

# A–Z of nutritional supplements: dietary supplements, sports nutrition foods and ergogenic aids for health and performance—Part 22

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Accepted 6 May 2011

Published Online First

6 June 2011

## INTRODUCTORY REMARKS

Practitioners who work with elite athletes know that the pressure and considerable rewards involved with success provide a high level of motivation to look for any safe and legal strategy that might enhance performance, even by small margins. Dietary supplements operate in this space, whether they promise a large performance boost or just create the fear that an athlete cannot afford to miss out on what everyone else is using. It is often tempting to overlook the lack of evidence to support the claims made about a supplement on the basis that the stakes are higher for elite athletes; therefore the cost:benefit ratio favours experimentation in the absence of clear proof. Over the past decade, however, we have become aware that the cost of getting it wrong has also escalated for elite athletes. A new hazard related to supplement use has emerged: inadvertent ingestion of substances that are banned under the antidoping codes in place in elite sport, but present in supplement products. In some cases, the level of the presence, or contamination, of banned substances in supplements presents a health hazard for all consumers. In some cases, the concentration may be too small to achieve any health or performance effect but large enough to record an infringement for athletes who submit to doping tests. Newspapers, the internet and Courts of Arbitration in Sport now bear stories of dedicated athletes whose careers have been or are being jeopardised because of the ingestion of a banned substance via a dietary supplement. This problem was first brought to scientific recognition by Hans Geyer and his colleagues from the Centre for Preventive Doping Research in Cologne. The following article provides an update of a recent review by this team.<sup>1</sup>

## INADVERTENT DOPING

### H Geyer and H Braun

In the past years, an increasing number of dietary supplements containing undeclared doping substances has been identified. The consumption of these supplements can lead to inadvertent doping cases. Although warnings about the risk of inadvertent doping have been communicated, recent studies show that athletes' knowledge of the problem is inadequate.<sup>2</sup> Furthermore, it seems that the risk has been growing due to the increased availability of pharmaceutical substances via the internet, which are admixed by criminal manufacturers to their, arguably, non-effective supplement products.

## DIETARY SUPPLEMENTS CONTAINING STIMULANTS

The main candidates from the dietary supplement market for inadvertent doping with stimulants are products containing ephedrine and analogues, sibutramine and methylhexaneamine. Such products are mainly advertised as fat burners or mood enhancers, and their use may lead to positive doping results in competition. The risk of inadvertent doping with such supplements is based on different reasons.

In the case of supplements containing ephedrine, the natural sources of ephedrine such as *Ma Huang* or *ephedra sinica* are frequently mentioned on the label rather than the names of the active ingredients (ephedrine, pseudoephedrine, methylephedrine, etc). Despite extensive education of athletes regarding unclear labelling, or the variety of names by which banned substances may be referred to, many athletes still fall into this doping trap.

In case of supplements enriched with sibutramine, the ingredient is not declared on the label and the consumer is only provided with the information that the product contains 'pure herbal ingredients' that are advertised to have considerable weight loss capabilities. Sibutramine can be found in therapeutic or even suprathreshold doses in slimming capsules, powders and even slimming teas.<sup>3–5</sup> Sibutramine is a synthetic anorectic drug, only approved as a pharmaceutical preparation and available only on prescription. Because of its enormous side effects (stroke and heart attack risk for patients with a history of cardiovascular disease), the European Medicines Agency recommended in January 2010 that this drug be withdrawn from the market. Sibutramine has been on the list of prohibited substances from the World Anti-Doping Agency (WADA) since 2006.

Since 2008–2009, there has been a high risk for inadvertent doping with the stimulant methylhexaneamine, which was added to the WADA prohibited list in 2009.<sup>6</sup> The issue of inadvertent doping arises from the fact that methylhexaneamine can be found on the labels in numerous different names such as dimethylamylamine, dimethylpentylamine, pentylamine, geranamine, forthane and 2-amino-4-methylhexane. On WADA's 2011 prohibited list, only the names methylhexaneamine and dimethylpentylamine are mentioned in the group of stimulants, which complicates the identification of the

substance as a prohibited compound. In some supplements, geranium root extract or geranium oil is mentioned as an alleged natural source of methylhexaneamine. However, recent investigations have shown that methylhexaneamine is not a natural ingredient of geranium oil,<sup>7</sup> which means that synthesised methylhexaneamine must have been added. Despite warnings by different national antidoping agencies in 2009 and 2010, numerous elite athletes in competition have been found to have a positive test for methylhexaneamine.

## DIETARY SUPPLEMENTS CONTAINING PROHIBITED ANABOLIC AGENTS

### Dietary supplements contaminated with prohormones

The extent of the contamination of dietary supplements with anabolic agents was evaluated in 2001 and 2002. A well-publicised study showed that about 15% of non-hormonal supplements such as vitamins, minerals, proteins and creatine contained anabolic androgenic steroids (mainly prohormones) that were not declared on the label.<sup>8</sup> The reason for the contamination was most probably the fact that manufacturers of prohormones (legally marketed as dietary supplements in the USA until 2004) also manufactured other supplements on the production line without sufficient cleaning. Another source of cross-contamination could have been the unclean transport containers from raw material suppliers of prohormones. The amount of detected prohormones, especially prohormones of nandrolone, could produce positive doping cases.

### Faked dietary supplements contaminated with 'classic' anabolic steroids

Since 2002, dietary supplements have appeared on the market, which are probably intentionally spiked with high amounts (more than 1 mg/g) of 'classic' anabolic steroids, not declared or declared with non-approved or fancy names on the label. Among these, steroids including stanozolol, metandienone, dehydrochloromethyltestosterone and oxandrolone have been identified. All these steroids are orally effective drugs based on their 17-alkyl group. These dietary supplements are advertised as leading to enormous enhancement of strength and lean body mass. The concentrations of the anabolic androgenic steroids are in the therapeutic or suprathereapeutic range per serving leading to positive doping cases detectable for several days and weeks, respectively, depending on the type of steroid administered.

Because the manufacturers of these faked products also prepare other nutritional supplements on the same production line, the risk of cross-contaminations with such 'classic' anabolic androgenic steroids is very high. Such contaminations have been found in fizzy tablets of vitamin C, magnesium and multivitamins produced for Spanish and German supermarkets containing, for example, small amounts of stanozolol and metandienone with the potential to produce a positive doping response.

Since 2002, the so-called designer steroids can also be found on the dietary supplement market. These steroids are neither listed as ingredients in any currently available medication, nor do their names appear in the WADA list of prohibited substances. Most of these 'designer steroids' have been synthesised in the 1960s and were tested only in animal studies for their anabolic and androgenic effects. Nowadays, these steroidal agents are produced exclusively for the nutritional supplement market and are advertised for their anabolic- or aromatase-inhibiting capacities. With regard to the effects and

side effects of these steroids for humans, there is limited or no knowledge. In most cases, the labelling of these products contains non-approved or fancy names of the steroids. More than 40 such designer steroids have been detected. The detection of metabolites of such a steroid in an athlete's urine sample is likely to lead to a positive doping case.

### Dietary supplements with clenbuterol

According to our knowledge, until now only two cases have been detected in which dietary supplements contained therapeutic (30 µg per tablet)<sup>9</sup> and suprathereapeutic (2 mg/capsule) doses of the β<sub>2</sub>-agonist clenbuterol (M K Parr, K Koehler, H Geyer *et al*, unpublished data). In the suprathereapeutically dosed product, clenbuterol was not declared on the label. Both supplements were advertised as weight loss products. Because of the extremely high concentration of clenbuterol in the second product (100-fold more than the therapeutic dose), severe side effects could be expected; in addition, a high risk of cross-contaminations of other products with clenbuterol is likely. Because WADA has classified clenbuterol as an anabolic agent, its detection in doping control may lead to severe sanctions.

## DIETARY SUPPLEMENTS CONTAINING PROHIBITED PEPTIDE HORMONES

In 2009 and 2010, dietary supplements containing the prohibited growth hormone-releasing peptide-2 (GHRP-2) were detected.<sup>10 11</sup> The products were advertised to produce anabolic, fat-reducing and anticatabolic effects and to improve regeneration. One product, in an ampoule of a drinking solution, contained an orally active concentration of GHRP-2. Such a product may lead to inadvertent doping cases because the name GHRP-2 is not specifically listed on the WADA prohibited list and is unknown to the majority of the sports community. However, GHRP-2 belongs as a releasing factor to the prohibited substance group S2 on the WADA list.

## EMERGING DRUGS

In 2009 and 2010, the first prohibited selective androgen receptor modulators (SARMs) and the gene doping substances AICAR and GW1516 were detected on the black market.<sup>11 12</sup> All these substances are still in clinical trials and have not yet been approved as medications. From our experience, we expect that these substances will appear very soon on the dietary supplement market, with advertising that the SARM products will achieve anabolic effects whereas the gene doping substances will enhance endurance. If these substances are added to other supplement products without being declared on the label, new sources of risk for inadvertent doping will be created.

## CONCLUSION – WHAT CAN ATHLETES DO?

According to our experience, the risk of inadvertent doping is predominantly connected to dietary supplements aggressively marketed for their physiological effects, for example, muscle gain and fat loss, but it cannot be confined exclusively to such products. Therefore, athletes should, in general, carefully consider the risks and benefits of dietary supplements. If use seems to be essential, athletes should purchase dietary supplements only from low-risk sources. Such sources are established in some countries such as Germany (<http://www.colognelist.com>), the Netherlands (<http://antidoping.nl/nzvt>), the UK (<http://www.hfl.co.uk>) and the USA (<http://www.nsf.org/certified/dietary>), where

databases list dietary supplements from companies whose products undergo frequent quality controls for the presence of doping agents. However, these sources still cannot guarantee that dietary supplements are free of risk, but they do offer a risk minimisation. Dietary supplements produced by pharmaceutical companies might represent an alternative as such products have not yet been found to be contaminated with doping substances.<sup>13</sup>

### Concluding comments

It is clear that there is a real risk that athletes who use dietary supplements may unknowingly ingest a banned substance that will cause them to record a positive doping outcome. There are cases in which a doping infringement can be traced back to supplement use and for which the athlete has undertaken some strategies to reduce this risk. For example, the athlete has received written advice from a supplement manufacturer that their produce does not contain banned substances, but following a positive doping test, a sealed container of the dietary supplement has been examined and found to contain the banned ingredient. Unfortunately, strict liability applies to these situations and even if athletes have been successful in having the terms of their ban from sport reduced, a doping infringement will still be recorded against their name. The loss of a career, livelihood and reputation are stakes that an athlete must take into account when using dietary supplements.

**Competing interests** None.

**Provenance and peer review** Commissioned; not externally peer reviewed.

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*Br J Sports Med* 2011 45: 752-754 originally published online June 6, 2011

doi: 10.1136/bjsports-2011-090180

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