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Drug adulteration of food supplements: A threat to public health in the European Union?

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ABSTRACT

Food supplements have been playing an increasingly important role in the consumers' awareness nowadays. They are widespread and – according to popular belief – healthier and safer than synthetic drugs. In the European Union (EU) food supplements are classified as foodstuffs and thus not subjected to any specific safety assessments prior to commercialisation. With the growing popularity of food supplements, there is an increased need for more effective control of their production and distribution. The aim of this study was to examine the food notifications, recorded since 2003 via the EU RASFF database with particular regard to recent years, as well as to evaluate the involvement of different EU state structures in the fight against drug-adulterated food supplements with regard to efficacy and safety. In recent years, the number of RASFF notifications in the category of dietetic foods, food supplements and fortified foods, especially related to unauthorised composition, has increased significantly. The majority of EU Member States authorities, who responded to the study, consider drug-adulterated food supplements to be a public health threat. However, the competences of different official structures within the Member States concerning such products do not appear to be clearly defined. Regulators should thus think of stricter legislative solutions to increase the safety of public health.

1. Introduction

According to Euromonitor International, the annual expenditure on food supplements in the European Union (EU) is currently estimated to be EUR 7 billion, and is constantly growing. This steady growth may be associated with a variety of factors, including current trends in the aging populations of the Member States that seek healthy lifestyle with more emphasis on self-medication, rising mistrust in conventional medicine (combined with the conviction that food supplements are safer than pharmaceutical drugs), as well as rapid development of information and communication technologies, providing easy access to these types of products. Food supplements are used by the general population for many different purposes including balancing diets (particularly when compensating for natural nutrients deficiencies or lack of exercise), health maintenance, preventing diseases, improving appearance and wellness as well as sexual or sports performance (Egan et al., 2011). Moreover, such products are heavily advertised, with claims of effectiveness, availability without prescription, being "natural" and "harmless". Therefore, the food supplements market is blooming, and in some EU states such products are consumed by more than a half of the population (Skeie et al., 2009). Recently published data from the PlantLIBRA FP7 project revealed that almost 19% of EU consumers used at least one plant food supplement, with higher values observed in Italy (~23%) (Garcia-Alvarez et al., 2014).

Because of the growing popularity of food supplements, consideration should be given to improving the legislation and surveillance systems in the EU in order to provide consumers with nutritional security and protection against adulterations. Currently, on the basis of the General Food Law Regulation (EC) No 178/2002, food supplements are classified as foodstuffs. This Regulation defines food (or foodstuff) as any substance or product, whether processed, partially processed or unprocessed, intended to be, or reasonably expected to be ingested by humans. Moreover, it indicates that products having characteristics of a medicinal product within the meaning of pharmaceutical legislation cannot be classified as a food supplement. According to Directive (2002)/46/EC on the approximation of the laws of the Member States relating to food supplements, the labelling, presentation and advertising must not attribute to food supplements the property of preventing, treating or curing a human disease, or refer to such properties. The Directive also introduces for Member States partial harmonisation

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of the rules applicable to marketing food supplements and provides a list of authorised mineral compounds and vitamins. The classification of food supplements as food implies that manufacturing has to be carried out under Hygiene Regulations (Regulation (EC) 852/2004) and that these products must comply with the above-mentioned Regulation (EC) 178/2002, Regulation (EC) 1881/2006 on maximum levels of nitrates, aflatoxins, heavy metals and dioxins, general food labelling Directive 2003/13/EC and the food fortification legislation (Regulation (EC) 1925/2006). In the case of food supplements which may reduce risk factors for specific diseases, they also must comply with Nutrition and Health Claims Regulation (EC) 1924/2006 (Silano et al., 2011).

However, studies on food supplements revealed that only 30% of such products are in compliance with food laws (Lachenmeier et al., 2013). Contrary to what is required for medicines, manufacturers are not legally required to provide evidence that their product is safe or effective. Generally, food supplements are not subjected to any specific regulatory pre-approval requirements prior to commercialisation. This enables unscrupulous manufacturers and distributors to adulterate supplements by means of the addition of pharmaceutical drugs or their analogues (predominantly not studied for efficacy or toxicity) in order to increase product effectiveness (Rocha et al., 2016). Naturally, if the supplement succeeds fast in providing the desired results, more units are likely to be sold, thus increasing profits. It has already been estimated that pharmaceutical drugs are the most common adulterants in food supplements (Brown, 2017). Meanwhile, adulterated supplements can cause serious adverse effects, including strokes, acute liver injury, kidney failure and even death. Most consumers are not aware of the presence of drugs and the risk they are taking when consuming such products (Da Justa Neves and Caldas, 2015).

The European food (therefore food supplements) market is controlled by the Directorate General for Health and Consumer Protection (*fr. Direction Générale de la Santé et Consommateurs, DG-SANCO*) and individual Member States national sanitary structures. One of the most important EU authorities dealing with food safety, subjected directly under the DG-SANCO, is the European Food Safety Authority (EFSA), whose main task is the scientific risk assessment at the request of the Member States, the Commission or the European Parliament. The European Medicines Agency (EMA), which regulates the registration of medicinal products does not deal with food supplements, except in a situation in which they contain pharmacologically active substances. An important place in the supervision over the safety of food supplements is carried out by SANCO IT platform called Rapid Alert System for Food and Feed (RASFF) that enables rapid exchange of information about dangerous food in Europe. The legal basis of the RASFF is Regulation (EC) No 178/2002, which establishes the RASFF as a network involving the Member States and the Commission as member and manager of the system.

In view of the growing popularity of food supplements, the process of their adulteration, especially with the use of substances with high pharmacological activity, has become a source of major concern for EU states. It is worth noting that there is no definition of an adulterated food supplement within the EU. This may contribute to complications in the classification of such products and issues related to the prosecution of criminals. The aim of this study was to examine the food notifications, recorded via the RASFF since 2003, with particular regard to recent years, as well as to evaluate the involvement of different EU state structures in the fight against drug-adulterated food supplements.

2. Material and methods

Food notification data was obtained by analysis of the EU RASFF database accessed in the first half of 2017. The period of assessment was set from January 2003 to December 2016. The database includes detailed information on each notification, such as the classification, notifying country, hazard category, date, product category and country of origin. The category 'dietetic foods, food supplements and fortified foods' was evaluated. Data analysis was performed with Excel 2016. Table 1 and Fig. 2 provide data from above one notification.

Table 1
RASFF notifications related to the unauthorised composition of dietetic foods, food supplements and fortified foods by notifying country in 2016. Repetitive substances have been bolded.

Notifying country	Main unauthorised substances
Germany	**caffeine (too high content)**, 1,3 dimethylamylamine (DMAA), 1,3-dimethylbutylamine (nor-DMAA), agmatine sulphate, beta-alanine, **yohimbine**, **synephrine**
Norway	**yohimbine**, alpha lipoic acid, acetyl L-carnitine
Netherlands	**phenethylamine** derivatives, **synephrine**, **caffeine (too high content)**, oxilofrine
Lithuania	**phenethylamine**, mineral compounds
Poland	**phenethylamine** and derivatives, citrulline aspartate
France	**sildenafil** and analogues
Ireland	microminerals and vitamins (too high content)
Slovenia	**sildenafil** and analogues
Spain	**sildenafil** analogues, **sibutramine**, **yohimbine**
Sweden	**synephrine**, **caffeine (too high content)**, Ephedra
Hungary	**sildenafil** and analogues
Cyprus	**sildenafil**, **sibutramine**, phenolphthalein
Czech Republic	benzalkonium chloride (BAC), magnesium in metal form
Italy	dehydroepiandrosterone (DHEA)

A questionnaire, consisting of 4 close-ended questions with the option of providing additional comments, was sent to the Ministries competent in the areas of Health, Food/Agriculture and related matters, as well as to all competent national and international agencies in every Member State of the EU, bringing the total number of potential respondents to 185. Answers are presented in Fig. 3. "No data" means that the respondent had quoted a lack of authorisation in the area or referred the researchers to another entity.

3. Results and discussion

In recent years, the number of RASFF notifications in the category of dietetic foods, food supplements and fortified foods, especially related to unauthorised composition, has increased significantly from none in 2003 to over 100 in 2014. After a sudden decline in 2015, the number of notifications in 2016 returned to values comparable to the previous year (Fig. 1).

Germany is the country with the highest number of notifications (Fig. 2). It is worth noting that in the past there was a strong positive correlation in the relationships between food imports and numbers of notifications and that Germany is also the main port of food entry into the EU (Taylor et al., 2013). However, recently the number of border rejections has been declining. In 2014, 2015 and 2016 in the EU, there were respectively 50, 22 and 16 border rejections in the category of dietetic foods, food supplements and fortified foods. Probably dishonest manufacturers use increasingly sophisticated methods to avoid detection of irregularities and the increase in the number of notifications in 2016 after a decline in 2015 is related to increased controls on the internal markets. The number of RASFF unauthorised composition of food supplements notifications by Germany in 2016, which came mostly from official control on the market, was significantly higher than in other EU countries. This can probably be explained, in part, by the fact that Germany has a specialised unit dealing with online sales, which actively monitors the sales of products that may pose a risk to consumers due to their composition (RASFF Annual Report, 2015, 2016).

Despite the fact that, according to Directive (2003)/4/EC on public access to environmental information, Member States public administration bodies are obligated to provide information on human health and safety, this information was obtained from only 31 (17%) of the 185 responders. These included 9 out of 30 (30%), 11 out of 72 (15%)