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Potential risks of dietary exposure to chlorpyrifos and cypermethrin from their use in fruit/vegetable crops and beef cattle productions

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Abstract The active ingredients (a.i.) used as pesticides vary across regions. Diet represents the main source of chronic exposure to these chemicals. The aim of this study was to look at the pesticides applied in fruit, vegetable, and beef cattle productions in Mendoza (Argentina), to identify those that were simultaneously used by the three production systems. Local individuals (*n* = 160), involved in these productions, were interviewed. Glyphosate was the a.i. most often used by fruit-vegetable producers, and ivermectin by beef cattle producers. Chlorpyrifos (CPF) and cypermethrin (CYP) were the only a.i. used by the three production systems. The survey revealed that CPF, CYP, alpha CYP, and CPF+CYP were used by 22, 16, 4, and 20% of the fruit and vegetable producers, respectively. Regarding beef cattle, CYP was used by 90% of producers, CYP + CPF formulation by 8%, and alpha CYP by 2%. The second approach of this study was to search the occurrence of CYP and CPF residues in food commodities analyzed under the National Plan for Residue Control (2012–2015). CYP residues found above the LOD were reported in 4.0% and CPF in 13.4% of the vegetable samples tested, as well as in 1.2 and 28.8%, respectively, of the fruit samples tested. Regarding beef cattle, CYP residues were reported in 2.3% and organophosphates (as a general pesticide class) in 13.5% of samples tested. In conclusion, consumers may be exposed simultaneously to CPF and CYP, from fruits, vegetables, and beef intake. Accordingly, the policy for pesticide residues in food and human risk assessment should account for the combined exposure to CPF and CYP. Moreover, appropriate toxicological studies of this mixture (including genotoxicity) are warranted.

Keywords Pesticides · Parasiticides · Residues in food · Chlorpyrifos · Cypermethrin · Combined exposure

Introduction

Agricultural and livestock production accounts for approximately 32% of Argentina's Gross Domestic Product and represents 90% of the food consumed across the country (Pórfido et al. 2014). Local production

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(Mendoza province) contributes significantly to the total national food supply (21% of fruit production and 14% of vegetable production) (http://www.iscamen.com.ar). However, food production systems require the use of pest control products for plant and animal health protection in order to avoid production losses and to increase crops yield, e.g., to obtain more than one harvest per year (Hjorth et al. 2011).

Pesticide use in Argentina for cereal and oilseed crops increased from 39 million kg–l/year in 1991 to 335 million kg–l/years in 2012 (http://www.casafe.org). On the other hand, insecticides and parasiticides are applied as veterinary medicines to control external and internal parasites. Veterinary medicines are often registered associated to other drugs in the same commercial formulation to enhance their effectiveness in the treatment of infestations by different pests. In line with this, certain active ingredients can be applied as plant protection products and/or veterinary medicines for primary food production (Committees on Toxicity Mutagenicity Carcinogenicity of Chemicals in Food, Consumer Products and the Environment 2002). Therefore, the same active ingredient (a.i.) and/or their metabolites can be found not only in fruit/vegetables but also in edible animal tissues (EFSA 2012).

Additional risks can occur if excessive doses of pesticides are used, or worst, if they have not been authorized for use by the competent health authority. Dietary habits over a sustained period of time represent the main source of chronic exposure of the population to low doses of pesticide residues (Hjorth et al. 2011). In Argentina, The National Service for Agri-food Health and Quality (SENASA) is the agency charged with the overall management of pesticides, including residue policy. This organism monitors the use of a.i. for crop production and veterinary practices and assures their compliance with the maximum residue limit (MRL) set for each food commodity (Pórfido et al. 2014).

For a.i. having dual use as plant protection products and veterinary medicines, co-exposure to compounds with the same mechanism of toxicity (or different mechanisms but eliciting the same toxic effect) may result in a combined action (Committees on Toxicity Mutagenicity Carcinogenicity of Chemicals in Food, Consumer Products and the Environment 2002). Under this scenario, potential toxicological risks may arise from the intake of different pesticide residues during one complete daily meal (Boobis et al. 2008; Crépet et al. 2013). Because of the numerous sources of exposure to pesticides (food, drinking water, residential, occupational) and routes of exposure (oral, inhalation, dermal), the associated risk may result from the sum of all of them (EFSA 2008). Hence, a new concept was coined in relation to multiple pesticide exposure: aggregate/cumulative risk (European Parliament 2005). However, regulations on combined exposure are not currently in place in Argentina.

The main objective of this paper was to address the potential human health concern associated with food commodities containing different pesticides that, in case of simultaneous exposure, can lead to combined effects. To this end, two main data sources were evaluated: (1) information provided by local (Mendoza) producers of fruit, vegetables, and beef cattle, on the pesticides most frequently applied in their respective work activities to identify which active ingredients (if any) were co-used in these productions and (2) reports of the National Plan for Residue Control (2012 to 2015) to check if these chemicals were found as residues in food commodities.

Materials and methods

Collecting information from local people involved in primary food production

A total of 160 individuals from Mendoza (Argentina) involved in fruit and vegetables production were interviewed over the period 2012–2015. The study area is located in Western Argentina, between parallels 24° and 43° south, and is considered one of the main food production systems of the arid region. Interviews were carried out using one questionnaire for fruit and vegetable producers and another one for beef cattle producers. They were interviewed in their work places by members of the research team. Ninety participants were farm workers involved in fruit and vegetables production from most of the cultivated areas, 10 were retailers of agrochemicals and 60 were beef cattle producers. For each farm worker interviewed, information was collected on crop type, number and type of pesticides/a.i. used, and its frequency of application. The study areas were identified according to the Rural Developmental Institute (http://www.idr.org.ar/) and a random sample was selected by cluster (Casal and Mateu 2003). In relation to livestock production, interviews were performed on beef cattle producers randomly selected from a local registry, veterinary professionals devoted to beef cattle production, and veterinary products sellers. Cattle producers were asked to provide information on the parasiticides they used (number and chemical class) and their frequency of application. Those a.i. mentioned by the three type of producers were chosen for the next part of this study.

Database search of the reports provided by the National Plan for Residue Control and Food Hygiene (Argentina)

Data on pesticide residues along with the analytical methods used were obtained from the 2012–2015 reports of the National Plan on fruit/vegetable (http://www.senasa.gob.ar/cadena-vegetal/forrajes/comercio/control-de-residuos-plan-creha) and animal (http://www.senasa.gob.ar/cadena-animal/fauna-silvestre/produccion-primaria/control-de-residuos-plan-creha) commodities from around the country (see supplementary). On the respective websites, only data from the last year are regularly shown.

The quantified residue levels were reported either as positive (≥ limit of detection, LOD) but without exceeding the respective MRL (< MRL), or positive and exceeding the MRL (≥). These MRL were defined in Resolutions 934/2010 and 608/2012 for vegetables where MRLs were set for 105 pesticides and plant protection products (SENASA 2010), and Resolution 559/2011 for bovine edible tissues, where MRLs were set for 68 veterinary parasiticides (SENASA 2011a). When the National Regulations did not set MRL, those established by the *Codex Alimentarius* FAO/WHO were used instead.

Results

In the survey, fruit and vegetable producers mentioned the use of 51 a.i. (Table 1), which were classified as insecticides (32.7%), fungicides (25.0%), herbicides (21.1%), and acaricides + insecticides (21.2%). Individually, glyphosate was the a.i. most widely used for fruit and vegetable crops, followed by imidacloprid, chlorpyrifos (CPF), cypermethrin (CYP), lambda cyhalothrin, and carbofuran, which showed similar percentages.

Major fruit crops grown in the region were as follows: olives (25.5%), peach (21.2%), plum (17.9%), pear (8.9%), apple (6.7%), almonds, and quince and walnuts (4.4% each one). Other fruits grown in a lesser percentage were as follows: banana, cherry, chestnuts, apricot, grape, hazelnuts, kiwi, lemon, oranges,

Table 1 Data for pesticide use according to the survey carried out on local fruit and vegetable producers, in Mendoza, Argentina (2013–2014)

Active ingredients	Indication of use	Number of producers (%) that use each active ingredient[a]
Glyphosate	H	31
Imidacloprid	I	23
Chlorpyrifos	I	22
Chlorpyrifos + cypermethrin	I,A	20
Lambda cyhalothrin	I	19
Carbofuran	I,A	19
Cypermethrin	I,A	16
Methidathion	I	15
Azinphos – methyl	I	14
Linuron	H	12
Avermectin	I,A	11
Dimethoate	I	10
Metalaxyl	F	9
Mancozeb	F	8
Pendimethalin	H	8
Propiconazole	F	8
Methamidophos	I,A	7
Carbendazim	F	6
Deltamethrin	I,A	6
Lufenuron+profenofos	I	6
Methoxyfenozide	I	6
Myclobutanil	F	6
Carbosulfan	I,A	5
Chlorfenapyr	I,A	5
Haloxyfop	H	5
Spinosad	I	5
Trifluralin	H	5
Paraquat dichloride	H	5
Alpha cypermethrin	I,A	4
Tebuconazole	F	4
Azoxystrobin	F	3
Endosulphan	I,A	3
Methomyl	I	3
Metolachlor (S)	H	3
Carboxin	F	2
Diconazole	F	2
Ethion	I	2
Metribuzin	H	2
Thiacloprid	I	2
Carbaryl	I	1
Chlorothalonil	F	1

Table 1 (continued)

Active ingredients	Indication of use	Number of producers (%) that use each active ingredient[a]
Clomazone	H	1
Fenarimol	F	1
Lindane	I,A	1
Methylparathion	I	1
Oxyfluorfen	H	1
Penconazole	F	1
Pirimicarb	I	1
Quizalofop	H	1
Triadimefon	F	1
Thiamethoxam	I	1

F fungicide, *H* herbicide, *I* insecticide, *A* acaricide

[a] survey: 90 farm workers involved in fruit and vegetables production and 10 retailers of agrochemicals. Each individual refers to use more than one active ingredient

strawberry, and tangerine. Major vegetable crops grown in the region were as follows: carrot (14%), onions (13.9%), garlic (12%), potatoes (11.4%), lettuce (10.7%), tomatoes (10.2%), chard (6.3%), and squash (5%). Other vegetables grown in a lesser percentage were as follows: artichoke, broccoli, cabbage, cauliflower, celery, chard/spinach, peppers, arugula, and pea. The reason for fungicide and insecticide application was preventive in 60.2% of cases (Table 1).

Beef cattle production was distributed in the following systems: breeding (72.6% of producers), re-breeding (23.3%), feedlot (2.7%) and wintering (1.4%). Ivermectin (IVM) was the a.i. most often used by beef cattle producers. CPF and CYP were preventively used against external parasites: ticks, flies, mites, lice, fleas, and mosquitoes. Producers of breeding and rearing systems referred to apply CPF and/or CYP between six and eight times per year (Table 2).

This survey indicated that CPF and CYP were used both for fruit/vegetables and for beef cattle. Hence, these a.i. were selected to check whether they are detected as residues in food of plant or animal origin.

In the National Plan for Residue Control, the summary reports indicated that from 1435 fruit samples studied for CYP, nine samples had positive residues but below the MRL and eight exceeded the MRL for the years 2013–2014 (Table 3). The same number of samples was analyzed for CPF and 412 positive results were found, all in compliance with the MRL except one sample, which exceeded the MRL. In the same time period, 298 vegetable samples were analyzed for CYP residues, which is a mixture of isomers including alpha CYP. Two samples were in compliance with MRL, ten exceeded the MRL, and residues were not detected in the remaining samples. As for samples analyzed for CPF residues, the report indicated that 23 were in compliance with the MRL and 17 exceeded the MRL (Table 3).

Table 2 Data for parasiticides used according to the survey carried out on local beef cattle producers in Mendoza, Argentina (2012–2015)

Active ingredients	Indication of use	Number of producers (%) that use each active ingredient[a]
Ivermectin	E	93
Cypermethrin	Ext. P.	90
Chlorpyrifos + cypermethrin	Ext. P	8
Albendazole	Int. P	3
Praziquantel	Int. P	2
Alpha cypermethrin	Ext. P	2
Doramectin	E	1

E endectocide, *Ext. P* external parasiticide, *Int. P* internal parasiticide

[a] Survey: 60 producers of beef cattle. Each individual refers to use more than one active ingredient

Over the years 2012–2015, 1483 fat samples from around the country were analyzed, of which 34 had organophosphates (OPs) residues above LOD (25 samples < MRL and 9 samples ≥ MRL) (Table 4). For CPF residues, 2072 fat samples were analyzed, of which 279 were positive (272 samples < MRL and seven samples ≥ MRL). Although the National Plan planned to search for CYP and CPF residues, the final results were reported as OPs and pyrethroids as a whole (without specifying individual a.i.).

Discussion

In the survey carried out in this study, fruit and vegetable producers confirmed the use of a wide number and variety of a.i. This indicates the high number of plant protection products available in the argentine market, accounting for about 1000

Table 3 Data on chlorpyrifos (CPF) and cypermethrin (CYP) residues in food commodities of plant origin according to the National Plan for Residue Control, Argentina

Commodities	Number of samples analyzed		% of samples positive for residues[a]				Maximum residue limits (MRLs) mg/kg			
			≥ LOD < MRL		≥ MRL		Senasa[b]	FAO/WHO[c]	Senasa[b]	FAO/WHO[c]
	CYP	CPF	CYP	CPF	CYP	CPF	CYP		CPF	
Fruits										
Almonds	38	38	0	0	0	0	0.5	ne	ne	0.05
Apple	148	148	0	51.3	0	0	1	0.7	0.2	1
Banana	328	328	0	58.2	0.6	0.3	ne	2.0	0.1	ne
Cherry	3	3	0	0	0	0	1	ne	0.5	ne
Chestnuts	11	11	0	0	0	0	ne	0.05	ne	ne
Damascus	na	na	na	na	na	na	1	3	0.5	ne
Hazelnuts	2	2	0	0	0	0	ne	0.05	ne	ne
Kiwi	34	34	0	8.8	0	0	ne	0.3	0.3	1
Lemon	95	95	0	7.4	0	0	ne	0.3	0.3	1
Oranges	62	62	3.2	22.5	0	0	ne	0.3	0.3	1
Olives	na	na	na	na	na	na	ne	0.05	0.5	ne
Peach	na	na	na	na	na	na	1	2	0.5	0.5
Pear	267	267	0	25.4	na	na	1	0.7	0.2	1
Plum	3	3	0	0	0	0	1	2	0.5	0.5
Quince	na	na	na	na	na	na	1	0.7	ne	1
Strawberry	35	35	0	8.6	5.7	0	ne	0.07	ne	0.3
Tangerine	409	409	1.7	12.2	0.9	0	ne	0.3	ne	1
Total	1435	1435								
Vegetables										
Artichoke	na	na	na	na	na	na	ne	0.1	0.05	ne
Arugula	43	43	2.3	23.2	0.0	2.3	ne	0.7	ne	ne
Broccoli	na	na	na	na	na	na	ne	1	0.5	2
Cabbage	na	na	na	na	na	na	ne	1	0.05	1
Carrot	na	na	na	na	na	na	ne	0.01	ne	0.10
Cauliflower	na	na	na	na	na	na	ne	1	0.5	0.05
Celery	20	20	0	30.0	5.0	40.0	ne	ne	ne	ne
Chard/spinach	74	74	0	1.3	5.4	5.4	ne	0.7	ne	ne
Garlic	na	na	na	na	na	na	0.1	ne	0.05	ne
Lettuce	85	85	0	5.9	5.9	4.7	ne	0.7	ne	ne
Onions	1	1	0	0	0	0	0.1	0.01	0.5	0.2
Peppers	na	na	na	na	na	na	ne	0.10	0.5	2
Potatoes	13	13	0	0	0	0	ne	0.01	0.02	2
Pumpkin	na	na	na	na	na	na	ne	0.07	ne	ne
Tomatoes	62	62	1.6	1.6	0	0	1	0.20	0.5	ne
Vetch	na	na	na	na	na	na	0.05	0.70	ne	0.01
Total	298	298								

ne not established, *na* not analyzed (therefore, the column % of samples positive for residues also indicates "na" because this information is not applicable)

[a] Senasa: National Service for Agri-food Health and Quality, 2013–2014

[b] Resolutions 934/ 2010 and 608/2012

[c] *Codex alimentarius* FAO/WHO 2015

registered chemicals (Pórfido et al. 2014). This figure is almost three times greater than the number of a.i. marketed in the European Union, where only 276 substances were registered before approving

Table 4 Data on chlorpyrifos (CPF) and cypermethrin (CYP) residues in food commodities of animal origin according to the National Plan for Residue Control, Argentina

Commodities	Number of samples analyzed		% of samples positive for residues[a]				Maximum residue limits (MRLs) mg/kg			
			≥ LOD < MRL		≥ MRL		Senasa[b]	FAO/WHO[c]	Senasa[b]	FAO/WHO[c]
	CYP[d]	OP[e]	CYP[d]	OP[e]	CYP[d]	OP[e]	CYP		CPF	
Bovine fat	2072	1483	10	2	0.1	0.6	1	2	1	1
Kidney	na	na	na	na	na	na	0.05	0.05	0.01	0.01
Liver	na	na	na	na	na	na	0.05	0.05	0.01	0.01
Total	2072	1483								

na not analyzed (therefore, the column % of samples positive for residues also indicates "na" because this information is not applicable).

[a] Senasa: National Service for Agri-food Health and Quality, National Program of Food Residues 2012–2015

[b] Resolution 559/ 2011

[c] *Codex alimentarius* FAO/WHO 2015

[d] CYP (or pyrethroids for 2014–2015)

[e] OPs: organophosphates,without identifying individual a.i.

the Regulation EC 1107/2009 currently into force (Karabelas et al. 2009).

From all pesticides mentioned by fruit/vegetables producers surveyed, CPF, CYP, and alpha CYP, and the commercial formulation containing CPF+CYP, were made a greater use for vegetable crops than for fruit crops. In particular, alpha CYP was mentioned two-fold more, and CPF+ CYP 16 times more by vegetable producers than by fruit producers. Some of the pesticides mentioned by fruit and vegetable producers are prohibited (or had restricted use) in Argentina, such as methamidophos, carbofuran, methyl parathion and lindane, as laid down in resolutions 127/1998, 10/1991, 606/1993, and 513/1998, respectively. Likewise, endosulfan was banned in 2011 (resolution 511/2011). The use of banned pesticides indicates that farmers did not follow Good Agricultural Practices (GAP). In this regard, it is important to note that because of the lack of professional pesticide applicators in Mendoza, the farmers themselves carry out this activity. The local agency in charge of regulating the use of pesticides provides fruit-vegetables and cattle producers with a handbook of GAP, which recommends not carrying out preventive or calendaring applications of plant protection products. Nevertheless, according to previous studies, we performed in the same region, 54% of workers acknowledged to apply insecticides and fungicides with a frequency of 3–4 months per year and 45% between 5–7 months per year, with herbicides being applied throughout the year according to the needs (Ferré et al. 2018). Argentina Regulation set out all the steps from the production to the application of pesticides and stipulates that a professional technical direction is required to give instructions on products, techniques, or methods of pesticide application as well as to respect the waiting times. Nevertheless, only 25% of the interviewees looked for professional technical advice (Ferré et al. 2018).

The a.i. commonly used for pest control in beef cattle was IVM, followed by CYP with almost similar percentage of use. None of the a.i. mentioned by cattle producers was prohibited or had a restricted use for animal health.

According to the survey carried out in this study, CPF, CYP, and alpha CYP were used not only for fruit and vegetable crops but also for beef cattle production. These two a.i. were the only ones used by three different production systems, which contrasts with the 16 a.i. reported for other geographical areas, where CYP was included but not CPF (Committees on Toxicity Mutagenicity Carcinogenicity of Chemicals in Food, Consumer Products and the Environment 2002).

When the database provided by the National Plan for Residue Control was compared with the information obtained in the survey carried out in this study, the most relevant information is the following. Glyphosate, the a.i. most often mentioned by fruit and vegetable producers, was not included within the 11 herbicides reported by the National Plan for Residue Control (data not shown). In relation to cattle beef producers, IVM and CYP, the two a.i. most often mentioned by these producers, were included in the National Plan (except for 2014, when endectocides in general were searched and reported, but not IVM in particular). Of the seven a.i. mentioned by the beef cattle producers, five were included in the National Plan for Residue Control. Alpha cypermethrin and praziquantel were not analyzed as residues, whereas albendazole was analyzed in liver samples (data not shown).

Some fruit and vegetables of local production were not analyzed for pesticide residues by the National Plan for Residue Control. This Plan used MRL established by national and international organizations. Three fruits: Damascus, peach, quinces, and nine vegetables: artichoke, broccoli, cabbage, carrot, garlic, pepper, olives, pumpkin, and vetch were not analyzed for CPF and/or CYP in the National Plan (Table 3). These primary food products have MRL established (FAO/WHO) for one or two of the pesticides analyzed except pumpkin and garlic. Since many of these 12 food products are typical regional productions, this may be the reason why they were not analyzed at national level. The National Plan residue report indicated that the presence of CPF and CYP residues were not analyzed in samples of local commodities such as olives, peach, quince, and walnuts, which corresponded to 25.5, 21.2, 4.4, and 4.4% of local production, respectively. It is worth of noting that less than 15 samples of onions and potatoes were analyzed over 2 years, which accounted for 13.9 and 11.4%, respectively, of vegetable production in Mendoza. Neither carrot nor garlic samples were examined, accounting for 14 and 12% of the region's vegetable production. Likewise, three samples of plum were analyzed in 2 years, while this type of production corresponded to 17.9% of total fruit production in the region. Regarding bovine meat, CPF/OP and CYP/pyrethroids were analyzed in a large number of samples although only a fairly low percentage of them exceeded the MRL; however, those a.i. were not searched for in kidney and liver samples (Table 4).

We emphasize the need of collecting representative samples of each geographical region in order to account for the type and magnitude of local agricultural production as well as to include in the residue analysis those a.i. particularly used in each region. Furthermore, the proportion of fruit and vegetable samples that were not analyzed and/or for which MLRs are not established is a matter of special concern. In some cases the MRLs adopted by the National Plan for Residue Control are higher and in other cases lower than those proposed by the Food and Agricultural Organization (FAO-WHO) (Tables 3 and 4). All the real combinations of food commodities/a.i. should have an established MRL since these represent an efficient tool to protect against the adverse effects of pesticides on human health. Moreover, the presence of pesticide residues in food commodities imported from Argentina was reported in the European Union Coordinated Monitoring Programme (EUCP). For the 2011 EUCP, the a.i. most often found in fruit samples was CPF (29.7%), followed by other insecticides (EFSA 2014). For combinations of local food products/MRLs of pesticides, only hazelnuts, chesnuts, arugula, chard, spinach, lettuce, and pumpkin lack MRL for CPF. As the analysis of the MRLs aims to monitor the correct use of pesticides according to GAP, it can be inferred that the use of CPF should not be allowed for these food products. However, CYP and CPF residues were analyzed for many of these products under the National Plan for Residue Control. It remains unclear which regulation was used as a reference. Table 3 shows that, from food commodities of local production, only celery has no MRLs established for those two pesticides; however, they were analyzed in the National Plan, and the same argument than before can be applied.

The conclusion that can be drawn from the present study is that the combination CYP+CPF should be taken into consideration for a proper dietary risk assessment. The European Food Safety Authority Panel on Plant Protection Products and their Residues (EFSA-PPR) identified a number of criteria for selecting groups of compounds for cumulative risk assessment, including (a) frequency of detection in surveillance programs, (b) frequency of use on the basis of information obtained from surveys or sales statistics, (c) high intakes, and based on biomonitoring data (EFSA 2008). The premises (a) and (b) are met in the present study, which support our proposal.

The main concern of this study is the possible chronic toxicity for consumers from dietary exposure to low doses of pesticides, as occurs with CYP and CPF which may be ingested daily through fruit, vegetables, and meat consumption. CYP and CPF were considered to have "no strong presumption of safety"(Cramer Class III) (EFSA 2012). CPF and CYP are not listed in the monographs on the evaluation of carcinogenic risks to humans of the International Agency for Research on Cancer (IARC 2016). The advisory group to recommend priorities for monographs during 2015–2019 considered that CPF has a medium priority recommendation (WHO-IARC, 2015). CPF is listed as evidence of non-carcinogenicity for humans, and CYP as possible human carcinogen by the U.S. Environmental Protection Agency (US EPA, 2015a). On the other hand, CYP and CPF were considered as suspected endocrine disruptors (Kegley et al. 2000) and included in the Endocrine Disruptor Screening Program (EDSP) Tier 1 of US-EPA and for CYP, additional Tier 2 testing is recommended (US EPA, 2015b).

CYP has been reported to induce oxidative stress and endocrine disruption in male mice (Jin et al. 2011). Furthermore, a disruptive action on androgen and estrogen receptors expression, and a reduction of ATP, mitochondrial enzymes activity, and mitochondrial membrane potential has been reported for CYP, which also exhibited procarcinogenic activities (Goodson et al. 2015). CYP also showed in vitro genotoxic effects in peripheral blood lymphocytes (Kocaman and Topaktaş 2009).

CPF has been reported to interfere with the activity of hormones involved in homeostasis, reproduction, and developmental processes (Kegley et al. 2000; Viswanath et al. 2010; Mnif et al. 2011). CPF and its oxon metabolite are toxic to the human sperm DNA (Salazar-Arredondo et al. 2008) and possess a threat to the reproductive system because of disruption of androgen biosynthesis (Viswanath et al. 2010). CPF also induced significant DNA damage in rat liver and brain cells after acute or chronic exposure, indicating an in vivo genotoxic potential (Mehta et al. 2008). However, EFSA peer review indicated that CPF does not show genotoxic and carcinogenic potential (EFSA 2014).

Co-exposure to pyrethroids (e.g., CYP) and OPs (e.g., CPF) may result in toxicokinetic interactions since the highly toxic oxon metabolite of CPF is an irreversible inhibitor of the esterase-mediated hydrolysis of CYP, thus enhancing its insecticidal activity, although these interactions are unlikely to occur at low doses (Hernández et al. 2013; Hernández et al. 2017). Mixtures of these two pesticides have shown to act together in a synergistic manner under experimental conditions in zebrafish (Zhang et al. 2017). They also caused an increase in micronucleated erythrocytes in rats acutely exposed to orally combined doses (Okonko et al. 2016).

Conclusion

In this study, we set out to find out which active ingredients could pose a higher risk to the consumers' health as a result of the presence of pesticide residues in food, in Mendoza, Argentina. Data from the survey conducted indicated that 55 active ingredients were commonly used for different locally produced foods. Glyphosate was used by 30% of farmers and ivermectin by 90% of breeders. However, concerns were raised on the active ingredients that can be found in different fresh food items we can eat throughout the day. We noted that the insecticides/parasiticides CPF and CYP were used significantly by fruit, vegetable, and beef producers over the period 2012–2015. In addition, both active ingredients were reported as food residues by the National Plan for Residue Control according to the annual report for the years 2012–2015. CYP was found as residue in nine and CPF in 13 out of 34 types of fruits and vegetables representative of local products analyzed in the National Plan. Both CPF and CYP were detected in bovine fat. However, not all types of the locally produced fruits and vegetables were analyzed for the presence of these pesticide residues. In the same way, not all the active ingredients used for crop or cattle production in Mendoza were analyzed under the National Residue Plan. It can most likely be inferred that local consumers are exposed simultaneously to CPF and CYP by the intake of fruits, vegetables, and beef, and the combined toxic effects of this binary mixture have not been assessed so far in regulatory toxicology studies. Further toxicological research is needed to assess the risks for human health from dietary exposure to low concentrations of this mixture, and to implement modernized parameters and regulations for an optimized policy of control of pesticide residues in food grounded on real exposure and dietary scenarios.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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