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Renal Lesions Induced by Pyrethroid Inhalation in Albino Rats

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Abstract: The effect of pyrethroid inhalation was studied on the kidney of Albino rats. The results revealed that animals inhaled tetramethrin for 15 days showed a significant increase in serum creatinine and blood urea nitrogen. Histological examination of the kidney of treated animals indicated marked symptoms of renal tissues impairment. The renal tubules lost their characteristic appearance and their linning epithelial cells appeared with cytoplasmic vacuolation. The glomeruli were degenerated and the renal blood vessels were congested. The intertubular spaces were infiltrated by inflammatory leucocytic cells. The magnitude of these changes was time-dependent, being more prominent after 15 days of treatment.

Key words: Pyrethroid, kidney, creatinine, histopathology.

Introduction

The wide spread utilization of insecticides in insect control has performed the need for evaluation of the hazards caused by such substances. Pyrethroids have been known as insecticides for many years. The source of pyrethroids is the flowers of the pyretherum plant *Chrysanthemum cinerariafolium* (McLaughlin, 1973). Due to the persistence of these insecticides in the environment, structures similar to pyrethroids have been synthesized and proved to be effective against different insects (Casida, 1973). On the other hand, pyrethroids were found to produce serious side effects of different types such as mutagenic, teratogenic, embryotoxic or gonadotrophic effects (Sakr and Azab, 2001). Moreover, animals exposed to these insecticides exhibited disturbance in their physiological activities beside other histopathological features (Kulkarni and Hodgson, 1980; Abu-El Zahab *et al.*, 1993; Sakr, 1999; El-Banhawy *et al.*, 2000). Extensive studies had been made to investigate the histopathological effects of pyrethroids, but little attention has been paid to its effect on the kidney. Therefore, it seems desirable to study the effect of one of these pyrethroids, tetramethrin, on the kidney of albino rat.

Materials and Methods

Sexually mature male albino rats (*Rattus norvigicus*) weighing 275 ± 5g. were used. Animals were kept in the laboratory under constant conditions of temperature (24 ± 2°C) for at least one week before and throughout the experimental work, being maintained on a standard diet and water were available ad-libitum. Animals were divided into two groups. Rats in the first group (25 animals) each inhaled 1ml of the pyrethroid, tetramethrin, once every two days for 15 days. Animals were kept individually in a closed cage and 1 ml of the pyrethroid was sprayed in each cage for 5 minutes (Sakr, 1999). This pyrethroid is obtained from local markets and is used as an insecticide for cockroaches and ants. It contains 0.20% tetramethrin, 1% propoxur and 98.8% solvents and propellants. Animals in the second group (15 animals) were used as controls.

The treated animals and their controls were sacrificed by decapitation after 3, 6, 9, 12 and 15 days of treatment. For creatinine and urea nitrogen determination, sera were obtained by centrifugation of the blood samples and stored at -20°C until essayed for the biochemical parameters. Serum creatinine and urea nitrogen were measured. Commercial Randox kits were used in these analyses. The results were analyzed statistically using Student's "t" test.

For histological study, kidneys were removed and fixed in Bouin's fluid for 24 hours. After fixation, the tissues were dehydrated through ascending grades of ethanol. Thereafter, it was cleared in xylene and finally embedded in paraffin wax. Using a rotary microtome, specimens were sectioned at 5 μm and sections were mounted on clean slides and stained with haematoxylin and eosin.

Results

Data (Table 1) shows that there was an elevation in creatinine in the serum of treated animals compared with that of control. This increase was significant ($p < 0.05$) after 9,12 and 15 days of treatment. Blood urea nitrogen exhibited a significant increase only after 12 and 15 days of treatment with tetramethrin.

Histological examination of the kidney of control rat revealed that it is divided into an outer, granular appearing cortex and an inner, striated-appearing medulla. It is composed of a huge number of functional filtering units called nephrone. Each nephrone consists of a dilated portion, the renal corpuscle; the proximal convoluted tubule; the thin and thick limbs of the loop of Henle; and the distal convoluted tubule. The renal corpuscle consists of a tuft of capillaries, the glomerulus, surrounded by a double walled epithelial capsule called Bowman's capsule. The internal layer of the capsule envelops the capillaries of the glomerulus and is called the visceral layer, whereas the external layer forms the outer limit of the renal capsule and is called the parietal layer. Between the two layers of the capsule is the urinary space. The parietal layer consists of a simple squamous epithelium supported by a basal lamina and a thin layer of reticular fibers. The proximal convoluted tubule is lined by simple cuboidal or columnar epithelium. Its cells have an acidophilic cytoplasm and the apex possesses abundant microvilli which form a brush border. The distal convoluted tubule is lined by simple cuboidal epithelium. The cells of the collecting tubules and ducts stain

Table 1: Effect of tetramethrin on creatinine and urea nitrogen in Sera of Albino rats

Days after treatment	Creatinine (mg dl^{-1})	Urea nitrogen (mg dl^{-1})
3	0.62 ± 0.01	30.22) ± 2.1
6	0.71 ± 0.03	28.12 ± 1.6
9	1.12 ± 0.06*	32.17 ± 4.1
12	1.43 ± 0.04*	36.9 ± 3.6*
15	1.51 ± 0.05*	37.8 ± 4.3*
Control	0.7 ± 0.02	30.6 ± 1.3

Each value represents mean ± standard deviation
* Significant at $p < 0.05$)

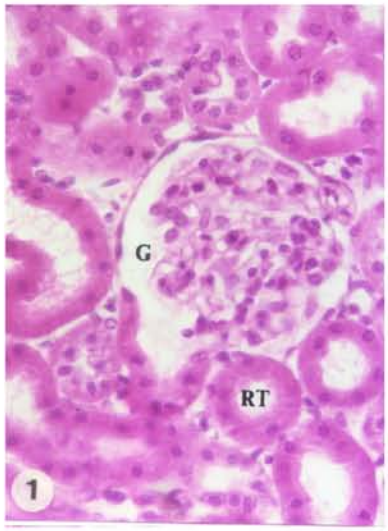

Fig. 1: T. S. in the kidney of a control rat showing a glomerulus (G) and renal tubules (RT), x 450

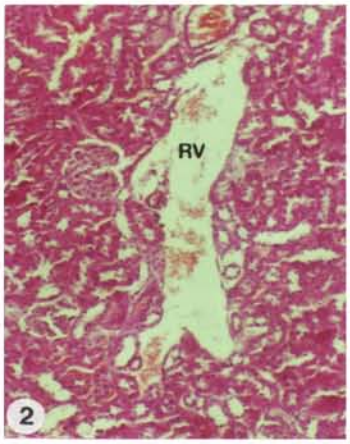

Fig. 2: Section in the kidney of a rat treated with tetramethrin for 9 days showing dilated and congested renal vein (RV), x 165

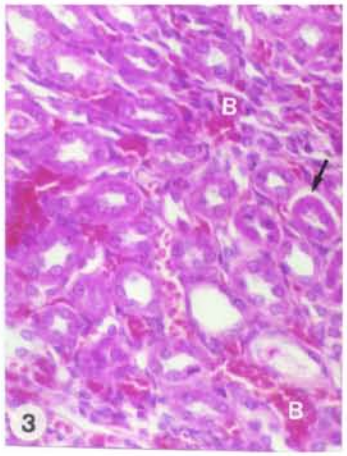

Fig. 3: Section in the kidney of a treated rat showing blood hemorrhage (B) in the intertubular space. The renal tubules appeared with swollen epithelial lining and desquamated from the underlying basement membrane (arrow) x 350

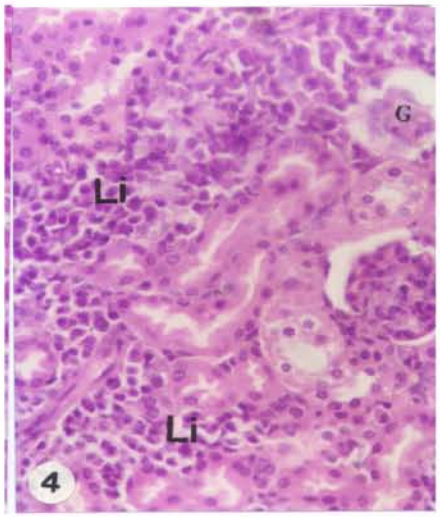

Fig. 4: Section in the kidney of a treated rat showing leucocytic infiltration (Li) and degenerated glomerular capillaries (G), x 350

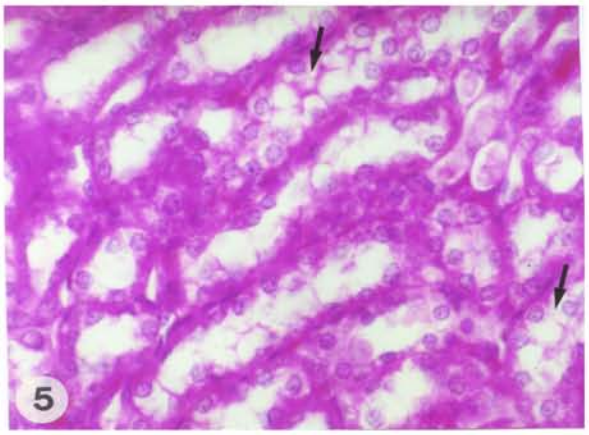

Fig. 5: Section in the kidney of a rat 21 days post-treatment with tetramethrin showing degenerated tubules with cytoplasmic vacuolation of the linning epithelia (arrows), x 350

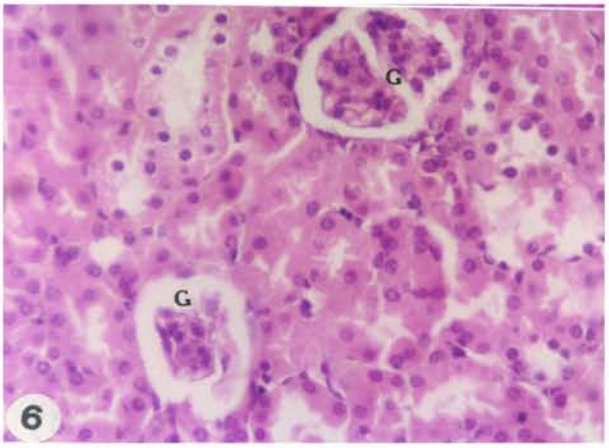

Fig. 6: Section in the kidney of a rat 15 days post-treatment with tetramethrin showing degenerated glomeruli (G), x 350

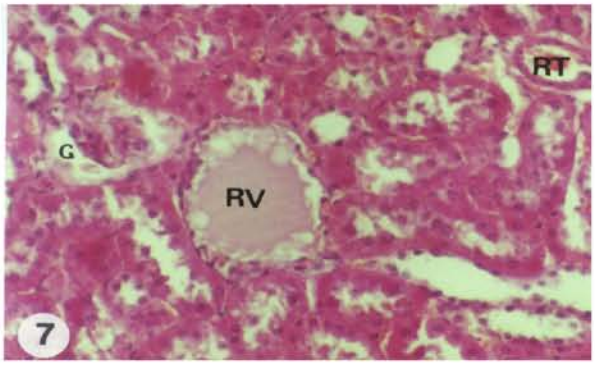

Fig. 7: Section in the kidney of a treated rat showing congested renal vein (RV) and renal artery (RT), x 350

weakly with the usual stains (Fig. 1).
Inspection of kidneys of animals after 3 and 6 days of treatment showed insignificant changes. After 9 days, examination of the kidney sections revealed that most of the renal blood vessels were dilated, congested and engorged with blood (Fig. 2). The intertubular spaces in the cortex and medulla were found to contain large quantities of homolyzed blood extravasted from the damaged blood vessels (Fig. 3). The tubular epithelial linning cells exhibited signs of cloudy swelling but with normal nuclei and some tubules were desquamated from their underlying basement membrane (Fig. 3). The glomerular capillaries were degenerated and the intertubular spaces were infiltrated by inflammatory leucocytic cells (Fig. 4). Such histopathological changes were increased after 12 and 15 days of treatment. The renal tubules rendered so highly damage that they have almost lost their characteristic appearance and their lining epithelial cells became undistinguished and their contents were intermixed with each other. In addition, many cells appeared with cytoplasmic vacuolation (Fig. 5). The walls of Bowman's capsule were eroded and the glomeruli were atrophied and in some sections appeared as empty spaces containing amorphous cellular debris (Fig. 6). The renal veins and arteries were congested and their linning epithelium were obviously eroded (Fig. 7).

Discussion

Results showed that rats inhaled pyrethroid exhibited an increase in serum creatinine and blood urea nitrogen. This increase was significant after 12 and 15 days of treatment. Abu-El-Zahab *et al.* (1993) obtained same results in rats that inhaled mixed pyrethroids (tetramethrin and sumithrin). These compounds were also elevated in rats treated with DD-T_{80} parallethrium (Seki *et al.*, 1987) and after dermal application of fenvalerate and decamethrin (Mohamed, 1988).
Treating animals with tetramethrin induced many histopathological alterations in the kidney. The most marked symptoms of renal tissues impairment were destruction of renal tubules, congestion of blood vessels, degeneration of glomeruli and marked abundance of leucocytic infiltration. The magnitude of these changes appeared to be time dependent, being more prominent after 15 days of treatment.
Although kidney is the second target organ in body for many toxic materials, relatively few studies have been done on the effect of pyrethroids on such organ. Abu El-Zahab *et al.* (1993) observed congestion of blood vessels, hemorrhage, necrosis and inflammatory leucocytes in kidneys of rats inhaled pyrethroids. Abdeen *et al.* (1994) reported that treating mice with fenvalerate induced renal damage of the epithelial linning of the renal tubule, ruptured of the distal tubules and enlargement of the glomerulei with hydropic degeneration. Abou-Zeid and El-Balshy (1995) reported that inhalation of Ezalo (a synthetic pyrethroid) caused acute tubular necrosis and glomerulonephritis in kidneys of new born mice. Subchronic feeding of decaboxy fenvalerate was found to induce glomerulonephrosis in kidney of rats (Parken *et al.*, 1986).
Among the pathological symptoms observed in the present work was the remarkable abundance of leucocytic infiltration in the kidneys of tetramethrin-treated rats. A similar result was also reported by some investigators in various animals subjected to different insecticides (Hurket, 1978; Abdel- Rahman and Zaki, 1992). These leucocytes are implicated in the process of phagocytosis of extracellular particles and dead cells and their increase in the body tissues is a good sign of body self-defense (Stevens and Lowe, 1992).
The results concluded that tetramethrin affected the glomeruli. The glomeruli injury is accompanied by a rapid decline in glomerular function progressing to renal failure in a few weeks. This renal failure is accompanied by oliguria with an elevation in serum creatinine and blood urea nitrogen (Couser, 1988). Thus, the present work collectively indicated that pyrethroid inhalation induced kidney injury in albino rats.

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