

PERFORMANCE-ENHANCING DRUGS: A NEW REALITY IN SPORT AND A REAL SHOWGROUND FOR PHARMACISTS

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INTRODUCTION

What Are Performance Enhancing Drugs?

Performance enhancing drugs (PED) are substances that increase a person's physical abilities and stamina. These drugs are taken for a variety of reasons, including to build muscle mass, dull pain, lower stress, and reduce weight[1].

The objectives to use for the athletes are mostly for:

- increase strength and endurance
- aid workout and injury recovery
- to alter intensity and aggression
- sharpen focus and concentration
- combat exhaustion and fatigue
- reduce weight and body fat
- relieve aches and pains
- increase muscle mass and oxygenation

Abusing them can cause severe side effects, however, so most drugs are available only by prescription if at all.

The use of enhancements dates as far back as ancient period, where writings refer to "performance potions" and "performance elixirs." These were given to athletes in preparation for major games. It was not until the latter part of the 20th century that technology advanced enough to screen athletes regularly and enforce bans on the unfair use of steroids and other substances.

Performance enhancing drugs have a variety of uses, each intended to improve a specific physical attribute, such as strength or endurance [2,3]. Some can even cover the traces of other drugs that are in an athlete's system. It is not uncommon for a person using performance enhancements to take a daily "cocktail" of different drugs.

Most performance enhancing drugs are taken orally as tablets or capsules. Others may be injected, applied as a cream, or taken in powder form mixed with health shakes.

Increasing oxygen delivery to active muscles, especially by increasing the number of red blood cells is the most effective way to increase aerobic performance [3]. For this reason, blood doping and using erythropoietin products are common among cyclists and other endurance athletes.

The Table 1 describes the drugs and techniques that athletes use illicitly most often. Anabolic steroids are the most commonly abused substances, and many athletes receive dosing recommendations from coaches, other athletes, online discussion groups, and Internet vendors [1]. Some receive the drugs without their knowledge or consent; coaches may give athletes supplements without revealing that they contain drugs [4]. Many websites imply that steroids are safe, often claiming that unskilled physicians, biased researchers, and government bureaucrats inflate their dangers.

AIM OF THE PAPER

The aim of this paper is to show the increasing need of the pharmacists for supporting athletes in maintaining their health, aiding recovery and providing essential information about the quality use of medicines in the context of their engagement with sport.

To know that athletes who are required to use medicines for selected medical conditions are able to obtain a therapeutic use exemption under certain circumstances and also be able to examine how medicines literacy is a critical aspect for athletes including an understanding of the nature, safety, quality and status of supplements and substances purchased from a variety of sources.

CONTROVERSY ABOUT PERFORMANCE ENHANCING DRUGS

There are a number of significant questions that accompany the use of performance enhancing drugs (PED). Many people feel that the drugs give an unfair advantage to their users. Others point to the potential side effects, and claim that overuse may cause significant health problems. In addition, some point out the role model factor: young people often look to professional athletes as role models, and, if an athlete uses enhancements, the young people may be more likely to follow.

On the other hand, many people are willing to risk the possible side effects in order to obtain peak performance. The use of performance enhancing drugs is so widespread, it has been argued, that it would be impossible to regulate them effectively. Still others raise the point that other forms of technology, the use of high-tech materials in shoes, for example, already give certain athletes an edge, so performance enhancing drugs should enjoy the same allowance[6].

Doping is controversial mainly because the medical community has not defined where restoration of normative function ends and performance enhancement begins. Those opposed to doping contend that it undermines the traditional principle of a level playing field and creates unnecessary health risks. Supporters maintain that medical practitioners' concerns about long-term health effects are unwarranted and that athletes who are informed about possible adverse effects should be able to make an informed decision [2].

Doping control (drug testing) and drug education of athletes have two primary objectives, one to protect the health and safety of athletes and second to preserve the dignity and integrity of sports by providing an environment for fair and equitable competition.

The first objective is intended not only to prevent athletes from harming themselves, but also to protect the safety of competitors. The second objective aims to "level the playing field." Both objectives embrace the virtue of ethics in sport.

NOT CONTROLLED USAGE, SERIOUS CONSEQUENCES

PED have many harmful consequences that many athletes experience. Pharmacists must keep in mind that athletes may use these drugs at doses well beyond those used in therapeutic settings. Some serious consequences can result, including irreversible androgenic/anabolic effects, toxic hepatitis, withdrawal, dependence, body dysmorphic disorders, depression, aggression, the unmasking or acceleration of cancer growth, diabetes mellitus, dyslipidemias, cardiomyopathy, and nephrotoxicity.

Steroids are associated with recurrent hepatitis, cholestasis, hemorrhage, or hepatoma in some individuals. Additionally, products obtained from illicit sources may contain toxic contaminants [3].

Health care professionals, including pharmacist, need to fully understand the complexity of PED (eg, their physiologic and psychotropic properties, individual characteristics, different drugs and doses), acknowledging that each athlete's biology is unique. Pharmacists should be aware that Internet information can strongly influence vulnerable athletes decisions. PED offer temporary glory or improved appearance, but their long-term effects are considerable and dangerous.

For the reason to have traceability and control of usage of PED and due to the consistency and conflicts

of interest of the International Olympic Committee (IOC) and the national Olympic committees, WADA (World Anti-Doping Agency) was established in 1999, led by the IOC and supported by governments and various sports federations [5]. The World Anti-Doping Agency was founded with the aim of bringing consistency to anti-doping policies and regulations within sport organizations and government's right across the world

Following the creation of the World Anti-Doping Code (Code) in 2004, WADA was tasked with oversee-

Table 1. Frequently Abused Performance-Enhancing Drug

All sports	Amphetamines (intensify alertness, concentration, and self-confidence)	<p>Long-term administration associated with growth retardation in adolescents and myocardial pathology</p> <hr/> <p>High chronic doses may lead to persistent personality changes (eg, amphetamine psychosis)</p>
All sports	Cannabinoids (recreational relaxation, stress relief)	Marijuana, hashish
All sports	Eugeroics (arousal)	<p>Modafinil and adrafinil</p> <p>Marketed as having low abuse liability and fewer side effects (eg, insomnia, anxiety, agitation)</p>
All sports	Stimulants (eg, amphetamines, ephedrine, cocaine)	Stimulants are often used by student athletes in high-contact sports to boost energy for handling academic commitments and remaining eligible for competition
Archery, billiards, pistol shooting	Beta-blockers (reduce tremor)	<p>In endurance sports, beta-blockers adversely affect performance</p> <p>Clenbuterol is also used as an anorectic</p> <p>Inhaled beta-blockers may be allowed</p>
Endurance sports, especially track and field and cycling	Oxygen enhancement (eg, blood doping, erythropoiesis stimulating agents)	<p>Traditionally, athletes saved and reinfused their own red blood cells</p> <p>Sleep chambers that mimic high-altitude environments are used to stimulate red blood cell production</p> <p>Erythropoietin is abused</p> <p>Help decrease inflammation</p>
Endurance sports, weight lifting	Glucocorticosteroids (allowed externally, but not internally; generally called steroids) and anabolic-androgenic steroids	<p>Increase muscle mass and alter appearance</p> <p>Needle sharing of injectable steroids increases risk for infection with HIV or hepatitis</p> <p>A new trend to avoid apprehension is to purchase cattle implants that contain anabolic drugs and estrogen, and then extract the estrogen using directions available on the Internet</p>
Wrestling, gymnastics, horse racing (for the jockey)	Diuretics (weight loss or fluid retention)	<p>Used to meet weight-class limits</p> <p>Modify urine excretion rate of prohibited drugs</p> <p>Overcome fluid retention as a consequence of anabolic steroid use</p>

ing activities in a number of key areas:

- Code Compliance Monitoring – including overseeing acceptance, implementation and compliance of the Code, the core document the glues together anti-doping policies, rules and regulations worldwide.
- Science and Medicine - scientific research, publishing the annual List of Prohibited Substances and Methods, and managing laboratory accreditation, Therapeutic Use Exemptions (TUEs) and the Athlete Biological Passport (ABP).
- Anti-Doping Coordination - coordinating anti-doping activities globally through the central clearinghouse Anti-Doping Administration and Management System (ADAMS).
- Global Anti-Doping Development - through its Regional Anti-Doping Organization (RADO) program, WADA is developing a clean sport culture in parts of the world previously untouched by anti-doping programs.
- Education - preventative methods such as values-based education programs targeted at young athletes, coaches, doctors, training and parents on the dangers and consequences of doping, as well as the legal and social ramifications, are increasingly prevalent in anti-doping programs.
- Athlete Outreach - engaging with athletes, their entourage and all those involved in sport on the world stage, WADA's Athlete Outreach program aims to raise awareness while ensuring athletes are involved and part of the solution.
- Cooperation with Law Enforcement - working closely with government, law enforcement and Anti-Doping Organizations (ADOs) in order to facilitate evidence gathering and information sharing.
- Other Initiatives - conducting a wide range of other activities including Independent Observer Missions at major sports events.

Despite the existence of the WADA, there is no universal program and institution to pay attention of the education of young athletes, that oversees drug education and prevention programs in high school sports, whereas professional sports are governed by their specific sports-governing organizations.

Moreover, there is currently no universal list of banned, restricted, and permitted substances that applies to all athletes or all sports-governing agencies.

Table 2. Prohibited list of the substances and by the methods of identification according to WADA

Substances Prohibited At All Times	
S0. Non-Approved Substances	Any pharmacological substance which is not addressed by any of the subsequent sections of the List and with no current approval by any governmental regulatory health authority for human therapeutic use (drugs under pre-clinical or clinical development or discontinued, designer drugs, substances approved only for veterinary use) is prohibited
S1. Anabolic Agents	1. Anabolic Androgenic Steroids (AAS)
	a. Exogenous* AAS and other substances with a similar chemical structure or similar biological effect(s).
	(* "exogenous" refers to a substance which is not ordinarily produced by the body naturally)
	b. Endogenous** AAS when administered exogenously:
	(** "endogenous" refers to a substance which is ordinarily produced by the body naturally)
	2. Other Anabolic Agents
	Erythropoiesis-Stimulating Agents [e.g. erythropoietin (EPO), darbepoetin (dEPO), hypoxia-inducible factor (HIF) stabilizers and activators (e.g. xenon, argon), methoxy polyethylene glycol-epoetin beta (CERA), peginesatide (Hematide)].

	Chorionic Gonadotrophin (CG) and Luteinizing Hormone (LH) and their releasing factors, in males
	Corticotrophins and their releasing factors
	Growth Hormone (GH) and its releasing factors and Insulin-like Growth Factor-1 (IGF-1).
	In addition, the following growth factors are prohibited
	Fibroblast Growth Factors (FGFs), Hepatocyte Growth Factor (HGF), Mechano Growth Factors (MGFs), Platelet-Derived Growth Factor (PDGF), Vascular-Endothelial Growth Factor (VEGF) as well as any other growth factor affecting muscle, tendon or ligament protein synthesis/degradation, vascularisation, energy utilization, regenerative capacity or fibre type switching;
	and other substances with similar chemical structure or similar biological effect(s).
S3. Beta-2 Agonists	All beta-2 agonists, including all optical isomers (e.g. d- and l-) where relevant, are prohibited except:
	inhaled salbutamol (maximum 1600 micrograms over 24 hours),
	inhaled formoterol (maximum delivered dose 54 micrograms over 24 hours)
	salmeterol when taken by inhalation in accordance with the manufacturers' recommended therapeutic regimen.
S4. Hormone and Metabolic Modulators	1. Aromatase inhibitors
	2. Selective estrogen receptor modulators (SERMs)
	3. Other anti-estrogenic substances
	4. Agents modifying myostatin function(s) including, but not limited, to:
	myostatin inhibitors.
	5. Metabolic modulators:
	Insulins
Peroxisome Proliferator Activated Receptor δ (PPAR δ) agonists, PPAR δ -AMP-activated protein kinase (AMPK) axis agonists)	
S5. Diuretics and Other Masking Agents	1. Masking agents are prohibited. They include:
	diuretics, desmopressin, plasma expanders (e.g. glycerol; intravenous administration of albumin, dextran, hydroxyethyl starch and mannitol), probenecid and other substances with similar biological effect(s).
	Local administration of felypressin in dental anaesthesia is not prohibited.
	Diuretics and other substances with a similar chemical structure or similar biological effect(s) (except drospirenone, pamabrom and topical dorzolamide and brinzolamide, which are not prohibited).
Methods Prohibited At All Times	
M1. Manipulation of Blood and Blood Components	The administration or reintroduction of any quantity of autologous, allogenic (homologous) or heterologous blood or red blood cell products of any origin into the circulatory system.
	Artificially enhancing the uptake, transport or delivery of oxygen, including, but not limited to, perfluorochemicals, efaproxiral (RSR13) and modified haemoglobin products (e.g. haemoglobin-based blood substitutes, microencapsulated haemoglobin products), excluding supplemental oxygen.
	Any form of intravascular manipulation of the blood or blood components by physical or chemical means.

M2. Chemical and Physical Manipulation	Tampering, or attempting to tamper, in order to alter the integrity and validity of Samples collected during Doping Control. These include but are not limited to urine substitution and/or adulteration (e.g. proteases).
	Intravenous infusions and/or injections of more than 50 mL per 6 hour period except for those legitimately received in the course of hospital admissions or clinical investigations.
M3. Gene Doping	The transfer of polymers of nucleic acids or nucleic acid analogues;
	The use of normal or genetically modified cells.

Table 3. Prohibited list of the Substances Prohibited In Particular Sports and Substances Prohibited In-Competition according to WADA

Substances Prohibited In Particular Sports	Substances Prohibited In-Competition
P1. Alcohol (ethanol)	S0. Non-Approved Substances
P2. Beta-Blockers	S2. Peptide Hormones, Growth Factors and Related Substances
S0. Non-Approved Substances	S3. Beta-2 Agonists
S1. Anabolic Agents	S4. Hormone and Metabolic Modulators
S2. Peptide Hormones, Growth Factors and Related Substances	S5. Diuretics and Other Masking Agents
S3. Beta-2 Agonists	S6. Stimulants
S4. Hormone and Metabolic Modulators	S7. Narcotics
S5. Diuretics and Other Masking Agents	S8. Cannabinoids
S6. Stimulants	S9. Glucocorticosteroids
S7. Narcotics	
S8. Cannabinoids	
S9. Glucocorticosteroids	

Since the list of banned substances for athletes can be extensive, athletes must be careful of consuming all drugs (prescribed and nonprescribed) as well as all dietary supplements. Inadvertent use of a banned substance can have devastating consequences for a class athlete, and pharmacists can help them avoid such problems [7,8].

The Prohibited List is a cornerstone of the World Anti-Doping Code and a key component of harmonization. The List is updated annually following an extensive consultation process facilitated by WADA [5]. The 2014 List is valid from January 1 to December 31, 2014 Table (2).

The prohibited list was presented by the substance and by the method of identification and containing three parts:

- Substances and methods prohibited at all times (in- and out-of competition)
- Prohibited in competition
- Prohibited in particular sports

DRUG USE IN SPORTS: A VERITABLE ARENA FOR PHARMACISTS

Pharmacists, in a variety of settings including community practice, dispense medications to athletes, and can offer advice on nonprescription products and dietary supplements. Pharmacists should question these patients as to whether they are competitive athletes subject to drug testing by a sports-governing body, and professional-sport organizations. If so, pharmacists can help the athlete to avoid banned substances, which are generally considered ergogenic and performance enhancing.

A network of trained pharmacists in local areas (e.g., community pharmacies) would be an asset for sports organizations.

Pharmacists with expertise in drug testing and doping control programs can serve as resources for universities, colleges, high schools, and other institutions that are interested in establishing their own in-house testing programs [12]. In this capacity, pharmacists can develop and implement the policies and procedures for specimen collection. They can also assist in formulary management in training rooms. Pharmacists can provide presentations and information to athletes, coaches, and athletic trainers on drug and supplement use at all levels of competition. Further, pharmacists can develop or participate in educational and rehabilitation programs for athletes that seek assistance or who have been referred due to a positive drug test [9].

Great caution must be exercised particularly when advising on the use of dietary supplements. There are sample opportunities for pharmacists to participate in other aspects of doping control as well. Athletes commonly use dietary supplements and other substances that have the potential to improve their performance. Due to the pressure and desire to win at any and all costs, some athletes turn to banned substances as well[10].

Pharmacists have many opportunities to provide care in this arena: counseling and advising athlete-patients, consulting with or serving as resources for high school and college athletic programs, and providing information to coaches and trainers [11]. Pharmacists can play a key role in doping control and prevent athletes from inadvertently consuming banned substances.

CONCLUSION:

The roles for pharmacists have been emerging in the field of sports pharmacy, including doping control. With the proliferation of drug and dietary supplement use and abuse in sports, pharmacists can play key roles in deterring illicit drug use and in preventing the inadvertent use of banned substances by athletes.

The Sports Pharmacist, even not yet officially recognized specialty, has a vital role in promoting the prevention of doping.

The Sports Pharmacist should further promote environmental development, such as activities to improve awareness of doping among young athletes and the establishment of medical drug consultation services for athletes (female athletes in particular).

REFERENCES:

1. Brennan, B.P., G. Kanayama, H.G. Jr. Pope. Performance-enhancing drugs on the web: a growing public-health issue. *Am J Addict.*, 22, 2013,158-161.
2. Savulescu, J., L. Creaney, A. Vondy. Should athletes be allowed to use performance enhancing drugs? *BMJ.* 2013, 347:f6150
3. Perera, N.J., K.S. Steinbeck, N. Shackel. The adverse health consequences of the use of multiple performance-enhancing substances: a deadly cocktail. *J Clin Endocrinol Metab.* 98, 2013, 4613.
4. Prakash, K. Performance enhancing drugs in sports and the role of doctors: are there guidelines? *Indian J Med Ethics.* 10, 2013, 115-117.
5. World Anti-Doping Agency. Accessed at: <http://list.wada-ama.org/>, The revised 2014 Prohibited List, May 17, 2014.
6. Page. D. Pharmacists play role in making sure athletes are running clean. *Drug Topics.* 144, 2000m 33.
7. D.H. Catlin, C.K. Hatton. Use and abuse of anabolic and other drugs for athletic enhancement. *Adv Intern Med.* 36, 1991, 399-424.
8. Rosenberg, J.M., R.J. Fuentes, Woolley, et al. Questions and answers -- what athletes commonly ask. In: R.J. Fuentes, J.M. Rosenberg, eds. *Athletic drug reference '99.* Durham, N.C.: Clean Data, Inc.; 1999:1-128.
9. Savulescu, J., B. Foddy, M. Clayton. Why we should allow performance enhancing drugs in sport. *www.bjs-portmed.com.* , May 14. 2014. 666-672
10. S.Mandarić, V. Delibašić, Sanctions for Doping in Sport, *PHYSICAL CULTURE* 68, (1), 2014, 39-49
11. T. C. Werner. Performance-Enhancing Drugs in Sports:How Chemists Catch Users. *Journal of Chemical Education.* Vol. XX 2012. A-G.
12. B. Kayser, A. Mauron, A.Miah. Viewpoint Legalisation of performance-enhancing drugs. *Lancet* 366, 2005.