

Effect of Dimethoate on Object Recognition Memory in Wistar Rats and Essay of Treatment with Nettle

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Abstract

Pesticides were economically important chemicals in agriculture. Their use has permitted agricultural progress, through the eradication of harmful insect and the fight against vectors of disease. However, several studies question the beneficial effects of organophosphorus compounds, showing that their deregulated use causes various problems of environmental pollution and human health. The present study shows that chronic exposure to a subtoxic dose of dimethoate is likely to affect cognitive and behavioral functions of rats (both males and females). Our results show that exposure to dimethoate affects both short and long-term memory capacities. The short-term memory results are more pronounced. Treatment with nettle extract allowed a significant improvement in cognitive and behavioral performance of the rats after their exposure to dimethoate.

Keywords

Dimethoate, Dioic Nettle, Acetylcholinesterase, Chelation, Memory

1. Introduction

It was in the 1940s that the first synthetic pesticides appeared on the market with very positive results in increasing agricultural yields. Twenty years later, the first accusations of harm to people's health and the environment were heard [1].

The debate about the risks and benefits of chemical control has since been ex-

tended and a great deal of research has been carried out to better understand the impact of pesticides on the environment.

The mechanism of acute neurotoxic action of Dimethoate is typically cholinergic. It involves inhibition of Acetylcholinesterase (AChE) of neuronal tissue through its active metabolic form; Omethoate which is 10 times more toxic than dimethoate (WHO, 2003).

Omethoate rapidly binds to the hydroxyl group of the active site of AChE, and undergoes a double displacement reaction involving the hydroxyl-serum and dimethylphosphoryl groups of AChE. Thus, phosphorylated AChE is stable and irreversible.

Inhibition of AChE causes an accumulation of acetylcholine released in the synaptic cleft upon nerve stimulation, leading to hyperstimulation of the nicotinic and muscarinic receptors. Consequently, the passage of nerve information is disrupted [2]. In addition, oxidative stress caused by lipid peroxidation and promoted by dimethoate is considered to be a second mechanism of toxicity of this organophosphorus [3] [4].

In this study, we will highlight the effect of sub-chronic intoxication by dimethoate on short-term and long-term memory. The poisoning took place on male and female Wistar rats. These intoxicated rats will undergo a trial of treatment by phytochelation. Extract of a medicinal plant, nettle, was obtained by decoction.

Chelation therapy has started as a branch of medicine to remove heavy metals and other toxins from the body by introducing powerful chemical agents that associate with toxins and are then excreted in the urine.

From the point of view of a medical use, several clinical trials carried out in this context confirmed these pharmacological properties in humans.

Urtica dioica L., is a ubiquitous plant of the Urticaceae family, renowned for its unpleasant irritating effects, the nettle is actually rich in vitamins, minerals and numerous medicinal virtues [5]. Over the last few decades, several studies have focused on the pharmacological implications and on the analysis of the chemical composition of the plant. Although all its potentialities have yet to be realized, numerous studies have strengthened its claims in traditional medicine. [6].

Indeed, put into practice *in vitro* and *in vivo* in animals, these studies have proved that this plant possesses numerous pharmacological properties in terms of antiproliferative, anti-inflammatory, antioxidant, analgesic, antiulcer, immunostimulating, anti-Infectious, anti-hypertensive and protective against cardiovascular disease. In addition, and in view of its richness in protein, minerals and vitamins, nettle provides a proven nutritional interest. In terms of toxicology, nettle remains innocuous and significant doses, administered orally to humans, showed no side effects.

Nettle extracts have a neutralizing role for reactive oxygen species (ERO). Their anti-free radical activity, with respect to the superoxide anion $O_2^{\cdot -}$, the

hydroxyl radical OH^\bullet and the nitric oxide radical NO^\bullet , was determined by spectrophotometry. Numerous studies have shown that the methanolic and ethanolic extracts of the leaves have a remarkable antioxidant effect with respect to the 1,1-diphenyl-2-picrylhydrazyl radical (DPPH) [7] [8] [9]. Chelation of ferrous iron was evaluated using ferrozine which forms a red chromophore with residual iron (Fe (II)-Ferrozine) having an absorption maximum at 562 nm. The absorbances obtained show that nettle has an important chelating activity with respect to the ferrous ion [10]. Another study, carried out on rats treated with tetrachloromethane (CCl_4), showed that nettle decreased lipid peroxidation and increased the activity of the antioxidant defense system thus playing a protective role against hepatotoxicity. This antioxidant activity is essentially correlated with the content of phenolic compounds [7] [11].

Nettle is very rich in polyphenols and is located in different parts of plants according to the plant species and the polyphenolic group considered. These compounds group together a multitude of molecules and represent one of the most important groups present in the plant kingdom. Although they are very diversified, they all have in common the presence of one or more benzene rings carrying one or more hydroxyl functions. Polyphenols are divided into several categories, including flavonoids [SFA, 2005].

Flavonoids act mainly as primary antioxidants, stabilizing peroxide radicals, but they can also deactivate reactive oxygen species, inhibit lipoxygenase or chelate metals [12].

Flavonoids are *in vitro* enzyme inhibitors of: histidine decarboxylase (by quercetin and naringenin), elastase, hyaluronidase (by flavones and proanthocyanidols) and catechol-O-methyltransferase.

2. Material and Methods

2.1. Animals Studied and Condition of Breeding

The animals used in this study are wistar albino rats (male and female), and are obtained from the Faculty of Science animal house. The animals are reared in transparent plastic cages ($32 \times 15 \times 13$ cm), covered by a stainless steel grill. The breeding takes place under standard conditions of ventilation, light (cycle of alternation 12H light/12H darkness), temperature (21 ± 2 degrees C) and relative humidity ($65\% \pm 15\%$). Rats have ad libitum access to fresh water and secalin-based food (SNV, Temara, Morocco).

2.2. Treatment of Animals

2.2.1. Chronic Toxicity to Dimethoate

In the adult stage, 120 Wistar rats aged 3 months of average weight (160 ± 40 g) are divided into two groups according to sex, 60 males and 60 females. Since the lethal dose of oral dimethoate was 300 mg/kg bw in rats [4] [13], we performed a sub-chronic study with a treatment of 100 mg/kg bw of dimethoate dissolved in the drinking water or in oil Of maize. The treatment time is 30 days. Two groups

were defined: control group “receiving only the drinking water or corn oil” and the intoxicated group “receiving dimethoate dissolved in the drinking water or in the corn oil”. Experimental procedures are also examined and approved by the internal ethical committee for animal welfare.

2.2.2. Procedure for the Treatment of Detoxification (Phyto-Processing)

After the period of intoxication and behavioral evaluation, rats (intoxicated by gavage or drinking water) received an extract by decoction of nettle. Indeed, 40 g of fresh leaves of Nettle have been roughly cut. After soaking in water for 24 hours, the whole is brought to boiling for 20 to 30 minutes under lid. After cooling the decoction under lid, filtering is carried out. This filtrate can be kept for only a few hours. A dose of 1 ml/100mg was administered orally to each of the intoxicated animals and this for duration of one month. The results of the treatment are finally compared with those of the control and intoxicated rats.

2.3. Parameters Studied

2.3.1. Body Weight Measurements

Signs of systemic toxicity such as convulsion, weakness and trembling were monitored. Weight is an important parameter in any experimental study because it is an indicator of physical health. The weight of each animal is monitored weekly with an electronic scale throughout the study.

2.3.2. Behavioral Testing: Novel Object Recognition Memory

- **Description of the device**

The object recognition memory test involves spontaneous exploration behavior in rodents, so it does not require food or water restriction or negative reinforcement of the animals. It is based on the spontaneous tendency of rats to preferentially explore a new object in relation to a familiar object. This device was used for the first time by [14].

This test takes place in a square open enclosure of $50 \times 50 \text{ cm}^2$ ($L \times l$), surrounded by four walls of 50 cm^2 height. It is made of wood painted with black color, which gives the image of an open cube. The device is illuminated by a light source positioned at a height of one meter.

- **Experimental procedure**

At the beginning of the test, each animal is allowed to freely explore the device for 5 minutes in the absence of any object. Twenty-four hours later, the animal must explore two identical objects (A1 and A2) placed at the two adjacent corners of the device at 10 cm from the walls, for 5 minutes; this is the “acquisition” session. Exploration is only called when the rat has a nose directed less than one cm to the object, while nibbling and marking are not considered exploration. After a delay of 2 hours (for evaluation of short-term memory effect) or 24 hours (for long-term memory evaluation), the rat is placed again in the device, but this time, one of the two identical objects is replaced by another entirely different B). The animal is allowed to explore the two different objects for 5 minutes. The two sets of objects used were in dup-

licate. The floor and objects are rinsed with 10% ethanol to remove any trace left by the animal in the device.

- **Parameters taken into account**

When the memory of the animal is not altered, it will explore the new object more than the old one, since it has memorized it. On the other hand, when the memory is defective, it will give more exploration time to the old object or it will explore both in an identical way. To evaluate the state of the memory, we calculated an index of recognition according to the following equation: Recognition index = time spent exploring the object B / Sigma time spent exploring object A and B [14].

2.4. Statistical Analysis

We performed the statistical analyzes using the SPSS 20.0 software. Parametric ANOVA repeat tests and 1-factor ANOVA were used to compare the data series. When there was a difference between more than two batches, a further analysis was carried out with Tukey's post hoc test. The normality of distribution was first atested by the Kolmogorov-Smirnov test and homogeneity by the Levens test. The values of $p < 0.05$ are considered significant.

2.5. Limitations of Study

Although the research has reached its aims, there are some unavoidable limitations.

The main of them are expressed as follows:

- Lack of prior research studies on the topic.
- The environmental factor (temperature, light...) influences the behavior of the rats and must be taken into consideration.
- The sample size is an important feature of any study. The higher the number, the more reliable the results.
- If the mode of administration is by gavage, the rats should be handled with care to avoid throat irritation.

3. Results

3.1. Macroscopic Observation

Signs of systemic toxicity such as weight loss, resting quake, decreased food intake were observed in groups of rats poisoned compared to controls.

3.2. Effect on Body Weight (Drinking Water)

In males rats: sub-chronic intoxication with dimethoate for four weeks induces a progressive decrease in body weight in treated rats groups, unlike control rats **Figure 1**. The Friedman test followed by the Bonferroni post-hoc test shows that the differences observed are highly significant between the two study groups ($p < 0.001$).

In female rats: A decrease in body weight was also observed in the group of

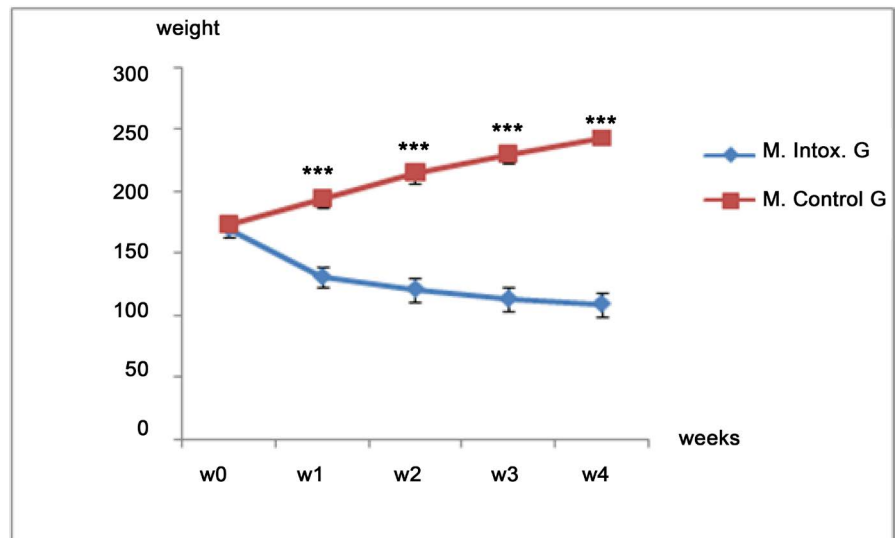


Figure 1. Effect of dimethoate on body weight in male rats Number of average errors \pm mean standard error (SEM). *** $p < 0.001$, comparison between intoxicated groups and controls.

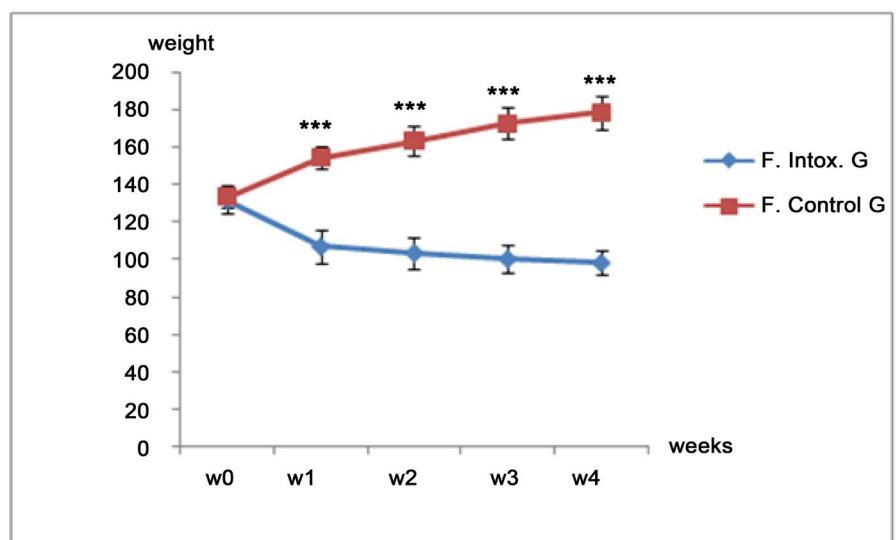


Figure 2. Effect of dimethoate on body weight in female rats Number of average errors \pm mean standard error (SEM). *** $p < 0.001$, comparison between intoxicated groups and controls.

rats intoxicated during the study **Figure 2**. The Friedman test followed by the Bonferroni post-hoc test shows that this decrease is very highly significant ($p < 0.001$).

3.3. Effect on Body Weight (Gavage)

In males: Body weight remained steady throughout the study period in intoxicated rats, while it increased steadily in control rats **Figure 3**. The differences observed between the two study groups are highly significant ($p < 0.001$).

In females: An increase in body weight was observed in female control rats

compared with those poisoned by dimethoate gavage. The statistical analysis also showed a highly significant difference between the two study groups ($p < 0.001$) **Figure 4**.

3.4. Evaluation of Memory Functions

3.4.1. Effect on Short Term Memory Recognition (STM): Case of Gavage

In male rats: **Figure 5** shows a decrease in the short-term recognition index. This index is below the recognition threshold in rats intoxicated with Dimethoate (IR = 40%). This decrease is highly significant $p < 0.001$.

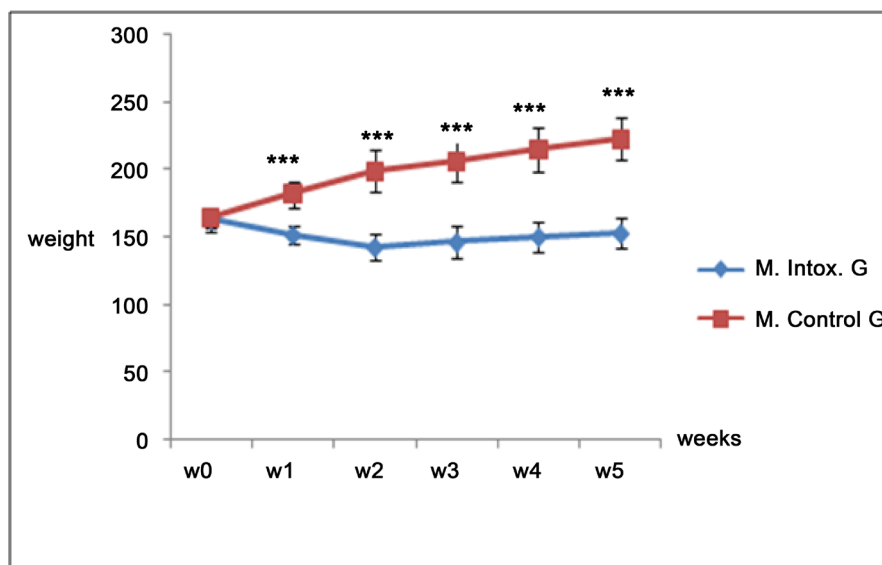


Figure 3. Effect of dimethoate on body weight in male rats Number of average errors \pm mean standard error (SEM). *** $p < 0.001$, comparison between intoxicated groups and controls.

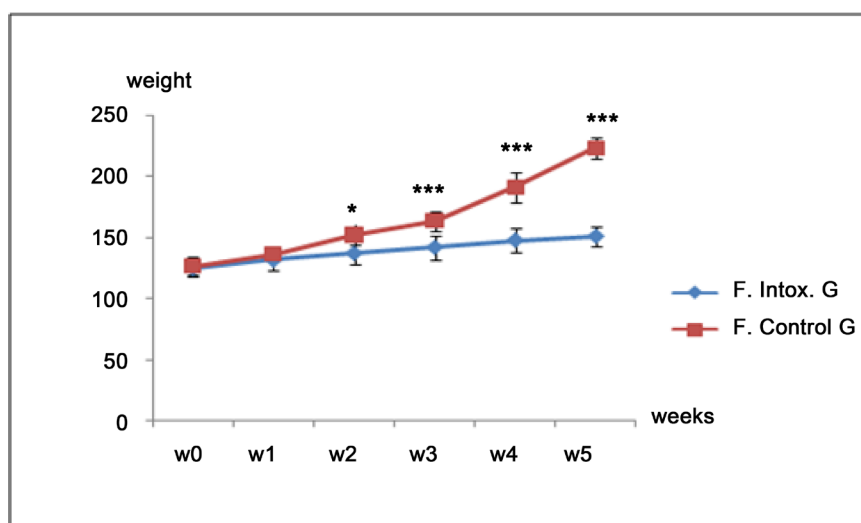


Figure 4. Effect of dimethoate on body weight in female rats Number of average errors \pm mean standard error (SEM). * $p < 0.05$, *** $p < 0.001$, comparison between intoxicated groups and control groups.

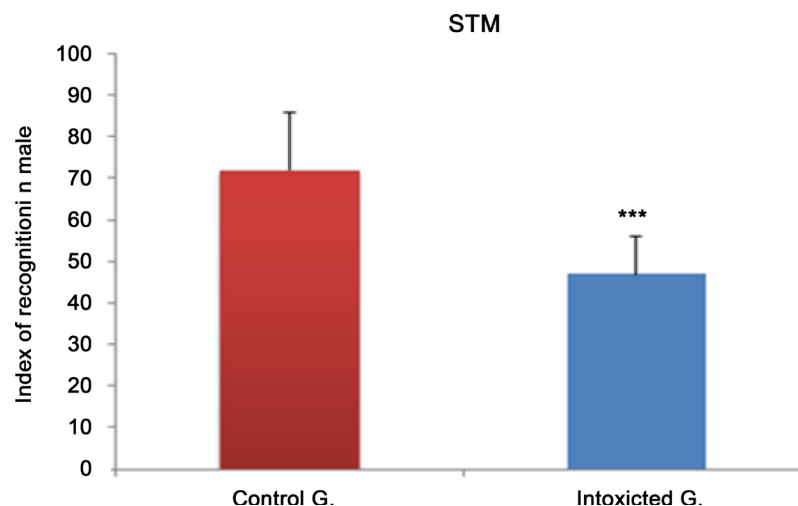


Figure 5. Effect of Dimethoate Exposure on Object Recognition STM in Male Rats Recognition index expressed on average \pm mean standard error (SEM). *** $p < 0.001$, comparison between intoxicated groups and controls.

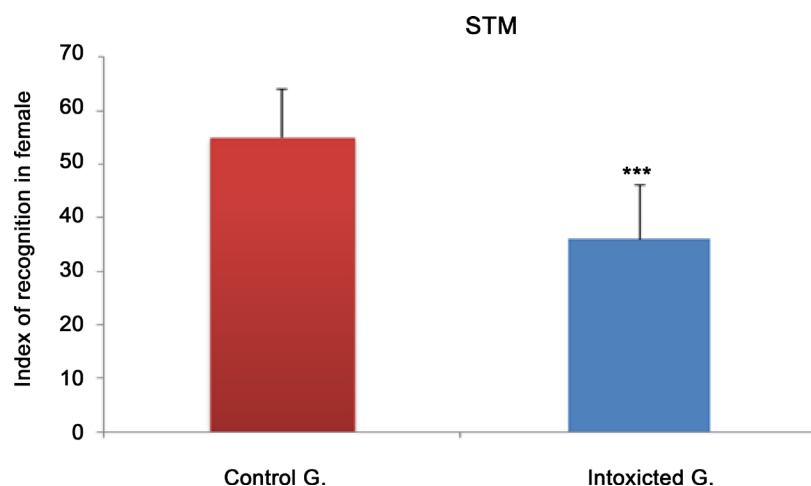


Figure 6. Effect of Dimethoate Exposure on Object Recognition STM in Female Rats Recognition index expressed on average \pm mean standard error (SEM). *** $p < 0.001$, comparison between intoxicated groups and controls.

In female rats: Dimethoate poisoning alters the short-term recognition memory in female rats. The expressed IR is highly significant between the two groups studied $p < 0.001$, either 43% to poisoned **Figure 6**.

3.4.2. Effects on STM Recognition: Drinking Water Case

In male rats: Dimethoate poisoning in drinking water induces an alteration of (STM) in rats. Indeed, the index of recognition is highly reduced in intoxicated rats. $P < 0.001$, compared to controls in **Figure 7**.

In female rats: There was also a highly significant reduction in the index of recognition in Dimethoate addicts $p < 0.001$, compared with controls in **Figure 8**.

3.4.3. Effects on Long Term Memory Recognition (LTM): Case of Gavage

In male rats: There was a significant decrease in long-term RI in rats treated with

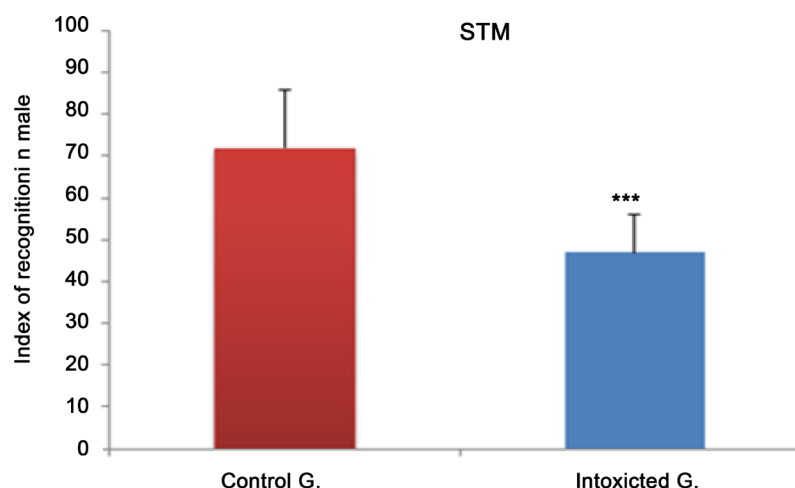


Figure 7. Effect of Dimethoate Exposure on Object Recognition STM In male rats Recognition index expressed on average \pm mean standard error (SEM). *** $p < 0.001$, comparison between intoxicated groups and controls.

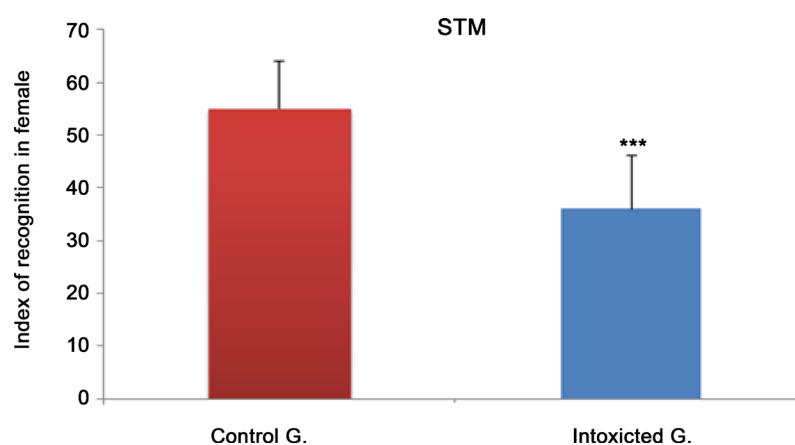


Figure 8. Effect of Dimethoate Exposure on Object Recognition STM in Female Rats Recognition index expressed on average \pm mean standard error (SEM). *** $p < 0.001$, comparison between intoxicated groups and controls.

Dimethoate gavage compared to controls, even though this index was above the 50% recognition threshold. The difference revealed is very statistically significant $p < 0.01$, **Figure 9**.

In female rats: the long-term RI of 54% in intoxicated females did not differ significantly with controls $p > 0.05$ **Figure 10**.

3.4.4. Effects on Long Term Memory Recognition (LTM): Case of Gavage

In male rats: As shown in **Figure 11**, RI is above the recognition threshold in rats treated with Dimethoate. However, this index differs significantly from that obtained by the control rats $p < 0.05$.

In female rats: It is also observed that the index of recognition is above the threshold of recognition of the objects in the rats intoxicated with Dimethoate, even if this index differs very significantly from that of the controls $p < 0.01$, **Figure 12**.

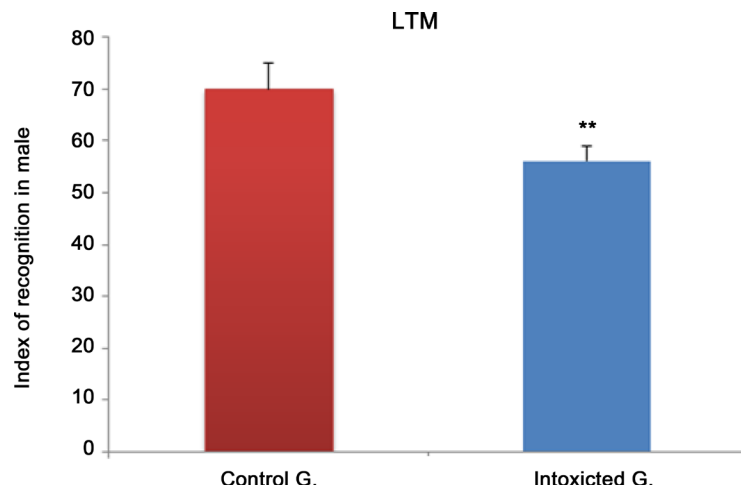


Figure 9. Effect of Dimethoate Exposure on Object Recognition LTM in Male Rats Recognition index expressed on average \pm mean standard error (SEM). ** $p < 0.01$, comparison between intoxicated groups and controls.

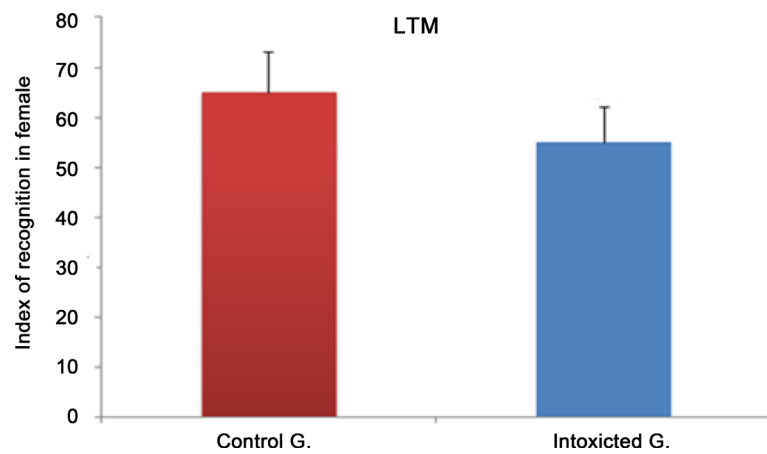


Figure 10. Effect of Dimethoate Exposure on LTM Recognition Objects in female rats Recognition index expressed as mean \pm mean standard error (SEM).

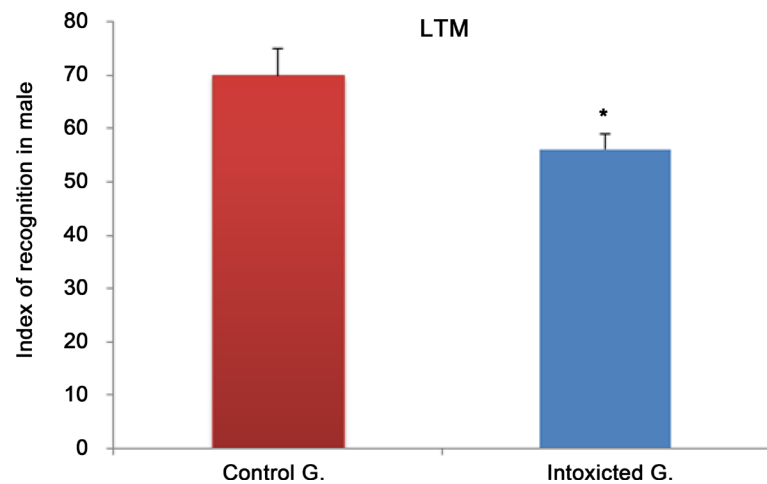


Figure 11. Effect of Dimethoate Exposure on LTM Recognition Objects in male rats Discrimination index expressed as average \pm mean standard error (SEM). * $p < 0.05$, comparison between intoxicated and control groups.

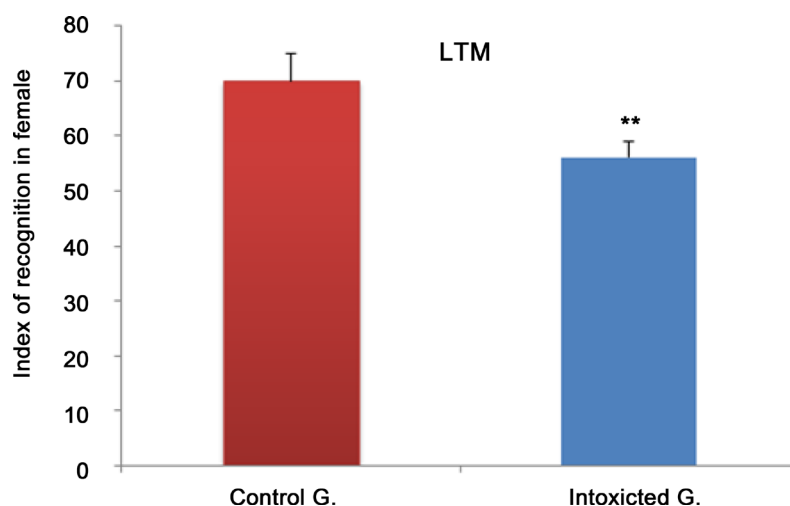


Figure 12. Effect of Dimethoate Exposure on LTM Recognition of Objects in female rats Discrimination index expressed as average \pm mean standard error (SEM). ** $p < 0.01$, comparison between intoxicated groups and controls.

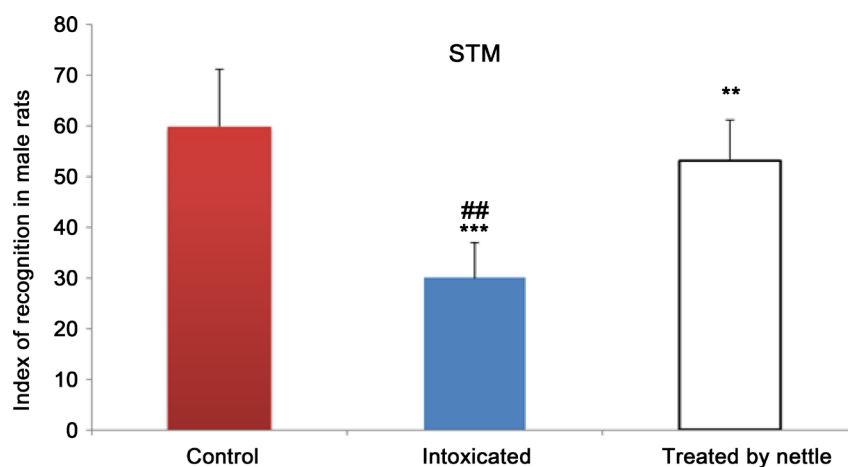


Figure 13. Effect of *Urtica Dioica* Medicinal Plant Treatment on Short-term Recognition Memory (STM) in Male Rats Recognition% expressed as average \pm mean standard error (SEM). *** $p < 0.001$, ** $p < 0.01$, comparison between the 3 groups treated; ### $p < 0.01$, comparison between the dimethoate addicted group and plant-treated group (1-factor ANOVA/Tukey post-hoc analysis).

3.5. Effects of Chelation Treatment on Memory Functions

3.5.1. Effects of Nettle Plant on STM Recognition: Drinking Water Case

In male rats: Recognition STM is highly altered in rats treated with Dimethoate, the recognition index is 40% below the recognition threshold with a highly significant difference from that of the control rats $p < 0.001$. However, treatment with the medicinal plant Nettle Dioica has led to an improvement in this index, which has increased from 40% to 53%, with a very significant difference $p < 0.01$,

Figure 13.

In females: Observations similar to that of males were made. As shown in **Figure 14**, the recognition index is 35%, which differs significantly from that of

the controls $p < 0.001$. In contrast, treatment with the plant significantly increased this index to 51% $p < 0.05$.

3.5.2. Effects of Nettle Plant on Recognition LTM: Drinking Water Case

In male rats: As shown in **Figure 15**, it is observed that the LTM of Recognition is weakly impaired with a 51% recognition in dimethoate $p < 0.05$, compared to controls. Treatment with the Nettle Dioica plant was able to slightly improve this index.

In females: The LTM index is very significantly decreased in Dimethoate addicts $p < 0.01$. However, it was possible to show a slight increase in this index after treatment with the plant Nettle dioica, this difference is not significant $p < 0.05$ (**Figure 16**).

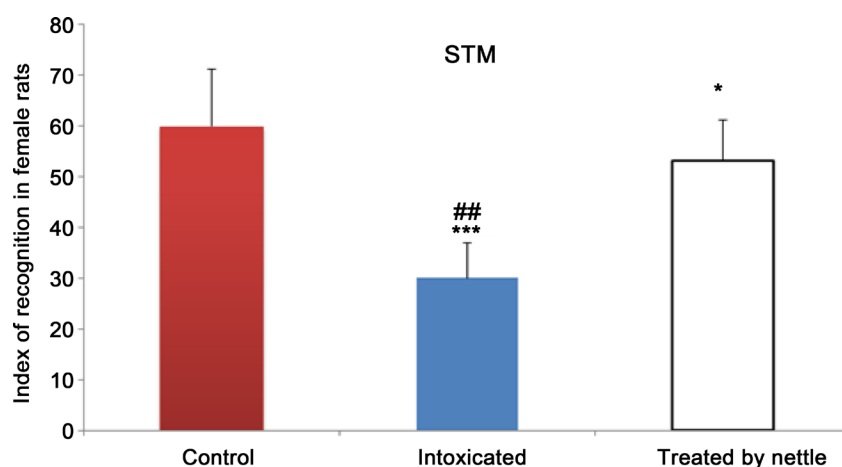


Figure 14. Effect of treatment by the medicinal plant *Urtica Dioica* on the short-term recognition memory (STM) in female rats Recognition% expressed as average \pm mean standard error (SEM). *** $p < 0.001$, * $p < 0.05$, comparison between the 3 treated groups; ## $p < 0.01$, comparison between the dimethoate addicted group and plant-treated group (1-factor ANOVA/Tukey post-hoc analysis).

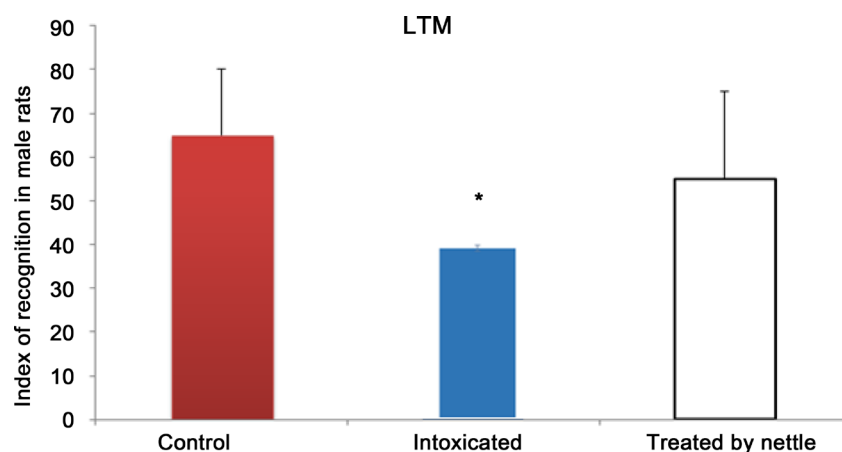


Figure 15. Effect of the *Urtica Dioica* Medicinal Plant Treatment on Long-Term Recognition Memory (LTM) in Male Rats Recognition% expressed as average \pm mean standard error (SEM). * $p < 0.05$ comparison between the 3 groups treated.

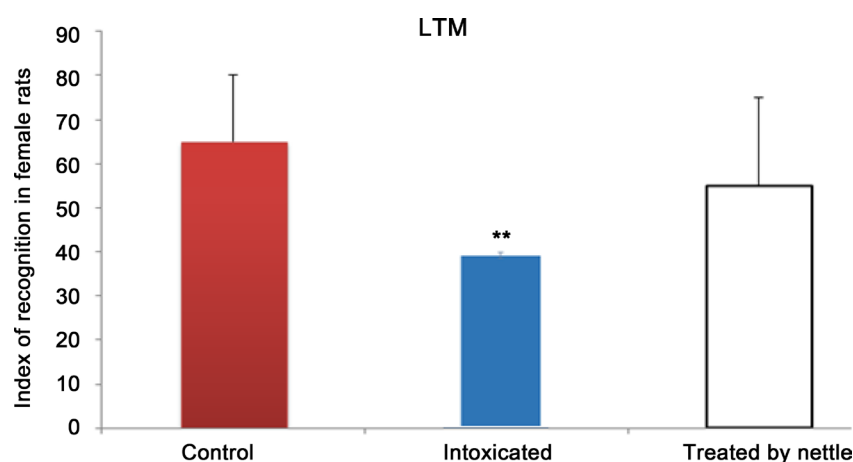


Figure 16. Effect of *Urtica Dioica* medicinal plant on long-term recognition memory (LTM) in female rats Recognition% expressed as average \pm mean standard error (SEM). ** $p < 0.01$, comparison between the 3 groups treated (ANOVA with 1 factor/Post-hoc analysis of Tukey).

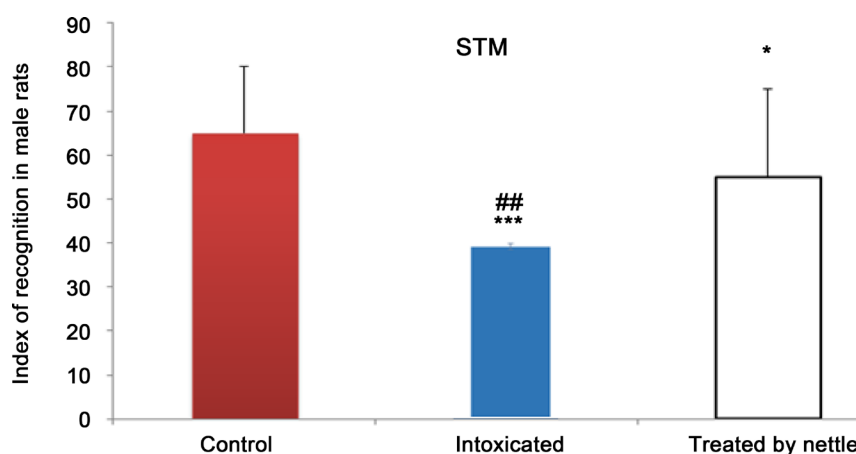


Figure 17. Effect of *Urtica Dioica* Medicinal Plant Treatment on Short-term Recognition Memory (STM) in Male Rats Recognition% expressed as average \pm mean standard error (SEM). *** $p < 0.001$, * $p < 0.05$, comparison between the 3 treated groups; ## $p < 0.01$, comparison between the dimethoate addicted group and plant-treated group (1-factor ANOVA/Tukey post-hoc analysis).

3.5.3. Effects of the Nettle Plant on the STM of Recognition: Case of Gavage

In male rats: In the case of gavage intoxication, it was demonstrated that the recognition STM was very much reduced (37%), compared to controls $p < 0.001$.

Treatment with the Nettle Dioica plant resulted in an improvement in this index, which rose from 37% to 60% in **Figure 17**.

In females: As shown in **Figure 18**, poisoning also induced a high alteration of STM recognition with 40% index versus 70% in $p < 0.001$ controls. On the other hand, the treatment with the plant caused an improvement of this index to 59% $p < 0.001$.

3.5.4. Effects of the Plant Nettle on the Recognition LTM: Case of Gavage

In male rats: Recovery LTM that was slightly impaired after intoxication was

slightly improved after treatment with nettle plant $p < 0.001$ **Figure 19**.

In females: As shown in **Figure 20**, the LTM index of recognition was not sig-

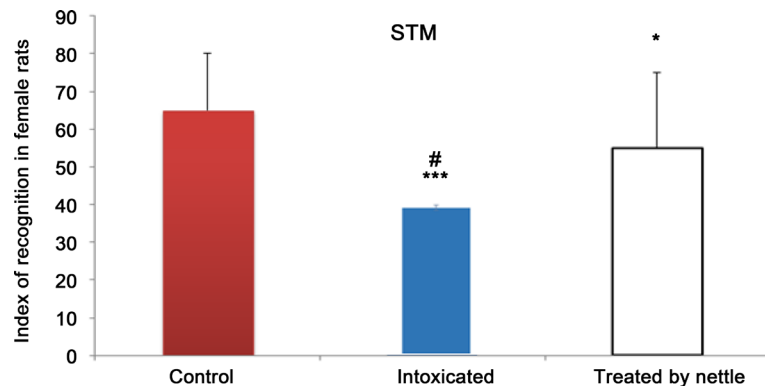


Figure 18. Effect of *Urtica Dioica* Medicinal Plant Treatment on Short-term Recognition Memory (STM) in Female Rats Recognition% expressed as average \pm mean standard error (SEM). *** $p < 0.001$, * $p < 0.05$, comparison between the 3 treated groups; # $p < 0.05$, comparison between the dimethoate poisoning group and plant-treated group (1-factor ANOVA/Tukey post-hoc analysis).

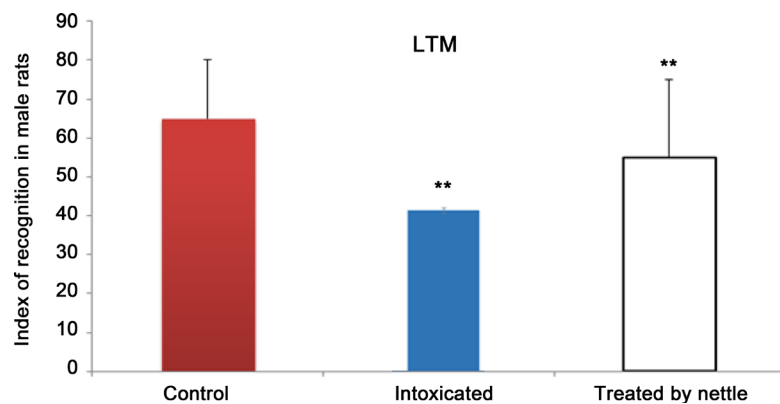


Figure 19. Effect of *Urtica Dioica* Medicinal Plant Treatment on Long-Term Recognition Memory (LTM) in Male Rats Recognition% expressed as average \pm mean standard error (SEM). ** $p < 0.01$, comparison between the 3 treatment groups (1-factor ANOVA/Tukey post-hoc analysis).

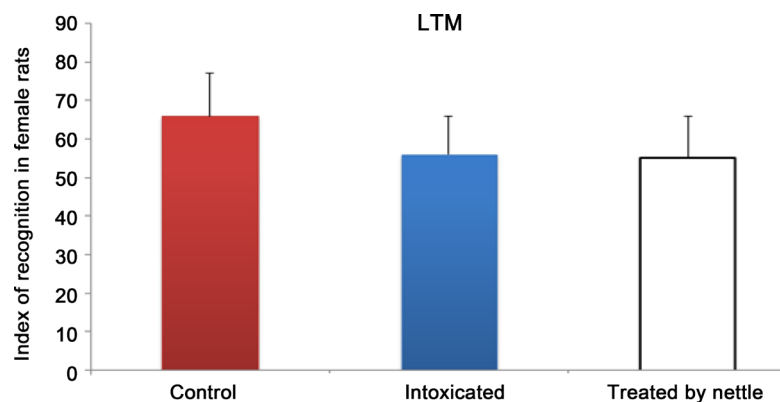


Figure 20. Effect of *Urtica Dioica* medicinal plant on memory Long-term recognition (LTM) in female rats. Recognition% expressed as average \pm mean standard error (SEM).

nificantly altered (54%) in intoxicated rats, compared to controls $p < 0.05$. However, treatment with the Nettle plant allowed a small increase in this index without significant effect $p < 0.05$.

4. Discussion

4.1. Effect of Dimethoate on Body Weight

The effect of the diméthoate on the physical weight gain for both modes of administration behaves appreciably in a different way. Indeed, in the case of the poisoning with diméthoate in drinking water, we observe a highly significant decrease in weight depending on the duration of the treatment for both rats' sexes, as shown in **Figure 1** and **Figure 2**. To the best of our knowledge, there have been no previous studies of this kind on the animal model. However these results indicate the significant impact of the diméthoate on the health of the agricultural populations living in the polluted middle. On the other hand, observations made in groups of rats exposed to dimethoate gavage show a slight decrease in body weight for both sexes males and females, as shown in **Figure 3** and **Figure 4**. Our results are in line with the works of Jallouli on mice poisoned by the diméthoate [15].

Another study of the developmental toxicity in Malathion also demonstrates a low physical weight gain for young rats to the (GD 6-PND 45) stage [16]. From the physio-pathological point of view, the low physical weight gain of the exposed groups could be attributed to the effect of overexpression of the ACh molecules which increases the gastric motility and decreases the intestinal absorption [17]. Indeed, the parasympathetic nervous system stimulates the processes of digestion, through the NT ACh. However, the excess of this NT due to the inhibition of AChE by the OP could be the cause of the dysfunction of this process [18].

4.2. Effect of Dimethoate on Memory Functions

The recognition memory capabilities of rats intoxicated with Dimethoate were highlighted by the NOR (Novel Object) recognition memory test. This methodology allowed to link chronic exposure to OPs insecticides and memory impairment which is a serious health problem for the general population. In this work, short and long-term types of memory have been studied, both of which are very much affected in Alzheimer's disease [19].

The test is based on the spontaneous tendency of rodents to explore a new object in relation to another already seen. This cognitive test, evaluating the ability to recognize a previous stimulus, is a fundamental study of human amnesia by animal model [20]. Indeed, the memory of recognition rests on the ability to judge whether we have already encountered any stimulus, in fact visual (face, object, place...).

The results of our study reveal that the sub-chronic exposure to Dimethoate induces a significant alteration of the recognition memory of the objects.

For STM short-term memory: In the case of rats poisoned by drinking-water, the recognition index was significantly decreased, with both sexes with a slightly pronounced effect in females: **Figure 5** and **Figure 6**. The same observations are made in rats intoxicated by gavage. But this impact is more important when the intoxication is made by the drinking water: **Figure 7** and **Figure 8**. Indeed, this index is below the recognition threshold of the objects, that is to say of 50% in the rats poisoned compared to the controls. This OP would therefore have disrupted the process of short-term memory formation. Our results are in agreement with a previous study which showed that Dimethoate poisoning produces an alteration of memory functions controlled by the hippocampus and the striatum [21].

To evoke hypotheses concerning the mechanism of action of alteration of memory, it is useful to know the cerebral structures considered as support for this cognitive function. Indeed, the NOR test model is influenced by hippocampal and cortical lesions [22] [23]. It is widely demonstrated that in rats and large apes, parahippocampal regions including the perirhinal cortex play a crucial role in the process of object recognition memory [24], *i.e.* their ability to evaluate a stimulus already encountered as a factor of familiarity based on the integrity of the medial temporal lobe [25]. This cerebral structure plays an important role in the formation of recognition memory. Its lesion leads to impaired performance [26]. A previous study has shown that exposure to subtoxic doses of Malathion induces a very significant inhibition of AChE in the hippocampus and associated regions [16]. The hippocampal system is rich in the cholinergic system, which has a central role in the encoding and consolidation of the new stimulus. This process therefore makes it possible to integrate and reorganize an already formed memory. By this means, in rodents, when a stimulus is previously experienced and reactivated, the hippocampus permits discrimination between the familiar and the new with a spontaneous and natural tendency to interact more with novelty [27]. Dysfunction in the OP induced cholinergic system in the hippocampus and/or perirhinal cortex may be suggested as a cause of alteration of short-term recognition memory. Indeed, the perirhinal cortex represents the main cerebral site of transit of information of environmental origin such as visual, olfactory and somatosensory stimuli, through which the hippocampus receives its “inputs” to form the memory [28].

For the long-term LTM recognition memory, our results also support a difference in the recognition index in the evaluation of the long-term recognition memory between the treated and control groups for the two forms of exposure, Even if this index turns out to be above the recognition threshold, as compared with the short-term recognition memory **Figures 9-12**. This implies that short-term recognition memory is more vulnerable to exposure to dimethoate than to long-term memory. Similar results have been demonstrated in a previous study which showed that malathion-exposed rats have a short-term memory disrupted compared to long-term recognition memory [16]. It could be suggested that

long-term recognition memory processes involve various components, such as subcortical and cortical structures. However, the sex effect that depends on the effect of dimethoate on recognition memory functions remains to be discussed. Indeed, the ability to recognize objects could be altered in both male rats and females exposed to Dimethoate. A developmental study showed that when the period of exposure to chlorpyrifos (CPF) occurs at the end of gestation (GD 17 - 20), only female mice with altered reference and working spatial memory. In this case, the muscarinic cholinergic system seems to be one of the systems whose functioning is modified or altered [29] [30]. On the other hand, if the period of exposure to CPF occurs postnatally, during the first days of life (PND 1 - 4), it is only the male mice that have spatial memory problems [31]. This implies that in order to better understand the sex-effect of dimethoate, exposure studies on different stages of development should be undertaken.

4.3. Effect of Nettle on the Functions of Memory

Although we have studied the effects of dimethoate intoxication in rats, we have tested the therapeutic effects of a medicinal plant, Nettle, which has antioxidant properties. In order to better support its properties, it is desirable to evoke the pro-oxidizing and proinflammatory effects induced by OPs in general and Dimethoate in particular. Most authors agree that chronic or acute exposure induces oxidative and proinflammatory stress effects in animals [4] [31] [32] [33] [34] [35].

In addition, dimethoate intoxication has been shown to cause cellular alterations and oxidative stress, leading to lipid peroxidation and the generation of free radicals [4] [36] [37]. In this study it was demonstrated that Nettle treatment resulted in a remarkable improvement in short-term memory recognition capacity, which was strongly altered by dimethoate. Indeed, antioxidants constitute the defense system that limits the toxicity associated with free radicals [38]. In addition, a dietary intake rich in antioxidant products has shown protective effects against oxidative stress [38] [39], this has been demonstrated for vitamin E [40] [41] and for Selenium [39].

These results suggest that nettle treatment has a positive effect by eliminating free radicals associated with exposure to Dimethoate. In addition, it would be appropriate to investigate the effects of dimethoate on the serotonergic system and on the catecholamines involved in the regulation of memory performance [42]. These systems have been disturbed during intoxication with CPF [43] [44] [45] [46] and methyl parathion [47].

5. Conclusions

Agriculture makes extensive use of pesticides and phytosanitary products. By destroying pests and weeds, these substances improve crops and guarantee the availability, quality, reliability and prices of agricultural products for the benefit of farmers and consumers.

Used improperly, pesticides constitute nevertheless a danger, because most can damage the health and the environment.

In this study, we have demonstrated that poisoning by dimethoate alters the short-term memory functions of wistar rats.

We have also tested the effect of nettle as a chelating treatment trial. An improvement in short-term memory was obtained.

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