Histopathological changes induced after oral administration of acetamiprid in kidneys of male albino mice

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Abstract
Repeated oral administration of (10 and 20 mg/ml) of Acetamiprid (ACP) - a neonicotinoid insecticide that is effective against both soil and plant insects (LD50=200mg\kg), for 14 days in male albino mice aged (6-7weeks) induced significa
\4nt changes in the histoarchitecture of the kidneys included marked congestion, tubular cell degeneration and sloughing of epithelial cells. haemorrhage and sever necrosis observed depend on the dose . The oral toxicity study of (ACP) revealed that this neonicotinoid insecticide is of highly risk in albino mice

Key words: Pesticide, Neonicotinoid, Acetamiprid, Histopathology.

التغيرات النسجية المرضية في كلى ذكور الفئران البيضاء والمستحثة بفعل الجرع الفموية للاسيتامبريد

مها عبد النبي غثوان
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الخلاصة:

عرضت مجموعه من ذكور الفئران البيض بعمر(6-7) أسابيع، ولمدة 14 يوم، لجرع متكررة بلغت 10-20 ملغم /مل من مبيد الاسيتامبريد (ACP)، وهو مبيد حشري من النيونيكوتينويدات الفعالة ضد كل من حشرات التربة والنباتات، وقد اظهرت النتائج وجود تغايرات مرضية نسجية شملت البنية النسجية للكلى، واحتقان ملحوظ فضلاً عن تنكس خلايا النبيبات الكلوية وانسلاخ الخلايا الظهارية مع نزف وتنخر نسيجي حاد، مع زيادة الجرعة المعطاة. وافادت الدراسة بخطورة المبيد على حيوانات التجربة.

Introduction

Insecticides are chemical substances used to control insects by killing them or preventing them from engaging in undesirable or destructive behaviors [1]. Insecticides could affect the physiological make-up of the target pests by causing changes in growth, development and reproduction parameters, or by causing changes in the nutritional contents of the host plants, which may result in enhanced developmental time, decreased survival, fecundity and reproduction or other changes in the behavior of the target pest Insecticidal effects on biological parameters of insects potentially have an ecological impact [2].

Neonicotinoids are the latest major class of insecticides with a novel mode of action. These insecticides are very important in agriculture because they are efficient against a broad spectrum of insect pests [3]. Most neonicotinoids are water-soluble and break down slowly in the environment, so they can be taken up by the plant and provide protection from insects as the plant grows. Neonicotinoids are currently used on corn, canola, cotton, sorghum, sugar beets and soybeans. They are also used on the vast majority of fruit and vegetable crops, including apples, cherries, peaches, oranges, berries, leafy greens, tomatoes, and potatoes. The use of neonicotinoids has been linked in a range of studies to adverse ecological effects, including honey-bee colony collapse disorder (CCD) and loss of birds due to a reduction in insect populations [4,5,6,7].

Acetamiprid is a neonicotinoid insecticide, which is a class of neuro-active insecticides modeled after nicotine. Nicotine was identified and used as an insecticide and rat poison as early as the 1600's. Its effectiveness as an insecticide spurred a search for insecticidal compounds that have selectively less effect on mammals, which led to the discovery of neonicotinoids. Neonicotinoids, like nicotine, bind to nicotinic acetylcholine receptors of a target cell [8,9]. These compounds are extensively applied to control pest insects in different agricultural crops; however they can also affect non target organisms (humans or biota). Still a limited number of studies are referring to neonicotinoids in terms of potential hazard for additive/cumulative effects on human health and to toxic effects of their transformation products on aquatic non target organisms [10-12].

Materials and Methods

Eighteen animals (aged 6-7 weeks) of albino male mice were used and distributed into three groups, each with 6 mice. First group was normal controls, which were administrated orally with 0.1 ml of distilled water. Second group (A GROUP) included mice orally administrated with acetamiprid (10 mg/ml), for two weeks. Third group (B GROUP) was orally administrated with acetamiprid (20 mg/ml) for two weeks.

Histopathology

Half of the mice were sacrificed (under anesthesia) on day 7, and the rest on day 14 ,and were examined by conducting postmortem examination for the presence of gross pathological changes and then tissue samples (kidney) were dissected out and cleaned with physiological saline solution (0.89%). The tissues were immediately put in 10% neutral formalin solution for subsequent processing and histopathological studies. The formalin fixed tissues were thoroughly washed in running tap water, dehydrated in ascending grades of alcohol and acetone, cleared in xylene, and embedded in paraffin wax at 58 °C. Five microns thickness sections from paraffin embedded tissues were stained with haematoxyline and eosin (H&E) stain [13].

Results

There was a significant change in the histoarchitecture of the kidneys, especially in the second half of the experiment for both concentrations (10, 20 mg/ml) of acetamiprid. Photomicrographs of a section of the kidneys after 7 days of insecticide exposure (Fig 1 and 4) showed mild tubular cell hydropic degeneration with cellular swelling. Some sections of kidneys of administration of acetmiprid (10 mg/ml) for

day 7 showed shrunken glomerulus and nucleated tubules filled with protein cast (fig 3).

The nephritic changes continued as the experiment progressed, with marked congestion, and necrotic tubular epithelium (pyknotic nuclei and acidophilic cytoplasm), and collecting duct degeneration and sloughing of epithelial cells becoming evident on day 14 of treatment, for the two concentrations, (Fig. 2, 5). At day7of 20mg/ml of pesicidal administration, there may be a small but significant increase of focal to multifocal foci of tubule basophilia, nuclear crowding, peritubular basement membrane thickening, and variable infiltration by mononuclear inflammatory cells, and hyaline casts are prominent (Fig 6).

Discussion

All new pesticides are tested to establish the type of toxicity and the dose necessary to produce a measurable toxic reaction. In order to compare the results of toxicity tests done in different labs, there are strict testing procedures. Toxicity testing is extensive (involving many phases) and therefore expensive. Humans, obviously, cannot be used as test subjects, so toxicity testing is done with animals and plants. Since different species of animals respond differently to chemicals, a new chemical is generally tested in mice, rats, rabbits, and dogs. The results of these toxicity tests are used to predict the safety of the new chemical to humans [14]. Histopathological biomarkers can be indicators of the effects on organisms of various pollutants and are a reflection of the overall health of the entire population in the ecosystem. The alterations in cells and tissues in vertebrates are recurrently used biomarkers in many studies. Histopathological biomarkers embody tissue lesions arising as a result of a previous or current exposure of the organism to one or more toxins. Well-documented lesions based on experimental data in liver, ovary, skeleton system and skin have been used as biomarkers to date [15]. Histopathological biomarkers are closely related to other biomarkers of stress since many pollutants have to undergo metabolic activation in order to be able to provoke cellular change in the affected organism. histopathological lesions may arise from pollutants or diseases, provoking necrotic and degenerative alterations to which the organism responds with an inflammatory, defensive reaction [16, 17]. An increased number of macrophagic aggregates can be found in the liver, kidney and spleen in fish exposed to chemical pollutants, bacteria, fungi or parasites [18].

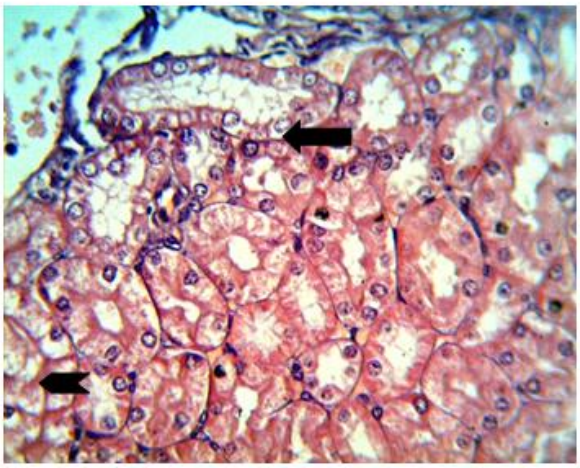
Degeneration of the epithelial cells of the renal **proximal convoluted tubule** (PCT) has been found in the toxicity of asbestos [19]. Severe congestion of the blood vessels, desquamation or necrosis of the epithelial cells of the tubules and proliferation of the endothelial cells of the glomeruli were seen in the kidney of goats due to cypermethrin intoxication [20]. Whereas, mild degenerative changes such as cellular swelling and necrosis were noticed in rats receiving cypermethrin [21, 22] mentioned that moderate degree of degenerative and necrotic changes in proximal convoluted tubules (PCT) and distal convoluted tubules (DCT) was found to be noted in the rats of 25 mg/kg of acetamiprid administration , while the rats of 100 mg/kg group there were congestion and hemorrhages in kidney. Moderate degenerative and necrotic changes were noted in the rats of 100 mg/kg group of (ACP). Rats of 200 mg/kg group revealed degenerative and necrotic changes in PCT and DCT of kidney. In some area of kidney tubular cells had undergone complete lyses leaving reticular framework and that was near to this study observation, Coagulative necrosis and degeneration of tubular epithelium were reported by [23,24] in NDEA induced oxidative stress in albino rats.

In the present study possibly progressive dehydration in (A&B groups) causing decrease in glomerular filtration rate and lesser blood supply through efferent artery to PCT and DCT resulted in low nutrient supply leading necrosis and lysis of the cell. similar to the results of[25] . As an analysis parameter the (ACP) has induced histopathological effects on mice all dose

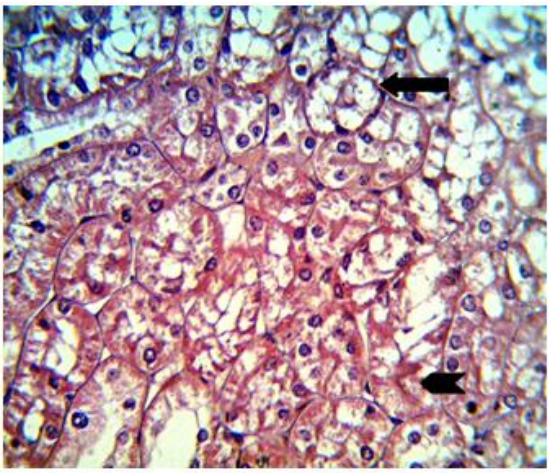
levels when exposed for a period of 14 days , It seems that the ACP at the dose dependent levels tested. in the present study for a period of 14 days The above findings suggested that the kidney as the excretory organ suffered the maximum damage. as mentioned by [26].

Conclusion:

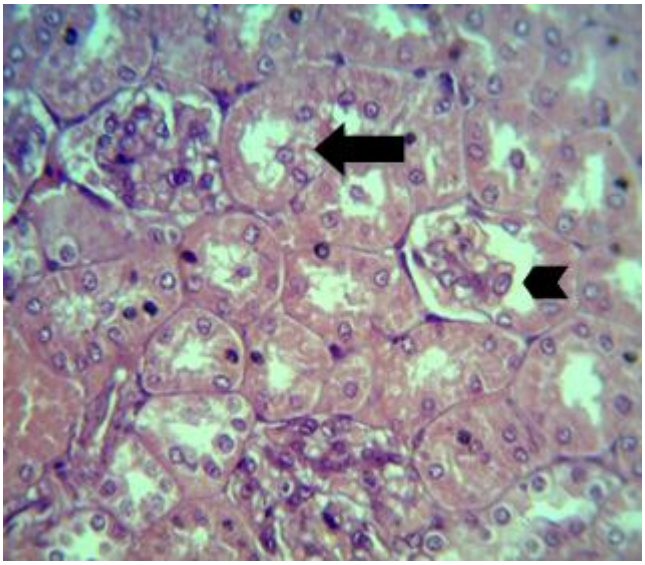
It is now clear that more studies are required to understand the toxicity of ACP on animal health hazards and establish guidelines for acceptable residues in the environment.



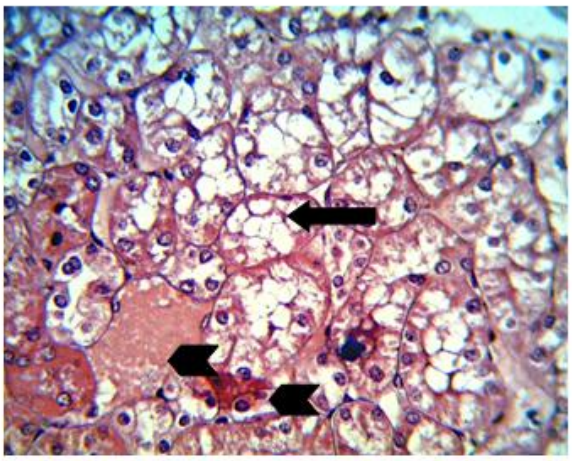
(Fig. 1): Photomicrographs of a section of a kidney of the albino mouse after the administration of acetmiprid (10 mg/ml) day7, showing: mild tubular epithelial cells degeneration(arrow)with cellular swelling (arrow head). H&E. x 400.



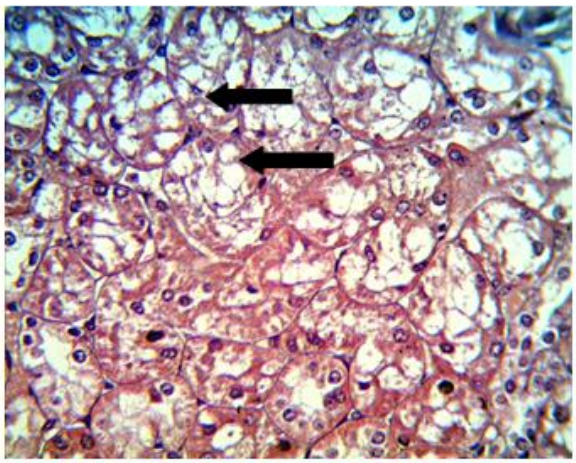
(Fig. 2): Photomicrographs of a section of a kidney of the albino mouse after the administration of acetmiprid (10 mg/ml) day14, showing: sloughed off tubular epithelial cells lying in the lumen of convoluted tubules (arrow) with mild tubular necrosis(arrow head). H&E. x 400.



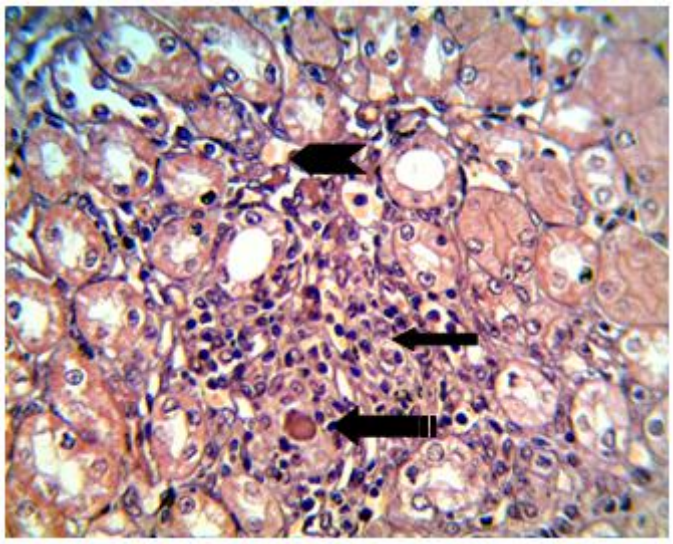
(Fig .3): Photomicrographs of a section of a kidney of the albino mouse after the administration of acetmiprid (10 mg/ml) day7, showing: shrunken glomerulus (arrow) and nucleated tubules filled with protein cast(arrow head). H&E. x 400.



(Fig.4): Photomicrographs of a section of a kidney of the albino mouse after the administration of acetmiprid (20 mg/ml) day7, showing: sever degeneration of tubular epithelial cells(arrow) with heamorage(arrow head). H&E. x 400.



(Fig. 5): Photomicrographs of a section of a kidney of the albino mouse after the administration of acetmiprid (20 mg/ml) day14, showing: severe acute tubular necrosis(arrows). H&E. x 400.



(Fig. 6) Photomicrographs of a section of a kidney of the albino mouse after the administration of acetmiprid (20 mg/ml) day7, showing: small but significant increase of focal to multifocal foci of tubule basophilia(striped arrow), nuclear crowding, peritubular basement membrane thickening, and variable infiltration by mononuclear inflammatory cells(arrow), and hyaline casts are prominent.(arrow head). H&E. x 400.

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