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Education Article

Pharmacological And Toxicological Aspects of Doping Substances And The Role of The Sports Pharmacist

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SUMMARY

Introduction: Despite the core essence of sport, athletes often turn to doping substances to advance quickly and improve performance. Doping remains a critical issue in sports, undermining fair competition and athlete integrity.
Methodology: A literature review was conducted using databases such as PubMed and Google Scholar. Key terms such as „anabolic steroids", „peptide hormones", „diuretics", and „sports pharmacist" were used to identify relevant studies.
Topic: The article discusses the growing issue of performance-enhancing drug abuse in sports, highlighting various substances such as anabolic steroids, stimulants, diuretics, and narcotics, emphasizing their pharmacological effects and toxicological consequences. These substances, often used in combination, can lead to serious health complications like cardiovascular issues, metabolic disorders, and addiction. Additionally, the misuse of banned substances may result in unintentional violations of doping regulations. The article highlights pharmacists' key role in sports, particularly in doping prevention and safe medication use. Sports pharmacy focuses on doping prevention, managing side effects, and safeguarding athlete health.
Conclusion: The misuse of performance-enhancing substances in sports poses serious health risks and undermines fair competition. Athletes may unknowingly violate doping rules, and substances can have harmful effects. To address this, better testing, education, and stricter regulations are needed. Pharmacists, though underutilized, play a key role in preventing doping and ensuring safe medication use. Establishing sports pharmacy as a specialized field with proper training is crucial for supporting athletes' health and safety.

Keywords: Anabolic Steroids, Peptide Hormones, Beta-Agonists, Diuretics, Sports Pharmacists

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INTRODUCTION

About sports today

Sport is often considered the most important secondary matter in the world. Across the globe, sport is a ubiquitous social activity that creates a unique connection between health, recreation, entertainment, and industry. It is also a significant economic activity that consciously or unconsciously impacts the social behavior of individuals at home, at work, and in play [1]. A practical and concise definition of sport is that it is the organized playing of competitive games according to rules. In that context, violating the rules implies cheating to achieve an unfair competitive advantage, whether it involves the use of illegal equipment, match-fixing, the abuse of prohibited substances, or any other banned means.

The illegal use of prohibited drugs (doping) to influence the outcome of a sporting competition constitutes fraud against competitors, spectators, the sport, sponsors, and the public, which is no different from other personal, professional, or commercial frauds. The rules in sports venues can be changed by agreement, but once they are established, they represent the boundaries of fair competition. Situational temptation, attitudes, and subjective norms were identified as strong predicting variables of doping intentions, with attitudes being a significant predictor for both doping susceptibility and behavior [2].

Sports abilities represent a combination of four main components: skill, strength, endurance, and recovery, with each sport utilizing a specific combination of these elements. These characteristics also show a significant correlation with the strongest and most effective forms of doping. Sports that require explosive strength are the most susceptible to androgen doping due to their effect on increasing muscle mass and strength, while endurance-requiring sports are most enhanced by doping with hemoglobin (blood) that increases the capacity to deliver oxygen to tissues under strain. Performance in contact sports and those involving intense physical activity or training can be improved through growth hormone and its secretagogues, in a way that their application accelerates tissue recovery from injury. Hormones remain the most commonly detected doping agents responsible for about two-thirds of anti-doping rule violations, identified using increasingly sophisticated detection methods. Currently, the vast majority of positive tests remain a result of the use of a wide range of androgens, including market and illicit nutraceuticals, designer drugs, specific androgen receptor modulators (SARMs), synthetic androgens as well as exogenous natural androgens, while peptide hormones (erythropoietin-stimulating hormone, growth hormone and its secretagogues) and autologous blood transfusion remain difficult to detect [3].

History of doping control

Although efforts have been made for years, even decades, to develop and establish some form of doping control, a precedent in this area only occurred after the increasingly frequent deaths in competitions. It is believed that the death of a Danish cyclist at the 1960 Summer Olympics in Rome, when it was proven that he had used amphetamines, prompted decision-makers to consider some form of reform. The first List of Prohibited Substances was published in 1962 by the European Council and included narcotics, stimulants, alkaloids, respiratory tonics, and hormones. In 1967, the International Olympic Committee (IOC) established a Health Commission that became the main body for researching doping substances and methods. That same year, it is believed that due to the use of prohibited substances contributed to a fatal incident during the Tour de France, which involved the death of a British cyclist. The first doping controls at the Olympics were conducted in 1968 at the Winter Olympics in Grenoble, France, as well as at the Summer Olympics the same year in Mexico. This marked the beginning of the introduction of doping control as regular practice at the Olympic Games, as well as at all other major international and world competitions [4].

Today, doping control analysis has become a conventional means of ensuring fairness and justice in sports. Although doping control sometimes seems like fighting windmills, every step taken to advance this area is of great importance. Doping in sport is influenced by a range of systemic factors beyond individual athletes, including the roles of support personnel, coaches, and the coach-athlete relationship, which significantly impact athletes' decisions to dope. The findings sug-

gest that doping is an emergent property of sport systems, highlighting its complexity as a systemic issue that requires Whole-of-system interventions rather than solely focusing on personal responsibility and strict liability of individual athletes [5].

In conclusion, the principles of existing doping analysis aim to preserve the fairness and integrity of sports by detecting and preventing the use of prohibited substances and methods among athletes. These principles rely on sophisticated analytical techniques, a comprehensive list of banned substances, and regular athlete testing programs for identification and appropriate sanctions [6].

Definition of doping and violations of anti-doping rules

Evolution of the term „doping"

Although the term „doping" is often considered a modern concept, its understanding has existed for as long as sports themselves. From ancient times to the present day, there has always been and always will be a desire to achieve great results.

The term „doping" itself was first mentioned in an English dictionary in 1889, describing a medicinal mixture containing opium used to enhance the performance of horses in horse racing. There are various opinions on the origin of this word. One of them suggests that „dop" is of Dutch origin and represented alcoholic beverages made from grape remnants, used by Zulu warriors as a „stimulant" in battles [4]. Later, the meaning of „dope" was expanded to include all beverages with stimulating effects. Over time, the term doping was accepted in sports and generally refers to the use of prohibited substances or methods to improve athletic performance [7].

Anti-doping rules

Doping involves the consumption of foreign substances or substances naturally present in the body with the aim of artificially enhancing an athlete's competitive abilities, which contradicts sporting ethics and the physical and mental integrity of athletes [8].

This is one of many definitions of doping accepted among the general population and experts; however, it is not exhaustive when it comes to violations of anti-doping rules.

According to the World Anti-Doping Agency (WADA), doping involves a violation of one or more anti-doping rules [7]. A violation of anti-doping rules includes much more than just the use and misuse of prohibited substances. Doping constitutes a breach of anti-doping rules, which are outlined in the World Anti-Doping Code (available on the World Anti-Doping Agency's website) and therefore are universal and widely accepted worldwide. The World Anti-Doping Code is a document that all organizations responsible for preventing doping in sport, such as the International Olympic Committee, national anti-doping agencies, or institutions involved in organizing major sporting events, are obligated to adhere to.

The document also defines doping as the occurrence of a breach of one or more anti-doping rules, which number 11, including:

1. Presence of a prohibited substance or its metabolites or markers in the athlete's bodily sample.
2. Use or attempted use of a prohibited substance or prohibited method.
3. Refusal or failure to submit a sample after notification, as required by valid anti-doping rules, without a compelling justification, or avoiding sample collection in any other way.
4. Whereabouts violation, which involves not meeting the specified conditions regarding the athlete's availability for out-of-competition testing, including failure to provide residence information and missing testing as per internationally accepted testing standards.
5. Tampering or attempt to tamper with any part of the doping control process.
6. Possession of a prohibited substance or method by the athlete or a person supporting the athlete.
7. Trafficking or attempted trafficking of any prohibited substance or method by the athlete or another person.
8. Administration or attempted administration of any prohibited substance or method by the athlete or another person to any athlete during competition, or administration or attempted administration of any prohibited substance or method to any athlete outside of competition or any prohibited method-of-Competition.
9. Assisting, encouraging, inciting, concealing, or any other form of complicity involving a violation of anti-doping rules or attempted vio-

lation, i.e. complicity or attempted complicity by an athlete or another person.
10. Prohibited association by an athlete or another person.
11. Actions by an athlete or another person to discourage or retaliate against reporting to authorities [7,9].

Despite existing regulations, there are significant differences in athletes' understanding of anti-doping rules. While some athletes have a thorough knowledge, many remain unaware of critical aspects, increasing the risk of unintentional violations. Current educational programs are inadequate, as they fail to address the diverse needs of athletes across different sports and regions. This lack of tailored education contributes to ongoing doping issues, highlighting the need for targeted interventions to improve awareness and ensure compliance with the World Anti-Doping Code [10].

List of prohibited substances

The introduction of the ban on the use of stimulants and doping control itself was a lengthy and exhaustive process that evolved throughout the twentieth century. It took a long time for organizations and sports federations to recognize the importance of this activity and incorporate it as an integral part of every competition and sports event. Unfortunately, this only occurred after several deaths recorded during competitions, which led to the establishment of the Health Commission by the International Olympic Committee in 1967 and the establishment of the first list of prohibited substances.

The list of prohibited substances and methods that are currently valid is published by the World Anti-Doping Agency as often as necessary, but no less than once a year. The most recent list can always be found on this institution's website [7]. The World Anti-Doping Agency Code [11] prohibits athletes from using substances or methods that meet two of three criteria, including: 1. performance enhancement 2. harm to the health of the athlete (safety) 3. undermining the spirit of sport (unsportsmanlike behavior, fair play) [3].

Currently prohibited substances and methods can be categorized as: - substances and methods that are always prohibited (in competition and out of competition) - substances and methods prohibited only in competition - substances prohibited in certain sports. Substances falling into the category of banned in and out of competition are classified into the following categories (Table 1): prohibited substances, anabolic agents, peptide hormones, growth factors and related substances, beta-2 agonists, hormones and metabolic modulators, diuretics, and other masking agents. Methods that are also always prohibited include blood and blood component manipulations, chemical and physical manipulations, and gene doping. In addition to the listed substances and methods that are always prohibited, stimulants, narcotics, cannabis, and glucocorticosteroids are also mentioned among the substances and methods prohibited in competition. There are substances that are only prohibited in certain sports, such as beta blockers. These drugs lead to reduced muscle tremors, reduced oxygen consumption, and diminished adrenaline impact on the body, therefore, they are most commonly abused in sports that require a steady hand, such as archery, motorsports, billiards, darts, golf, shooting, skiing, and ski jumping [7].

The aim of this education article is to offer a comprehensive overview of pharmacological and toxicological properties of doping substances, providing a deeper understanding of their effects. Gaining insight into these factors is crucial for developing effective prevention strategies and preserving the integrity of

Table 1. List of prohibited substances for the year 2024 [summarized from 12]

PROHIBITED AT ALL TIMES (IN- AND OUT-OF-COMPETITION)
S0 NON-APPROVED SUBSTANCES
S1 ANABOLIC AGENTS
S2 PEPTIDE HORMONES, GROWTH FACTORS, RELATED SUBSTANCES, AND MIMETICS
S3 BETA-2 AGONISTS
S4 HORMONE AND METABOLIC MODULATORS
S5 DIURETICS AND MASKING AGENTS
M1 MANIPULATION OF BLOOD AND BLOOD COMPONENTS
M2 CHEMICAL AND PHYSICAL MANIPULATION
M3 GENE AND CELL DOPING
PROHIBITED IN-COMPETITION
S6 STIMULANTS
S7 NARCOTICS
S8 CANNABINOIDS
S9 GLUCOCORTICOIDS
PROHIBITED IN PARTICULAR SPORTS
P1 BETA-BLOCKERS

competitive sports. Additionally, the paper emphasizes the role of the sports pharmacist in doping prevention, athlete education, and ensuring safe and ethical pharmacological practices in sports.

Law on the Prevention of Doping in Sports

The International Olympic Committee (IOC) established the World Anti-Doping Agency (WADA) in 1999 with its headquarters in Montreal, which has become the supreme institution in the field of anti-doping. By publishing the WADA Code, anti-doping rules were introduced and unified globally. In addition to accrediting national anti-doping laboratories, the World Anti-Doping Agency also established the Court for Arbitration for Sport (CAS) to settle legal disputes related to anti-doping [3]. This Code has been adopted by over 660 sports organizations, including all Olympic, Paralympic, and national anti-doping organizations, among which our National Anti-Doping Agency (Antidoping Agency of the Republic of Serbia, ADAS) is included [13]. Doping in sports in the Republic of Serbia is prohibited by the Law on the Prevention of Doping in Sports (Official Gazette of RS, No. 111/2014 and 47/2021), which prescribes measures and activities for preventing doping in sports.

Punitive provisions are established, including two criminal offenses:
1. Facilitating the use of doping substances
2. Unauthorized production and trafficking of doping substances [7].

Disciplinary measures imposed for violations of anti-doping rules established by this law and the World Anti-Doping Code include disqualification of sports results, temporary suspension, ban on participating in competitions, prohibition of engaging in sports-related activities, and other measures. The law also emphasizes that an individual subject to a measure due to a violation of anti-doping rules is not entitled to participate in any capacity in any sport during the duration of the measure [9].

METHODOLOGY

Information for this article was gathered from scientific articles accessed through internet-based databases, including PubMed and Google Scholar. The search was conducted using key terms such as „anabolic steroids", „peptide hormones", „diuretics", and „sports pharmacist". The references selected for this research paper were carefully selected based on their relevance to the research topic and the current state of knowledge in the field. The studies included in the literature review provide a solid foundation of evidence regarding the effects of doping substances on athletic performance, particularly focusing on their impact on general health and their potential toxicity. Several references were chosen because they offer critical theoretical frameworks and empirical findings that directly relate to healthcare professionals in sports, such as sports pharmacists. A literature search was conducted using only Serbian and English sources, which may represent a limitation of this study, potentially affecting the comprehensiveness of included research. Overall, these references were selected to ensure a balanced perspective, offering both historical context and contemporary viewpoints, and to strengthen the overall validity of the study's conclusions.

TOPIC

According to the World Anti-Doping Code, at the top of the List of Prohibited Substances is group **S0**, or the group of **Non-Approved Substances**. This group includes any pharmacological substance that currently does not have approval from any government regulatory health body concerning therapeutic applications in humans, making this category very broad. Substances in this category can be drugs currently under preclinical or clinical trials, drugs whose use has been suspended, or drugs approved for use only in veterinary use. Therefore, substances in this group are those for which there are currently no solid evidence of (beneficial) effects on humans in general, so in practically all cases, and there is a lack of evidence for performance enhancement [14].

The next categories of prohibited drugs will be covered in separate chapters.

Anabolic Androgenic Steroids

According to recent World Anti-Doping Agency reports, anabolic steroids account for 60% of positive doping tests in athletes [15]. The prevalence of non-medical use of anabolic steroids is estimated to be between 1.27

and 4% among young adults. When considering specific populations approximately 20% of bodybuilders and 11% of prisoners are believed to use anabolic steroids [16].

Physiological function of steroids

The most important natural androgen secreted in both male and female bodies is testosterone. In a male with healthy sex glands, Leydig cells in the testicles produce about 95% of the total testosterone in the body. The adrenal glands (of both sexes) and the ovaries in females produce very little testosterone, but they also secrete weaker androgens compared to testosterone, such as dehydroepiandrosterone (DHEA and its sulfo-conjugate) and androstenedione, which can be converted into stronger androgens in the periphery, such as testosterone and 5-alpha-dihydrotestosterone, DHT [17].

As the name suggests, anabolic androgenic steroids exhibit both androgenic and anabolic effects. Androgenic effects can manifest in bones, reproductive tissue, muscles, hair follicles in the skin, liver, kidneys, hematopoietic, immune, and central nervous systems; primarily involving the development of secondary sexual characteristics and masculinization. Androgenic effects include the growth of the larynx causing deepening of the voice, growth of terminal hair (in pubic, axillary, and facial regions; growth in other areas depends on various factors), increased activity of sebaceous glands, especially in facial areas leading to acne, as well as libido and increased aggressiveness. Anabolic effects can also be seen as protein building in skeletal muscles and bones and stimulation of linear growth that eventually stops due to epiphyseal closure. In men, androgens are essential for maintaining reproductive function. They play a vital role in maintaining skeletal muscles and bones, supporting cognitive function and a sense of well-being [17].

Classification

Androgenic anabolic steroids can be divided in many ways. The simplest classification is based on their solubility: steroids that are soluble in water and administered orally (17-alpha-alkylated) and parenteral forms soluble in lipids (17-beta-esterified). Another way of classification concerns their structures that can be based on testosterone, dihydrotestosterone (DHT), or 19-nortestosterone (nandrolone). This classification implies that they will have different properties and expected side effects.

The situation is further complicated by beliefs among users, often stemming from unverified sources, that some steroids are primarily better for „bulking" or gaining mass (e.g., Deca-Durabolin), while others are more suitable for losing body fat (e.g., Winstrol). It is very difficult to track and predict the amount of steroids that someone is taking into their body, as they are often used in „cycles", meaning there are periods of usage followed by periods of abstinence. The main reason for this type of use is primarily because it is said to reduce the likelihood of unwanted effects while maximizing the substance's anabolic potential. An additional problem arises when the users combine these cycles with additional pharmaceutical agents: when they want to increase weight, they use insulin or human growth hormone, and when they want to lose weight, they add clenbuterol, cytomel, or 2,4-dinitrophenol.

There is also a surprising number of drugs used in an attempt to limit the unwanted effects of steroid use or to normalize the hypothalamic-pituitary-gonadal axis after the cycles. Some of these are: estrogen receptor antagonists (tamoxifen), selective estrogen receptor modulators (clomiphene), aromatase inhibitors (arimidex), 5-alpha reductase inhibitors (finasteride), and stimulators of the hypothalamic-pituitary-gonadal axis such as human chorionic gonadotropin [15].

Therapeutic use of Steroids

Hormone Replacement Therapy

Testosterone preparations are used in male hypogonadism and male hormonal contraception (where progestogens are used to inhibit gonadotropin secretion). Anabolic steroids also stimulate erythrocyte synthesis, which may be useful in the treatment of hypoplastic anemias. However, their use in affluent countries is likely to be limited due to the relatively recent availability of recombinant human erythropoietin and its analogues. In postmenopausal women, the treatment of osteoporosis with anabolic steroids such as nandrolone decanoate is not recommended given the success of estrogen replacement and, more recently, the introduction of bisphosphonates.

Regarding the clinical use of steroids,

a positive therapeutic effect can be expected, with the prior decision of the physician based on the balance of benefits and risks relative to the patient's condition. In contrast, athletes and bodybuilders who wish to enhance their performance or use steroids for cosmetic reasons, typically do so covertly and make decisions on the method of administration based on subjective assessment [17]. The study found that the first choice of anabolic androgenic steroids differed between genders, with men primarily using testosterone and women opting for oxandrolone [18].

Reasons for Steroid Abuse

Ergogenic effects (effects that enhance athletic performance) associated with the use of anabolic steroids include: an increase in lean body mass, an increase in cross-sectional area of muscles, a decrease in body fat percentage, an increase in muscle strength and power, faster recovery between training sessions, quicker recovery from injury, an increase in protein synthesis, an increase in muscle endurance, increase in erythropoiesis, as well as hemoglobin and hematocrit synthesis, an increase in bone mineral density, an increase in glycogen storage, an increase in lipolysis, increase in neuronal transmission, reduced muscle damage, an increase in pain tolerance, behavior modification – specifically increased aggression (desirable in combat sports)… [19] One study found that nandrolone was the most frequently used anabolic androgenic steroid. Additionally, male testosterone users exhibited significantly elevated testosterone/epitestosterone (T/E) ratios, whereas women using dermal testosterone had supra-physiological total serum testosterone concentrations but did not exceed a T/E ratio of 4, underscoring the need for gender-specific biomarkers in doping detection [18].

Adverse Effects and Consequences of Abuse

Despite extensive evidence on the adverse effects of steroid use, particularly on the cardiovascular system [20], steroids remain the most commonly detected substances in positive doping tests. Table 2 outlines potential adverse effects, including growth and developmental disorders in adolescents, hirsutism and amenorrhea in females, an increased risk of liver cancer with oral use, and various psychological issues such as heightened aggression, anxiety, and depression. A meta-analysis found that anabolic steroid use significantly suppresses luteinizing hormone, follicle-stimulating hormone, and testosterone (all $p < 0.001$). While gonadotropins normalize within 13–24 weeks after discontinuation, testosterone remains significantly low, indicating prolonged reproductive effects [21]. The HAARLEM study found that most male amateur athletes using anabolic steroids experienced side effects, with 97% of former users reporting adverse effects. Only 47% of tested samples contained the labeled substance, and 48% of participants reported addiction, highlighting quality concerns and dependency risks [22].

Target organ	Side effects
Bones	Premature closure of the epiphysis in children (early cessation of growth).
Breasts	In women: atrophy. In men: gynecomastia and enlargement of the nipples.
Cardiovascular system	Increased risk of thrombotic conditions, such as myocardial infarction or stroke (elevated LDL, decreased HDL, and apolipoprotein-1, elevated hematocrit due to polycythemia, and decreased fibrinogen in plasma). Heart damage (left ventricular hypertrophy, fibrosis, and heart failure). Sudden cardiac death.
Central nervous system	Increased libido in both men and women, which can be difficult to control. Hypomania (a milder form of mania). Increased irritability. Increased aggression and hostility. Destructive impulses. Self-destructive impulses. Withdrawal symptoms may include severe depression.
Hair	Hirsutism in women (conversion of vellus hair to terminal hair and male body hair pattern). Accelerated male pattern baldness.
Liver	Impaired function. Hepatic cholestasis (obstruction of the bile duct causing jaundice). Peliosis hepatitis (blood-filled cysts in the liver). Liver tumors (increased risk).
Reproductive system	Decreased spermatogenesis. Amenorrhea. Clitoral hypertrophy. Testicular atrophy. Disproportionate growth of the inner prostate. Infertility.
Skin	Acne, severe forms on the back, chest, and face.
Vocal cords	Deepening of the voice in women.

Table 2. Overview of the side effects of anabolic-androgenic steroid use by target organ [summarized from 17].

Peptide Hormones, Growth Factors, Related Substances, and Mimetics

This category includes a large number of substances which are divided into three groups. The first group includes erythropoietin and other substances that can induce hypoxia such as cobalt; the second group includes peptide hormones and their stimulating factors like luteinizing hormone or growth hormone while the third group consists of factors that can influence growth, such as insulin-like growth factor-1 [12].

Erythropoietin

Erythropoietin is a glycoprotein hormone and the main precursor in the synthesis of red blood cells from bone marrow cells. In adults, erythropoietin is primarily secreted in the kidneys and to a lesser extent in the liver, with the main stimulus for its secretion being oxygen deficiency or hypoxia. Physiologically, hypoxia can occur at higher altitudes or with exposure to intense physical exertion, such as training. Erythropoietin stimulates hematopoiesis, leading to an increase in red blood cell production, typically observed after three to four weeks [23].

Therapeutic Indications

The therapeutic use of erythropoietin mainly involves treating anemias of various etiologies, such as anemia of chronic disease, anemias caused by hepatitis C or HIV infection, malignant diseases, renal insufficiency, or dialysis. It can also be used if a patient chooses not to undergo blood transfusion therapy due to personal or religious beliefs [24].

Erythropoietin as a doping substance

The use of recombinant human erythropoietin (rHuEpo) in athletes was officially banned in 1988, among other reasons because it was believed that numerous cyclist deaths during that period were linked to its use. Empirical trials have shown that moderate doses of rHuEpo can increase VO_2 max by 6–8 units by boosting hemoglobin levels, significantly enhancing endurance and maximal aerobic capacity [25]. More oxygen allows for extended training time and reduces fatigue that athletes experience, leading to its frequent abuse in endurance sports such as cycling or ski jumping [26].

In sports performance, accurate determination of the anaerobic threshold (AT) is crucial for assessing endurance, as it indicates when the body transitions to anaerobic metabolism. Understanding AT can help identify risks related to doping substances. For example, endurance-enhancing substances like erythropoietin (EPO) can alter the anaerobic threshold, allowing athletes to maintain high performance longer than physiologically possible. Precise measurement of blood lactate levels, as shown in the study by Mladenović Ćirić and Jovanović (2024), can help detect physiological changes from doping use, even without a standard warm-up protocol. This method enables a more accurate assessment of an athlete's physical state and supports preventive measures against doping [27].

The most commonly abused types of erythropoietin and its analogs are rHuEpo, darbepoetin alfa, and the long-acting erythropoietin CERA (continuous erythropoietin receptor activator) [24].

One of the most well-known cases of abuse of doping substances, including erythropoietin, is the American cyclist Lance Armstrong. He was the winner of seven consecutive titles in the prestigious cycling race „Tour de France" from 1999 to 2005, but after proven presence of doping substances in his samples in 2012, the United States Anti-Doping Agency took all of his medals and banned him for life from participating in sports competitions [28].

Adverse Eeffects of Erythropoietin

Increased red blood cell count leads to an increase in hematocrit, which will result in increased blood viscosity and density. Prolonged exposure to intense physical exertion can lead to dehydration due to increased sweating, which combined with increased blood density can lead to cardiovascular and thromboembolic complications. Some of these complications include heart failure, hypertension, hypertrophy, pulmonary embolism, or myocardial infarction. If these changes are not addressed in time, they can lead to fatal outcomes [26].

Growth Hormone

Human growth hormone or somatotropin is a polypeptide hormone secreted by somato-

tropic cells in the anterior pituitary gland, or adenohypophysis. The most common use is in the treatment of growth hormone deficiency or idiopathic short stature [29]. During adolescence, the secretion of this hormone is regulated by numerous factors such as the release of growth hormone-releasing hormone, regular sleep, physical activity, and levels of L-dopa and arginine. Growth hormone acts directly on insulin-like growth factor 1. Its effects at the biochemical level include lipolysis and increased protein anabolism, resulting in decreased fat content and increased muscle mass. What also may occur with its use include increased energy, increased muscle strength, cardiac output, and improved oxygen utilization [30]. Growth hormone significantly reduced fat mass and increased lean body mass through an increase in extracellular water and body cell mass in men, particularly when co-administered with testosterone. However, the effects on physical performance, particularly sprint capacity, were temporary and did not persist after the cessation of treatment, suggesting that reliance on growth hormone for long-term performance enhancement may be ineffective [31].

Unwanted Effects of Somatotropin

Side effects of growth hormone administration in healthy adults include swelling, arthralgias, paresthesias, fatigue, and changes in cardiac morphology and function. Chronic somatotropin abuse can lead to serious health risks, such as myocardial hypertrophy, cardiac complications, arthropathy, insulin resistance, and an increased risk of diabetes and malignancy. These adverse effects are likely exacerbated when growth hormone is used in combination with anabolic androgenic steroids [32].

Beta-2 Agonists

Beta-2 adrenergic agonists are among the oldest medications used in the treatment of obstructive respiratory diseases such as asthma, chronic obstructive pulmonary disease (COPD) and bronchitis. Beta-2 agonists are classified into short-acting or first-generation drugs like salbutamol, terbutaline, fenoterol, etc; and long-acting or second-generation drugs like salmeterol and formoterol [33].

The mechanism of action of these drugs is based on their bronchodilator effect, achieved by stimulating beta-2 adrenergic receptors in the smooth muscles of the lungs and respiratory system [14]. Research has shown that when administered by inhalation or in high oral doses, beta-2 agonists can exert anabolic effects, increasing muscle strength and maximal power [34]. While low therapeutic doses have minimal impact, supratherapeutic doses have been linked to muscle hypertrophy and improved sprint performance, raising concerns about their use in sports. This potential for performance enhancement, particularly in short, intense exercises, underscores the need for vigilance in anti-doping efforts [35].

The most common side effects that can occur with the use of these substances are cough and throat irritation. Possible side effects on the cardiovascular system include tachycardia, palpitations, bronchospasm, and tremors. Anxiety, angioedema, itching, headache, as well as paradoxical bronchospasm can also occur, but less frequently [33].

Hormones and Metabolic Modulators

This category includes various groups of drugs, including aromatase inhibitors and selective estrogen receptor modulators, whose main therapeutic indications for use are hormone (estrogen) dependent carcinomas, such as estrogen-dependent breast cancer [36,37]. Due to their inhibitory effect on estrogen, they found their place on list of prohibited substances, often used as additional therapy with androgenic anabolic steroids. As their name suggests, aromatase inhibitors suppress the action of the aromatase enzyme, preventing the conversion of testosterone to estrogen and reducing the risk of gynecomastia. The primary reason for the abuse of these drugs is to reduce the unwanted effects of steroids. Selective estrogen receptor modulators are also found in this group and are abused for the same reason, with their mechanism of action being the inhibition of the binding of created estrogen to receptors [14]. One of the most well-known and commonly abused drugs in this group, belonging to hormones, is insulin.

Insulin

Insulin is a peptide hormone that is naturally synthesized in the human body and secreted when there is an increased level of glucose in the body, from the beta cells of the pancreas.

Table 3. Classification of diuretics and their most common clinical applications [summarized from 42]

Diuretic group	Examples	Most common clinical applications
Loop diuretics	furosemide, bumetanide, torasemide	Chronic heart failure, kidney failure, acute pulmonary edema, refractory edema
Thiazides	hydrochlorothiazide, bendroflumethiazide, chlortalidone, indapamide, metolazone, chlorothiazide	Hypertension, edema, diabetes insipidus
Potassium-sparing diuretics	amiloride, triamterene, eplerenone, canrenone, spironolactone	Edema, in combination with Henle loop diuretics or thiazides to maintain potassium balance in patients with hypertension, congestive heart failure, or cirrhosis with ascites; primary hyperaldosteronism (Conn's syndrome); cirrhosis with edema; moderate to severe heart failure (with other medications); mild heart failure (in combination with other medications)
Carbonic anhydrase inhibitors	acetazolamide, dorzolamide, brinzolamide	Glaucoma therapy
Osmotic diuretics	mannitol	Brain edema; to reduce intraocular pressure

Its first clinical application was more than a hundred years ago, and it is still used in the therapy of patients with diabetes mellitus type 1 or 2, or other forms of diabetes [38].

Insulin preparations are mainly categorized based on their duration of action: short-acting insulins like lispro and aspart, intermediate-acting (insulin lente), or long-acting insulins like glargine or detemir [39].

While research is ongoing to determine whether insulin alone can affect athletic performance, it is often used as an additional substance of abuse, usually in combination with growth hormone. As mentioned earlier, the use of growth hormone can lead to the development of diabetes or insulin resistance due to high glucose concentrations, so insulin is used to prevent the manifestation of these unwanted effects [40].

The most common adverse effect that may occur with insulin abuse is hypoglycemia, which can be presented as mild nausea, dizziness and headache, but can progress to a life-threatening condition like hypoglycemic coma. Weight gain may occur, which is typically corrected promptly in professional athletes, while sometimes allergic reactions or anaphylaxis may occur [39].

Diuretics

Diuretics are a relatively broad group of substances with a large number of registered drugs that can be classified based on their site of action and mechanism of action. These include loop diuretics, carbonic anhydrase inhibitors, thiazide and thiazide-like diuretics, potassium-sparing diuretics, osmotic diuretics, and vasopressin receptor antagonists. In addition to their therapeutic use, their use as doping agents in sports has been increasing in recent years [41].

Mechanism of Action

All diuretics, except mannitol and vasopressin receptor antagonists, work by increasing the excretion of sodium ions and water from the body through the kidneys. Their primary action is the reduction of sodium (Na+) and chloride (Cl-) reabsorption from the filtrate, and their secondary action is the increase in water excretion, which is directly proportional to the increased excretion of sodium chloride (NaCl). These effects are achieved in two ways: either by acting directly on the nephron cells or indirectly by altering the filtrate composition. Mannitol belongs to osmotic diuretics, while vasopressin receptor antagonists inhibit the action of antidiuretic hormone, thus preventing water reabsorption and promoting water excretion from the body.

Therapeutic Indications

Diuretics can be used in the treatment of various medical conditions either as monotherapy or in combination with other drug groups. They are most commonly used in conditions such as hypertension, acute and chronic edema, kidney failure, and heart failure (Table 3). Additionally, diuretics may be applied in cases of forced diuresis for poison elimination in poisoning incidents, as well as in diabetes insipidus (thiazide diuretics).

Diuretics as Doping in Sports

Since diuretics were added to the List of Prohibited Substances in 1985, many well-known athletes and medalists at prestigious competitions have tested positive for doping. Examples include Ben Johnson (Canadian sprinter), Shane Warne (Australian cricketer), Ivan Ivanov (Bulgarian weightlifter), Deco (Portuguese footballer), and others.

There are two main reasons why diuretics are abused in sports: to reduce an athlete's weight or to quickly eliminate another substance from their body. In sports that categorize competitors by weight, such as combat sports (judo, wrestling), bodybuilding, weightlifting, or jockeys in horse racing, some athletes try to lose weight quickly and efficiently to enter a lower weight category. During this process, athletes often resort to diuretics such as furosemide, bumetanide, spironolactone, and ethacrynic acid, in addition to non-pharmacological (often excessive) measures like saunas or physical exertion without water intake. Another reason for diuretic abuse in sports is to speed up and increase the excretion of prohibited substances from the body. Using diuretics can increase urine volume, thereby diluting the concentration of any potential doping substances and their metabolites in the urine, which could potentially help avoid a positive doping test. Therefore, it is not surprising that there is a significant number of positive doping cases involving diuretics worldwide (between 5% and 8% of all doped athletes) [42].

Adverse Effects

Diuretics, like all other medications, can cause various adverse effects during use, as well as toxic effects resulting from medication overdoses. Abuse of diuretics without appropriate indications or therapeutic doses, can lead to several adverse effects. Some of these include hyponatremia, hypokalemia, hyperkalemia, acid-base balance disturbances, calcium and magnesium metabolism disorders, metabolic disturbances such as insulin resistance, dyslipidemia, hyperuricemia, androgenic effects, ototoxicity, allergic interstitial nephritis, and more.

All diuretics affect potassium homeostasis in muscles that are exposed to intense training. Potassium-sparing diuretics can lead to hyperkalemia and consequently to arrhythmias. Conversely, non-potassium-sparing diuretics can cause hypokalemia (with muscle cramping), which may also result in arrhythmias.. During exercise, the temperature of skeletal muscles quickly exceeds body temperature, after which the thermoregulatory system is activated. If diuretics are added, it can lead to exhaustion, heart rhythm disturbances, heart attack, and death. Additionally, most diuretics also affect uric acid metabolism, which can lead to gout attacks [42].

Stimulants

Stimulants represent a group of substances and medications that can be divided into non-selective and selective within the List of Prohibited Substances. Non-selective stimulants include amphetamines, cocaine, prenilamine, and others, while selective stimulants include ephedrine, pseudoephedrine, sibutramine, nicetamide, epinephrine...

The primary effect of stimulants lies in stimulating neurotransmission, primarily dopamine and norepinephrine in the brain [14]. Amphetamines are central nervous system stimulants, and their sympathomimetic effects are mainly expressed through the release of norepinephrine from synaptic vesicles. Released norepinephrine will exhibit effects such as increased excitement, increased blood pressure, accelerated heart and respiratory rate. The most common route of administration is oral, although they can also be injected.

Reasons for the Abuse of Stimulants

The effects observed during the use of amphetamines include increased strength, muscle power, speed, aerobic capacity, and endurance. Undesired effects that occur during the use of stimulants are mainly associated with increased excitation of the central nervous system. Some of these effects include restlessness, agitation, gastrointestinal disturbances and nausea, headaches, recurrence of previous fatigue, while more severe adverse effects include overheating due to increased sweating and loss of water and minerals, arrhythmias, seizures, hallucinations, and addiction [43].

Pseudoephedrine

Pseudoephedrine is a substance that was on the list of banned substances until 2004 when it was removed and then reinstated in 2010

[44]. This substance is a sympathomimetic and it is used as a nasal decongestant due to its vasoconstrictive effect. It can be short-acting or specially formulated for extended release. Patients should be informed of the risk of central nervous system stimulation [45]. A study by Gill, Shield, and Blazevich, showed that pseudoephedrine increases maximal torque, maximal strength, and lung function. Some studies have demonstrated improved middle-distance running times with prior intake of caffeine and ephedrine. A systematic review found that the ergogenic effects of pseudoephedrine are dose-dependent. No significant performance enhancement was observed at therapeutic doses (60–120 mg), while supratherapeutic doses (≥180 mg) demonstrated clinically significant effects [46]. Another study reported that pseudoephedrine's impact on exercise performance was generally negligible, except for a small increase in heart rate (ES = 0.43). However, well-trained athletes (VO_2 max ≥ 65 ml/kg/min) and younger participants exhibited larger effect sizes for heart rate and time trial performance, suggesting that while pseudoephedrine may provide marginal benefits in specific populations, its effects remain inferior to those of other stimulants [47].

Symptoms of intoxication vary, presenting as either CNS depression (sedation, apnea, coma, circulatory collapse) or stimulation (insomnia, hallucinations, tremors, convulsions). Severe cases can be fatal. Overdose effects include headache, dizziness, anxiety, tachycardia, blood pressure changes, nausea, and vomiting. In children, dry mouth, dilated pupils, fever, and digestive issues are more common. Additional effects include arrhythmias, allergic reactions, and psychological dependence [48]. Many unintentional doping cases arise from the use of cold medications. Athletes often overlook that over-the-counter medications from the pharmacy may contain one or more substances on the list. The most common positive doping cases here were associated with the use of cold medications containing pseudoephedrine in their composition: Defrinol (Galenika), Aspirin Complex (Bayer), Rinasek (Hemofarm), Caffetin Cold (Alkaloid) [49].

Narcotics

The category of narcotics includes a group of strong analgesics, all classified as opioids, including buprenorphine, dextromoramide, diamorphine (heroin), fentanyl and its derivatives, hydromorphone, methadone, morphine, nicomorphine, oxycodone, oxymorphone, pentazocine, pethidine, and since last year, tramadol.

While the analgesic effects of these substances could theoretically improve performance, common opioid side effects, including nausea, sedation, and respiratory depression, would equally counter any beneficial effects. One study showed that intrathecal fentanyl injection did not affect average power output during a 5 km cycling time trial in trained cyclists; however, power output during the first half of the time trial was increased, then decreased during the second half, compared to placebo. The authors attributed this to weakened afferent feedback from exercising muscles, followed by excessive development of fatigue and overall deterioration in their ability to „dose" their effort [14]. Another study found that participants completed a 25-mile time trial significantly faster when under the influence of 100 mg of tramadol (63 min 38 s) compared to a placebo (64 min 30 s), indicating a performance enhancement effect of tramadol in time trial cycling [50].

Cannabinoids

Marijuana and all its metabolites fall into the category of substances banned only in competition. The only exception with appropriate documentation and diagnosis is CBD (cannabidiol). The reason marijuana is banned in competitions is not solely because it enhances the athlete's physical performance (not yet fully proven), but because it meets the other two conditions for being on the doping list: it is harmful to the athlete's health and is not in line with the spirit of sports [51]. The plant Cannabis sativa, or cannabis, has been on the List of Prohibited Substances since 2004 [52].

What is cannabidiol (CBD) and why is it an exception among cannabinoids?

Cannabidiol is a substance that belongs to cannabinoids and is extracted from hemp or industrial hemp. Most derivatives extracted from hemp, besides being on the list of prohibited substances, are actually illegal in most countries worldwide. The exception in both cases is CBD, primarily because it has shown health benefits in humans when used for therapeutic purposes in an appropriate

manner. As a result, its use, sale, and distribution have become legal in the United States, Spain, Germany, China, Uruguay, Costa Rica, and Morocco.

While we are in a period where these effects will be fully clarified and analyzed, it has been determined so far that CBD can be used in the therapy of insomnia because of its anxiolytic and antidepressant effects that can improve sleep quality and duration. To some extent, cannabidiol can inhibit neurotransmitter activity and thereby slow down the pain transmission process, leading to an analgesic effect. Furthermore, it has been proven that by activating 5-HT1A receptors, cannabidiol restores damaged neurotransmission in the 5-HT1A (serotonin) system, increases serotonin transmission, and thus reduces stress and improves mood. It is believed that a dose of 10mg/kg of CBD can alleviate inflammation, i.e., inflammatory processes that occur after intense physical exertion, due to increased concentrations of IL-6, IL-1, and TNF-alpha that activate type 2 cannabinoid receptors [53].

The potential adverse effects of cannabidiol itself are still not sufficiently researched, but to some extent can be associated with other metabolites from this group. Acute adverse effects include memory impairment, coordination problems, slowed reflexes, disorientation, paranoia, and psychotic episodes. On the other hand, chronic effects may reflect these acute effects and their escalation, resulting in dependency, slowed cognitive development, increased occurrence of psychosis, as well as negative effects on the respiratory tract such as bronchitis [52].

Glucocorticoids

Glucocorticoids represent a group of corticosteroids that regulate numerous metabolic functions in the body. As medicinal substances, they include both natural and synthetic forms of these hormones. Due to their anti-inflammatory and immunosuppressive effects, glucocorticoids are used today in various forms of inflammatory diseases, whether local or systemic.

Therapeutic Indications for the Use of Glucocorticoids

Some of the most significant and common indications for the use of these drugs are (allergic) asthma, rheumatoid arthritis, connective tissue inflammations, inflammatory dermatological and ocular diseases, as well as systemic inflammatory diseases such as inflammatory bowel diseases including Crohn's disease, ulcerative colitis, and indeterminate colitis [54]. Glucocorticoids are available in numerous pharmaceutical forms, such as injections, tablets, creams, eye and ear drops, nasal sprays, or inhalers [55]. Considering the nature of athletes' injuries, which are most often related to the musculoskeletal system, as well as the increasing prevalence of asthma, it is not surprising that there is a growing (justified) need for drugs from this group. However, it is not unknown that glucocorticoids have been used as doping agents since the 1960s and it has been proven that they can enhance athletes' physical performance.

Mechanism of Action and Abuse

The anti-inflammatory action of corticosteroids is not fully understood, but it is believed to involve multiple mechanisms. These drugs inhibit phospholipase A2, reducing the synthesis of inflammatory mediators like leukotrienes and prostaglandins. Additionally, corticosteroids can inhibit cyclooxygenase (COX) and nitric oxide synthase (NOS), both of which play roles in inflammation. These effects reduce the immune response and alleviate inflammation, helping with muscle injuries by decreasing swelling, pain, and enabling athletes to train without feeling injury. Glucocorticoids also promote lipolysis, proteolysis, and increased glucose availability, providing additional energy substrates [56]. A study found that intramuscular injection of 40 mg triamcinolone acetonide significantly accelerated erythropoiesis, as evidenced by a higher reticulocyte percentage observed three and seven days post-administration compared to the placebo group. Additionally, hemoglobin mass was also higher in the glucocorticoid group at both seven and 21 days after treatment. Despite the increase in hemoglobin mass and accelerated erythropoiesis, the research indicated that there was no improvement in aerobic exercise performance, as mean power output during a 450-kcal time trial remained similar between the glucocorticoid and placebo groups at both seven and 21 days post-treatment [57].

Adverse Effects of Glucocorticoids

While glucocorticoids can be used in various bone and musculoskeletal disorders, they can also have many adverse effects, which mostly depend on the duration of therapy, type of glucocorticoid, dosage, and mode of administration [58]. It is known that administering corticosteroids into the body can affect bone metabolism and it is considered that therapy with these drugs may be associated with a higher risk of bone fractures. Adverse effects related to the musculoskeletal system usually involve cartilage damage, multiple ruptures of the patellar and Achilles tendons, subcutaneous atrophy... In patients on chronic inhalation therapy, there may be an increased risk of developing cataracts or pneumonia in patients with chronic obstructive pulmonary disease [56]. Additionally, adverse effects due to systemic administration may also occur, such as hypertension, glucose intolerance, initial stages of Cushing's disease... [59].

Beta-Adrenergic Blockers

Beta-adrenergic blockers or beta-blockers are medications commonly used in everyday practice to treat high blood pressure, congestive heart failure, or myocardial infarction. The mechanism of their action is based on reducing the influence of the sympathetic nervous system by blocking beta 1, beta 2, and beta 3 receptors. They achieve this effect by inhibiting the binding of catecholamines (primarily norepinephrine) to beta receptors present (mostly) on heart structures, thus reducing the heart rate [60].

Beta 1 receptors are predominantly located in the heart and juxtaglomerular apparatus of the kidney, so inhibiting catecholamines from binding to these receptors will result in bradycardia, prolonged diastolic filling time, and reduced oxygen consumption and demand. Examples of beta blockers that selectively act on beta 1 receptors are bisoprolol and nebivolol. Beta 2 receptors are mostly found in the smooth muscles of blood vessels, and their stimulation leads to vasodilation. Beta 3 receptors are localized in the heart and adipocytes, so their non-selective blockade can lead to obesity and hyperglycemia [61].

It has been proven that the use of beta-blockers in endurance or strength sports has no benefit. There may even be unwanted effects and a decrease in athlete performance, particularly in sports where aerobic capacity utilization is crucial. The (mis)use of beta-blockers is mainly observed in sports that require a steady hand, i.e., calmness and gentle movements, such as ballet, shooting, archery, golf, or in sports where it is desirable to reduce the effect of adrenaline, decrease tremors, anxiety, and heart rate [60].

Adverse Effects of Beta-Blocker Use

The adverse effects of beta-blockers can vary greatly, and which side effect will manifest depends mainly on the metabolism pathway of a specific beta blocker. If we are talking about lipophilic beta-blockers, their presence in higher concentrations can lead to crossing the blood-brain barrier and cause problems in the nervous system. Those that are more hydrophilic and are primarily metabolized by the kidneys are less likely to cause such changes [62]. Common adverse effects include bradycardia and hypotension. Fatigue, dizziness, nausea, and constipation are also common. Some patients report sexual and erectile dysfunction. Patients with asthma who use beta-blockers are at a higher risk of experiencing bronchospasm. Patients with Raynaud's syndrome are at risk of worsening symptoms. Beta blockers can cause hyperglycemia and thereby mask hemodynamic signs typically seen in patients with hypoglycemia, such as tachycardia. Some patients report insomnia, disrupted sleep patterns, and nightmares while using beta blockers. This effect is more pronounced with beta blockers that cross the blood-brain barrier. Some patients may experience fatigue or weight gain. Carvedilol may increase the chance of edema in some patients. Sotalol blocks potassium channels in the heart, thereby prolonging the QT interval and increasing the risk of torsades de pointes. All beta blockers, especially in patients with heart risk factors, carry the risk of heart block [63].

Exemptions for Therapeutic Use in Sports (Therapeutic Use Exemptions, TUE)

After reviewing the medicinal substances that are not allowed for athletes (during competitions or in general), the question arises whether an athlete has the right to become ill and to receive treatment? The answer is, of course, yes, provided that the use of these medications

must be justified and documented. The World Anti-Doping Agency (WADA) has introduced „Therapeutic Use Exemptions". TUE represents a document that an athlete submits to the World Anti-Doping Agency so that they can use the medication they need without restrictions and without sanctions, free from fear and worry that he will test positive for doping. Due to this, there are appropriate criteria for submitting and approving TUE in sports according to the TUE approval regulations issued by WADA [49]:

1. When there is no adequate substitute for the prohibited substance or method for treating a specific condition.
2. When the health status of the athlete is verified with valid documentation and diagnosed in accordance with international standards.
3. When not taking prohibited doping substances or methods during treatment significantly worsens the athlete's health condition.
4. When the necessity of using prohibited substances and/or methods is not in whole or in part the consequence of their previous non-therapeutic use.
5. When the therapeutic use of substances or methods will not contribute to improving the competitive abilities of the athlete except for those that expect after the end of treatment.

According to the statistics of the World Anti-Doping Agency, the number of TUE requests is increasing year by year. It is believed that better awareness among athletes and their teams about this procedure has contributed to these statistics, or the enlarged demands of today's sport that increasingly lead to injuries. It should not be overlooked that the TUE can be used as an opportunity for the „legal application" of prohibited doping substances. What is certainly the goal and imperative of this procedure by WADA is respect for one of the fundamental human rights of every person, including athletes, which is the right to health [64]. Some of the most common medical conditions that athletes file an application for TUE and their treatment are listed in Table 4.

Pharmacists in Sports

Although athletes are considered one of the healthiest groups of people, the use of medications among them is exceptionally high [65]. Medications are most commonly taken for specific medical conditions, illnesses, or injuries, when their use is justified. However, there is also potential for misuse. Inadequate use of medication can not only make the athlete-patient test positive for doping, putting their career at risk, but also endanger their health. Therefore, it is essential that all existing therapies are under the supervision of a healthcare professional. Pharmacists have the potential to provide specialized advice to athletes, primarily because of their adequate knowledge of medications and because they are the most accessible healthcare professionals. However, they are still underrepresented and underutilized in the circle of athletes [66].

Sports pharmacy is a new subspecialty within pharmacy that requires additional education to meet the needs of athlete-patients, both professionals and those who engage in sports recreationally [65]. Historically, the relationship between pharmacists and sports practice has been mainly focused on doping control, laboratory analyses, and their results. Recently, it has also shifted towards the clinical aspect of monitoring the recovery process of athletes [67].

Pharmacists face critical issues in doping prevention, primarily due to limited knowledge of anti-doping organizations and prohibited substances. The absence of clear

Illness / Medical condition	Prohibited substance for which a TUE (Therapeutic Use Exemption) is requested
Musculoskeletal injuries	Glucocorticoids and narcotics
Asthma	Beta-2 agonists, glucocorticoids
Diabetes mellitus	Insulin
Hypogonadism in men	Testosterone, growth hormone
Kidney transplant	Beta blockers, erythropoietin, glucocorticoids
Arterial hypertension	Diuretics, beta blockers
Attention deficit disorder	Amphetamines, methylphenidate
Growth hormone deficiency in adults	Growth hormone, gonadotropin
Growth hormone deficiency in children	Recombinant growth hormone

Table 4. List of diseases/medical conditions for which there is a legitimate need for a TUE and the medications from the list of doping-positive substances that may be used for the treatment of the listed diseases [summarized from 49]

guidelines outlining specific roles and responsibilities further complicates their ability to assist athletes effectively. Key barriers include insufficient education on doping regulations and the need for enhanced training programs. Addressing these issues is essential for pharmacists to fulfill their potential role in providing accurate medication-related information and preventing unintentional doping among athletes [68].

The growing recognition of athlete-patients as a special population has indeed led to the formation of sports pharmacy as a crucial branch within the pharmaceutical field.. The need for trained sports pharmacists arises from the potential risks involved with improper medication use, doping, and misinterpretation of banned substances in sports. At the intersection of substance use and athletic performance, the expertise of pharmacists can ensure the appropriate use of medications [65].

Pharmacists require additional training and knowledge enhancement, which can be achieved through special accreditation or through workshops, short courses, and/or continuous professional development activities. The International Olympic Committee (IOC) has introduced a course previously known as the Sports Pharmacist Course, now named the Course on Drugs in Sport [69]. However, there is currently no formally defined (job) position for a sports pharmacist at the global level.

Many athletes, especially at the beginning of their careers in professional sports, have no other option but to rely (solely) on general practitioners and pharmacists in public pharmacies, who are often not sufficiently informed about anti-doping. A study conducted in Australia, which included 135 pharmacists, showed that pharmacists expressed a willingness and readiness to provide every athlete with a complete check and professional assistance. The main obstacles were insufficient information gained through formal education, and therefore, a lack of confidence that they had checked everything appropriately and given the right advice.

This study also showed that it is necessary to provide educational programs aimed at pharmacists, which could meet the demands of athletes and ensure their safety. Designing credible education programs is something that should be worked on in the future [66].

To demonstrate that this idea is not just a theoretical concept but also feasible and applicable in practice, the example from Japan is the best illustration. Sports pharmacy was established in Japan in 2009 [70]. The way the structure of sports pharmacists was formed in Japan can serve as an example for other countries. Sports pharmacists provide anti-doping education to athletes and their support staff, such as coaches, physiotherapists, etc. In institutional settings, they provide care when athletes are admitted to the hospital for acute conditions or perioperative care. In the community setting, they are an accessible resource for athletes, especially those interested in self-medication and additional advice. Sports pharmacists also give lectures in pharmacy schools, as anti-doping is a potential topic on the national licensing exam. Additionally, they can visit elementary and high schools to teach students about the dangers of using prohibited drugs. As a result, the profession of sports pharmacists is valued beyond traditional pharmacy practices in Japan [65].

This topic is not widely discussed in our country or the region. There is currently no established education program for sports pharmacists in the form of a specialization, separate program, or course, nor are they part of sports societies, clubs, and national teams. At the first congress on doping prevention in sports held in Belgrade in 2015, under the auspices of the Ministry of Youth and Sports, the topic of sports pharmacy was also discussed. Dr. Biljana Stojanović from the Faculty of Pharmacy, University of Belgrade, spoke on this topic, presenting an elective course which she also teaches called „Sports Pharmacy". She emphasized that this elective course, held since 2011 at the Faculty of Pharmacy, is a pioneering project, not only in our country but in the entire region [71].

CONCLUSION

The abuse of performance-enhancing substances, such as anabolic steroids, erythropoietin, growth hormones, diuretics, stimulants, narcotics, cannabinoids, glucocorticoids, and beta-adrenergic blockers, remains a significant issue in sports. These substances pose serious health risks, including cardiovascular issues, reproductive dysfunction, metabolic disorders, and more, while also compromising the integrity of fair competition. Athletes may unknowingly violate doping regulations, espe-

cially with over-the-counter medications containing banned substances. To address these concerns, improved testing methods, athlete education, and stricter regulations are essential. Additionally, pharmacists play a crucial, though often underutilized, role in supporting athletes' health, preventing doping, and ensuring safe medication use. The development of sports pharmacy as a specialized branch, with appropriate training and education for pharmacists, is crucial to bridge gaps in knowledge regarding doping regulations and athlete care. The example of Japan offers an inspiring model for other countries, demonstrating the potential benefits of integrating sports pharmacists into the athletic community. Strengthening the knowledge and training of pharmacists through accredited courses, workshops, and continuous professional development is critical to ensuring a safe, fair, and doping-free sporting environment.

CONFLICT OF INTEREST

All authors declare no conflict of interest.

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Farmakološko-toksikološki aspekti primene doping supstanci i uloga sportskog farmaceuta

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KRATAK SADRŽAJ

Uvod: Stavljajući suštinu sporta u drugi plan, sportisti se često okreću upotrebi doping supstanci kako bi brzo napredovali i poboljšali svoje performanse. Doping ostaje ključan problem u sportu, narušavajući fer takmičenje i integritet sportista.
Metodologija: Pregled literature vršen je pomoću baza podataka kao što su PubMed i Google Scholar. Korišćeni su ključni pojmovi kao što su „anabolički steroidi", „peptidni hormoni", „diuretici" i „sportski farmaceut" za identifikaciju relevantnih studija.
Tema: Rad se bavi sve većim problemom zloupotrebe supstanci za poboljšanje performansi u sportu, ističući različite supstance kao što su anabolički steroidi, stimulansi, diuretici i narkotici, naglašavajući njihove farmakološke efekte i toksikološke posledice. Ove supstance, često korišćene u kombinaciji, mogu dovesti do ozbiljnih zdravstvenih komplikacija, poput kardiovaskularnih problema, metaboličkih poremećaja i zavisnosti. Takođe, zloupotreba zabranjenih supstanci može rezultirati nenamernim kršenjem antidoping propisa. Tekst ističe ključnu ulogu farmaceuta u sportu, naročito u prevenciji dopinga i sigurnoj upotrebi lekova, iako su često nedovoljno uključeni. Sportska farmacija se fokusira na prevenciju dopinga, upravljanje nuspojavama i zaštitu zdravlja sportista.
Zaključak: Zloupotreba supstanci koje poboljšavaju performanse u sportu predstavlja ozbiljan rizik po zdravlje i ugrožava fer konkurenciju. Sportisti mogu nesvesno kršiti pravila dopinga, a doping supstance mogu imati štetne efekte. Da bi se rešili ovi problemi, potrebna su bolja testiranja, edukacija sportista i stroža regulativa. Farmaceuti, iako često nedovoljno uključeni, igraju ključnu ulogu u prevenciji dopinga i osiguravanju bezbedne upotrebe lekova. Uspostavljanje sportske farmacije kao specijalizovane oblasti sa odgovarajućom obukom farmaceuta ključno je za zaštitu zdravlja i sigurnosti sportista.

Ključne reči: anabolički steroidi, peptidni hormoni, beta agonisti, diuretici, sportski farmaceuti

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