PRZYGODZKA, Sabina, RUTKIEWICZ, Maciej, GADŻAŁA, Katarzyna, GARBINO, Karolina, BRUDNIAK, Katarzyna, SZUŚCIK, Antoni Szuścik and CZYCZERSKA, Magdalena. Contamination of dietary supplements: the impact of the undeclared compounds on health, consequences of daily usage and prevention strategies. Quality in Sport. 2025;38:57810. eISSN 2450-3118.
https://doi.org/10.12775/QS.2025.38.57810
https://apcz.umk.pl/QS/article/view/57810

The journal has been 20 points in the Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.
Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.
Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 14.01.2025. Revised: 12.02.2025. Accepted: 14.02.2025 Published: 17.02.2025.

Contamination of dietary supplements: the impact of the undeclared compounds on health, consequences of daily usage and prevention strategies

Sabina Przygodzka[1], Maciej Rutkiewicz[2], Katarzyna Gadżała[3], Karolina Garbino[4], Katarzyna Brudniak[5], Antoni Szuścik [6], Magdalena Czyczerska[7]

[1] T. Marciniak Hospital in Wroclaw, gen. Augusta Emila Fieldorfa 2, 54-049 Wroclaw, Poland, sabinaprzygodzka@gmail.com, ORCID: https://orcid.org/0009-0002-0865-9451
[2] Lower Silesian Center of Oncology, Pulmonology and Haematology, Plac Ludwika Hirszfelda 19, 53-413 Wrocław, macrutkiewicz@gmail.com, ORCID: https://orcid.org/0009-0007-7249-0490
[3] Wroclaw Medical University, wybrzeże Ludwika Pasteura 1, 50-367 Wrocław, kasia.gadzala@gmail.com, ORCID: https://orcid.org/0009-0005-4863-6045
[4] 4. Military Clinical Hospital with Policlinic in Wroclaw, Weigla Street 5, 53-114 Wrocław, Poland e-mail: karolinamgarbino@gmail.com, ORCID: https://orcid.org/0000-0002-2846-6035
[5] University of Opole, plac Kopernika 11A, 45-040 Opole, lek.katarzynabrudniak@gmail.com, ORCID: https://orcid.org/0009-0001-1878-5294
[6] University of Opole, plac Kopernika 11A, 45-040 Opole, antoni.szuscik@gmail.com, ORCID: https://orcid.org/0009-0001-2780-8208
[7] University of Opole, plac Kopernika 11A, 45-040 Opole, magdalena.czyczerska@gmail.com, ORCID: https://orcid.org/0009-0001-1579-2501

Abstract
Throughout recent years, dietary supplement usage significantly increased. The reason behind it is a desire to enhance physical performance due to the healthy-body trend. As the primarily unregulated market grows, so does the possibility of consumer exploitation. By releasing products intentionally or unintentionally contaminated by undeclared active compounds, producers endanger the health of many people worldwide. Components found in ergonutritional products have a broad spectrum of properties but also many adverse effects, which may occur in long-term use, including cardiovascular, neurological complications, and hormonal imbalance, among others. It is pivotal for users to be aware of the possible risks of DS consumption and crucial for governments to tighten regulations regarding manufacturing, testing, and labeling food supplements to ensure the safety of consumers.

Keywords: dietary supplements, contamination, doping, sibutramine, higenamine, anabolic androgenic steroids, AAS, SMARs, DMAA, health risks

1. Introduction

The European Parliament Directive (2002/46/EC) defines a food supplement as a concentrated source of nutrients or other substances with physiological or nutritional effects whose purpose is to supplement a regular diet alone or in combination [1]. Annexes I and II to this directive specify minerals and vitamins that may be used to make DS. Although the labeling and advertising cannot suggest that the product has properties of curing or preventing human disease [1], there are no strict regulations before DS hit the market in the means of checking actual ingredients or if the process of manufacturing DS is correct (conditions in factory and possibility of DS contamination in the production line) [2]. The lack of law adaptation to the constantly growing market, to this day, leads to exploitation of the consumer and - in some cases - even puts his health in danger. The liberal approach to the topic is also noticeable in the US. There are similarities between the Food and Drug Administration (FDA) and European supervision of the DS industry, such as no premarket regulations including safety requirements (for example, obligatory tests regarding the quality or quantity of the compounds) [3]. It relies on information provided by the public and manufacturers, requiring producers to report serious side effects [4,5], which paints an inadequate picture of the products themselves because of the low number of these reports [6,7]. It also does not guarantee a lack of contamination by forbidden substances and, furthermore, label compliance [6,8]. However, there are countries such as Canada where DS are described as natural health products (NHPs) and belong to a specific category of drugs. As a result, they are under Natural Health Products Regulations, which means that manufacturers and their products must be licensed and need to provide evidence of the safety and efficacy of the food supplement [9].

The usage of the DS has risen remarkably through the last few years, leading to predictions that the global food supplement market will reach $307,8 billion value by 2028 [10]. The cause of this high demand is greater society's awareness regarding staying in good health and shape. So it's not only professional athletes trying to enhance their performance and

minimize the side effects of intense training [11], but also a group of people who exercise daily or need to fill in the gaps in their diet.

Nonetheless, the athletes are more often tested by the World Anti-Doping Agency (WADA), so even unintentional doping by using contaminated DS may be detected and, moreover, lead to negative consequences, including their career [12,13]. This implies that a broad group of consumers do not know the repercussions of long-term usage of undeclared substances in supplements that are not appropriately checked before they appear on the market. In recent years, studies have found that many DS contain compounds such as anabolic androgenic steroids (AAS) but also prohormones [14,15,16].

2. Purpose of the study

This review paper aims to explore the subject of food supplement contamination and describe the possible impact of undeclared compounds on health in unintentional everyday usage of dietary supplements. Based on current literature, it also evaluates ways of preventing it and highlights the importance of spreading awareness and education about inadvertent doping.

3. Materials and methodology

The literature on which this review was based was gathered through searches on PubMed and Google Scholar, supplemented by references from the initially retrieved articles. Phrases used in searches on databases mentioned above are "dietary supplements", "contamination", "doping", "sibutramine", "higenamine", "anabolic androgenic steroids", "SARMs" and "DMAA".

4. Discussion

Dietary supplements are often contaminated by compounds not labeled on the product or the difference listed and the actual amount of the ingredients. Studies from 12 different countries have found that the contamination rate of DS is between 12% and 58% [17]. So long-term usage may cause significant health risks by affecting the cardiovascular system, hormonal balance, hepatic function, and many more ways that may occur after years. The most common substances found in food supplements are sibutramine, β2-agonists, selective androgen receptor modulators, anabolic androgenic steroids, and 1,3-dimethylamylamine. The effects and risks associated with consuming undeclared substances are thoroughly described in the subsections of this review.

4.1 Sibutramine

Sibutramine belongs to the group of serotonin and norepinephrine reuptake inhibitors and was initially developed as an antidepressant. Through the years of therapy, it turned out that sibutramine has a low effect on depression but decreases appetite, and so on, reduces caloric intake, resulting in weight loss. In 1997, in the United States, sibutramine was approved for short- and long-term obesity therapy [18,19]. Side effects such as headache, insomnia, nausea, constipation, and increased heart rate and blood pressure (systolic and diastolic) were very

common [18,20]. The studies showed that in subjects with preexisting cardiovascular risks receiving long-term sibutramine treatment, the individual rates of nonfatal myocardial infarction, but also stroke were much increased [21,22].
Furthermore, there is a possibility of liver injury by this medication. The mechanism is unclear, but sibutramine undergoes extensive hepatic metabolism, and its active intermediate may induce hepatotoxicity [23]. Since 2010, sibutramine has been withdrawn in the majority of countries (the US and the European Union) due to an increase in cardiovascular events such as myocardial infarction, arrhythmias, tachycardia, hypertension, and even induced nonischemic cardiomyopathy [24].

4.2 Higenamine

Higenamine is an alkaloid identified as a β2-(adrenoreceptor) agonist, which can be extracted from several different species of plants used, for example, in traditional Chinese medicine in a broad range of conditions such as heart failure and asthma [25]. It has an inotropic and chronotropic effect on cardiac function [25,26,27]. Also, studies have shown that higenamine has a relaxant effect on the smooth muscle of the trachea [28,29] and colon [30]. Moreover, it enhances metabolism and glucose uptake, comparable to the impact of endogenous catecholamines such as norepinephrine and epinephrine [31]. Because of its ability to alter the cardiovascular, respiratory, and even central nervous systems by enhancing performance, higenamine was included in the Prohibited Substances and Methods List by WADA in 2017 [32]. The intake of this drug can increase blood pressure and may cause irregular heartbeats [33,34]. There was also a case of paraspinal muscle rhabdomyolysis without renal damage [35]. The side effects such as heart palpitations, nausea, and dizziness were reported during human clinical studies of the impact of higenamine [34,36]. The substance may also reduce the effectiveness of blood thinners and blood pressure medications [37,38].

4.3 Anabolic androgenic steroids (AAS)

Food supplements often contain not only parent anabolic steroids but also their precursors. A study performed by Baume et al. showed that the main prohormones in the DS are those of nandrolone and testosterone [39]. Besides these, compounds such as metandienone, widely used in the 1980s by bodybuilders, can be found in supplements [39]. Exogenous steroid use, especially long-term usage, may disrupt the natural production of hormones (hormonal imbalance), which may cause reversible or irreversible changes, such as infertility or gynecomastia [40,41]. Moreover, the intake of AAS is associated with higher cardiovascular risk by causing hypertension, thrombosis, impaired diastolic filling, left ventricular hypertrophy, and in long-term use - cardiomegaly and even sudden cardiac death [6,42]. AAS admission may have a toxic impact on the liver, resulting in cholestasis, hepatic peliosis, adenoma, and hepatocellular carcinoma [43]. These substances can interact with anticoagulants such as warfarin, increasing its effect and ipso facto - risk of bleeding complications [44]. Adverse effects also include AAS-induced behavioral disorders like increased anxiety and aggression [45].

4.4 Selective androgen receptor modulators (SARMs)

Compared to the AAS, selective androgen receptor modulators have anabolic effects but without androgenic ramifications, making them popular in the bodybuilding and athlete community [46]. Studies showed that more than 90% of men were satisfied with SARM usage because of the increased muscle mass, but also more than half of the users reported significant side effects, such as mood swings, acne, and decreased testicular size [47]. Furthermore, SARMs are associated with higher risk of myocardial infarction and stroke, as well as liver injury and acute liver failure, psychosis, hallucinations, sleep disturbances, infertility, pregnancy miscarriage, and sexual dysfunction [48]. Currently, the most common substances found in DS are ostarine and ibutamoren [6], but andarine and arimistane were also detected [49]. In the U.S., selective AR modulators are considered unapproved drugs and cannot be legally marketed as a dietary supplement or drug at this time [48].

4.5 1,3-dimethylamylamine (DMAA)

1,3-Dimethylamylamine is an alkylamine stimulant commonly found in dietary supplements (especially weight loss products because of appetite suppressant properties) and pre-workout sports nutrition [50,51]. DMAA is often labeled as a part of the geranium plant and used as a nasal decongestant [6,52]. Reported adverse effects include a higher risk of increased blood pressure, tachycardia, hemorrhagic stroke, and cardiac arrest [53,54,55]. It's perilous for consumers who use medications or supplements, that may raise blood pressure and groups of people who are hypertensive [6]. DMAA is determined as illegal by the FDA [53].

5. Conclusions

The contamination of dietary supplements become a real pressing issue. The number of different undeclared compounds, in various amounts and with a broad spectrum of properties (also the adverse effects) in this group of products is now a safety matter. The lack of regulation on the DS market regarding mandatory analytical control over production lines may result in numerous health problems for consumers already with higher risks of complications or even potentially the ones in perfect shape. It is critical that each country's government should have increased surveillance over the quantity and quality of components, and the labeling of the product entering the market should be more supervised and checked regularly. In some ways, it is intentionally misleading the public by producers, marketing enhancement in the physical form of customers, but simultaneously causing them harm. It is as dangerous as it sounds. There are third-party testing organizations that, as a neutral body, examine specific products on request. Still, they are usually available for a particular circle of users, such as athletes, with sponsors and their livelihoods on the line. Ordinary citizens do not have access to those methods, and

buying supplements in good faith to improve their condition. Therefore, besides effective government oversight, there is a need for educational interventions carried out by medical doctors, nutritional specialists, as well as personal trainers and coaches who often come across food supplements.

The goal is to increase awareness of the present law regulations of DS manufacturing and about the possibility of food supplement contamination, especially in the product without special certification, through lectures, demonstrations, videos, and writing materials like booklets or flyers, etc., so before purchase, everyone interested in long-term usage could check if the dietary supplement is good for them. However, to do that, there must be a general principle of information transparency (included in the labeling of nutritional supplements), which must be guaranteed and prosecuted by authorities.

DISCLOSURE

Author's contribution
Sabina Przygodzka: conceptualization, writing rough preparation
Maciej Rutkiewicz: writing rough preparation
Katarzyna Gadżała: supervision, resources
Katarzyna Brudniak: visualization, data curation
Karolina Garbino: methodology
Maciej Rutkiewicz: check
Antoni Szuścik: investigation,
Antoni Szuścik: writing and editing
Magdalena Czyczerska: formal analysis
Katarzyna Gadżała: software
Project administration: Sabina Przygodzka

All authors have read and agreed with the published version of the manuscript.

Conflict of interest

The authors deny any conflict of interest

Institutional Review Board Statement

Not applicable – Not required

Financing statement

The study received no specific funding

Informed Consent Statement

Not applicable – Not required

Data Availability Statement
Not applicable

REFFERENCES

1. Directive 2002/46/EC of the European Parliament and of the Council of 10 02 on the Approximation of the Laws of the Member States Relating to Food Supplements. European Parliament and of the Council; Brussels, Belgium: 2002. pp. 51–57.
2. Wierzejska R. E. Dietary supplements—for whom? The current state of knowledge about the health effects of selected supplement use. International Journal of Environmental Research and Public Health . 2021;18(17):p. 8897. doi: 10.3390/ijerph18178897.
3. Petkova-Gueorguieva E. S., Getov I. N., Ivanov K. V., et al. Regulatory requirements for food supplements in the European Union and Bulgaria. Folia Medica . 2019;61(1):41–48. doi: 10.2478/folmed-2018-0032
4. Lewis J. D., Strom B. L. Balancing safety of dietary supplements with the free market. Annals of Internal Medicine . 2002;136(8):616–618. doi: 10.7326/0003-4819-136-8-200204160-00011.
5. Mehta N., Germain M. S., Quiel L. Dietary supplements: when too much of a good thing becomes harmful. Clinical Case Reports . 2021;9(9) doi: 10.1002/ccr3.3614.
6. Kozhuharov VR, Ivanov K, Ivanova S. Dietary Supplements as Source of Unintentional Doping. Biomed Res Int. 2022 Apr 22;2022:8387271. doi: 10.1155/2022/8387271. PMID: 35496041; PMCID: PMC9054437.
7. Oketch-Rabah H. A., Roe A. L., Muldoon-Jacobs K., Giancaspro G. I. Challenges and opportunities for improving the safety assessment of botanical dietary supplements: a United States Pharmacopeia perspective. Clinical Pharmacology and Therapeutics . 2018;104(3):426–429. doi: 10.1002/cpt.1113.
8. Starr R. R. Too little, too late: ineffective regulation of dietary supplements in the United States. American Journal of Public Health . 2015;105(3):478–485. doi: 10.2105/AJPH.2014.302348
9. Health Canada Natural and Non-Prescription. Health Products Directorate (NNHPD) About natural health product regulation in Canada. https://www.Canada.ca/En/Health-Canada/Services/
10. Zion Market Research. Dietary supplements market by ingredients (botanicals, vitamins, minerals, amino acids, enzymes) for additional supplements, medicinal supplements and sports nutrition applications - global industry perspective, comprehensive

analysis and forecast . March 2022, https://www.zionmarketresearch.com/report/dietary-supplements-market
11. Knapik J.J., Steelman R.A., Hoedebecke S.S., Austin K.G., Farina E.K., Lieberman H.R. Prevalence of Dietary Supplement Use by Athletes: Systematic Review and Meta-Analysis. Sports Med. 2016;46:103–123. doi: 10.1007/s40279-015-0387-7.
12. WADA. World Anti-Doping Code. 2015. Available online: https://www.wada-ama.org/sites/default/files/resources/files/ wada-2015-world-anti-doping-code.pdf (accessed on 1 December 2022).
13. Maughan, R.J.; Burke, L.M.; Dvorak, J.; Larson-Meyer, D.E. IOC Consensus Statement: Dietary Supplements and the HighPerformance Athlete. Int. J. Sport Nutr. Exerc. Metab. 2018, 28, 23
14. Martello S., Felli M., Chiarotti M. Survey of nutritional supplements for selected illegal anabolic steroids and ephedrine using LC-MS/MS and GC-MS methods, respectively. Food Additives and Contaminants . 2007;24(3):258–265. doi: 10.1080/02652030601013729.
15. Alaedini S., Amirahmadi M., Kobarfard F., Rastegar H., Nasirahmadi S., Shoeibi S. Survey of protein-based sport supplements for illegally added anabolic steroids methyltestosterone and 4-androstenedione by UPLC-MS/MS. Steroids . 2021;165, article 108758 doi: 10.1016/j.steroids.2020.108758.
16. Cohen P. A., Travis J. C., Vanhee C., Ohana D., Venhuis B. J. Nine prohibited stimulants found in sports and weight loss supplements: deterenol, phenpromethamine (Vonedrine), oxilofrine, octodrine, beta-methylphenylethylamine (BMPEA), 1,3-dimethylamylamine (1,3-DMAA), 1,4-dimethylamylamine (1,4-DMAA), 1,3-dimethylbutylamine (1,3-DMBA) and higenamine. Clinical Toxicology . 2021;59(11):975–981. doi: 10.1080/15563650.2021.1894333.
17. Martínez-Sanz JM, Sospedra I, Ortiz CM, Baladía E, Gil-Izquierdo A, Ortiz-Moncada R. Intended or Unintended Doping? A Review of the Presence of Doping Substances in Dietary Supplements Used in Sports. Nutrients. 2017 Oct 4;9(10):1093. doi: 10.3390/nu9101093. PMID: 28976928; PMCID: PMC5691710.
18. LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012–. Sibutramine. 2020 Jun 5. PMID: 31643572.
19. Luque CA, Rey JA. Sibutramine: a serotonin-norepinephrine reuptake-inhibitor for the treatment of obesity. Ann Pharmacother. 1999 Sep;33(9):968-78. doi: 10.1345/aph.18319. PMID: 10492502.
20. Scheen AJ. Cardiovascular risk-benefit profile of sibutramine. Am J Cardiovasc Drugs. 2010;10(5):321-34. doi: 10.2165/11584800-000000000-00000. PMID: 20860415.
21. James WP, Caterson ID, Coutinho W, Finer N, Van Gaal LF, Maggioni AP, Torp-Pedersen C, Sharma AM, Shepherd GM, Rode RA, Renz CL; SCOUT Investigators. Effect of sibutramine on cardiovascular outcomes in overweight and obese subjects. N Engl J Med. 2010 Sep 2;363(10):905-17. doi: 10.1056/NEJMoa1003114. PMID: 20818901.

22. Wooltorton E. Obesity drug sibutramine (Meridia): hypertension and cardiac arrhythmias. CMAJ. 2002 May 14;166(10):1307-8. PMID: 12041851; PMCID: PMC111085.
23. Chounta A, Tsiodras S, Zouridakis S, Doumas M, Giamarellou H. Sibutramine use associated with reversible hepatotoxicity. Ann Intern Med. 2005 Nov 15;143(10):763-4. doi: 10.7326/0003-4819-143-10-200511150-00030. PMID: 16287809.
24. Shah MS, Patel ZK, Bharucha R, Talati T, Benz M. Sibutramine-Induced Nonischemic Cardiomyopathy. Cureus. 2022 Jan 26;14(1):e21650. doi: 10.7759/cureus.21650. PMID: 35242455; PMCID: PMC8884463.
25. Hudzik TJ, Patel M, Brown A. β_2 -Adrenoceptor agonist activity of higenamine. Drug Test Anal. 2021 Feb;13(2):261-267. doi: 10.1002/dta.2992. Epub 2021 Jan 12. PMID: 33369180; PMCID: PMC7898339.
26. Praman S, Mulvany MJ, Williams DE, Andersen RJ, Jansakul C. Crude extract and purified components isolated from the stems of Tinospora crispa exhibit positive inotropic effects on the isolated left atrium of rats. J Ethnopharmacol. 2013 Aug 26;149(1):123-32. doi: 10.1016/j.jep.2013.06.010. Epub 2013 Jun 15. PMID: 23778316.
27. Praman S, Mulvany MJ, Williams DE, Andersen RJ, Jansakul C. Hypotensive and cardio-chronotropic constituents of Tinospora crispa and mechanisms of action on the cardiovascular system in anesthetized rats. J Ethnopharmacol. 2012 Mar 6;140(1):166-78. doi: 10.1016/j.jep.2012.01.006. Epub 2012 Jan 14. PMID: 22265931.
28. Ueki T, Akaishi T, Okumura H, Morioka T, Abe K. Biphasic tracheal relaxation induced by higenamine and nantenine from Nandina domestica Thunberg. J Pharmacol Sci. 2011;115(2):254-7. doi: 10.1254/jphs.10251sc. Epub 2011 Jan 26. PMID: 21282929.
29. Tsukiyama M, Ueki T, Yasuda Y, Kikuchi H, Akaishi T, Okumura H, Abe K. Beta2-adrenoceptor-mediated tracheal relaxation induced by higenamine from Nandina domestica Thunberg. Planta Med. 2009 Oct;75(13):1393-9. doi: 10.1055/s-0029-1185743. Epub 2009 May 25. PMID: 19468973.
30. Bai G, Yang Y, Shi Q, Liu Z, Zhang Q, Zhu YY. Identification of higenamine in Radix Aconiti Lateralis Preparata as a beta2-adrenergic receptor agonist1. Acta Pharmacol Sin. 2008 Oct;29(10):1187-94. doi: 10.1111/j.1745-7254.2008.00859.x. PMID: 18817623.
31. Kato E, Kimura S, Kawabata J. Ability of higenamine and related compounds to enhance glucose uptake in L6 cells. Bioorg Med Chem. 2017 Dec 15;25(24):6412-6416. doi: 10.1016/j.bmc.2017.10.011. Epub 2017 Oct 14. PMID: 29066136.
32. Cohen PA, Travis JC, Keizers PHJ, Boyer FE, Venhuis BJ. The stimulant higenamine in weight loss and sports supplements. Clin Toxicol (Phila). 2019 Feb;57(2):125-130. doi: 10.1080/15563650.2018.1497171. Epub 2018 Sep 6. PMID: 30188222.
33. Lee SR, Schriefer JM, Gunnels TA, Harvey IC, Bloomer RJ. Acute oral intake of a higenamine-based dietary supplement increases circulating free fatty acids and energy expenditure in human subjects. Lipids Health Dis. 2013 Oct 21;12:148. doi: 10.1186/1476-511X-12-148. PMID: 24139127; PMCID: PMC4016229.

34. Feng S, Jiang J, Hu P, Zhang JY, Liu T, Zhao Q, Li BL. A phase I study on pharmacokinetics and pharmacodynamics of higenamine in healthy Chinese subjects. Acta Pharmacol Sin. 2012 Nov;33(11):1353-8. doi: 10.1038/aps.2012.114. Epub 2012 Oct 22. PMID: 23085737; PMCID: PMC4011356.
35. Jeter J, DeZee KJ, Kennedy L. A Case of Paraspinal Muscle Rhabdomyolysis in a 22-Year-Old Male After Ingesting a Supplement Containing Higenamine. Mil Med. 2015 Jul;180(7):e847-9. doi: 10.7205/MILMED-D-14-00647. PMID: 26126260.
36. Bloomer RJ, Schriefer JM, Gunnels TA. Clinical safety assessment of oral higenamine supplementation in healthy, young men. Hum Exp Toxicol. 2015 Oct;34(10):935-45. doi: 10.1177/0960327114565490. Epub 2015 Jan 14. PMID: 25591969.
37. Yun-Choi HS, Pyo MK, Park KM, Chang KC, Lee DH. Anti-thrombotic effects of higenamine. Planta Med. 2001 Oct;67(7):619-22. doi: 10.1055/s-2001-17361. PMID: 11582538.
38. Zhang N, Lian Z, Peng X, Li Z, Zhu H. Applications of Higenamine in pharmacology and medicine. J Ethnopharmacol. 2017 Jan 20;196:242-252. doi: 10.1016/j.jep.2016.12.033. Epub 2016 Dec 19. PMID: 28007527.
39. Baume N, Mahler N, Kamber M, Mangin P, Saugy M. Research of stimulants and anabolic steroids in dietary supplements. Scand J Med Sci Sports. 2006 Feb;16(1):41-8. doi: 10.1111/j.1600-0838.2005.00442.x. PMID: 16430680.
40. Karila T, Hovatta O, Seppälä T. Concomitant abuse of anabolic androgenic steroids and human chorionic gonadotrophin impairs spermatogenesis in power athletes. Int J Sports Med. 2004 May;25(4):257-63. doi: 10.1055/s-2004-819936. PMID: 15162244.
41. Mottram DR, George AJ. Anabolic steroids. Baillieres Best Pract Res Clin Endocrinol Metab. 2000 Mar;14(1):55-69. doi: 10.1053/beem.2000.0053. PMID: 10932810.
42. Torrisi M, Pennisi G, Russo I, Amico F, Esposito M, Liberto A, Cocimano G, Salerno M, Li Rosi G, Di Nunno N, Montana A. Sudden Cardiac Death in Anabolic-Androgenic Steroid Users: A Literature Review. Medicina (Kaunas). 2020 Nov 4;56(11):587. doi: 10.3390/medicina56110587. PMID: 33158202; PMCID: PMC7694262.
43. Solimini R, Rotolo MC, Mastrobattista L, Mortali C, Minutillo A, Pichini S, Pacifici R, Palmi I. Hepatotoxicity associated with illicit use of anabolic androgenic steroids in doping. Eur Rev Med Pharmacol Sci. 2017 Mar;21(1 Suppl):7-16. PMID: 28379599.
44. Serlin MJ, Breckenridge AM. Drug interactions with warfarin. Drugs. 1983 Jun;25(6):610-20. doi: 10.2165/00003495-198325060-00004. PMID: 6347619.
45. Bertozzi G, Sessa F, Albano GD, Sani G, Maglietta F, Roshan MHK, Volti GL, Bernardini R, Avola R, Pomara C, Salerno M. The Role of Anabolic Androgenic Steroids in Disruption of the Physiological Function in Discrete Areas of the Central Nervous System. Mol Neurobiol. 2018 Jul;55(7):5548-5556. doi: 10.1007/s12035-017-0774-1. Epub 2017 Oct 2. PMID: 28971285; PMCID: PMC5994209.
46. Solomon ZJ, Mirabal JR, Mazur DJ, Kohn TP, Lipshultz LI, Pastuszak AW. Selective Androgen Receptor Modulators: Current Knowledge and Clinical Applications. Sex

Med Rev. 2019 Jan;7(1):84-94. doi: 10.1016/j.sxmr.2018.09.006. Epub 2018 Nov 30. PMID: 30503797; PMCID: PMC6326857.
47. Efimenko IV, Valancy D, Dubin JM, Ramasamy R. Adverse effects and potential benefits among selective androgen receptor modulators users: a cross-sectional survey. Int J Impot Res. 2022 Dec;34(8):757-761. doi: 10.1038/s41443-021-00465-0. Epub 2021 Sep 1. PMID: 34471228.
48. Commissioner, O. "Of the FDA in brief: FDA warns against using SARMs in body-building products." (2019).
49. Leaney AE, Beck P, Biddle S, Brown P, Grace PB, Hudson SC, Mawson DH. Analysis of supplements available to UK consumers purporting to contain selective androgen receptor modulators. Drug Test Anal. 2021 Jan;13(1):122-127. doi: 10.1002/dta.2908. Epub 2020 Aug 16. PMID: 32748554.
50. Monakhova YB, Ilse M, Hengen J, El-Atma O, Kuballa T, Kohl-Himmelseher M, Lachenmeier DW. Rapid assessment of the illegal presence of 1,3-dimethylamylamine (DMAA) in sports nutrition and dietary supplements using 1H NMR spectroscopy. Drug Test Anal. 2014 Sep;6(9):944-8. doi: 10.1002/dta.1677. Epub 2014 Jun 9. PMID: 24913715.
51. Small C, Cheng MH, Belay SS, Bulloch SL, Zimmerman B, Sorkin A, Block ER. The Alkylamine Stimulant 1,3-Dimethylamylamine Exhibits Substrate-Like Regulation of Dopamine Transporter Function and Localization. J Pharmacol Exp Ther. 2023 Aug;386(2):266-273. doi: 10.1124/jpet.122.001573. Epub 2023 Jun 22. PMID: 37348963; PMCID: PMC10353075.
52. Zhang Y, Woods RM, Breitbach ZS, Armstrong DW. 1,3-Dimethylamylamine (DMAA) in supplements and geranium products: natural or synthetic? Drug Test Anal. 2012 Dec;4(12):986-90. doi: 10.1002/dta.1368. Epub 2012 Jul 12. PMID: 22786761.
53. Karnatovskaia LV, Leoni JC, Freeman ML. Cardiac arrest in a 21-year-old man after ingestion of 1,3-DMAA-containing workout supplement. Clin J Sport Med. 2015 Jan;25(1):e23-5. doi: 10.1097/JSM.0000000000000103. PMID: 24878759.
54. Bloomer RJ, Harvey IC, Farney TM, Bell ZW, Canale RE. Effects of 1,3-dimethylamylamine and caffeine alone or in combination on heart rate and blood pressure in healthy men and women. Phys Sportsmed. 2011 Sep;39(3):111-20. doi: 10.3810/psm.2011.09.1927. PMID: 22030947.
55. Forrester M. Exposures to 1,3-dimethylamylamine-containing products reported to Texas poison centers. Hum Exp Toxicol. 2013 Jan;32(1):18-23. doi: 10.1177/0960327112454895. Epub 2012 Oct 11. PMID: 23060409.