



## PESTICIDES: CLASSIFICATIONS, EXPOSURE AND RISKS TO HUMAN HEALTH

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**Abstract:** Pesticides are used in the control and prevention of pests, improving the productivity and the quality of agricultural production. The adoption of the Brazilian agricultural model, which uses pesticides on a large scale and indiscriminately, has been worrying public authorities about their impacts on human health and environmental sustainability. Thus, studies that contribute to a better understanding of agrochemicals and their effects on ecosystems and human health are timely. The aim was to investigate the

history of the production and use of pesticides, their classifications, sources of exposure and their risks to human health. The research was carried out through literature review in databases to verify scientific information about the history of pesticides, structural and toxicological classifications, sources of exposure and their risks to human health. The use of pesticides dates back many years. During the nineteenth century until the mid-twentieth century, some chemicals nowadays used as pesticides were used for public health or for war purposes. About the classification of pesticides, due to the different biological targets, the agrochemicals market is segmented into different action targets (herbicides, fungicides and insecticides). Pesticides can be classified as contact, ingestion or systemic according to the mode of action. As for the chemical structure, the main classes of pesticides are organochlorines, organophosphates, pyrethroids and carbamates. The toxicity of pesticides ranges from low toxic to extremely toxic. Exposure to pesticides can occur directly through occupational exposure, or indirectly, through environmental exposure and food. The impacts on human health are divided into acute and chronic form. The prolonged human exposure to pesticides may result in neurological, reproductive, teratogenic and immunological disorders. The results presented in this literature review contribute to a better understanding of agrochemicals and their effects on human health.

**Keywords:** Agrochemicals. Class. Contamination. Health disorders.

## 1 INTRODUCTION

Pesticides are used in the control and prevention of pests during cultivation and after harvesting, improving the productivity and the quality of agricultural production.<sup>1,2</sup>

In Brazil, the pesticides are extensively used, making the country the largest consumer of these substances in the world, accounting for 19% of world use.<sup>3,4</sup>

In the 2015 harvest, 899 million liters of agrochemicals were sprayed in the national crops, representing an average of 12.6 liters per hectare and average environmental, occupational and food exposure of 4.4 liters of pesticides per inhabitant per year.<sup>5</sup>

These substances used have several denominations, among them are pesticides, biocides, poisons and agrochemicals.<sup>6</sup> Several are the active principles used as pesticides. These present different spectra of action, chemical structure and toxicological classifications, which will interfere in its mode of action and in the risks that exposure to these substances can cause.<sup>7</sup>

Every year in Brazil, according to the Brazilian health organization, 400,000 new cases of poisoning by pesticides are registered with a rate of 1% of deaths.<sup>4</sup> However, it is believed that there is underreporting of the intoxications occurrence, considering that Brazil does not have an adequate system of records, these being the companies acting in the cases and also not differentiated as acute and chronic intoxications.<sup>4</sup> In addition, the prolonged human exposure to agrochemicals can trigger neurological, reproductive, teratogenic and immunological disturbances.<sup>8-10</sup>

The adoption of the Brazilian agricultural model, which uses pesticides on a large scale and indiscriminately, has been worrying public authorities about their impacts on human health and environmental sustainability.<sup>3,11</sup> Thus, studies that contribute to a better understanding of agrochemicals and their effects on ecosystems and human health are timely.

Thus, the objective of this work was to investigate the history of the production and use of pesticides, their classifications, sources of exposure and their risks to human health.

## 2 MATERIAL AND METHODS

The research was carried out through review in specialized literature, conducted between May and June 2018, in which a search was conducted with online books and periodicals, by scientific articles selected in the databases of SciELO (Scientific Electronic Library Online) and CAPES (Coordination for the Improvement of Higher Education Personnel). The keywords used in the search were “pesticides history”, “structural classification”, “toxicological classification”, “sources of exposure” and “risks to human health”.

## 3 RESULTS

### 3.1 PESTICIDES HISTORY

The use of chemicals in pest control and elimination dates back to Roman, Greek and Chinese times over 3000 years ago. There have been reports that these civilizations used sodium chloride to kill weeds and sulfur dust to control insects.<sup>6</sup>

In the nineteenth century, with the discovery of the copper acetoarsenite, popularly known as the “Paris Green”, to combat the potato beetle, the first major landmark in the history of synthetic pesticides.<sup>6</sup>

During the nineteenth century until the mid-twentieth century, the chemicals developed were used for public health or for war purposes. Examples include dichlorodiphenyltrichloroethane (DDT), discovered in 1874, widely used by soldiers during Second World War, which pulverized the compound by the body to prevent and control diseases such as malaria and typhus. The properties as pesticide of this compound were only discovered sixty-five years later.<sup>6</sup>

In 1943, organophosphates, also known as “nerve gas”, were used to combat enemy troops during Second World War.<sup>12</sup> After the period of the world wars, strategies of growth of the companies of the chemical branch were created in search of new markets in which they could use the molecules developed until the moment. From this, the agrochemical industries, which already existed since the First World War, began to expand.<sup>6</sup>

In Brazil, the use of pesticides was disseminated during the years 1945 to 1985, known as the period of modernization of national agriculture. It was also during this period that the installation of agrochemical industry in the country was carried out by the main manufacturers of these products worldwide.<sup>6</sup>

In the mid-1950s, with the growth of the world population and, consequently, the increase in demand for food, the development of increasingly efficient agricultural systems was boosted.<sup>13</sup> Since then, the use of agrochemicals has been the main strategy to control and prevent pests during cultivation and after harvesting, improving productivity and quality of agricultural production.<sup>1,2</sup>

## 3.2 PESTICIDES CLASSIFICATIONS

Agrochemicals can be classified according to action targets, mode of action, chemical structure and toxicity.<sup>14</sup> This classification makes it possible to know information about the chemical behavior of the substance used as a pesticide, such as persistence in the environment and its action on the target organism and on humans that may become contaminated.<sup>7</sup>

### 3.2.1 Action targets

Due to the different biological targets, the agrochemicals market is segmented into different action targets, the main ones being: herbicides (control of weeds), fungicides (control of fungal diseases) and insecticides (control of insects). Of these, herbicides and fungicides have the highest volume of exports and imports in the world, with 45% and 14%, respectively.<sup>11</sup>

### 3.2.2 Action mode

Pesticides can be classified as contact, ingestion or systemic according to the mode of action. Contact pesticides act on the surface of the food, directly affecting the target organism, while those of ingestion act after the biocide is ingested by the biological target. However, systemic pesticides penetrate the sap of the plant and travel through all vascular tissues, exerting a phytotoxic action in the case of herbicides or acting against insects when they feed on the sap.<sup>6</sup>

Systemic pesticides and part of the contact pesticides are absorbed by the plant's internal tissues and, if the appropriate dosage and shelf life are not respected or have not been degraded by the plant metabolism itself, they may remain in the food even if they are sanitized.<sup>14</sup>

### 3.2.3 Chemical structure

As for the chemical structure, the main classes of pesticides are organochlorines, organophosphates, pyrethroids and carbamates.<sup>6</sup> In Figure 1, some characteristics about chemical behavior, persistence in the environment and action on organisms, and examples of chemical structures of each class are presented.

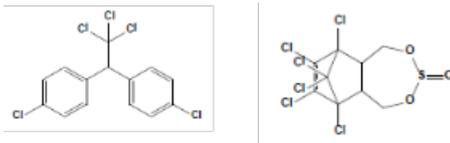
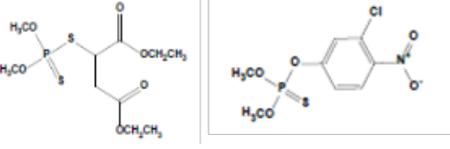
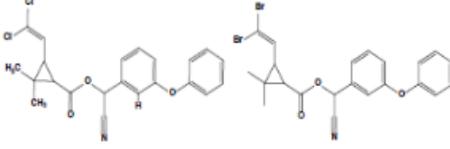
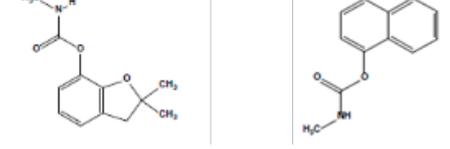
| Class            | Characteristics  | Examples  |
|------------------|--|---|
| Organochlorines  | They have the element chlorine in their molecules. They exhibit high physico-chemical stability, with high persistence in the environment and low rates of degradation and biotransformation. They are liposoluble with a tendency to bioaccumulate along the food chain, but with a low acute toxicity. <sup>15</sup> |  <p>DDT (Dichlorodiphenyltrichloroethane)</p> <p>Endosulfan</p> |
| Organophosphates | They are organic derivatives of phosphoric, dithiophosphoric and thiophosphoric acids. They exhibit low volatility and low persistence in the environment, decomposing within a few days. They are liposoluble, possessing higher acute toxicity for the mammals than the organochlorines. <sup>16</sup>               |  <p>Malathion</p> <p>Clorthon</p>                             |
| Pyrethroids      | They are synthetic derivatives of pyrethrins, toxic esters isolated from flowers of the species of <i>Chrysanthemum cinerariaefolium</i> . They are less persistent in the environment and less toxic to mammals than organophosphates and carbamates. <sup>17</sup>   |  <p>Cypermethrin</p> <p>Deltamethrin</p>                      |
| Carbamates       | They are carbamic acid derivatives. They exhibit high efficiency and wide spectrum of use. They have low persistence in the environment, presenting rapid decomposition in aquatic environments. They show low long-term toxicity. <sup>16,18</sup>  |  <p>Carbofuran</p> <p>Carbaryl</p>                            |

Figure 1 – Classification of chemical structure, behavior characteristics, persistence in the environment and action on organisms, and examples of chemical structures of each class of pesticide.

### 3.2.4 Toxicity

A significant criterion for the classification of pesticides is their degree of toxicity. This classification is essential for the knowledge of the acute effects that pesticides can cause.<sup>19</sup>

The classification proposed by the World Health Organization<sup>19</sup> considers three factors: the average lethal dose (LD50) of the formulated pesticide, the contact form of the pesticide (oral or dermal) and the type of formulation (solid or liquid). Referring to LD50, this consists of the amount of the toxic substance producing a 50% mortality of the test animals, under controlled conditions for a time of 24 hours, expressed in milligrams of pesticide per kilogram of animal weight (mg/Kg).<sup>20</sup>

In Brazil, the toxicological classification is in charge of the Ministry of Health, which determines that all products must present on the labels a colored band indicative of its toxicological class.<sup>16</sup> In Table 1, it is possible to visualize the toxicological classes, the staining of the strip and the LD50 according to the type of formulation and the form of contact.

| Pesticide class                          | LD50 to rats (mg.kg-1 of body weight) |            |            |            |
|--|---------------------------------------|------------|------------|------------|
|  | Way                                   |            |            |            |
|  | Oral                                  | Dermal     |            |            |
|  | Solid                                 | Liquid     | Solid      | Liquid     |
| Class I - Extremely toxic (red band)     | < 5                                   | < 20       | < 10       | < 40       |
| Class II - Highly toxic (yellow band)    | 5 a 50                                | 20 a 200   | 10 a 100   | 40 a 400   |
| Class III - Moderately toxic (blue band) | 50 a 500                              | 200 a 2000 | 100 a 1000 | 400 a 4000 |
| Class IV - Low toxic (green band)        | > 500                                 | > 2000     | > 1000     | > 4000     |

Table 1 - Toxicological classification of pesticides

Source: Larini (1999).<sup>7</sup>

Another existing classification, provided by the International Agency for Research on Cancer (IARC), is the carcinogenic potential of chemicals, agents and exposures to humans. This classification is based on evidence from epidemiological and laboratory studies on the carcinogenicity of substances<sup>21</sup> (Figure 2).

| Group    | Characteristics                            |
|----------|--|
| Group 1  | Carcinogenic to humans                     |
| Group 2A | Probably carcinogenic to humans            |
| Group 2B | Possibly carcinogenic to humans            |
| Group 3  | Not classifiable as carcinogenic in humans |
| Group 4  | Probably not carcinogenic to humans        |

Figure 2 – Classification according to the carcinogenic potential of chemical substances, agents and exposures. Source: International Agency for Research on Cancer.<sup>21</sup>

It is necessary to observe that even the active ingredients being classified as medium or low toxic, prolonged exposure for months, years and even decades can trigger chronic effects such as the development of cancer, congenital malformations, endocrine and neurological disorders.<sup>4</sup>

### 3.3 BRAZIL AND THE PESTICIDES

Brazil is characterized as a country with a large rural area and a favorable climate for agricultural production. Due to this and the agricultural model, agrochemicals are extensively used in Brazilian crops.<sup>3</sup>

The Brazilian market for agrochemicals showed a significant growth of 10% per year between 1977 and 2006, so that Brazil was, from the mid-1970s to 2007, among the six largest consumers of agrochemicals in the world.<sup>11</sup>

Since 2008, Brazil has assumed the position of the largest consumer of pesticides in the world, a position formerly occupied by the United States, representing 19% of world use and moving more than US \$ 7 billion in agrochemicals.<sup>3,4,11</sup>

However, this data contradicts the relationship between productivity and consumption, considering that the main agricultural producer in the world is the United States, with 27%, while Brazil ranks second, with 19% of the share of world food production.<sup>22</sup>

In Brazil, agricultural crops that most use agrochemicals are soy, corn and sugarcane, accounting for 82% of total agrochemical use in 2015.<sup>5</sup> The Brazilian regions with the greatest intensity of these crops coincide with the highest concentrations of

pesticide use: Mato Grosso (18.9%), São Paulo (14.5%), Paraná (14.3%), Rio Grande do Sul (10.8%), Goiás (8.8%), Minas Gerais (9.0%), Bahia (6.5%), Mato Grosso do Sul (4.7%) and Santa Catarina (2.1%).<sup>23</sup>

Another characteristic point about the use of agrochemicals in Brazil is that several pesticides scientifically recognized as harmful to public health and the environment, banned in different countries, are still in circulation in Brazil. According to ANVISA, 22 of the 50 most widely used and allowed active ingredients in the country's crops are banned in the European Union, making Brazil the largest consumer of agrochemicals banned in other countries.<sup>11</sup>

The adoption of the Brazilian agricultural model, which uses pesticides on a large scale and indiscriminately, has been worrying public authorities about their impacts on human health and environmental sustainability.<sup>3,11</sup>

### 3.4 HUMAN EXPOSURE TO PESTICIDES

Exposure to pesticides can occur directly through occupational exposure, or indirectly, through environmental exposure and food.<sup>24</sup>

Agricultural work is one of the most dangerous occupations today, being the workers or residents of areas close to plantations exposed directly and indirectly to pesticides.<sup>4</sup>

The population in general, which does not work directly with agrochemicals or does not live in rural areas, is not exempt from the impacts of these compounds, having contact with pesticides through the environment and food.<sup>4</sup>

The main routes of human exposure to pesticides occur by residues in food, air, water, soil, flora and fauna.<sup>24</sup> This is because once in the environment, pesticides can be distributed, degraded or accumulated in the environment compartments and in living beings.<sup>25</sup>

In Brazil, from 2002 to 2011, there was an increase in the average consumption of agrochemicals in relation to the planted area, from 10.5 liters per hectare (L/ha) in 2002 to 12 L/ha in 2011 increasing the risk of contamination of soil, water and food by pesticides, as well as exposure of humans to these compounds.

Food analyzes have been demonstrating quantities of excessive agrochemical residues in plant foods, especially in fruits and vegetables. Data indicate that one-third of the food consumed daily by Brazilians presents contamination by pesticides above that allowed by legislation.<sup>26</sup> In a study by Granella *et al.*,<sup>27</sup> it was observed contamination above legal values and by pesticides banned in Brazil in samples of conventional and organic milk. In addition, analyzes performed on breast milk showed the presence of organochlorine pesticide residues, indicating that exposure to pesticides begins early in childhood.<sup>28</sup>

### 3.5 PESTICIDES AND RISKS TO HUMAN HEALTH

The use of agrochemicals in Brazil has had serious consequences for the health of the population. These consequences are most often conditioned by occupational activity, by the toxicity of the active ingredients used as pesticides, by inadequate use or lack of personal protective equipment (PPE).<sup>10</sup>

The impacts on human health are divided into two forms: the acute form, which occurs through direct intoxication by the pesticide, be it at the time of application of this or the intake of a highly contaminated food, and the chronic form, due to long exposure.<sup>29</sup>

The World Health Organization (WHO) estimates that about 3% of workers exposed to pesticides end up suffering some form of intoxication, making a total of approximately three million human poisonings per pesticide worldwide over a year.<sup>30</sup>

Studies have shown that the epidemiological profile of pesticide intoxications in Brazil occurs in the majority of cases in males, at a productive age, with a higher percentage of accidental intoxication, followed by intentional circumstances.<sup>31,32</sup>

In addition to acute effects, such as intoxication, prolonged human exposure to pesticides may result in neurological, reproductive, teratogenic and immunological disorders.<sup>8-10</sup>

In a study by Fassa *et al.*<sup>33</sup> showed that pesticides used in tobacco cultivation are significantly associated with neurobehavioral disturbances in tobacco growers. Some substances have properties that can affect the central nervous system, causing psychiatric disorders and leading to suicide.<sup>34</sup> In addition, epidemiological studies have found a positive

relationship between occupational exposure to pesticides and the risk of developing Parkinson's disease.<sup>35,36</sup>

In studies conducted by Raafat, Abass and Salem<sup>37</sup> and Malekirad *et al.*,<sup>38</sup> it has been shown that organophosphate pesticides may cause insulin resistance in farmers, who are more susceptible to developing diabetes mellitus.

Cancer is among one of the major diseases caused by chronic exposure to pesticides. Evidence suggests that exposure to low concentrations of pesticides may already increase the risk of developing prostate, pancreatic, liver, breast and rectal cancer, as well as leukemias and lymphomas.<sup>39-41</sup>

Studies have suggested that pesticides act by influencing the activity of the immune system, inducing the production of proinflammatory cytokines such as interleukin-6 (IL-6), interleukin-1 $\beta$  (IL-1 $\beta$ ) and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), promoting the progression of the tumor through the activation of the inflammatory process.<sup>42,43</sup>

## 4 CONCLUSION

The use of pesticides, whether in wars, to combat diseases related to public health or agriculture, dates back many years. Pesticides have several classifications of action spectrum, mode of action, chemical structure and toxicological classification, which provide information on the degradation, accumulation and risk of each substance. Although agrochemicals have the role of eliminating harmful biological forms in agriculture, they can cause adverse health effects when used improperly, in accordance with the recommendations. Human exposure to pesticides can occur through direct or indirect contact, mainly by the presence of pesticide residues in food. The impacts on human health are divided into two forms: the acute form, which occurs through direct intoxication by the pesticide, and the chronic form, due to long exposure, which may result in neurological, reproductive, teratogenic and immunological disorders.

The results presented in this literature review contribute to a better understanding of agrochemicals and their effects on human health.

## CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

## FUNDS

This reserach was supported by Brazilian financial support from “Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES)”, and “Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq)”.

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Recebido em: 06 de julho de 2018

Avaliado em: 28 de novembro de 2018 (AVALIADOR A)

Avaliado em: 15 de fevereiro de 2019 (AVALIADOR B)

Aceito em: 15 de fevereiro de 2019

