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Short inventory of EU legislation on plant toxins in food

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REVIEW ARTICLE

Abstract

Plant toxins, secondary metabolites that are not essential for the survival of the organism itself but are toxic to human health, are produced by many plants. Plant toxins can be present as inherent metabolites in daily foods such as potatoes, herbs and spices or in herbal preparations. Plant toxins can be present as contaminants in foods as a result of unintentionally co-harvested weeds, transfer from feed to products of animal origin, or as residue after application of plant toxins as natural pesticides. Incidents with plant toxins are reported in Europe, mainly as a result of mixing-up of plant species used in herbal remedies or similarities between edible crops and certain weeds. EU legislation on plant toxins in food, if existing at all, is scattered over different legal acts, such as acts on contaminants, flavourings and residues. Limits for plant toxins are, furthermore, mentioned in product specifications of approved novel foods and thus related to one specific plant product. It was concluded that there is a need for a more coherent legislation on plant toxins in food in the EU to ensure consumer health.

Keywords: plant toxins, legal limits, regulations, botanical impurities, food

1. Introduction

Plants produce a wide range of metabolites of which some are not essential for the survival of the organism. Those metabolites are synthesised by the plant for various reasons and are called secondary metabolites. The variation in molecular structures of these secondary metabolites is enormous (Frohne and Pfänder, 2005).

Secondary plant metabolites that cause adverse effects to the human health after ingestion are referred to as plant toxins. Plant toxins can cause acute (Adamse *et al.*, 2014; Plenert *et al.*, 2012) or long term effects (Wiedenfeld, 2011) in humans. Several plant substances are metabolised to toxic metabolites in the liver or other tissues (EFSA, 2011b; Molyneux *et al.*, 2011; Wiedenfeld, 2011).

Humans are exposed to plant toxins, such as pyrrolizidine and tropane alkaloids, via food products of plant or animal origin (Bodi *et al.*, 2014; Hoogenboom *et al.*, 2011; Mulder *et al.*, 2015a). Most of these products have been part of the human diet for a long time. In some cases exposure occurs accidentally due to misidentification of plants at harvest (for instance when collected in the wild (Adamse *et al.*, 2014), contamination of the harvested product with toxic plant species growing on fields with the crop (Mulder *et al.*, 2015a) or accidental mixing of edible and non-edible varieties at harvest or during processing (Adamse *et al.*, 2014). Plant toxins also naturally occur in minor ingredients that are added during food preparation such as herbs, spices and certain oils (Alhusainy *et al.*, 2014). Likewise, parts or extracts of plants or herbs containing plant toxins can be present in food supplements. Exposure to plant toxins can also be the result of the use of some substances, isolated from plant materials, in minute quantities in foods like flavours or food additives. Mixtures or substances containing plant toxins derived from plants can be used as plant protection product (EU, 2009b). Exposure could thus result from residues of these products in harvested plant materials which can end up in food. Feed, both roughage and preserved feed, can be contaminated with plant materials or residues of plant protection compounds of plant origin (Mulder *et al.*, 2009; Van Raamsdonk *et al.*, 2015). Herbs and herbal preparations can also be administered to farm animals as veterinary drugs (Groot *et al.*, 2015; Hashemi and Davoodi, 2011). Some plant toxins are transferred to food of animal origin, such as in milk or eggs (Diaz *et al.*, 2014;

Hoogenboom *et al.*, 2011; Mulder *et al.*, 2015b), through the feed and drugs routes and can enter the food chain.

Plant toxins are not defined as such in EU legislation but are part of the group of contaminants as defined in article 1 of Regulation (EEC) No 315/93 (EU, 1993): 'a substance not intentionally added to food and present in food as a result of all processes along the food chain from farm to retail'. Natural toxins in plants are thus included in this definition. Although it cannot be excluded that plant toxins incidentally can occur in the diet of the EU population in levels that may harm their health, legal maximum levels for plant toxins in food are scarce and scattered across various legal acts.

In this paper the relevant EU regulations on plant toxins will be discussed in relation to the route of exposure of the EU population. The focus will be on food safety and, therefore, the issues related to intended recreational use, abuse and medical use will not be discussed.

2. EU legislation on hazardous substances in food in general

Requirements for food, food businesses and food business operators (FBOs), and the official control on compliance with these requirements, are laid down in the EU in legal acts. These legal acts are regulations (binding as such in each EU member states), directives (binding after implementation in member states laws) or decisions (binding as such). FBOs are primarily responsible for the safety of food products they produce; they should not place unsafe food onto the EU market. EU member states are to make sure that FBOs comply with this rule. To harmonise the official control on compliance in the EU, there are rules for sampling, analysis, and maximum levels of hazardous substances in food and feed. In order to set maximum levels for a hazardous substance in food (and feed) information on toxicity, occurrence and levels in food and feed products and consumption of these products are evaluated by risk assessors. In the EU in general this evaluation is made by the European Food Safety Authority (EFSA), which publishes its risk assessments as opinions, statements or other documents. Thus far EFSA, and its predecessor, the Scientific Committee on Food (SCF), has published a number of opinions on plant toxins in food and feed (Table 1) and food flavourings (Table 2).

As part of risk management the EU then proposes, if necessary, maximum levels of hazardous substances in food. If EU member states (and depending on the legal environment also the European Parliament) agree with proposed levels, these are laid down in legal acts. Maximum

Table 1. European Food Safety Authority (EFSA) and Scientific Committee on Food (SCF) opinions on plant toxins.

Food (and feed)	
Caffeine	(EFSA, 2015b)
Cyanogenic glycosides in apricot kernels	(EFSA, 2016)
Ethyl carbamate and hydrocyanic acid in food and beverages	(EFSA, 2007a)
Nitrate	(EFSA, 2008d)
Statement on nitrates in leafy vegetables	(EFSA, 2010)
Opium alkaloids in poppy seeds	(EFSA, 2011c)
Pyrrolizidine alkaloids in food and feed	(EFSA, 2011b)
Tetrahydrocannabinol in food and feed	(EFSA, 2015a)
Tropane alkaloids in food and feed	(EFSA, 2013)
Feed	
Cyanogenic compounds in feed	(EFSA, 2007b)
Glucosinolates in feed	(EFSA, 2008c)
Gossypol in feed	(EFSA, 2009a)
Phorbol esters in *Jatropha* kernel meal	(EFSA, 2015c)
Pyrrolizidine alkaloids in feed	(EFSA, 2007c)
Ricin in feed	(EFSA, 2008e)
Saponins in *Madhuca longifolia* L in feed	(EFSA, 2009b)
Theobromine in feed	(EFSA, 2008f)
Tropane alkaloids in feed	(EFSA, 2008g)

Table 2. European Food Safety Authority (EFSA) and Scientific Committee on Food (SCF) opinions on food flavourings.

β-asarone	(SCF, 2002e)
Capsaicin (2002)	(SCF, 2002a)
Camphor (2008)	(EFSA, 2008a)
Coumarin	(EFSA, 2008b)
Estragole	(SCF, 2001a)
Eucalyptol	(SCF, 2002b)
Furfural	(EFSA, 2004a)
Glyzyrrhinic acid	(SCF, 2003a)
Hydrocyanic acid	(EFSA, 2004b)
Hypericin	(SCF, 2002d)
Isosafrole	(SCF, 2003b)
Menthofuran	(EFSA, 2005)
Methyleugenol	(SCF, 2001b)
Pulegone	(EFSA, 2005)
Quassin	(SCF, 2002c)
Rebaudioside A (steviol)	(EFSA, 2011a)
Safrole	(SCF, 2002g)
Teucrin A	(SCF, 2003c)
Thujone	(SCF, 2002f)

limits are set to minimise or avoid the risk of adverse effects in consumers due to exposure. Limits are set at the EU level and not at member state level to facilitate trade within the EU. For some hazardous substances, the 'contaminants' (see below), not only risk minimisation but also feasibility, societal, economic and other factors are taken into account when setting limits. Also a sampling method and a harmonised and validated method of analysis should preferably be available. EU member states are required to monitor foods for compliance with legal maximum limits (Regulation (EC) No 882/2004; EU, 2004b). Hazardous food products are notified in the European Rapid Alert System on Food and Feed (RASFF) (EU, 2015g). Cases reported are those in which two or more EU member states are involved concerning all materials traded within the EU of both EU and non-EU origin. This system allows fast communication with other EU member states in case of violations and it further helps to improve the food and feed safety system.

3. EU acts relevant for food business operators marketing food products that may contain plant toxins[1]

Regulation (EC) No 178/2002, the General Food Law

Food placed on the market of the EU by FBOs should not be unsafe. It is the responsibility of the FBO to make sure that food is not unsafe (Regulation (EC) No 178/2002; EU, 2002d). Food products consisting of or derived from plants that have been part of the human diet for a long time are *a priori* considered to be safe. Experience learned that either the levels of plant toxins or intake of these products are too low to cause toxicity, or proper processing or pre-treatment, such as peeling potatoes (Haase, 2010) or processing cassava tubers (Ezeigbo *et al.*, 2015) reduces the toxins to safe levels. Advances in plant breeding and selection, processing and trade expanded the number of plant species considered to be fit for human consumption as compared to past centuries. Only for novel plant species introduced as food on the EU market a safety assessment is required prior to market introduction (see below, Regulation (EC) No 258/97; EU, 1997). However, recent EFSA opinions like those on pyrrolizidine alkaloids (PAs) (EFSA, 2011b) and tropane alkaloids (TAs) (EFSA, 2013) point at potential risks of food products containing plant toxins. Furthermore, studies showed the presence of PAs in tea and milk on the EU market (Mulder *et al.*, 2015b), and TAs in foods for young children (Mulder *et al.*, 2015a), indicating the presence today of unsafe food on the EU market.

[1] The legal acts quoted in this paper refer, where applicable, to the latest amended version.

Regulation (EC) No 852/2004 – the hygiene regulation

Regulation (EC) No 852/2004 on the hygiene of foodstuffs lays down rules for FBOs on the hygiene of foodstuffs (EU, 2004a). In this regulation it is also stipulated that food safety is primarily the responsibility of the FBO. Hygiene is defined as all measures and conditions necessary to control hazards and to ensure fitness of food products, including harvested primary plant products. FBOs should protect primary products against contamination (thus the presence or introduction of a hazard). Measures to control contamination arising from air, soil, water, fertiliser, plant protection products, veterinary medicinal products and biocides should be included in the control of hazards (Annex I, Part A II 3(a)). No mention is made of measures to prevent the use of seeds of plants not intended for human consumption (for example rapeseed with high levels of erucic acid), or impure seeds, or harvesting from fields infested with toxic weeds. For primary production the application of hazard analysis and critical control principles was not deemed feasible at the time, instead the use of (national and EU) 'Guides to good hygiene practice' was recommended. In the examples of hazards and measures that may be included in these guides (Annex I, Part B 2), inherently present plant toxins or plant toxins present due to contamination with (co-harvested) toxic weeds are not mentioned. This does not mean that there are no requirements for seeds used in plant production for food, only that no referral is made to these requirements in this Regulation. However, EU and Netherlands seed marketing acts do set requirements for seeds, and also, for maximum contents of seeds of other plant species in seeds, and registration of varieties (see for example Directive 2002/55/EC on the marketing of vegetable seeds; EU, 2002b).

Regulation (EC) No 258/97 concerning novel foods and novel food ingredients

According to Regulation (EC) No 258/97 on novel foods and novel food ingredients prior to market introduction the safety of the novel food has to be proven (EU, 1997). FBOs wishing to sell novel foods in the EU have to compile application dossiers containing scientific data on evidence of safety. Safety assessments are made by member state competent authorities and, if objections are raised by other EU member states on the initial assessment report, a new assessment is performed by the Food Additives and Nutrient Sources panel of EFSA. For foods and food ingredients consisting or derived from (new) plants (except those derived from plants with a history of safe food use and obtained by traditional propagating practices) the safety assessment includes an evaluation of the risk of due to presence of inherent plant toxins. Novel in this regulation is defined as not being on the EU market prior to May 15, 1997. In authorisations for novel plant species

or products derived thereof, maximum limits for plant toxins are sometimes mentioned in the specifications of the product. Examples are: coagulated potato proteins and hydrolysates thereof – glycoalkaloid (total): not more than 150 mg/kg (Decision 2002/150/EC; EU, 2002a); refined *Echium* oil – pyrrolizidine alkaloids: not detectable with a detection limit 4 µg/kg (Decision 2008/558/EC; EU, 2008b); dried and roasted leaves of *Morinda citrifolia* – oxalic acid <0.14% (Decision 2008/985/EC; EU, 2008a); leaf extract from lucerne – saponins: not more than 1.4%, coumestrol not more than 100 mg/kg (Decision 2009/826/EC; EU, 2009a); flavonoids from *Glycyrrhiza glabra* L. – glycyrrizinic acid: less than 0.005% (Decision 2011/761/EU; EU, 2011a). Also authorisations by members states (valid in the EU, and issued when no objections were raised to the initial assessment report) sometimes contain specifications concerning plant toxins, e.g. ≤10 mg/kg methyl eugenol and ≤100 mg/kg total alkaloids in the novel food magnolia bark extract (FSA, 2011). Including these requirements for levels of plant toxins in product specifications of novel foods is problematic from the view point of official (and private) control. Each enforcement body has to keep track of all individual novel food specifications as listed on the website of DG SANTE (EU, 2015f).The recently published Regulation (EU) 2015/2283 repeals Regulation (EC) No 258/97, most articles in this new regulation will apply from January 1, 2018 (EU, 2015h). This new regulation also applies to new plant food products except for those obtained by traditional propagating practices already used in the EU before 15 May 1997 or by non-traditional breeding practices not used in the EU before 15 May 1997 when these practices do not give rise to significant changes in the composition. For traditional food products (including new plant products) from non-EU countries with a history of safe use lighter notification procedure is foreseen is this new Regulation. The EU Commission will furthermore establish and maintain the Union list of novel foods.

Directive 2002/46/EC on the approximation of the laws of the Member States relating to food supplements and Regulation (EC) No 1925/2006 on the addition of vitamins and minerals and certain other substances to food

A special kind of food, but legally regarded as being food, is a food supplement. The variety of food supplements available on the EU market is enormous, varying from simple vitamin C pills to complex herbal preparations. In an attempt to harmonise requirements for sale of food supplements in the EU, the Directive 2002/46/EC was published in 2002 (EU, 2002c). A food supplement is defined in this directive as 'a foodstuff meant to supplement the normal diet with concentrated sources of nutrients (vitamins and minerals) and 'other substances' with a nutritional or physiological effect and marketed in dosing forms resembling medicines'. Only several vitamins and minerals are currently listed in the annexes of the Directive. For other nutrients and other substances no specific rules are established yet. Therefore, no specific EU legislation is currently in place for herbal supplements containing plant parts or plant extracts, also referred to as 'botanicals'. However, if the FBO claims a beneficial effect of the food supplements, this health claim has to be substantiated by data that are evaluated by EFSA. Approval of health claims occurs at the EU level. Requirements for substantiation of health claims on food are laid down in Regulation (EC) No 1924/2006 (EU, 2006c). Almost all applications for health claims for botanicals were, however, set 'on hold' by EFSA in September 2010. This resulted from a gridlock in visions on how herbal supplements should be treated: as herbal medicine (already in use in some EU member states), as traditional herbal medicinal product or as food supplement? For an herbal medicine, quality, safety and efficacy must be proven. For a traditional herbal medicinal product, quality of the product is an issue but safety and efficacy are assumed to be established by the long term use (>30 years) (Directive 2001/83/EC; EU, 2001). In contrast, for an herbal food supplement safety is assumed (unless it is a novel food) but the claim of efficacy (beneficial effects) has to be substantiated.

Related is the Regulation on addition of vitamins and minerals, and 'certain other substances' to food, Regulation (EC) No 1925/2006 (EU, 2006d). Also here the annexes contained only minerals and vitamins until recently when *Ephedra* herbs and preparations were added to annex III part C containing prohibited substances as significant safety concerns were identified associated with the use of *Ephedra* in food (Regulation (EU) 2015/403; EU, 2015b). Yohimbe bark and preparations were at the same time included in annex III part C with substances under Community scrutiny, meaning it was not possible yet to decide whether to allow or prohibit adding these products to food.

Regulation (EEC) No 315/93 – on Community procedures for contaminants in food

Regulation (EEC) No 315/93 lays down the basic principles of EU legislation on contaminants in food (EU, 1993). It is the EU Commission only that is entitled to formulate proposals for maximum levels of contaminants in food. Once regulated at the EU level, EU member states are not allowed to set deviating maximum levels for the regulated contaminant in the specified food product. Most important aspect is that it states that levels for contaminants must be kept as low as reasonably achievable following good practices at all stages. Also reference is made to sampling and methods of analysis. Food products in which official maximum levels of contaminants are exceeded are not allowed to be placed on the EU market.

4. EU food regulations containing provisions for certain plant toxins

Regulation (EC) No 1881/2006 – on maximum levels for certain contaminants in foodstuffs

Regulation (EC) No 1881/2006 contains legal limits for contaminants set via the procedure of Regulation (EEC) No 315/93 (EU, 1993, 2006a). Even though many foods in the EU contain inherent plant toxins, there are only three limits for inherent plant toxins in place, namely: (a) nitrate (despite the fact that this is not considered a toxin by some toxicologists and/or risk assessors (Sindelar and Milkowski, 2012) in some leafy vegetables and baby-food; (b) recently included via Regulation (EU) No 696/2014 amending Regulation (EC) No 1881/2006 (EU, 2014b), erucic acid in vegetable oils and fats, food containing added vegetable oils and fat, and infant formulae and follow up infant formulae (formerly this toxins was regulated in Directive 76/621/EEC; EU, 1976); and (c) tropane alkaloids via Regulation (EU) 2016/239 amending Regulation (EC) No 1881/2006 as regards maximum levels of tropane alkaloids in certain cereal-based foods for infant and young children (EU, 2016). Methods of sampling and analysis are described in Regulation (EC) No 1882/2006 (nitrate) (EU, 2006b) and Regulation (EU) 2015/705 (EU, 2015d).

EFSA opinions are one of the most important inputs for EU regulations on contaminants. Recently, EFSA published its opinions on tetrahydrocannabinol (THC) (EFSA, 2015a), PAs (EFSA, 2011b) and TAs (EFSA, 2013) in food and feed, opium alkaloids in poppy seeds (EFSA, 2011c) and on carvone (EFSA, 2014). The opinion on TAs has resulted in maximum levels for tropane alkaloids in certain cereal based foods for infants and young children by Regulation (EU) 2016/239 (EU, 2016). Legal EU maximum levels for PAs are thus far only set in the specifications of the novel foods *Echium* oil (see section on Regulation (EC) No 258/97 concerning novel foods and novel food ingredients; EU, 2008b) and refined oil from the seeds of *Buglossoides arvensis* (EU, 2015a). Legal limits for THC and opium alkaloids are not (yet) included in Regulation (EC) No 1881/2006. For use of carvone as plant protection product (potato sprout regulator) the default maximum residue levels (MRL) of 0.01 mg/kg applies (Regulation (EC) No 396/2005; EU, 2005), for use as food flavour no specific use levels were defined (Regulation (EU) No 872/2012; EU, 2012). An EU Recommendation was issued on good practices in order to prevent and reduce the presence opium alkaloids in poppy seeds (EU, 2014a).

Regulation (EC) No 1334/2008 on flavourings and certain food ingredients with flavouring properties for use in and on foods

Prior to use, the safety of food additives and flavourings must be evaluated, only those substances for which safe use levels are established are added to a positive list. Several plant toxins are regulated according to Regulation (EC) No 1334/2008 on flavourings and certain food ingredients with flavouring properties for use in and on foods (EU, 2008c). Natural aromas (extracted from plants) or synthetic substances can be added to foods under certain conditions. This regulation provides a lists of substances and plants that are not allowed to be added to food, or for which maximum levels are set: aloin, capsaicin, beta-asarone and its source *Acorus calamus*, hypericine and its source *Hypericum perforatum*, teucrin and its source *Teucrium chamaedrys*, quassin and its sources *Quassia amara* and *Picrasma excelsa*, and a range of substances present in many essential oils (e.g. estragol, methyleugenol, pulegone, thujone). Methyl-eugenol, estragol, safrole, β-asarone and coumarin are known carcinogens while there is no consensus on the carcinogenic properties of pulegone. Of these the alkenyl benzenes, methyl-eugenol, estragol and safrole are also genotoxic. The genotoxicity of β-asarone is still indicative (Van den Berg *et al.*, 2011). It should be noted that for a number of substances the limits set only apply to addition of the substances as such (pure compound), and not when added as natural ingredient through herbs and spices.

5. Regulations on residues of plant toxins due to use in agriculture

Regulation (EC) No 1107/2009 on plant protection products (PPP) and Regulation (EC) No 396/2005 on maximum residue levels of PPPs

Active ingredients in plant protection products (PPP) are only allowed to be used in the EU when listed on one of the annexes of Regulation (EU) No 540/2011 (EU, 2011b). In order to be listed, producers of PPP have to supply data on, among others, efficacy, environmental fate and safe use of the active ingredient to the competent authorities according to Regulation (EC) No 1107/2009 (EU, 2009b). All active ingredients on the annexes have been re-evaluated or are in the process of being re-evaluated, the latter is true for PPP derived from plants. Not all formerly used plant-derived PPPs passed the re-evaluation. Products like citrus extract, garlic extract, mustard powder and rapeseed extracts were not approved, while others like pyrethrins, azadirachtin, eugenol, orange oil, clove oil and carvone were approved. When using PPP of plant origin, residues may remain on harvested products. Regulation (EC) No 396/2005 sets MRL of PPPs at the EU level (EU, 2005). For products that have not been registered on a particular

crop, or for which proper use should not leave residues, a default MRL at an established limit of determination applies (typically 0.01 mg/kg). Higher tolerances have only been set for few of plant-derived substances, including azadirachtin, carvone and pyrethrins. For nicotine limits have been set for certain plant commodities that might naturally contain this toxin (evidence not yet conclusive in most cases). For some PPPs it was established that no MRL was required (like eugenol). Legal status of plant-derived PPPs and MRLs for plant protection products can be found in the EU Pesticide Database (EU, 2015e)

Regulation (EU) No 37/2010 on pharmacologically active substances and maximum residue limits in foodstuffs of animal origin

Regulation (EU) No 37/2010 set the rules for limits for residues of pharmacologically active substances in foodstuffs of animal origin (EU, 2010). Annex table 1 of this Regulation lists all active substances that are allowed on the EU market as pharmacologically active ingredient of a veterinary drug, the intended use and, if necessary, the MRL in food products derived from animals treated with the substance. Although many products of plant origin are listed in Annex 1, an MRL has been set for only one substance: isoeugenol in fish (6,000 µg/kg). The veterinary drugs of plant origin listed in Regulation (EU) No 37/2010 are mainly of homeopathic nature. Residue concentrations of plant substances in animal products after application of these homeopathic veterinary drugs are considered to be too low to cause adverse effects in the consumers of the derived product, and thus no MRL is required. Annex table 2 of this Regulation contains a list of substances that are forbidden to be used in food producing animals, included in this list are *Aristolochia spp*. and preparations thereof.

6. Regulation (EU) No 1169/2011 on the provision of food information to consumers

For some plant substances it is required to mention them on food labels if present in higher than specified levels (EU, 2011c). For confectionary and beverages containing glycyrrhizinic acid or its ammonium salt at concentrations of 100 mg/kg or 10 mg/l or above, due to addition of the liquorice plant, 'contains liquorice' shall be added to the list of ingredients on the label of the product. For confectionary in which these substances are present at concentrations of 4 g/kg or above, or beverages containing >50 mg/l (or >300 mg/l if the alcohol content is >1.2% by volume) 'contains liquorice – people suffering from hypertension should avoid excessive consumption' shall be added immediately after the list of ingredients. In the absence of a list of ingredients, the statement shall accompany the name of the food.' Also beverages, with the exception of beverages based on coffee or tea (-extract), with high caffeine content should be labelled if caffeine is present in excess to 150 mg/l with the terms 'contains caffeine. Not recommended for children or pregnant women or breast-feeding women.' Label of foods other than beverages, where caffeine is added with a physiological purpose, should contain the sentence 'Contains caffeine. Not recommended for children or pregnant women.' Labelling is not required if the name of the food contains 'coffee' or 'tea' (Annex III Regulation (EU) No 1169/2011; EU, 2011c). Caffeine and quinine should be mentioned by name in the list of ingredients if used as food flavouring (Annex VII PART D 3 Regulation (EU) No 1169/2011). Also foods or food ingredients with added phytosterols, phytostanols or esters thereof should be labelled with, among others, the amount added per 100 g or ml food, and a warning that the product is not intended for people who do not need to control their blood cholesterol levels, that patients on cholesterol lowering medication should use the product only under medical supervision and that consumption of more than 3 g of added sterols/stanols should be avoided (Annex III, Regulation (EU) No 1169/2011).

7. Discussion

EU legal limits on plant toxins in food are limited to nitrate, erucic acid and tropane alkaloids, residues of some plant toxins present in plant protection products and or as veterinary drug, and several flavouring substances isolated from plants. Limits on several plant toxins or groups of toxins are furthermore embedded in novel food authorisations. For other plant substances with known adverse effects labelling is required. Despite the fact that plant toxins are hardly regulated at an EU level, multiple RASFF notifications on incidents with plant toxins have been reported during the last decades: alerts on the tropane alkaloids scopolamine and atropine in: popcorn from Spain; baby foods from Spain, Austria and Germany (millet); sorghum baking mix and flour from Czech Republic and Slovakia; polenta from Germany (2×); millet balls from Hungary; millet/cereal porridge from Germany; millet honey poppies from Germany; millet from Austria (2×), Hungary and the Netherlands; and millet dumpling from Hungary (2×) (RASFF alerts 2016.0444, 2016.0106, 2015.1487, 2015.1190, 2015.0684, 2015.0399, 2015.0388, 2015.0387, 2015.0339, 2015.0338, 2015.0210, 2015.0203, 2014.1724, 2014.1694, 2014.1652, 2014.1596), pyrrolizidine alkaloids in chamomile tea from Turkey and herbal food supplements from USA, the Netherlands and China (RASFF alerts 2015.1591, 2013.0234, 2012.1702, 2012.0402) and THC in alcoholic drink from Czech Republic, food supplements from Poland, Hungary and Germany and in *Tribulus terrestris* extract from Romania (RASFF notifications 2015.0166, 2014.1665, 2014.1663, 2014.1205, 2014.1137, 2014.1104; EU, 2015g). Notifications on plant toxins are, however, reported in the RASFF system in various categories, such as in botanical impurities as well

as in 'GMO/novel foods', which does not facilitate gaining a clear insight in the seriousness of the problem.

It is largely unknown if the EU population is exposed to harmful concentrations of plant toxins through their food, since data on toxicity of inherent plant toxins and on occurrence are lacking to a large extent. For preparation of a scientific opinion on tropane alkaloids, the EFSA working group only had data on 124 samples, collected in two member states in food (EFSA, 2013), and later published by Mulder *et al.* (2015a). The measured levels of hyoscyamine varied for the lower bound level between 0-3.6 µg/kg and upper bound 0.3-3.8 µg/kg, while the scopolamine level varied lower bound between 0-1.5 µg/kg and upper bound from 0.3-1.8 µg/kg. EFSA concluded that he Acute Reference Dose for TAs (ARfD), a dose considered to be safe in case of short term incidental consumption, could be exceeded by toddlers up to seven times, potentially resulting in adverse effects. The EFSA survey on PA occurrence showed that PAs are commonly present at high levels in ordinary black teas as well as herbal teas, up to a maximum of 64 µg/l tea infusion (4,800 µg/l dry tea), without clear indications for severe negative effects on human health in Germany or any other EU country (Bodi *et al.*, 2014; Mulder *et al.*, 2015b). Drinking tea with these PA levels however results in a margin of exposure/$BMDL_{10}$ (benchmark dose lower confidence limit for a 10% extra cancer risk) below 10,000. Normally a margin of exposure above 10,000 is considered to be safe. Although tea seems to have a history of safe use, it cannot be guaranteed that the quality of the tea has not changed over the years, and that PA might not have been present in such quantities before. On the other hand, not much is known on the toxicity of the various PAs and the occurrence of PAs with a low toxicity may explain the bias. Therefore, analytical methods for quality control must be developed and applied to gain more insight in variability of levels of inherent plant toxins, occurrence of plant toxins as contaminant, and to study effects of plant breeding and new ways of cultivation. Part of the quality assessment may include the use of unambiguous product identifiers (e.g. Latin names of plants), quality management throughout the chain, and regulatory measures in both the exporting and importing nations (Kleter and Marvin, 2009).

EU legislation on flavours is complicated and concerns various plant toxins. Several plant toxins are limited to be added as flavouring substance when isolated from the plant, such as eugenol. However, no limits are set for addition of herbs containing eugenol as food ingredient. For other substances, maximum limits have been set, but they do not apply when these substances are naturally occurring in flavourings and food ingredients, even when this results in much higher levels. Furthermore, substance and source plant are both prohibited in several cases (e.g. beta-asarone and *Acorus calamus*). Regulation (EC) No 1334/2008 set restrictions for plants primarily at species level (EU, 2008c). As a result, closely related plant species that can pose the same hazard, can still be used freely.

The establishment of legal limits on plant toxins can be complicated. Herbs that have been used in foods for long time may contain both toxic and beneficial compounds. Concentrations of toxins in plants can vary from year to year, between plant cultivars and plant parts (Petersson *et al.*, 2013). In case the use of a certain plant in food is regulated, it is recommended to regulate it as genus level rather than species level because the same plant toxin often occurs in multiple species of the same genus. Moreover, one has to consider that plant classification can change according to developments in plant systematics and nomenclature, e.g. *Senecio jacobaea* (ragwort) has been renamed *Jacobaea vulgaris* (Pelser *et al.*, 2007). The authors advised to be conservative in legislation with name changes (Van Raamsdonk *et al.*, 2015).

Currently, more emerging issues are recognised regarding plant toxins in food. Supply chains become more complicated thus increasing the chances for comingling, consumption habits change, meaning that plant toxins may enter the food chain in an area where they have not been before, or that other parts of the population are at risk.

8. Conclusions

It is concluded that the current EU legislation on plant toxins in food is scarce and scattered over various types of legislation. The effects of most plant toxins in food have not been investigated, unlike the effects of regulated active substances of, for example, additives, plant protection products and veterinary drugs. Attributing adverse health effects to presence of plant toxins in food is therefore problematic. The health risks of plant toxins from food to the European consumer are not clear, but the incidence of rapid alerts, despite the lack of legislation, indicates that it is an issue that needs to be addressed both by more data and more clarity in legislation. The establishment of legal limits for plant toxins is, however, a challenge. Plants that are used as food ingredient may contain both toxic and beneficial compounds. The same is true for the food supplements.

When legal limits are set in EU legislation one needs to carefully consider the use of botanical nomenclature as well as the occurrence of a chemical substance and the source plant(s). The presence of certain toxic substances can be limited to a specific plant species or can occur in various genera of which not all plants are relevant to food.

Few risk assessments on plant toxins have been carried out by EFSA. It is, therefore, of utmost importance that more data become available on exposure of the European population and on the toxicity of the plant toxins.

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