

Pharmacology of Bodybuilding

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1. INTRODUCTION

Bodybuilders consume a wide variety of drugs and nutritional supplements in the quest for the "perfect body." They take these substances to enhance muscle hypertrophy, speed recovery and prevent the effects of overtraining, increase training intensity and aggressiveness, control fat, body water, and appetite.

Bodybuilding has become a very popular, high-profile sport. Several champions have become international film stars and many make a great deal of money endorsing athletic food supplements. Numerous bodybuilding and fitness periodicals serve as promotional vehicles for many products of questionable value.

Philen *et al.* (1) surveyed popular health and bodybuilding periodicals to quantify products and ingredients of advertised supplements. They counted 89 brands, 311 products, and 235 unique ingredients, the most frequent of which were unspecified amino acids. The most frequently promoted health benefit was muscle growth.

Unfortunately, some of these periodicals have gone beyond giving advice about harmless food supplements. Several bodybuilding magazines openly espouse the use of substances such as anabolic steroids, growth hormone, insulin-like growth factor, and insulin. Articles advise athletes about dosage, side-effects, avoiding detection, and black market sources of drugs. These magazines have achieved a significant market share among bodybuilding publications. This brazen philosophy about potentially dangerous drugs suggests that serious problems exist in bodybuilding. This chapter will review the use patterns, efficacy, and side-effects of the major drugs and supplements used by bodybuilders.

2. AGENTS TAKEN TO PROMOTE MUSCLE HYPERTROPHY

This category is of greatest concern to bodybuilders and constitutes the most significant area of abuse.

2.1. Anabolic-Androgenic Steroids

Bodybuilders take anabolic-androgenic steroids (AAS) in the hope of gaining weight, muscle size, strength, power, speed, endurance, and aggressiveness.

Several studies have examined use patterns among athletes and the general population (2). At the elite level of bodybuilding use of AAS is thought to be almost universal. A survey of non-elite bodybuilders showed that 58 % of the men and 10% of the women used anabolic steroids (3). The authors reported that the principal reason bodybuilders used steroids was related to their perception that these drugs were an important factor in winning competitions.

Buckley *et al.* (2) found that 6% of high school students in their survey used AAS. While most AAS users were athletes, 35 percent were non-athletes. Thirty percent of steroid users cited improved appearance (i.e., bodybuilders) as the main reason for taking the drugs. Twenty percent of steroid users obtained the drugs from health care professionals. The findings of Buckley *et al.* have recently been replicated in a large epidemiological study conducted by the US Center for Disease Control (4)

In the United States in 1990, the Anabolic Steroid Control Act classified anabolic steroids as a Schedule III substance. The law gave the Drug Enforcement Administration (DEA) power to restrict the importation, exportation, distribution, and dispensing of anabolic steroids (5). This has led to a thriving "black market" for illegal anabolic steroids in the United States. It is clear that bodybuilders have little trouble obtaining these drugs almost anywhere in the world.

Efficacy: AAS drugs increase protein synthesis, which enhances lean body mass and induces a positive nitrogen balance (6). AAS bind with receptor molecules, causing synthesis of enzymes, such as those involved in the ribonucleic acid-polymerase system, which stimulates protein synthesis in the cells (7). AAS may also have an anticatabolic effect by crossbinding with glucocorticoid receptors, interfering with post-exercise glucocorticoid catabolic activity (7). These steroids may also create a "psychosomatic state," which allows athletes to train harder (6).

Side-effects: Side effects include liver toxicity and tumours, decreased high density lipoproteins, cardiac arrhythmia, depressed spermatogenesis, lowered testosterone production, hypertension, increased risk of AIDS (shared needles), depressed immune function, glucose intolerance, psychological disturbances, masculinization in women and children, premature closure of the epiphyses, and an increased cancer risk (6). Severe side-effects of anabolic steroid use have been reported in bodybuilders, including myocardial infarction, ventricular tachycardia, liver cancer, and severe psychiatric disturbances (6, 8, 9). Bodybuilders may be particularly prone to side-effects because of the tendency of this subculture to take high dosages of the drugs for prolonged periods of time.

2.2. Human Chorionic Gonadotropin

Prolonged use of anabolic steroids suppresses serum testosterone and spermatogenesis (10) and training gains are lost rapidly (11). Bodybuilders take HCG to boost natural testosterone production and prevent muscle atrophy common during withdrawal from anabolic steroids.

High doses of HCG are no more effective than lower doses in increase serum testosterone. Administration of 1500, 3000 or 4500 IU of HCG on successive days did not increase serum testosterone above the level elevated by the 1500 IU dosage (12).

2.3. Growth Hormone

Growth hormone (GH) is popular with bodybuilders, who use it to increase muscle mass and strength. Reports in the news media suggest that, as with anabolic steroids, its use has filtered down to non-athlete high school students (13). The development of recombinant human growth hormone has made the hormone more widely available.

Efficacy: Growth hormone facilitates the transport of amino acids into cells and their incorporation into protein(14). Amino acid transport rate is associated with muscle hypertrophy (15). It exerts a stimulatory effect on insulin-like growth factors, which are also potent anabolic agents. Growth hormone affects carbohydrate and fat metabolism. It stimulates glucose uptake in muscle and fat. It mobilizes of free fatty acids from adipose tissue (58).

Two studies of growth hormone administration in humans have shown no beneficial effects on muscle or exercise performance (18, 62). Animal studies have suggested that growth hormone administration stimulates muscle hypertrophy (54). Observations on athletes suggest that GH is highly anabolic in intensely training elite bodybuilders. Nitrogen balance becomes highly positive when GH is administered to adult humans, which lends some credence to these observations.

Side-effects: Prolonged growth hormone administration may result in fasting hyperglycaemia, hyperinsulinaemia, cardiomegaly, and elevated nonesterified fatty acid concentrations (18). Prolonged use could also lead to acromegaly, characterized by enlarged bones in the head, face, and hands, myopathy, peripheral neuropathy, osteoporosis, arthritis, and heart disease (19). The administration of growth hormone may also cause antibody formation to the hormone that could affect normal growth hormone metabolism (19).

Some bodybuilders also take drugs that increase exogenous growth hormone secretion. These drugs include propranolol, vasopressin, clonidine, and levodopa (20). There is no evidence that these practices enhance muscle hypertrophy.

2.4. Insulin-like Growth Factor (IGF-1)

Recombinant IGF-1, also called somatomedin C, has recently become a popular drug among bodybuilders.

Efficacy: IGF-1 production is stimulated by growth hormone. It is released mainly by the liver but may also be secreted by the testes, fat cells, bone, and heart. IGF-1 is an extremely anabolic hormone. It facilitates amino acid and glucose transport, positive nitrogen balance, glycogen synthesis, and has anabolic effects in bone and cartilage (21). While IGF-1 is a powerful anabolic agent, its effects in bodybuilders is unknown; but it is a popular topic in bodybuilding magazines.

Side-effects: The side-effects are thought to be similar to those of growth hormone. Long-term use promote cancer growth (21).

2.5. Dehydroepiandrosterone (DHEA)

This is a relatively weak adrenal androgen. Bodybuilders take this drug to stimulate muscle hypertrophy and aid in weight control.

Efficacy: Administration of DHEA in middle age and older adults resulted in improved "energy levels," increased muscle mass, mental acuity, and immune function(22). However,

these subjects had blood levels of the hormone at least 20 % below the average level of a 20 year old.

Young men given 1600 mg/d supplements of DHEA experienced a 30% decline in fat mass (23), but these results have not been replicated by others (24). Its value as an ergogenic aid may lie in its ability to increase serum testosterone concentrations (24). It may act as an anti-obesity agent by increasing futile cycling in mitochondria (25).

Side-effects: High doses (1600 mg/d) in young men led to a reduction in LDL and HDL cholesterol (26). However, in elderly subjects, DHEA reduced LDL and had no effect on HDL (22). Doses of 150-300 mg/d have a marked effect on testosterone concentration. This could lead to masculinization in female bodybuilders and interfere with the hypothalamic-pituitary-gonadal axis in both sexes.

2.6. Insulin

Bodybuilders take exogenous insulin or elevate levels during exercise by dietary stimulation to promote muscle hypertrophy(27). Exogenous insulin injection is not, fortunately, a widespread practice among bodybuilders.

Efficacy: Insulin, aside from its influence on glucose and fat metabolism, affects protein metabolism (28). These effects include enhanced amino acid transport into cells, increased rate of incorporation of amino acids into protein, and suppression of protein catabolism (15, 29). The effectiveness of insulin supplementation or elevation in stimulating muscle hypertrophy is not known. Sherwood (30) studied the effects of dietary induced increases in insulin during weight training and found no effect on lean mass, anthropometric measurements, or strength beyond those of training.

Side-Effects: The most serious side-effect of exogenous insulin administration in exercising bodybuilders is insulin shock (31). Sherwood (30) found that practising dietary insulin loading for 12 weeks had no effect on glucose tolerance or serum enzymes.

2.7. Clenbuterol

Bodybuilders take this β_2 adrenergic agonist to prevent muscle atrophy, increase lean body mass, and decrease body fat (3).

Efficacy: The proposed benefit from this substance emanates from its capacity to stimulate the central nervous system. Adrenergic agonists are widely used as bronchodilators to prevent and treat symptoms of exercise-induced asthma. Clenbuterol may promote muscle hypertrophy by stimulating protein metabolism in the cell via increased calcium transport, increased cyclic adenosine monophosphate levels and activation of protein kinase (32).

In the rat, clenbuterol increases muscle mass, decreases body fat, and exerts metabolic effects that augment the endurance training effect (33). The drugs quickly lose their capacity to promote muscle hypertrophy. Rothwell *et al.* (34) showed that muscle β receptor density decreased 50% after 18 days of clenbuterol administration in rats. For this reason, bodybuilders often "cycle" clenbuterol, taking it on and off in 2-day cycles. This cycle is generally continued for 8 to 10 weeks, followed by 10 to 12 weeks without the drug (35)

Side-effects: These include insomnia, arrhythmias, anxiety, anorexia, nausea. More serious side-effects include cardiomegaly and myocardial infarction (35).

2.8. Other Agents:

Other substances sometimes used by bodybuilders include periactin, conjugated linoleic acid (CLA), vanadyl sulfate, dibenzozide, and organ extracts (36). These agents are much less popular with bodybuilders and their efficacy is questionable.

3. AGENTS TAKEN TO SPEED RECOVERY

The primary purposes of taking these agents is to replenish depleted substrate pools and serve as a substrate pool for post-exercise protein synthesis.

3.1. Creatine

A recent survey suggests that currently, creatine (i.e., creatine monohydrate) is among the most popular supplements used by bodybuilders (37). They use these supplements to enhance recovery and increase power output (38).

Efficacy: While creatine feeding was attempted early this century, interest in this technique as an ergogenic aid stems from the work of Harris *et al.* (39). Creatine feeding (creatine monohydrate) increased the creatine phosphate content of the muscle by 20 %. The optimal dosage for achieving maximum values of muscle creatine appear to be approximately 3-5 g/day (38). Creatine supplementation improved performance in short-term, high intensity, repetitive exercise (40, 41), which would make it a valuable supplement for bodybuilders. It may improve performance by augmenting the availability of creatine phosphate and possibly regulating the rate of muscle glycolysis (38). It may enhance muscle hypertrophy in bodybuilders by allowing them to train harder.

3.2. Amino Acid and Polypeptide Supplements

Bodybuilders take amino acid and polypeptide supplements to accelerate muscle development, decrease body fat, and stimulate the release of growth hormone (36).

Efficacy: There is little scientific proof to support amino acid or polypeptide supplementation in bodybuilders. The protein requirement of these athletes is not much higher than for sedentary individuals (42), so the rate of amino acid absorption from the gastrointestinal tract is not important.

Side-effects: Substituting amino acid or polypeptide supplements for protein rich foods may cause deficiencies in important nutrients, such as iron and the B vitamins.

3.3. Other Substances:

Carbohydrate beverages during and immediately following exercise enhance recovery from intense training, speeding the replenishment of liver and muscle glycogen (43). While these beverages are useful to endurance athletes, there is little reason to believe they would help the bodybuilder (beyond eating a normal diet). The use of other substances to speed recovery, such as vitamin C, N-acetyl-L-cysteine (NAC), inosine, and beta-hydroxy beta-methylbutyrate (HMB), is not currently supported by positive research findings.

4. SUBSTANCES TAKEN TO INCREASE AGGRESSIVENESS AND TRAINING INTENSITY

Bodybuilders spend many hours per day training in the gymnasium. Monotony and fatigue sometimes make it difficult to make significant improvement. Many bodybuilders use stimulants to help them increase training intensity and combat fatigue.

4.1. Amphetamines

Bodybuilders take amphetamines to prevent fatigue and to increase confidence and training intensity. Examples of amphetamines include benzedrine, dexedrine, dexamyil and methedrine.

Efficacy: These drugs act as both central nervous system and sympathomimetic stimulants (44). Amphetamines stimulate the central nervous system by directly affecting the reticular activating system and post-ganglionic nerves. Central effects include increased arousal, wakefulness, confidence, and the feeling of an enhanced capability to make decisions. Sympathomimetic effects include increased blood pressure, heart rate, oxygen consumption in the brain, and glycolysis in muscle and liver, vasoconstriction in the arterioles of the skin and spleen, and vasodilation in muscle arterioles.

Studies have generally supported the effectiveness of amphetamine as a psychotropic drug that masks fatigue, but have been equivocal on their ability to improve endurance performance. Most studies have shown increases in static strength but mixed results in muscle endurance. They appear to aid power oriented movement skills in activities that employ constant motor patterns such as shot putting and hammer throwing (45). Theoretically, they could provide some benefit to bodybuilders.

Side-effects: Amphetamines can cause severe neural and psychological effects that include aggressiveness, paranoia, hallucinations, compulsive behaviour, restlessness, irritability, arrhythmias, hypertension, and angina(45).

4.2. Caffeine

Caffeine is a favourite stimulant of bodybuilders. Caffeine is a xanthine and is found naturally in numerous plant species. It stimulates the central nervous system by causing the adrenal medulla to release adrenaline. It stimulates the heart (positive chronotropic and inotropic agent), causes peripheral vasodilation, and acts as a diuretic by blocking renal tubular reabsorption of sodium. Caffeine increases calcium transport by increasing calcium permeability in the sarcoplasmic reticulum. It increases cellular cyclic AMP. In subjects who have not taken caffeine regularly, this stimulates glycogenolysis, resulting a rise in blood glucose. The increase in cyclic AMP also causes increased fatty acid mobilization from fat cells. Caffeine may also block adenosine receptors. Adenosine has a calming effect. Blocking adenosine may partially explain the stimulating effects of the drug (11).

Efficacy: In athletics, caffeine is used as a stimulant and as a fatty acid mobilizer. While there is some evidence that caffeine may improve endurance (11), the drug does not appear to enhance short-term maximal exercise capacity. While some older, poorly controlled studies found improvements in strength and power from this substance, these findings have not been replicated by well-controlled studies (46).

Side-effects: Caffeine increases the incidence of arrhythmias, insomnia and is addictive (11).

4.3. Other Agents:

Other agents in this category include cocaine, ephedrine and ginseng. Cocaine use is not thought to be widespread in bodybuilders, but some reportedly use it to increase training intensity. Ephedrine, a weak stimulant, is widely used by bodybuilders during work-outs (37). Sidney and Lefcoe (47) found that despite a slight stimulating effect on blood pressure and on exercise and recovery heart rates, ephedrine had no effect on physical work capacity.

Ginseng is also very popular with bodybuilders, but there is little evidence to support its use as an ergogenic aid (48).

5. SUBSTANCES TAKEN TO AID WEIGHT CONTROL

Drugs used in weight control include those that suppress appetite, thermogenic drugs, drugs affecting the gastrointestinal (GI) tract, and diuretics to control weight and increase muscle definition. Bodybuilders use a variety of techniques to decrease body fat and body water prior to a contest.

5.1. Anorectic, Thermogenic, and Gastrointestinal Agents

Anorectic drugs suppress appetite and work by acting on catecholamine neurotransmitters, serotonin neurotransmitters, or blocking opioid receptors. Thermogenic drugs affect metabolic rate. Gastrointestinal drugs attempt to affect nutrient absorption. Other weight-loss agents of questionable effectiveness and desirability include human chorionic gonadotropin, growth hormone, glucagon, progesterone, and biguanides (49). Appetite suppressants include amphetamine, diethylpropion, fenfluramine, and phenylpropanolamine (49). Thermogenic drugs include thyroid hormone, ephedrine, and dinitrophenol. They reduce lean body mass and cause an increased incidence of cardiac arrhythmias. Uncoupling agents, such as dinitrophenol, are toxic at effective dosages and are associated with neuropathy and cataracts. Drugs affecting the gastrointestinal tract include dietary fibre and sucrose polyester. Dietary fibre causes gastrointestinal distention and may restrict energy intake. Sucrose polyester (Olestra) is a new diet ingredient of some promise.

5.2. Diuretics

Before a contest, bodybuilders attempt to accentuate their muscle definition by using diuretics, potassium supplements, and low calorie diets (50). Some bodybuilders also take potassium supplements to promote fluid retention in their muscle cells, thus increasing muscle size. Athletes combine these practices with very low calorie diets and dehydration in the quest for leanness.

Efficacy and side-effects: There is no evidence that these unhealthy practices improve performance in bodybuilding. Serious complications have developed from these practices including, rhabdomyolysis, hypotension, marked haemoconcentration, hyperkalaemia, cardiac arrhythmias, and heart failure (50).

6. THE POLYDRUG PHENOMENON IN BODYBUILDING

The effects of the large variety and combination of supplements and drugs used in bodybuilding make it extremely difficult to determine the efficacy of these practices or predict their side-effects. Many reports in the literature describe catastrophic side-effects from unsafe drug use and nutritional supplementation. Clearly, the sport has gravitated from the quest for a healthy, attractive looking body to one where muscle size and definition are the only goals, regardless of the cost.

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Discussion: Pharmacology of Bodybuilding**J.P. Clarys:**

One of the reasons why they take all those substances is, as you say, to prevent overtraining. How must I understand "overtraining" in bodybuilding?

T.D. Fahey:

These athletes typically train six hours a day. So, the sport lends itself to overtraining. One of the things that we try to get athletes to do (I mainly work with throwing athletes, but the principle is quite similar in bodybuilders) is to cut down on the volume of the exercises that they do. One reason bodybuilders take the anabolic steroids, is to get the so-called anti-catabolic effect so that they can recover and train harder. Unfortunately, many times this backfires because heavy training stimulates corticosteroid overproduction.

J.P. Clarys:

When they have workouts of six hours a day, is that strength training in its different variations or do they do something else? Cardiovascular, for example.

T.D. Fahey:

They do some aerobic training, but most of it is just a high-volume moderate-intensity weight training. Very often the muscular adaptations in bodybuilders are quite similar to those we see in aerobic-type athletes in contrast to strength athletes, such as discus-throwers and power-lifters.

A.J.M. Wagenmakers:

Does not the attempt to increase insulin during the workouts lead to problems with the maintenance of the fat mass?

T.D. Fahey:

Interestingly enough, when we looked at this (and we have only looked at this for a 12-week period) we actually found that people lost body fat. Also, we saw no effect on glucose tolerance. I am not really sure why they lost body fat because it appeared they increased their total caloric intake. They consumed about 2,000 calories during a workout. So, they were obviously cutting down their caloric consumption during other parts of the day.

A. Batterham:

Several athletes that I have worked with in recent years have accused us as a scientific community of a kind of selective use of the evidence, in that we are quite prepared to cite case studies and nonexperimental cross-sectional work for evidence of adverse side effects, but for evidence of effectiveness, we require randomised controlled trials. Is it possible that a policy of education through what athletes would sometimes regard as scare tactics, together with claims of potential ineffectiveness of these agents, is likely to prove an ineffective strategy?

T.D. Fahey:

I agree with you 100%. I think that we really do not have the evidence for widespread catastrophic side effects of anabolic steroids. If you extrapolate to the number of people worldwide who have taken anabolic steroids (in high school students, about 8% of the population), you have millions of people who have taken the drugs since the 1960s. We should have a heart attack epidemic among old weightlifters and discus throwers. Your point is well taken. We use scare tactics because we perceive that it is good for sport. We have a vested interest in removing drugs from athletics.

B. Ekblom:

I saw on one of your slides that they use carnitine to increase body mass or reduced body fat. What is the rationale for that?

T.D. Fahey:

I do not think that bodybuilders necessarily have a valid rationale for many of their practices. Certainly, there is no evidence to suggest that this would work at all. On theoretical grounds, this supplement might have something to do with its possible effect on mitochondrial activity but there is no logic behind many practices of bodybuilders.

A.J.M. Wagenmakers:

How extensive is the use of hydroxycitrate? I think there is research showing that it inhibits acetylcholine production in neuronal cells.

T.D. Fahey:

I have seen some mention of this. I do not think that it is too wide spread at this time. It is just like DHEA. Six months ago this was basically a non-issue in the United States and now it is the hottest supplement that we have. Hydroxycitrate may be another agent that falls in that category.