



## Review article

# Potential health risks of foodborne performance-enhancing drugs in competitive sports

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## ABSTRACT

Athletes need to consume a significant amount of energy during prolonged training and in high-intensity competition. It is necessary for them to take nutritional foods that recharge their bodies. However, in sporting events of recent years, both domestic and international, many positive drug tests are found to be caused by the ingestion of foods that contain performance-enhancing drugs (PEDs). As a result, the prevention and control of PEDs in food supply have drawn increasing attention. For better prevention and control, the first step is to understand the food contaminants – PEDs. This study has categorized PEDs through their presence in animal-derived foods, plant-derived foods, and synthetic nutritional supplements in competitive sports. It investigates the potential risks of foodborne doping using techniques such as external addition and endogenous component analysis. This research explored the causes of PEDs in food and their negative effects on athletes and proposed measures to ensure the safety of nutritional substances in competitive sports. PEDs in animal-derived foods include  $\beta$ -adrenergic agonists, anabolic steroids, and glucocorticoids, which can be found in meat and ox penis, amongst other food sources. In contrast, PEDs in plant-derived foods include alkaloids, higenamine, and zeranol, which can be found in coffee, tea, Sichuan pepper, custard apple, and cereal. Performance-enhancing drugs (PEDs) that are often added to synthetic supplements include creatine, traditional Chinese herbs, 1, 3-dimethylbutylamine (DMAA), sibutramine, ephedrine, and methylhexanamine. Targeted anti-doping training should be provided to athletes. In addition, the latest domestic and international standards and regulations regarding PEDs or prohibited and restricted ingredients in foods should be tracked in real-time. The control list for performance-enhancing drugs in food should be continually updated and refined. Research on detection methods for performance-enhancing drugs in food should also be advanced. Moreover, market surveillance and law enforcement should be strengthened to ensure that sports foods meet national safety standards before they enter the market. This paper provides workable solutions to clarify the types and scope of performance-enhancing drugs in food, aiming to improve the prevention and control of PEDs in animal-derived foods, plant-derived foods, and supplements in major sporting events.

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## 1. Introduction

The use of performance-enhancing drugs prevails among athletics around the world, which is a controversial issue involving athletes, coaches and physicians [1]. Performance-enhancing drugs are substances that induce physical changes to enhance performance [2]. Performance-enhancing drugs are prohibited in competitive sports for the rules of fair play. To gain a competitive edge, some athletes adopt more advanced and hidden substances and tactics and the World Anti-Doping Agency, which makes global anti-doping regulations finds it complicated and challenging to enforce the policies. However, most athletes are reluctant to take performance-enhancing drugs, because they know the dangers of performance-enhancing drugs to their health, which they do not want to sacrifice for increasing performance. Some athletes were detected and suspected of taking performance-enhancing drugs. However, according to investigation by anti-doping agencies, they just accidentally consumed food that contained banned substances. Moreover, most studies focus on the effect of performance-enhancing drugs, but few of them discuss what types of nutritional food would lead to the violation of doping code or harm athletes' health. Some studies show that the performance-enhancing drug abusers may develop renal failure [3]. Although performance-enhancing drugs may give dishonest athletes an advantage over other players, they will also damage their health. By affecting the myocardium, vasculature, and metabolism, these drugs may damage the cardiovascular system [4]. Besides, some studies seek to determine if cobalt may act as a performance-enhancing drug [5] and the role that it plays in performance-enhancing drugs in MLB [6]. To predict attitudes towards the use of performance-enhancing substances, some scholars have built sport drug control models based on the data of Australian athletes [7].

Athletes in competitive sports need a higher standard of nutritional intake to support their sustained physical and cognitive performance. In addition to essential energy, athletes also need nutritional food products that can promote rapid recovery from intensive training and enhance their performance in competition events. With the improvement of national fitness, China is growing into a sports powerhouse, laying a solid foundation for its sports industry [8]. Therefore, it is of paramount importance to provide its athletes with targeted and nutritionally adequate food. In recent years, a growing number of athletes have been tested positive for performance-enhancing drugs (PEDs). Performance-enhancing drugs harm the health of athletes, and once athletes are found to take such drugs, the image of the country will be seriously harmed. According to investigations by anti-doping agencies, the primary source of performance-enhancing drugs in athletes is animal-derived food, followed by plant-derived food and synthetic supplements. Intakes of such food products in both endogenous and exogenous ways are the major sources of performance-enhancing drug contamination. Repeated consumption of such foods can cause irreversible harm to athletes who push themselves to their physical limits in training and competitions. This paper has reviewed literature, explored the functions and potential health risks of nutritional food products that athletes consume, and searched for the causes of positive doping tests to raise the awareness of nutritional food safety in competitive sports. The findings of this research have pointed out the potential risks of performance-enhancing drugs to prevent similar occurrences in the future.

## 2. Methods

### 2.1. Information searching

The querying, which refers to a well-defined, targeted information seeking for clearly articulated information about performance-enhancing drugs needed for this paper, included database searches and manual searches. Data was obtained from two Chinese database: China National Knowledge Infrastructure (CNKI) and China Biology Medicine (CBM). Two databases were searched from inception to May 31st, 2023.

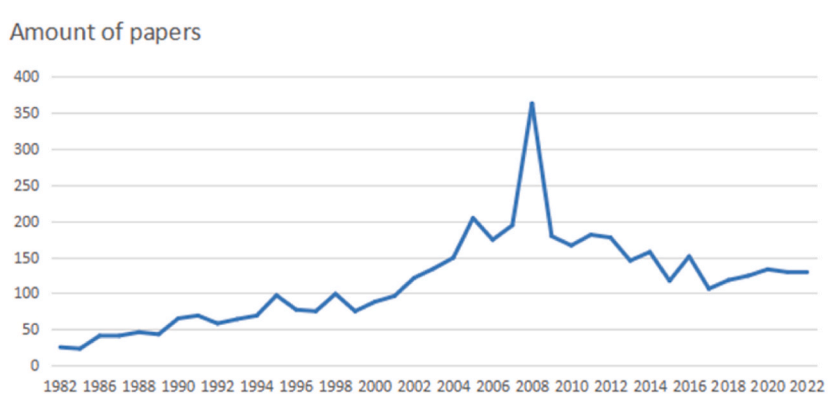


Fig. 1. Trend of publication of related studies.

## 2.2. Eligibility criteria

This paper took references from various scientific studies in both English and Chinese to support the claims about performance-enhancing drugs or anti-doping. It excluded duplicate publications of the same study, and included the most recent results of the study.

## 3. Discussions

### 3.1. Overview of related studies

We have obtained 4647 related studies from CNKI and CBM. The trend of publication is shown in Fig. 1.

Fig. 1 shows that the number of related publications was on an upward trend and peaked in 2008. With the development of science, people gradually realize the side effects of performance-enhancing drugs (PEDs), which can be dangerous and negative for athletes and may cause health issues. However, some players still take PEDs to win competitions and simple test approach is not able to detect the drugs. Researchers have proposed various approaches to detect performance-enhancing drugs and revealed the side effects to warn players against such drugs. The Olympic Games Beijing 2008 were a catalyst for proposals that addressed the use of performance-enhancing drugs, as China adopted international doping testing measures and raised environmental awareness among its population. As many scholars refined the methods for PED detection, performance-enhancing drugs have become a hot topic in the academic circle since then.

### 3.2. Author analysis

According to Table 1, besides those from universities, most scholars studying performance-enhancing drugs or anti-doping are from the General Administration of Sport of China, which has a total of 91 articles published. The administration holds the highest authority for doping testing. It has launched a wide range of education and publicity programmes for various target groups, including anti-doping talks, workshops and outreach programmes, which are executed by scholars in its Sports Science Division. Researchers from universities and other research platforms have also greatly contributed to the national prevention of intentional and unintentional doping.

### 3.3. Nutrition for better athletic performance

Besides being mentally tough and emotionally controlled, athletes need to have physical and technical fitness, intellectual ability and master tactical skills to achieve exceptional results in competition. To tap their potential to the fullest, athletes require a balanced

**Table 1**  
Author character.

Author	Place of work	Amount of papers
Youxuan Xu	General Administration of Sport of China	38
Shuli Guo	Soochow University	25
Binling Song	Xiangtan University	23
Zhimin Liu	Peking University	19
Changjiu Zhang	Institute of Sports Science of General Administration of Sport of China	19
Liu Xin	General Administration of Sport of China	19
Moutian Wu	General Administration of Sport of China	18
Shixi Huang	Shandong University	15
Jiang Xi	Shanghai University of Political Science and Law	14
Yinong Zhang	General Administration of Sport of China	14
Li Zhi	Fuzhou University	13
Qilin Xu	Institute of Sports Science of Hebei Province	13
Zhao Min	Shanghai Mental Health Center	12
Qingshan Zhou	Xiangtan University	11
Dong Ying	General Administration of Sport of China	11
Hao Wei	The Second Xiangya Hospital of Central South University	10
Pinggu Wu	Zhejiang Provincial Center for Disease Control and Prevention	10
Jingzhu Wang	General Administration of Sport of China	10
Shumin Yang	General Administration of Sport of China	10
Yan Kuan	Beijing Sport University	10
Han Yong	Capital University of Physical Education and Sports	9
Shibo Jiang	Shandong University	9
Huiying Xiang	Shanghai University of Political Science and Law	9
Jianli Zhang	Institute of Sports Science of General Administration of Sport of China	9
Zhanliang Wang	General Administration of Sport of China	9
Qin Yang	Institute of Sports Science of General Administration of Sport of China	9
Zeyi Yang	Beijing Cupid Sports Nutrition Research Institute	8
Yu Jian	Sanxia University	8
Chunran Yang	China University of Petroleum	8

supply of various nutrients. Food sources that provide energy can be categorized into three types: 1) grains, such as wheat and rice; 2) animal-derived products, such as meats, eggs, and dairy; and 3) synthetic supplements designed to enhance athletic performance. These nutrient sources may have health risks or residues of prohibited substances, which can result in positive doping tests.

### 3.4. Risks of nutrition for sports

#### 3.4.1. The risk of performance-enhancing drugs in animal-derived food

Proteins are the fundamental building blocks for all cells within tissues or organs across the human body. Endurance exercise stimulates protein breakdown and synthesis, and helps build muscle mass and strength. As the structure of animal proteins resembles human proteins, athletes can benefit from the daily intake of good-quality proteins to promote muscle protein recombination [9]. Protein intake depends on the level of physical activity and should be proportional to daily protein consumption by the organism. If the protein intake in diet is 30 % below the minimum protein intake, protein deficiency occurs and will have negative effects on life activities. Animal-based foods (meat, poultry, fish, eggs, and dairy foods) tend to be good sources of complete protein, fat, and micronutrients to athletes. During endurance exercise, the organism consumes a substantial amount of nutrients. Both fat and proteins are main sources of energy for the human body. However, fat has some limitations. For example, it can only be broken down into energy through oxidation and cannot be metamorphosed into glucose to maintain blood sugar levels. In contrast, the amino acids from ingested protein could be converted into glucose to keep blood sugar levels in a healthy range [10]. Therefore, protein plays an indispensable role in endurance exercise, during which protein consumption should be about 12–14 % of the total energy expenditure [11].

**3.4.1.1.  $\beta$ -receptor agonists.** Beta-receptor agonists belong to the class of phenethylamine drugs, whose chemical structures are similar to those of adrenaline and noradrenaline. Often used in animal husbandry, beta-receptor agonists can promote animal protein synthesis and increase feed conversion efficiency. Despite their potential benefits, the intake of residual  $\beta$ -receptor agonists through meat products can cause harmful physiological side effects to human body [12]. Clenbuterol hydrochloride, known in China simply as “lean meat powder,” can promote animal muscle growth, reduce fat deposition, and increase lean meat [13]. It is also the most common  $\beta$ -receptor agonist detected in anti-doping tests. Numerous athletes have tested positive for clenbuterol after eating meat. Such atypical results can negatively impact their reputation and damage their health [14,15].

According to reports from world sports events and data from WADA-accredited laboratories and anti-doping laboratories of the General Administration of Sport of China (GASC), accidental or inadvertent doping has become the main cause of positive results since 2008. Accidental doping happens more in team sports [16], and inadvertent use of prohibited drugs by athletes also occurs in individual sports, such as cycling and wrestling, which require high amounts of physical endurance. According to the regulations of the International Olympic Committee (IOC) and the *World Anti-Doping Code* (WADC), though athletes may be exonerated after testing positive for contaminants in food or endogenous substances, they are responsible for whatever is in their body, regardless of how it got there. According to the regulations, athletes who test positive for prohibited substance will receive a suspension [17]. The allegations will still upend their lives and shatter their athletic momentum. To prevent inadvertent intake of contaminated meat by athletes, many training centers raise pigs, cattle, and other animals in their own facilities or purchase animal-derived foods from designated suppliers.

**3.4.1.2. Anabolic steroids.** Anabolic steroids, officially known as anabolic–androgen steroids or colloquially simply as “steroids,” are drugs that mimic the effects of the male sex hormones testosterone and androstenedione. As one of the most common performance-enhancing drugs in sports, anabolic steroids can seriously disrupt hormonal balance in the human body. According to the investigation of the International Olympic Committee, out of the 634 dietary samples, 14.8 % (94) contained anabolic steroids, but they were not shown on the product label [18]. Therefore, athletes should always know what they are putting into their system before consuming the products to avoid inadvertent anti-doping rule violations [19]. For example, they should avoid the intake of natural steroids by not eating reproductive organs of animals such as ox and dog.

**3.4.1.3. Glucocorticoids.** Glucocorticoids are a type of adrenal cortex hormone that maintains energy supply by breaking down proteins and liver glycogen into glucose [20]. Commonly found in foods such as licorice and custard apples, glucocorticoids include dexamethasone, prednisone, and hydrocortisone. In modern veterinary medicine, glucocorticoids play a vital role in the management of an array of clinical conditions. In sports, they form a type of performance-enhancing drug that is banned by the International Olympic Committee (IOC) and the World Anti-Doping Agency (WADA) [21]. Residues of dexamethasone and betamethasone can be found in the muscles and kidneys of ox, pigs, and horses.

To prevent and control foodborne doping, the Anti-Doping Center of the General Administration of Sport of China issued the *Guidelines for the Prevention and Control of Foodborne Performance-Enhancing Drugs in Major Sporting Events* (T.F.X.F.J.Zi [2021] No. 584) on November 23, 2021. The document helps determine 6 major classes of 48 prohibited substances in sports, including 1) protein anabolic agents, 2)  $\beta$ 2 agonists, 3)  $\beta$ -blockers, 4) glucocorticoids, 5) stimulants, and 6) diuretics and other masking agents. These substances will be strictly monitored by the authority to reduce the risks of unintended doping originating from tainted food or nutritional supplements [22,23].

In summary, the use of veterinary drugs in food-producing animals has the potential to generate residues in animal-derived products (meat, milk, eggs and honey) and poses a health hazard to the consumer. Moreover, the ingestion of veterinary drug residues in edible animal parts not only constitutes a potential health hazard for athletes but also leads to positive doping results, which

will damage their careers and the image of their countries. For the development of food and sports industries, it is necessary to strictly monitor the veterinary drug residues in animal-derived foods (ADFs).

### 3.4.2. Risks of performance-enhancing drugs in plant-derived food products

Plant-based foods are those that come from seeds, fruits, or other parts of plants, either directly or after being processed, to give people essential energy and minerals. Plant-based foods include various items, but are not limited to, grains, potatoes, legumes and their derivatives, fruits, vegetables, tea, spices, and herbs.

Plant-based foods are major sources of carbohydrates, such as glucose. Besides providing human body with energy, they also contain various other nutrients, including vitamins, minerals, polyphenols, plant estrogens, sulfides, active polysaccharides, lycopene, chlorophyll, and alkaloids. Vegetables and fruits are the best sources of water-soluble vitamins and minerals, such as vitamin C, potassium, calcium, and magnesium. Plant-based foods can significantly boost metabolism and enhance physical fitness.

**3.4.2.1. Alkaloids.** Common alkaloids include solanine, xanthine alkaloids, and areca alkaloids. The xanthine alkaloids are well-known components of tea, coffee, and cocoa. The effects of alkaloids in reducing fatigue have been extensively studied [24,25]. As modern people care more about their health and various cutting-edge scientific tools emerge, researchers have deepened their studies of alkaloids' impact on human beings. Caffeine is the most crucial one among xanthine alkaloids. It is mainly distributed in plants and used to protect plants' tender tissues from the damage of beetles. Its chemical composition is  $C_8H_{10}N_4O_2$ , and its molecular composition is 1,3,7-trimethylxanthine [26]. Caffeine has a strong central nervous system stimulatory effect and acts clinically as moderate tranquilizer, used for neurasthenia therapy and coma recovery. It is the world's most widely used psychoactive drug [27]. Although caffeine is generally safe in low-to-moderate amounts, high levels of consumption can cause dangerous side effects, such as brain and nervous system problems, high blood pressure, heart disease, and dependence. Caffeine withdrawal can cause several symptoms, such as fatigue, decreased energy/activeness, decreased alertness, drowsiness and others. Caffeine has a long half-life in the body's metabolism and is prone to accumulation in the body. Theophylline can be endogenously generated during the metabolism of caffeine. Theophylline is highly toxic because it has a narrow therapeutic index. In other words, the margin of safety above therapeutic doses is small [28]. Therefore, caffeine has been listed as a controlled substance in national psychotropic drug standards and as regulated drugs by WADA [29].

**3.4.2.2. Higenamine or tretoquinol.** Belonging to the class of benzyloisoquinoline alkaloids (BIAs), Higenamine is a type of natural plant-derived  $\beta_2$ -receptor agonist that has the effect of reducing the tension of smooth muscles, thus often being used as a cardiac stimulant [30]. Due to its pharmacological effects, like increasing heart rate and lung capacity, Higenamine is used by some athletes to enhance their performance for sports that require explosive strength. However, as a cardiotonic, higenamine may also put an athlete at an increased risk of heart problems. Consequently, higenamine has been categorized as a prohibited substance, falling under the S3 class ( $\beta_2$ -agonists) by the WADA since 2019 [31]. Higenamine can be found in various traditional Chinese medicine herbs, such as asarum, radix aconiti lateralis preparata, cortex phellodendri. It is also present in essential spices that every home cook needs, such as Sichuan pepper, pepper, and cinnamon. As they are widely used by people, many athletes may be unaware of the potential for unintentional doping [32,33]. Thus, for athletes, higenamine poses a food safety hazard as a dietary intake of a performance-enhancing substance. Based on WADA guidelines, the presence of higenamine in urine samples at concentrations greater than or equal to 10 ng/mL constitutes an adverse analytical finding (AAF) [34]. The General Administration of Sport of China Anti-Doping Center has included higenamine in the list of Performance-Enhancing Drugs in Food and put many efforts to prevent such ingredients found in foods during the hosting of large sporting events.

**3.4.2.3. Zeranol.** Zeranol, also known as "Ralgro", is a secondary metabolite of zearalenone - a mycotoxin produced by *Fusarium* fungi during the growth of maize. Zeranol belongs to resorcylic acid lactones (RALs). As a non-steroidal anabolic agent [35], its misuse in sports is prohibited by regulatory agencies for decades. On December 27, 2019, Zeranol was officially banned from being used in animal production [36]. In advertent doping with zeranol can happen due to the natural presence of mycotoxins in grains: Zearalenone, which can be metabolically converted into Zeranol, may be unintentionally ingested by athletes after the consumption of contaminated cereals, such as maize, wheat, and sorghum. Moreover, the unintended use of this drug may also occur due to illegal administration to livestock. As Zeranol misuse is rarely found in cases of anti-doping rule violations, the possibility of accidental intake should be considered when encountering adverse analytical results in sports [37].

### 3.4.3. Additive risks in synthetic nutrients

To achieve better performance, athletes often have various motivations for using different supplements, such as protein powder, energy boosters, and muscle-building and fat-burning foods. Synthetic nutritional supplements are made from chemical compounds produced in a lab to supplement a diet and to improve the body's function or athletic ability and promote exercise endurance, but they must not contain banned performance-enhancing drugs. Ingredients in synthetic nutritional supplements mainly include creatine, herbal compounds, and others. However, these added substances also carry potential risks, and unscrupulous producers may illegally add prohibited components into these products to provide quick effects and increase sales.

**3.4.3.1. Creatine.** Americans consume over 4 million kilograms (kg) a year of creatine. In sports nutrition market, creatine is the most popular nutritional supplement with the annual sales of \$200 million [38]. While creatine is widely used, its safety is still a subject of

debate. Overall, in healthy individuals, there appears to be no adverse effects from consuming recommended doses of creatine monohydrate both in short term and in long term (up to 30 g per day for up to 5 years) [39]. Short-term (5 days–2 weeks) and high-dose (0.3–0.8 g (kg d)<sup>-1</sup>) creatine administration may stimulate the production of methylamine and formaldehyde (potential cytotoxic metabolites of creatine) in the urine of healthy individuals, but there are no adverse effects on their kidney function.

**3.4.3.2. Herbal plant compounds.** The use of sports nutrition products containing herbal active ingredients has increased in recent years. These products are marketed as “natural” and are gaining popularity in the market. However, “natural” does not necessarily mean “safe”. Because herbal supplements are not regulated and their ingredients are unknown, there is no guarantee about their safety or effectiveness. Research has shown that adverse events associated with multi-compound herbal supplements occur more frequently than single-ingredient supplements [40]. For example, synephrine is an alkaloid that is structurally similar to adrenaline. It occurs naturally in some plants (citrus fruits) and animals and can be used as an active ingredient in sports nutrition products to aid in weight loss, enhance athletic performance and boost energy. Synephrine became popular as an alternative to ephedra after the banning of ephedrine-containing dietary products due to adverse cardiovascular reactions [41]. Studies in humans and animals show that synephrine intake can cause cardiovascular side effects, especially when combined with caffeine. Hydroxycitric acid (HCA) is a naturally occurring fruit acid found in the fruits of the tropical plant *Garcinia cambogia*. It is commonly added to supplements for weight loss, as it can inhibit lipid synthesis and perhaps suppress appetite [42–44]. Animal studies have suggested that administration of high doses of certain HCA-containing products can cause testicular toxicity (testicular atrophy and spermatogenic disorders) [39]. Given the lack of clinical trials with human subjects, particularly regarding the male reproductive system, the safety of HCA-containing supplements is currently uncertain.

**3.4.3.3. 1,3-Dimethylamylamine.** With its structure analogous to ephedrine and amphetamines, DMAA has been incorporated into weight loss products as it can accelerate lipolysis and stimulate metabolism [45]. However, taking DMAA can raise blood pressure and lead to cardiovascular problems ranging from tachycardia, cardiac arrest, heart attack, stroke, to cerebral hemorrhage. In the severe cases, it may also lead to acute liver injury and liver failure [46]. Consequently, a number of sporting authorities and countries have banned or heavily restricted the use of DMAA as a dietary supplement. In recent years, compounds such as 1,3-dimethylbutylamine (DMBA) [47], 1,4-dimethylpentylamine, and 2-amino-6-methylheptane [48] that share structural similarity to DMAA have been added to sports nutrition products, yet no proven studies have been done to confirm their biosafety and effectiveness. As such, the addition of these agents to such products violates standing regulations.

**3.4.3.4. Sibutramine, ephedrine and methylhexanamine.** Somatotropin (STH) is chemically known as *N*-l-(1-chlorophenyl)-3-methylbutyl-N, *N*-dimethylamine hydrochloride hydrate and its molecular composition is C<sub>17</sub>H<sub>26</sub>ClN·HCl·H<sub>2</sub>O. STH becomes a component in a novel weight-loss drug that suppresses appetite by regulating the central nervous system to reduce food intake. By inhibiting the reuptake of dopamine, norepinephrine, and serotonin, STH induces excitation of the satiety center in the hypothalamus, decreases fat storage and carbohydrate absorption, and increases muscle growth to some extent [49].

Methylhexanamine (MHA) is a simple aliphatic amine and vasoconstrictor that can be administered by inhalation to the nasal mucosa to exert its effect as a nasal decongestant. It is also used to treat hypertrophy or hyperplastic oral tissues. MHA is widely used as a dietary supplement under trade names like Forthane, Forthan, Floradrene, and dimethylhexaneamine. In 2010, it was included in the WADA prohibited list, and remained as stimulant prohibited in competition from 2011 to 2013. According to WADA's laboratory annual report in 2010, the number of positive cases for MHA (123 cases reported) was the highest among other stimulant drugs, accounting for 21.4 % of all stimulants detected in anti-doping tests. In the next year, 2011, it again topped the list of stimulants, with 283 positive cases reported, comprising 39.4 % of all [50].

Ephedra contains a large number of chemical constituents, predominantly in the form of alkaloids, including ephedrine, pseudoephedrine, *N*-methyl ephedrine, *D*-*N*-methyl pseudoephedrine, norpseudoephedrine, *D*-norpseudoephedrine, and ephedine, among others [51].

STH, ephedrine, and MHA are representative additives in health products. According to statistics from the laboratories accredited by WADA, MHA is the most commonly used prohibited substance in the stimulant category, causing over 10 % of all positive drug tests in competitive sport. Both in international and domestic sporting events, athletes have been found positive for MHA over the years. Ephedrine-type alkaloids are present in traditional Chinese medicine and are often added as ingredients in dietary supplements. STH is a newly discovered illegal additive that has been banned in recent years. It is very often detected during random inspections of health products and domestic doping tests.

According to the standards of the General Administration of Sports, food additives in synthetic nutritional supplements must meet regulatory requirements [52–58]. However, related regulations on synthetic nutritional supplements in China still need to be refined to ensure better enforcement. The market is still flooded with subpar products with exaggerated advertising and some products even contain illegal additives harmful to human health. The sellers exploit consumers' lack of knowledge and understanding [59] and athletes are among these consumers. Athletes often consume certain synthetic nutritional supplements to improve or maintain their condition during training and competition. For them, the quality of synthetic nutritional supplements is of great importance. If they inadvertently use substandard nutritional supplements, they may be tested positive for stimulants and face suspension. Their results in competition may also be invalidated. The consumption of such products will not only harm their health but also their careers.

#### 4. Summary

As many stages and subjects are involved in the food chain, a specific type of stimulants may be present in this complex process and it is difficult to analyze and confirm their presence. To meet the requirements and prevent PEDs from entering the food supply at major sporting events, it is necessary to monitor the veterinary drugs and plant-derived foods. These measures include: (1) continuous monitoring of veterinary drugs and plant-derived ingredients that have been banned or suspended in China; (2) cautious of the nature and potential modulatory effects of performance-enhancing drugs in newly approved veterinary drugs and plant-based ingredients; (3) timely updating the list of illegal animal- and plant-derived ingredients; (4) mindful of substances that share similar structures or functional features with the existing PEDs. Regarding to the risks of the additives in synthetic nutritional supplements: First, we need to take steps to enhance supervision and law enforcement. Relevant departments should improve supervision and management to ensure the quality of sports nutrition products on the market. They should strictly control food products that contain banned substances, increase the frequency of random inspections, standardize market entry modes, and reduce the severity and prevalence of products' side effects. Secondly, the government should strengthen rules on illegal advertising of health products, guide the public to make rational consumption decisions and encourage people to eat healthy balanced diets to meet nutritional needs. Laws and regulations should be strictly enforced to punish producers who overstate the efficacy and safety of their products, or add prohibited substances to their products. Third, teams must fully understand the types of available sports foods, know the benefits and risks of active ingredient substances, ensure food safety, and prevent unintentional ingestion of foodborne performance-enhancing drugs. By regularly updating the list of prohibited substances, athletes can be protected from potential harms to their health and doping issues, so that they can perform outstandingly in international sporting events.

Preventing unconscious intake of foods containing doping substances is a key issue for athletes and hosts of major sporting events. It is both about food safety and the prevention of doping. Stimulants are not only present in drugs but also in foods, and athletes who consume such foods may be disqualified from sporting events and experience adverse health effects. The sources of stimulant contamination include animal-derived foods, plant-derived foods, and synthetic nutritional supplements. Performance-enhancing drugs (PEDs) that appear in animal-derived foods include  $\beta$ -agonists, anabolic steroids, and glucocorticoids, which are commonly found in the reproductive organs of animals for meat production, such as ox. PEDs that appear in plant-derived foods include alkaloids, higenamine, and zeranol. They can be found in coffee, tea, Sichuan peppercorns, custard apples, and grains. Synthetic nutritional supplements add stimulants like creatine, traditional Chinese herbs, 1,3-dimethylamylamine (DMAA), sibutramine, ephedrine, methylhexanamine and others. Athletes should be cautious about what they eat, and receive regular and targeted anti-doping education to understand the potential risks of certain food products. It is also necessary to track the world's latest standards and regulations about PEDs, and prohibited substances and ingredients in food products. Moreover, a comprehensive and updated list of foodborne doping substances should be created, while further research on detection methods for food-derived stimulants should be carried out to provide technical support for the control of foodborne performance-enhancing drugs in major sporting events in China.

#### Data availability statement

The data used to support the findings of this study are all in this manuscript.

#### Ethics declarations

Review and/or approval by an ethic committee was not needed for this study, because the subjects of this study do not involve research on humans and the primary study subjects are food.

#### Additional information

No additional information is available for this paper.

#### CRediT authorship contribution statement

**Maoqiong Wei:** Conceptualization, Data curation, Formal analysis, Writing – original draft. **Ju'an Wang:** Formal analysis, Methodology, Writing – original draft, Writing – review & editing.

#### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

#### References

- [1] N.A. Ghaphery, Performance-enhancing drugs, *Orthop. Clin. N. Am.* 26 (3) (1995) 433–442.
- [2] M. Lusetti, M. Licata, E. Silingardi, A. Bonsignore, C. Palmiere, Appearance/image-and performance-enhancing drug users: a forensic approach, *Am. J. Forensic Med. Pathol* 39 (4) (2018) 325–329, <https://doi.org/10.1097/PAF.0000000000000424>.

- [3] A. Ostovar, M.J. Haerinejad, M.R. Farzaneh, M. Keshavarz, Adverse effects of performance-enhancing drugs on the kidney in the male bodybuilders, *Sci. Sports* 32 (2) (2017) 91–98, <https://doi.org/10.1016/j.scispo.2016.12.001>.
- [4] L.G. André, J.B. Maria, Cardiovascular effects of performance-enhancing drugs, *Circulation* 135 (2017) 89–99, <https://doi.org/10.1161/circulationaha.116.022535>.
- [5] K.H. McKeever, K. Malinowski, C.K. Fenger, W.C. Duer, Maylin GA. Evaluation of cobalt as a performance enhancing drug (PED) in racehorse 16 (4) (2020) 243–252.
- [6] S.A. Brave, K.A. Roberts, The competitive effects of performance-enhancing drugs: MLB in the posttesting era, *J. Sports Econ.* 20 (6) (2019) 747–781.
- [7] G. Jalleh, R.J. Donovan, I. Jobling, Predicting attitude towards performance enhancing substance use: a comprehensive test of the Sport Drug Control Model with elite Australian athletes, *J. Sci. Med. Sport* 17 (6) (2014) 574–579.
- [8] L. Yuan, Current situation and future development trend of sports nutrition food, *China Food Safety Magazine* 36 (2018) 43.
- [9] R.M. Daniel, Nutrition to support recovery from endurance exercise: optimal carbohydrate and protein replacement, *Curr. Sports Med. Rep.* 14 (4) (2015) 294–300.
- [10] T.M. McLellan, S.M. Pasiakos, H.R. Lieberman, Effects of protein in combination with carbohydrate supplements on acute or repeat endurance exercise performance: a systematic review, *Sports Med.* 44 (4) (2014) 535–550.
- [11] H. Ai, Review of current sports nutrition research, *Chin J Sports Med* (3) (2010) 228.
- [12] M. Li, Analysis of 3 kinds of  $\beta$ -stimulants in animal food by rapid test card and enzyme-linked immunosorbent assay kit, *Chin Food Ind* (7) (2020) 2.
- [13] D.W. Li, Research progress on the effect of clenbuterol on the physiological function of athletes and its detection methods, *J Food Saf Qual* 10 (7) (2019) 1965–1968.
- [14] X. Sun, X. Sun, L. Zhai, K. Song, Discussion on the harmfulness and prevention and control measures of veterinary drug abuse, *Chinese Journal of Animal Husbandry and Veterinary Medicine* 502 (10) (2018) 14–16.
- [15] L. Guo, Current situation and analysis of veterinary drug residues in livestock and poultry products, *Chinese Journal of Animal Husbandry and Veterinary Medicine* (3) (2019) 140.
- [16] World Anti-Doping Agency (WADA), Anti-doping Rule Violations (ADRVs) Report, WADA, Montreal, 2018, pp. 5–60.
- [17] World Anti-Doping Agency (WADA), World Anti-doping Code 2015with 2019 Amendments, WADA, Montreal, 2019, pp. 99–261.
- [18] M. Thalmayr, Analysis of non-hormonal nutritional supplements for anabolic-androgenic steroids-results of an international study, *J. Sports Med.* 25 (2) (2004) 124–129.
- [19] C.R. Casey, W.C. Andersen, N.T. Williams, T.J. Nickel, P.R. Ayres, Multiclass, multiresidue method for the quantification and confirmation of 112 veterinary drugs in game meat (bison, deer, elk, and rabbit) by rapid polarity switching liquid chromatography-tandem mass spectrometry, *J. Agric. Food Chem.* 69 (4) (2021) 1175–1186.
- [20] Y. Shen, J. Zhang, J. Xie, J. Liu, In vitro assessment of corticosteroid effects of eight chiral herbicides, *Journal of Environmental Science and Health, Part B* 55 (1/3) (2020) 91–102.
- [21] World Anti -Dope Agency, Prohibited List. <http://www.wada-amea.org/en/>.
- [22] 2021-11-23[2022-05-16].<https://www.chinada.cn/contents/9/3263.html>.
- [23] Y. Li, J. Geng, T. Mu, Y. Xu, S. Xu, X. Liu, R. Sun, J. Ma, Analysis of food-derived doping based on the regulations on the use of veterinary drugs in animal-derived foods in China, *Food Sci. (N. Y.)* 43 (13) (2022) 319–325.
- [24] H.Y. Zheng, Y. Gao, H.B. Wang, Optimization of extraction process and antioxidant activity of caffeine from okra seeds, *Food Sci Technol* 41 (6) (2016) 230–236.
- [25] M. Xu, Study on Extraction and Antifatigue Activity of Alkaloids from Okra Seeds, Jilin Agricultural University, Changchun, 2014.
- [26] M. Jiang, C. Liu, R. Gong, Research progress on caffeine, *Agricultural Engineering Technology (Agro-processing Industry)* 10 (2009) 34–36.
- [27] H. Li, R. Chen, D. Zhou, L. Wu, Synthesis and pharmacological effects of caffeine: research progress, *West China J. Pharm. Sci.* 26 (2) (2011) 182–187.
- [28] J. Zhai, W. Cui, J. Zhu, Recent advances on the study of the poisoning, analysis and application of caffeine, *Chin. J. Forensic Sci.* (5) (2017) 30–35.
- [29] F. Lin, J. He, Research progress of coffee and health, *Journal of Health Care Research and Practice* 16 (4) (2019) 15–18.
- [30] P. Guo, Y. Yue, Y. Gao, S. Liu, J. Leng, Pharmacological activity and metabolism of major benzyloquinoline alkaloids: research progress, *Journal of Logistics University of PAP (Medical Sciences)* 28 (12) (2019) 70–76.
- [31] K. Grucza, K. Kowalczyk, M. Wicka, M. Szutowski, E. Bulska, D. Kwiatkowska, The use of a valid and straightforward method for the identification of higenamine in dietary supplements in view of anti-doping rule violation cases, *Drug Test. Anal.* 11 (6) (2019) 912–917.
- [32] K.V. Rangelov, K. Ivanov, S. Ivanova, Higenamine in plants as a source of unintentional doping, *Plants* 11 (3) (2022) 354.
- [33] C. Yen, C. Tung, C. Chang, C.C. Tsai, M.C. Hsu, Y.T. Wu, Potential risk of higenamine misuse in sports: evaluation of Lotus Plumule extract products and a human study, *Nutrients* 12 (2) (2020) 285.
- [34] R. Wang, X. Xiong, M. Yang, S. He, X. Xu, A pharmacokinetics study of orally administered higenamine in rats using LC–MS/MS for doping control analysis, *Drug Test. Anal.* 12 (4) (2020) 485–495.
- [35] O.T. Soyelu, A.O. Aderibigbe, The effects of zeranol and oestradiol implants on performance and nutrient digestibility of zero-grazed White Fulani cattle, *Animal Production Science* 60 (8) (2020) 1081–1086.
- [36] Ministry of Agriculture and Rural Affairs, Announcement No.250 of the Ministry of Agriculture and Rural Affairs of the People's Republic of China (list of drugs and other compounds prohibited to be used in food animals), *China Feed Additives* (2) (2020) 47–50.
- [37] K. Walpurgis, A. Thomas, H. Geyer, U. Mareck, M. Thevis, Dietary supplement and food contaminations and their implications for doping controls, *Foods* 9 (8) (2020) 1012.
- [38] D. Davani-Davari, I. Karimzadeh, S. Ezzatzadegan-Jahromi, M. Sagheb, Potential adverse effects of creatine supplement on the kidney in athletes and body builders, *Iranian journal of Kidney Diseases* 12 (5) (2018) 253–260.
- [39] R.B. Kreider, D.S. Kalman, J. Antonio, T.N. Ziegenfuss, R. Wildman, R. Collins, D.G. Candow, S.M. Kleiner, A.L. Almada, H.L. Lopez, International society of sports nutrition position stand: safety and efficacy of creatine supplementation in exercise, sport, and medicine, *Sports Nutr. Rev. J.* 14 (1) (2017) 18.
- [40] N. Bakhiya, R. Ziegenhagen, K.I. Hirsch-Ernst, B. Dusemund, K. Richter, K. Schultrich, S. Pevny, B. Schäfer, A. Lampen, Phytochemical compounds in sport nutrition: synephrine and hydroxycitric acid (HCA) as examples for evaluation of possible health risks, *Mol. Nutr. Food Res.* 61 (6) (2017), 1601020.
- [41] L.G. Rossato, V.M. Costa, R.P. Limberger, L. Bastos Mde, F. Remião, Synephrine: from trace concentrations to massive consumption in weight-loss, *Food Chem. Toxicol.: An International Journal Published for the British Industrial Biological Research Association* 49 (1) (2011) 8–16.
- [42] L.O. Chuah, W.Y. Ho, B.K. Beh, S.K. Yeap, Updates on antiobesity effect of garcinia origin (-)-HCA, *Evid. base Compl. Alternative Med.* (2013), 751658.
- [43] Z. Tian, Y. Zhang, Z. Zheng, M. Zhang, T. Zhang, J. Jin, X. Zhang, G. Yao, D. Kong, C. Zhang, Z. Wang, Q. Zhang, Gut microbiome dysbiosis contributes to abdominal aortic aneurysm by promoting neutrophil extracellular trap formation, *Cell Host Microbe* 30 (10) (2022) 1450–1463.
- [44] Q. Guo, T. Li, Y. Qu, M. Liang, Y. Ha, Y. Zhang, Q. Wang, New research development on trans fatty acids in food: Biological effects, analytical methods, formation mechanism, and mitigating measures, *Prog. Lipid Res.* 89 (2023), 101199.
- [45] S. Eichner, M. Maguire, L.A. Shea, M.G. Fete, Banned and discouraged-use ingredients found in weight loss supplements, *J. Am. Pharmaceut. Assoc.* 56 (5) (2016) 538–543.
- [46] L.V. Karnatovskaia, J.C. Leoni, M.L. Freeman, Cardiac arrest in a 21-year-old man after ingestion of 1,3-DMAA-containing workout supplement, *Clin. J. Sport Med.* 25 (1) (2015) e23–e25.
- [47] P.A. Cohen, J.C. Travis, B.J. Venhuis, A synthetic stimulant never tested in humans, 1,3-dimethylbutylamine (DMBA), is identified in multiple dietary supplements, *Drug Test. Anal.* 7 (1) (2015) 83–87.
- [48] P.A. Cohen, J.C. Travis, P.H.J. Keizers, P. Deuster, B.J. Venhuis, Four experimental stimulants found in sports and weight loss supplements: 2-amino-6-methylheptane (octodrine), 1,4-dimethylamylamine (1,4-DMAA), 1,3-dimethylamylamine (1,3-DMAA) and 1,3-dimethylbutylamine (1,3-DMBA), *Clin. Toxicol.* 56 (6) (2018) 421–426.



- [49] I.C. Hwang, J.Y. Park, H.Y. Ahn, et al., Effects of CYP3A5, CYP2C19, and CYP2B6 on the clinical efficacy and adverse outcomes of sibutramine therapy: a crucial role for the CYP2B6 allele, *Clin. Chim. Acta* 428 (4) (2014) 77–81.
- [50] Z. Wang, J. Zhang, Y. Zhang, Screening and confirmation of methylhexanamine in sports supplements through gas chromatography-mass spectrometry, *Chinese Journal of Sports Medicine* 33 (10) (2014) 1004–1008.
- [51] L. Zhou, J. Chen, J. Chen, C. Chen, Effect of ephedrine and methoxyphen in stabilizing heart rate and blood pressure of elderly patients undergoing lower extremity orthopaedic operation with tourniquet, *Journal of Beihua University (Natural Science)* 21 (4) (2020) 510–513.
- [52] GB, National Food Safety Standard-Standards for the Use of Food Additives, 2760, 2014.
- [53] GB, National Food Safety Standard-General Principles for Compound Food Additives, 26687, 2011.
- [54] GB, National Food Safety Standard-General Rules for Nutrition Labelling of Prepackaged Food, 28050, 2016.
- [55] GB, National Food Safety Standard-Prepackaged Special Dietary Food Labels, 13432, 2013.
- [56] SN/T, General Rules for the Inspection of Import and Export Prepackaged Food, 1642, 2005.
- [57] GB, National Food Safety Standard-Health Food, 16740, 2014.
- [58] GB/T, National Food Safety Standard-General Rules for Sports Nutrition, 24154, 2015.
- [59] Y. Cui, H. Zhang, Y. Han, Analysis on risk factors of sports nutrition food quality and safety, *Modern Food* (22) (2020) 31–33.