Chapter 3

Crop Protection Compounds: A Source of Endocrine Disruptors in Uruguay?

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Additional information is available at the end of the chapter

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Abstract

The intensive use of agrochemicals in agriculture has been raised the concern about their potential effects on human health and the environment. In this way, regarding crop protection compounds a complex frameworks and restrictions had been established in several countries, particularly for compounds identified as endocrine disruptors. In Uruguay, the General Direction of Agricultural Services is the agency responsible for registry, but the authorization process does not consider the potential effects on endocrine system. Uruguay has significantly increased the use of crop protection compounds, of which several of them have been identified as endocrine disruptors and the environmental risks associated have not been studied. The aim of this study was to be bridging the gap between registry process and environmental protection policies. An eco-epidemiological analysis of the database of compounds imported in 2017, use guideline, national agricultural census as well as the public endocrine disruptor databases were carried out. Main class of crop protection compounds were ranked according to imported volumes and the top 10 of each class were contrasted with the disruptor databases. In function to recommended doses and geographical localization of the crops was identified the main hot spots associated to the use of agricultural compounds identified as endocrine disruptors.

Keywords: endocrine disruptors, crop protection compounds, summer rain-fed crops, environmental risk assessment

1. Introduction

In the agricultural production, a wide variety of crop protection compounds are used and several of them may interfere with endocrine system functioning [1–15]. According to Kavlock et al. [16], an “endocrine disrupting compound” (EDC) is “an exogenous agent that interferes with the synthesis, secretion, transport, binding, action, or elimination of natural hormones in the body, which are responsible for the maintenance of homeostasis, reproduction, development and or behavior."

Throughout the 1990s, the concern about the adverse effects on human and wildlife resulting from interaction between environmental chemicals and endocrine system has been increasing. However, given that hundreds of synthetic compounds have been released into the environment, the possible mechanisms for disruption and their physiological effects are enormous and not well understood. In this way, several regulatory agencies have developed different screening and testing strategies to assess the potential of crop protection compounds to interfere with the endocrine system.

In Uruguay, the registry and use of these chemical compounds are regulated by the General Direction of Agricultural Services (Res DGSA N° 01/2009 y Dec. 294/2004), but the authorization process does not consider the potential to induce adverse effects in humans and wildlife via interaction endocrine system. In this way, some laboratory and field studies have detected masculinization process [17], induction of the synthesis of plasmatic vitellogenin in immature organism and changes in somatic index in fish exposed to potential sources of endocrine disruptors [18, 19].

In order to bridge the gap between authorization process of crop protection compounds and environmental protection policies, the aims of this study were as follows:

1. to identify the crop protection compounds used in Uruguay that have a documented or presumed effect on endocrine functions,
2. to identify the main geographical areas potentially affected by endocrine disrupting compounds, and
3. to propose a research strategy to guide the effort and identify the potential scope of the problem.

We do this by an eco-epidemiological analysis of the Uruguayan database of crop protection compound imported in 2017 (DGSA database), the use guidelines (SATA Guide 2016) [20], the national agricultural census [21] as well as the public endocrine disruptor databases (PAN Pesticide Database (PANNA) and Pesticide Properties Database (PPDB)). The main class of crop protection compounds (herbicides, insecticides and fungicides) was ranked according to the imported volumes, and the top 10 of each class were contrasted with the endocrine disruptor databases and scientific articles. In function of the use guidelines (recommended doses) and the geographical localization of the main crops, the hot spot areas and the crop protection compound priorities were identified due its potential effects on endocrine system.

2. Survey of crop protection compounds currently used in Uruguay

The agriculture is one of the most important economic activities in Uruguay, and in the past decades, the summer rain-fed crops have experienced an important expansion and

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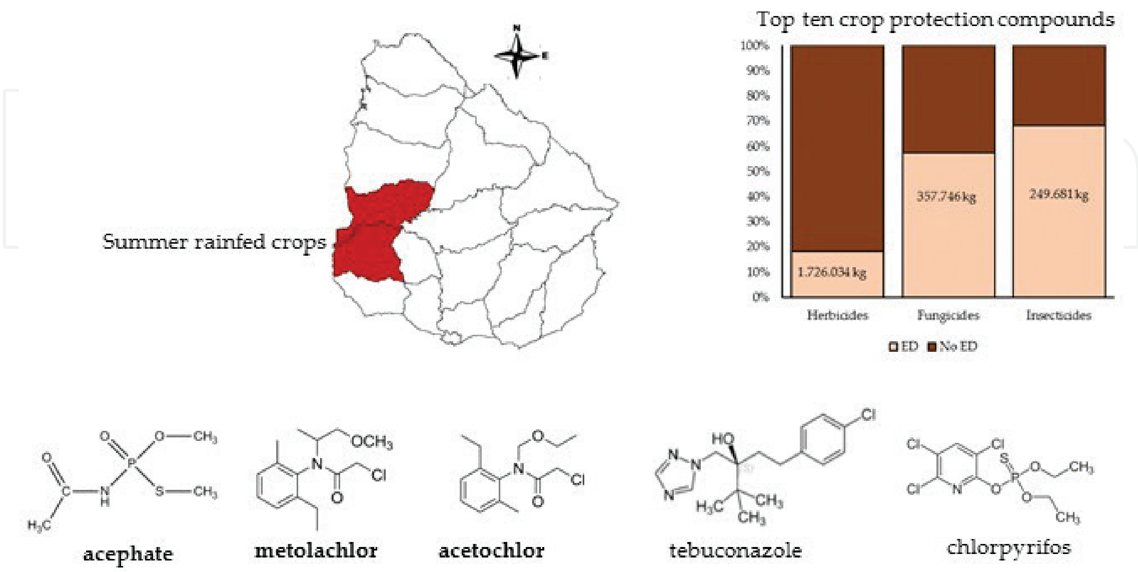
intensification process. In this way, the soybean crop occupied 1,140,000 ha and its exportable volumes exceed 3 million tons/year [21]. This process implied an increase in the use of crop protection compounds, mainly herbicides [22].



The survey of crop protection compounds currently used in Uruguay was conducted based on the active ingredients (AI) imported in 2017 and considered only herbicides, insecticides and fungicides. A total of 175 AI (11,358,732 kg), corresponding to 48% herbicides, 29% insecticides and 23% fungicides, were analyzed [22]. In **Table 1**, top 10 compounds for each class ranked in function to the imported volumes are shown.

Active ingredients	Category	Kg imported
Glyphosate, dimethylammonium salt	Herbicide	2,792,921
Glyphosate, ammonium salt	Herbicide	2,572,365
Glyphosate, isopropylamine salt	Herbicide	1,217,482
Glyphosate, potassium salt	Herbicide	980,073
2,4-D, dimethylamine salt	Herbicide	896,773
Acetochlor	Herbicide	407,484
S-Metolachlor	Herbicide	244,339
Paraquat	Herbicide	134,036
2,4 DB Butyl ester	Herbicide	98,910
Metolachlor	Herbicide	78,528
	Total	9,422,911
Mancozeb	Fungicide	164,400
Sodium metabisulfite	Fungicide	117,600
Chlorothalonil	Fungicide	71,544

Active ingredients	Category	Kg imported
Copper oxide	Fungicide	68,264
Captan	Fungicide	67,115
Folpet	Fungicide	43,008
Sulfur	Fungicide	36,032
Azoxystrobin + cyproconazole	Fungicide	20,275
Tebuconazole	Fungicide	18,812
Mancozeb + metalaxyl	Fungicide	15,600
	Total	622,650
Chlorpyrifos	Insecticide	181,795
Triflumuron	Insecticide	53,478
Lambda-cyhalothrin + Thiamethoxam	Insecticide	26,453
Paraffin oil	Insecticide	24,226
Aluminum phosphide	Insecticide	19,536
Acephate	Insecticide	17,423
Chlorpyrifos-methyl	Insecticide	15,360
Emamectin benzoate	Insecticide	9,873
Chlorantraniliprole	Insecticide	8,816
Bifenthrin + thiamethoxam	Insecticide	8,650
	Total	365,610

Elaborated with data from DGSA-MGAP 2017.

Table 1. List of active ingredients with the highest import volume for each main class.

Active ingredients	US EPA status	EC status	PANNA	PPBD
2,4 DB Butyl ester (H)	Not classified	Approved	Suspected	Suspected
2,4-D, dimethylamine salt (H)	Not classified	Approved	Suspected	n/d
Acephate (I)	Not classified	Not approved	Suspected	Yes
Acetochlor (H)	Restricted use	Not approved	Suspected	Suspected
Aluminum phosphide (I)	Restricted use	Approved	No	n/e
Azoxystrobin + cyproconazole (F)	Not classified	Approved/approved	No/no	No/suspected
Bifenthrin + thiamethoxam (I)	Not classified	Approved/approved	Suspected/no	Yes/no
Captan (F)	Not classified	Approved	Suspected	Suspected
Chlorantraniliprole (I)	Not classified	Approved	No	No
Chlorothalonil (F)	Restricted use	Approved	Suspected	Suspected

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Active ingredients	US EPA status	EC status	PANNA	PPBD
Chlorpyrifos ethyl (I)	Restricted use	Approved	Suspected	Suspected
Chlorpyrifos-methyl (I)	Restricted use	Approved	No	Suspected
Copper oxide (F)	Not classified	Approved	No	No
Emamectin benzoate (I)	Restricted use	Approved	No	n/d
Folpet (F)	Not classified	Approved	No	n/e
Glyphosate, ammonium salt (H)	Not classified	Approved	No	n/d
Glyphosate, dimethylammonium salt (H)	Not classified	Approved	No	n/d
Glyphosate, isopropylamine salt (H)	Not classified	Approved	No	No
Glyphosate, potassium salt (H)	Not classified	Approved	No	No
Lambda-cyhalothrin + thiamethoxam (I)	Restricted use	Approved/approved	Suspected/no	No/no
Mancozeb (F)	Not classified	Approved	Suspected	Suspected
Mancozeb + metalaxyl (F)	Not classified	Approved/approved	Suspected/no	Suspected/no
Metolachlor (H)	Restricted use	Not approved	Suspected	Suspected
Paraffin oil (I)	Not classified	Approved	No	No
Paraquat (H)	Restricted use	Not approved	No	No
S-Metolachlor (H)	Restricted use	Approved	Suspected	Suspected
Sodium metabisulfite (F)	Not classified	Not approved	No	n/d
Sulfur (F)	Not classified	Approved	No	n/e
Tebuconazole (F)	Not classified	Approved	Suspected	n/e
Triflumuron (I)	Not classified	Approved	No	No

Suspicion of endocrine disruption effects according to the PAN Pesticide Database (PANNA) and the Pesticide Properties Database (PPDB) is noted. If the active ingredient is not found in any database, it is reported as n/d.

n/e: reported without evidence.

The substances are listed in alphabetical order. F-fungicide, H-herbicide, I-insecticide.

Table 2. List of active ingredients according to the categorization of the US EPA and the European Commission (EC).

The status regulatory according to international agencies as well as the potential to interfere with the endocrine system functioning were analyzed and the results are presented in **Table 2**.

From the regulatory point of view, a total of 18 compounds present a status "Approved," 7 "Approved with restricted use" and 5 "Not approved." The last status regulatory includes three herbicides, one fungicide and one insecticide. Whereas in relation to potentially endocrine disrupting compounds, six fungicides, five herbicides and five insecticides were identified. The analysis of effects on endocrine system was complemented with information from several scientific articles [9, 10, 23–26] and according to the crop protection compound priorities are: acetochlor, chlorpyrifos methyl, mancozeb, metolachlor and tebuconazole (**Table 3**).

Active ingredients	References	Effect
2,4 DB butyl ester (H)	PPDB	
2,4-D, dimethylamine salt (H)	PANNA; Cocco [23]; McKinlay et al. [25]; Mnif et al. [9]	2,5
Acephate (I)	PANNA; PPDB; McKinlay et al. [25]; Mnif et al. [9]	1,2,5
Acetochlor (H)	PANNA; PPDB; Cocco [23]; McKinlay et al [25]; Mnif et al. [9]	1,2
Azoxystrobin + **cyproconazole** (F)	PPDB; McKinlay et al. [25]; Mnif et al. [9]	1,3,5
Bifenthrin + thiamethoxam (I)	PANNA; PPDB; McKinlay et al. [25]	1,2
Captan (F)	PPDB; McKinlay et al. [25]; Mnif et al. [9]	1
Chlorothalonil (F)	PPDB; McKinlay et al. [25]; Mnif et al. [9]	5
Chlorpyrifos ethyl (I)	PANNA; PPDB	3,5
Chlorpyrifos-methyl (I)	PPDB; Morales y Rodríguez [24]; McKinlay et al. [25]; Mnif et al. [9]; Marx-Stoelting et al. [10]; Ewence et al. [11]	5
Lambda-cyhalothrin + thiamethoxam (I)	PANNA; Morales y Rodríguez [24]; Ewence et al. [11]	1
Mancozeb (F)	PANNA; PPDB; Cocco [23]; Morales y Rodríguez [24]; McKinlay et al. [25]; Mnif et al. [9]; Marx-Stoelting et al. [10]; Ewence et al. [11]	2
Mancozeb + metalaxyl (F)	PANNA; PPDB; Cocco [23]; Morales y Rodríguez [24]; McKinlay et al. [25]; Mnif et al. [9]; Marx-Stoelting et al. [10]; Ewence et al. [11]	2
Metolachlor (H)	PANNA; PPDB; Cocco [23]; Mnif et al. [9]	5
S-Metolachlor (H)	PANNA; PPDB; Cocco [23]; Mnif et al. [9]; Ewence et al. [11]	5
Tebuconazole (F)	PANNA; McKinlay et al. [25]; Mnif et al. [9]; Marx-Stoelting et al. [10]; Ewence et al. [11]; Ventura et al. [29]; Yang et al. [30]	1,3,5

Target effect metabolism is included as follows: 1-estrogen, 2-thyroid hormones, 3-aromatase, 4-pregnane receptor, 5-androgen. The substances are listed in alphabetical order.

Table 3. List of active ingredients suspected of generating endocrine disruption effects in at least one of the consulted databases (F-fungicide, H-herbicide, I-insecticide).

3. Geographical areas potentially affected by endocrine disrupting compounds

Several of the crop protection compounds identified as endocrine disruptors are applied in different crops, widely distributed within the territory. Therefore, were analyzed the spatial impacts combining the area occupied by each crops and the recommended doses (**Tables 4** and **5**). The crops considered were: grasslands (2,500,000 ha), soybean (1,140,000 ha), wheat (215,000 ha), barley (190,000 ha), rice (164,400 ha), corn (83,000 ha), sorghum (67,000 ha), fruit and citrus trees (17,000 ha), vegetables (14,190 ha) and sugarcane (7,600 ha) [21] **Figure 1**.

According to estimated loads, the crop protection compounds priority: 2,4 butyl ester, chlorpyrifos, 2,4-D, dimethylamine salt, acetochlor, tebuconazole, chlorpyrifos methyl, metolachlor and S- metolachlor. Considering only the agricultural lands (without grasslands), 60% of them are occupied for soybean and are mainly concentrated at the west littoral zone (Rio Negro, Soriano and Flores Department), represented in **Figure 1**, like the land use rain-fed crops.

Active ingredients	Crops	Recommended dose	Units
2,4 Butyl ester (50%) (H)	1, 3–4	2–2.5	L/ha
2,4-D, dimethylamine salt (50%) (H)	1, 3–7, 11	0.6–3	L/ha
Acephate (75%) (I)	2	0.5–1	kg/ha
Acetochlor (H)	2, 6, 11	0.8–3.8	L/ha
Azoxystrobin + cyproconazole (200/80) (F)	2–5	0.2–0.4	L/ha
Bifenthrin + thiamethoxam (6%/13%) (I)	2	0.20	L/ha
Captan (80%) (F)	9–10	0.8–1.5	kg/ha
Chlorothalonil (72%) (F)	8–10	1.5–5	L/ha
Chlorpyrifos (50%) (I)	1–4, 6–7, 9	0.3–2.5	L/ha
Chlorpyrifos-methyl (I)	1, 3–4	0.35–1	L/ha
Lambda-cyhalothrin + thiamethoxam (I)	2–7	0.05–0.25	L/ha
Mancozeb (80%) (F)	8–10	1–5	L/ha
Mancozeb + metalaxyl (F)	9	2–3	kg/ha
Metolachlor (H)	2, 6–7	0.8–1.6	L/ha
S-Metolachlor (90%) (H)	2, 6–7	0.8–1.6	L/ha
Tebuconazole (25%) (F)	2–5	0.5–2	L/ha

The substances are listed in alphabetical order. F-fungicide, H-herbicide, I-insecticide.
Source: SATA Guide.
1-pastures, 2-soybean, 3-wheat, 4-barley, 5-rice, 6-corn, 7-sorghum, 8-citrus, 9-vegetable, 10-fruit, 11-sugarcane.

Table 4. Crops and recommended doses of the compounds cataloged as suspect of generating endocrine disruption effects.

Active ingredients	Recommended average dose	Units	Total cultivated area (ha)	Estimated AI added (L or kg)
2,4 Butyl ester (50%) (H)	2,3	L/ha	2,905,000	**6,536,250**
2,4-D, dimethylamine salt (50%) (H)	1,8	L/ha	3,227,000	**5,808,600**
Acephate (75%) (I)	0,8	kg/ha	1,140,000	855,000
Acetochlor (H)	2,3	L/ha	1,230,600	**2,830,380**
Azoxystrobin + cyproconazole (200/80) (F)	0.3	L/ha	1,709,400	555,555
Bifenthrin + thiamethoxam (6%/13%) (I)	0,2	L/ha	1,140,000	228,000
Captan (80%) (F)	1,2	kg/ha	26,387	30,345
Chlorothalonil (72%) (F)	3,3	L/ha	27,000	87,750
Chlorpyrifos (50%) (I)	1,4	L/ha	4,209,187	**5,892,862**
Chlorpyrifos-methyl (I)	0,7	L/ha	2,905,000	**1,960,875**
Lambda-cyhalothrin + thiamethoxam (I)	0,2	L/ha	1,859,400	278,910

Active ingredients	Recommended average dose	Units	Total cultivated area (ha)	Estimated AI added (L or kg)
Mancozeb (80%) (F)	3,0	L/ha	27,000	81,000
Mancozeb + metalaxyl (F)	2,5	kg/ha	14,187	35,468
Metolachlor (H)	1,2	L/ha	1,290,000	**1,548,000**
S-Metolachlor (90%) (H)	1,2	L/ha	1,290,000	**1,548,000**
Tebuconazole (25%) (F)	1,3	L/ha	1,709,400	**2,136,750**

For the estimation, the average dose reported was used. The total sown area corresponds to the sum of the crops in which the compound is used. The substances are listed in alphabetical order. F-fungicide, H-herbicide, I-insecticide.

Table 5. Estimation of formulated applied according to hectares sown in the agricultural year 2016/2017.

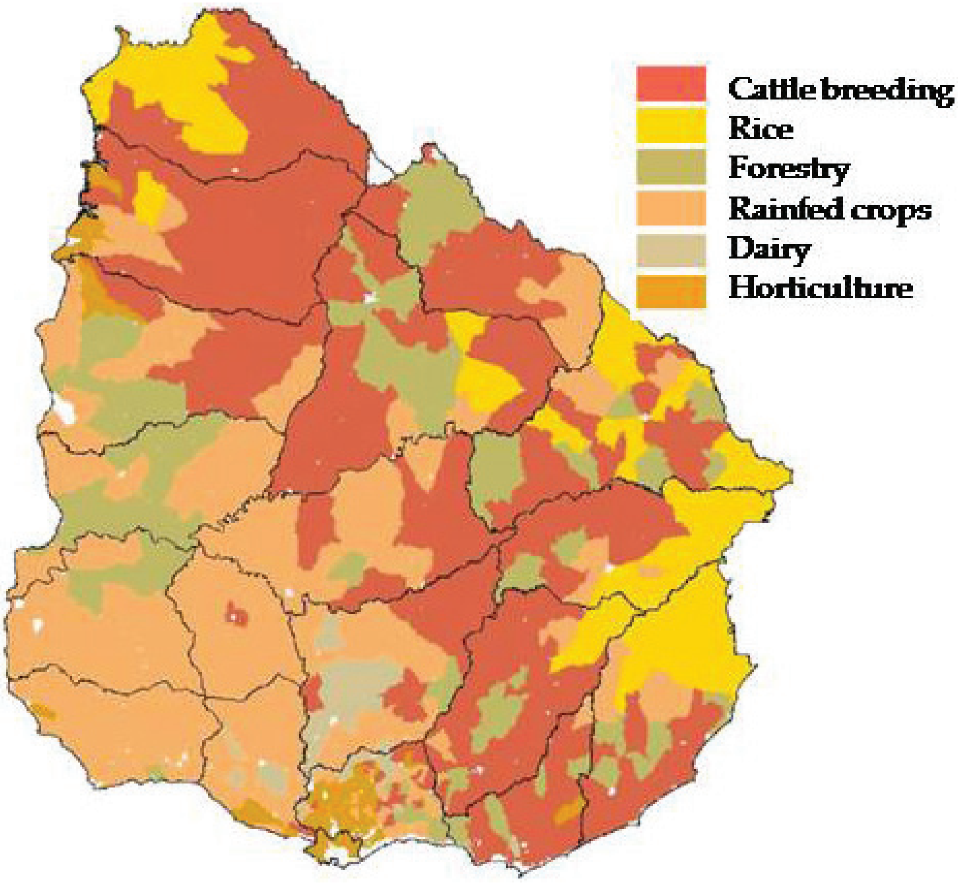

Figure 1. Uruguay regionalization according to the land use.

4. Scope and perspectives

The agricultural intensification and expansion are global processes associated with growing worldwide demands (food, feed, fiber and fuel), and these are highly dependent on external additions of nutrients and crop protection compounds [27, 28]. In Uruguay, these processes began from 2000, mainly in the west littoral zone with the inclusion of soybean in agricultural sequences under no-tillage. Currently, more than 2 million hectares are destined to agriculture and approximately 50% correspond to soybean crops. In addition, the imported volumes of agrochemicals significatively increase, particularly herbicides (10,200,404 kg AI in 2017).

Considering the herbicides, insecticides and fungicides being more used, the doses/application numbers recommended and the agricultural area (crops and grasslands), we have estimated that in 2017, 15 million L of herbicides, 8 million L of insecticides and 750,000 L of fungicides were added. Several of them, as stated by the European and US regulatory agencies, have a status "Approved with restricted use" (7) or "Not approved" (5). In addition, PAN Pesticide Database (PANNA) and Pesticide Properties Database (PPDB) classified as "Suspected" interferes with the endocrine system functioning and four of these are: acephate, acetochlor, chlorpyrifos ethyl and metolachlor. On the other hand, although the aforementioned regulatory agencies confers tebuconazole the "Approved" status, it is one of the fungicides more used (2.136.750 L in 2017) and was reported as endocrine disruptor in PANNA and PPDB database, and by several authors [9–11, 25, 29, 30]. These last five compounds are used in the soybean cropping, and the bigger surfaces occupied by this crop are located around the two most important river basins in the country (Uruguay and Negro river).

On the other hand, it is important to highlight that the available information at National level on residues of crop protection compounds is basically for export products and some foods for internal market. While as data about environmental concentration (soil, water or biota) are scarce, environmental surveillance programs are not carried out.

According to our review about the crop protection compounds used in the agricultural systems in Uruguay, this activity is a potential source of endocrine disruptors. One of the first actions tending to reduce the environmental risk associated with the use of these compounds is to replace acephate, acetochlor, and metolachlor by other active ingredients. In the same way and in function of the scientific evidences, it is necessary to establish monitoring programs for determining environmental levels of chlorpyrifos and tebuconazole, as well as to assess the potential human health and wildlife risks. Finally, we consider that the west littoral is the zone with the highest risk associated with exposure to endocrine disrupting compounds (hot spot area), principally the Rio Negro and Soriano Department.

Conflict of interest

None.

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