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Position of the Working Group Sports Nutrition of the German Nutrition Society (DGE): Safety Aspects of Dietary Supplements in Sports

Position der Arbeitsgruppe Sporternährung der Deutschen Gesellschaft für Ernährung (DGE): Sicherheitsaspekte von Nahrungsergänzungsmitteln im Sport

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Summary

› **This position paper** deals with safety aspects of the use of dietary supplements (DS) in sports. DS are legally classified as foodstuffs and may contain vitamins, minerals and other substances with a nutritional or physiological effect. In the case of other substances with a nutritional or physiological effect, it is currently not specifically regulated, with a few exceptions, which individual substances may be added, provided the products are still classified as foods. DS are offered in a wide variety and can be purchased worldwide via the internet. In Germany, they are only subject to a notification requirement before being launched on the market; they are not subject to safety assessment by state authorities. The manufacturers/distributors of the DS are responsible for their safety and for ensuring that consumers are not misled by the product presentation and promotion.

› **For athletes,** a balanced diet that is adapted to their needs is a basic requirement and one of the preconditions for good athletic performance. DS are no replacement for a balanced diet.

› **In sports,** the use of DS or products that contain micronutrients and other substances with a nutritional or physiological effect should not be conducted uncritically. Possible risks, such as an unintentional violation of anti-doping regulations or potential health risks, should be considered.

KEY WORDS:
Doping Risk, Wada Prohibited List, Health Risks, Vitamins, Minerals, Caffeine

Zusammenfassung

› **Dieses Positionspapier** befasst sich mit Sicherheitsaspekten bei der Anwendung von Nahrungsergänzungsmitteln (NEM) im Sport. NEM zählen rechtlich zu den Lebensmitteln und können Vitamine, Mineralstoffe und sonstige Stoffe mit ernährungsspezifischer oder physiologischer Wirkung enthalten. Bei sonstigen Stoffen mit ernährungsspezifischer oder physiologischer Wirkung ist gegenwärtig bis auf wenige Ausnahmen nicht speziell geregelt, welche Stoffe im Einzelnen zugesetzt werden dürfen, sofern die Produkte noch als Lebensmittel einzuordnen sind. NEM werden in großer Vielfalt angeboten und können via Internethandel weltweit bezogen werden. Sie unterliegen hierzulande vor dem Inverkehrbringen nur einer Anzeigepflicht; eine staatliche Prüfung der Sicherheit erfolgt dabei nicht. Die Verantwortung für ihre Sicherheit und dass Verbraucher durch Aufmachung und Bewerbung nicht getäuscht werden, liegt bei den Herstellern/Inverkehrbringern der NEM.

› **Für Sportler** ist eine ausgewogene und den Bedürfnissen angepasste Ernährung ein grundlegendes Erfordernis und eine der Voraussetzungen für gute sportliche Leistungen. NEM stellen keinen Ersatz für eine ausgewogene Ernährung dar.

› **Die Verwendung von NEM** bzw. Produkten, die Mikronährstoffe und sonstige Stoffe mit ernährungsspezifischer oder physiologischer Wirkung enthalten, sollte im Sportbereich nicht unkritisch erfolgen. Mögliche Risiken wie eine unabsichtliche Verletzung von Anti-Dopingregularien oder mögliche gesundheitliche Risiken sollten berücksichtigt werden.

SCHLÜSSELWÖRTER:
Dopingrisiko, Wada-Verbotsliste, Gesundheitsrisiken, Vitamine, Mineralien, Koffein

Introduction

There is widespread use of dietary supplements (DS) in sports. The advertising messages of these products are diverse. Athletes use them with the intention of improving their general state of health and immune function, for disease prevention, improved regeneration, increased performance capacity or to improve a diet that is considered imbalanced, among other things (2, 37).

There is relatively reliable information about the use of supplements in athletic sports from an evaluation of doping control sheets that were compiled for adolescent and adult athletes from 2003-2008 during world championships and on other occasions. In 66% of these cases, the consumption of a DS during the last seven days was confirmed. In that time period, adult athletes had taken supplements from 1.7 different supplement substance categories on average. Thirty percent of the control sheets (in all age groups) indicated the intake of more than two supplement categories and, in individual cases, up to 24 supplements from 11 supplement categories (44).

At the Soccer World Cup in 2006, responsible team physicians reported an average consumption of 1.3 supplements per player and game, and some players took up to 10 supplements before a game (45). In Germany, in a survey of young top athletes in various Olympic disciplines, 91% of the respondents stated

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that they had consumed a supplement during the last month, and more than a quarter (26.8%) of the supplement users consumed at least one supplement per day (13).

In a literature study that included different types of sports and countries, vitamins/minerals, multivitamins/multiminerals, vitamin C, protein products, sports drinks and sports bars were among the most frequently used supplements (33). In the above-mentioned survey of young top athletes in Germany, the most common "supplements" consumed at least once per month were magnesium (69% of the supplement users), dextrose (64%), energy drinks (64%), vitamin C (56%) and calcium (46%) (13).

In the available investigations, the applied definitions of supplements were partially not identical with the EU-wide regulatory definition of DS and they ranged from various DS with a wide range of ingredients to more conventional products, such as sports drinks or sports bars.

In the following, safety-related aspects of DS and their ingredients are discussed. In principle, however, the aspects described can also be transferred to other food categories such as snack bars, drinks or other products having such ingredients added.

It is worth noting that not only questions of safety but also of "effectiveness", i.e. a proven positive effect on athletic performance, are significant in regard to the use of DS in sports. It can be assumed that – apart from compensating for proven deficiencies or ensuring sufficient supplies of essential nutrients, e.g. certain vitamins and minerals, or, apart from certain products to cover energy, carbohydrate or fluid/electrolyte demands in endurance sports – such a positive effect has so far only been sufficiently scientifically proven for very few substances advertised as ergogenic (1, 26, 36, 38, 43).

Legal Background

DS are legally classified as foodstuffs and are subject to food legislation. In addition to general food law regulations, DS are subject to the Regulation on Nutritional Supplements (Verordnung über Nahrungsergänzungsmittel, NemV), with which the EU directive 2002/46/EC was implemented in German law (39).

According to this directive, a DS is defined as a foodstuff that

1. is intended to supplement a normal diet and
2. is a concentrate of nutrients or other substances with a nutritional or physiological effect either alone or in combination and
3. is marketed in dose form (capsules, tablets, pills, sachets of powder, powder, ampoules of liquids, drop dispensing bottles, etc.) to be taken in measured small unit quantities.

DS have to be labelled with certain information, including the recommended daily intake of the product and the associated supply of nutrients or other substances with a nutritional or physiological effect.

Nutrients within the meaning of the regulation are vitamins and minerals, including trace elements. There are specifications for these as to which vitamins or minerals and which vitamin/mineral compounds may be used in the production of DS. When it comes to other substances with a nutritional or physiological effect (e.g. amino acids, fiber, fatty acids, animal-derived substances (glucosamine, etc.), dried powdered plants/plant parts, plant extracts, isolated plant substances), aside from a few cases, there are no specific regulations on which individual substances may be added to DS. This needs to be asses on a case-by-case basis.

Currently, there are no regulatory maximum amounts for the addition of vitamins, minerals or other substances with a nutritional or physiological effect to DS, neither at German national nor at European Union level (although legal provisions on national maximum amounts of vitamins and minerals or various other substances with a nutritional or physiological effect exist in individual countries of the EU). However, the general food law regulations apply, which prohibit the placing on the market of foodstuffs that are not safe (article 14, Regulation (EC) 178/2002).

Before bringing DS to market, there is merely a duty of notification. They are not subject to a safety assessment by state authorities before being placed on the market. The manufacturers/distributors of the products are responsible for the safety of DS and for ensuring that consumers are not misled by their presentation and promotion. The DS on the market are monitored by the food surveillance authorities of the German federal states. Health-related advertising messages about DS ingredients, i.e. whether their consumption is associated with health benefits, including positive effects in sports, are and have been evaluated by the European Food Safety Authority (EFSA) in the context of the evaluation of health claims for foodstuffs and food ingredients (14).

In view of global trade and availability of products via the internet, it must also be borne in mind that while there are certain national and EU-wide regulations regarding foodstuffs and DS, a purchase from abroad raises the question of which national regulations those products are subject to, especially in terms of product safety and the validity of advertising messages/promised effects, and whether those are actually adhered to. Additionally, there is the question of whether applicable German food regulations are complied with. For example, DS from abroad may possibly be considered as medicinal products in Germany. Accordingly, an import would be prohibited. In such cases, purchasers may even be threatened with prosecution (4). More information regarding the online purchase of DS and existing seals of quality for online purchases are available e.g. from the German Federal Office of Consumer Protection and Food Safety (3, 4).

Potential Risk of Using DS In Sports

DS must be safe, and the promotion, labelling and product claims may not mislead consumers. Nonetheless, with the wide range of products offered as DS or available as such via global internet, it is possible that the consumption is associated with potential risks even if the specified recommended daily intake is adhered to. For athletes who are subject to the doping control system, this primarily concerns the potential unintentional ingestion of substances banned by the World Anti-Doping Agency (WADA) Prohibited List, and health risks posed by the ingredients of DS.

Substances Banned by the WADA-Prohibited List

Products that are referred to as DS may contain substances that are banned according to the WADA-Prohibited List (48). On the one hand, these may be products where such substances are openly labelled and advertised as ingredients as such or in the form of synonyms. On the other hand, these may be products where these substances are not declared as ingredients. In these cases, the substances banned by the WADA-List were introduced into the products unintentionally as impurities (contamination) during the manufacturing process or they were added intentionally (adulteration) to achieve certain product effects. In some cases, the substances relevant to doping are not, or only with difficulties recognizable to athletes as substances on the WADA-List, because of the use of synonyms or fancy names or irregular names (e.g. the substance 4-methylhexan-2-amine [methylhexaneamine]; used synonyms: dimethylamylamine = DMAA = dimethylpentylamine = pentylamine = geranamine; in some cases, geranium root extract or geranium oil were cited as alleged natural sources of methylhexanamine (28). ›

The doping-relevant substances detected in the past years are variegated (e.g. stimulants, prohormones, "classic" anabolic steroids, "designer" steroids, clenbuterol, prohibited peptide hormones, etc.). The products involved were similarly diverse (28, 29, 30, 32, 35). Especially when it comes to intentionally adulterated products, "slimming products" with added stimulants, DS products with anabolic steroids marketed for building muscles, fat-reducing and muscle-building products with added β2-agonists or motivation-enhancing products and so-called neuroenhancers with added stimulants are the main candidates for these adulterations (12). In positive doping cases, DS with diuretics were also detected (12). However, other products that listed as their main ingredients e.g. vitamins, minerals, amino acids/protein hydrolysates or a broad range of substances used in sports, have also been affected in the past, e.g. by contamination (29, 30).

The detected amounts ranged from high, sometimes supra-therapeutic, doses to low doses, which are highly unlikely to produce positive effects on performance, although they can sometimes still be sufficient to cause positive doping test results (28-30). For example, small doses of 2.5 µg of a nandrolone prohormone (19-norandrostendione), administered in a mix with 5 g creatine (corresponding to a contamination of 0.00005%) were sufficient to produce urine levels of the diagnostically used main nandrolone breakdown product (19-norandrosterone) in the first two urine samples after ingestion of some of the study participants, which would have resulted in a positive doping test (46).

Insofar as a physician is aware that an athlete whom he advises is subject to the doping control system, he should inform the athlete of the risk of a possible positive doping result owing to contamination when advising on the use of DS. If this does not happen and a positive result is obtained, a liability claim by the athlete against the physician is to be assumed. To what degree this principle can be extended to other persons serving in an advisory capacity, such as nutritionists, has not yet been legally clarified.

Depending on the dose, the aforementioned doping-relevant substances may also pose health risks. It is possible that the main doping-relevant substances detected are subject to change over time, e.g. as a result of regulatory measures in certain countries, which will affect their availability. Reference should also be made e.g. to the detection of non-declared sibutramine in various products labelled as DS for weight loss ("slimming products"), which appeal to different population groups. Sibutramine is included on the WADA-Prohibited List (in the stimulants section) and is a substance belonging to the group of appetite suppressants which was previously used as medicinal product. Owing to significant side effects, particularly in overweight persons with cardiovascular diseases, the European Medicines Agency recommended in 2010 that the approval of medicinal products containing sibutramine be revoked (4, 5).

In the meantime, various countries have implemented quality assurance programs which ensure that DS are examined for the presence of various doping-relevant substances and that other quality-related information about the product's manufacturing process is collected in order to provide athletes access to DS that carry a reduced but not eliminated risk of containing doping substances. In Germany, for example, there is the "Kölner Liste" ("Cologne List") (www.koelnerliste.com) or in the USA the National Sanitation Foundation (NFS) International with the program Certified for Sport® (www.nsfsport.com/), the program Informed Choice (http://informed-choice.org/) and the program of the Banned Substances Control Group (www.bscg.org) (40). According to a rough estimate, which is afflicted with considerable uncertainty, approximately 6-9% of doping cases sanctioned in Australia, Great Britain and the USA between 2006 and 2013 were associated with products marketed as DS (41).

Potential Health Risks of Used Ingredients

It cannot be assumed that all products sold as DS or distributed worldwide via the internet are without health risks, even if the recommended daily intake is adhered to.

An extreme example of the health risks posed by ingredients was the unauthorized use of 2,4-dinitrophenol (DNP) in products that were sold as DS and "slimming products", so-called fat burners, and appealed in particular to people in the "bodybuilding scene" as the target group. Several deaths were attributed to the consumption of products with DNP in various countries. In some cases, the addition of DNP was not labelled and thus not recognizable for consumers. DNP is a chemical which functions as an uncoupler of oxidative phosphorylation in the mitochondria, thus obstructing the physiological respiratory chain and the cell's energy metabolism, resulting in an increased cellular metabolic rate (lethal oral dose: 1-3 g, serious and life-threatening effects may also occur after repeated consumption of low doses owing to accumulation in the body) (7).

Another example of using risky substances in DS is the use of the Ephedra herb and its preparations originating from Ephedra species in food, which is now banned in the EU (Regulation (EU) 2015/403). In the past, extracts of Ephedra herb, referred to as Ephedra or Ma-huang, were added to DS for weight reduction (fat burners) or to improve athletic performance, often in combination with caffeine/guarana extract and/or other substances. These products were available on the Internet. The EFSA concluded that for the Ephedra herb and ephedra alkaloid-containing preparations used in DS, there are significant safety concerns regarding the estimated levels of intake (e.g. potential adverse cardiovascular and/or central nervous effects in the case of high ephedra alkaloid intake) (23).

Health risks of DS can arise not only from the sample substances listed here, some of which are extreme, but also from various other substances from the wide range of ingredients that are added to DS. As with most substances, the health risks depend on the dose, i.e. the daily intake. In this regard, the common expectation of consumers that a product containing a higher amount of a certain ingredient per daily dose also indicates a higher-quality product does not always apply. In this respect, DS and their ingredients are comparable with spices; the key is not to think "the more, the better", but rather to use the right amount. Adverse effects can thus be prevented.

In some cases, it is possible that substances are used as ingredients of DS for which only few safety data are available and whose safety profile has only been investigated incompletely or not adequately. Also, when several ingredients are combined in one product, particularly when similar undesired effects are to be taken into account for some of the ingredients (e.g. in the case of substances that stimulate the cardiovascular system), questions may arise regarding potential health risks of the product as a whole.

When using several DS per day, consumers ought to bear in mind that an ingredient may be included in more than one of these products (e.g. when using combination products) and that in such cases, they should consider the total daily intake of those ingredients in order not to exceed safe intake levels. When it comes to ingredients derived from plants, such as dried and powdered plants/plant parts, extracts or isolated plant ingredients (botanicals), it must be kept in mind that there are no binding specifications for such plant-based preparations in the food sector and that – even if they are derived

Table 1

Vitamins and minerals for which the SCF/EFSA derived tolerable upper intake levels (UL). Tolerable upper intake levels derived by the EFSA/SCF (adults, ≥18 years) (16,20-22) and D-A-CH reference values available for these vitamins and minerals (adults, ≥19 years) (11) and available recommendations for maximum amounts of these vitamins and minerals in dietary supplements (DS) (adolescents and adults, ≥15 years) (47). BfR = Bundesinstitut für Risikobewertung (German Federal Institute for Risk Assessment); DS = dietary supplement; D-A-CH = Deutsche Gesellschaft für Ernährung; Österreichische Gesellschaft für Ernährung, Schweizer Gesellschaft für Ernährung (German Nutrition Society, Austrian Nutrition Society, Swiss Nutrition Society); EFSA = European Food Safety Authority; SCF = Scientific Committee on Food. [a] Notice stating that during pregnancy, vitamin A should only be taken after consulting a doctor; [b] health-based guidance value; according to the EFSA (22), the additional consumption of 15 mg β-carotene/day, e.g. via DS and food colourants, is safe; [c] according to EFSA (20); [d] in the absence of endogenous synthesis; [e] the UL only applies to synthetic folic acid; [f] recommended intake of folate; [g] recommended intake of niacin; [h] according to EFSA (21); [i] In adults, zinc absorption is influenced by phytate levels in food. The values stated here refer to a median phytate intake (corresponding to 660 mg/day [1.0 mmol/day]); j In Germany, a UL of 500 µg/day applies for adults and especially older persons who have been exposed to iodine deficiency for a longer period and thus may be at a risk of altered autonomic function (11).

NUTRIENT	UL (EFSA/SCF) (ADULTS ≥18 YEARS)	D-A-CH REFERENCE VALUE FOR NUTRIENT INTAKE (ADULTS ≥19 YEARS)	RECOMMANDED MAXIMUM LEVELS FOR DS BY BFR (ADOLESCENTS AND ADULTS ≥15 YEARS)
Vitamin A (mg/day)	3.0	0.8-1.0	0.2 [a]
β-carotene (mg/day)	15 [b]	2-4	addition to DS only under the condition that there is no fortification of of non-alcoholic drinks with β-carotene or that it is restricted
Vitamin D (µg/day)	100 [c]	20 [d]	20
Vitamin E (mg/day)	300	11-15	30
Vitamin B6 (mg/day)	25	1.4-1.6	3.5
Folic acid (µg Folate equivalents/day)	1000 [e]	300f	200
Nicotinic acid (mg/day)	10	11-16 [g]	4
Nicotinamide (mg/day)	900		160
Calcium (mg/day)	2500 [h]	1000	500
Magnesium (mg/day)	250 (for supplemental intake)	300-400	250
Zinc (mg/day)	25	8.0-14.0 [i]	6.5
Copper (mg/day)	5	1.0-1.5	0 (for persons aged 15-17) 1 (for persons ≥18 years)
Iodine (µg/day)	600 [j]	150-200	100
Molybdenum (µg/day)	600	50-100	80
Selenium (µg/day)	300	60-70	45

from the same plant or the same related plant species – depending on the raw material used (e.g. regional provenance), processing and manufacturing method (e.g. extraction, purification process), they can have different contents or compositions of health-relevant substances, purity levels and amounts of accompanying/undesirable substances. It may thus be possible that health effects and safety profiles observed with one preparation may not be readily transferred to other preparations.

Safety-Related Aspects of Individual Ingredients frequently Used in Sports

Safety-related aspects of individual DS ingredients frequently used in sports are presented below. With respect to the wide range of substances often used as ingredients of DS in sports, reference is also made, for example, to the brochure of the German Olympic Sports Association "Nutritional Supplements" (12) and its chapter "Fact Check" (12).

Vitamins and Minerals

(This refers to the minerals for which reference values for daily intakes have been derived by the DGE, EFSA and other scientific bodies.) Vitamins and minerals in the form of multivitamin/multimineral products or products that contain individual vitamins or minerals are among the most frequently used supplements in sports.

The human body depends on the intake of vitamins and minerals. There are health risks on the one hand in the case of deficiencies and on the other hand in the case of excessive intakes and associated adverse effects. When vitamins and minerals are used as food ingredients, the intake range considered safe for humans is limited upwards by the tolerable upper intake level. The tolerable upper intake level (UL) is defined as the maximum level of chronic daily intake of a nutrient from all intake sources judged to be unlikely to pose a risk of adverse health effects in humans (16). Table 1 lists the ULs for adults for vitamins and minerals derived by the EFSA and its predecessor institution, the Scientific Committee on Food (SCF), on the basis of available human and animal data and in consideration of uncertainty factors (16, 20, 21). The ULs apply to the general adult population but not to individuals who receive vitamins/minerals under medical supervision or for therapeutic purposes.

For several vitamins and minerals, no ULs could be derived owing to insufficient data. This includes substances for which no adverse effects were observed even with intake levels far above the reference values (vitamin B1, vitamin B2, biotin, ›

Table 2

Caffeine content of selected foods ((6), modified according to (24)). All values relating to caffeine content are approximations as the caffeine contents may fluctuate.

	SERVING UNIT	CAFFEINE CONTENT/ SERVING
Filter coffee	Cup (200 ml)	90 mg
Energy drink	Can (250 ml)	80 mg
Espresso	Cup (60 ml)	80 mg
Black tea	Cup (200 ml)	45 mg
Cola beverage	Can (330 ml)	35 mg
Cocoa drink	Cup (200 ml)	8–35 mg
Green tea	Cup (200 ml)	30 mg
Dark chocolate	½ bar (50 g)	25 mg
Milk chocolate	½ bar (50 g)	10 mg

pantothenic acid) as well as substances for which no UL could be derived due to scarce data, insufficient knowledge on dose-effect relationships, open questions regarding adverse effects or other reasons (vitamin C, vitamin K, vitamin B12, iron, manganese, chromium, sodium, potassium, chloride, phosphorus). Some evaluations of these substances contain (to some extent) information that can be used alternatively as a guidance value in risk assessment (e.g. for vitamin C).

As a rule, ULs were derived for the intake of a nutrient from all sources, i.e. the intake from the normal diet, DS and enriched foods. They should not be confused with maximum levels for individual DS. When considering health-based acceptable maximum levels for individual DS products, the daily vitamin or mineral intakes from all above-mentioned sources must be taken into account adequately. Proposals for maximum levels of vitamins and minerals in DS based on this stipulation which are applicable to persons aged 15 or older have been published by the German Federal Institute for Risk Assessment (Bundesinstitut für Risikobewertung, BfR) (9, 47). They are listed in Table 1 for the vitamins and minerals for which ULs were derived by the EFSA/SFC.

Safety-Related Aspects of Individual Minerals and Vitamins Frequently Used in Sports

Magnesium

The UL derived by the SCF for magnesium of 250 mg/day (16) for adults and children from four years of age applies only to the supplemental intake of easily dissociable magnesium salts and compounds such as magnesium oxide via DS or enriched foods, since in healthy consumers, no adverse effects have been observed to date with magnesium intakes which result from normal diet or from the natural magnesium content of foods. This should be considered when comparing the UL with the reference values for magnesium intake of adults (300-400 mg/day). The SCF's UL derivation is based on gastrointestinal effects (mild diarrhea) that may occur in a small percentage of adults with the additional intake of about 360-365 mg magnesium/day. No laxative effects were observed in adults with an intake of up to 250 mg/day. On this basis, and since the adverse effects are not associated with pathological sequelae and considerable adaptation can occur within days, the SCF derived a UL of 250 mg/day. Since in most studies used to derive the UL, the magnesium was taken in two or more servings per day, the panel pointed out that the UL applies to additional intakes consumed in two or more separate servings per day (16). There has been some evidence that mild diarrhea in a small percentage of adults can already occur with an additional (= supplemental) intake of 300 mg/day, which can be interpreted as a confirmation of the UL derived by the SCF (250 mg/day for additional intake) (8).

Iron

The EFSA was unable to derive a UL for iron due to insufficient data (16). Adverse effects of short-term excessive iron intake are relatively well-described. The EFSA concluded that adverse gastrointestinal effects (nausea, epigastric discomfort, constipation) were observed after short-term supplemental doses of 50-60 mg of non-heme iron preparations/day, particularly if taken without food. The American Institute of Medicine based its UL derivation for iron, conducted in 2001, on acute gastrointestinal effects and derived a UL of 45 mg iron/day (31).

In regard to possible adverse effects of long-term intake, the EFSA pointed out that according to limited scientific data, supplemental doses of 30 mg of non-heme iron/day may be associated with indicators of high iron stores (elevated serum ferritin concentration) in older persons, but that it is currently not known at which point elevated serum ferritin concentrations are associated with increased health risks, such as fibrosis of the liver.

According to the evaluation by the EFSA, the risk of adverse effects due to high iron intake from normal diet is low in the general population, but additional iron intake via DS may increase the proportion of individuals among men and postmenopausal women who are likely to develop biochemical indicators of elevated iron stores. Furthermore, EFSA pointed out that menstruating women and children, who are at risk of poor iron status, may benefit from additional iron intake or improved bioavailability of dietary iron (for specific questions about the iron status and iron supply of athletes, see: Position of the working group sports nutrition of the German Nutrition Society (DGE): minerals and vitamins in sports (10)).

Homozygous carriers of hereditary hemochromatosis (up to 0.5% of the population) represent a particularly sensitive risk group for iron overload, even at normal dietary iron intakes (16)

In its recommendations for maximum levels for DS, the BfR derived a recommended maximum level for iron in DS of 6 mg/day, especially with regard to menstruating women, combined with the statement that men, postmenopausal women and pregnant women should only take iron supplements with medical advice (47).Taken together, owing to the health risks posed by iron supplements, and to ensure optimal supplementation – if this should be necessary – athletes are advised against taking iron supplements of their own accord without medical advice.

Vitamin C

The EFSA could not derive a UL for vitamin C owing to a lack of data (16). In the risk assessment of high vitamin C intakes, the focus is on adverse gastrointestinal effects and open questions concerning increased renal oxalate excretions. The EFSA stated that acute adverse gastrointestinal reactions (abdominal distension, flatulence, diarrhea, transient colic) represent the most clearly defined adverse effects of high vitamin C intake, but that only limited data about the dose-response relationship is available, making it impossible to derive a UL. However, human studies suggest that an additional intake (= in addition to the normal dietary intake) of up to about 1 g/day does not lead to adverse effects, whereas such effects could occur with higher intakes (3-4 g/day) (16).

Furthermore, there are scientific uncertainties whether high vitamin C intake is associated with increased renal oxalate excretion, which in turn could increase the risk of kidney stones. However, according to EFSA, no increased risk of kidney stones was observed with a habitual intake of 1.5 g/day. The EFSA also pointed

out that vitamin C absorption is saturated at high doses, and that therefore intakes of more than 1 g/day are associated with negligible increases in absorption and tissue concentrations, but with increased risks of adverse gastrointestinal effects (16).

It should be noted that there is a current discussion about whether high intakes of antioxidants (e.g. vitamin C, vitamin E; often administered in combination) during training have potential adverse effects on performance- and health-promoting adaption processes in sports training (see: Position of the working group sports nutrition of the German Nutrition Society (DGE): minerals and vitamins in sports (10)).

Taking into account possible intakes of vitamin C from other food sources, a maximum level (for persons ≥15 years) of 250 mg vitamin C/day was proposed for DS (47).

Caffeine

Caffeine (1,3,7-trimethylxanthine), a natural alkaloid, has been consumed as an ingredient of various foods and drinks for centuries, primarily owing to its stimulating effect, and its use is also widespread in sports.

Natural sources include coffee beans, tea leaves, cocoa beans, guarana berries, cola nuts and leaves of the yerba mate plant. Caffeine is also added to numerous foods as a pure substance or in the form of extracts, e.g. to energy drinks, mate drinks, cola beverages, sweets, baked goods and, combined with synephrine, to various DS, which are offered for weight loss or enhanced sporting performance (sometimes in combination with other substances) (Table 2). Caffeine stimulates the cardiovascular and central nervous system. This is primarily accomplished by antagonistic effects on adenosine receptors. Consumed in moderate amounts, this is associated with an increased ability to concentrate, increased alertness, reduced fatigue or increased physical performance (in the endurance area).

Excessive caffeine intake can result in adverse effects, e.g. increased nervousness, irritability, anxiety, insomnia, sweating or tachycardia. However, the occurrence of adverse effects greatly depends on individual sensitivity, the usual caffeine consumption and the associated habituation effect as well as the respective caffeine dose ingested. Excessive caffeine consumption over longer time periods is associated with cardiovascular problems. In pregnant women, excessive caffeine consumption over a longer period creates the risk of stunted foetus development (6, 24).

According to the safety evaluation of caffeine by the EFSA (25), there are no safety concerns for healthy adults with single doses (or caffeine intakes within a short period) of up to 200 mg caffeine (about 3 mg/kg body weight [bw] for adults weighing 70 kg). This also applies to intakes of up to 200 mg caffeine consumed within two hours prior to intense physical exercise under normal environmental conditions. With regard to the total daily consumption distributed throughout the day, habitual intakes of up to 400 mg caffeine (approx. 5.7 mg/kg bw and day) appear to be safe for healthy adults.

In the case of intakes of 200 mg caffeine, derived by the EFSA for single doses or for caffeine intakes over a short period of time, athletes should consider that, according to the EFSA, these intakes can elicite positive effects in terms of attention/alertness (intake considered necessary for these effects: at least 75 mg caffeine per serving) and that, to a large extend, it is possible to reach intake levels that can result in positive effects on endurance performance or capacity in sports (intake considered necessary for this: 3 mg caffeine/kg body weight, taken one hour prior to starting the sports exercise) (18, 19).

With regard to intakes of up to 6 mg caffeine/kg bw or more, which are sometimes recommended in sports to increase endurance capacity, it should be noted that the intake level derived by the EFSA for single doses or intakes of caffeine over a short period of time of 200 mg caffeine, should not be exceeded.

Creatine

The SCF evaluated the safety of creatine (N-(aminoiminomethyl)-N-methyl glycine) in the year 2000. Based on the data available at the time, the scientific panel concluded that although no significant adverse effects had been reported in studies on the efficacy of creatine, this evidence was insufficient to provide reassurance about the safety of creatine supplementation and that various open questions remained. The panel recommended avoiding high loading doses. With a low intake of up to 3 g creatine/day, similar to the daily turnover rate of creatine (about 2 g/day), health risks were considered unlikely (42). In a 2004 evaluation of creatine monohydrate, the EFSA pointed to a study in which athletes received 15.75 g creatine monohydrate/day for five days, followed by an average of 5 g/day for up to 21 months (34). According to the panel, this study indicates that the intake of about 5 g creatine monohydrate/day (corresponding to about 4.4 g creatine/day) appears to be safe for athletes engaged in intense training and competition, but does not give reassurance about possible long-term effects of high doses of creatine monohydrate in non-highly trained individuals or other population groups. On the whole, the panel confirmed the earlier SCF recommendation, according to which high loading doses should be avoided and that – provided creatine with a high purity level is used – health risks are unlikely at intakes of up to 3 g creatine/day (15).

Significant for athletes: According to EFSA assessments, this intake (3 g creatine/day) is also sufficient to achieve an increase in physical performance in successive bursts of short-term, high intensity exercise or to enhance the effect of specifically defined resistance training on muscle strength in adults over the age of 55 (Regulation (EU) 432/2012) (17, 27).

Conclusion

A balanced diet that is adapted to their needs is a basic requirement for athletes and one of the preconditions for good athletic performance. DS are no replacement for a balanced diet.

If the use of DS is being considered – even though, to date, only a few substances that are advertised as ergogenic have been sufficiently scientifically proven to have a positive effect on athletic performance – the targeted use of DS should ideally be conducted in supplementing a well-composed diet plan. In sports, the use of DS or products that contain micronutrients and other substances with a nutritional or physiological effect should not be conducted uncritically. Possible risks, such as the unintentional violation of anti-doping regulations or potential health risks should be considered.

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Conflict of Interest

The authors have no conflict of interest.

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