (Special Issue): 53-70.
- [18]Lemon PWR: Do athletes need more dietary protein and amino acids? *Int J Sport Nutr* 1995; S39-S61.

Nutritional strategies to promote muscle hypertrophy

- [19]Low SY, Rennie MJ, Taylor PM: Modulation of glycogen synthesis in rat skeletal muscle by changes in cell volume. *J Physiol* 1996; 495: 299-303.
- [20]Low SY, Rennie MJ, Taylor PM: Signalling elements involved in amino acid transport responses to altered muscle cell volume. *FASEB Journal* 1997; 11: 1111-1117.
- [21]Maganaris CN, Maughan RJ: Creatine supplementation enhances maximum voluntary isometric force and endurance capacity in resistance trained men. *Acta Physiol Scand* 1998; 163: 279-287.
- [22]Mertz W: Chromium: history and nutritional importance. *Biol Trace Elem Res* 1992; 32: 3-8.
- [23]Nielsen F, Hunt C, Mullen L, Hunt J: Effect of dietary boron on mineral, estrogen, and testosterone metabolism in postmenopausal women. *FASEB J* 1987; 1: 394-397.
- [24]Nissen S, Sharp R, Ray M, Rathmacher JA, Rice D, Fuller JC, Connolly AS, Abumrad N: Effect of leucine metabolite b-hydroxy b-methyl butyrate on muscle metabolism during resistance-exercise training. *J Appl Physiol* 1996; 81: 2095-2104.
- [25]Oopik V, Timpmann S, Medijainen L, Viru A: Effect of in vivo creatine administration on creatine content in skeletal muscle of rat. *Clin Sci* 1994; 87 (Suppl): 116.
- [26]Oopik V, Timpmann S, Medijainen L, Aleksejeva T: Effect of creatine administration on blood urea and post-exercise glycogen repletion in liver and skeletal muscle in rats. *Ann Nutr Metab* 1996; 40: 359-363.
- [27]Rehunen S, Harkonen M: High-energy phosphate compounds in human slow-twitch and fast-twitch muscle fibres. *Scand J Clin Lab Invest* 1980; 40: 45-54.
- [28]Rennie MJ, Low SY, Taylor PM, Khogali SE, Yao PC, Ahmed A: Amino acid transport during muscle contraction and its relevance to exercise. *Adv Exp Med Biol* 1998; 441: 299-305.
- [29]Vandenberghe K, Goris M, Van Hecke P, Van Leemoutte M, Vangerven L, Hespel P: Long-term creatine intake is beneficial to muscle performance during resistance training. *J of Applied Physiology* 1997; 83: 2055-2063.
- [30]Volek JS, Kraemer WJ, Bush JA, Boetes M, Incledon T, Clark KL, Lynch JM: Creatine supplementation enhances muscular performance during high-intensity resistance exercise. *J of the American Dietetic Association* 1997; 97: 765-770.
- [31]Waldegger S, Lang F: Cell volume and gene expression. *J Membr Biol* 1997; 162: 95-100.
- [32]Walker JB: Creatine biosynthesis, regulation and function. *Adv Enzymol* 1979; 50: 117-142.
- [33]Walker LS, Bemben MG, Bemben DA, Knehans AW: Chromium picolinate effects on body composition and muscular performance in wrestlers. *Med Sci Sports Ex* 1998; 30: 1730-1737.
- [34]Ziegenfuss TN, Lemon PWR, Rogers MR, Ross R, Yarasheski KE: Acute creatine ingestion: effects on muscle volume, anaerobic power, fluid volumes, and protein turnover. *Med Sci Sports Ex* 1997; 29: S127.