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FOOD AND DRUG SUPPLIMENTS TOXICITY FOR ATHLETES

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Abstract

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Food and Drug Supplement Toxicity for Athletes

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Supplement use by athletes is complex and research supports the alarming notion of misinformed decisions regarding supplements. A frequent divergence between the type of supplements chosen by athletes and the rationale dictating the supplement use is hypothesized. Thus, a potentially dangerous incongruence may exist between rationale and practice. In the continued absence of reliable data on supplement use, an alternative approach of studying the reasons underlying supplement use in athletes is proposed to determine whether there is an incongruence between rationale and practice. Existing data from large scale national surveys can be used to investigate this incongruence.

In this report, analyses of distinctive patterns between the use and rationale for use of supplements among athletes are recommended to explore this potentially dangerous phenomenon.

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1. Introduction

1.1 Introduction to Supplements

'Supplement' is an overarching name for vitamins, minerals, herbal remedies, traditional Asian remedies, amino acids and other substances to be taken orally. They may also be referred to as dietary, food or nutritional supplements or ergogenic aids (supplements purported to improve athletic performance) and are typically sold in the form of tablets, capsules, soft gels, liquids, powders, and bars. In the UK, most supplements are regulated as foods and subject to the general provisions of the Food Safety Act 1990, the Food Labelling Regulations 1996 and the Trade Descriptions Act 1968. Supplements are not required to exhibit efficacy before marketing, nor are they subject to prior approval unless they are genetically modified or claimed to be new. Medicinal claims on packaging or in an advertisement for a supplement, however, are prohibited.

This fact sheet provides an overview of selected ingredients in dietary supplements designed or claimed to enhance exercise and athletic performance. Manufacturers and sellers promote these products, sometimes referred to as "ergogenic aids," by claiming that they improve strength or endurance, increase exercise efficiency, achieve a performance goal more quickly, and increase tolerance for more intense training. These effects are the main focus of this fact sheet. Some people also use ergogenic aids to prepare the body for exercise, reduce the chance of injury during training, and enhance recovery from exercise.

1.1.1 Variety of drug supplements

Dietary supplements to enhance exercise and athletic performance come in a variety of forms, including tablets, capsules, liquids, powders, and bars. Many of these products contain numerous ingredients in varied combinations and amounts. Among the more common ingredients are amino acids, protein, creatine, and caffeine.

Widespread debate has accompanied the introduction of new legislation on the use of dietary supplements within the EU. Comprehension of detailed studies, ranging from quantities and patterns of use to side-effects of supplement consumption, has been impeded by variations in terminology and practice amongst countries and user groups.

Many exercise and athletic-performance dietary supplements in the marketplace contain multiple ingredients (especially those marketed for muscle growth and strength). However, much of the research has focused only on single ingredients. One therefore cannot know or predict the effects and safety of combinations in these multi-ingredient products unless clinical trials have investigated that particular combination. Furthermore, the amounts of these ingredients vary widely among products. In some cases, the products contain proprietary blends of ingredients listed in order by weight, but labels do not provide the amount of each ingredient in the blend. Manufacturers and sellers of dietary supplements for exercise and athletic performance rarely fund or conduct scientific research on their proprietary products of a caliber that reputable biomedical journals require for publication

Dietary supplements and herbal medicines play important roles in health care. Vitamins and minerals are important, as they are necessary for enzymatic reactions and bodily functions; lack of these compounds can lead to deficiency-related diseases. Herbal medicine was the predominant form of health care for the world's population before the advent of modern medicine and still is the predominant form of health care in many underserved populations. Herbal medicine continues to infuse new ideas and treatments into modern medicine for the benefit of our patients.

1.1.2 The World Health Organization (WHO) on Dietary Supplement

The World Health Organization (WHO) and the United States (US) Dietary Supplements Health and Education Act (DSHEA) of 1994 both define dietary supplements as a product (other than tobacco) that is meant to supplement the diet. Both organizations include vitamins, minerals, herbs, botanical products, amino acids, or dietary substances in their definitions.

The WHO also defines herbal medicines as plant-derived materials or preparations intended for human therapeutic use or for other health benefits in humans. However, most indigenous herbal traditions not only have plant matters in their material medica, but also include animal matters and mineral compounds. Herbal products are usually ingested raw, as tea or as decoctions (concentrated extracts). Sometimes they are applied as a paste or powder on the skin. Some herbal traditions, such as traditional Chinese Mmdicine (TCM) and Ayurvedic medicine, have medicinal products that are packaged in the form of pills or liquids for ease of consumption and retailing. These are sometimes called proprietary medicine, finished products, or patent medicine. Many exercise and athletic-performance dietary supplements in the marketplace contain multiple ingredients (especially those marketed for muscle growth and strength). However, much of the research has focused only on single ingredients. One therefore cannot know or predict the effects and safety of combinations in these multi-ingredient products unless clinical trials have investigated that particular combination.

Furthermore, the amounts of these ingredients vary widely among products. In some cases, the products contain proprietary blends of ingredients listed in order by weight, but labels do not provide the amount of each ingredient in the blend. Manufacturers and sellers of dietary supplements for exercise and athletic performance rarely fund or conduct scientific research on their proprietary products of a caliber that reputable biomedical journals require for publication.

2.Food Supplements

A wide range of nutrients and other ingredients might be present in food supplements, including, but not limited to, vitamins, minerals, amino acids, essential fatty acids, fibre and various plants and herbal extracts.

Food supplements are intended to correct nutritional deficiencies, maintain an adequate intake of certain nutrients, or to support specific physiological functions. They are not medicinal products and as such cannot exert a pharmacological, immunological or metabolic action. Therefore their use is not intended to treat or prevent diseases in humans or to modify physiological functions.

In the EU, food supplements are regulated as foods. Harmonised legislation regulates the vitamins and minerals, and the substances used as their sources, which can be used in the manufacturing of food supplements. For ingredients other than vitamins and minerals, the European Commission has established harmonised rules to protect consumers against potential health risks and maintains a list of substances which are known or suspected to have adverse effects on health and the use of which is therefore controlled.

2.2.1 There are three main types of food supplement, which are herbal, synthetic and mineral supplements.

Herbal health products and supplements have become a billion-dollar industry. An herb, or botanical, is a plant or part of a plant that people use to try to stay healthy, or to treat health conditions and illnesses. An herbal health product or supplement (also called a botanical product) is a type of dietary supplement that contains one or more herbs.

These supplements can have strong effects on the body but are not regulated by the Food and Drug Administration (FDA). They are available in many forms, including in tea bags, capsules, tablets, liquids, and powders. Examples of common herbal health products and supplements include black cohosh, echinacea, garlic, ginkgo, saw palmetto, and St. John’s wort.

Synthetic nutrients do not include "whole food supplements," which are made from concentrated, dehydrated whole foods. The majority of supplements available on the market today are made artificially. These include vitamins, antioxidants, minerals andamino acids, among others

Multivitamin/mineral (MVM) supplements contain a combination of vitamins and minerals, and sometimes other ingredients as well. They go by many names, including multis and multiples or simply vitamins.

Table 1 Most Commonly Used Vitamins/Minerals and Herbal Supplements.

Vitamin or Mineral	Percent Use	Herbal Supplement	Percent Use
Multivitamin	26	Ginseng	3.3
Vitamin E	10	Gingko biloba	2.2
Vitamin C	9.1	Garlic	1.9
Calcium	8.7	Glucosamine	1.9
Magnesium	3.0	St. John's wort	1.3
Zinc	2.2	Echinacea	1.3
Folic acid	2.2	Lecithin	1.1
Vitamin B_{12}	2.1	Chondroitin	1.0
Vitamin D	1.9	Creatine	0.9
Vitamin A	1.8	Saw palmetto	0.9
Any vitamin or mineral	40	Any herbal supplement	14

SOURCE: Adapted from Kaufman et al. (2002).

2.2Drug Supplements

Supplements aren't regulated by the FDA. Under the Dietary Supplement Health and Education Act (DSHEA), the FDA treats supplements like food and the DSHEA defines supplements as "products taken orally for supplementing the diet." Supplements can include minerals, vitamins or other natural biological substances and they're available in a variety of shapes and sizes, including concentrates, extracts, capsules, tablets, liquids and powders.

3.Supplements and their Consequences

Beyond contaminated products that easily lead to adverse results in doping tests, vitamin products with accurately listed compounds and substances can also be harmful. High levels of vitamin and mineral intake can lead to toxic side effects. For example, the use of iron supplementation by elite athletes is not uncommon and whilst iron is beneficial for athletes with iron deficiency, it can also cause harm with long-term use or certain medical conditions. Similarly, excess intake of vitamin C can be harmful as well as in combination with iron, which may cause damage to the gastrointestinal tract (GI) and initiate or aggravate symptoms associated with chronic GI disorders. The long-term effects of creatine are still unknown but short term side-effects such as cramping and dehydration have been reported along with the suggestion for its use to be under medical supervision. Caffeine is no longer on the list of the IOC's prohibited substances. However, as athletes can use it in training and competition, the relationship between caffeine intake and resulting side-effects such as high blood pressure warrant further study.

3.1.1 Selected Ingredients in Dietary Supplements for Exercise and Athletic Performance

Many exercise and athletic-performance dietary supplements in the marketplace contain multiple ingredients (especially those marketed for muscle growth and strength). However, much of the

research has focused only on single ingredients. One therefore cannot know or predict the effects and safety of combinations in these multi-ingredient products unless clinical trials have investigated that particular combination. Furthermore, the amounts of these ingredients vary widely among products. In some cases, the products contain proprietary blends of ingredients listed in order by weight, but labels do not provide the amount of each ingredient in the blend. Manufacturers and sellers of dietary supplements for exercise and athletic performance rarely fund or conduct scientific research on their proprietary products of a caliber that reputable biomedical journals require for publication.

Table 2 briefly summarizes the findings discussed in more detail in this fact sheet on the safety and efficacy of selected ingredients in dietary supplements to enhance exercise and athletic performance. Some research-derived data is available on these ingredients on which to base a judgment about their potential value to aid exercise and athletic performance. These dietary supplement ingredients are listed and discussed in Table 2.

Table 2 Selected Ingredients in Dietary Supplements for Exercise and Athletic Performance.

Ingredient	**Proposed Mechanism of Action**	**Evidence of Efficacy****	**Evidence of Safety****
Antioxidants (vitamin C, vitamin E, and coenzyme Q_{10})	Minimize free-radical damage to skeletal muscle, thereby reducing muscle fatigue, inflammation, and soreness	Several small clinical trials **Research findings**: Do not directly improve performance; appear to hinder some physiological and physical exercise-induced adaptations	Safe at recommended intakes; some safety concerns reported with high doses **Reported adverse effects**: Potential for diarrhea, nausea, abdominal cramps, and other gastrointestinal disturbances with vitamin C intakes of more than 2,000 mg/day in adults; increased risk of hemorrhagic effects with vitamin E intakes of more than 1,500 IU/day (natural form) or 1,100 IU/day (synthetic form) in adults; nausea, heartburn, and other side effects with coenzyme Q_{10}

Table 2 Selected Ingredients in Dietary Supplements for Exercise and Athletic Performance.

Ingredient	Proposed Mechanism of Action	Evidence of Efficacy**	Evidence of Safety**
Arginine	Increases blood flow and delivery of oxygen and nutrients to skeletal muscle; serves as a substrate for creatine production; increases secretion of human growth hormone to stimulate muscle growth	Limited clinical trials with conflicting results **Research findings**: Little to no effect on vasodilation, blood flow, or exercise metabolites; little evidence of increases in muscle creatine content	No safety concerns reported for use of up to 9 g/day for weeks; adverse effects possible with larger doses **Reported adverse effects**: Gastrointestinal effects, such as diarrhea and nausea
Beetroot or beet juice	Dilates blood vessels in exercising muscle, reduces oxygen use, and improves energy production	Limited clinical trials with conflicting results **Research findings**: Might improve performance and endurance to some degree in time trials and time-to-exhaustion tests among runners, swimmers, rowers, and	No safety concerns reported for short-term use at commonly recommended amounts (approximately 2 cups) **Reported adverse effects**: None known

Table 2 Selected Ingredients in Dietary Supplements for Exercise and Athletic Performance.			
Ingredient	**Proposed Mechanism of Action**	**Evidence of Efficacy****	**Evidence of Safety****
		cyclists; appears to be most effective in recreationally active non-athletes	
Beta-alanine	Increases synthesis of carnosine, a dipeptide that buffers changes in muscle pH, thereby reducing muscle fatigue and loss of force production; considerable individual variation in associated muscle carnosine synthesis	Numerous clinical trials with conflicting results **Research findings**: Inconsistent effects on performance in competitive events requiring high-intensity effort over a short period, such as team sports; little or no performance benefit in activities lasting more than 10 minutes	No safety concerns reported for use of 1.6–6.4 g/day for up to 8 weeks **Reported adverse effects**: Paresthesia (tingling) in face, neck, back of hands, and upper trunk with at least 800 mg or over 10 mg/kg body mass; pruritus (itchy skin)
Beta-hydroxy-beta-methylbutyrate (HMB)	Helps stressed and damaged skeletal muscle cells restore their structure and	Numerous clinical trials with conflicting results	No safety concerns reported for typical dose of 3 g/day for up to 2 months

Table 2 Selected Ingredients in Dietary Supplements for Exercise and Athletic Performance.			
Ingredient	**Proposed Mechanism of Action**	**Evidence of Efficacy****	**Evidence of Safety****
	function	**Research findings**: Might help speed up recovery from exercise of sufficient amount and intensity to induce skeletal muscle damage	**Reported adverse effects**: None known
Betaine	Might increase creatine production, blood nitric-acid levels, or water retention in cells	Limited clinical trials in men with conflicting results **Research findings**: Potential but modest strength and power-based performance improvements in bodybuilders and cyclists	No safety concerns reported for 2–5 g/day for up to 15 days **Reported adverse effects**: None known
Branched-chain amino acids (leucine, isoleucine, and valine)	Can be metabolized by mitochondria in skeletal muscle to provide energy during exercise	Limited number of short-term clinical trials **Research findings**: Little	No safety concerns reported for 20 g/day or less for up to 6 weeks **Reported adverse effects**: None known

Table 2 Selected Ingredients in Dietary Supplements for Exercise and Athletic Performance.			
Ingredient	**Proposed Mechanism of Action**	**Evidence of Efficacy****	**Evidence of Safety****
		evidence of improved performance in endurance-related aerobic events; possibility of greater gains in muscle mass and strength during training	
Caffeine	Blocks activity of the neuromodulator adenosine; reduces perceived pain and exertion	Numerous clinical trials with mostly consistent results **Research findings**: Might enhance performance in endurance-type activities (e.g., running) and intermittent, long-duration activities (e.g., soccer) when taken before activity	Reasonably safe at up to 400–500 mg/day for adults **Reported adverse effects**: Insomnia, restlessness, nausea, vomiting, tachycardia, and arrhythmia; risk of death with acute oral dose of approximately 10–14 g pure caffeine (150–200 mg/kg)
Citrulline	Dilates blood vessels to increase delivery of	Few clinical trials with	Few safety concerns reported for up to 9 g for 1

Table 2 Selected Ingredients in Dietary Supplements for Exercise and Athletic Performance.			
Ingredient	**Proposed Mechanism of Action**	**Evidence of Efficacy****	**Evidence of Safety****
	oxygen and nutrients to skeletal muscle	conflicting results **Research findings**: Little research support for use to enhance performance	day or 6 g/day for up to 16 days **Reported adverse effects**: Gastrointestinal discomfort
Creatine	Helps supply muscles with energy for short-term, predominantly anaerobic activity	Numerous clinical trials generally showing a benefit for high-intensity, intermittent activity; potential variation in individual responses **Research findings**: May increase strength, power, and work from maximal effort muscle contractions; over time helps body adapt to athlete-training	Few safety concerns reported at typical dose (e.g., loading dose of 20 g/day for up to 7 days and 3–5 g/day for up to 12 weeks) **Reported adverse effects**: Weight gain due to water retention; anecdotal reports of nausea, diarrhea, muscle cramps, muscle stiffness, heat intolerance

Table 2 Selected Ingredients in Dietary Supplements for Exercise and Athletic Performance.			
Ingredient	**Proposed Mechanism of Action**	**Evidence of Efficacy****	**Evidence of Safety****
		regimens; of little value for endurance sports	
Deer antler velvet	Contains growth factors (such as insulin-like growth factor-1 [IGF-1]) that could promote muscle tissue growth	Few short-term clinical trials that show no benefit for physical performance **Research findings**: No evidence for improving aerobic or anaerobic performance, muscular strength, or endurance	Safety not well studied **Reported adverse effects**: Hypoglycemia, headache, edema, and joint pain (from prescription IGF-1); banned in professional athletic competition
Dehydroepiandrosterone (DHEA)	Steroid hormone that can be converted into testosterone and estradiol	Small number of clinical trials that show no benefit for physical performance **Research findings**: No evidence of increases in	Safety not well studied; no safety concerns reported for up to 150 mg/day for 6–12 weeks **Reported adverse effects**: Over several months, raises testosterone levels in women, which can cause acne and growth of facial hair

Table 2 Selected Ingredients in Dietary Supplements for Exercise and Athletic Performance.

Ingredient	Proposed Mechanism of Action	Evidence of Efficacy**	Evidence of Safety**
		strength, aerobic capacity, lean body mass, or testosterone levels in men	
Ginseng	Unknown mechanism of action; *Panax* ginseng used in traditional Chinese medicine as a tonic for stamina and vitality; Siberian ginseng used to reduce fatigue	Numerous small clinical trials, most showing no benefit for physical performance **Research findings**: In various doses and types of preparations, no effects on peak power output, time to exhaustion, perceived exertion, recovery from intense activity, oxygen consumption, or heart rate	Few safety concerns reported with short-term use **Reported adverse effects**: For *Panax* ginseng: headache, sleep disturbances, and gastrointestinal disorders; for Siberian ginseng: none known
Glutamine	Involved in metabolism and energy production; contributes nitrogen for	Few studies of use to enhance performance	No safety concerns reported with about 45 g/day for 6 weeks; safe use of up to 0.42

Table 2 Selected Ingredients in Dietary Supplements for Exercise and Athletic Performance.

Ingredient	Proposed Mechanism of Action	Evidence of Efficacy**	Evidence of Safety**
	many critical biochemical reactions	directly **Research findings**: In adult weight lifters, no effect on muscle performance, body composition, or muscle-protein degradation; may help with recovery of muscle strength and reduce muscle soreness after exercise	g/kg body weight (e.g., 30 g/day in a person weighing 154 lb) by many patients with serious conditions (e.g., infections, intestinal diseases, and burns) **Reported adverse effects**: None known
Iron	Increases oxygen uptake, reduces heart rate, and decreases lactate concentrations during exercise	Numerous clinical trials with conflicting results **Research findings**: Improved work capacity with correction of iron deficiency anemia; conflicting evidence on whether milder	No safety concerns reported for use at recommended intakes (8 mg/day for healthy men and postmenopausal women and 18 mg/day for healthy premenopausal women) **Reported adverse effects**: Gastric upset, constipation, nausea, abdominal pain, vomiting, and fainting at intakes above 45 mg/day

Table 2 Selected Ingredients in Dietary Supplements for Exercise and Athletic Performance.			
Ingredient	**Proposed Mechanism of Action**	**Evidence of Efficacy****	**Evidence of Safety****
		iron deficiency without anemia impairs exercise performance	
Protein	Builds, maintains, and repairs muscle	Numerous clinical trials **Research findings**: Optimizes muscle training response during exercise and subsequent recovery period	No safety concerns reported at daily recommended intakes for athletes of up to about 2.0 g/kg body weight (e.g., 136 g for a person weighing 150 lb) **Reported adverse effects**: None known
Quercetin	Increases mitochondria in muscle, reduces oxidative stress, decreases inflammation, and improves blood flow	Numerous small, short-term clinical trials **Research findings**: Little to no effect on endurance performance or maximal oxygen consumption	No safety concerns reported for 1,000 mg/day or less for up to 8 weeks **Reported adverse effects**: None known
Ribose	Involved in production of adenosine triphosphate (ATP)	A few small, short-term, clinical trials	Safety as a dietary supplement not well studied; no safety concerns reported

Table 2 Selected Ingredients in Dietary Supplements for Exercise and Athletic Performance.			
Ingredient	**Proposed Mechanism of Action**	**Evidence of Efficacy****	**Evidence of Safety****
		Research findings: Little to no effect on exercise capacity in both trained and untrained adults	for up to 10 g/day for 8 weeks **Reported adverse effects**: None known
Sodium bicarbonate	Enhances disposal of hydrogen ions generated from intense muscle activity, thereby reducing metabolic acidosis and resulting fatigue	Many small, short-term clinical trials **Research findings**: Might provide minor to moderate performance benefit for short-term and intermittent high-intensity activity, especially in trained athletes	No safety concerns reported for short-term use of up to 300 mg/kg body weight **Reported adverse effects**: Nausea, stomach pain, diarrhea, and vomiting
Tart or sour cherry	Phytochemicals in tart cherries may facilitate exercise recovery by reducing pain and inflammation	A few clinical trials with conflicting results **Research findings**: Variable results	No safety concerns reported for about 1/2 quart of juice or 480 mg freeze-dried Montmorency tart-cherry-skin powder per day for up to 2 weeks **Reported adverse effects**:

Table 2 Selected Ingredients in Dietary Supplements for Exercise and Athletic Performance.			
Ingredient	**Proposed Mechanism of Action**	**Evidence of Efficacy****	**Evidence of Safety****
		for aiding muscle strength recovery, reducing soreness, or reducing inflammatory effects on lungs after exercise; insufficient research on ability to improve aerobic performance	None known
Tribulusterrestris	Increases serum testosterone and luteinizing hormone concentrations, thereby promoting skeletal muscle hypertrophy	A few small, short-term clinical trials **Research findings**: No effect on strength, lean body mass, or sex hormone levels	Safety not well studied; no safety concerns reported at up to 3.21 mg/kg/day for 8 weeks **Reported adverse effects**: One case report of harm from product labeled but not confirmed to contain *Tribulusterrestris*

4. Toxic Effects of Drug Supplements Used by Athletes

Certain patterns of use or use of certain products tend to produce adverse effects and toxicities. When adverse effects and toxicities may arise. In table 3.1, factors predisposing to adverse effects and toxicities is shown.

Table 3.1 Factors predisposing to adverse effects and toxicities.

Factors predisposing to adverse effects and toxicities	When to anticipate them
Inappropriate usage and inherent toxicity of herbs	Inappropriate indications (non-traditional indications)—weight loss, athletic performance, recreational use
	Inappropriate duration—use for prolonged periods of time, usually several weeks to months
	Inappropriate dosage—excessive dose in order to achieve some particular results
	Inadequate processing—herbs that are usually consumed in a certain way in a particular herbal tradition being processed in other non-recommended ways
	Herbs with pronounced pharmacological effects or toxic components
Adulteration with modern pharmaceuticals (NSAIDs, steroids, antihistamines, Sildenafil, sulfonylurea)	Finished products claiming fast relief of symptoms or sexual enhancement
Drug interaction	Patients on multiple modern pharmaceuticals, especially drugs with a narrow therapeutic index, such as warfarin, and taking dietary supplements and herbal products
	Patients taking multiple dietary supplements or herbal medicines

Factors predisposing to adverse effects and toxicities	When to anticipate them
Heavy metal toxicities	Finished products from TCM, Ayurvedic traditions, or Mexican folk remedies

In most instances, problems arise due to inappropriate usage of these herbs and supplements. Herbs and supplements can be toxic when used for inappropriate indications, or prepared inappropriately, or used in large excessive dosages, or for a prolonged duration of time. When patients provide such a history of use, physicians should be on a look out for possible toxicities. For example, excessive doses of vitamin D due to overzealous fortification in milk resulted in hypercalemia; similarly, excessive and prolonged intake of vitamin A can lead to osteoporosis and hepatotoxicity .

Many serious adverse effects have arisen because of using of traditional herbs for non-traditional indications. Ephedra is used in small dose in TCM for indications, such as wheezing and cough, but it was never used as a stimulant, a dieting agent, or recreational agent; however, such uses in excessive doses and durations have resulted in serious toxicities, including death, seizures, psychosis, myocardial infarction, cardiac arrhythmia, and stroke. Similarly, the use of Datura species for recreational purposes instead of therapeutic effects has resulted in anti-cholinergic poisoning and death.

In Belgium in the early 1990s, the TCM herb Stephaniatetrandra was used for weight loss. Aristolochiafangchi was mistakenly used instead, and this resulted in more than 100 cases of renal failure and more than 20 cases of urothelial dysplasia. Similar problems were later reported in the UK. The culprit is thought to be the aristolochic acid found in Aristolochiafangchi. In TCM practice, Stephaniatetrandra and Aristolochiafangchi were never meant to be used for weight loss.

Inappropriate processing of herbs can also result in problems. In TCM practice, Aristolochiafangchirequires extensive boiling into a decoction before being applied in small amounts. In the Belgian sliming clinic, it was used as a powder. Aristolochic acid concentration is much lower in decoctions as it has low water solubility; hence, a decoction is a safer way to administer it.

Herbal medicines do not usually produce immediate relief of symptoms as most of them are generally concerned with homeostasis. When products claim to provide immediate relieve of symptoms, physicians should watch out for possible intentional adulteration with pharmaceuticals. Such adulterations can cause problems and toxicities. These products are usually in the form of finished products meant for ingestion or occasionally for topical applications. A survey in Taiwan found that of 2,609 herbal samples analyzed, 23.7% were adulterated with pharmaceuticals. A study of 243

proprietary products in California found that 7% contained undeclared pharmaceuticals. In 1999, out of 3,320 TCM herbal products screened in Singapore, 1.2% were found to contain undeclared pharmaceuticals. Usually only one adulterant is found, although there are instances of multiple adulterants. Another form of adulteration is the substitution of one herb for another that may be cheaper or more readily available, but has a less desirable safety profile.

The most common adulterants are pharmaceuticals that are used to relieve uncomfortable symptoms, such as non-steroidal anti-inflammatory drugs (NSAIDs) and antihistamines. Adulteration in steroids and sexual-enhancing drugs, such as Sildenafil, are also commonly reported. Serious adverse effects including death can result from such adulterations, especially since the drugs added can have serious toxic effects; for example, sulfonylurea, phenylbutazone, phenytoin, and corticosteroids can have serious toxic effects. Problems that can arise from adulterants in these products include allergic reactions, Addisonian crisis, and Cushing's syndrome from unsuspecting use of products with added steroids. Hypotension can occur in patients on nitrates for cardiac ischemia and unsuspected use of products adulterated with Sildenafil, and severe or fatal hypoglycemia can result from unsuspected use of products with sulfonylurea.

For patients taking multiple medications and dietary supplements or herbal medicines, physicians should look out for herb-drug interactions. Sixteen percent of adults in US who take prescription medicine also take herbal medicines. Patients with chronic illnesses, who are most likely to be taking multiple medications, are also most likely to consume dietary supplements or herbal medications, putting them at risk of drug-herb interactions. Patients may consume multiple dietary supplements or herbal medicines and take products that contain multiple components, putting themselves at risk of herb-herb interactions.

Patients most at risk of harmful drug-herbs interactions are those at extremes of age, on multiple prescriptions, with chronic illnesses or with impaired organ functions and those on prescription medications with a narrow therapeutic margin, such as warfarin. Coagulative problems arising from drug-herb interactions with warfarin are commonly reported, sometimes with serious consequences, such as intracranial hematoma. Garlic, gingko, ginger, and Angelica sinensis (Dong quai) are commonly implicated as they are commonly used, but any herb that may contain compounds related to salicylate or coumarin can augment anti-coagulative effects, resulting in bleeding.

Augmentation of sedative effects of modern pharmaceuticals is another problem, especially with popular herbs with sedative effects, such as Piper methysticum (kava) and Valerianaofficinalis (valerian). Kava has been reported to increase the frequency and duration of "off-periods" in Parkinson's patients, and long-term use of this herb can also lead to hepatotoxicity and dermatopathy. Another form of interaction is with metabolic enzymes. For example, Hypericumperforatum (St John's wort), popularly used as an herbal anti-depressant, is a strong inducer of CYP3A, which metabolizes about 50% of all modern pharmaceuticals. This

induction can lead to a sub-therapeutic effect in drugs that are inactivated or potential toxic effects in drugs that are activated by this family of enzymes.

Contamination of dietary supplements and herbal medicines with unwanted substances is another area of concern. Problems arising from contaminations are difficult to anticipate except that they appear to be more widely reported with products from some herbal traditions, such as TCM, Ayurvedic practices, and Mexican folk remedies. Physicians need to be aware of this problem when they encounter patients using products of these herbal traditions and presenting with non-specific symptoms. One form of contamination that is often reported is heavy metal contamination; it can lead to heavy metal poisoning and should be suspected in patients presenting with features suggestive of heavy metal toxicities after using dietary supplements and herbal medicines. Heavy metal contamination arises due to defective manufacturing processes or because the herbs were grown in polluted soil. However, in some instances, like in TCM and Ayurvedic medicine, heavy metals exist as part of their formulary and are deliberately added into preparations for therapeutic effects . Lead poisoning is frequently reported and presents with anemia, abdominal pain, and encephalopathy. It is reported in children given Mexican folk remedies for gastrointestinal symptoms and also in calcium supplements derived from animal sources . Mercury, arsenic, and thallium use are reported in TCM . Arsenic poisoning from herbal medicine is usually chronic and presents with features, such as skin changes, leucopenia, anemia, sensory neuropathy, and malignancies. Other heavy metals reported to contaminate dietary supplements and herbal products include, cadmium, copper and molybdenum.

Other contaminants include micro-organisms, pesticides, industrial chemicals, and toxic herbs. These usually result in gastroenteritis, but more severe problems have been reported, such as eosinophilia-myalgia syndrome and death due to unknown chemical contamination of L-tryptophan supplements. Chinese herbal products have been reported to be contaminated with toxic herbs such as podophyllum and Daturametel. These can produce features of toxicities due to the inherent toxicities of these herbal contaminants; for example, podophyllum poisoning can lead to agranulocytosis, and Daturaingestion can lead to anti-cholinergic toxicities.

Dietary supplements and herbs that possess pronounced pharmacological effects or toxic constituents can be inherently poisonous, and physicians should anticipate problems with such toxicities if they encounter patients using these products. The clinical features encountered will depend on the inherent compounds present in the products. outlines some of the frequently reported herbs and their expected toxicities. Toxic herbs frequently encountered in reports are those with stimulant effects, such as Ephedra species, caffeine, ginseng, and gingko; those with cardiac effects, such as herbs containing cardioactive glycosides or Aconitum species; those with autonomic effects, such as Datura species, Lobelia species, and yohimbine; those with hepatotoxic effects, such as herbs with pyrrolizidine alkaloids; those with nephrotoxic effects, such as herbs with aristolochic acid; and those that are used as abortifacients, such as pennyroyal oil.

Table 3.2 Organ toxicities and toxidromes, and common dietary supplements or herbal medicines that can cause them.

Clinical features	Xenobiotics
Cardiac	Sodium channel effects—Aconitum species (widen QRS, shock)
	Digoxin-like effects—Digitalis species, bufo toads
Central nervous system	Seizures—strychnine, thujone, essential oils (camphor, eucalyptus)
	Sedation—Valeriana species, kava kava
Dermatological	Blistering—cantharidin (Chinese blister beetle)
Hematological	Coagulopathies—G-herbs (ginger, garlic, gingko)
	Agranulocytosis—anti-mitotic agents (colchicine, podophyllotoxin)
Hepatotoxic	Hepatitis—multiple agents, germander commonly reported
	Veno-occlusive disease—pyrrolizidine alkaloids (comfrey, Senecio species, Heliotropiumspecies)
Nephrotoxic	Renal failure—Aristolochia speices
	Hypertension, hyperkalemia—licorice
Anticholinergic	Daturametel commonly used in TCM
	Hexing herbs (Atropa sepcies, Hyoscyamus species, Mandragoofficinarum) common in Western herbal practice
Sympathomimetic	Ephedra species, Citrus aurantium (bitter orange)
Salicylate	Willow bark, checkerberry

Clinical features	Xenobiotics
poisoning	

The problem of the inherent toxicity is compounded by the variation in content of the active ingredients found in these products. The chemical constituents in a plant are dependent on the soil they are grown in, rainfall and sunshine, the season of harvesting, the stage of the plant growth during harvest, diseases afflicting it, and the parts that were harvested. Even in finished products, such as pills and liquids, there can be large batch-to-batch variations in content, and this can result in toxicity. For example, a survey of ginseng products found up to 200 times variation in content between different products. In another survey of Ephedra products, within the same product, up to ten times variation in active ingredients among batches was found .

Allergic reactions to dietary supplements and herbal medicines appear to be common and under-reported. These reactions may present as mild reactions, such as pruritus and urticaria, to more severe reactions, such as angioedema and anaphylaxis. Patients may react to compounds inherent in the dietary supplements and herbal medicines, such as proteins found in animal products. Patients may also develop allergic reactions to compounds that were added into these products as intentional adulterants or contaminants. It is difficult to anticipate allergic reactions to these products unless previous allergies are known.

5. Management of Patient with Toxicities

Toxicities from dietary supplements and herbal medicines present unique management challenges. Patients may not inform their physicians about herbal supplement use because they do not perceive these products as medications. When toxicities arise, patients may not be aware that the dietary supplements or herbal products are causing the problems, so they continue to use the products. Such behaviors can hamper diagnosis or make the toxicities worse.

Information about product content and dose may also be difficult to obtain. Labeling of these products can be inaccurate or incomplete. The quantity of content can be different from the label given the lack of quality assurance and labeling consistency. Multiple components within a product make identification of the offending agent difficult. Unsuspected adulterants or contaminations may make the presentation more confusing. Raw herbs, dried herbs, or herbs processed into powders or liquids may prove difficult or impossible to identify. Even when labeling is accurate or herbs can be identified, scientific and toxicological information regarding them may not be readily available from conventional resources. A study in the US of adverse effects from dietary supplements found that less than half of the products or ingredients were listed in the poison information software that is used in most US poison centers.

Nevertheless, the spectrum of toxicities from dietary supplements and herbal medicines is similar to that of toxicities from pharmaceuticals in that similar organ system effects or toxidromes can be expected. Furthermore, some herbs or formulations are well known to result in certain organ toxicities or toxidromes, and their presence should be suspected when these clinical features occur.

The approach to patients with toxicities from dietary supplements and herbal medicine is similar to the approach to patients with other forms of toxicities. outlines steps generally recommended by authors for treating these patients. Patients who present with unstable medical conditions, such as cardiac dysrhythmias or seizures, require immediate stabilization. Once they are stabilized, extended history taking, physical examination, and laboratory investigation can be done. Once the problem is identified, the use of the product can be stopped or altered, and appropriate therapy can be initiated.

Table 4 Useful steps in managing patients with toxicities from dietary supplements or herbal medicines.

1. Ask specifically regarding use of such products
2. Secure sample for identification
a. Actual herbs or product used
b. Prescription or packaging
3. Laboratory studies
a. Basic blood count, renal function, liver function, and electrocardiogram
b. Heavy metal screening if suspected or if symptoms are non-specific
c. Analysis methods exist for some herbal toxins only—colchicines (HPLC, GCMS), tropane alkaloids (GCMS, oxalate (GCMS), vinca alkaloids (HPLC), cardioactive steroids (immunoassay)—check with local laboratory
4. Good resuscitative, symptomatic, and supportive care
5. Use antidote if appropriate

6. Instruct patients and family to stop using the product
7. Consider outpatient monitoring of renal function, liver function, and blood counts
8. Report case to regulating authority
9. Report unusual cases in the medical literature

Good resuscitative, symptomatic, and supportive care is paramount in these patients, as in all patients with poisoning. In such circumstances, offending agents would most likely not be identified early, and even if identified, specific antidote treatment may not exist, making resuscitative, symptomatic, and supportive care more important. Some generalizations for management can be made. Patients who present early with toxic ingestion of dietary supplements or herbal products that can cause severe life-threatening effects, such as Aconitium species or colchicines, should undergo gastric lavage with adequate airway protection. Similarly, activated charcoal can be given in an acute overdose of toxic dietary supplements and herbal medicines if there is adequate airway protection. In patients with stimulant effects, agitation or seizures can be managed with benzodiazepines. In patients suffering from digoxin toxicity, digoxin antibody is expected to work, but a non-standard dose may be required. In patients with sodium channel effects (wide QRS complexes, shock), sodium bicarbonate can be used, and class IB anti-arrhythmics such as lignocaine can be used if sodium bicarbonate fails. The local poison information centers can be good resources to assist with diagnostic or management issues.

When obtaining history from patients suspected of suffering from dietary supplement or herbal medicine toxicities, it is important to remember that patients often do not volunteer information regarding the use of these products to their physicians. When suspected, physicians need to ask patients specifically if they were or currently are consuming such products. And these products include specialty teas for weight loss or calming effects. Studies have shown that up to 70% of patients who use alternative therapies do not inform their physicians about it.

During physical examination, features suggestive of toxidromes should be looked for, such as pupils size, mucosa moisture, skin moisture, and bowel sounds. Features of organ toxicities should also be sought, especially signs of liver injuries or failure. These toxidromes and organ toxicities can often be related to certain commonly used dietary supplements and herbal medicines.

Whenever possible, a sample of the actual product used by the patient should be secured; otherwise, prescription or packaging should be secured. If this is not possible, samples from where the patient

actually obtained the product may be useful. If raw herbs were involved, obtain information about the parts used and how they were processed. These can be used to identify offending agents. Although immediate identification or analysis is often not possible, efforts should still be made to identify them later as some herbs and products can have long-term effects, such as hepatotoxicity or nephrotoxicity.

Basic diagnostic studies, such as blood count, electrolytes and renal function, liver function, and electrocardiograms, should be performed, as well as other tests based on the patient's clinical presentation. If symptoms are non-specific or suggestive of heavy metal toxicities, a heavy metal screen may be useful. Analytical methods exist for herbal toxins, such as colchicines, tropane alkaloids (anti-cholinergic), vinca alkaloids, and cardioactive glycosides; however, the availability of these tests depends on local laboratories. When such analyses are indicated, it is essential to check with the local laboratory if the tests are available. The salicylate level should be available in most laboratories.

For patients who can be discharged, they should be specifically instructed to stop using the dietary supplements or herbal medicines. This discussion should involve family members as well, as they may be taking similar products or be supplying them to the patients. Consideration should also be given to referring patients for outpatient monitoring of liver function, renal function, and blood counts in a week or two, as toxicities in these organs may be delayed and not clinically apparent. Some authors and herbal practitioners advocate that patients using TCM should have their liver function monitored regularly as many herbs can cause hepatotoxicity.

The relevant regulating authorities should be informed of such events so that offending products can be investigated and if necessary taken off the market to prevent more people from being affected. The range of dietary supplements and herbal products are expanding rapidly, and medical and scientific knowledge of these products is still growing. Unusual cases should be reported to the medical literature to inform the medical community of potential problems.

6. Conclusion

In Conclusion, its known that all the supplements that are used in the sport field are useful for athletes and the advantages are a lot. Many consider the that most of the food and drug supplements that is used by the athletes is the main way for them to keep fit and have more efficient performance. There are many things that needs to be considered before taking the suppliments when doing sport. Depending on who uses the medication, the dose and effect differs if the person is a beginner, amateur or a professional athlete.

As anything else the food and drug suppliments have their own risks, and toxic effect is one of them. Most food and drug suppliments are not considered as harmful or toxic, what makes it toxit is

the way of using it or taking some fake product while doing sport. By this it needs to be known that taking these suppliments is good to use as recommended and being careful on what to take and to use.

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