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Lethality of Imidacloprid and Fipronil on *Apis mellifera*: A Retrospective Analysis on the French Case

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Abstract: The aim of this study was to draw a retrospective analysis on the lethality of Imidacloprid (Gaucho®) and Fipronil (Régent TS®) on *Apis mellifera* between 1992 and 2016 in France. Early monitoring reports in the 1992-2002 period notified these two embedded insecticides to be at the origin of massive colony collapse disorders. Ecotoxicological analyses based on the LD_{50} of Imidacloprid and Fipronil highlighted their differential lethality by both contact (Imidacloprid: 81 ng/honeybee vs. Fipronil: 5.9 ng/honeybee) and ingestion (Imidacloprid: 3.7 ng/honeybee vs. Fipronil: 4.2 ng/honeybee), but failed to point Imidacloprid's high solubility as a higher lethal agent. Chemical properties and action mode of these two insecticides originated neural disfunction in the case of Imidacloprid, and honeybee brood immune depression for Fipronil. Despite the conduction of these monitoring reports and laboratory researches, Fipronil was completely banned in 2005 but Imidacloprid only in 2016.

Key words: *Apis mellifera*, Imidacloprid, Fipronil, monitoring, colony collapse disorder, LD_{50}.

1. Introduction

This study draws a retrospective analysis on the lethality of Imidacloprid (IMI) (under commercial denomination Gaucho®) and Fipronil (FIP) (under the commercial denomination Régent TS®) on *Apis mellifera* between 1992 and 2016 in France [1]. This study fact per periods the succession of responses between stakeholders. It provides an analysis on why even with scientific conclusive proof of lethality, the outcome was a time-shifted ban of these pesticides well after damage had been evidenced.

After the successive reforms of the European Union (EU) Common Agricultural Policy (CAP), and a massive decrease of its budget, agricultural practices have been intensified and massively oriented towards monocultures. These practices have brought a scarcity of available melliferous resources and ultimately a loss of entomological biodiversity. In this context, and in an effort to improve productivity and efficiency of monocultures, agrochemical multinationals found an opportunity to sell their pesticides [2, 3].

2. Early Crisis: Colony Collapse Disorder Reports in the 1992-2002 Period

2.1 Gaucho on Market: First Devastating Effects

Early monitoring reports reveal after July 1992 [4], the first marketing campaign of Gaucho, an insecticide massively employed in sunflower cultures. This commercial product composed of IMI targeted insects-suckers, beet predators, sunflower and maize crops. In the first time, it was treated on seeds, in an effort to protect the seed envelope, later on the seedling in order to penetrate the whole plant through the sap. It will be later extended to rice, fall cereals and maize.

Immediately after its use in July 1992 [4], bee mortality in hives boosted from 40% in 1994 to 50% in some cases in 1997. Beekeepers declare themselves to be psychologically devastated as they walk along a "carpet of dead bees". Beekeepers witnessed that honeybees "stay on the flower, as if stuck unable to extricate themselves and shake by ending in convulsions before dying". Such witnesses reinforced evidence of colony disorders.

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2.2 Régent's First Shakes

First use of Régent came back to 1993 for the sunflower cultures and different mixed exploitations. This pesticide based on FIP was applied on seed coating and for soil treatment. FIP is a neurotoxic molecule applied in insecticides not only particularly in France but also in Europe. This product was brought to market and largely commercialised by BASF despite its neurotoxic effects and harm to environment.

The first local consequences felt by the exposition to Régent date back to April 2002, period during which use of FIP results in the direct colony collapse of local beehives. Furthermore, direct exposition to this substance leads to the intoxication of beekeepers with oedemas, cutaneous irritations and swelling when harvesting their honey [4, 5].

3. Proving and Rooting the Impacts: A Race against Time and Noise (2003-2007)

3.1 National Institute of Agronomic Research (INRA), National Counsel of Scientific Research (CNRS) and French Food Security and Safety Agency (AFSSA) Assessments on IMI and FIP

In 2003, INRA, CNRS and AFSSA [4, 5] demonstrated the high toxicity, persistence and long permanence of Gaucho® [6], where both its active components and metabolites act on plants, non-target insects and environment. The released reports denounced Bayer's negligence and contested its ethics. Bayer had estimated the lethal doses to 5,000 ppb whereas in reality they were at 0.1 ppb. In fact, with a budget of €150 million, Bayer created a more effective generation of pesticides and marketed it strongly, without sufficient accuracy on the analyses and ecotoxicological data reported.

In 2005, new INRA and CNRS studies confirmed extreme toxicity of FIP on pollinators and environment, as well as its induced risks on human health [7].

3.2 Comparative Analysis of IMI and FIP Lethality

In order to measure the toxicity of a substance and its lethality, LD_{50} measures were conducted. Louvet in 2004 [8] submitted an ecotoxicological report to compare the toxicity between IMI and FIP on honeybee *A. mellifera*. IMI lethality was quantified at 3.7 ng/honeybee through ingestion, against 81 ng/honeybee through contact. FIP lethality was quantified at 4.2 ng/honeybee through ingestion, against 5.9 ng/honeybee per contact.

3.3 IMI and FIP Action Mode

Nicolino and Veillerette [9] also described IMI and FIP action mode. They qualified the disease process of honeybees exposed to IMI witnessed by beekeepers due to a neurotoxic trigger. IMI's action mode brings an over-excitation of the acetylcholine nicotinic receptors (nAChRs) inside insect's nervous system. Seeds treated with IMI diffuse the substance into the vascular system of the plant so that parasites such as aphids sucking the stems die by paralysis. Unfortunately, given the fact that the entire vascular system of plants is affected by the spread of IMI to the anthers, pollinators are exposed to the harmful effects of the molecule.

Regarding FIP, it is important to highlight that when exposed to the sun (surface of the soil or plants), it undergoes a photo-degradation in desulfinyl-FIP which is clearly more toxic than FIP itself. In soil and water, FIP is first degraded into other molecules, many of which are as active as FIP. Since it is very difficult to define the moment when a substance has completely disappeared from an environment, it is conventional to consider its half-life time, that is to say the duration after which half of the quantity initially produced has disappeared. Some results reported short half-lives (less than one month). Ecotoxicological studies were concerned only with the substance and not with its degradation product. But in reality, as a neurotoxic substance, this molecule acts specifically by completely altering the behaviour of bees resulting

in a decrease in their foraging activity following exposure by contact or ingestion. In particular, it can lead to intoxication of the hive during the brood of the fact that the nectar and pollen are in the hive. If the new bee comes to birth, it does so with great immune weaknesses and immunosuppression syndromes.

4. Final Outcome: Time-Shifted Resolutions (2005-2016)

4.1 The Initial Ban of FIP: April 2005

FIP is officially banned in France after three successive decrees:

- April 6th, 2005 decree prohibiting the marketing of seeds treated with phytopharmaceutical products containing FIP;
- April 15th, 2005 decree prohibiting the placing on the market of phytopharmaceutical products containing FIP and intended for soil treatment in the context of the fight against wireworms and weevils;
- April 19th, 2005 decree prohibiting the use of phytopharmaceutical products containing FIP as soil treatment in the fight against wireworms and weevils, and seeds treated with these products.

It is worth to mention that after this initial ban, further laws, regulations and directives were applied with exceptions, or restrictions to a specific context [10, 11].

4.2 Final Ban of IMI: France's 2016 Law on Biodiversity

According to the press journal *Le Monde*, the new France law on biodiversity [10, 12], known as "LOI n° 2016-1087 du 8 août 2016 pour la reconquête de la biodiversité, de la nature et des paysages" (Eng. "Law n° 2016-1087 of August 8th, 2016 for the Conquest of Landscapes, Biodiversity, Nature and Landscapes"), passed on August 9th, 2016, has served to draw a list of insecticides that were to be prohibited as of September 1st, 2018. These insecticides are Clothianidine, IMI, Thiomethoxam, Thiacloprid and Acetamiprid.

5. Attention Points

According to the US National Pesticide Information Center, IMI and FIP have the following chemical properties. IMI is an insecticide that belongs to the family of the nicotinyls, being the first of the known list of neonicotinoids. It is a synthetic derivative of nicotine, possesses a molar mass of 255.66 g/mol, a density of 1.54 g/cm^3 and a water solubility of 610 mg/L at 20 °C.

On the other side, FIP is a broad-spectrum insecticide that belongs to the phenylpyrazole chemical family. It possesses a molar mass of 437.14 g/mol and a density between 1.477 g/cm^3 and 1.626 g/cm^3. It has a 20 °C solubility in water of 1.9 mg/L at pH 5 versus 2.4 mg/L at pH 9.

Solubility states that an agent with a higher solubility is more prone to saturate the solvent than a low solubility agent. Since the water cycle defines how water reaches plants and pollinators through the continuous movement of water; all chemical which is highly soluble in water will be more easily transported with water than a lower one. All facts considered, since IMI solubility in water is much higher than FIP, IMI possesses a higher fitness both through and in water. Therefore, IMI is a higher exposing factor to pollinators including honeybees.

6. Conclusions and Lessons Learnt

From the retrospective study of the lethality of IMI and FIP on *A. mellifera*, the following conclusions are stated:

In the first place, and despite thorough monitoring reports revealed by beekeepers and scientists on the one hand, and ecotoxicological assessments conducted by independent research centres on the other hand, this first group of stakeholders were trapped in a noise loop and time pressure in the effort to carry on scientific, objective and standardised methods and ultimately bring to the public conclusive and significant results, with limited resources. In this context, IMI's higher solubility in water, and therefore

its spread in the water cycle failed to be highlighted. This failure, combined with the lack of early on the field ecotoxicological assessments, plus focussing uniquely on the lethality of FIP instead of its degradation by-products, blocked the scientific community from acquiring more data.

In the second place, multinational agrochemical companies took advantage of a legal vacuum to fulfil their business objectives by large-scale marketing of Gaucho® and Régent TS® embedded pesticides. Colony collapse disorders and related disruptions caused by IMI and FIP to plants and non-target insects such as honeybees were a contingency non or poorly evaluated based on the current legislation in the moment of commercialisation. Low entry barriers were exploited as a business opportunity with incomplete focus on the consequences to the ecosystems.

The third group of stakeholder's worth to be mentioned are the decision poles and legal architects. This group designed, implemented, shifted and enforced the successive legal frameworks that went from absence of regulation to a shifted in time restrictions and bans according to the context and pressure to which they were exposed.

Finally, and as part of the responsibility the scientific community faced related to this topic, the following recommendations can be provided. The defence of universal interests towards sustainable, renewable and foundational sources of life requires accurate and effective strategy focus. In the aim to avoid tit for tat, risks of backfire and other crisis situations between and among all involved stakeholders, full resources and capabilities are of the essence. When confronted to disruptive events, such resources and capabilities need to be made fully available and communicated assertively. Only then can an accurate root of choices and clear resolution path be executed in order to secure the preservation of human common heritage and legacy.

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