Common Feed and Animal Derived Food Contaminants in Israel

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ABSTRACT

Inspection of feed and animal derived food products is of utmost importance in providing safe feed and food products. Chemical as well as microbial contaminants are frequently encountered in various food and feed commodities thereby potentially endangering public health as well as animal well-being. In February 2014 a new law, namely the Control of Animal Feed Law, was approved by the Israeli parliament and which will come into force in 2017. The law regulates the production, safety and marketing of animal feed and animal derived products. In the present review, we have summarized the major feed and animal-derived food product contaminants most frequently encountered in Israel. The need for a governmental regulated feed safety laboratory, is crucial for ensuring public and animal health, thereby guarantying the safety of animal feed and consequently the quality of animal-derived food products.

Keywords: Food Contaminants ; Israel; Control of Animal Feed Law; Regulation of Food Safety.

INTRODUCTION

The implementation of adequate surveillance measurements on the safety of feed and animal-derived food products has been demonstrated over the years to ensure the well-being of food-producing animals, thereby reducing potential health hazards to the general public (1, 2).

The new feed law, namely the Control of Animal Feed Law, is expected to enter into an effect only in 2017 (3). The new law was enacted inorder to provide concise regulation of animal feed production and marketing, guaranteeing the safety and quality of animal products throughout the production chain. Moreover, the new law addresses the requirements of the production, marketing and utilization of safe feed products for farm and domestic animals. The Veterinary Services and Animal Health (VSAH) is currently responsible for the implementation of the new feed law, including the control of feed quality and implementing maximum residue limits (MRLs) of potential feed toxicant and/or contaminants (1).

In Israel, the most commonly utilized feeds and feed ingredients are grains, oilseeds, fruit/vegetable by-products, forage, directly dried products (e.g. bakery by-products), bio-fuel by-products (e.g. distillers' grains), food processing by-products, minerals, animal by-products (e.g. meat and bone meal, fats, poultry litter), aquatic products (e.g. fishmeal, shellfish, fish by-products, seaweed and krill), fermentation/biomass products, viable microbes and silage additives (1).

Routine feed analysis provides crucial information for: a) veterinary and public health inspection services, in evaluating the risk exposure to animals and humans; b) farmers, to optimize nutrient utilization in animal feeds; c) feed compounders, to prepare feed mixtures suitable for different animal production systems; d) researchers to relate animal performance to feed characteristics and the potential carryover of contaminants into the food chain (2).

In order to ensure feed safety, it is important to use analytical techniques that have a high sensitivity, i.e., that can reliably detect low levels of harmful material in diverse matrices (4-7). The VSAH, is presently faced with a demand for efficient enforcement tools, for quick decisions when confronted by large numbers of samples, e.g. at entry points of shipments, trading situations, on contamination sites or in case of a food safety crisis. In the last decade countless fatal intoxication events occurred in farm animals and household pets in Israel, due to the presence of hazardous feed contaminants (8-21).

In the following review we characterize the most common feed contaminants encountered in feeds in Israel. The following criteria were selected for enlisting major feed contaminants affecting feed safety 1) relevance of the hazard to animal and public health 2) extent of the occurrence of the hazard 3) impact of the hazard on international trade in food and feed.

Major feed contaminants in Israel

In the following paragraphs the currently most important undesirable feed contaminants are described based on safety assessment and prevalence.

MICROBIAL HAZARDS

Salmonella

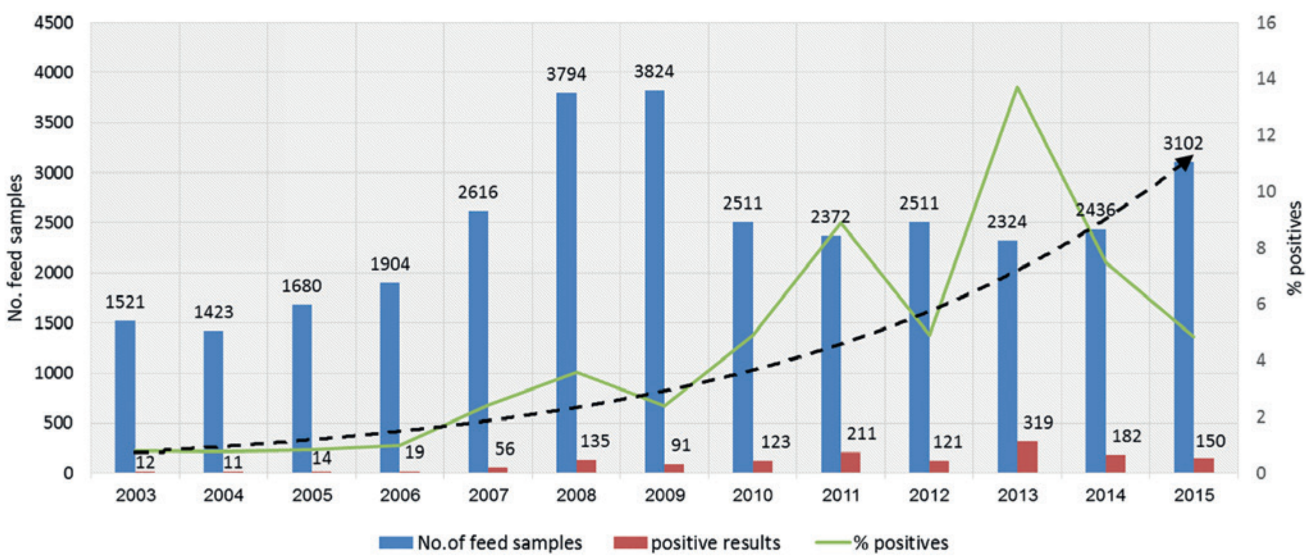
Contamination of feed and animal derived food products by *Salmonella* spp. was identified as a major hazard for microbial contamination. *Listeria monocytogenes*, *Escherichia coli* and *Clostridium* spp. are additional microbial hazards occasionally found in various foods and feed commodities (40-43, 22).

Animals may become infected with pathogenic Salmonella spp. when exposed to Salmonella-contaminated feed, possibly resulting in clinical manifestation (22). In addition, animals may also become infected by contact with Salmonella-infected animals, directly or via their excretions (22). Certain Salmonella spp. commonly detected in animal feed may also present major health risks to humans as has been shown recently by numerous studies (22). *Salmonella enterica* was reported in feedstuffs in Israel, while *Salmonella infantis* is commonly found in up to 64% of feather meal and poultry meal samples (40-43). *Salmonella infantis* is widely distributed and a common serovar in the US and Europe as well (22). The food hygiene laboratory at the Kimron Veterinary Institute, documented since 1990 the presence of *Salmonella* spp. in a wide variety of animal feeds and animal derived food products (40-43). The prevalence of *Salmonella* spp. contamination in feed increased from less than 1% in 2003 up to 13.7% in 2013 (Figure 1).

Botulism

Botulism is a deadly motor paralysis caused by exposure to botulinum neurotoxin (BoNT) produced primarily by *Clostridium botulinum* types A-G (23). The spore-forming anaerobic organism is frequently encountered in untreated poultry litter as well as in animal feed such as hay, silages and other bulky forages contaminated with decomposing animal tissue (24). Among the seven immunologically distinct

Figure 1: Prevalence of *Salmonella* spp. isolated from feedstuffs in Israel



BoNT serotypes, the serotype BoNT-D is most commonly associated with livestock poisoning in Israel, while serotype BoNT-C1 is frequently encountered in poultry poisoning, mostly water fowls (23-25). Clinically botulism is characterized as a lower motor neuron disease resulting often in fatal respiratory muscle paralysis (24).

In September 2013, an unusual mass botulinum toxicosis outbreak occurred in 91 beef cattle and dairy farms resulting in the death of 528 dead beef and dairy cows over a time period of about 42 days (26). The source of the botulinum toxicosis was untreated poultry litter highly contaminated with BoNT-D producing *C. botulinum*. In the following year, two major botulinum intoxication events occurred in January and October 2014, due to the consumption of poultry litter contaminated with BoNT-D producing *C. botulinum* resulting altogether in 27 and 14 fatally intoxicated calves, respectively (27, 28). In both cases decreased morbidity and mortality were observed in animals vaccinated by the above-mentioned protocol.

Throughout 2015 numerous large scale botulinum toxicosis events occurred in various animal species including cattle, goats, sheep, horses and reindeer (unpublished data). Reindeer bred in a local zoo located in the northern part of Israel were fed alfalfa contaminated with animal carcass harboring BoNT-D producing *C. botulinum*. Within two weeks 30 reindeer were fatally poisoned resulting in almost a complete wipeout of the entire reindeer population. Animal carcasses in forages were also the source of BoNT-D producing *C. botulinum* in other fatal poisoning events in horses, goats and sheep resulting in the death of 20, 17 and 68 animals respectively (unpublished data). Moreover, dozens of calves were fatally poisoned in 2015 following exposure to an unknown source of BoNT-D producing *C. botulinum* in their feed. Taken all together, it seems according to our records, that botulism in recent years constitutes the most common cause of death in livestock as compared to other feed contaminates described in the present review.

TRACE ELEMENTS

Some trace elements have nutritional functions and are essential to the health such as copper, selenium, manganese and zinc, while others such as lead, cadmium, arsenic and mercury have no nutritional relevance and can cause serious illnesses (29).

Mercury

Mercury exists in the environment as elemental mercury (metallic), inorganic mercury and organic mercury (primarily methyl mercury) (30, 31). Among organic forms, the most toxic is methylmercury (31). Methylmercury is able to cross the blood-brain and the placental barriers; hence the nervous system is the primary site of toxicity in animals and humans (31). Methylmercury bio accumulates along the food chain particularly in the aquatic food chain; long-lived carnivorous fish and marine mammals exhibit the highest content (32). In Israel the MRL value for mercury in non-predator fish is 0.5 ppm (33). A survey conducted between 2010 to 2014 measuring total mercury levels in 223-367 fish samples of 9-13 different common edible species along the Israeli Mediterranean coastline revealed that 4.9%-7.9% of all fish samples analyzed exceeded the MRL value of 0.5 ppm mercury, whereas in the Haifa bay area alone the percentage of polluted fish samples exceeding the MRL value was significantly higher, namely 6.6%-19.5% (33-36).

Arsenic

Arsenic is found in both organic and inorganic forms occurring in different ores, minerals, rocks and ground water (37, 38). Inorganic arsenicals are more than ten times more toxic the organic form (37, 38). Acute poisoning in animals and humans is characterized by gastrointestinal adverse effects, neurological signs collapse and death. Subacute exposure is characterized by depression, anorexia, incoordination and hemorrhagic diarrhea (39).

In the years 2010-2014 a total of 725 of the most common fish species were analyzed for total arsenic levels, yielding levels ranging between 0.025-153 ppm, of which 26% were above 10 ppm per wet weight (33-36). According to the US Environmental Protection Agency (EPA) estimation, the maximal percentage of inorganic arsenic of the total arsenic in fish is 10%, hence about 26% of the analyzed fish species are potentially above the MRL levels of 1 ppm inorganic arsenic (40).

Cadmium

Cadmium is commonly found in the form of mineral forming cadmium oxides, phosphates, chlorides and sulphates (41). Cadmium usually enters the environment from zinc refining, coal combustion, mine wastes, steel production and the use of dicadmium phosphate minerals as feed additive (41-43).

Chronic cadmium poisoning is associated with osteoporosis, renal lesions, mineral imbalance and death (42). According to the published reports of 2010-2013, a total of 705 liver poultry samples in Israel were analyzed, of which 8.3% were found above the MRL value of 500 ppb (44-47). In 2010 of the 42 beef liver samples analyzed, 17% exceeded the MRL value of 500 ppb (47). However, in the following years (2011-2013), no residual levels of cadmium in beef liver samples were reported (44-46).

Reports published by the Plant Protection Inspection Service (PPIS), indicated low prevalence of cadmium in various imported grain commodities such as wheat, barley, soy and alfalfa with 1.3% of 670 samples analyzed exceeding the MRL of 1 μg/kg (Unpublished data).

Copper

Although copper does not belong to the heavy metals that are generally known to pose the greatest risk to animal and human health, it is interesting that in Israel copper causes more health problems than all the heavy metals altogether (48). Chronic copper toxicosis in sheep, mainly in the East Friesan/Awassi breed crosses, is frequently diagnosed in Israel every year. Between 2010-2013, 64 different sheep herds were chronically intoxicated following ingestion of a Total Mixed Ration (TMR) containing toxic copper levels. The most common causes of copper toxicosis in Israel comprise excess copper in sheep concentrates or poultry litter commonly fed to ruminants. Recently a major and rare copper toxicosis occurred in dairy cows following exposure to TMR containing toxic levels of copper sulphate (500 mg/kg), as a result of dosage miscalculation by the grower (unpublished case report). Dietary molybdenum and sulphate play a crucial role in the metabolic balance of copper in ruminants; hence it is important to determine copper and molybdenum, as well as sulphur and zinc in tissues (liver and kidney) and feedstuffs for diagnosis and for monitoring interactions between them (48).

VETERINARY DRUGS

Veterinary drugs are currently used for therapeutic indications, disease prevention or as growth promotors (49). Hazardous exposure may result from improper usage for non-target animals, accidental over dosage or as a result of carryover in feed during feed production (2, 49). This section focuses on antimicrobial drugs, due to their high prevalence as drug residues in animal-derived food products and their direct involvement in drug-related intoxication events in farm animals. The antimicrobial drugs presently approved for usage in farm animals include β-lactams, sulfonamides, tetracyclines, aminoglycosides, chloramphenicol analogues, fluoroquinolones, macrolides, nitrofuranes, bacitracin and polymyxin antibiotics (49, 50). The antibiotics most commonly detected in animal-derived products such as eggs, beef and poultry liver belong to the sulfonamide, tetracycline and fluoroquinoloe classes (44-47).

Although sulfonamides and fluoroquinolones are totally forbidden for the treatment, prevention or growth promotion in lying hens, the drugs are occasionally found at levels exceeding their MRL values in eggs with a prevalence of up to 1% and 1.2% respectively (44-47). Tetracyclines are also frequently reported to exceed their MRL value in eggs of 400 μg/kg with occurrence rate of up to 2.9% as reported in 2012 (45). Consequently, the occurrence rate of up to 2.9% as reported in 2012 resulted in 54 million eggs contaminated with tetracyclines, which entered the local Israeli market. Poultry, turkey and beef liver analysis in 2010-2013 revealed sulfonamide, fluoroquinolones and macrolides residues exceeding their corresponding MRL values in up to 1.9% of all samples analyzed (44-47). Recently a mass intoxication event in pregnant sheep occurred in Israel, following exposure to lethal dosage of oxytetracycline resulting in a high mortality rate (unpublished case study). A dosage of 1 kg oxytetracycline was mixed with 250 kg TMR and administered to a herd of 280 pregnant sheep for the prevention of abortions. The dosage was about 8 times the recommended maximal dosage of 10 mg/kg body weight for sheep, subsequently leading to the high mortality rate. Coccidiostats are widely used in Israel mainly as poultry feed additives for preventing or treating coccidiosis (9). It is generally acknowledged that under practical conditions during the production of mixed feeds, a certain percentage of a feed batch remains in the production circuit and these residual amounts can contaminate the subsequent feed batches (51). This cross contamination may result in the exposure of non-target animal species, and hence the potential health risks for non-target animal species as well as the potential residue deposition in foods derived from these non-target species. In Israel, poultry litter from coccidiostats treated broilers is commonly used as feed additive to livestock. Consequently, lethal cardiomyopathic syndrome in beef cattle is frequently diagnosed in Israel almost every year (13-15, 44-47). Recently a major fatal maduramicin intoxication event occurred in a pig farm located in the southern part of Israel affecting 22 gilts and two boars, resulting in a total mortality of 65% within 2 days following ingestion of feed contaminated with lethal levels of maduramicin (9). Not only farm animals were reported to be fatally intoxicated with ionophors. In 2004, 17 dogs were intoxicated following ingestion of commercial dog food contaminated with toxic levels of lasalocid, resulting in 30% mortality rate (11). A survey of locally produced poultry litter conducted in the years 2010-2013 by the PPIS revealed exceptionally high levels of maduramicin (range: 0.2 – 13 µg/kg), lasalocid (11-39 µg/kg) and monensin (range: 3.6-76.3 µg/kg), exceeding the MRL values in non-target animal feed (unpublished data).

A direct impact of the extensive usage of ionophors in animal feed is frequently observed by the carryover of ionophors into animal derived products such as eggs and poultry/turkey meat (44-47, 52). An alarmingly high prevalence rate of ionophors (21.7%) was found in Israel in 2012 in eggs for human consumption, whereas in the following year, the prevalence rate declined to 4.8% (45, 46). The analysis of poultry and turkey meat on the presence of ionophors in the years 2010 to 2013 yielded an average of 2.5% of all meat products (n=893) exceeding their MRL values (44-47). Clopidol is frequently found in Israeli eggs for human consumption, although it is not approved for usage for laying hens (44-47). Furthermore, no MRL value for clopidol has been so far defined for eggs, despite its frequent prevalence in eggs. The high occurrence rate of clopidol in eggs (12.8-34% in the years 2010 – 2013) is worrisome, due to the lack of toxicological data following long term exposure in humans.

MYCOTOXINS

The risk of contamination by mycotoxins is an important feed and food safety concern for grains and other field crops. Mycotoxins are toxic secondary metabolites of mold infestations affecting as much as one-quarter of global food and feed crop output (53, 54). Mycotoxins are produced by fungi of various genera when they grow on agricultural products before or after harvest or during transportation or storage (53).

Mycotoxins may be carcinogenic (e.g. aflatoxins, ochratoxins, fumonisins), oestrogenic (zearalenone), neurotoxic (fumonisin B_1), nephrotoxic (ochratoxins, citrinin), dermanecrotic (trichothecenes) or immuno-suppressive (aflatoxin B_1, ochratoxin A, and trichothecenes) (55, 56). Mycotoxins are regularly found in feed ingredients such as maize, sorghum grain, barley, wheat, rice meal, cottonseed meal, groundnuts and other legumes (57).

To protect consumers from these health risks, many countries have adopted regulations to limit exposure to mycotoxins (58-60). However, diverging perceptions of tolerable health risks associated largely with the level of economic development and the susceptibility of a nation's crops to contamination have led to widely varying standards among different national or multilateral agencies (59).

Aflatoxins

Aflatoxins (AF) are hepatotoxic and carcinogenic secondary metabolic products from fungi belonging in particular to the *Aspergillus flavus* and *A. parasiticus* species (61).

More than 20 aflatoxin-like secondary metabolites have been identified and aflatoxin B1 (AFB1) was shown to possess the most toxic and carcinogenic properties to humans and animals (61). AF's are found as natural contaminants in many feedstuffs of plant origin, especially in cereals but also in fruits, hazelnuts and almonds (61). AFB1 can cause chronic diseases in humans and animals and can have different effects such as hepatotoxicity, genotoxicity and immunotoxicity (61, 62). The analysis of imported grain samples in Israel in 2010 and 2011 revealed AFB1 levels above the MRL value of 20 µg/kg in 3% of all analyzed samples (n = 536) with a maximum concentration of up to 149 µg/kg, possibly posing a health risk to farm animals (unpublished data).

Aflatoxin M1 (AFM1), a possible human carcinogen, is the major oxidized metabolite of AFB1 and is excreted primarily in the urine and less so in the milk (61). Israeli regulations concerning the dairy industry are harmonized with the EU regulations, hence a MRL of 0.05 µg/kg for AFM1 in milk is applied (63). Between the years 2010-2013, 3.5% of dairy milk samples exceeded the MRL value of 0.05 ppb, clearly indicating an existing problem with AFB1 contaminated feed (44-47).

Household pet are occasionally affected by AFB1, e.g. in 2005/06 a major aflatoxicosis event occurred in dogs in Israel, following ingestion of commercial pet diet containing corn contaminated with 30-300 µg/kg AFB1, resulting in high mortality rate and severe clinical signs (64).

Fumonisins

Fumonisins are mycotoxins produced mainly by *Fusarium proliferatum* and *F. verticilloides*, occurring mainly in maize, wheat and other cereals (65). Fumonisin B1 is the most common and economically important form, followed by B2 and B3 (65). Fumonisins exposure in feed and food has been associated with the occurrence of pulmonary edema in pigs, leukoencephalomacia in horses, hepatic cancer in rats and esophageal cancer in humans (65, 66). Surprisingly, in Israel the regulatory authorities do not conduct a routine yearly analysis of feed and food products for fumonisins, despite their widespread occurrence and their health hazards for humans and animals.

Trichothecens

Trichothecens are produced on many different grains like wheat, oats or maize by various *Fusarium* species such as *F. graminearum*, *F. sporotrichioides*, *F. poae* and *F. equiseti* (54). Trichothecens are powerful toxic protein and DNA synthesis inhibitors highly toxic to a wide range of animal species (67). Chemically trichothecenes can be classified into four types, among which type A and type B are the most prevalent types in agriculture commodities (67). Type A trichothecenes, mainly diacetoxyscirpenol and T-2 toxin, are considered more toxic than type B trichothecenes, the most common of which is deoxynivalenol (DON) and nivalenol (67, 68). The reports of the PPIS indicated in the years 2010-2013 in Israel, that 1% of the imported grains contained T-2 levels above the MRL value displayed a concentration range of 0.1-514 µg/kg (unpublished data). Numerous intoxication events occurred in Israel during the late ‘80s affecting poultry exposed to toxic levels of trichothecenes in their feed (16). A flock of laying hens exposed to T-2 and HT-2 toxin at 3.5 and 0.7 mg/kg, respectively, for 5 consecutive days displayed severe clinical signs, including depression, recumbency, feed refusal and cyanotic combs (16). Egg production dropped by 96% after 5 days. In 1996 and 1999, T-2 and diacetoxyscripenol were found in feed of affected broiler and layer flocks at levels of 70-350 µg/kg, resulting in high mortality rate and severe oral lesions (unpublished case study).

Zearalenone

Zearalenone is an estrogenic compound produced by several species of *Fusarium* fungi occurring on a wide range of substrates such as wheat, maize, rice and sorghum (66, 69). Zearalenone can cause hyperestrogenism and impaired fertility and increased rate of abortions (66, 69, 70). Zearalenone levels exceeding 1 ppm have been shown in various animal species to induce hazardous estrogenic effects over time (66). In 1986 an exceptionally high mortality rate of 40% occurred in a flock of 24,000 broilers in Israel; following ingestion of feed contaminated with zearalenone at levels up to 5 mg/kg feed (70).

Ochratoxins

Ochratoxins are a group of mycotoxins produced by several *Aspergillus* and *Penicillium* species occurring most commonly on a variety of cereal grains, grapes, dried fruits and coffee (71, 72). Ochratoxin A is the most prevalent and relevant fungal toxin of this group (71, 72). In 1996 a major ochratoxicosis event occurred in Israel affecting a flock of geese and broilers resulting in a 30% mortality rate following ingestion of corn contaminated with ochratoxin at concentrations of up to 930 µg/kg (73). A mycotoxin survey (analyzing only AFs and ochratoxin A) conducted by the Israeli Ministry of Health between 2008-2012 in major food commodities, revealed ochratoxin levels below the MRL value (50 µg/kg) in all samples analyzed (74).

PESTICIDES AND PERSISTENT ORGANIC POLLUTANTS (POPS)

Pesticides and persistent organic environmental pollutants (e.g, organophosphates, organochlorides) – may get into the feed due to common agricultural practices of pesticide applications in the fields (2).

Persistent organic pollutants (POPs)

As a result of industrial activity, POPs are widely spread in the environment and persist for many years (75-79). POPs are toxic chemicals consisting of highly diverse group of chemicals which are currently or were in the past used as pesticides, solvents, pharmaceuticals, and industrial chemicals, such as organochlorine insecticides (e.g. aldrin, dieldrin), brominated flame retardants, dioxins and dioxin-like compounds (77, 79). POPs are known to accumulate in the fatty tissue of living organisms, e.g. fish meal and fish oil are well known to contain substantial levels of POPs (77-79).

In 2012 the Israeli Ministry of Health published the results of a 5 years long survey (2006-2010), in which 5558 different samples of fruits, vegetables, spices and grains for human consumption were analyzed (80). The results of the aforementioned survey revealed pesticide levels above the MRL values in 11.2% of all analyzed samples, indicating potentially hazardous chronic exposure of the population to pesticides (80). Among the detected pesticides exceeding their MRL values, the organochlorine insecticide endosulfan was frequently detected in various food commodities such as fruits and vegetables (80). Although endosulfan has been banned in Israel since 2015, it is still occasionally detected in fatal toxicosis events in wild animals (unpublished data) (80, 81).

Dioxins and dioxin-like compounds (DLCs)

Dioxins and dioxin-like compounds (DLCs), by-products of various industrial processes are commonly regarded as highly toxic compounds, including polychlorinated dibenzo-p-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), and polychlorinated biphenyls (PCBs; considered dioxin-like compounds) (82-85). Dioxins have been implicated in reproductive and developmental toxicities, as well as compromised immune system (83-85). Dietary intake represents the most common route of human and animal exposure to dioxins and PCBs (85). Foods of animal origin are the greatest source of human exposure to these contaminants (85).

Contaminated fats or oils added either intentionally or unintentionally incorporated into manufactured feeds can be a major source of dioxins and PCBs (85). The Israeli Public Health Services together with the Ministry of Agriculture conducted in 2013 a small survey on the presence of dioxins and DLCs in 120 samples of animal derived food products such as milk, meat, eggs and dairy products (86). According to the results published by the Public Health Services, the eggs were the only animal-derived food product with dioxins and DLCs levels above their MRLs, namely 24% exceeded their MRL value of 5 ρg/g (86).

Organophosphorus and carbamate pesticides

Organophosphorus pesticides are extensively used in Israel in agriculture, public and veterinary health as well as in home and garden insecticides (87, 88).

Organophosphorus pesticides may cause severe, sudden toxicosis, but evidence exists that non-lethal exposure may deleteriously affect behavior, the immune system and reproduction, making diagnosis of harmful effects in populations difficult to perform (89). Many toxicosis in animals diagnosed in Israel are due to malicious poisonings in farm, wild and particularly pet animals (20, 44-47). Outbreaks of toxicosis in raptors caused by illegal spraying of fodder crops against rodents have resulted in repeated large-scale toxicoses events in Israel (20, 90).

The survey results conducted between 2006-2010 and the survey summery of 2011-2014 on the presence of pesticides in food commodities (mainly fruits and vegetables) by the Ministry of Health and Ministry of Agriculture, provide some indication regarding the burden of pesticide residues in local fodder products such as maize, wheat and sorghum in Israel (80, 81). The survey results between 2006-2010 revealed that 11.2% of the total samples analyzed exceeded the regulated MRL values, potentially exposing the Israeli population to hazardous health effects (80). Among the organophosphorus pesticides found to exceed the recommended average daily intake were dimethoate, fenamiphos, methamidophos, methidathion and oxydemethon-methyl (80). Methamidophos was reported to be implicated in numerous occasions in fatal wildlife intoxications affecting mainly raptors, waterfowls, jackals, foxes and boars (20, 90).

Between 4.2-15.6% of the food commodities (mainly fruits and vegetables) tested in 2011-2014, exhibited pesticide levels above their MRL values (81). The majority of the food samples exceeding the pesticides MRL values were vegetables (carrot, cucumber, fennel bulbs, radish), fruits (pumpkins, zucchini, kiwifruit, pear, strawberry) and leaves (lettuce, beet leaves, garden parsley, mint). The most common pesticides exceeding their MRL values were metalaxyl, bifenthrin, dimethomorph, carbofuran, chlorpyrifos, endosulfan, difenoconazole, methomyland azoxystrobin (81). Recently a study estimating the exposure of the adult Israeli population to organophosphorus pesticides revealed that the urinary organophosphorus pesticides levels in the Israeli population were higher as compared to the general population in the US and Canada and that fruit intake was a major source of exposure (91).

Carbamates are commonly used pesticides complementing the organophosphorus pesticides with similar toxicological properties (89). Worldwide they are extensively used in agriculture, in public and veterinary health and as home and garden insecticides (92, 93). Some carbamates such as methomyl and dithiocarbamates are extensively used in intensive agriculture systems in Israel (87, 88). Most of the intoxication events diagnosed in wildlife and household animals in Israel are due to malicious poisonings with aldicarb and methomyl, as well as following illegal usage of carbamate insecticides by farmers (20, 44-47). According to the yearly reports of the Veterinary Services, between 2010 – 2013, about 180 fatal intoxication cases were diagnosed in farm and household animals, due to exposure to methomyl and aldicarb (44-47).

PHYTOTOXINS

Natural pastures in Israel contain few toxic plants, most of which exhibit strongly aversive smell or taste toxins (94). Notwithstanding, reports of plant toxicosis in Israel have been made over the years in various animals species (94). By far the most common fatal toxicosis including abortions are caused by plants of high nitrate levels (> 1.0% w/w on dry weight basis) (94). Following ingestion, nitrate is reduced by rumen microorganisms to the much more toxic nitrite, which is subsequently absorbed into the blood stream, leading to the formation of methemoglobin and hypoxia (95).

The most important nitrate-containing plants in Israel frequently associated with abortions and intoxication events are the winter annual weeds *Malva nicaeensis* and *Silybum marianum*, as well as the summer annual weeds of the *Amaranthus* species (94). These weeds contaminate fields of fodder grown for hay and are often harvested together with the good feed. A survey of cattle feed in 50 Israeli farms revealed a wide range of nitrate levels in the hay (94). High nitrate levels (>1.5% w/w on dry basis) were most frequently determined in corn and *Setaria* straw (> 50 %), followed by clover, oat and vetch samples (25%) (94). None of the corn, wheat and sorghum silages displayed nitrate levels above 1.5% (94). In recent years several cases of fatal intoxication events in beef herds were recorded following ingestion of *Xanthium strumarium*, an introduced summer annual weed (94). There have been three recorded mass pyrrolizidine-toxicosis events in beef cattle due to ingestion of hay contaminated with *Heliotropium europium* (8, 17, 94). *Heliotropium* species are pyrrolizidine alkaloid producing weeds widely distributed in the Mediterranean region, often implicated with lethal pyrrolizidine alkaloids intoxications in livestock and humans (96, 97). The main plant toxicosis in sheep and goats is caused by an endemic plant, *Ferula communis*, a winter perennial plant dominating pastures in the Jerusalem foothills and in the Golan Heights (94). The plant contains natural anticoagulants, namely 4-hydroxy-coumarin derivatives, causing reduced blood coagulation with extensive hemorrhages leading to fatal anemia (98).

CONCLUSIONS

There are many pathways by which a contaminant can enter the food chain. This includes feed processing that may induce chemical changes, raw materials that may contain naturally occurring toxicants, cross contamination of subsequent feed batches and packaging material that may leach into the feed. A feed safety laboratory needs to deal with many challenges such as determination of analyte at trace levels in food and feed in complex matrices, conducting surveys, supporting the legislative arm by setting up MRL levels for newly discovered contaminants and conducting health risk assessments. VSAH laboratories are at the front line of public health on a very broad scale. Because of their availability to decision makers to react, they are typically the front line in a food and feed crisis or major animal and public health issue.

Furthermore, the feed safety laboratory should be equipped with state-of-the-art analytical instruments to enable rapid method development to detect chemical contamination in feed stuffs and be able to respond quickly to feed and food threats. Enforcing the new feed safety law is of utmost importance for ensuring public health, as feed contaminants might easily enter animal-derived products such as meat, milk and eggs, thereby directly endangering the end consumer.

ACKNOWLEDGEMENTS

The authors kindly thank Efrat Habusha and Faina Golender for their excellent technical assistance.

REFERENCES

1. Barel, S.: Review of the needs and composition of the feed safety and noxious compounds inspection system in the Israeli VSAH. http://www.vetserv.moag.gov.il/NR/rdonlyres/6E7801D9-882B-487E-A315-8B83129A7CB3/0/Barel.pdf. Accessed on 10.07.2016
2. Fink-Gremmels, J.: Introduction to animal feed contamination. In: Fink-Gremmels eds. Animal feed contamination. Woodhead Publishing Limited, Cambridge, UK: pp. 1-8, 2012.
3. Control of Animal Feed Law, Israel, March 5th 2014. http://www.vetserv.moag.gov.il/NR/rdonlyres/5C40C135-8CD6-4C71-9C6B-CE260FAA7E0A/0/hok_pikuah_baaley_haim_2014.pdf. Accessed on 10.07.2016
4. Lopez-Alonso, M.: Animal feed contamination by toxic metals. In: Fink-Gremmels eds. Animal feed contamination. Publishing Limited, Cambridge, UK; pp. 183-201, 2012.
5. Pettersson, H.: Mycotoxin contamination of animal feed. In: Fink-Gremmels eds. Animal feed contamination. Woodhead Publishing Limited, Cambridge, UK: pp. 233-270, 2012.
6. Monbaliu, S., Van Peteghem, C. and De Saeger, S.: Detection and determination of natural toxins (mycotoxins and plant toxins) in feed. In: Fink-Gremmels eds. Animal feed contamination. Woodhead Publishing Limited, Cambridge, UK: pp. 286-315, 2012.
7. O'Mahony, J., Clarke, L., Whelan, M., O'Kennedy, R., Lehotay, S.J. and Danaher, M.: The use of ultra-high pressure liquid

chromatography with tandem mass spectrometric detection in the analysis of agrochemical residues and mycotoxins in food – challenges and applications. J. Chromatogr. A. 1292: 83-95, 2013.
8. Shimshoni, J.A., Mulder, P.P., Bouznach, A., Edery, N., Pasval, I., Barel, S., Abd-El Khaliq, M. and Perl, S.: Heliotropium europaeum poisoning in cattle and analysis of its pyrrolizidine alkaloid profile. J. Agric. Food Chem. 63:1664-1672, 2015.
9. Shimshoni, J.A., Britzi, M., Pozzi, P.S., Edery, N., Berkowitz, A., Bouznach, A., Cuneah, O., Soback, S., Bellaiche, M., Younis, A., Blech, E., Oren, P., Galon, N., Shlosberg, A. and Perl, S.: Acute maduramicin toxicosis in pregnant gilts. Food Chem. Toxicol. 68: 283-289, 2014.
10. Shimshoni, J.A., Soback, S., Cuneah, O., Shlosberg, A. and Britzi, M.: New validated multiresidue analysis of six 4-hydroxycoumarin anticoagulant rodenticides in hen eggs. J. Vet. Diagn. Invest. 25:736-743, 2013.
11. Segev, G., Baneth, G., Levitin, B., Shlosberg, A. and Aroch, I.: Accidental poisoning of 17 dogs with lasalocid. Vet. Rec. 155:174-176, 2004.
12. Yeruham, I., Shlosberg, A., Hanji, V., Bellaiche, M., Marcus, M. and Liberboim, M.: Nitrate toxicosis in beef and dairy cattle herds due to contamination of drinking water and whey. Vet. Hum. Toxicol. 39: 296-298, 1997.
13. Shlosberg, A., Perl, S., Harmelin, A., Hanji, V., Bellaiche, M., Bogin, E., Cohen, R., Markusfeld-Nir, O., Shpigel, N., Eisenberg, Z., Furman, M., Brosh, A., Holzer, Z. and Aharoni, Y.: Acute maduramicin toxicity in calves. Vet. Rec. 140: 643-646, 1997.
14. Shlosberg, A., Harmelin, A., Perl, S., Pano, G., Davidson, M., Orgad, U., Kali, U., Bor, A., Van Ham, M. and Hoida, G.: Cardiomyopathy in cattle induced by residues of the coccidiostat maduramicin in poultry litter given as a feedstuff. Vet. Res. Commun. 16: 45-58, 1992.
15. Perl, S., Shlosberg, A., Hoida, G., Davidson, M., Yakobson, B. and Orgad, U.: Cardiac failure in beef cattle fed dried poultry litter. Vet. Rec. 13: 35-36, 1991.
16. Shlosberg, A., Weisman, Y., Handji, V., Yagen, B. and Shore, L.: A severe reduction in egg laying in a flock of hens associated with trichothecene mycotoxins in the feed. Vet. Hum. Toxicol. 26: 384-386, 1984.
17. Shlosberg, A. and Egyed, M.N.: Examples of poisonous plants in Israel of importance to animals and man. Arch. Toxicol. Suppl. 6: 194-196, 1983.
18. Malkinson, M., Shlosberg, A., Egyed, M.N., Avidar, Y., Perl, S., Weisman, Y., Nobel, T. and Bogin, E.: Hepatic cirrhosis suggesting aflatoxicosis in a flock of geese. Vet. Rec. 110:101-103, 1982.
19. Schlosberg, A., Elkin, N., Malkinson, M., Orgad, U., Hanji, V., Bogin, E., Weisman, Y., Meroz, M. and Bock, R.: Severe hepatopathy in geese and broilers associated with ochratoxin in their feed. Mycopathol. 138: 71-76, 1997.
20. Shimshoni, J.A., Evgeny, E., Lublin, A., Cuneah, O., King, R., Horowitz, I. and Shlosberg, A.: Determination of brain choline esterase activity in normal and pesticide exposed wild birds. Isr. J. Vet. Med. 67: 214-219, 2012.
21. Bruchim, Y., Segev, G., Sela, U., Bdolah-Abram, T., Salomon, A. and Aroch, I.: Accidental fatal aflatoxicosis due to contaminated commercial diet in 50 dogs. Res. Vet. Sci. 93: 279-287, 2012.
22. Scientific Opinion of the Panel on Biological Hazards. Microbiological risk assessment in feedingstuff for food-producing animals. EFSA J. 720: 1-84, 2008.
23. Rossetto, O., Pirazzini, M. and Montecucco, C.: Botulinum neurotoxins: genetic, structural and mechanistic insights. Nat. Rev. Microbiol. 12: 535-549, 2014.
24. Lindström, M., Myllykoski, J., Sivelä, S. and Korkeala, H.: Clostridium botulinum in cattle and dairy products. Crit. Rev. Food Sci. Nutr. 50: 281-304, 2010.
25. Steinman, A., Chaffer, M., Elad, D. and Shpigel, N.Y.: Quantitative analysis of levels of serum immunoglobulin G against botulinum neurotoxin type D and association with protection in natural outbreaks of cattle botulism. Clin. Vaccine Immunol. 13:862-868, 2006.
26. Gilboa, A.: Botulism events in September-October 2013. The Veterinary Services, Ministry of Agriculture. http://www.vetserv.moag.gov.il/NR/rdonlyres/8041254D-F2BB-4624-A712-14727A0845D9/0/botulism_eventssepoct2013draniellagilboa.pdf. Accessed on 10.07.2016
27. Scheinin, S.: Another botulinum intoxication ? 2014 what have we learned. http://www.hachaklait.org.il/articles/files/3629758070.pdf. Accessed on 10.07.2016
28. Eitan, T.: Botulism event in cattle in Ramat Ishai, Israel. http://www.hachaklait.org.il/files/021404.pdf. Accessed on 10.07.2016
29. Leeman, W.R., Van Den Berg, K.J. and Houben, G.F.: Transfer of chemicals from feed to animal products: The use of transfer factors in risk assessment. Food Addit. Contam. 24: 1-13, 2007.
30. EFSA (European Food Safety Authority). Mercury as undesirable substance in animal feed. Scientific opinion of the panel on contaminants in the food chain. The EFSA J. 654: 1-76, 2008.
31. Bosch, A.C., O'Neill B., Sigge, G.O., Kerwath, S.E. and Hoffman, L.C.: Heavy metals in marine fish meat and consumer health: a review. Sci. Food Agric. 96: 32-48, 2016.
32. Kim, M.K. and Zoh, K.D.: Fate and transport of mercury in environmental media and human exposure. J. Prev. Med. Public Health. 45: 335-343, 2012.
33. National Monitoring Program of Israel in the Mediterranean Sea, Scientific Report, 2013/2014. http://www.sviva.gov.il/infoservices/reservoirinfo/doclib2/publications/p0801-p0900/p0801b.pdf. Accessed on 10.07.2016.
34. National Monitoring Program of Israel in the Mediterranean Sea, Scientific Report, 2012. http://www.sviva.gov.il/InfoServices/ReservoirInfo/DocLib2/Publications/P0701-P0800/P0750.pdf. Accessed on 10.07.2016.
35. National Monitoring Program of Israel in the Mediterranean Sea, Scientific Report, 2011. http://www.sviva.gov.il/InfoServices/ReservoirInfo/DocLib2/Publications/P0601-P0700/P0696.pdf. Accessed on 10.07.2016.
36. National Monitoring Program of Israel in the Mediterranean Sea, Scientific Report, 2010. http://www.sviva.gov.il/InfoServices/ReservoirInfo/DocLib2/Publications/P0601-P0700/P0630.pdf. Accessed on 10.07.2016.
37. Tchounwou P.B., Yedjou, C.G., Patlolla, A.K. and Sutton, D.J.: Heavy metal toxicity and the environment. EXS. 101: 133-164, 2012.
38. Agency for Toxic Substances and Disease Registry (ATSDR),

Toxicological Profile for Arsenic TP-92/09. Georgia: Centre for Disease Control, Atlanta, 2000.
39. Abdul, K.S., Jayasinghe, S.S., Chandana, E.P., Jayasumana, C. and De Silva, P.M.: Arsenic and human health effects: A review. Environ. Toxicol. Pharmacol. 40: 828-846, 2015.
40. US EPA.: Guidance for assessing chemical contaminant data for use in fish consumption advisories, Vol. I: Fish Sampling and Analysis, 3rd ed. EPA-823-B-00-007. Office of Water, Wash. DC., 2000.
41. Jensen, A. and Bro-Rasmussen, F.: Environmental cadmium in Europe. Rev. Environ. Contam. Toxicol. 125: 101-181, 1992.
42. Lane, E.A., Canty, M.J. and More, S.J.: Cadmium exposure and consequence for the health and productivity of farmed ruminants. Res. Vet. Sci. 101:132-139, 2015.
43. EFSA (European Food Safety Authority). Cadmium in food. Scientific Opinion of the Panel on Contaminants in the Food Chain. The EFSA Journal, 980: 1-139, 2009.
44. Report 2013, Kimron Veterinary Institute, Veterinary Services and Animal Health, Ministry of Agriculture, Israel. http://www.moag.gov.il/agri/files/doch_shnati_2013.pdf. Accessed on 10.07.2016.
45. Report 2012, Kimron Veterinary Institute, Veterinary Services and Animal Health, Ministry of Agriculture, Israel. http://www.moag.gov.il/agri/files/doh_shnati_2012.pdf. Accessed on 10.07.2016.
46. Report 2011, Kimron Veterinary Institute, Ministry of Agriculture. Veterinary Services and Animal Health, Ministry of Agriculture, Israel. http://www.moag.gov.il/agri/files/report_2011.pdf. Accessed on 10.07.2016.
47. Report 2010, Kimron Veterinary Institute, Ministry of Agriculture. Veterinary Services and Animal Health, Ministry of Agriculture, Israel. http://www.moag.gov.il/agri/files/report_2010.pdf. Accessed on 10.07.2016.
48. Shlosberg, A.:Ssyndromes of ill –health associated with copper Isr. J. Vet. Med. 65:170-171, 2010.
49. Anadón, A., Martínez-Larrañaga, M.R. and Castellano, V.: Regulatory aspects for the drugs and chemicals used in food-producing animals in the European Union. In: Veterinary Toxicology Basic and Clinical Principles, ed Gupta RC, Elsvier, pp. 135-155, 2012.
50. The Israel Drug Registry, The Ministry of Health, 2016. https://webcache.googleusercontent.com/search?q=cache:WUr9SxwZRkIJ:https://www.old.health.gov.il/units/pharmacy/trufot/Trufut-Veter.asp%3Fp%3D1+&cd=2&hl=iw&ct=clnk&gl=il. Accessed on 10.10.2016.
51. EFSA (European Food Safety Authority). Cross-contamination of non-target feedingstuff by maduramicin authorized for use as a feed Additive. Scientific Opinion of the Panel on Contaminants in the Food Chain. EFSA J. 594: 1-30, 2008.
52. Kantiani, L., Llorca, M., Sanchís, J., Farré, M. and Barceló, D.: Emerging food contaminants: a review. Anal. Bioanal. Chem. 398: 2413-2427, 2010.
53. Smith, M.C., Madec, S., Coton, E. and Hymery, N.: Natural co-occurrence of mycotoxins in foods and feeds and their in vitro combined toxicological effects. *Toxins* (Basel); 8. pii: E94., 2016. doi: 10.3390/toxins8040094.
54. Bryden, W.: Mycotoxin contamination of the feed supply chain: implications for animal productivity and feed security. Animal Feed Sci. Technol., 173:134-158, 2012.
55. Miller, J.D.: Mycotoxins in small grains and maize: old problems, new challenges. Food Addit. Contam. 25: 219–230, 2008.
56. Marin, S., Ramos, A.J., Cano-Sancho, G. and Sanchis, V.: Mycotoxins: occurrence, toxicology, and exposure assessment. Food Chem. Toxicol. 60: 218-237, 2013.
57. Gallo, A., Giuberti. G., Frisvad, J.C., Bertuzzi, T. and Nielsen, K.F.: Review on mycotoxin issues in ruminants: occurrence in forages, effects of mycotoxin ingestion on health status and animal performance and practical strategies to counteract their negative effects. Toxins (Basel), 7: 3057-3111, 2015.
58. Marroquín-Cardona, A.G., Johnson, N.M., Phillips, T.D. and Hayes, A.W.: Mycotoxins in a changing global environment-a review. Food Chem. Toxicol. 69: 220-230, 2014.
59. Streit, E., Naehrer, K., Rodrigues, I. and Schatzmayr, G.: Mycotoxin occurrence in feed and feed raw materials worldwide: long-term analysis with special focus on Europe and Asia. J. Sci. Food Agric. 93: 2892-2899, 2013.
60. Shimshoni, J.A., Cuneah, O., Sulyok, M., Krska, R., Galon, N., Sharir, B. and Shlosberg, A.: Mycotoxins in corn and wheat silage in Israel. Food Addit Contam Part A, Chem. Anal. Control Expo. Risk Assess. 30:1614-1625, 2013.
61. Kensler, T.W., Roebuck, B.D., Wogan, G.N. and Groopman, J.D.: Aflatoxin: a 50-year odyssey of mechanistic and translational toxicology. Toxicol. Sci. 120 Suppl. 1: S28-48, 2011.
62. Wu, F., Groopman, J.D. and Pestka, J.J.: Public health impacts of foodborne mycotoxins. Annu. Rev. Food Sci. Technol. 5:351-372, 2014.
63. European Union, Commission Regulation (EU) No 165/2010 of 26 February 2010 amending Regulation (EC) No 1881/2006 setting maximum levels for certain contaminants in foodstuffs as regards aflatoxins, 2010. http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2010:050:0008:0012:EN:PDF. Accessed on 10.07.2016.
64. Bruchim, Y., Segev, G., Sela, U., Bdolah-Abram, T., Salomon, A. and Aroch, I.: Accidental fatal aflatoxicosis due to contaminated commercial diet in 50 dogs. Res. Vet. Sc. 93: 279–287, 2012.
65. Scott, P.M.: Recent research on fumonisins: a review. Food Addit. Contam. Part A Chem. Anal. Control Expo. Risk Assess. 29: 242-248, 2012.
66. Yiannikouris, A. and Jouany, J.P.: Mycotoxins in feeds and their fate in animals: a review. Anim. Res. 51: 81-99, 2002.
67. McCormick, S.P., Stanley, A.M., Stover, N.A. and Alexander, N.J.: Trichothecenes: from simple to complex mycotoxins. Toxins (Basel) 3: 802-814, 2011.
68. Kongkapan, J., Polapothep, A., Owen, H., and Giorgi, M.: A brief overview of our current understanding of nivalenol: a growing potential danger yet to be fully investigated. Isr. J. Vet. Med. 71: 3-9, 2016.
69. Bennett, J.W. and Klich, M.: Mycotoxins. Clin. Microbiol. Rev. 16:497-516, 2013.
70. Bock, R.R., Shore, L.S., Samberg, Y. and Perl, S.: Death in broiler breeders due to salpingitis: possible role of zearalenone. Avian Pathol. 15: 495-502, 1986.
71. Wang, Y., Wang, L., Liu, F., Wang, Q., Selvaraj, J.N., Xing, F., Zhao, Y. and Liu, Y.: Ochratoxin A producing fungi, biosynthetic pathway and regulatory mechanisms. Toxins (Basel) 8, 2016. pii: E83. doi: 10.3390/toxins 8030083.

72. Kőszegi, T. and Poór, M.: Ochratoxin A: molecular interactions, mechanisms of toxicity and prevention at the molecular level. Toxins (Basel) 8 (2016). pii: E111. doi: 10.3390/toxins8040111.
73. Schlosberg, A., Elkin, N., Malkinson, M., Orgad, U., Hanji, V., Bogin, E., Weisman, Y., Meroz, M. and Bock, R.: Severe hepatopathy in geese and broilers associated with ochratoxin in their feed. Mycopathologia, 138: 71-76 ,1997.
74. Hamama-Elishov, Z. and Versano, R.: Summary results of monitoring mycotoxins in food in Israel 2008-2012. Public Health Services-Food Control Services, Ministry of Health, 2013. http://www.health.gov.il/PublicationsFiles/mycotoxins2008_2012.pdf. Accessed on 10.09.2016.
75. Fernández-González, R., Yebra-Pimentel, I., Martínez-Carballo, E., Regueiro, J. and Simal-Gándara, J.: Inputs of polychlorinated biphenyl residues in animal feeds. Food Chem. 140: 296-304, 2013.
76. Mantovani, A., Maranghi, F., Purificato, I. and Macrì, A.: Assessment of feed additives and contaminants: an essential component of food safety. Ann. Ist Super. Sanita. 42: 427-432, 2006.
77. Weber, R., Gaus, C., Tysklind, M., Johnston, P., Forter, M., Hollert, H., Heinisch, E., Holoubek, I., Lloyd-Smith, M., Masunaga, S., Moccarelli, P., Santillo, D., Seike, N., Symons, R., Torres, J.P., Verta, M., Varbelow, G., Vijgen, J., Watson, A., Costner, P., Woelz, J., Wycisk, P. and Zennegg, M.: Dioxin – and POP-contaminated sites-contemporary and future relevance and challenges: overview on background, aims and scope of the series. Environ. Sci. Pollut. Res. Int. 15: 363-393, 2008.
78. Carpenter, D.O.: Polychlorinated biphenyls (PCBs): routes of exposure and effects on human health. Rev. Environ. Health 21: 1-23, 2006.
79. Giesy, J.P., Kannan, K., Blankenship, A.L., Jones, P.D. and Hilscherova, K.: Dioxin-like and non-dioxin-like toxic effects of polychlorinated biphenyls (PCBs): implications for risk assessment. Cent. Eur. J. Public Health, 8th Suppl: 43-45, 2000.
80. Versano, R. and Tal, A.: Risk analysis posed by pesticide residues in food in Israel. Ministry of Health, 2012. http://www.health.gov.il/PublicationsFiles/21112012_pesticides.pdf. Accessed on 10.07.2016
81. Versano, R. and Hamama-Elishov, Z.: Analysis of pesticide residues monitoring in food in Israel. Public Health Services – Food Control Services, 2014. http://www.health.gov.il/PublicationsFiles/pest_findings2014.pdf. Accessed on 10.07.2016.
82. Malisch, R. and Kotz, A.: Dioxins and PCBs in feed and food-review from European perspective. Sci. Total Environ. 491-492: 2-10, 2014.
83. Sapkota, A.R., Lefferts, L.Y., McKenzie, S. and Walker, P.: What do we feed to food-production animals? A review of animal feed ingredients and their potential impacts on human health. Environ. Health Perspect. 115: 663-670, 2007.
84. Gies, A., Neumeier, G., Rappolder, M. and Konietzka, R.: Risk assessment of dioxins and dioxin-like PCBs in food-comments by the German Federal Environmental Agency. Chemosphere. 67: S344-349, 2007.
85. Fernández-González, R., Yebra-Pimentel, I., Martínez-Carballo, E. and Simal-Gándara, J.: A Critical Review about Human Exposure to Polychlorinated Dibenzo-p-Dioxins (PCDDs), Polychlorinated Dibenzofurans (PCDFs) and Polychlorinated Biphenyls (PCBs) through Foods. Crit. Rev. Food Sci. Nutr. 55: 1590-1617, 2015.
86. Versano, R., Hamama-Elishov, Z. and Ben-Ezra, R.: Survey summery of dioxins and PCB-like dioxins in food in Israel, 2013. Public Health Services and Food Control Services. http://www.health.gov.il/PublicationsFiles/dioxine2013.pdf. Accessed on 10.07.2016.
87. Spector Bass, S.: Utilization of pesticides in agriculture. The Center of Research and Knowledge, HaKnesset Israel, 2010. http://www.knesset.gov.il/mmm/data/pdf/m02510.pdf. Accessed on 10.07.2016.
88. Ben-Sidon, O., Tal, T. and Yanai, M.: Pesticides in Israel 2008-2010. Central Bureau of Statistics, Israel, 2013. http://www.cbs.gov.il/publications13/pesticides2010_1497/pdf/h_print.pdf. Accessed on 10.07.2016.
89. Gupta, R.C.: Toxicology of Organophosphate & Carbamate Compound. In: Veterinary Toxicology, Basic and Clinical Principles, Elsevier Academic 2nd ed., Chapter 45: pp 573-585, 2012.
90. Shlosberg, A. and Bahat, B.: The Risk of toxicosis from pesticides and pollutants in raptors and wildlife in Israel-The present situation and recommendations for the future. Proceedings of an International Workshop, Jerusalem Biblical Zoo, Israel, April 9-10th, 2000.
91. Berman, T., Goldsmith, R., Göen, T., Spungen, J., Novack, L., Levine, H., Amitai, Y., Shohat, T. and Grotto, I.: Urinary concentrations of organophosphate pesticide metabolites in adults in Israel: demographic and dietary predictors. Environ. Int. 60: 183-189, 2013.
92. Berman, T., Karakis, I. and Reicher, S.: Environmental Health in Israel. Environment and Health Fund and Ministry of Health, 2014. http://www.health.gov.il/publicationsfiles/bsv_sviva2014e.pdf. Accessed on 10.07.2016.
93. King, A.M. and Aaron, C.K.: Organophosphate and carbamate poisoning. Emerg. Med. Clin. North Am. 33:133-151, 2015.
94. Shlosberg, A.: Plant Toxicoses in Israel. Israel J. Vet. Med. 66: 171-174, 2011.
95. Burrows, G.E.: Nitrate intoxication. J. Am. Vet. Med. Assoc. 177: 82-83, 1980.
96. Kakar, F., Akbarian, Z., Leslie, T., Mustafa, M.L., Watson, J., van Egmond, H., Omar, M.F. and Mofleh, J.: An outbreak of hepatic veno-occlusive disease in Western Afghanistan associated with exposure to wheat flour contaminated with pyrrolizidine alkaloids. J. Toxicol. 2010: 1-7, 2010.
97. Molyneux, R.J., Gardner, D.L., Colegate, S.M. and Edgar, J.A.: Pyrrolizidine alkaloid toxicity in livestock: a paradigm for human poisoning? Food Addit. Contam. 28: 293-307, 2011.
98. Akaberi, M., Iranshahy, M. and Iranshahi, M.: Review of the traditional uses, phytochemistry, pharmacology and toxicology of giant fennel (*Ferula communis* L. subsp. communis). Iran J. Basic Med. Sci. 18:1050-1062, 2015.