AN OVERVIEW ON TOXICOLOGICAL EFFECTS OF PYRETHROID INSECTICIDE DELTAMETHRIN

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Abstract. The aim of this study was to identify the impact of pyrethroid-type insecticides upon organisms but also the negative influence upon the quality of people lives. Pyrethroids are synthetic chemical mixtures similar to pyrethrins - a compound from a Chrysanthemum flowers extract. The degree of aggressiveness of pyrethroid insecticides depends on a number of factors such as dose, route of administration and exposure time. So, the nervous system is the most vulnerable to the toxicity of these compounds, especially to type II pyrethroids. Disturbances due to exposure to compounds of the pyrethroid range lead to disruption of essential functions of the nervous system mainly affecting locomotor coordination and activity of antioxidant enzymes. Deltamethrin (DLM) is a synthetic type II pyrethroid. In insects DLM poisoning may cause paralysis or death. Also, fish and rats have experienced malfunctions of the reproductive system. In humans, exposure to deltamethrin, depending on the amount taken, may lead to headache, nausea, dizziness, tremors, convulsions, fatigue and paralysis.

Keywords: insecticide, pyrethroid, deltamethrin, oxidative stress


Cuvinte cheie: insecticid, piretroid, deltametrin, stres oxidativ

Introduction

In recent years, various methods and chemicals have been developed to protect plants against pests. Today, there is a wide range of chemicals that negatively act on insects and not only. Among the most well-known are: organochlorine, organophosphate, pyrethroid and neonicotinoid insecticides. The pyrethroids insecticides are synthetic substances similar to the natural active component, pyrethrins, spread in the species of some chrysanthemum
flowers. Significant amounts of active substance are extracted from *Chrysanthemum cinerariaefolium*, but small quantities of pyrethrin are also found in other chrysanthemum flowers as well, such as: *Chrysanthemum coccineum* and *Chrysanthemum marshalli* (Polosky, 2015). *Chrysanthemum cinerariaefolium* is a member of Asteraceae family, known for their fruits named achenes which contains the seeds rich in the active principle - pyretrins (Bajaj, 1994). According to the Agency for Toxic Substances and Disease Registry (2003) pyrethrins are a complex consisting of 6 components which are formed following the esterification of the chrysanthemic acid (pyretrin I, cinerin I, jasmolin I) and pyrethric acid (pyrethrin II, cinerin II, jasmolin II). Taking into account that pyrethrin is rapidly degraded by light and plant material is an exhaustible source, specialists have experimentally developed other similar chemicals called pyrethroids (Matsuo & Mori, 2012). Pyrethroids were produced at Rothamsted Research in America in the 1960s and 1970s by Michael Elliot and colleagues (BBSRC, 2014). The new synthetic esters are formed from natural pyrethrin in combination with other chemical substances named synergistics. This new formula is much more aggressive than pyrethrin. Pyrethroids have many advantages and disadvantages compared to pyrethrin as illustrated in Figure 1.

![Figure 1. Advantages and disadvantages of pyrethroids (modified after Rehman et al., 2014).](image)

Despite the obvious advantages, the disadvantages weigh a lot more in this balance and that because the indirect actions of pyrethroids affect organisms much more. The principal target of insecticides is the nervous system according to a series of toxicological studies conducted on animal models (Rehman et al., 2014). Pyrethroid insecticides have neurotoxic effects by disrupting the normal functioning of the sodium channels. Due to this fact the molecules of insecticide interfere with the transmission of nervous impulse, leading to repetitive nervous influxes or depolarization (Soderlund, 2012). The consequences are not delayed. Depending on dose or time of exposure, effects are even more pronounced. Tremors,
convulsions, nausea, locomotor deficits, paralysis or death are some symptoms of the pyrethroid insecticide poisoning (ATSDR, 2003, Soderlund, 2012, Rehman et al., 2014).

**Structures and properties of pyrethroids**

Pyrethrine is the active substance which is found in the extract of several species of *Chrysanthemum* and it has a powerful insecticide action. From all the natural extracts with insecticide effect, plant extracts of *Chrysanthemum* genus are most wanted. Today Australia is the second largest pyrethrin production centre after Kenya (Gilbert, 2010). Despite the massive production of natural pyrethrine extracts there are also similar synthetic compounds on the market called pyrethroids (Table 1). Pyrethroids have two forms associated with the presence/absence of an α-cyano group similar to pyrethrine.

**Table 1.** Examples of pyrethrine and pyrethroids insecticides (modified after Klaassen, 2008).

<table>
<thead>
<tr>
<th>COMPOUND</th>
<th>SOURCE</th>
<th>EXAMPLES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyrethrine</td>
<td>Natural pyrethrum extract</td>
<td>Pyrethrin I, Pyrethrin II, Cinerin I, Cinerin II, Jasmolin I, Jasmolin II</td>
</tr>
<tr>
<td>Pyrethroids type I</td>
<td>Derivatives of pyrethrins that do not include a cyano group</td>
<td>Alletrin, Bifenthrin, Permethrin, Phenothrin, Resmethrin, Tefluthrin, Tetramethrin</td>
</tr>
<tr>
<td>Pyrethroids type II</td>
<td>Derivatives of pyrethrins that include a cyano group</td>
<td>Cyfluthrin, Cyhalothrin, Cypermethrin, Deltamethrin, Fenvalerate, Fenpropathrin, Flucythrinate, Flumethrin, Fluvalinate, Tralomethrin</td>
</tr>
</tbody>
</table>

Compared to pyrethrines, pyrethroids are more toxic and due to their lipophilicity are easier absorbed from the water column (Viran et al., 2003). Excess of type I pyrethroid leads to a poisoning named T syndrome, which is characterized by hyperexcitation, convulsions and tremors, while type II produce CS syndrome consisting of salivation, hypersensitivity, choreoathetosis and seizures (Soderlund et al., 2002; Kim et al., 2008; Cao et al., 2010).

Both forms have insecticide function by attacking the nervous system of insects. The mechanism is not totally elucidated. It is known that the main target is the malfunction of the sodium channels in the nervous system, which causes hyperstimulation of nerve membrane (Miller & Salgado, 1985; Cox, 1998; Soderlund, 2012). Certain studies revealed that pyrethroids also act on the calcium channels (Clark & Symington, 2007; Neal et al., 2010).

**Deltamethrin**

One of the most popular type II pyrethroid insecticides is DLM. DLM was synthetized for the first time in 1974 and it is widely spread all over the world. Due to its effectiveness as insecticide is commonly used in agriculture to protect plant crops (Kumar et al., 2015). For example, in India DLM is used against pests of tea plantations and grain (Parvez & Raisuddin, 2006; Gurusubramanian et al., 2008) or to control mosquitoes responsible for the spread of malaria (Yadav et al., 2001). In China it is used as pesticide in the agricultural fields for pest control (Huang et al., 2014).

Despite its high effectiveness DLM is a potential source to induce negative consequences because humans and animals are exposed to it. Several studies demonstrated
the implications of DLM in the immune system perturbation. Occurrence of autoimmune diseases, immunosuppression and hypersensitivity reactions are some of immunotoxicity signs (Kumar et al., 2015). Toxic effects on spleen and thymus were observed by Kumar and his contributors (2017) in mice, when animals were exposed to 5 mg/Kg DLM for 7 days. Also, the team of Kumar has demonstrated the benefic action of piperine and curcumin against DLM poisoning. Some of its properties are summarized in Table 2.

Table 2. Properties of DLM (after NPIC, 2011).

<table>
<thead>
<tr>
<th>PROPERTY</th>
<th>DLM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (g/mol)</td>
<td>505.2</td>
</tr>
<tr>
<td>Color</td>
<td>Colorless</td>
</tr>
<tr>
<td>Physical state</td>
<td>Crystals</td>
</tr>
<tr>
<td>Melting point (°C)</td>
<td>101-102</td>
</tr>
<tr>
<td>Solubility in water (mg/L)</td>
<td>&lt;0.002</td>
</tr>
<tr>
<td>Solubility in organic solvent</td>
<td>Soluble</td>
</tr>
</tbody>
</table>

How toxic is DELTAMETHRIN?

Most of experimental studies conducted in vivo or in vitro had the same results. DLM is toxic for insects and aquatic organisms and less toxic for birds, mammals or humans. Cases of pollution due to a large amount of DLM were reported. An ecocatastrophe occurred in Hungary in the Lake Balaton (1995): 30 tons of eel (Anguilla anguilla) died due to DLM toxicity (Nemcsók et al., 1999). In order to identify the main effects of poisoning with DLM scientists have put the bases of animal models development. They intended to discover lethal and sub-lethal concentrations when the organisms show obvious effects. So, the organisms predominantly used in research are: insects, fish, mice and rats.

The farmworkers use insecticides in large amounts to protect plant crops and stored products, but they do not take into account the effects of the active substance. The study of Paudyal and contributors (2016) demonstrated the benefic effect of DLM upon three insect species: Tribolium castaneum (Herbst), Sitophilus oryzae (L.) and Rhyzopertha dominica (F.). These insects are known to be harmful. The concentrations of DLM were: 1, 25, 50, 100, 250, 500, 1,000 and 3,000 mg/L. 25 mg/L was the lethal concentration when the insects were knocked down after 4 hours of exposure. The producers of insecticides were interested to develop new formulas of DLM solutions. A surprising idea was to combine diatomaceous earth with DLM which has similar effects. This mixture was a perfect solution to combat Sitophilus zeamais in stored corn (Ceruti & Lazzari, 2005). The same mixture was used to fight against Rhyzopertha dominica and Tribolium castaneum (Korunic & Rozman, 2010).

After insects, fishes are the second group affected by the DLM exposure because they have a high compound absorption from the water which passes through gills (Srivastav et al., 1997; Sayeed et al., 2003).

Several studies demonstrated the impact of the insecticide upon the swimming behavior (Oliveira et al., 2012). In addition, the presence of oxidative stress is a marker of DLM influence. Oxidative stress is defined as imbalance between oxidants (ROS) and antioxidants. A large level of ROS leads to reduction of antioxidant enzymes activities (Sukla et al., 2011; Sies et al., 2017). The most used indicators to determine the presence of oxidative
stress are: catalase, superoxide dismutase, glutathione peroxidase and malondialdehyde (Gul et al., 2004). Evaluation of enzyme activities in fish is an important parameter to determine the presence of the compound in the aquatic environment.

Also, the biochemical activity is observed (Gul et al., 2004; Suvetha et al., 2015). For example, in snakehead (Channa punctatus) the activity of catalase is reduced and lipid peroxidation increases as a result of ROS action (Sayeed et al., 2003). The acute exposure of the zebrafish (Danio rerio) to different concentrations (0, 0.15, 1.5, 3.75, 7.5 and 15 μg/L) of DLM leads to locomotor deficits in 24 h. Rapid gill and opercular movement, swimming at the surface of water or swimming in a corkscrew manner were the main symptoms recorded (Huang et al., 2014). Same observations were made for tilapia species (Oreochromis niloticus) by Yildirim et al., (2006) and for guppies by Viran et al., (2003). The chronic exposure of zebrafish females (Danio rerio) for 5 days at two concentrations of DLM (0.5 and 1 μg/L) has determined degeneration of follicles, oogenesis delay and decreased number of primary oocyte (Yön et al., 2009). Eggs’ hatching is affected too (Görge et al., 1990; Sharma & Ansari, 2010). The effects of DLM can be observed due disrupting the intern metabolism. Low levels of plasma glucose and cholinesterase and high levels of hemoglobin content, proteins, ammonia and calcium were recorded in the case of rainbow trout (Oncorhynchus mykiss) at acute exposure (Vellšek et al., 2007).

Another study investigated the effect of DLM upon the Indian major carp (Labeo rohita) at acute exposure (0.438 mg/L). Fish manifested hyperactivity, loss of movement coordination, increased gill mucus secretion, increased cortisol and prolactin levels (Suvetha et al., 2015).

Effects of DLM on nervous, respiratory, immune and hematological systems are reported in rats. Exposure of rats to different concentrations of insecticide and their effects are found in several papers. Locomotor activity and social interactions are reduced following the administration of 10 mg/kg DLM in rats (Ricci et al., 2013; Habr et al., 2014). At low doses (0.08 mg/kg), the effect of DLM is reflected by the reduction of locomotor activity and increase of the rest period (Lazarini et al., 2001). Influence of the insecticide also can be observed in biochemical metabolism. The activity of enzymes superoxide dismutase and glutathione-S transferase was significantly low. Malondialdehyde which is a parameter of

Figure 2. The action of DLM in the nervous system of insects.
lipid peroxidation showed high levels in different tissues (Mokhtar et al., 2006). After injection, DLM was rapidly distributed in the organism reaching approximately in all the tissues. Despite the fact that is very quickly absorbed, its excretion is low. Thus, small doses of DLM were recorded in brain and high doses in muscle, skin and fat (Kim et al., 2008). The cytotoxic effects can be diminished by adding vitamin E in the rats’ diet. According to a study, the administration of DLM combined with vitamin E led to the reduction of oxidative stress (Galal et al., 2014).

Regarding human exposure there are several ways to be exposed to DLM poisoning. Substances can reach the skin surface, can get into the eyes, can be ingested or inhaled. The most common route is the dermal exposure. The effects can be observed by appearance of paraesthesia, erythema and desire to scratch the skin. The literature also reported several cases of suicide through ingestion of different solutions which contained DLM. After ingestion, most of the people have manifested dizziness, itching, nausea, fatigue, sweating, convulsions, tremors, facial paraesthesia and even coma (He et al., 1989; ATSDR, 2003, Watts, 2012).

Conclusions
The pyrethroid insecticides are an effective source of pest control, especially insects. High demands and the widespread use of these compounds in agriculture raised many questions among researchers. A part of their interest is focused on the effects produced by DLM upon organisms. Most of the experimental studies were run with model animals. Unfortunately, though little is known about poisoning symptoms, a cure for treating it was not found yet. An eventual perspective would be to find an appropriate treatment to fight against the toxicity of pyrethroid compounds without affecting other organisms.

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