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Sports supplements: a health risk?

Suplementos deportivos: ¿riesgo a la salud?

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ABSTRACT

Sports supplements are a category of dietary supplements that in recent years has not only increased in quantity and availability, but also in the number of new products. Athletes of all levels are interested in the consumption of supplements that are useful to increase muscle mass gain, thus making the consumption of these products a frequent practice. Unfortunately, there are some products that are doping substances which are offered as sports supplements; on the other hand, certain sports supplements may contain active pharmaceutical ingredients, or their analogues, not declared in their ingredients to effectively enhance the benefits that these products ensure, exposing consumers to a significant potential health risk, especially those unfamiliar with sports supplements. It is important that health professionals are aware of the possible implications of consuming certain products offered in the sports nutrition market when evaluating their patients for a variety of pathologies.

Keywords: dietary supplements, sports supplements, ergogenic aids, doping substances, adulteration, contamination

RESUMEN

Los suplementos deportivos son una categoría de los suplementos alimenticios que en los últimos años no solo ha incrementado en cantidad y disponibilidad, sino también en el número de nuevos productos. Deportistas de todos los niveles se interesan en el consumo de suplementos que son útiles para incrementar la ganancia de masa muscular convirtiendo así el consumo de estos productos en una práctica común. Desafortunadamente existen algunos productos que en realidad son sustancias dopantes que son ofertadas como suplementos deportivos, por otra parte ciertos suplementos deportivos pueden contener sustancias con actividad farmacológica o sus análogos no declarados en sus ingredientes probablemente para potenciar de manera efectiva los beneficios que estos productos aseguran, exponiendo a los consumidores a un riesgo potencial significativo a la salud, sobre todo a aquellos que no están familiarizados con los suplementos deportivos. Es importante que los profesionales de la salud tengan el conocimiento de las posibles implicaciones por el consumo de ciertos productos ofertados en el mercado de la nutrición deportiva al momento de evaluar a sus pacientes para una variedad de patologías.

Palabras clave: suplementos alimenticios, suplementos deportivos, ayudas ergogénicas, sustancias dopantes, adulteración, contaminación

INTRODUCTION

An adequate nutrition is a key component to optimize sports performance, since individual nutritional needs differ widely depending on the type of sports discipline, sports training period, training days and rest, among other factors. The nutritional strategies implemented include adjustments in energy balance, proportion and nutrient timing, as well as supplementation (Bytomski, 2018). Dietary supplements, also known as nutritional or food supplements, are a category of food products that include over-the-counter formulations consumed in addition to the usual diet, with the aim of providing additional nutrients (Augustin and Sanguansri, 2012).

The companies that market these products, associates their properties to the wide variety of ingredients in the different formulations, such as improvement in the general state of health, enhancement of the physical and mental performance, increased energy, weight loss, decreased pain and other favorable effects (Knapik *et al*., 2016b), although the need and efficacy of certain ingredients remains under considerable debate (Kerksick *et al*., 2018). Dietary supplements should not contain active pharmaceutical ingredients in their formulation, since these are used to diagnose, prevent, or cure a disease. These products are not drugs and should not make any of the above claims (Edenfield, 2020).

For most countries and regions worldwide, dietary supplements are regulated as a food category. When attempting to bring a product to the market, a notification or registration-based system is required for its approval, the acceptance and safety of the product depends in great part on the ingredients used in the formulation, which are ruled by the requirements in food additives considered by local regulations such as the Federal Commission for the Protection against Sanitary Risks (COFEPRIS) in the case of Mexico and the Food and Drug Administration (FDA) in the United States of America. This approach contrasts with the premarket approval approach required for drugs in most countries, and appropriately fits the category of foods, as these inherently pose low safety risks relative to drugs (Shao, 2017).

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In sports sciences, dietary supplements are considered nutritional ergogenic aids (Lopez-Samanes *et al*., 2015) since some of these products have an impact in the improvement of physical-athletic performance, which is the reason of why they are also known as sports supplements (Jovanov *et al*., 2019).

A wide variety of these products are available in the market ensuring that they improve the physical performance, but only a few have scientific evidence of their benefits, in addition to the fact that the performance improvements are a function of the type of sports practice, competition level and timing at which they are consumed, which can vary widely between individuals due to several factors, including age, sex, genetics, intestinal microbiota, regular diet, among others (Maughan *et al*., 2018).

The sports supplement industry is constantly growing and over the last decades its consumption has increased considerably, estimating that the global sports nutrition market will reach approximately 34.5 billion dollars by 2028, mainly due to the increase in product demand by bodybuilders and other athletes (Grand View Research, 2020). However, the constant innovation in these products by manufacturers to catch and keep consumers' attention, as well as trends of interest, may carry a risk in pleasing consumers in terms of what they firmly believe they need to improve their physical performance (Garthe, 2019).

SPORTS SUPPLEMENTS

Sports supplements are products formulated with food-source ingredients, as well as nutrients that are ingested in addition to the regular diet in an adequate effective dose, that can be used in certain specific training phases with the purpose of increasing physical performance by improving adaptations to exercise, skills, recovery capacity and correction or prevention of nutritional deficiencies, as well as aiding in the body composition improvement, helping individuals to train and compete more effectively (Muñoz Maldonado *et al*., 2021). These products can be classified according to their level of scientific evidence (Garthe and Maughan, 2018), although probably the most widely known classification by its consumers is the bodybuilding supplement classification (Navarro *et al*., 2014). Previous research has documented that the most popular supplements consumed by bodybuilders include protein and peptide-based supplements, branched chain amino acids (BCAAs), individual amino acids, polyunsaturated fatty acids (PUFAs), complex, oligomeric, or simple carbohydrates-based supplements, individual or complex vitamins and minerals, creatine, "pre-workout" supplements, "fat burners", supplements for "joint health", "testosterone boosters", among other supplements rarely used to be classified (Chappell *et al*., 2019; 2018).The consumption and type of these products vary widely between practitioners and sports disciplines, especially in those where strength and power predominate, where the use of supplements can be considered a rule (Maughan *et al*., 2004),

Prevalence of sports supplements consumption

Sports nutrition market primarily targets three diverse types of consumers:

a) Bodybuilders and other professional athletes who seek to increase muscle mass through the combination of high calorie intake and resistance training (also known as weight training).
b) Recreational athletes, since most of them do physical exercise as a hobby or are "fitness" enthusiasts, even though they do not achieve the same levels of physical effort as professional athletes.
c) Consumers with healthy lifestyles, who do not necessarily use these products for improving their physical performance since they incorporate these supplements into their lifestyle to improve their health, replace food with beverages, nutritional bars, among others.

To attract consumers, sports nutrition companies continue to innovate their marketing and product strategies to offer products with high expectations (Agriculture and Agri-Food Canada, 2019). Unfortunately, it is difficult to obtain a complete description of the consumption prevalence of these products since different data collection methods have been used in the many studies related to this topic. When supplement use is pooled by sport discipline, sport populations, as well as the various supplement classifications, there is high variability between studies. In general, the use of supplements among men and women who are professional athletes is 69% and 71% respectively, whereas for recreational athletes is 48% and 42%, thus being similar the consumption of these products among people from both groups. Furthermore, some athletes tend to consume supplements in up to 100% of individuals depending on the type of sport and the level of competition (Knapik *et al*., 2016a). On the other hand, among recreational teen athletes, around 60% have mentioned the use of sports supplements, 42% of which, state using more than one type of supplement with high frequency of consumption, and up to 86% do not verify the nutritional label of the chosen supplement (Tsarouhas *et al*., 2018).

In the case of bodybuilders, up to 87% of these athletes at the amateur level are consumers of sports supplements (Montuori *et al*., 2021), while of professional bodybuilders, 100% use these products (Sánchez-Oliver *et al*., 2019). Recently, other sports disciplines at a professional level have exhibited a high prevalence of consumption such as cycling (86%), watersports (77%), and weightlifting (75%). In turn, in team sports such as American football and soccer, similar frequencies of up to 57% and 75% have been observed, respectively (Baltazar-Martins *et al*., 2019). Interestingly, in athletics, long and medium distance athletes are the largest consumers of sports supplements with frequencies of 76% and 72%, respectively, followed by sprinting and obstacle course with up to 58% in both disciplines (Tabata *et al*., 2020).

A large part of the studies related to the consumption prevalence of these products concludes a marked trend

towards greater use of sports and herbal supplements. In general, athletes have conventionally been the largest consumers of sports supplements, representing more than a third of the overall market. However, the growing population of recreational athletes and individuals with a "fitness" lifestyle creates a new dimension of potential consumers for the manufacturers and sellers of these products, with an increasing trend of multi-ingredient supplements and varied content of biologically active compounds (Garthe, 2019). Another aspect to be considered is the commonness of the situation in which consumers exceed the recommended doses and timing of supplement consumption, which may be due to the belief that "more is better" (Maughan *et al*., 2004). Moreover, it is a fact that supplementation is a frequently self-prescribed practice and without adequate medical or nutritional assessment, since the relevant information and recommendations usually come from other athletes, personal trainers, friends, or even relatives (Tsarouhas *et al*., 2018). Likewise other media such as bodybuilding magazines (Iraki *et al*., 2019), as well as online resources such as forums and social networks, are important sources of information and influence, although unfortunately the information presented in these media does not always have scientific support (Waller *et al*., 2019).

Although estimates of the general use of dietary supplements are available in national surveys, these studies have used different categorizations, and most lacking specific data for these products (Geller *et al*., 2015). It is important to note that during 2008, Mexico was the second largest international market for sports supplements with 192 million dollars in sales to retailers alone. If we consider that sports supplements sales have increased significantly, it would not be surprising that currently our country continues to maintain or has even surpassed this position (Muñoz Maldonado *et al*., 2021).

PERFORMANCE-ENHANCING DRUGS OFFERED AS SPORTS SUPPLEMENTS

Currently, a wide range of possible performance-enhancing substances is available, mostly offered through the internet as sports supplements (Joseph and Parr, 2014), as "safe" and "legal" alternatives to performance-enhancing drugs (Abbate *et al*., 2015). This, present a high prevalence of consumption by, but not limited to, bodybuilders (Sánchez-Oliver *et al*., 2019), and between sports where strength and power predominate (Jokipalo and Khudayarov, 2021).

As such, these products from the black market often contain active pharmaceutical ingredients without prior authorization by the corresponding national regulatory entities, no clinical approval and/or even without authorization for human use, and therefore without a known complete toxicological profile. Additionally, the lack of quality control and the incorrect labeling of these products implies potential health risks, although unfortunately, this situation does not limit the use and abuse by the consumers. Although until the early 2000s these products were almost exclusively steroidal prohormones and designer steroids, nowadays the selective androgen receptor modulators (SARMs) are also available, which are synthesized from several pharmacophores (Geldof *et al*., 2017).

Designer steroids

Taking advantage of the ease and convenience for obtaining food supplements, certain manufacturers carry out chemical modifications to existing anabolic androgenic steroids (AAS), in order to avoid legal controls regarding the manufacture and supply of current medicines; the synthesized compounds are called "designer steroids" and are marketed as sports supplements (Voelker *et al*., 2019). The term "designer drug" was originally introduced to describe new substances that are synthesized from known substances of abuse, preserving, or enhancing pharmacological effects while remaining outside of legal control; currently this term is broadened to include substances that are derived from industrial or academic research, but never receive medical approval. Some designer drugs may be approved in some countries, and in a strict sense, they should not be considered as such as they do not conform to the classical definition (Luethi and Liechti, 2020). Designer steroids are offered as supplements or ingredients in some of these products for muscle mass gain, commonly referred to misleading and incorrect terms such as "testosterone boosters", "natural steroids" and "prohormones" (Rahnema *et al*., 2015). The term prohormone refers to the precursors, in this case, of the steroid hormone testosterone such as dehydroepiandrosterone (DHEA), androstenedione, androstenediol or other similar compounds. They have also been sold as "andro-supplements", stating that these active ingredients are converted into testosterone or its analogues, to improve adaptations to resistance training. Even though it has been shown that the use of steroidal prohormones does not provide any ergogenic benefit, their use is widely extended, despite their consumption is prohibited by the World Anti-Doping Agency (WADA) and different sports governing organizations (Brown *et al*., 2006).

Designer steroids are typically manufactured and sold by smaller scale companies that often dissolve or change their name when they meet resistance from regulatory agencies (Rahnema e*t al*., 2015). In the United States, the Designer Anabolic Steroid Control Act of 2014 expanded the list of anabolic steroids regulated by the Drug Enforcement Administration (DEA), thus decreasing their sale and acquisition. However, the continued synthesis of new designer steroids by manufacturers means that these compounds are not on the current banned substance lists (Brown, 2017).

Just like testosterone, designer steroids share common mechanisms of action by interacting at the androgen receptor, as well as aromatization and 5-α reduction for some of these compounds. Like all androgens, the parameters by which they are characterized differ among the different compounds as they exhibit varying proportions of anabolic and androgenic activity. Most designer steroids are formulated to

be consumed orally with varying degrees of bioavailability through 17-α alkylation, however this modification increases the compound toxicity. On the other hand, it seems that the benefits from the use of these products are minimal and even non-existent, compared to the considerable number of adverse health effects. Like exogenous androgens, designer steroids have the potential to cause reversible adverse effects such as hypertension, secondary hypogonadism, infertility, as well as polycythemia and adverse changes in lipoprotein subfractions. There is evidence that some designer steroids can cause more permanent adverse effects, such as hepatotoxicity, cardiotoxicity, and ischemic stroke (Rahnema et al., 2015). It is noteworthy to mention that evaluations of their side effects or metabolism in humans is scarce, making the continuous synthesis of new compounds even more difficult to determine. In addition to the above mentioned effects, designer steroids may also show side effects related to the activation of other steroid receptors, such as the glucocorticoid receptor (Joseph and Parr, 2014). Since designer steroids are derived from anabolic androgenic steroids, their use has been banned by sports' governing organizations since athletes who consume these products may result in a positive doping test for anabolic steroids (Kazlauskas, 2010).

A study published in the UK (Abbate *et al*., 2015) investigated the presence and estimate of specific active substances amounts present in a total of 24 "prohormone supplements" selected according to information available on the internet from sellers, bodybuilding forums discussing these products, as well as consumers familiar with these products. The samples were purchased from different distributors such as gym equipment stores and online stores that claimed on the product label the different designer steroids content. Of the samples analyzed, one of them did not contain any steroids and about 70% were substituted products containing classic steroids (such as DHEA, methyl-1-testosterone, 4-androstenedione, desoxymethyltestosterone, methasterone, androst-4-en-3, 11,17-trione and furazabol) other than those indicated on the label. In addition, the spelling of some of the chemical names for the active compounds was incorrect, probably in order to hide the true ingredients from both consumers and regulatory agencies. All identified compounds were controlled or potentially controlled substances in the UK under the Misuse of Drugs Act 1971. Furthermore, the estimated amounts for 17-alkylated steroids equaled or exceeded the established therapeutic doses for this type of drugs.

Selective androgen receptor modulators

In an attempt to mitigate the risks associated with the administration of testosterone and other AAS in pathologies that result in the loss of muscle mass and function, as well as in hormone replacement therapies, SARMs were developed, which have a targeted therapeutic effect through binding to the androgen receptor in muscle and bone tissues (Thevis and Schänzer, 2018). The pharmacophores present in SARMs have an unprecedented potential for chemical modifications, these include steroidal substances such as testosterone itself and non-steroids such as aniline, aryl-propionamides, benzimidazole, bicylclic hydantoins, bridged tricyclics, diarylaniline, indole, quinolones, tetrahydroquinolones, tricyclics and pyrazoline derivatives (Machek *et al*., 2020).

In various clinical trials, certain SARMs have shown improvements in fat-free mass in healthy men, sarcopenic and postmenopausal women, as well as the cancer population, although the effects on the muscular strength and physical performance increase remain inconsistent, and with unknown effects of its long-term use. Just like androgens, SARMs have adverse effects, although to a lesser degree compared to the use of testosterone. In clinical trials, a decrease in high-density lipoproteins (HDL), hepatotoxicity with an increase in liver transaminases and alterations in plasma levels of anabolic hormones involved in the hypothalamic-pituitary-gonadal axis have been reported. To date, and despite their clinical potential, none of the existing SARMs are approved for human use in any country, even though some have progressed to phase II and III trials (Fonseca *et al*., 2020). Unfortunately, SARMs have attracted the attention of athletes as novel compounds due to their anabolic effects and few side effects, and because of this, the WADA has placed SARMs on the list of banned substances since 2008 due to the potential high risk of abuse (Temerdashev and Dmitrieva, 2020).

There are two recent studies (Leaney *et al*., 2021; Van Wagoner *et al*.,2017) conducted to contrast the precision of the labeling with respect to composition and concentration, considering the claims of various products offered as SARMs. It is worth mentioning that in the samples from both investigations up to 20 – 55% of the products mentioned the liability exemptions of "not suitable for human consumption" and/or "for research purposes only", nevertheless, some of them detailed the information of the suggested portion. Also, between 45 – 85% of the products were sold as sports supplements and some of the products were stacks containing different multiple SARMs.

A study carried out in the United States of America (Van Wagoner *et al*., 2017) reported that 44 products purchased from 21 online distributors in the same country were analyzed. Some manufacturers and distributors used the term SARM on the product label and advertising, although they were not selective modulators of androgen receptor. These included the agonist compounds of the peroxisome proliferator-activated receptor gamma (PPARδ) GW501516, growth hormone secretagogue ibutamoren, nuclear receptor agonist Rev-ErbA-α SR9009, and the anabolic compound 5α- hydroxy-laxogenin, all of them included in the WADA list of prohibited substances and without scientific evidence of the efficacy or safety of these substances. Chemical analysis determined that, of the 44 products, 73% matched the active substance indicated on the label, however, only 18 products contained the declared amount, three products contained additional prohibited substances, and 11 products differed with a lower amount. Furthermore, in eight products, the

active substances were not found, but were replaced by other prohibited substances in lower amounts, and in four products, no active substances were found.

Similar findings were found in the UK (Leaney *et al*., 2021), derived from an analysis of 20 products available in the UK market purchased from 12 manufacturers online. Of the total of the products evaluated, only 30% were consistent with the label content, while 35% had at least one active substance absent in the content. In addition, two products substituted with different prohibited active substances, one product did not contain the presence of any active substance, and nine products with amounts less than those indicated.

HEALTH CONCERNS RELATED TO THE CONSUMPTION OF SOME SPORTS SUPPLEMENTS

It is important to know that certain sports supplements may contain substances prohibited by WADA, which are performance-enhancing drugs not labeled in the ingredients of the product (Martínez-Sanz *et al*., 2017; Rocha *et al*., 2016), and they can even contain plant compounds that have no history of human useage and are often used as ingredients to mask banned substances (Jędrejko *et al*., 2021).

When the content of active ingredients in a supplement is variable, it is due to inadequate quality control during the manufacturing process. However, there is also evidence that some products do not contain the indicated amount of the highest value ingredients declared on the label and, in some cases, the active ingredient is completely absent and the product contains only low-cost materials, even relatively inexpensive ingredients may be absent or present in trivial amounts (Maughan *et al*., 2011). Poor manufacturing practices can likely lead to cross-contamination of supplements on the same production line (Geyer *et al*., 2008), but in most cases it is deliberately by the manufacturers themselves in order to obtain more noticeable effects claimed by their product (Odoardi *et al*., 2015). Supplements that are intentionally added with illegal substances or with pharmacological activity not declared on the nutritional label are called adulterated supplements (Ronis *et al*., 2018). These products could be problematic as they expose professional athletes to inadvertent doping, as well as potential health risks for consumers in general, due to the inadvertent intake of substances with pharmacological activity. These risks go beyond the inherent effects of consuming these substances in high amounts, polypharmacy, and the fact that some of these are often not tested in humans and the effects when combined with exercise are unknown (Mathews, 2018).

The health consequences caused by adulterated and/or contaminated sports supplements are unclear, due to the lack of precise reports on adverse events. Also, some side effects are not acute events, but could appear as delayed and chronic health problems (Eichner and Tygart, 2016). The presented data in the case reports of adverse events associated with the use of adulterated sports supplements are difficult to collect, due to incomplete information such as the lack of the product name or manufacturer, and confounding variables such as drug addiction of the individual, concomitant medication, and other pre-existing risks. The main factors that influence the reliability of these reports are the product identity and quality, unfortunately most of the supplements are not properly identified, analyzed or characterized in the reports, which makes it difficult to assign or determine the product (Gardiner *et al*., 2008). Also, most patients do not report on supplement use, causing physician to be unable to identify associated adverse events as frequently as they do with pharmaceuticals, in addition to possible limited knowledge of drug-supplement interactions (Geller *et al*., 2015).

It is well known that the acquisition of sports supplements is due to their easy accessibility and availability through websites, supplement stores and gyms without the need for any type of prescription or clinical approval. Additionally, the number of supplements from the informal market has increased dramatically in recent decades due to high demand from consumers (Odoardi *et al*., 2015). An example of sports supplements that may present a greater risk of adulteration and/or contamination are supplements for muscle mass gain (Kulkarni *et al*., 2017; Pomeranz *et al*., 2015).

Sports supplements for muscle mass gain

These products have the objective of increasing the anabolic response in the muscle induced by resistance training, these include a wide variety of supplements with nutritional ingredients (Yager and McLean, 2020). Some products included in the supplement category for muscle mass gain are:

a) *Protein and multi-ingredient protein-based supplements*

Most of these products are milk, egg, and plant-based protein and peptide powders that are reconstituted with the addition of water, juice, or milk (De Ceglie *et al*., 2015). They are also found in combination with other safe and authorized nutritional ingredients, such as mixtures with different proteins and/or peptides, carbohydrates, amino acids (individual or combined), creatine, β-hydroxy-β-methylbutyrate (HMB), PUFAs, vitamins, minerals (O'Bryan *et al*., 2020), and some plant compounds (Directo *et al*., 2019), to mention just a few examples.

b) *Mass gainers, weight gainers or muscle gainers*

These hypercaloric supplements are designed for those individuals who find it difficult to gain muscle mass. Most of these products contain a high amount of carbohydrates and proteins making them a good replacement for some meals (Wójcicki, 2020).

c) *Testosterone boosters (T-boosters)*

They are supplements with different herbal ingredients in combination with minerals and vitamins, in complexes or individually, being the plant material Tribulus terrestris the most widely known (Balasubramanian *et al*., 2019; Santos *et al*., 2019). T-boosters claim to improve muscle strength and endurance while increasing blood testosterone levels,

as well as inhibiting its conversion to estrogen, thus stimulating muscle hypertrophy, statements from the internet or other means that try to encourage the use of T-boosters. The supposed beneficial effects is attractive for bodybuilders and professional athletes, however, the effectiveness and safety of these supplements is questionable (Herriman *et al*., 2017; Pokrywka *et al*., 2014). Various other ingredients and their combinations, to date, have not been shown to be conclusively effective in supporting the claims these products make (Clemesha *et al*., 2020).

Different international research groups have analyzed the undeclared presence of AAS, steroidal prohormonal compounds and designer steroids in sports supplements for muscle mass gain, since 1999 through chromatographic methods, due to the relationship between positive doping cases and sports supplements. Studies carried out in the early 2000s provided the first evidence that some non-hormonal supplements based on proteins, creatine and even vitamins and minerals had the presence of prohibited substances in around 15% of a sample of 634 supplements purchased from 13 countries, including 215 different distributors (Geyer *et al*., 2008). The presence of AAS as adulterants was reported with five steroid hormones in up to 18% of products, from a sample of 28 protein and amino acid supplements combining other permitted ingredients (Martello *et al*., 2007).

This situation seems to be highly prevalent in sports supplements for muscle mass gain, since currently, in the Netherlands, Duiven *et al*. (2021) evaluated a total of 66 products that claimed to modulate hormonal regulation, stimulate muscle mass gain, increase fat loss and/or increase energy, selected from 21 different brands and purchased from 17 online stores. A total of 21 products (32%) contained the presence of at least five different AAS, 1,4-androstenediene-3,17-dione (boldione) being mostly detected in 11 products, followed by 5-androstene-3β,17α-diol, in addition to DHEA, testosterone, and 5-androstenedione. On the other hand, in Iran (Alaedini *et al*., 2021) was determined that up to 37% of a sample of 30 non-hormonal sports supplements selected from 12 different brands, purchased in pharmacies and the formal market, contained at least one of the AAS. The greatest relevance in the list of substances banned from WADA found, included 4-androstenedione and methyl-1-testosterone. Also, stanozolol and 5α-hydroxy-laxogenin have been found in protein and amino acid supplements in South Korea (Lee *et al*., 2020) and in Italy, in up to 10% of products identified as amino acids. These, are also consumed by professional athletes, and are adulterated with DHEA, while the same percentage for herbal products have come to contain dehydroepiandrosterone acetate (DHEA-acetate), methylandrostenediol, clausterone, testosterone propionate, 5α-androstane-3α,17β-diol y progesterone (Micalizzi *et al*., 2021).

Designer steroids have also been found with increasing regularity, in products offered as all natural herbal supplements marketed for muscle mass and strength gain, as is the recently reported androsta-3,5-diene-7,17-dione, an aromatase inhibitor, which is included in the WADA banned list. Although little is currently known about the pharmacological effects and/or toxicity of this compound, its structure is similar to that of AAS which are known to cause significant health risks (Lorenz *et al*., 2019).

Supplements adulterated with these substances, should be considered for having significant pharmacological activity when consumed chronically. Health consequences of inadvertent use of steroidal prohormones and designer steroids (in addition to the adverse effects mentioned above), could include cholestasis, kidney failure, gynecomastia, acne, psychological dependence, among others. Ingestion by women could cause absence of menstruation, virilization, alopecia and clitoromegaly (Mathews, 2018). In adolescents, the risk is greater since consumption, even in insignificant amounts, can suppress testosterone production for months, as well as cardiovascular risks and mood alterations. Similarly, it can cause premature epiphyseal closure, brain remodeling and an increased risk of maladaptive behaviors and neurological disorders (Eichner and Tygart, 2016).

On the other hand, the SARM ostarine has been detected as an undeclared ingredient in several supplements, which opens the possibility that other SARMs are present as adulterants in sports supplements for muscle mass gain, leading to cases of inadvertent doping (Walpurgis *et al*., 2020),

Inadvertent doping prevention programs as tools for advice and recommendations when selecting sports supplements

According to current scientific evidence, the risk that any sports and dietary supplement, in general containing a variety of substances with undeclared pharmacological activity, is close to 15% of the total of these products (Outram and Stewart, 2015). Not only AAS have been found as adulterants, but also has a variety of substances such as phosphodiesterase-5 inhibitors and antihistamines, found in supplements to improve sexual performance and blood pressure respectively (Kim *et al*., 2017). Also found, are glucocorticoids and non-steroidal anti-inflammatory analgesics in herbal supplements for pain management (Garza-Ocañas *et al*., 2013), as well as sympathomimetic agents, anorectics, and pancreatic lipase inhibitors in weight loss supplements (Ronis *et al*., 2018). All of these substances are also prohibited by WADA since their consumption through these products has incurred in cases of positive doping, such is the case of Mexican professional athletes (Proceso, 2011).

Some programs try to protect athletes who consume sports supplements from inadvertent doping, the best known being the Sports Supplements Regulatory Framework of the Australian Institute of Sport (2021). This is designed for the specific needs of Australian sports organizations, to promote their use based on scientific evidence and other practical considerations that determine whether the product is safe, permissible and effective in enhancing athletic performance.

In recent years, laboratory tests for the detection of prohibited substances in sports supplements have been

available to anyone interested, such as athletes, sports organizations, national anti-doping agencies and manufacturers of these products (Garthe and Ramsbottom, 2020). Various third-party companies offer supplement analysis services for quality, purity, and composition. These must be free of conflicts of interest, have external accreditation, perform audits for good manufacturing practices, and have validated and accredited methods to analyze prohibited substances. When approved, the supplement brand will receive the corresponding approval seal to be displayed on the product label; some of these companies are Consumer Labs (consumerlab.com), National Sanitation Foundation (NSF.org), Banned Substances Control Group (bscg.org) and Informed-Choice/Informed-Sport (informed-sport.com). These companies offer a variety of services that include certification of facilities and raw materials, compliance with good manufacturing practices, label verification and testing of the final product. The cost of these services can be an issue for small companies and larger companies may not see any market advantage in certification and will not consider this additional scrutiny. However, it is impossible to affirm that a product is free of all prohibited substances because it is not possible to analyze all of them due to the continuous synthesis of new adulterants. In summary, supplement certification cannot completely eliminate the risk of a product being contaminated, but it does have strong evidence of reduced risk (Mathews, 2018).

In Mexico, the National Association of Food Supplements Industry (ANAISA) integrated of accredited dietary supplement companies (including sports supplements), determine those products that meet the regulatory requirements indicated by authorities in our country such as the Secretariat of Health, COFEPRIS and the Office of the Federal Prosecutor for the Consumer (PROFECO). These, have the purpose of protecting the consumer from the increasing bombardment of advertising and sale of products that potentially endanger the population's health, like the programs above. The accredited products have a certification seal, in addition to outreach program of technical and scientific information, to promote regulatory improvement through the generation of proposals aligned with global trends (Asociación Nacional de la Industria de los Suplementos Alimenticios, 2021).

CONCLUSIONS

The consumption of active pharmaceutical ingredients, steroidal prohormones and designer steroids, offered as sports supplements for muscle mass gain, in addition to other ergogenic effects, as well as the inadvertent consumption of the same substances in sports supplements, is a potentially risk situation difficult to estimate, not only for professional sports but also for the consumers' health. This, due to the acute or chronic exposure of a wide range of substances with pharmacological activity in unknown quantities that have a variety of adverse effects that are not even fully determined yet. It is important to note that, although the percentage of supplement adulteration and/or contamination in general may seem minimal (around 15% of the total), there are minimal studies that have analyzed significant amounts of the great diversity of these products from the national market. Thus, there is no precise data on the approximation to this figure in Mexico, which is one of the main consumers of these products internationally.

When elaborating a routine medical history, it usually includes a patient questioning about drug use and drug addiction. However, due the disclosure of sports supplements or products, they probably will not be considered due to the belief that these do not cause damage to health. The latter, under the argument that they are not drugs or because are offered with statements such as being of natural origin and without adverse effects, or being safe and legal alternatives for other types of substances. Therefore, the authors encourage physicians and other health professionals who consider asking about the use of these products when relevant to perform a differential diagnosis. Similarly, it is necessary to standardize studies related to the consumption prevalence of these products with appropriate definitions and contextualization, since these play a key role in the assessment and quantification of risks to public and individual health.

It is not the intention of the authors to suggest that all sports supplements are likely to cause harm to the consumer's health, or lead to cases of positive doping in professional sports. There are ingredients and products whose scientific evidence has shown their effectiveness and safety when properly consumed and for their purpose. Instead, we highlight the importance of health professionals' involvement to mitigate the potential risks that the consumption of certain sports supplements entails, that could be adulterated and/or contaminated. In addition, this will produced additional elements to consider when assessing the causes of some pathologies, as well as issue the pertinent recommendations for the differentiation and consumption of these products.

REFERENCES

Abbate, V., Kicman, A.T., Evans-Brown, M., Mcveigh, J., Cowan, D.A., Wilson, C., Coles, S.J., Walker, C.J. 2015. Anabolic steroids detected in bodybuilding dietary supplements – A significant risk to public health. Drug Testing and Analysis. 7: 609-618. https://doi.org/10.1002/dta.1728

Agriculture and Agri-Food Canada. Custom reports service – Sports nutrition products market – Europe. [Accessed 30 July 2021] 2019. Available at: https://agriculture.canada.ca/en/international-trade/market-intelligence/reports/custom-reports-service-sports-nutrition-products-market-europe

Alaedini, S., Amirahmadi, M., Kobarfard, F., Rastegar, H., Nasirahmadi, S., Shoeibi, S. 2021. Survey of protein-based sport supplements for illegally added anabolic steroids methyltestosterone and 4-androstenedione by UPLC-MS/MS. Steroids. 165: 108758. https://doi.org/10.1016/j.steroids.2020.108758

Asociación Nacional de la Industria de los Suplementos Alimenticios. [Accessed 11 August 2021] 2021. Available at: https://anaisa.mx/

Augustin, M.A., Sanguansri, L. 2012. Challenges in developing delivery systems for food additives, nutraceuticals and dietary supplements. In: Encapsulation Technologies and Delivery Systems for Food Ingredients and Nutraceuticals. N. Garti and M. Julian (ed.), pp 19-48. Woodheah Publising Limited, Philadelphia. https://doi.org/10.1533/9780857095909.1.19

Australian Institute of Sport. Australian Institute of Sport Position Statement: Supplements and sports foods in high performance sport. [Accessed 15 July 2021] 2021. Available at: https://www.ais.gov.au/__data/assets/pdf_file/0014/1000841/Position-Statement-Supplements-and-Sports-Foods-abridged_v2.pdf

Balasubramanian, A., Thirumavalavan, N., Srivatsav, A., Yu, J., Lipshultz, L.I., Pastuszak, A.W. 2019. Testosterone imposters: An analysis of popular online testosterone boosting supplements. The Journal of Sexual Medicince. 16: 203-212. https://doi.org/10.1016/j.jsxm.2018.12.008

Baltazar-Martins, G., Brito de Souza, D., Aguilar-Navarro, M., Muñoz-Guerra, J., Plata, M.D.M., Del Coso, J. 2019. Prevalence and patterns of dietary supplement use in elite Spanish athletes. Journal of the International Society of Sports Nutrition. 16: 30. https://doi.org/10.1186/s12970-019-0296-5

Brown, A.C. 2017. An overview of herb and dietary supplement efficacy, safety and government regulations in the United States with suggested improvements. Part 1 of 5 series. Food and Chemical Toxicology 107: 449-471. https://doi.org/10.1016/j.fct.2016.11.001

Brown, G.A., Vukovich, M., King, D.S. 2006. Testosterone prohormone supplements. Medicine & Science in Sports & Exercise. 38: 1451-1460. https://doi.org/10.1249/01.mss.0000228928.69512.2e

Bytomski, J.R. 2018. Fueling for Performance. Sports Health. 10: 47-53. https://doi.org/10.1177/1941738117743913

Chappell, A.J., Simper, T., Barker, M.E. 2018. Nutritional strategies of high level natural bodybuilders during competition preparation. Journal of the International Society of Sports Nutrition. 15: 4. https://doi.org/10.1186/s12970-018-0209-z

Chappell, A.J., Simper, T., Helms, E. 2019. Nutritional strategies of British professional and amateur natural bodybuilders during competition preparation. Journal of the International Society of Sports Nutrition. 16: 35. https://doi.org/10.1186/s12970-019-0302-y

Clemesha, C.G., Thaker, H., Samplaski, M.K. 2020. 'Testosterone boosting' supplements composition and claims are not supported by the academic literature. The World Journal of Men's Health. 38: 115-122. https://doi.org/10.5534/wjmh.190043

De Ceglie, C., Calvano, C.D., Zambonin, C.G. 2015. MALDI-TOF MS for quality control of high protein content sport supplements. Food Chemistry. 176: 396-402. https://doi.org/10.1016/j.foodchem.2014.12.038

Directo, D., Wong, M.W.H., Elam, M.L., Falcone, P., Osmond, A., Jo, E. 2019. The effects of a multi-Ingredient performance supplement combined with resistance training on exercise volume, muscular strength, and body composition. Sports. 7: 152. https://doi.org/10.3390/sports7060152

Duiven, E., van Loon, L.J.C., Spruijt, L., Koert, W., de Hon, O.M. 2021. Undeclared doping substances are highly prevalent in commercial sports nutrition supplements. Journal of Sports Science & Medicine. 20: 328-338. https://doi.org/10.52082/jssm.2021.328

Edenfield, K.M. 2020. Sports supplements: Pearls and pitfalls. Primary Care - Clinics in Office Practice. 47: 37-48. https://doi.org/10.1016/j.pop.2019.10.002

Eichner, A., Tygart, T. 2016. Adulterated dietary supplements threaten the health and sporting career of up-and-coming young athletes. Drug Testing and Analysis. 8: 304-306. https://doi.org/10.1002/dta.1899

Fonseca, G.W.P.D., Dworatzek, E., Ebner, N., Von Haehling, S. 2020. Selective androgen receptor modulators (SARMs) as pharmacological treatment for muscle wasting in ongoing clinical trials. Expert Opinion on Investigational Drugs. 29: 881-891. https://doi.org/10.1080/13543784.2020.1777275

Gardiner, P., Sarma, D.N., Dog, T.L., Barrett, M.L., Chavez, M.L., Ko, R., Mahady, G.B., Marles, R.J., Pellicore, L.S., Giancaspro, G.I. 2008. The state of dietary supplement adverse event reporting in the United States. Pharmacoepidemiology and Drug Safety. 17: 962-970. https://doi.org/10.1002/pds.1627

Garthe, I. 2019. Dietary supplements and elite athletes: when nature becomes high risk. Current Opinion in Endocrine and Metabolic Research. 9: 66-73. https://doi.org/10.1016/j.coemr.2019.07.004

Garthe, I., Maughan, R.J. 2018. Athletes and supplements: Prevalence and perspectives. International Journal of Sport Nutrition and Exercise Metabolism. 28: 126-138. https://doi.org/10.1123/ijsnem.2017-0429

Garthe, I., Ramsbottom, R. 2020. Elite athletes, a rationale for the use of dietary supplements: A practical approach. PharmaNutrition. 14: 100234. https://doi.org/10.1016/j.phanu.2020.100234

Garza-Ocañas, L., Badillo-Castañeda, C.T., Montoya-Eguía, S.L., Saenz-Chávez, P.L., Garza-Ulloa, H. 2013. Confirmación de dexametasona y diclofenaco por LC-MS-MS como adulterantes en un producto herbolario. Salud Pública de México. 55: 498. https://doi.org/10.21149/spm.v55i5.7250

Geldof, L., Pozo, O.J., Lootens, L., Morthier, W., Van Eenoo, P., Deventer, K. 2017. In vitro metabolism study of a black market product containing SARM LGD-4033. Drug Testing and Analysis. 9: 168-178. https://doi.org/10.1002/dta.1930

Geller, A.I., Shehab, N., Weidle, N.J., Lovegrove, M.C., Wolpert, B.J., Timbo, B.B., Mozersky, R.P., Budnitz, D.S. 2015. Emergency Department Visits for Adverse Events Related to Dietary Supplements. The New England Journal of Medicine. 373: 1531-1540. https://doi.org/10.1056/nejmsa1504267

Geyer, H., Parr, M.K., Koehler, K., Mareck, U., Schänzer, W., Thevis, M. 2008. Nutritional supplements cross-contaminated and faked with doping substances. Journal of Mass Spectrometry. 43: 892-902. https://doi.org/10.1002/jms.1452

Grand View Research. Sports Nutrition Market Size & Growth Report, 2020-2027. [Accessed 31 August 2021] 2021. Available at: https://www.grandviewresearch.com/industry-analysis/sports-nutrition-market

Herriman, M., Fletcher, L., Tchaconas, A., Adesman, A., Milanaik, R. 2017. Dietary supplements and young teens: Misinformation and access provided by retailers. Pediatrics. 139: e20161257. https://doi.org/10.1542/peds.2016-1257

Iraki, J., Fitschen, P., Espinar, S., Helms, E. 2019. Nutrition Recommendations for Bodybuilders in the Off-Season: A Narrative Review. Sports. 7: 154. https://doi.org/10.3390/sports7070154

Jędrejko, K., Lazur, J., Muszyńska, B. 2021. Risk associated with the use of selected ingredients in food supplements. Chemistry & Biodiversity. 18: e2000686. https://doi.org/10.1002/cbdv.202000686

Jokipalo, I., Khudayarov, A. 2021. A Netnography and a survey on doping use among competitive doping-untested strength-sport athletes. Interational Journal of Sports Medicine. 42: 645–650 https://doi.org/10.1055/a-1342-7312

Joseph, J., Parr, M., 2014. Synthetic androgens as designer supplements. Current Neuropharmacology. 13: 89-100. https://doi.org/10.2174/1570159x13666141210224756

Jovanov, P., Đorđić, V., Obradović, B., Barak, O., Pezo, L., Marić, A., Sakač, M. 2019. Prevalence, knowledge and attitudes towards using sports supplements among young athletes. Journal of the International Society of Sports Nutrition. 16: 27. https://doi.org/10.1186/s12970-019-0294-7

Kazlauskas, R. 2010. Designer steroids, in: Doping in sports: Biochemical Principles, Effects and Analysis. Handbook of Experimental Pharmacology, vol 195. D. Thieme and P. Hemmersbach (ed.), pp. 155-185. Springer, Berlin. https://doi.org/10.1007/978-3-540-79088-4_7

Kerksick, C.M., Wilborn, C.D., Roberts, M.D., Smith-Ryan, A., Kleiner, S.M., Jäger, R., Collins, R., Cooke, M., Davis, J.N., Galvan, E., Greenwood, M., Lowery, L.M., Wildman, R., Antonio, J., Kreider, R.B. 2018. ISSN exercise & sports nutrition review update: Research & recommendations. Journal of the International Society of Sports Nutrition. 15: 38. https://doi.org/10.1186/s12970-018-0242-y

Kim, E.H., Seo, H.S., Ki, N.Y., Park, N.H., Lee, W., Do, J.A., Park, S., Baek, S.Y., Moon, B., Oh, H. Bin, Hong, J. 2017. Reliable screening and confirmation of 156 multi-class illegal adulterants in dietary supplements based on extracted common ion chromatograms by ultra-high-performance liquid chromatography-quadrupole/time of flight-mass spectrometry. Journal of Chromatography A. 1491: 43-56. https://doi.org/10.1016/j.chroma.2017.02.032

Knapik, J.J., Steelman, R.A., Hoedebecke, S.S., Austin, K.G., Farina, E.K., Lieberman, H.R. 2016a. Prevalence of dietary supplement use by athletes: Systematic review and meta-analysis. Sports Medicine. 46: 103-123. https://doi.org/10.1007/s40279-015-0387-7

Knapik, J.J., Trone, D.W., Austin, K.G., Steelman, R.A., Farina, E.K., Lieberman, H.R. 2016b. Prevalence, adverse events, and factors associated with dietary supplement and nutritional supplement use by US Navy and Marine corps personnel. Journal of the Academy of Nutrition and Dietetics. 116: 1423-1442. https://doi.org/10.1016/j.jand.2016.02.015

Kulkarni, A., Huerto, R., Roberto, C.A., Austin, S.B. 2017. Leveraging corporate social responsibility to improve consumer safety of dietary supplements sold for weight loss and muscle building. Translational Behavioral Medicine. 7: 92-97. https://doi.org/10.1007/s13142-016-0434-4

Leaney, A.E., Beck, P., Biddle, S., Brown, P., Grace, P.B., Hudson, S.C., Mawson, D.H. 2021. Analysis of supplements available to UK consumers purporting to contain selective androgen receptor modulators. Drug Testing and Analysis. 13: 122-127. https://doi.org/10.1002/dta.2908

Lee, J.H., Han, J.H., Min, A.Y., Kim, H., Shin, D. 2020. Screening for twenty-eight target anabolic-androgenic steroids in protein supplements using QuEChERS extraction followed by liquid chromatography-tandem mass spectrometry. Food Additives & Contaminants - Part A. 37: 1425-1436. https://doi.org/10.1080/19440049.2020.1773543

Lopez-Samanes, A., Ortega Fonseca, J.F., Fernandez Elias, V.E., Borreani, S., Mate-Munõz, J.L., Kovacs, M.S. 2015. Nutritional ergogenic aids in tennis: A brief review. Strength and Conditioning Journal. 37: 1-11. https://doi.org/10.1519/SSC.0000000000000141

Lorenz, L.M., Toomey, V.M., Lanzarotta, A.C., Flurer, R.A., Falconer, T.M. 2019. Identification of the designer steroid androsta-3,5-diene-7,17-dione in a dietary supplement. Drug Testing and Analysis. 11: 1109-1115. https://doi.org/10.1002/dta.2589

Luethi, D., Liechti, M.E. 2020. Designer drugs: mechanism of action and adverse effects. Archives of Toxicology. 94: 1085-1133. https://doi.org/10.1007/s00204-020-02693-7

Machek, S.B., Cardaci, T.D., Wilburn, D.T., Willoughby, D.S. 2020. Considerations, possible contraindications, and potential mechanisms for deleterious effect in recreational and athletic use of selective androgen receptor modulators (SARMs) in lieu of anabolic androgenic steroids: A narrative review. Steroids. 164: 108753. https://doi.org/10.1016/j.steroids.2020.108753

Martello, S., Felli, M., Chiarotti, M. 2007. Survey of nutritional supplements for selected illegal anabolic steroids and ephedrine using LC-MS/MS and GC-MS methods, respectively. Food Additives & Contaminants. 24: 258-265. https://doi.org/10.1080/02652030601013729

Martínez-Sanz, J.M., Sospedra, I., Ortiz, C.M., Baladía, E., Gil-Izquierdo, A., Ortiz-Moncada, R. 2017. Intended or unintended doping? A review of the presence of doping substances in dietary supplements used in sports. Nutrients. 9: 1093. https://doi.org/10.3390/nu9101093

Mathews, N.M. 2018. Prohibited contaminants in dietary supplements. Sports Health. 10: 19-30. https://doi.org/10.1177/1941738117727736

Maughan, R.J., Burke, L.M., Dvorak, J., Larson-Meyer, D.E., Peeling, P., Phillips, S.M., Rawson, E.S., Walsh, N.P., Garthe, I., Geyer, H., Meeusen, R., Van Loon, L., Shirreffs, S.M., Spriet, L.L., Stuart, M., Vernec, A., Currell, K., Ali, V.M., Budgett,

R.G.M., Ljungqvist, A., Mountjoy, M., Pitsiladis, Y., Soligard, T., Erdener, U., Engebretsen, L. 2018. IOC consensus statement: Dietary supplements and the high-performance athlete. International Journal of Sport Nutrition and Exercise Metabolism. 28: 104-125. https://doi.org/10.1123/ijsnem.2018-0020

Maughan, R.J., Greenhaff, P.L., Hespel, P. 2011. Dietary supplements for athletes: Emerging trends and recurring themes. Journal of Sports Sciences. 29: S57-S66. https://doi.org/10.1080/02640414.2011.587446

Maughan, R.J., King, D.S., Lea, T. 2004. Dietary supplements. Journal of Sports Sciences. 22: 95-113. https://doi.org/10.1080/0264041031000140581

Micalizzi, G., Huszti, K., Pálinkás, Z., Mandolfino, F., Martos, É., Dugo, P., Mondello, L., Utczás, M. 2021. Reliable identification and quantification of anabolic androgenic steroids in dietary supplements by using gas chromatography coupled to triple quadrupole mass spectrometry. Drug Testing and Analysis. 13: 128-139. https://doi.org/10.1002/dta.2929

Montuori, P., Loperto, I., Paolo, C., Castrianni, D., Nubi, R., De Rosa, E., Palladino, R., Triassi, M. 2021. Bodybuilding, dietary supplements and hormones use: behaviour and determinant analysis in young bodybuilders. BMC Sports Science, Medicine and Rehabilitation. 13: 147. https://doi.org/10.1186/s13102-021-00378-x

Muñoz Maldonado, G.E., Ochoa Ahmed, F.A., Díaz Ochoa, E.A., Ramírez Orozco, R.E., Gómez Renaud, V.M. 2021. Suplementos deportivos: ¿Cómo definimos a estos productos? Lux Médica.16. https://doi.org/10.33064/48lm20213235

Navarro, V.J., Barnhart, H., Bonkovsky, H.L., Davern, T., Fontana, R.J., Grant, L., Reddy, K.R., Seeff, L.B., Serrano, J., Sherker, A.H., Stolz, A., Talwalkar, J., Vega, M., Vuppalanchi, R. 2014. Liver injury from herbals and dietary supplements in the U.S. Drug-Induced Liver Injury Network. Hepatology. 60: 1399-1408. https://doi.org/10.1002/hep.27317

O'Bryan, K.R., Doering, T.M., Morton, R.W., Coffey, V.G., Phillips, S.M., Cox, G.R. 2020. 54: 573–581 Do multi-ingredient protein supplements augment resistance training-induced gains in skeletal muscle mass and strength? A systematic review and meta-analysis of 35 trials. British Journal of Sports Medicine. 54: 573-581. https://doi.org/10.1136/bjsports-2018-099889

Odoardi, S., Castrignanò, E., Martello, S., Chiarotti, M., Strano-Rossi, S. 2015. Determination of anabolic agents in dietary supplements by liquid chromatography-high-resolution mass spectrometry. Food Additives & Contaminants - Part A. 32: 635-647. https://doi.org/10.1080/19440049.2015.1014868

Outram, S., Stewart, B. 2015. Doping through supplement use: A review of the available empirical data. International Journal of Sport Nutrition and Exercise Metabolism. 25: 54-59. https://doi.org/10.1123/ijsnem.2013-0174

Pokrywka, A., Obmiński, Z., Malczewska-Lenczowska, J., Fijałek, Z., Turek-Lepa, E., Grucza, R. 2014. Insights into supplements with tribulus terrestris used by athletes. Journal of Human Kinetics. 41: 99-105. https://doi.org/10.2478/hukin-2014-0037

Pomeranz, J.L., Barbosa, G., Killian, C., Austin, S.B. 2015. The dangerous mix of adolescents and dietary supplements forweight loss andmuscle building: Legal strategies for state action. Journal of Public Health and Management & Practice. 21: 496-503. https://doi.org/10.1097/PHH.0000000000000142

Proceso. Los estragos de un "producto milagro". [Accessed 8 July 2021] 2011. Availale at: https://www.proceso.com.mx/reportajes/2011/3/10/los-estragos-de-un-producto-milagro-84745.html

Rahnema, C.D., Crosnoe, L.E., Kim, E.D. 2015. Designer steroids – over-the-counter supplements and their androgenic component: Review of an increasing problem. Andrology. 3: 150-155. https://doi.org/10.1111/andr.307

Rocha, T., Amaral, J.S., Oliveira, M.B.P.P. 2016. Adulteration of dietary supplements by the illegal addition of synthetic drugs: A review. Comprensive Reviews in Food Science and Food Safety. 15: 43–62. https://doi.org/10.1111/1541-4337.12173

Ronis, M.J.J., Pedersen, K.B., Watt, J. 2018. Adverse effects of nutraceuticals and dietary supplements. Annual Review of Pharmacology and Toxicology. 58: 583-601. https://doi.org/10.1146/annurev-pharmtox-010617-052844

Sánchez-Oliver, A.J., Grimaldi-Puyana, M., Domínguez, R. 2019. Evaluation and behavior of spanish bodybuilders: Doping and sports supplements. Biomolecules. 9: 122. https://doi.org/10.3390/biom9040122

Santos, H.O., Howell, S., Teixeira, F.J. 2019. Beyond tribulus (*Tribulus terrestris L.*): The effects of phytotherapics on testosterone, sperm and prostate parameters. Journal of Ethnopharmacology. 235: 392-405. https://doi.org/10.1016/j.jep.2019.02.033

Shao, A. 2017. Global market entry regulations for nutraceuticals, functional foods, dietary/food/health supplements. in: Developing New Functional Food and Nutraceutical Products. B. Debasis and N. Sreejayan (ed.), pp 279-290. Academic Press, London. https://doi.org/10.1016/B978-0-12-802780-6.00015-8

Tabata, S., Yamasawa, F., Torii, S., Manabe, T., Kamada, H., Namba, A., Kato, J., Kaneko, H., Tahara, K., Tsukahara, Y., Sato, K. 2020. Use of nutritional supplements by elite Japanese track and field athletes. Journal of the International Society of Sports Nutrition. 17: 38. https://doi.org/10.1186/s12970-020-00370-9

Temerdashev, A.Z., Dmitrieva, E. V. 2020. Methods for the determination of selective androgen receptor modulators. Journal of Analytical Chemistry. 75: 835-850. https://doi.org/10.1134/S1061934820070187

Thevis, M., Schänzer, W. 2018. Detection of SARMs in doping control analysis. Molecular and Cellular Endocrinology. 464: 34-45. https://doi.org/10.1016/j.mce.2017.01.040

Tsarouhas, K., Kioukia-Fougia, N., Papalexis, P., Tsatsakis, A., Kouretas, D., Bacopoulou, F., Tsitsimpikou, C. 2018. Use of nutritional supplements contaminated with banned doping substances by recreational adolescent athletes in Athens,

Greece. Food and Chemical Toxicology. 115: 447-450. https://doi.org/10.1016/j.fct.2018.03.043

Van Wagoner, .R.M., Eichner, A., Bhasin, S., Deuster, P.A., Eichner, D. 2017. Chemical composition and labeling of substances marketed as selective androgen receptor modulators and sold via the internet. Journal of the American Medical Association. 318: 2004-2010. https://doi.org/10.1001/jama.2017.17069

Voelker, S.E., Lorenz, L.M., Litzau, J.J. 2019. Semi-quantitative determination of designer steroids by high-performance liquid chromatography with ultraviolet detection in the absence of reference material. Drug Testing and Analysis. 11: 428-434. https://doi.org/10.1002/dta.2511

Waller, M.C., Kerr, D.A., Binnie, M.J., Eaton, E., Wood, C., Stenvers, T., Gucciardi, D.F., Goodman, C., Ducker, K.J. 2019. Supplement use and behaviors of athletes affiliated with an australian state-based sports institute. International Journal of Sport Nutrition and Exercise Metabolism. 29: 518-525. https://doi.org/10.1123/ijsnem.2018-0336

Walpurgis, K., Thomas, A., Geyer, H., Mareck, U., Thevis, M. 2020. Dietary supplement and food contaminations and their implications for doping controls. Foods. 9: 1012. https://doi.org/10.3390/foods9081012

Wójcicki, K. 2020. FTIR spectroscopy for quality evaluation of sports supplements on the Polish market. Foods and Raw Materials. 8: 177-185. https://doi.org/10.21603/2308-4057-2020-1-177-185

Yager, Z., McLean, S. 2020. Muscle building supplement use in Australian adolescent boys: relationships with body image, weight lifting, and sports engagement. BMC Pediatrics. 20: 89. https://doi.org/10.1186/s12887-020-1993-6