Regulatory Toxicology and Pharmacology 73 (2015) 93–104

Contents lists available at ScienceDirect

Regulatory Toxicology and Pharmacology

journal homepage: www.elsevier.com/locate/yrtph

Dietary supplements: International legal framework and adulteration profiles, and characteristics of products on the Brazilian clandestine market

Diana Brito da Justa Neves [a], Eloisa Dutra Caldas [b, *]

[a] National Institute of Criminalistics, Federal Police Department, 70610-200 Brasilia, DF, Brazil
[b] Laboratory of Toxicology, Faculty of Health Sciences, University of Brasília, 70910-900 Brasilia, DF, Brazil

ARTICLE INFO

Article history:
Received 12 January 2015
Received in revised form
16 June 2015
Accepted 17 June 2015
Available online 21 June 2015

Keywords:
Dietary supplements
Legislation
Irregular products
Adulteration
Hormones
Fat-burners
Brazil
European Union
United States

ABSTRACT

The objectives of this work were to evaluate current legislation on dietary supplements in the United States, the European Union and Brazil, and the profile of adulterated and/or irregular products on these markets. Due to a less restrictive legal framework, a supplement product that is freely available in the US may be considered a drug or even be proscribed in the EU and Brazil, thus giving rise to a clandestine market based on smuggling. From 2007 to 2014, the United States Food and Drug Administration reported 572 cases of supplement adulterations in the country, mainly products for sexual enhancement (41.6%). Data from the European Union Rapid Alert System for Food and Feed showed 929 adulterations during the same period, over 40% due to unauthorized ingredients or undeclared medicines. From 2007 to 2013, the Brazilian Federal Police Department seized 5470 supplement products, 92.2% with an American-declared origin. Qualitative chemical analyses performed on 2898 products found 180 adulterations, 41.1% due to undeclared drugs, mainly anabolic steroids, anorectics and products for erectile dysfunction, all considered medicines in Brazil. Educating the public regarding the potential risks they are taking when consuming adulterated or irregular products is necessary to protect the health of consumers.

1. Introduction

Dietary, food or nutrient supplements, referred to in this work as supplements, may be defined as concentrated sources of nutrients or other substances with a nutritional or physiological effect, marketed in dose form, with the purpose of supplementing the normal diet (EC, 2002). The use of supplements has been increasing worldwide in the last decades, even though the efficacy and safety of some of these products are still under discussion in the scientific community (Petroczi et al., 2011; Eudy et al., 2013; Cohen, 2012; Sepkowitz, 2013; Lachenmeier et al., 2013; Finley et al., 2014).

Most studies addressing the consumption of supplements worldwide involve athletes or physically active people, who are the main consumers of these products. Consumption rates for these populations in Brazil range from 20 to 94%, with an increase in recent years (De Rose et al., 2006; Goston and Correia, 2010; Silva and Marins, 2013; Carvalho-Silva et al., 2012; Fayh et al., 2013; Nogueira et al., 2013). Similar results were reported in Spain (28%; Oliver et al., 2011), Iran (66.7%; Saeedi et al., 2013), Germany (91.1%; Diehl et al., 2012), Canada (98.6%; Kristiansen et al., 2005), and the USA (46.7%; Jacobson et al., 2012).

The legal framework for supplements varies among countries. In Brazil, the category “dietary supplement” does not exist, and these products are placed in other food categories such as food for athletes, vitamins and/or mineral supplements, and foodstuffs with functional properties or health claims (SVS, 1998; ANVISA, 1999a,b; ANVISA, 2010a,b,c). Substances with therapeutic functions cannot be included in these products, as they are classified as medicines and are specifically regulated (BRAZIL, 1976). The distinction between foodstuffs and medicinal products is also clear in the European Union (EC, 2001), although there are the so-called “borderline products”, which contain substances that may have pharmacological effects at a given dose (Lachenmeier et al., 2012). In the United States, legislation allows a wider range of products to be marketed as supplements, which may contain a substance that has been

* Corresponding author.
E-mail addresses: diana.dbjn@dpf.gov.br (D.B. Justa Neves), eloisa@unb.br (E.D. Caldas).

http://dx.doi.org/10.1016/j.yrtph.2015.06.013
0273-2300/

approved as a new drug, certified as an antibiotic, or licensed for biological use if, prior to such approval, it has been marketed as a supplement or food, unless stated otherwise by specific regulation (USA, 1994). Thus, many products that are legally commercialized in the United States as supplements are considered medicines in Brazil and in Europe and, as such, need to comply with all the obligatory requirements for a medicine product.

In addition to the legal issues, another potential problem related to supplements is the risk of adulteration. Supplements can be adulterated either unintentionally due to cross contamination, or intentionally with drugs to ensure or enhance the product's results. The substances reported to be most frequently used in supplement adulteration are steroids, stimulants, anorectics and phosphodiesterase inhibitors, used for erectile dysfunction (Geyer et al., 2004, 2008; Petroczi et al., 2011; Damiano et al., 2014).

The aims of this work were to overview the legislation related to supplements in Brazil, the European Union and the United States, the international scenario of supplement adulteration, and to evaluate supplements seized and analyzed by the Brazilian Federal Police Department (DPF) from 2007 to 2013.

2. Legal framework for dietary supplements

2.1. United States legislation

The first attempts made by the United States Food and Drug Administration (FDA) to regulate dietary supplements as drugs occurred in the 1960s and 1970s, which met strong resistance from consumers, including protests, and from manufacturers. In 1994, the US Congress approved the Dietary Supplement Health Education Act (DSHEA), which established that dietary supplements be treated as foods (USA, 1994), not drugs, which are regulated more stringently (USA, 1938). This Act effectively assured the public unrestricted access to dietary supplements (Brownie, 2005).

According to the DSHEA, dietary supplements may contain a vitamin, mineral, herb, botanical, amino acid, or a dietary substance to supplement the diet by increasing the total dietary intake, or a concentrate, metabolite, constituent, extract or combination of any of these ingredients. In addition, they may include substances that have been approved as a new drug or certified as an antibiotic if they were, prior to such approval, marketed as a dietary supplement or food (USA, 1994). This means that many substances with pharmacological actions can be regularly sold as food supplements in the US.

Under the DSHEA, supplement manufacturers are not required to notify, gain approval, or register their products with the FDA, nor are they obliged to obtain FDA approval to release the product on the market (USFDA, 2011a,b; Brownie, 2005; USA, 1994). They must comply with specific dietary supplement Good Manufacturing Practices (GMPs), which were established by the FDA in 2007 (USFDA, 2007). These GMPs include quality control procedures and recording requirements for each step in the manufacturing process, to ensure that the final product contains the appropriate ingredients at the right dose, without the presence of contaminants, such as toxins, bacteria, pesticides, glass, and heavy metals, or improper packaging and labeling.

Also according to the DSHEA, the FDA must prove – at its own expense – that a supplement presents an unreasonable risk of illness or injury before acting to remove it from the market as being unsafe. Contrary to what is required for drugs, manufacturers are not legally required to provide evidence that their product is safe or effective. Structure or function claims can be made on the supplement's label as long as the manufacturer has substantiation that such claims are "truthful and not misleading" and declares that "This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease" (Brownie, 2005; USA, 1994). The supplement label can also contain health claims, which must be authorized by the FDA and meet a significant scientific agreement (SSA), based on evidence from well-designed studies and agreement among experts (USFDA, 2009). Additionally, health claims can be used when they are based on authoritative statements from federal scientific bodies, within the FDA Modernization Act (USFDA, 1997), or when there are qualified health claims based on less scientific evidence but approved by the FDA, using standardized qualifying language (USFDA, 2003; Corby-Edwards, 2013).

The only case of necessary notification to the FDA is when manufacturers intend to include a new dietary ingredient in their products, meaning an ingredient that was not marketed as food in the US before October 15, 1994 (USDA, 1994). In this situation, manufacturers are required to notify the FDA of their plans 75 days before the product goes to market, and to submit evidence that the dietary ingredient would be reasonably expected to be safe under the conditions of use recommended or suggested in the supplement labeling (USFDA, 2013a,b; USA, 1994). Many manufacturers fail to report their intention to include new dietary ingredients, which has led to the withdrawal of some well-known products from the market (USFDA, 2013).

Only in 2011 did the US government introduce slightly more stringent measures to regulate the supplement market. The Food Safety Modernization Act (FSMA), which went into effect on January 4, 2011, changed part of the Federal Food, Drug and Cosmetic Act (USA, 1938), declaring that an officer or a qualified FDA employee may order the withdraw of any food item if they have reason to believe that it is adulterated or misbranded. If there is a reasonable doubt that consumption of a food item will cause serious adverse health consequences to humans and animals, the Agency may require that its distribution or sale be immediately ceased (USA, 2011; USFDA, 2013b). It was based on this new Act that the FDA managed to take OxyElite Pro off the market, due to the reasonable probability that it was related to several cases of liver failure caused by a new ingredient, aegeline, whose safety for consumers had not been demonstrated (USFDA, 2013b).

2.2. European Union legislation

In the European Union (EU), food is defined as "any substance or product, whether processed, partially processed or unprocessed, intended to be, or reasonably expected to be ingested by humans". 'Food' includes drink, chewing gum and any substance, including water, intentionally incorporated into the food during its manufacture, preparation or treatment". It is clearly stated in Regulation (EC) 178/2002 that "food" shall not include medicinal products (EC, 2002b). There are also several norms to regulate food products, such as Regulation 1925/2006 (which refers to fortified foods; EC, 2006b), Directive 2002/46/EC (which refers to food supplements, specifically vitamins and minerals; EC, 2002), and Regulation 1924/2006 (which refers to nutrition and health claims; EC, 2006). Some of these norms already foresee the need for establishing additional guidelines to cover a wider range of products already available on the market. The area is deemed well-regulated, although the norms may be difficult to interpret (Petroczi et al., 2011).

Medicinal products are defined as "(a) Any substance or combination of substances presented as having properties for treating or preventing disease in human beings; or (b) Any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis" (EC, 2004). These products may not be placed on the market