

*Review***DRUGS IN SPORTS****A. Tsvetkova, M. Georgieva\*, S. Mihaylova**

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**ABSTRACT**

The use of doping - medications intended to artificially enhance athletic performance, remains a serious and widespread phenomenon in elite sports, despite strict prohibitions. The World Anti-Doping Agency (WADA) annually updates its list of banned substances and monitors their use through blood and urine testing, conducted by certified laboratories using proven methods, such as gas chromatography and mass spectrometry.

Despite these efforts, violations persist, and the list of substances used continues to grow and diversify. The main groups of doping agents include: anabolic steroids, hormones, stimulants, beta-blockers, diuretics and analgesics.

Gene doping is a new and difficult-to-detect form of doping which raises serious ethical and health concerns and requires new approaches for detection and control.

Conclusion. Doping remains a significant and multifaceted problem in modern sports. Despite strict bans and evolving control methods, athletes and coaches often rely on substances with limited scientifically proven effectiveness, which pose numerous health hazards. The emergence of new technologies, such as gene doping further complicates the situation. More effective regulations, increased awareness, and a strictly scientific approach are essential in the fight against doping.

**Keywords:** Doping, athletic performance, WADA, banned substances, control and regulation

**INTRODUCTION**

The term "lifestyle" is applied to drugs used not for medical reasons but by personal choice. This is a diverse group that includes narcotics, performance-enhancing drugs (especially in sports), as well as substances taken for cosmetic needs or purely social reasons. Many of these drugs are additionally used as standard therapeutic agents.

Performance-enhancing drugs in sports, though officially banned, represent a specific subcategory of lifestyle-related drugs. A wide range of substances, including established medications, belong to this group. This raises important questions regarding their use in competitive sports (1).

It may be difficult to define the term *lifestyle drugs*. Generally, this category includes a wide spectrum of medications and substances used for personal reasons rather than medical necessity.

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In this paper we adopt the concept of drugs as substances taken voluntarily to bring pleasure (e.g., cannabis, alcohol, cocaine), enhance performance (e.g., sports drugs, cognitive enhancers), or improve appearance. Therefore, they are not used for clinical treatment, but to satisfy a personal desire or goal unrelated to a medical condition. Simply put, these are drugs are taken voluntarily by healthy people.

This category also includes dietary supplements and other similar products consumed for their supposed benefits, even without reliable evidence for their effectiveness. Many commonly used lifestyle or sports supplements are natural in origin (e.g., extracts from Ginkgo, melatonin, St. John's Wort, Cinchona). Because they are not strictly regulated, their contents often vary, and their effectiveness and safety remain unproven. Despite being natural, these products can cause both positive and adverse effects, just like synthetic drugs.

Regarding drugs in sports, the use of performance-enhancing substances ("doping") in elite athletic competitions, such as the

Olympic Games is clearly widespread, despite being officially prohibited (1, 2).

The World Anti-Doping Agency (WADA) – <http://www.wada-ama.org> – was partially established in response to high-profile doping cases and athlete deaths linked to drug abuse. WADA publishes an annually updated list of

banned substances, which athletes are prohibited from using both during and outside competition. Doping tests are based primarily on blood and urine analyses conducted under strict protocols. Chemical testing relies on established methods like gas chromatography, mass spectrometry, and immunoassays, which must be performed in certified laboratories. (5)

**Table 1. Examples of Drugs Used in Sports**

Drug Class	Examples	Effects	Detection	Notes
<b>Anabolic agents</b>	Androgenic steroids (testosterone, nandrolone, etc.)	Increase muscle mass, aggression, competitiveness. Serious long-term side effects.	Blood or urine	Many are endogenous hormones—detection relies on significantly elevated levels.
	Clenbuterol	Combined anabolic and $\beta$ 2-adrenergic effect, may increase muscle strength.		
	Human chorionic gonadotropin (hCG)	Sometimes used to stimulate androgen secretion.		
<b>Hormones and related substances</b>	Erythropoietin (EPO)	Boosts red blood cell production and oxygen transport. Increases blood viscosity—risk of hypertension, strokes, heart attacks.		Short plasma half-life makes detection difficult. Mainly used for endurance.
	Human growth hormone (hGH)	Increases lean muscle mass, reduces fat, may accelerate recovery. Risks: heart hypertrophy, acromegaly, liver damage, cancer.	Blood	Differentiating endogenous from exogenous hormone is difficult.
	Insulin	Sometimes used with glucose to prevent hypoglycemia and stimulate glucose uptake/metabolism in muscles.	Plasma	Likely does not enhance performance.
$\beta$ 2-adrenergic agonists	Salbutamol, etc.	Used by runners, cyclists, swimmers to enhance oxygen intake (bronchodilation) and heart function.	Urine	Controlled studies show no significant performance gain.
$\beta$ -adrenergic antagonists	Propranolol, etc.	Used to reduce tremors and anxiety in precision sports (shooting, gymnastics, diving).	Urine	Not banned in most sports, as they may impair performance.
<b>CNS stimulants</b>	Ephedrine and derivatives, amphetamines, cocaine, caffeine	Slight improvements in strength and short-duration performance (e.g., sprints, swimming, field sports).	Urine	Most widely used group along with anabolic steroids.
<b>Diuretics</b>	Thiazides, furosemide	Mainly used for rapid weight loss before weigh-ins. Also used to mask other substances by diluting urine.	Urine	
<b>Narcotic analgesics</b>	Codeine, morphine, etc.	Used to mask pain from injuries.	Urine	

**Note:** a. *Blood doping* (removing 1–2 liters of blood before an event and reinfusing it just before competition) has similar effects and is even more difficult to detect.

Despite these precautions, violations persist, involving not only individual athletes but, in some cases, entire teams. For example, American cyclist Lance Armstrong was once a national hero who won the Tour de France seven times after overcoming testicular cancer. Persistent accusations of doping were firmly denied until January 2013, when Armstrong admitted to having used a cocktail of performance-enhancing drugs for many years. This led one commentator (Sparling, 2013) to express despair at the "farce of doping-free sport" (3).

In 2016, WADA published the findings of an investigation into Russia, concluding that a large-scale, state-sponsored doping program existed. This led to a ban on the Russian team's participation in subsequent Summer Olympic Games and other sporting events.

**Table 1. Summary of Main Classes of Drugs Currently Banned by WADA**

Athletes may often be easily deceived of the potential of various substances to improve their chances of winning, and indeed, **controlled clinical trials** confirming these claims are difficult to conduct. In many cases, these substances likely have minimal or no real effect — but even slight performance improvements (often under 1%), which are hard to measure experimentally, can determine the difference between victory and defeat. As a result, the **competitive instinct** of athletes and coaches often outweighs scientific evidence.

Below are the most important and frequently used performance-enhancing drugs. More detailed information can be found in:

- *British Medical Association (2002)*
- *Reardon and Creado (2014)*
- *Mottram (2005)*
- Gould (2013) also reviewed the potential use of gene therapy for performance enhancement - another potential nightmare for regulators (4).

**Banned Substances in Sports and Doping Tests (1, 2, 4)**

Certain substances are listed in the prohibited drug abuse protocols of WADA. During and outside competitions doping tests are primarily based on hematology and urinalysis, whereas certified laboratories can process chemical analyses, relying on gas chromatography/mass spectrometry and immunoassays (5).

**ANABOLIC STEROIDS**

Anabolic steroids include a large group of compounds with effects similar to testosterone, with around 50 named compounds listed as banned substances. New chemical derivatives ("designer steroids"), such as tetrahydrogestrinone (THG) are regularly developed and illegally offered to athletes. This poses a constant challenge for the authorities responsible for their detection and identification (5). Some of these drugs are also endogenous compounds or their metabolites, whose concentrations can vary drastically for physiological reasons. This complicates proving that the substance was used illegally. To address this, techniques measuring isotope ratios are used. Based on the fact that endogenous and exogenous steroids have slightly different ratios of isotopes  $^{12}\text{C}$  -  $^{13}\text{C}$ , it is analytically possible to distinguish between them. Since anabolic steroids cause long-lasting effects and are usually used throughout the training period rather than during the competition itself, conducting tests outside competitions is essential (1, 2).

Combined with training and high protein intake, anabolic steroids undoubtedly increase muscle mass and body weight, but there is little evidence that they increase muscle strength beyond what training alone can achieve or improve sports performance. On the other hand, they have serious long-term effects, including male infertility, masculinization in women, liver and kidney tumors, hypertension, increased cardiovascular risk, and (in adolescents) premature bone maturation leading to irreversible growth cessation. Anabolic steroids cause feelings of physical well-being, increased competitiveness, and aggressiveness, which sometimes progress to real psychosis. Depression commonly occurs when the use of these drugs is discontinued, sometimes leading to long-term mental health issues. Despite the emergence of new and different banned substances, anabolic steroids (AAS) remain the main group of drugs abused by people seeking to increase muscle mass and strength (5). Despite improved detection and evidence of health risks, their abuse does not decrease and is even on the rise, especially among people who exercise for pleasure or attend gyms to improve appearance. Scientific research confirms that AAS improve sports performance, but there is still no conclusive evidence linking them to severe and long-term health problems. The most concerning issue is the presence of a "black market" with

products whose safety is not guaranteed, as well as the use of new substances like SARMs, which have not yet been sufficiently studied for safety. Clenbuterol is a  $\beta$ -adrenergic receptor agonist. Through an unknown mechanism of action, it causes anabolic effects similar to androgenic steroids but with apparently fewer side effects. It can be detected in urine, and its use in sports is prohibited (1, 2).

### HUMAN GROWTH HORMONE

The use of human growth hormone (hGH) by athletes began after the availability of recombinant hGH, used to treat endocrine disorders. It is administered via injection, and its effects appear similar to anabolic steroids. hGH reportedly also induces a similar feeling of well-being, though without accompanying aggression and changes in sexual development and behavior. It increases lean body mass and reduces body fat, but its effect on muscle strength and sports performance is unclear. It is claimed to speed recovery from tissue injuries, allowing more intensive training regimens (1, 2). The main side effect of hGH is the development of acromegaly, causing excessive growth of the jaw and thickening of fingers but can also lead to heart hypertrophy, cardiomyopathy, and potentially increased cancer risk. Detecting hGH use is difficult because its physiological secretion is pulsatile, causing normal plasma concentrations to vary significantly. The plasma half-life is short (20–30 minutes), and only traces appear in urine (5). However, secreted hGH consists of three isoforms with different molecular weights, while recombinant hGH contains only one, allowing detection of exogenous material by measuring the relative amounts of isoforms. Growth hormone acts partly by releasing insulin-like growth factor from the liver, which athletes have also started using.

Another hormone, erythropoietin, which increases erythrocyte production, is administered via injections over days or weeks to increase red blood cell count and thus oxygen-carrying capacity. Recombinant erythropoietin development made it widely available, though detecting its use is difficult. Its use carries risks such as hypertension and neurological disorders (1,2).

### STIMULANTS

The main officially banned stimulants used by athletes are: ephedrine and methylephedrine; various amphetamines and similar drugs like fenfluramine and methylphenidate; cocaine; and

other central nervous system stimulants, such as nicethamide, amiphenazole (no longer used clinically), and strychnine (5,6).

Caffeine is also used; some commercial energy drinks contain taurine along with caffeine. Taurine is an agonist of glycine and extrasynaptic GABA-A receptors. Therefore, its effects on the brain are likely inhibitory, rather than stimulatory. For this reason, taurine may be responsible for the "crash" of energy felt after caffeine's stimulating effect wears off. Unlike steroids, some studies show stimulant drugs improve performance in disciplines like sprinting and weightlifting, and under experimental conditions increase muscle strength and significantly reduce muscle fatigue. The psychological effect of stimulants is likely more significant than their physiological effects. Surprisingly, caffeine appears more consistently effective at improving muscle performance, compared to other more potent stimulants. There have been several deaths among athletes taking amphetamines and ephedrine-like drugs in endurance competitions. The main causes are coronary insufficiency linked to hypertension; hyperthermia associated with skin vasoconstriction; and dehydration (1, 2).

Pharmacologically, the use of drugs to enhance sports performance carries many risks and questionable effectiveness. The growing prevalence of this practice reflects many of the same factors driving the use of "lifestyle" drugs - the desire to enhance performance in healthy people combined with ignoring scientific evidence of effectiveness and risk.

There are several reasons why these drugs - regardless of how we define them - are of increasing concern. Increased accessibility through "electronic pharmacies," along with direct advertising by the pharmaceutical industry to the public in some countries, will ensure demand remains high. Most sales occur in developed countries, and the pharmaceutical industry will undoubtedly develop more lifestyle drugs to serve this lucrative market.

Doping is banned in professional sports because it provides unfair advantage to athletes who "cheat." However, many other factors also play important roles in why one athlete may have an advantage over another - such as genetic makeup - so there is actually no truly "level playing field" from the start. Some even argue that athletes should have unrestricted access to performance-enhancing stimulants, provided these substances do not harm their health (7). However, this view

is controversial and raises ethical, medical, and regulatory questions, such as coercion, long-term health risks, and sports integrity.

Many different types of drugs are frequently used by athletes to improve competition performance. Drug use in sports is officially banned - usually both during and outside competitions. Detection mainly depends on analysis of the drug or its metabolites in urine or blood samples (5). Proving abuse of endogenous hormones like erythropoietin, growth hormone, and testosterone is difficult. Controlled studies show drugs have little effect on improving sports performance. Anabolic agents increase body weight and muscle volume without clearly increasing muscle strength. The effect of stimulants is often more psychological, than physiological (8,9,10).

## GENE DOPING

Mottram (2018) and Gould (2013) examined the potential use of gene therapy to improve sports performance - another challenge for regulators (2,4). Gene doping is the use of genes to enhance sports performance by making the body produce beneficial substances on its own. Unlike usual drugs taken in high doses which are easily detected, gene doping is hard to detect because the levels of substances are low and appear natural, though they may be more dangerous and harder to detect with current doping tests. Gene doping is the use of gene therapy to enhance sports performance by altering genes that affect muscle growth, metabolism, or cardiovascular function.

- Early research shows that increasing IGF-1 via viruses in mice increases muscle mass and strength, even in adults.
- Gene transfer of IGF-1 (insulin-like growth factor) combined with training improves muscle strength and recovery.
- Key doping genes are those that increase muscle mass, alter muscle metabolism, or improve cardiovascular function.
- An example is the myostatin gene, which suppresses muscle growth; its absence leads to large muscles and greater strength.
- Mutations in the erythropoietin receptor (EPO) gene increase endurance.
- The PPAR $\delta$  gene increases endurance in transgenic animals.

## Current concerns:

- Most gene manipulations have only been tested in animals, but their potential use in humans worries anti-doping authorities.
- New gene targets and pathways are being discovered, such as bone morphogenetic protein (BMP) signaling, which plays a role in muscle hypertrophy.

## CONCLUSIONS

Pharmacists can and should play an important role in doping control, in addition to counseling, advising, and treating athletes. When athletes take drugs for medical conditions, pharmacists can help prevent the inadvertent use of banned substances for those athletes subject to drug testing. Thus, pharmacists need to be familiar with how they can obtain information on banned, restricted, and permitted substances by the various sports-governing organizations.

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