# Natural Supports for Gaining and Maintaining Muscle Mass

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Muscle-building research is useful for athletes and bodybuilders as well as for elderly patients and those with muscle-wasting conditions. Research shows that a healthy diet, resistance exercise, and nutritional supplements are beneficial for improving body composition and the body of research on nutritional supplements for athletes is growing.

However, supplementation will not improve muscle size and strength without resistance training, such as weight lifting or weight-bearing aerobics. The sports-nutrition and weight-loss industries in the United States comprise a growing market and there were reports of $14.3 billion dollars in sales of such products in 2004.[1] In addition, according to the *Nutrition Business Journal*, this product market increased sales by 14 percent to reach $15.6 billion in 2005 and is estimated to grow at a rate of approximately 5–7 percent per year for the next 8 years.[2]

## Body Composition and Its Effects on Muscles

*Insulin Resistance*

Insulin resistance is a state in which the pancreas secretes increasingly higher levels of insulin to facilitate glucose uptake into skeletal, hepatic, and adipose tissue cells. Specific glucose receptors, such as the glut-4-insulin–dependent receptors in muscle and adipose tissue are poorly responsive to high levels of glucose in the blood. This glucose is then transported to the liver and metabolized to glycogen and is stored as fat in the liver or in adipose tissue.

Moderate weight loss has been shown to reduce insulin resistance. Hyperinsulinemia increases intracellular lipid and fat accumulation, which, in turn, may increase insulin resistance. Insulin-resistant skeletal muscle has lower oxidative capacity and has fatty-acid oxidation favoring lipid accumulation.[3] In addition, high lipid levels in skeletal muscle also result in a lower oxidative capacity.[4]

Hormones have also been shown to have a great impact on insulin resistance. Stress and its resulting increase in epinephrine and cortisol affects insulin resistance. These adrenal hormones have been shown to increase glycogen breakdown from the liver and affect glucose utilization unfavorably.[5,6] Estrogen supplementation may also increase insulin resistance, particularly in postmenopausal women.[7] Increased testosterone in females and increased estrogens in males decrease peripheral glucose utilization.[8]

Studies have shown that dehydroepiandrosterone (DHEA) supplementation increases peripheral glucose utilization.[9] Insulin-like growth factor–1 (IGF-1) is a polypeptide stimulated by growth hormone, which affects growth and glucose metabolism. Studies have shown that IGF-1 increases peripheral glucose utilization as well as decreases protein catabolism.[10]

*Aging*

Many physiologic changes seen with aging affect muscle size and strength. Many hormones, such as testosterone, estrogen, DHEA, growth hormone, and IGF-1, decrease with age. Research suggests that age-related muscle loss, or sarcopenia, may be related to declines in growth hormone, IGF-1, estrogen, and testosterone and other androgens.[11] In addition, decreased nutritional intake and lowered vitamin D levels cause muscle atrophy in aging patients. Other causes of muscle loss include decreased nerve innervation, lowered physical activity, and increased levels of the proinflammatory cytokines tumor-necrosis-factor–alpha (TNF-$\alpha$) and interleukin-6.[12] Loss in skeletal muscle is estimated to be 35–40 percent between ages 20 and 80.[13]

*Diet*

Macronutrient dietary recommendations for athletes vary greatly. High-protein diets are often recommended to provide protein and amino acids necessary for protein synthesis. However, most organizations still recommend diets with ample carbohydrates to provide glycogen in the muscles during exercise. Sufficient fat in the diet is also necessary to provide essential fatty acids as well as fat soluble vitamins. High-protein, low-carbohydrate diets have been shown to decrease appetite and caloric intake as well as increasing losses in total body weight and fat mass.[14] Another study on high-protein, low-carbohydrate diets showed increased muscle-protein synthesis, increased whole-body muscle proteolysis, and a 50 percent decrease in plasma insulin levels, with no changes in total plasma IGF-1, growth hormone, or fat free-mass.[15]

High-protein diets are generally designed with the assumption that 30 percent of the total energy intake will be from protein. A study on college-age women showed that postprandial thermo-

## Muscle-Building Supplements

| Supplements | Doses |
|---|---|
| Whey protein | 10–20 g/day |
| Branched chain amino acids | 7–12 g/day |
| Creatine monohydrate | 20 g for 5 days, followed by 2 g/day |
| Beta-hydroxy-beta-methyl butyrate | 3 g/day |
| Glutamine | 6–10 g/day |
| L-Carnitine | 2 g/day |
| Conjugated linoleic acid | 2–4 g/day |
| Alpha lipoic acid | 600 mg/day |
| Testosterone | Physician should adapt to individual patients |
| Dehydroepiandrosterone | 25–100 mg/day |
| Growth hormone | Physician should adapt to individual patients |
| Chrysin | 300 mg/day |
| Chromium picolinate | 400 µg/day |

genesis was twofold higher from a high-protein diet compared to a high-carbohydrate diet, leading to increased energy expenditure and probable weight loss.[16]

## Nutritional and Botanical Supplements for Muscle Building

*Whey Protein and Branched-Chain Amino Acids*

Whey is a byproduct of cheese manufacturing. Whey contains lactose; minerals; and proteins such as alpha-lactalbumin, beta-lactoglobulin, and lactoferrin. In addition, whey contains approximately 24 percent branched chain amino acids (BCAAs), which have been shown to stimulate protein synthesis.[17]

Studies indicate that whey protein supplementation increases insulin sensitivity and decreases body weight in insulin-resistant rats.[18] Research also shows an increase in satiety following a whey-protein meal compared to a meal containing casein protein.[19] Side-effects are rare with whey supplementation but may include fatigue, nausea, increased stool frequency, headaches, and thirst.[17] Whey protein should be avoided in individuals with dairy allergies and may decrease absorption of some medications.[20]

BCAAs are essential amino acids, including leucine, isoleucine, and valine. These amino acids play multiple roles in protein metabolism. Specifically, leucine has been shown to signal protein synthesis in skeletal muscle.[21] BCAAs stimulate protein synthesis in adipose tissue and in the liver as well as inducing the pancreas to release insulin, resulting in increased protein synthesis.[22] These amino acids also decrease muscle breakdown during exercise.[23] BCAA supplementation can increase plasma ammonia levels in dosages in the 40–60 g per day ranges or in the presence of metabolic disorders; hence, caution is advised when considering long-term supplementation. Liver enzymes should be measured in patients on long-term BCAAs.

*Creatine Monohydrate*

Creatine is a nitrogenous amine found in meat, dairy products, and fish. The body also synthesizes creatine in the liver, kidneys, and pancreas. This amine is found primarily in skeletal muscle. There are many studies supporting the use of creatine to increase muscle mass, strength, stamina, and endurance. Creatine in skeletal muscle exists as free creatine and phosphocreatine. Phosphocreatine is involved with the conversion of adenosine diphosphate to adenosine triphosphate (ATP). ATP provides quick energy to cells.

Creatine supplementation is believed to allow quicker renewal of ATP, improving high-intensity short-duration activity.[24] Creatine also improves the nitrogen balance, which indicates that the body has sufficient protein for muscle growth. Skeletal muscle has a saturation limit for creatine.

Patients are often given an initial high loading dose for 5–7 days, which is then followed by a maintenance dosage schedule. Muscle mass gain resulting from creatine supplementation is believed to be caused by an increase in water retention. Studies show that creatine increases intracellular water, which is hypothesized to signal cells to increase protein synthesis.[25]

Studies also indicate that creatine plus endurance training increases lean-body mass. Creatine levels return to baseline levels after 4 weeks upon discontinuation of supplementation.[26] Creatine is metabolized to creatinine and excreted by the kidneys. Caution is advised when considering creatine use in individuals with kidney disease. Side-effects of creatine supplementation include muscle cramping, nausea, diarrhea, gastrointestinal (GI) upsets, and possible dehydration. The typical dosage is 20 g per day as a loading dose for the first 5–7 days, followed by 2 g per day as a maintenance dose.

*Beta-Hydroxy-Beta-Methyl Butyrate*

Beta-hydroxy-beta-methyl butyrate (HMB) is a byproduct of metabolism of the amino acid leucine. Studies have indicated that resistance training combined with HMB supplementation increases muscle strength and lean-muscle mass, and decreases muscle damage and breakdown compared to resistance training alone. In addition, lean-muscle gain was shown to be correlated directly with increasing dosages of HMB.[27] Some studies have suggested that this effect is more pronounced in individuals who have not undergone prior endurance training.[28,29] A typical dosage of HMB is 3 g per day, in divided doses.

*Glutamine*

Glutamine is an amino acid produced primarily in skeletal muscle. Nitrogen is transported in the body primarily as glutamine or alanine. Physical injuries and traumas have been shown to increase nitrogen excretion and induce muscle catabolism. Glutamine supplementation induces a positive nitrogen balance, restores deficient intracellular glutamine levels, and increases skeletal muscle synthesis.[30] Glutamine also stimulates the immune system and improves intestinal-barrier function.

*L-Carnitine*

L-Carnitine is an amino acid made by the body and found in meat and dairy products in the diet. L-Carnitine plays a significant role in cellular energy metabolism. Although there is con-

flicting evidence, some studies indicate that L-carnitine improves athletic performance. L-Carnitine levels have been shown to decrease with intense short-duration exercise.[31]

One study found that L-carnitine supplementation prior to aerobic training increased power output and maximal oxygen uptake while decreasing plasma lactate, carbon-dioxide production, and pulmonary ventilation.[32] In addition, research has shown that L-carnitine supplementation improves glucose disposal in both healthy individuals and those with type 2 diabetes.[33]

*Conjugated Linoleic Acid*

Conjugated linoleic acid (CLA) is commonly found in beef and dairy products. Many studies have indicated that CLA improves body composition. CLA has been shown to decrease the size and possibly the number of adipocytes.[34] Animal studies indicate that CLA consumption causes increased apoptosis in adipose tissue.[35,36] CLA supplementation has been shown to decrease body fat mass, decrease hunger, and increase a feeling of fullness.[37,38]

CLA exists is multiple isomers. Animal and human studies on the *trans*-10, *cis*-12 isomer indicate that it can increase insulin resistance and glycemia, and may decrease high-density lipoprotein (HDL) levels. However, most CLA supplements are combinations of the two isomers, and studies on combination isomer products have not demonstrated increased insulin resistance.[39] Animal studies have indicated that CLA combination isomer products actually improve insulin sensitivity.[40] Side-effects of CLA may include GI upsets, diarrhea, loose stools, and nausea.

*Alpha-Lipoic Acid*

Alpha-lipoic acid (ALA) is a coenzyme involved in ATP production and carbohydrate metabolism, and is a potent antioxidant. Research suggests that ALA improves insulin efficiency and sensitivity.[41] Many studies on patients with type 2 diabetes have shown that ALA increases insulin-dependant glucose disposal. Specifically, one study showed that the rate of metabolic clearance of glucose increased by 50 percent with ALA supplementation.[42]

ALA can also affect glucose uptake into skeletal muscle directly. One study demonstrated that glucose uptake increased by 40–300 percent in muscle cells after subjects were given ALA supplementation.[43] Animal studies have shown that ALA stimulates adenosine monophosphate (AMP)–activated protein kinase in skeletal muscle, which regulates cellular energy metabolism as well as decreasing triglyceride accumulation.[44] Skeletal-muscle triglyceride accumulation has been shown to contribute to insulin resistance.

Similar studies have shown that ALA suppresses AMP-activated protein kinase in the hypothalamus, causing a decrease in food intake, increasing energy expenditure, and resulting in significant weight loss.[45] Human studies have shown that ALA supplementation combined with creatine monohydrate and sucrose increases creatine uptake by skeletal-muscle cells more than creatine plus sucrose or creatine alone.[46] Large doses, such as 600–1200 mg per day, of ALA may cause GI upsets, rashes, or headaches.

**Siberian ginseng (*Eleutherococcus senticosus*) may stimulate protein building as well as stimulating the pituitary–adrenocortical axis.**

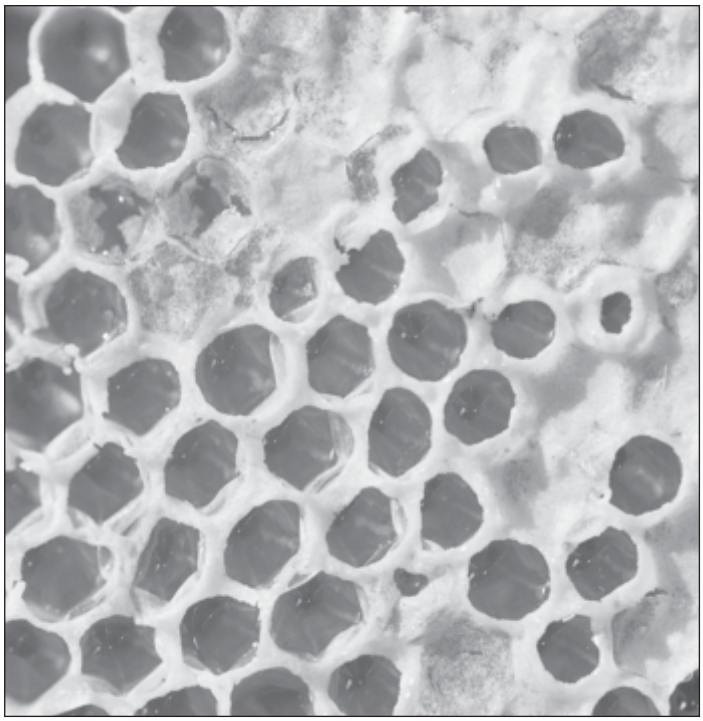
*Testosterone*

Testosterone is an anabolic steroid synthesized in the testes. Anabolic hormones increase muscle mass, protein synthesis, and retention of nitrogen. It is estimated that 4–12 percent of adolescent males abuse steroids to improve athletic performance or appearance.[47] Studies on men with low testosterone showed that testosterone supplementation combined with resistance training produced a significant increase in lean-body mass and strength compared to resistance training or testosterone alone.[48]

Additional studies have shown that testosterone supplementation increases strength, lean-muscle mass, and bone density as well as reducing fat mass.[49] One study showed that muscle strength and power increased in a dose-dependant manner with increasing testosterone dosage. This study also demonstrated that testosterone supplementation does not improve muscle fatigability or specific tension.[50]

Restoring testosterone levels can improve athletic performance but should be considered only for individuals with low testosterone levels. Side-effects of supraphysiologic doses of testosterone can be severe, including liver disease, low sperm counts, changes in mood and behavior, increased hematocrit levels and prostate-specific antigens, decreased HDL, increased low-density lipoprotein, and adverse changes in thyroid hormones.[51,52] Unfavorable cardiovascular changes can occur, such as left-ventricular hypertrophy, which remain after discontinuing testosterone supplementation.[53]

Androgen precursors to testosterone, such as androstenediol and androstenedione, have also been studied. A study on adult males with normal testosterone levels during high-intensity resistance training found that supplementation with these products initially increased testosterone but that these levels returned to baseline within 16 weeks. In addition, the researchers did not find improvement in muscle strength or body composition, and



**Chrysin is a flavonoid found in many plants, such as passionflower (*Passiflora incarnata*) and geranium *Pelargonium crispum* as well as in honey and propolis. Honeycomb shown above.**

found that there was an increase in estrogen-related compounds and adverse changes in lipid profiles and results of cardiovascular risk assessments.[54]

*Dehydroepiandrosterone*

Dehydroepiandrosterone (DHEA) is synthesized in the adrenal glands, liver, testes, and the brain. This substance is converted to androstenedione, which is the precursor to other androgens, and improves insulin sensitivity. DHEA levels begin declining at approximately age 25. Studies have indicated that DHEA supplementation improves insulin sensitivity and decreases both subcutaneous and visceral fat.[55] Specifically, animal studies have shown that DHEA decreases both body weight and the cytokine TNF-α, which is implicated in causing insulin resistance.[56]

A 6-month study on adults showed that DHEA supplementation at 100 mg per day increased IGF-1. However, only the male subjects had decreased fat-body mass and increased muscle strength. Women had increases in total-body mass and had androgen levels that were above normal. No changes were seen in cortisol levels, lipid profiles, glucose levels, fasting insulin levels, bone-mineral density, or basal metabolic rates.[57]

*Growth Hormone*

Growth hormone (GH) is an anabolic hormone made in the pituitary gland. Secretion of GH is stimulated by exercise, trauma, sleep, acute illness, hypoglycemia, and other hormonal interactions.[51] GH facilitates carbohydrate, fat, and protein metabolism, as well as increasing IGF-1, bone thickness, linear growth, and soft-tissue growth.

Studies have shown that GH supplementation increases strength and lean-muscle mass in individuals who are deficient in GH. However, studies are conflicting regarding the effects of supplementation for individuals with normal growth hormone levels. A study on endurance-trained adult males showed that GH supplementation caused a 50 percent decrease in leucine oxidation with exercise, which demonstrated the effects of GH on skeletal muscle.[58] In addition, studies on elderly men show that GH injections increases lean-muscle mass and decreases fat mass more than strength training alone.[59]

A study on obese adults combined low-dose GH supplementation with diet restriction. The results indicated that GH produced a positive nitrogen balance, increased lean-muscle mass, increased body weight lost as fat, increased loss of visceral fat, and increased IGF-1.[60] However, several other studies have not supported these findings.[61,62]

Supplementation with the amino acids ornithine, lysine, and arginine may increase GH levels, although studies have not supported this finding.[63] GH supplementation is still debated because of its potential for causing serious side-effects, such as insulin resistance, carpal-tunnel compression, and water retention.[64]

*Chrysin*

Chrysin is a flavonoid found in many plants, such as passionflower (*Passiflora incarnata*) and geranium (*Pelargonium crispum)* as well as in honey and propolis. Researchers and athletes are interested in this flavonoid because of its potential for increasing testosterone by decreasing the conversion of testosterone to estrogen. Several animal studies have shown that chrysin is a potent inhibitor of the enzyme aromatase.[65] Aromatase converts androstenedione and testosterone to estrogen and dihydrotestosterone. However, human studies have not supported this finding. Studies on aging animals have also shown that chrysin supplementation increased libido, sperm count, and fertilization potential.[66]

*Chromium picolinate*

Chromium is a commonly used product for balancing blood sugar. Chromium picolinate is well-studied and is often used in the supplemented form of chromium, although other forms, such as amino-acid chelates, can be used. Researchers have found chromium picolinate supplementation to be effective for treating many individuals with both diabetes and reactive hypoglycemia. Research has also shown that intense aerobic exercise increases chromium excretion.[67]

Data from human studies are inconsistent and many studies do not show that chromium supplementation improves strength, lean-muscle mass, or body-fat loss. However, some studies do indicate that chromium picolinate supplementation may improve body composition as a result of the product's glucose-balancing effects.[68,69]

*Additional Supplements*

Several other nutritional and botanical supplements have been shown to increase athletic performance. Although scientific evidence is lacking, these supplements may be used to support the body in optimizing metabolism to improve body composition. These supplements include:

- *Pyruvate*—Human studies have found pyruvate supplementation increases glucose extraction in the muscle at rest and during exercise as well as increasing overall endurance.[70]
- *Siberian ginseng*—Siberian ginseng (*Eleutherococcus senticosus*) is believed to stimulate protein building as well as stimulating the pituitary–adrenocortical axis.[71] However, studies have not found supplementation to improve endurance or athletic performance in endurance-trained individuals.[72]
- *Cordyceps*—Animal studies show that cordyceps (*Cordyceps sinensis*), an adaptogenic herb, increases endogenous corticosteroid production, and provides improved glucose metabolism and increased insulin sensitivity.[73] Human studies on cordyceps and athletic performance did not show improvement of endurance or oxidative capacity, however.[74]
- *Puncture vine*—Puncture vine (*Tribulus terrestris*) is believed to act as an androgen. Animal studies indicate that tribulus supplementation causes androgenic effects, stimulating sexual function in rats.[75] However, human studies did not indicate that the herb improved athletic performance or body composition.[76]

## Conclusions

There are a number of ways to address problems with muscle size and strength as well as assisting athletes who wish to improve their performance and endurance. Treatment approaches should be individualized to each patient's needs with caution used for patients who have coexisting conditions. Additional research and human studies are needed for some supplements. □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