The Effect of Herbicide Metribuzin on Environment and Human: A Systematic Review

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Abstract

Metribuzin is a synthetic organic compound used as a selective Triazinone herbicide, incorporated as a post-emergent soil applied herbicide to control weeds in wheat, potato, tomato and others. The aim of this study was to assess the impact of Metribuzin on the environment and human health. Human exposure to Metribuzin occurs through inhalation and ingestion, usually in agricultural settings. Farmers' occupational exposure to Metribuzin is highly variable and complex depending on the farm but Few studies have assessed the exposure of the population to this herbicide. Metribuzin can accumulate in soil and water and cause damage to flora and fauna. furthermore, Herbicides Metribuzin have a very variable toxicity, in the short term it can cause acute intoxication which can cause breathing and difficult drowsiness but the high exposures can cause stomach aches, fatigue and depression of the central nervous system, on the other hand in the long term and with strong exposure or other repeated it can cause modifications of the hepatic enzymes, disturbance in the kidneys, can affect the reproduction, the endocrine function and oxidant/antioxidant system imbalance. This study highlights on the undesirable effect of Metribuzin which allows to affirm their toxicity even at low doses, is not only following an occupational exposure, but also for the general population by their use of treated agricultural products by these pesticides, which poses a real public health problem. Accordingly, it is imperative that farmers avoid their use and replace them with biological fertilizers that are less harmful to human and animal health

1 Introduction

Pesticides are complex chemicals used in agriculture, destroying or combating pests, including vectors of human or animal diseases¹ and unwanted species of plants or d animals which cause damage or are otherwise harmful during the production, processing, storage, transport or marketing of food, agricultural products, wood and wood products, or animal feed, or which may be given to animals to fight insects, arachnids and other parasites in or on their bodies². Metribuzin is incorporated as a post-emergent soil applied herbicide to control weeds in wheat, potato, tomato and others. Although the herbicide may have a beneficial impact on the agricultural productivity, nonetheless³, Pesticides

are substances that have a biological activity that acts on various physiological functions and most often results in the death of the living organism that was able to absorb it ⁴. Pesticides can be very harmful, and they are suspected of posing a risk to human health and the environment by accumulating in ecosystems⁵. The existence of organic and inorganic pollutants in the aquatic system can be detrimental to a variety of living species⁶. Exposure to pesticides is one of the risk factors that promote increased oxidative stress by producing oxygenated free radicals.

This risk of oxidative stress is widely accepted as being a critical component of most pathological pathways⁷. Reactive oxygen species (ROS) are free radicals resulting from the metabolism of oxygen⁸. They are constantly generated inside cells following exposure to xenobiotics in our ambient environment⁹. The current review focuses on the explain the harmful effects of pesticides used on the environment and human health and its relationship to oxidative stress. TO this, we will study the Metribuzin chosen as the pesticide model.

2 Chemical properties of metribuzin

Metribuzin is a member of the group like substituted triazinone herbicides¹⁰. Their activity is due to an interference with the transport of photosystem II electrons in the chloroplasts of plants. The metabolism of metribuzin in plants has been the subject of numerous short-term and long-term studies from the early 1970s¹¹. Metribuzin (4-amino-6 (1,1-dimethylethyl) -3- (methylthio) -1,2,4-triazine-5 (4H) one) (Fig 1), is a white crystalline solid with a pressure of vapor of 1.2.10-7 mm Hg at 20 ° C, a solubility in water of 1100 mg / l (ppm) at 20 ° C, which makes the soil mobile, a half-life of 30 to 60 day, and an oral LD50 (rat) of 1090 mg / kg¹².

Fig 1: Metribuzin structure¹⁵

3 The effects of Metribuzin on the environment

Pesticides have largely contributed to the increase in agricultural productivity and the quality of crop production¹⁶, but once introduced into the environment, they can accumulate in soil and water and cause damage to flora and fauna, when concentrations in food chains become high enough to harm wild flora and fauna (Table 1)¹⁷.

Table 1: Harmful effects of pesticides on the environment¹⁷

Agricultural practices	Pesticides
Soils	pesticides Accumulation and degradation products
Groundwater	Leaching of mobile pesticide residues and degradation products
Surface water	
Flora and fauna	- Effect on soil microflora; resistance of certain weeds -Poisoning resistance
Others: air, noise, landscape	Evaporation, bad, aerial spreading, residues

Bačmaga et al. (2018) also noted that recommended or medium dose positively affected the barley yield. Reason behind this may be that higher dose of herbicide may have exerted a negative influence on soil nutrients by disturbing the soil physicochemical and biological properties¹⁸. Metribuzin is highly toxic to freshwater macrophytes and algae¹⁹. Concentrations of Metribuzin lower than those affecting invertebrates and fish, for which it is moderately toxic, cause the inhibition of aquatic plant growth. Metribuzin is more toxic to aquatic plants than other pesticides such as atrazine, alachlor, or metolachlor²⁰.

In addition, pesticide residues affect the quality of drinking water, contaminate food intended for human consumption, have negative effects on the health of agricultural workers who are directly exposed to it, while certain pesticides contain bromide compounds. which, once volatilized, transform into the stratosphere into gases responsible for the depletion of the ozone layer²¹.

4 Mode of Metribuzin exposure to animal and human

4.1 Professional exposure

Farmers' occupational exposure to Metribuzin is highly variable and complex depending on the farm. The reconstruction of the exhibition is also complicated by the evolution of agricultural practices over time²². Occupational exposure is also a potential source of indirect exposure for infants if one of the parents works in an area that uses pesticides. Exposure to these can be through skin absorption, inhalation and ingestion. More than 50 pesticides have been declared carcinogenic in animals²³. In general, exposure is mainly cutaneous, to a lesser extent aerial and secondarily oral (meals, tobacco, etc. in the workplace)²⁴.

4.2 Non-professional exposure

Few studies have assessed the exposure of the lay population to Metribuzin. For the general public, various factors contribute to

general exposure to pesticides: proximity to a treatment area, poorly controlled domestic use (insecticide treatments in homes for example)²⁵, poor gardening practices (exposure during treatment and via self-consumption) and the ingestion of pesticides via food²⁶. Food consumption of pesticides is via water, animal products (milk, meat, fish, etc.) or plants and can be acute or chronic. Accurate knowledge of the overall "Metribuzin" risk for the general public requires independent information on the different exposure solutions. Exposures are multiple because each factor acts on the intensity of the risk and the factors can combine with each other²⁷. WHO indicate that pesticide contamination of food is by far the most important route of exposure, with some exceptions. Risk assessments assign 90% of exposure to food versus 10% to water²⁵.

5 Metribuzin toxicity

Metribuzin can affect you when you breathe in and through your skin. Acute intoxication can cause difficulty breathing and drowsiness²⁸. High exposures can cause stomach upset, fatigue, and depression of the central nervous system, causing poor coordination, tremors, and weakness. Human Tox = 200.00000 ppb (very low)²⁹. High or other repeated exposure can cause changes in liver enzymes, goiter, and can affect thyroid function and central nervous system³⁰.

6 Effects of Metribuzin on human health

6.1 Effects of Metribuzin on fertility and reproduction

Pesticides and their byproducts have also been identified as agents likely to impair the male fertility process, via testicular toxicity³¹. The link between pesticides and infertility in women is poorly understood and deserves to be better studied³². Studies in rats have clearly shown the harmful effects of methyl parathion on the reproductive system³³. It has been noted that in women exposed to pesticides, the risk of intrauterine mortality increases and that fetal growth decreases. Note also that pesticides have been found in the umbilical cord but also in breast milk, which could explain the poor development of the fetus, birth defects and abnormalities of the central nervous system³⁴. The main reproductive disorders concern the fetus, which is exposed by its mother. The consequences are spontaneous abortions, stillbirths and birth defects. It is often cited as a decline in fertility which may be due to an endocrine disruption³⁵.

6.2 Carcinogenic effect of Metribuzin

The harmfulness of Metribuzin on human health has been demonstrated for a long time, as early as 1962, Rachel Carson showed the deleterious effects of these on the environment and man, in particular with the development of cancers³⁶. A study by derouiche *et al.* (2018)³⁷ shows a disruption of glomerular function induced by sub chronic exposure of metribuzin with a dose of 6.44mg/kg in rabbit, which may be the cause of kidney cancer appears in many people exposed to metribuzin. The

number of these molecules (metribuzin) released into the environment has become considerable. The carcinogenic effect of several pesticides is certain, probable or possible according to the CIRC³⁸. This link between exposure to pesticides and cancer is today demonstrated by the work of certain epidemiologists. In addition, farmers who use pesticides for their crops more frequently develop certain types of cancer and in particular leukemias, lymphomas and multiple myelomas³⁹. The lymphocyte count is an important auxiliary diagnostic test as changes occur with systemic inflammation and other disease⁴⁰.

6.3 Effects of Metribuzin on the endocrine system

The toxic effects induced by chronic exposure to environmental pollutants involve physiological disturbances that will affect the essential functions of the organism, including endocrine and immune functions⁴¹. The disturbances induced by the presence of pollutants in the surrounding environment will affect the role that the endocrine system plays in the maintenance of homeostasis and physiological integrity⁴². These effects will affect growth, metabolism and reproduction, thus endangering the survival of the population. Among environmental pollutants, endocrine modulators such as pesticides and metals are now widely studied⁴³. Capable of mimicking or altering hormone synthesis and metabolism, these toxins affect the body's normal response to stress by affecting the role that the endocrine system plays in coordinating physiological processes and in maintaining hemostasis. After entering the body, these pollutants can interfere with hormonal processes by acting on several levels of anatomical and functional organization, such as the hypothalamus-pituitary-interrenal axis⁴⁴.

6.4 Effects of Metribuzin on antioxidant defense

Metribuzin as a xenobiotic⁴⁵, explain that the stimulation of free radical production induced lipid peroxidation and disturbance of total antioxidant capability of human and animals body are mechanisms of toxicity in most xenobiotics which are chemical compounds foreign to the body such as herbicides and environmental pollutants⁴⁶. The exposition of a xenobiotic toxic, the antioxidant enzymes decreased when the ROS increased which modulates the generation of oxidative stress⁴⁷. Also the study of Iwona and Narcyz (2012) demonstrated a greater risk of oxidative stress and kidney damages during exposure to xenobiotics in drinking water⁴⁸. Currently the water borne xenobiotics can be uptake via deferent tissues and capable to contribute to oxidative stress when overexpression of ROS and inhibition of antioxidant enzymes activity and associated with cell dysfunction⁴⁹. The defense mechanisms of antioxidant (GSH, CAT, GST and SOD) can be subverted by xenobiotics that induce the production of excessive of untimely free radicals and result in damage to macromolecules including DNA⁵⁰. The conjugation of metribuzin metabolites with GSH followed by the conversion of mercapturic acid derivatives appears to play a major role in detoxification and excretion⁵¹. So xenobiotics can induced

oxidative stress results in decreasing the antioxidant capacity GST and SOD and increasing in lipid peroxidation and catalase activity by alteration the expression of antioxidant enzymes which leading to disruption of the cell function⁵².

7 Conclusion

These results leave a great idea on the undesirable effect of Metribuzin which allows to affirm their toxicity even at low doses, is not only following an occupational exposure, but also for the general population by their use of treated agricultural products by these pesticides, which poses a real public health problem.

8 Recommendations and Future Perspective

Accordingly, through this study, we recommend avoiding the use of agricultural products treated with chemical fertilizers, and also that farmers avoid using them. Hence, as future studies, we must develop a system to detect the presence of fertilizer residues in agricultural products and also deepen research in order to reach more ecological and healthy methods such as developing biological fertilizers so that they increase the agricultural yield and have no negative effects on the farmer and the consumer.

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10 Conflict of interest

The authors declare no conflicts of interest

11 Author's contributions

SD carried out literature review, design and drafting the manuscript. OSRM and AS participated in collection of data . All authors read and approved the final manuscript.

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