Review of Contemporary Philosophy
ISSN: 1841-5261, e-ISSN: 2471-089X
Vol 23 (2), 2024
Pp 1899 - 1908

The Ethical Implications and Health Risks Associated with Off-Label Pharmaceutical use in Sports Medicine: Review of Performance-Enhancing Drug Misuse among Athletes

[1-] Mohammad Ismail Alhazmi ,[2-] Mohammed Mahdi Ali Khawaji- ,[3-] Luay Mohammed Abdu Faqihi,[4-]Waleed Ahmed Khallufah Otayn,[5-] Sarah Ahmed Alafaleq,[6-] Abdullah Ahmed Alafaleq,[7-]Sami Fahad Saleh Alanazi,[8-]Halaa Awwadh G Alotaibi,[9-]Bassam Mohammed Al-Rashid

[1] Ksa, Ministry Of Health, King Fahad Central Hospital
[2] Ksa, Ministry Of Health, Prince Mohammed Bin Nasser Hospital
[3] Ksa, Ministry Of Health
[4] Ksa, Ministry Of Health, Jazan Specialized Hospital
[5] Ksa, Ministry Of Health, Dammam Phc
[6] Ksa, Ministry Of Health
[7] Ksa, Ministry Of Health, Prince Sultan Military Medical Hospital
[8] Ksa, Ministry Of Health
[9] Ksa, Ministry Of Health

Abstract

Background: The ethical dilemmas in sports medicine have garnered increasing attention, particularly regarding the off-label use of pharmaceutical agents to enhance athletic performance. This phenomenon poses significant risks to athletes' health, integrity, and the competitive nature of sports.

Methods: A narrative literature review was conducted to evaluate the prevalence and implications of off-label drug use among athletes. A comprehensive search of scholarly articles was performed across databases such as PubMed, Scopus, and Web of Science, focusing on both hormonal and non-hormonal substances commonly employed in sports.

Results: The findings reveal a concerning trend: athletes, driven by societal pressures and the pursuit of competitive advantage, frequently misuse performance-enhancing drugs (PEDs), including anabolic steroids and growth hormones. These substances are often acquired through unregulated channels, leading to significant health risks, including cardiovascular complications, hormonal imbalances, psychological disorders, and dependency. The misuse of these drugs is further exacerbated by misinformation and the lack of stringent regulatory oversight.

Conclusion: The off-label use of pharmaceuticals in sports presents multifaceted challenges that necessitate urgent attention from healthcare professionals, regulatory bodies, and sports organizations. Educational interventions, enhanced health literacy, and robust regulatory frameworks are essential to mitigate the health risks associated with off-label drug use and to uphold the ethical standards of competitive sports.

Keywords: Off-label drug use, Performance-enhancing drugs, Sports medicine, Ethical dilemmas, Health risks

Received:08 October 2024 **Revised**:27 November 2024 **Accepted**:15 December 2024

Introduction

Recently, there has been a rise in the off-label use of some drugs [1,2]. Off-label usage is described as the purposeful use of a medicine for a therapeutic reason that deviates from the product's marketing authorization. A medicine that has received formal approval for certain ailments or populations may be administered off-label according to clinical judgment, forthcoming research, or anecdotal evidence [3,4]. This method provides adaptability in medical care, enabling individualized therapy and novel therapeutic alternatives, particularly when conventional therapies are restricted or unsuccessful [3]. Off-label usage, however, diverges from established medical practices due to its often absence of stringent clinical studies and extensive data that substantiate permitted applications [3,5]. Regulatory agencies, such as the Food and Drug Administration (FDA) or the European Medicines Agency (EMA), generally do not actively regulate off-label uses. The doctor has full responsibility for off-label prescription [6,7]. Regulatory authorities may give warnings on safety issues; nevertheless, the choice to dispense off-label mostly rests with the clinical judgment and discretion of healthcare professionals [7].

The administration of medications beyond their approved indications is prevalent among both professional and amateur athletes, including gym enthusiasts and bodybuilders [8,9]. Athletes are increasingly using drugs for off-label purposes to improve performance, physical attractiveness, or expedite recovery, which raises substantial safety and ethical issues [8,9]. Performance-enhancing drugs (PEDs) involve chemicals that augment athletic performance by improving endurance, strength, and/or concentration. [1, 10, 11]. Common examples include anabolic steroids, growth hormones, stimulants, and other substances often used outside their sanctioned medical applications to achieve a competitive advantage [12]. Performance-enhancing drugs (PEDs) are often linked to the risk of usage, insufficient data about long-term effects, and breaches of anti-doping rules [13,14]. Their use poses significant dangers, especially for long-term health implications and equity in contests, including the erosion of competitive integrity.

The off-label usage enables athletes to use the pharmacological features of medications for competitive gain, since pharmaceuticals designed for illnesses such as asthma are frequently repurposed to enhance aerobic capacity [15,16]. The quest for competitive advantage often transpires in a high-pressure milieu, where victory may provide substantial financial and social benefits, compelling sportsmen to pursue every possible advantage [17]. The technique is, nevertheless, laden with hazards, including developmental and side effects, ethical quandaries, and the possibility of fines in sports where the drug's usage contravenes anti-doping standards [18].

These compounds are often provided orally or by injection, sometimes in a combination of pharmaceuticals to achieve a purported synergistic effect via complimentary modes of action [19,20]. Such practices, particularly those involving injectable administration, are generally performed in non-aseptic conditions, with drugs being shared among users, reused without adequate sterilization, or improperly stored, thereby substantially elevating the risk of infections and other medical issues, including adverse effects [19,20]. The origins of these medications complicate the issue, since some persons get these medicines from unregulated or dubious sources, using non-medical avenues such as counterfeit internet pharmacies, illicit market vendors, or acquaintances [21,22]. The absence of regulation and control in these transactions leads to the circulation of counterfeit or contaminated items, which pose substantial health hazards to consumers [20,23]. The ramifications of off-label use can be grave, encompassing infections, allergic reactions, and more critical conditions such as cardiovascular complications, hormonal dysregulation, psychological disorders, dependency, episodes of social violence, and potentially fatal outcomes [7,8,14,24-30].

Access to these medications is restricted to prescription only due to these hazards [1]. Although numerous substances are produced by reputable pharmaceutical companies, there is an increasing incidence of smuggled and counterfeit medications, which frequently lead to adulterated or infected products comprising incorrect dosages, alternative substances, harmful impurities, or toxic agents [31]. Although these drugs, both hormonal as well as non-hormonal, are sanctioned for particular medical conditions, their off-label application by athletes poses heightened risks, especially due to inappropriate dosing, absence of medical oversight, and utilization of these substances beyond their designated therapeutic context [32].

Hormonal drugs, such as anabolic steroids and growth hormones, affect the body's endocrine system and are linked to perilous hormonal imbalances and many adverse effects, including hypertension, metabolic alterations, and an elevated risk of cancer [33]. Anabolic steroids may result in hypertension, hepatic damage, and reproductive health complications, while the abuse of growth hormone might induce arthralgia, insulin resistance, and an elevated cancer risk [1,9,29,30,34]. Conversely, non-hormonal medicines, like benzodiazepines and β2-agonists, may induce dependency, psychological impacts, and cardiovascular problems [33].

This study is to provide an overview of the off-label use of pharmacological agents by athletes, including both hormonal and non-hormonal compounds employed to augment performance, improve physical appearance, and expedite recovery from injuries.

1. Methods

This research used a narrative literature review technique to assess the off-label utilization of pharmaceuticals by athletes in sporting activities. A thorough bibliographic search was performed to collect pertinent scholarly papers from PubMed (Medline), Scopus, and Web of Science.

2. Off-label substances

Off-label substances used in athletic practice differ according to the athlete's category, the sport involved, and the intended results. The chemicals include both hormonal and non-hormonal molecules. Nonetheless, a significant issue in athletics is the prevalent habit of concurrently using many drugs, often without enough medical supervision. This approach is especially hazardous since it increases the likelihood of harmful medication interactions. This may enable the synergistic effects of many medications to intensify, resulting in compounded dangers. The combination of anabolic steroids and erythropoietin may increase the risk of cardiovascular events, including thrombosis and myocardial infarction [35]. Diuretics may be used with performance-enhancing medications, resulting in significant dehydration and electrolyte imbalance, hence increasing the risk of cardiac arrest or other life-threatening disorders [18,36]. The cumulative consequences of this are particularly alarming since they may remain unnoticed until significant and/or irreparable damage has occurred. The extensive distribution, abuse, and off-label application of polypharmacy in sports poses significant risks to athlete health.

Consumers concurrently use drugs, sometimes combining several to attain a presumed synergistic benefit or to mitigate any detrimental consequences [19,20]. The most often used chemicals are mostly hormonal, including testosterone, growth hormone, insulin, erythropoietin, and thyroid hormone [37]. Erythropoietin (EPO) is administered in safe dosages to regulate erythropoiesis, enhance the oxygen transport capacity of red blood cells, and address anemia caused by chemotherapy or chronic kidney disease. In athletics, it is used to elevate hemoglobin levels, hence enhancing oxygenation in the bloodstream and augmenting performance in endurance training and contests [38]. Notwithstanding the prohibition by the World Anti-Doping Agency, athletes persist in using EPO to enhance their performance in endurance sports, including running, cycling, and skiing [40]. In healthy non-athletic individuals, erythropoietin treatment enhances submaximal exercise performance by about 54%, irrespective of the roughly 12% rise in VO2max [41].

HCG is often used as an ovulation inducer and in gonadotropin therapies [42]. It is crucial for placental development and fetal growth, as well as spermatogenesis, and serves as a tumor marker in several cancer types [42-44]. hCG is used off-label to enhance muscular strength and elevate testosterone levels [44]. It is especially esteemed for its capacity to promote endogenous testosterone production, rendering it a favored option among sportsmen aiming to improve performance and physical aesthetics [44]. The introduction of exogenous anabolic-androgenic steroids into the male body inhibits the natural synthesis of testosterone by disrupting the hypothalamic-pituitary-adrenal axis via innate negative feedback mechanisms. This results in testicular atrophy [1,9]. HCG is often used throughout and after steroid cycles to preserve and restore testicular size and normal testosterone production [45].

Controlled dosages of growth hormone are used in the treatment of male hypogonadism, inflammatory bowel disease, musculoskeletal disorders, newborn hypoglycemia, and infertility. In athletic training, the

objectives are to enhance muscular strength, augment lean body mass, promote lipolysis, and expedite healing from soft tissue injuries [1,9,46,47].

3. Motivations of Athletes for Off-Label Drug Utilization

Athletes across diverse competitive tiers, from top professionals to recreational amateurs, encounter social constraints that often drive them to engage in off-label drug usage [1]. These pressures include the quest for an ideal body image, weight control, and muscle mass enhancement, in addition to efforts to diminish indications of aging and address tiredness or hormonal imbalances [1,10]. The evidence indicates that male athletes are often more predisposed to participate in doping practices than female athletes. Research indicates that males are more inclined to use performance-enhancing chemicals, often driven by the aspiration to improve physical performance and gain a competitive advantage, while females generally resort to dietary supplements mainly for health-related purposes [48,49]. The motives of professional athletes seeking a competitive advantage and amateur athletes emphasizing aesthetics or fitness may vary, although the related hazards are equally substantial. This use is sometimes predicated on data from dubious websites, ads, and commercials [1].

The expedited recovery process is a significant rationale for sportsmen using off-label medications. Pharmaceuticals designed for muscle-wasting conditions, such as anabolic steroids, may be used to expedite recovery from injuries or intense workouts, enabling athletes to adhere to demanding training regimens [50,51]. The aspiration to regulate weight, particularly in sports with stringent weight classifications or aesthetic requirements, may prompt players to use drugs for hunger suppression or metabolic augmentation [52]. Diuretics and other drugs not specifically designed for weight reduction may be used off-label for the fast loss or management of weight [18]. Athletes often use drugs to improve physical appearance, reduce weight, augment muscle mass, postpone aging, and enhance performance [1,10,19]. Societal and media pressures to achieve an ideal body image, along with the pursuit of rapid and sometimes unattainable outcomes, compel sportsmen to use these drugs, notwithstanding the inherent health dangers and ethical dilemmas. Athletes may justify the use of performance-enhancing drugs due to their aspirations for better physical appearance, greater strength, and improved recovery, despite the acknowledged health dangers involved.

The growing focus on physical aesthetics and optimal athletic performance, particularly intensified by social media and modern cultural discourses, seems to substantially propel players towards the usage of off-label drugs. This discovery highlights the need for more study to comprehend the aggregate effects of these social influences on the physical and emotional well-being of athletes, especially within younger and susceptible demographic segments.

4. Misrepresentation in Off-Label Utilization

General consumers often seek information online, sometimes sourcing it from untrustworthy websites, deceptive marketing, and misleading social media postings, which may result in the dissemination of false or harmful advice and promote risky habits. [1]. Nevertheless, a significant portion of the accessible material originates from organizations that often emphasize sales above reliable medical advice. This is especially troubling for athletes using hormone therapies, since uneven rules and prescribing practices may lead to confusion, prompting reliance on unsubstantiated claims from forums, social media, or anecdotal suggestions [21]. Misinformation significantly contributes to the rising off-label use of prescription medications, as well as the growing occurrence of adverse events associated with these treatments and the larger social and economic hazards. [8,21]. This dependence on unreliable information results in poor dose, inaccurate use, and a misapprehension of the related risks and adverse effects [8]. The absence of regulation and control compels athletes to acquire these compounds from dubious sources, including the black market, leading to the use of counterfeit or contaminated items [20,21]. This usage has extensive social and economic ramifications, including heightened healthcare expenses, societal stigmatization, and perhaps legal repercussions [53]. Moreover, athletes often depend on unreliable sources for information, resulting in the misapplication and misinterpretation of the related hazards. The use of performance-enhancing

drugs (PEDs) also engenders ethical dilemmas of equity in athletics and the coercion of athletes to adhere to drug usage to maintain competitiveness [54].

The availability of both credible and dubious health information on the internet and social media underscores a significant deficiency in health literacy among athletes. Mitigating this gap may need more stringent controls around the distribution of medical material, particularly on platforms frequented by younger or novice athletes, who may be more susceptible to disinformation. Future research should assess the effects of misinformation on off-label medication use and investigate strategies to improve health literacy.

5. Physical, Psychological, and Social Hazards of Off-Label Drug Utilization

The trend of off-label drug use among athletes is influenced by various psychological, social, and physical factors, stemming from the desire to meet societal expectations and attain a more aesthetically pleasing physique, including weight loss, muscle mass enhancement, reduction of aging signs, and performance improvement [1,10,16]. The use of substances such as anabolic steroids, growth hormones, and erythropoietin is linked to cardiovascular issues, including hypertension, myocardial infarctions, and strokes [55,56]. Infections often occur, especially when medications are injected in non-sterile environments [57]. Additionally, users may encounter hormonal abnormalities, such as gynecomastia, testicular shrinkage, and monthly irregularities in women, potentially resulting in infertility. The improper use of these drugs often leads to both physical and psychological dependency, compelling users to persist in their use to maintain their physical look or performance levels [58]. The off-label use of prescription medications in sports and fitness extends beyond personal health, with significant societal and economic ramifications. The heightened strain on healthcare systems from managing side effects, the risk of social stigmatization, and the legal ramifications of illegal drug use are substantial issues [54]. Moreover, the ethical dilemmas about fairness in sports and the coercion on players to adhere to drug usage norms further complicate the situation [36].

Social changes and aggressive actions contribute to isolation, damaged relationships, and reported incidents of violence. Individuals often disengage from social interactions, preferring physical objectives over interpersonal ties, resulting in their isolation [59]. The prolonged use of anabolic steroids heightens the risk of adopting an antisocial lifestyle and increases the incidence of violent crimes and weapon offenses [60-63]. Individuals who misuse steroids have a higher propensity for engaging in criminal activities, as shown by epidemiological research, and steroids are sometimes recognized as an indirect cause of mortality [64-66].

The proven medical hazards of off-label medication use are substantial; nevertheless, the psychological and social repercussions, such as possible isolation and violent behaviors, need more scrutiny. The results indicate that preventative methods must include not just bodily damage but also provide extensive mental health care and counseling for athletes experiencing dependence or psychological consequences of such activities.

6. Economic Implications

A significant issue is the origin of these substances; while physician prescriptions are required for these compounds, athletes often seek alternate sources. Another health risk factor pertains to the sources from which these substances are acquired, including online vendors, gym associates, trainers, or even through inappropriate prescriptions from physicians who issue them without legitimate necessity or medical justification, merely at the request of the individual [67]. The increase in the smuggling and counterfeiting of pharmaceuticals, especially via the black market and illicit laboratories, highlights the vital necessity of regulations such as the Falsified Medicines Directive (FMD), which seeks to safeguard public health by obstructing the circulation of counterfeit medications within the European Union. This regulation is a crucial legislative action aimed at safeguarding the pharmaceutical supply chain from unlawful and hazardous chemicals that often infiltrate via illicit channels, including black market activities from other nations [20,23].

Concerning the economic aspect, off-label usage may constitute a substantial segment of healthcare cost for managing adverse effects related to its use. [53]. Sivalokanathan et al. investigated the cardiac implications of performance-enhancing drugs (PEDs), contrasting substances such as caffeine and anabolic steroids, and highlighted the health hazards linked to PEDs that may result in elevated healthcare expenditures [68]. Off-label medication utilization imposes a significant strain on healthcare systems owing to the need for managing diverse unfavorable consequences [69]. Sampaio et al. demonstrate that the annual expenses associated with this off-label use, inclusive of problems, for 18-year-old boys in Sweden total around half a million USD [70]. These expenditures include healthcare costs, productivity losses, and legal system charges. Healthcare expenses account for 54% of the total, while productivity losses are 28% and court costs make up 18%, all of which are substantial contributors [69]. The economic ramifications of off-label prescription use, along with heightened healthcare expenditures and regulatory obstacles related to counterfeit pharmaceutical marketplaces, highlight the pressing need for enhanced international regulatory cooperation.

7. Prospective Investigations and Interventions

Future study must concentrate on the long-term health ramifications to comprehend the implications of off-label medication use among athletes, especially across various demographics and sports categories [14]. It is essential to investigate effective solutions, such as educational initiatives, legislative reforms, and support frameworks for athletes [70,71]. Sampaio et al. propose that preventative interventions, especially those aimed toward gym attendees, may be economically advantageous and socially beneficial [69].

Another priority should be to examine the sources from which athletes get information on off-label drug usage and to enhance the reliability and accessibility of correct information. Furthermore, research should evaluate the efficacy of existing rules and suggest new frameworks to enhance the oversight of the distribution and use of these chemicals in sports [54]. Comprehending the psychological drivers of off-label medication use, including body image concerns, performance anxiety, and societal pressures, is crucial for formulating focused psychological therapies [54,72]. Comparative studies must be undertaken to assess the prevalence and effects of off-label medication usage across various sports, geographies, and competitive levels to customize treatments appropriately. Future study should investigate the psychological drivers of off-label drug use among athletes, especially emphasizing young athletes who may be significantly affected by societal influences. Educational interventions must be customized for athletes, their coaches, and support networks, with the objective of fostering a preventative strategy that encompasses psychological, social, and physical aspects.

8. Conclusions

This research highlighted significant medications often used off-label in sports, underscoring their non-approved usage and related detrimental consequences. Athletes frequently utilize hormonal agents (e.g., erythropoietin, insulin, human chorionic gonadotropin, human growth hormone, oxandrolone, testosterone, and thyroid hormones) and non-hormonal substances (e.g., furosemide, clenbuterol, glucocorticoids, and tamoxifen) to augment performance, elevate muscle mass, and accelerate recovery. The off-label use of these medications entails considerable dangers, such as cardiovascular complications, hormone disruptions, psychiatric disorders, dependence, and severe adverse outcomes including organ damage and mortality. The report underscores an escalating issue, emphasizing the need for more stringent rules and preventative strategies. The off-label use of these medications presents considerable hazards and necessitates specific treatments to safeguard athletes' health and integrity.

References

1. Irwig M.S., Fleseriu M., Jonklaas J., Tritos N.A., Yuen K.C.J., Correa R., Elhomsy G., Garla V., Jasim S., Soe K., et al. Off-label use and misuse of testosterone, growth hormone, thyroid hormone, and adrenal supplements: Risks and costs of a growing problem. Endocr. Pr. 2020;26:340–353.

2. Agency E.M. Guideline on Good Pharmacovigilance Practices (GVP), Module VI—Management and Reporting of Adverse Reactions to Medicinal Products (Rev 1) European Medicines Agency and Heads of Medicines Agencies London; London, UK: 2014.
3. Claverie H. On-Label vs Off-Label Drug Prescribing. IG Living. 2016;2016:28–31.
4. Stafford R.S. Regulating off-label drug use—Rethinking the role of the FDA. N. Engl. J. Med. 2008;358:1427–1429.
5. Kesselheim A.S. Off-label drug use and promotion: Balancing public health goals and commercial speech. Am. J. Law. Med. 2011;37:225–257.
6. Beck J.M., Azari E.D. FDA, off-label use, and informed consent: Debunking myths and misconceptions. Food Drug Law. J. 1998;53:71–104.
7. Silva A.F. Ph.D. Thesis. Universidade do Algarve; Faro, Portugal: 2018. Uso Off-Label de Medicamentos: Um Tema Controverso.
8. Clement C., Marlowe D., Patapis N., Festinger D., Forman R. Nonprescription steroids on the internet. Subst. Use Misuse. 2012;47:329–341.
9. Ip E.J., Doroudgar S., Lau B., Barnett M.J. Anabolic steroid users' misuse of non-traditional prescription drugs. Res. Soc. Adm. Pharm. 2019;15:949–952.
10. Vari C.-E., HOsz B.-E., Miklos A., Berbecaru-Iovan A., Tero-Vescan A. Aromatase inhibitors in men-off-label use, misuse, abuse and doping. Farmacia. 2016;64:813–818.
11. Ashid M., Katariya D., Agarwal P., Soni K., Joshi A. A brief study on performance enhancing drugs (PED'S) World J. Pharm. Res. 2016;5:495–533.
12. Watson C.J., Stone G.L., Overbeek D.L., Chiba T., Burns M.M. Performance-enhancing drugs and the Olympics. J. Intern. Med. 2022;291:181–196.
13. Miskulin I., Grbic D.S., Miskulin M. Doping attitudes, beliefs, and practices among young, amateur Croatian athletes. Sports. 2021;9:25.
14. Ventura R., Matabosch X., Segura J. Bioanalytical techniques in discrimination between therapeutic and abusive use of drugs in sport. Bioanalysis. 2016;8:965–980.
15. Catlin D.H., Murray T.H. Performance-enhancing drugs, fair competition, and Olympic sport. JAMA. 1996;276:231–237.
16. Baker J.S., Graham M.R., Davies B. Steroid and prescription medicine abuse in the health and fitness community: A regional study. Eur. J. Intern. Med. 2006;17:479–484.
17. Milano G., Chiappini S., Mattioli F., Martelli A., Schifano F. β-2 agonists as misusing drugs? Assessment of both clenbuterol-and salbutamol-related European medicines agency pharmacovigilance database reports. Basic. Clin. Pharmacol. Toxicol. 2018;123:182–187.
18. Cadwallader A.B., De La Torre X., Tieri A., Botrè F. The abuse of diuretics as performance-enhancing drugs and masking agents in sport doping: Pharmacology, toxicology and analysis. Br. J. Pharmacol. 2010;161:1–6.
19. Baker J.S., Graham M., Davies B. Gym users and abuse of prescription drugs. J. R. Soc. Med. 2006;99:331–332.
20. Parkinson A.B., Evans N.A. Anabolic androgenic steroids: A survey of 500 users. Med. Sci. Sport. Exerc. 2006;38:644–651.
21. Ahmed J., Mohac L., Mackey T., Raimi-Abraham B. A critical review on the availability of substandard and falsified medicines online: Incidence, challenges and perspectives. J. Med. Access. 2022;6:239920262210745.
22. Fittler A., Lankó E., Brachmann B., Botz L. Behaviour analysis of patients who purchase medicines on the internet: Can hospital pharmacists facilitate online medication safety? Eur. J. Hosp. Pharm. 2012;20:8–12.
23. Fink J., Schoenfeld B.J., Hackney A.C., Matsumoto M., Maekawa T., Nakazato K., Horie S. Anabolic-androgenic steroids: Procurement and administration practices of doping athletes. Phys. Sportsmed. 2019;47:10–14.
24. Quaglio G., Fornasiero A., Mezzelani P., Moreschini S., Lugoboni F., Lechi A. Anabolic steroids: Dependence and complications of chronic use. Intern. Emerg. Med. 2009;4:289–296.

25. Sansoucy M., Naud J. Using proteins as markers for anabolic steroid abuse: A new perspective in doping control? Chem. Res. Toxicol. 2023;36:1168–1173.
26. Pomara C., Neri M., Bello S., Fiore C., Riezzo I., Turillazzi E. Neurotoxicity by synthetic androgen steroids: Oxidative stress, apoptosis, and neuropathology: A review. Curr. Neuropharmacol. 2015;13:132–145.
27. George A. The actions and side effects of anabolic steroids in sport and social abuse. Andrologie. 2003;13:354–366.
28. Van Amsterdam J., Opperhuizen A., Hartgens F. Adverse health effects of anabolic–androgenic steroids. Regul. Toxicol. Pharmacol. 2010;57:117–123.
29. Abasnejad M., Mohammadi A., Khajehlandi A. Investigation of the chronic effects of winstrol and oxandrolone anabolic steroids on liver enzymes in male bodybuilding athletes. Jundishapur J. Chronic Dis. Care. 2020;9:e106517.
30. Bird S., Goebel C., Burke L., Greaves R. Doping in sport and exercise: Anabolic, ergogenic, health and clinical issues. Ann. Clin. Biochem. Int. J. Lab. Med. 2015;53:196–221.
31. Lentillon-Kaestner V. The development of doping use in high-level cycling: From team-organized doping to advances in the fight against doping. Scand. J. Med. Sci. Sports. 2011;23:189–197.
32. European Parliament and Council . Directive 2011/62/EU of the European Parliament and of the Council of 8 June 2011 amending Directive 2001/83/EC on the Community Code Relating to Medicinal Products for Human Use, as Regards the Prevention of the Entry into the Legal Supply Chain of Falsied Medicinal Products. Official Journal of the European Union; Musdrok, The Netherlands: 2011.
33. Neto J., Silva C., Lima A., Caminha J., Pinto D., Alves F., Araújo J.S., Daher E.d.F. Disorder of hypothalamic-pituitary-gonadal axis induced by abusing of anabolic-androgenic steroids for short time: A case report. Andrologia. 2018;50:e13107.
34. Hashim A., Almukhtar S. The influence of anabolic-androgenic steroids on males' hormones among gym-goers in mosul city; Proceedings of the 1st International Ninevah Conference on Medical Sciences (INCMS 2021); Mosul, Iraq. 5-7 September 2021.
35. Rosenzweig M.Q., Bender C.M., Lucke J.P., Yasko J.M., Brufsky A.M. The decision to prematurely terminate a trial ofR-HuEPO due to thrombotic events. J. Pain. Symptom. Manag. 2004;27:185–190.
36. Ramara T., Munayi S., Bailasha N., Chumba J. The prevalence of drug abuse as it relates to psychosocial reasons among university athletes in selected competitive sports in kenya. Int. J. Psychol. 2024;8:1–18.
37. Morente-Sánchez J., Zabala M. Doping in sport: A review of elite athletes' attitudes, beliefs, and knowledge. Sports Med. 2013;43:395–411.
38. Birzniece V. Doping in sport: Effects, harm and misconceptions. Intern. Med. J. 2015;45:239–248.
39. Palmi I., Berretta P., Tini A., Ricci G., Marinelli S. The unethicality of doping in sports. Clin. Ter. 2019;170:e100–e101.
40. Malve H. Sports pharmacology: A medical pharmacologist's perspective. J. Pharm. Bioallied Sci. 2018;10:126.
41. Thomsen J.J., Rentsch R.L., Robach P., Calbet J.A., Boushel R., Rasmussen P., Juel C., Lundby C. Prolonged administration of recombinant human erythropoietin increases submaximal performance more than maximal aerobic capacity. Eur. J. Appl. Physiol. 2007;101:481–486.
42. Gregor C., Cerasoli E., Schouten J., Ravi J., Slootstra J., Horgan A., Martyna G.J., Ryadnov M.G., Davis P., Crain J. Antibody recognition of a human chorionic gonadotropin epitope (hcgβ66–80) depends on local structure retained in the free peptide. J. Biol. Chem. 2011;286:25016–25026.
43. Camperi J., Combès A., Fournier T., Pichon V., Delaunay N. Analysis of the human chorionic gonadotropin protein at the intact level by hilic-ms and comparison with rplc-ms. Anal. Bioanal. Chem. 2020;412:4423–4432.
44. Chen Y., Niu Y., Xu H., Wang D., Jiang H., Pokhrel G., Wang T., Wang S.-G., Liu J.H. Testosterone undecanoate supplementation together with human chorionic gonadotropin does not impair spermatogenesis in males with isolated hypogonadotropic hypogonadism: A retrospective study. Asian J. Androl. 2019;21:413–418.

45. Woldemariam G., Butch A. Immunoextraction–tandem mass spectrometry method for measuring intact human chorionic gonadotropin, free β-subunit, and β-subunit core fragment in urine. Clin. Chem. 2014;60:1089–1097.
46. Holt R.I.G., Ho K.K.Y. The use and abuse of growth hormone in sports. Endocr. Rev. 2019;40:1163–1185.
47. Siebert D.M., Rao A.L. The use and abuse of human growth hormone in sports. Sports Health. 2018;10:419–426.
48. Wibowo E., Pollock P., Hollis N., Wassersug R. Tamoxifen in men: A review of adverse events. Andrology. 2016;4:776–788.
49. Daher J., Mallick M., Khoury D. Prevalence of dietary supplement use among athletes worldwide: A scoping review. Nutrients. 2022;14:4109.
50. Mazzeo F., Santamaria S., Montesano P. Gender difference, nutritional supplements and drug use in sport to enhancing performance: An italian revision over the last decade. Sport Mont. 2019;17:69–73.
51. Wenbo Z., Yan Z. The uses of anabolic androgenic steroids among athletes; its positive and negative aspects-a literature review. J. Multidiscip. Healthc. 2023;31:4293–4305.
52. Pope H.G., Wood R.I., Rogol A., Nyberg F., Bowers L., Bhasin S. Adverse health consequences of performance-enhancing drugs: An Endocrine Society scientific statement. Endocr. Rev. 2014;35:341–375.
53. Gadela N., Coban H., Wasserman E., Schreyer E., Jaiswal A. The tragedy of a strong muscle and a weak heart: Complications of anabolic-androgenic steroid misuse. Cureus. 2021;13:e17389.
54. Braillon A., Lexchin J. Off-label drug use. Am. J. Med. Qual. 2016;31:285.
55. La Gerche A., Brosnan M.J. Drugs in sport—A change is needed, but what? Heart Lung Circ. 2018;27:1099–1104.
56. Lichtenfeld J., Deal B., Crawford S. Sudden cardiac arrest following ventricular fibrillation attributed to anabolic steroid use in an adolescent. Cardiol. Young. 2016;26:996–998.
57. Mędraś M., Tworowska U., Jóźków P., Dumański A., Dubiński A. Postoperative course and anabolic-androgenic steroid abuse–a case report. Anaesthesia. 2004;60:81–84.
58. Baharlou S., Boulle K., Heijningen I., Cervini I., Termohlen P. Standards for aseptic techniques in medical aesthetic practices in the benelux: Consensus recommendations. J. Cosmet. Dermatol. 2022;22:289–295.
59. La Vignera S., Condorelli R.A., Cannarella R., Duca Y., Calogero A.E. Sport, doping and female fertility. Reprod. Biol. Endocrinol. 2018;16:108.
60. Souza G., Hallak J. Anabolic steroids and male infertility: A comprehensive review. BJU Int. 2011;108:1860–1865.
61. Talih F., Fattal O., Malone D. Anabolic steroid abuse: Psychiatric and physical costs. Clevel. Clin. J. Med. 2007;74:341.
62. Solakovic S., Serhatlic H., Solakovic N., Hajrulahovic F., Godinjak A., Pavlović R., Vrcic M., Kozina Z., Yarymbash K., Dorofieieva O. Therapeutic measures from cardiovascular damage using statins, acetylsalicylic acid during the abuse of irrational cycles of anabolic steroids in bodybuilder Who Were Infected with the COVID-19. Med Res. Arch. 2024;12
63. Lehmann S., Thomas A., Schiwy-Bochat K.H., Geyer H., Thevis M., Glenewinkel F., Rothschild M.A., Andresen-Streichert H., Juebner M. Death after misuse of anabolic substances (clenbuterol, stanozolol and metandienone) Forensic Sci. Int. 2019;303:109925.
64. Klötz F., Garle M., Granath F., Thiblin I. Criminality among individuals testing positive for the presence of anabolic androgenic steroids. Arch. Gen. Psychiatry. 2006;63:1274–1279.
65. Placidi-Frot D. Université Paris-Saclay Graduate School of Law, Proceedings of 1st International Summer School. IEDP—Institut d'Etudes de Droit Public; Sceaux, France: 2023. International Conventions Applicable to the Trade in Illicit Medical Products: A Political Scientist's View.
66. Layachi O.B. International and National Obligations to Protect from the Risks of Pharmaceutical Crime: The Crime of Counterfeit Pharmaceutical Products in the COVID-19 Crisis. Syst. Rev. Pharm. 2020;11:648.

67. Holubeck P., Eksi A., Gillett K., O'Hara J., McGoldrick D., Brown D., McCarthy A.D. Social interest data as a proxy for off-label performance-enhancing drug use: Implications and clinical considerations. Cureus. 2024;16:e52011.
68. Sivalokanathan S., Małek Ł., Malhotra A. The cardiac effects of performance-enhancing medications: Caffeine vs. anabolic steroids. Diagnostics. 2020;11:324.
69. Andlin-Sobocki P., Wittchen H.U. Cost of affective disorders in Europe. Eur. J. Neurol. 2005;12:34–38.
70. Sampaio F., Ssegonja R., Thiblin I., Nystrand C. A model for evaluating the economic value of prevention programs for illicit use of anabolic androgenic steroids. Health Policy. 2021;125:807–813.
71. Savulescu J., Creaney L., Vondy A. Should athletes be allowed to use performance enhancing drugs? BMJ. 2013;347:f6150.
72. Monaghan L. Bodybuilding, Drugs and Risk. Routledge; London, UK: 2002.

الآثار الأخلاقية والمخاطر الصحية المرتبطة بالاستخدام غير المرخص للأدوية في طب الرياضة: مراجعة لسوء استخدام العقاقير لتعزيز الأداء بين الرياضيين

الملخص

الخلفية :حظيت المعضلات الأخلاقية في طب الرياضة باهتمام متزايد، خاصة فيما يتعلق باستخدام الأدوية بطريقة غير مرخصة لتعزيز الأداء الرياضي. يشكل هذا الظاهرة مخاطر كبيرة على صحة الرياضيين ونزاهتهم وطبيعة المنافسة الرياضية.

الطرق :تم إجراء مراجعة أدبية سردية لتقييم مدى انتشار واستخدام الأدوية غير المرخصة بين الرياضيين. تم البحث بشكل شامل في مقالات علمية عبر قواعد بيانات مثل **PubMed** و**Scopus** و**Web of Science**، مع التركيز على المواد الهرمونية وغير الهرمونية المستخدمة بشكل شائع في الرياضة.

النتائج :تكشف النتائج عن اتجاه مثير للقلق: الرياضيون، مدفوعون بالضغوط الاجتماعية والسعي لتحقيق ميزة تنافسية، غالبًا ما يسيئون استخدام العقاقير لتعزيز الأداء، مثل المنشطات الابتنائية وهرمونات النمو. غالبًا ما يتم الحصول على هذه المواد عبر قنوات غير منظمة، مما يؤدي إلى مخاطر صحية كبيرة، بما في ذلك مضاعفات قلبية وعائية، واختلالات هرمونية، واضطرابات نفسية، والإدمان. يتم تفاقم سوء استخدام هذه العقاقير بسبب المعلومات الخاطئة ونقص الرقابة التنظيمية الصارمة.

الخلاصة :يمثل الاستخدام غير المرخص للأدوية في الرياضة تحديات متعددة الجوانب تتطلب اهتمامًا عاجلاً من المهنيين الصحيين والهيئات التنظيمية والمنظمات الرياضية. تعد التدخلات التعليمية، وتعزيز الإلمام الصحي، وإطار تنظيمي قوي ضرورية لتخفيف المخاطر الصحية المرتبطة باستخدام الأدوية غير المرخصة والحفاظ على المعايير الأخلاقية في الرياضة التنافسية.

الكلمات المفتاحية :استخدام الأدوية غير المرخصة، العقاقير لتعزيز الأداء، طب الرياضة، المعضلات الأخلاقية، المخاطر الصحية.