Effect of *Moringa oleifera* (Moringa) on tandem lead mixture in rats body

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**Abstract**

The main target of the present investigation was to study the effect of *Moringa oleifera* leaves to get rid of toxic heavy metals (Cadmium and lead mixture) in albino rats. Thirty healthy adult male albino rats "Sprague Dawley strain" weighing 150±5g, were used and divided into 5 equal groups, one was kept as a negative control group, while the second Group(6 rats) fed on basal diet with cadmium and lead at the level of 0.2%( control positive group). Groups (3, 4 and 5) were fed on diet with toxin mixture and moringa leaves at different levels 2.5, 5 and 10%. At the end of the experiment, feed intake (FI), body weight gain (BWG), feed efficiency ratio (FER) and relative weights of liver, kidneys and spleen were calculated. Also, Serum liver functions (GOT, GPT, ALK), kidney functions (Urea, CR, ALb), lipid profile (T.Ch, Tri, LDL, HDL, ) were determined in serum. Histopathological changes of liver samples were examined. The results indicated that rats infected toxins mixture which fed on diet with tested leaves at 10% significantly increased in body weight gain, organs weight, serum glucose, cholesterol, triglycerides, LDL, liver enzymes kidney functions and decreased HDL. Treating rats which were fed on diet with this level of tested leaves improved all other parameters and internal organs weights. The histopathological examination confirmed the improvements in biological parameters and cell structure.

**Key Words**: Sprague Dawley Strain, toxin mixture, moringa leaves, liver enzymes, kidney functions.
1. Introduction

Human activity in the last few decades has led to global contamination by organic and inorganic compounds (Chaerunet al., 2011) and (Sahuet al., 2007). The presence of the pollutants generated from industrial and agriculture activities in the waterways has been identified to produce potential harmful effects on the aquatic living organisms and the food webs (Katnoria et al., 2011) and (Oliveira et al., 2004). Nowadays, heavy metal contamination is considered to be among the most serious environmental problems. Heavy metals are any inorganic metallic compounds that can exert their toxicity via binding to the thiol group and disulfide bond that contribute to the stability of the enzyme (Frasco et al., 2005). The metals have high affinity to the disulfide bridge between two cysteine residues in any protein compound. Heavy metals are very dangerous to living organisms especially for humans since they can cause DNA damage and exert carcinogenic effects. Medicinal plants play an important role in individuals and communities' health. The medicinal value of these plants depends on some chemical compounds that produce a definite physiological action in the human body. The most important of these bioactive constituents of plants are alkaloids tannins flavonoids and phenolic compounds (Hill, 1952). The state of medicinal plants research has been emphasized in many developing countries (Edeoga et al., 2005). The appropriate utilization of local resources to cover drugs needs is dependent on the preliminary scientific study to determine the efficacy and safety of any preparation (Burkill, 1984). The awareness of the role of medicinal plants in health care delivery of developing countries has resulted in researches into traditional medicine with a view to integrating it with modern orthodox medicine (Sofowara, 1993). Metal poisoning is a global problem with humans being exposed to a wide range of metals in varying doses and varying time frames. Traditionally, treatment involves removal of the toxic source or chelation therapy. An intermediate approach is needed. This study reported that the use of essential metal supplementation was very important as a strategy to induce metallothionein expression and displace the toxic metal from important biological systems, improving the metal burden of the patient. Specific recommendations are given for supplementation with calcium, zinc and
vitamin E as a broad strategy to improve the status of those exposed to toxic metals (Wayne, 2014).

Pure cadmium is a soft, silver-white metal. The level of this toxic hazardous metal in the environment have increased dramatically in the last few years as it is naturally emitted into the environment through volcanic activities, forest fires and generation of sea salt aerosols. Cadmium is mostly used in the production of batteries, pigments, coatings and plantings, stabilizers for plastics, nonferrous alloys and photovoltaic devices. Studies have also shown that tobacco leaves accumulate high levels of cadmium from the soil. Cadmium is a major concern for people living near cadmium-emitting industries. Highest risk of occupational exposure occurs from processes involving heating cadmium containing materials such as smelting and electroplating. Exposure to this environmental pollutant can be prevented through personal protective equipment, though cigarette smoking is known to double the toxic effects (ATSDR, 2008).

The injurious effect of cadmium is related with diverse clinical manifestations like renal and hepatic dysfunction, bone diseases, anaemia, immune toxic effects along with the alterations of the lipid profile, pulmonary oedema and testicular damage (Vinodini et al. 2013).

"Lead poisoning" or "lead intoxication" has been defined as exposure to high levels of lead typically associated with severe health effects. Poisoning is a pattern of symptoms that occur with toxic effects from mid to high levels of exposure; toxicity is a wider spectrum of effects, including subclinical ones (those that do not cause symptoms). However, professionals often use "lead poisoning" and "lead toxicity" interchangeably, and official sources do not always restrict the use of "lead poisoning" to refer only to symptomatic effects of lead (Guidotti and Ragain, 2007).

The amount of lead in the blood and tissues, as well as the time course of exposure, determine toxicity. Lead poisoning may be acute (from intense exposure of short duration) or chronic (from repeat low-level exposure over a prolonged period), but the latter is much more common. Diagnosis and treatment of lead exposure are based on blood lead level (the amount of lead in the blood), measured in micrograms of lead per deciliter of blood (µg/dL). Urine lead levels may be used as well, though less commonly. In cases of chronic exposure lead often
sequesters in the highest concentrations first in the bones, then in the kidneys. If a provider is performing a provocative excretion test, or "chelation challenge", a measurement obtained from urine rather than blood is likely to provide a more accurate representation of total lead burden to a skilled interpreter (Lowry, 2010).

The US Centers for Disease Control and Prevention and the World Health Organization state that a blood lead level of 10 μg/dL or above is a cause for concern; however, lead may impair development and have harmful health effects even at lower levels, and there is no known safe exposure level. Authorities such as the American Academy of Pediatrics define lead poisoning as blood lead levels higher than 10 μg/dL.

Numerous plant in nature possess medicinal properties. One among many is Moringa oleifera. This Moringa oleifera plant is one of the naturalized species of Moringaceae family. The tree thrives best under the tropical insular climate. Moringa, originally from India, is now distributed throughout the world. In some parts, it is often referred to as the drumstick or the kelor tree while in other places it also known as Shagara al Rauwaq (Anwar et al., 2007).

The leaves of this miraculous plant are a source of protein, B-carotene, vitamins (A, B, C, E, riboflavin), nicotinic acid, folic acid, pyridoxine, amino acids, minerals, various phenolic compounds. Leaves of Moringa oleifera are known to have hypolipidemic, anti-atherosclerotic, antioxidant, hypotensive, tumour suppressive and immune boosting effect and also for its role in the prevention of cardiovascular diseases (Khalafalla et al., 2010).

Best known as miracle tree, Moringa is an important tropical crop that is used as human food, medicine and in oil production (Anwar et al., 2007). It has a wide range of health benefits and hence extracts from different parts of Moringa could be used to combat various metal intoxications like cadmium, arsenic, lead etc. (Sirimongkolvorakulet et al., 2012).

It not only has a positive effect in lowering the lipid levels but also alters the levels of the liver enzymes and hence can also improve the liver functions (Vinodiniet et al., 2014).
So, This study aimed to investigate the effect of different levels of *Moringa oleifera* on the biological parameters of rats toxic with cadmium and lead mixture.

### 4-Materials and Methods

#### 4-1. Materials:
Moringa leaf and Casein were obtained from Morgan Company, Cairo, Egypt. Vitamins mixture, salt mixture and biological kits were purchased from El – Gomhoria Company., Cairo, Egypt. Thirty healthy adult male albino rats "Sprague Dawley strain" weighing 150±5g were used in the study. The rats were obtained from Research Institute of Ophthalmology, Medical Analysis Department, Giza, Egypt. They were housed in galvanized iron cages measuring 40 × 24 × 20 cm (5 rats to each cage).

#### Methods:

A. Preparation of samples:
Moringa leaves were cleaned for removing dust and impurities and dried at 50°C using a fan oven. Then, they were milled by a precession mill to give powder. A grinder mill and sieves were used to obtain a powder particle size of less than 0.2mm.

B. Biological Experiments
Basal diet was prepared from fine ingredients per 100g. The diet had the following composition: Corn starch 67%, Casein 13% (*AIN, 1993*), corn oil 10%, Fiber 5%, Salts mixture 4% (*Hegstedet al., 1941*), vitamin mixture 1% (*Campbell, 1963*). Moringa leaves were added to the tested diet at the level 2.5, 5 and 10%.

C. Experimental Design
Biological experimental was done at the central laboratory of Research Institute of Ophthalmology, Medical Analysis Department, Giza, Egypt. Rats (n = 30 rats) were housed individually in wire cages in a room maintained at 25 ± 2°C and kept under normal healthy conditions. All rats (30 rats) were fed on basal diet for one – week before starting the experiment for to learn non-lethal dose. After this week, they were divided into nine main groups:
Group(1): Rats were fed on basal diet as negative control group.

Group(2): Rats were fed on basal diet with toxin mixture at the level 0.2% as a positive control.

Group(3): Rats were fed on diet with toxin mixture and moringa at the level 2.5%.

Group(4): Rats were fed on diet with toxin mixture and moringa at the level 5%.

Group(5): Rats were fed on diet with toxin mixture and moringa at the level 5%.

D. Biological evaluation

During the experiment period (28days), the quantities of diet which were consumed and / or wasted were recorded every day. In addition, rat's weight was recorded weekly. The body weight gain (BWG), feed intake(FI), feed efficiency ratio(FER) were determined according to (Chapman et al., 1959).

E. Biochemical evaluation and Histopathological examination

At the end of the experiment period, the rats were fasted overnight before sacrifice and the blood samples were collected from each rat and centrifuged to obtain the serum. Serum was carefully separated and transferred into dry clean ebendorf tubes and kept frozen at-20ºc for analysis as described by (Schermer, 1967). Liver , and Brain were removed from each rat by careful dissection , cleaned from the adhesive matter by a saline solution(0.9%) , dried by filter paper ,weighed and kept in formalin solution (10%), according to the method described by (Drury and Walling,1980)

F. Hematological analysis

Different tested parameters in serum were determination using specific methods as follow: Glotamicoxaloacetictransaminas (GOT), glutamic pyruvic transaminas (GPT), urea and createne according to Kakkaret al., (1984); Aebi (1974); Ellman (1959) &Reitman and Frankel (1957) respectively.

G. Statistical analyses

Statistical analysis was carried out using the programmer of Statistical Package for the Social Sciences (SPSS), PC statistical software (Version 20; Untitled–SPSS Data Editor). The results were expressed as mean ± Standard deviation (mean ± S.D.). Data were analyzed using one way classification, analysis of variance (ANOVA).
The differences between means were tested for significance using least
significant difference (LSD) test at p<0.05 (Sendcor and Cochran,
1979).

Results and Discussion

In the current study the effect of moringa leaves to get rid of toxic
heavy metals in rat's body.

1-Effect of moringa leaves at different levels on body weight gain
(BWG) of rats toxic with cadmium and lead mixture.

Data presented in table (1) showed the effect of different levels
of tested leaves on body weight gain (BWG) of rats.

It could be noticed in table (1) that differences between all mean
values of these groups were significant when compared to control
negative group. With expecting, 0.02% toxins mixture group was the
lowest value of body weight gain. There is no significant differences in
BWG among group 3 and 4. The best result was group 5 which fed on
mixture 0.02% and moringa at the level 10%.

Potential health problems associated with a high intake of
vegetables and meat products which contain salt of Lead and cadmium
have been linked to decreased energy intakes, weight gain and the
weight loss epidemic as indicated by Katnoriaet al. (2011).

Meanwhile, Oliveira et al. (2004) found that the rising
consumption of vegetables fertilizer and meat additives provides a rising
intake of Lead which can contribute to weight loss and underweight.

Also, study done by Frasco et al. (2005) increased cadmium
consumption would decrease total energy intake by decreased appetite
and decreased fat intake.

Karakaya (2004) who found that moringa leaves increased
weight gain to contained many biological active compounds including
chymopapain and papain which is the ingredient that aids digestive
system and a good supply of vitamin A and C that are highly essential
for maintaining a good health.
Table (1): Effect of moringa leaves at different levels on body weight gain (BWG) of rats toxic with cadmium and lead mixture.

<table>
<thead>
<tr>
<th>Groups</th>
<th>BWG g / 28 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative control (G1)</td>
<td>43.64 ± 4.21</td>
</tr>
<tr>
<td>Positive control (G2)</td>
<td>4.61 ± 0.13</td>
</tr>
<tr>
<td>Toxins mixture and moringa leaves at the level 2.5% (G3)</td>
<td>9.12 ± 1.19</td>
</tr>
<tr>
<td>Toxins mixture and moringa leaves at the level 5% (G4)</td>
<td>12.74 ± 0.21</td>
</tr>
<tr>
<td>Toxins mixture and moringa leaves at the level 10% (G5)</td>
<td>17.54 ± 1.11</td>
</tr>
</tbody>
</table>

Means in the same column with different litters are significantly different (P ≤0.05).

2- Effect of moringa leaves at different levels on Feed Intake (FI) and feed efficiency ratio (FER) of rats toxic with cadmium and lead mixture.

Data present in table (2) showed the effect of tested leaves to high doses of lead and cadmium on feed intake (FI) and feed efficiency ratio (FER) (mean± SD).

It is clear that no significant differences in feed intake (FI) between positive controls and group 3. From the table, it could be noted that the differences in values of feed intake between all treated groups were considerable as compared to negative and positive control groups. The obtained data revealed a high variation in feed intake between treatments and the controls group, this may be due to the acceptability of the added material. These results are in accordance with those reported by Frasco et al. (2005) who found that lead decreased appetite and decreased fat intake. Callisteet et al. (2001) reported that moringa is a source of antioxidants vitamin as A that prevents damage caused by free radicals that may cause some forms of cancer.

According to data present in the same table (2), these results denote that there were significant increases in feed efficiency ratio (FER) for all groups when compared with control positive group. The highest value of feed efficiency ratio (FER) was found in 10% group. It is noticed that a significant decreases in BWG% for control group compared to all groups, was indicated and confirmed that the real effect for BWG% due to moringa leaves administration.

From the obtained results, it could be observed that treating rats with the tested vegetables and fruit led to increase in BWG%, FI and FER when compared with both positive controls while lower than negative control. These results were in agreement with those reported by...
Callisteet et al. (2001) who said that dietary fiber (DF) derived from fruits and vegetables have a relatively high proportion of SDF.

Table (2): Effect of moringa leaves at different levels on Feed Intake (FI) and feed efficiency ratio (FER) of rats toxic with cadmium and lead mixture (mean± SD).

<table>
<thead>
<tr>
<th>Groups</th>
<th>FI (g/day)</th>
<th>FER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative control (G1)</td>
<td>11.71± 0.22</td>
<td>0.133± 0.001</td>
</tr>
<tr>
<td>Positive control (G2)</td>
<td>2.63± 0.11</td>
<td>0.063± 0.001</td>
</tr>
<tr>
<td>Toxins mixture and moringa leaves at the level 2.5% (G3)</td>
<td>2.89± 0.02</td>
<td>0.112± 0.001</td>
</tr>
<tr>
<td>Toxins mixture and moringa leaves at the level 5% (G4)</td>
<td>4.76± 0.12</td>
<td>0.096± 0.002</td>
</tr>
<tr>
<td>Toxins mixture and moringa leaves at the level 10% (G5)</td>
<td>7.68± 0.27</td>
<td>0.082± 0.002</td>
</tr>
</tbody>
</table>

Means in the same column with different litters are significantly different (P ≤ 0.05).

3-Effect of moringa leaves at different levels on kidney functions of rats toxic with cadmium and lead mixture (mean± SD).

Data given in table (3) showed the effect of moringa leaves to high doses of lead and cadmium mixture on serum urea levels (mean± SD). It could be observed that the highest value of serum urea levels was found in rats which received toxins mixture as positive control group. No significant changes were found in serum urea levels between groups 2 and 3 also, there is no significant between group 4 and 5.

It is clear that in control negative group creatinine levels was 0.46± 0.02 mg/dl which significantly decreased when compared with rats which received the toxins mixture as positive control and group fed on moringa leaves at the level 2.5%. Meanwhile, rats of groups 4 and 5, creatinine levels of these groups were non significant between each other and showed significantly increasing as compared to control negative group. Groups 5 was the lowest creatinine value which showing a significant decreased as compared to the other groups and a significant increased when compared with control negative group.
Table (3): Effect of moringa leaves at different levels on kidney functions of rats toxic with cadmium and lead mixture (mean± SD).

<table>
<thead>
<tr>
<th>Groups</th>
<th>Urea (mg/dl)</th>
<th>Creatinine (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative control (G1)</td>
<td>27 ± 4.23</td>
<td>0.46 ± 0.12</td>
</tr>
<tr>
<td>Positive control (G2)</td>
<td>50.33 ± 3.21</td>
<td>2.45 ± 0.22</td>
</tr>
<tr>
<td>Toxins mixture and moringa leaves at the level 2.5% (G3)</td>
<td>48.33 ± 3.31</td>
<td>2.05 ± 0.15</td>
</tr>
<tr>
<td>Toxins mixture and moringa leaves at the level 5% (G4)</td>
<td>43.33 b ± 4.12</td>
<td>1.53 b ± 0.35</td>
</tr>
<tr>
<td>Toxins mixture and moringa leaves at the level 10%(G5)</td>
<td>40.3 b ± 1.1</td>
<td>1.35 b ± 0.50</td>
</tr>
</tbody>
</table>

Means in the same column with different litters are significantly different (P ≤0.05).

4-Effect of moringa leaves at different levels on liver functions of rats toxic with cadmium and lead mixture (mean± SD).

Data presented in table (4) showed the effect of moringa leaves to high doses of lead and cadmium mixture levels of serum AST (mean± SD).

It could be observed that in control negative group AST was 39 ± 3.00 u/l which significantly decreased when compared with positive control group. But, the levels of AST in groups 3,4 and 5 showed significant increasing as compared to control negative group and significant decreased as compared to control positive groups. The strongest effect in serum AST levels recorded for group 5 which fed on basal diet with 10% of moringa leaves.

<table>
<thead>
<tr>
<th>Groups</th>
<th>AST(UL)</th>
<th>ALT(UL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative control (G1)</td>
<td>39 ± 3.00</td>
<td>45 ± 0.6</td>
</tr>
<tr>
<td>Positive control (G2)</td>
<td>109 ± 3.21</td>
<td>95 ± 2.3</td>
</tr>
<tr>
<td>Toxins mixture and moringa leaves at the level 2.5% (G3)</td>
<td>102 ± 5.01</td>
<td>90 ± 5.4</td>
</tr>
<tr>
<td>Toxins mixture and moringa leaves at the level 5% (G4)</td>
<td>94 b ± 5.34</td>
<td>82.66 b ± 0.34</td>
</tr>
<tr>
<td>Toxins mixture and moringa leaves at the level 10%(G5)</td>
<td>88 c ± 7.76</td>
<td>77 b ± 3.8</td>
</tr>
</tbody>
</table>

It is clear that the serum level of (ALT) in group 5 which fed on toxins mixture with 10% moringa leaves was the lowest level which being 77 ± 3.8 U/L and showing no significant change with group which fed on toxins mixture with 5% tested leaves which was 82 ± 0.34 U/L. At the
same time, rats which received toxins mixture with 2.5% leaves and positive control groups significantly didn’t differ in serum level of ALT.

Edeoga et al. (2005) revealed that mercury had a potential role to cause injuries in several organs and tissues. The increased consumption of cadmium and Lead sources in foods and drinks is linked with the hepatic metabolism and caused lipogenesis and ATP depletion, which leads to fat accumulates in the liver by the primary effect of NO oxidation. It could be hypothesized that increased mercury and Lead sources consumption contributes to the development of non-alcoholic fatty liver disease (NAFLD) which can progress to cirrhosis over time in some individuals.

Anwar et al. (2007) showed that moringa plant is one of the most important plants which containing phenolic antioxidant compound which protected liver from any free radical.

Khalafalla et al. (2010) found that the moringa extraction contained dietary fiber or essential oils, the flavonoids hesperidin and narirutin which reduced the residual mercury levels and the degree of lipid oxidation.

Anwar et al. (2007) found that moringa leaves contained significant antioxidant activity and had hepatoprotection effect by restoring the normal hepatic architecture.

Table (4): Effect of moringa leaves at different levels on liver functions of rats toxic with cadmium and lead mixture (mean± SD).

<table>
<thead>
<tr>
<th>Groups</th>
<th>AST(UL)</th>
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</tr>
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<tr>
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<td>Toxins mixture and moringa leaves at the level 2.5% (G3)</td>
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<td>90±5.4</td>
</tr>
<tr>
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</tr>
<tr>
<td>Toxins mixture and moringa leaves at the level 10%(G5)</td>
<td>88±7.76</td>
<td>77±3.8</td>
</tr>
</tbody>
</table>

Means in the same column with different litters are significantly different. (P ≤ 0.05).
Histopathological results:
*Liver:* Liver’s rat which fed on basal diet, the Liver structure showing the normal histological (photo 1). In photo (2), Liver’s rat which fed on basal diet with 0.2% toxins mixture as positive control group showed that congestion of central vixen and hepatic sinusoids and kupijer cells activation and with local hepatic necrosis associated mononuclear cells infiltration. In Photo (3), Liver’s rat which fed on basal diet with 0.2% mixture with 2.5% tested leaves showed that slight vacuolation of hepatocytes. In Photo (4), Liver’s rat which fed on basal diet with 0.2% mixture and 5% from leaves showed that hydropic degeneration of hepatocytes. In Photo (5), liver’s rat which fed on basal diet with mixture 0.02% and 10% leaves showed that no histopathological changes.

**Photo (1):** liver of rat fed on diet as control negative  
**Photo (2):** liver of rat fed on diet with lead 0.2% as positive control  
**Photo (3):** liver of rat fed on diet with 0.02% toxin and 2.5% moringa leaves  
**Photo (4):** liver of rat fed on diet with 0.02% toxin and 5% moringa leaves  
**Photo (5):** liver of rat fed on diet with 0.02% toxin and 10% moringa leaves
References


تأثير المورينجا على خليط الرصاص والكادميوم في جسم الفئران

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قاسم السيد عبد الرشيد
قسم التغذية وعلوم الأغذية، كلية الاقتصاد المنزلي، جامعة المنوفية

الملخص العربي:

الهدف الرئيسي لهذه الدراسة هو معرفة تأثير المورينجا أوالغيرة للخلاص من
سموم المعادن الثقيلة ( خليط الكادميوم والرصاص) في الفئران البيضاء. استخدمت هذه
الدراسة عدد 30 من ذكور الفئران البيضاء من فصيلة (أسرايجلوني). وزنها 150 ± 5جم،
وتم تقسيمهم إلى 5 مجموعات متساوية، المجموعة الرئيسي الأولي تم تغذيتها على الغذاء
الأساسي وامضت المجموعة ضابطة (سالبة)، في حين تم تغذية المجموعة الثانية (6فئران)
على الغذاء الأساسي مضاد اليد خليط من الكادميوم والرصاص بنسبة 0.2% كمجموعة
ضايقة (موجهة).

وتغذية المجموعات (3و4و5) على الغذاء الأساسي مع خليط السموم وأوراق
المورينجا في نسبة مختلفة 2.5 و 5 و 10%. وفي نهاية فترة التجربة، تم قياس عدد أكاساب
الوزن- معدل كفاءة الغذاء - الغذاء الماكول - الوزن النسبى للأطعمة- مستوى الجلوكوز-
أنزيمات الكبد (GOT,GPT,ALP) - وظائف الكلى (اليوليرك - حامض البهرامك - الكريتيتين) -
الكليستيرول الكلي (TG) - TC (الجليريدات الثلاثية) - الاميلوربينات (مرتفعة،$

تم فحص السهولة الوظيفية على الكبد وأشارة النتائج إلى أن الفئران المصابة بخليط
السموم التي تتشوى على الغذاء الأساسي مع 10% من أوراق المورينجا تظهر بزيادة كبيرة
في وزن الجسم ووزن الأعضاء وجلوكوز الدم والكليستيرول والدهون الثلاثية ووظائف الكلي
وانزيمات الكبد وانخفاض في الليپوپروتينات المرتفعة حدث تحسن لكلي القيادات (أكد التشريح
الهستولوجي هذه التحسينات).

الكلمات المفتاحية: فئران أسرايجلوني، خليط السموم (الرصاص والكادميوم)، أوراق
المورينجا، انزيمات الكبد ووظائف الكلي.