



## Imidacloprid Induced Histopathological Alterations in the Kidneys of Male Swiss Albino Mice

## KEYWORDS

Imidacloprid, histopathology, kidneys, albino mice

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**ABSTRACT** Six groups of male Swiss albino mice (A, 0.4 mg/kg bw; B, 0.8 mg/kg bw; C, 1.6 mg/kg bw; D, 3.2 mg/kg bw; E, 4.0 mg/kg bw and F, 8.0 mg/kg bw) (6 in each group) were orally administered with different doses to understand the nephrotoxicity of imidacloprid insecticide. Another group (G) of 6 mice served as controls. Two mice from each of test group were necropsied on day 4, 16 & 30 after treatment; two mice from the control group were also necropsied on the same designated days. Kidney tissues were fixed, sectioned and stained for histopathology. Kidney tissue of test mice in all the groups showed haemorrhages, glomerular atrophy and tubular degeneration and necrosis on day 4, 16 and 30 of experiments. The toxicity of imidacloprid is found to be severe on day 30 of treatment in mice of all the test groups.

## INTRODUCTION:

Imidacloprid, a systemic insecticide was the first chloronicotinyl insecticide, and is the largest selling insecticide world wide (Mencke and Jeschke, 2002). It affects the central nervous system, leading to paralysis and death of insect. Liver and kidneys of male rats exposed to carbendazim showed congestion, enlargement of the sinusoids, hyperplasia of kupffer cells, mononuclear cell infiltration and hydropic degeneration in liver at low doses (300 mg/kg) and congestion, mononuclear cell infiltration, tubular degeneration and fibrosis in kidneys, at higher doses (600 mg/kg) (Selmanoglu et al., 2001). Premlata et al., (2004) reported no histological lesions in liver, kidneys or heart of rats exposed to low doses (20 mg/kg) of imidacloprid; congestion and cloudy swelling in liver, mild congestion in kidneys and mild haemorrhages in heart at high dose (40 mg/kg). Khogali et al., (2005) found congestion, swollen and shrank glomeruli in the kidneys of Swiss albino mice treated with dimethoate. Bowman's capsular cells showed hypoplasia. Malnourished and diabetic rats treated with pesticides showed severe demarcated tubular necrosis in kidneys (Benjamin et al., 2006). Carbosulfan treated (orally) albino mice showed vacuolization, hypertrophy, hyalinization and loss of radial arrangement of hepatocytes in liver (Ksheerasagar and Kaliwal, 2006). Male wistar rats treated with fenitrothion showed tubular dilation and atrophy in renal cortex, degeneration of parenchymatous cells of renal tubules and infiltration in between the proximal tubules (which was more significant in high dose 100 mg/kg) in kidneys (Kerem et al., 2007). Kidneys of test rats revealed marked tubular dilation, hydropic degeneration in tubular epithelium, moderate congestion and haemorrhage in the cortex and medulla during fenitrothion treatment (Simin, 2008). Desai and Desai (2008) investigated the toxic effect of intraperitoneally administered dichlorvos in mice and found damaged glomerulus, necrosis and sloughing of tubular epithelium in kidneys. Kidney of rats exposed to deltamethrin @ 1.28 mg/kg bw per day for 30 days showed mild necrotic changes and severe ultra structural changes (El-Gerbed, 2012). Al-Sharqi et al., (2012) reported histopathological alterations in liver and kidneys of albino mice exposed to actara 25 WG insecticide; lobulated glomeruli, haemorrhage, congested blood vessels, degenerative changes and infiltration of inflammatory cells. These changes became severe with the increase in dose and duration of exposure. The present investigations are designed to study the histopathology of kidneys in male Swiss albino mice treated with various oral doses of imidacloprid.

## Material and Methods:

Male Swiss albino mice weighing about 23-26 gms (6-8 weeks old) were used for this study. They were maintained on a standard diet and water ad libitum. The experiments were conducted according to the guidelines laid down by CPCSEA. Imidacloprid was orally administered to six groups (six in each) of mice (A, 0.4 mg/kg bw/mouse; B, 0.8 mg/kg bw/mouse; C, 1.6 mg/kg bw/mouse; D, 3.2 mg/kg bw/mouse; E, 4.0 mg/kg bw/mouse and F, 8.0 mg/kg bw/mouse). Another group (G) six mice served as controls. Tissues of kidney and spleen from both experimental and control mice were fixed in Bouin's solution and embedded in paraffin wax. Tissues were sectioned at 5 µm, processed and stained in Haematoxylin and Eosin for histopathology.

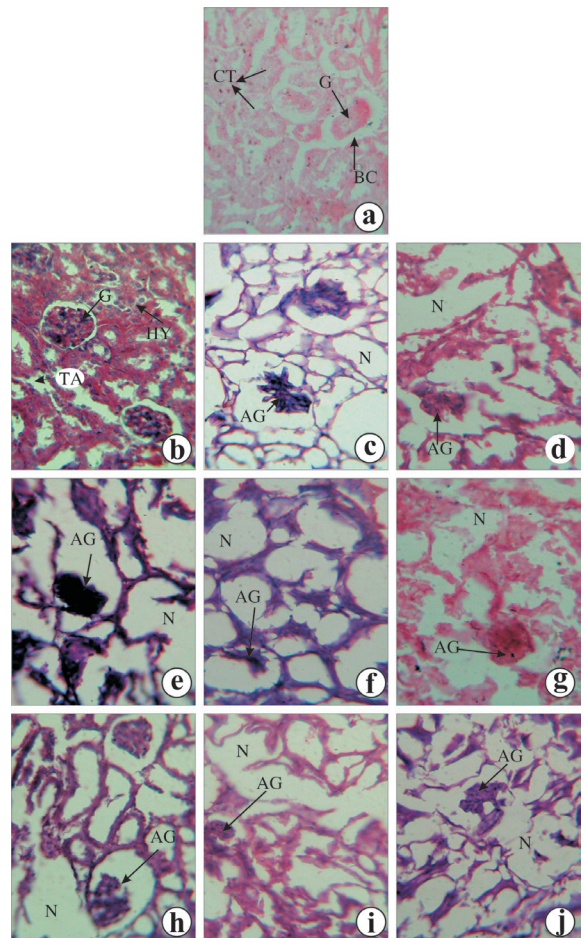
## Result and Discussion:

**In control group (G):** In the normal (untreated) mouse, the sections of kidney cortex exhibited normal structure of renal corpuscles, renal tubules (proximal and distal) and collecting ducts (Fig. 1a). The tissue response of mouse kidney in control (group G) and experimental mice treated with 0.4 mg/kg (group A), 0.8 mg/kg (group B), 1.6 mg/kg (group C), 3.2 mg/kg (group D), 4.0 mg/kg (group E) and 8.0 mg/kg (group F) was studied on day 4, 16 and 30 of experimental period and showed in figures 1 and 2.

Figures 1 and 2 (except in Fig. 1a) showed the degenerative changes in the kidney of the treated series. The following changes were recognised: (i) progressive decrease in the number of Bowman's capsules, (ii) progressive increase in the irregular shape of these bowman's capsules; (iii) progressive increase in the demarcation of proximal and distal convoluted tubules; (iv) appearance of large vacuoles and the degraded products on day 30 (Fig. 1d, 1g, 1j; Fig. 2c, 2f, 2i); (v) no congestion; (vi) haemorrhages in cortex and medulla. These degenerative changes resulted in the loss of appearance of proximal and distal convoluted tubules on day 4, 16 and 30 of treatment period in all the experimental groups. Among these, most apparent were the following: (i) reduction of bowman's capsules on day 16 in mice treated with 0.8 mg/kg (Fig. 1f), 1.6 mg/kg (Fig. 1i), 3.2 mg/kg (Fig. 2b), 4.0 mg/kg (Fig. 2e) and 8.0 mg/kg (Fig. 2h). (ii) destruction of proximal and distal convoluted tubules on day 4, 16 and 30 in mice treated with all the test doses; (iii) Loss of cuboidal epithelial cells in the bowman's capsule on day 4, 16 and 30 of test mice treated with varied doses of like 0.4 mg/kg, 0.8 mg/kg, 1.6 mg/kg, 3.2 mg/kg, 4.0 mg/kg and 8.0 mg/kg.

The histopathological observations on the kidneys of all the experimental groups clearly indicate the progressive decrease in the number of bowman's capsules, progressive increase in the irregular shape of bowman's capsule and demarcation of proximal and distal convoluted tubules and the formation of large vacuoles (with degraded products) on day 30. These changes are similar to that of Aughey et al., (1984), Selmanoğlu et al., (2001) and Brzoska et al., (2003) who also reported tubular necrosis and degeneration of epithelial cells in renal tubules in rats exposed to carbendazim and cadmium and ethanol respectively. Absence of congestion in the kidney of all the treated mice (0.4 mg/kg - 8.0 mg/kg) on day 4, 16 and 30 of treatment confirm that of Premlata et al., (2004) who reported mild congestion in rat kidneys when administered with imidacloprid at 40 mg/kg. In the present study, the test kidneys showed swelling of the tubules and lining of the bowman's capsules which are probably related to disturbance of the ionic milieu of the cells caused by the imidacloprid as suggested by Khogali et al., (2005) in mice treated with dimethoate 40 EC. The microscopic changes observed in test kidneys are (in all the groups of experimental mice), degeneration of parenchymatous cells of renal tubules, glomerular atrophy, haemorrhages and necrosis in tubules. These effects are similar to that of Benjamin et al., (2006) and Kerem et al., (2007) who reported pesticide mixture of monocrotophos, endosulfan and hexachlorocyclohexane and fenthion toxicity in rats. Degenerative changes in the proximal and distal convoluted tubules in the kidneys of test mice in the present study confirm that of Jankeer and El-Nouri (2009), and Inayat et al., (2007) who reported similar observations during pesticide toxicity. Degeneration of renal tubules, shrunken glomerulus and renal tubular necrosis confirm that of Damain et al., (1992), Abdel-Mageid (1994) and Lamfon and Al-Rawi (2007) (in rats treated with pesticides). Simin et al., (2008) reported tubular dilation, moderate congestion and haemorrhages in the cortex and medulla of kidneys. Desai and Desai (2008) also reported damaged glomeruli, necrosis and sloughing of tubular epithelium in mouse kidney exposed to dichlorvos. The presence of haemorrhages in cortex and medulla of kidneys (in groups A to F) is similar to that of Afshar et al., (2008) who also found haemorrhages in the cortical and medullary part of the kidneys. The occurrence of vacuolation and haemorrhages in cortex and medulla (in all the treated groups) confirm that of Mahmoud and Mahmoud (2010) who also found high vacuolation and haemorrhages and damaged cells in cortex and medulla of female rat kidneys administered with thiamethoxam and emamectin benzoate. Soliman et al., (2010) reported glomerular sclerosis and tubular injury in rat kidneys exposed to gibberillic acid. Uzun and Kalender (2011) and Tripathi and Srivastav (2011) found mononuclear cell infiltration, glomerular atrophy and degeneration of renal tubules in rat kidneys exposed to malathion and cadmium chloride respectively. Disarrangement of renal cortex and medulla, haemorrhages and abnormal structure of renal corpuscles were found in the kidneys of rats exposed to one month carbendazim exposure (Zari and Al-Attar, 2011). Cyromazine and chlorpyrifos induced vacuolization, swelling and degeneration in the endothelium of glomerular tuft and the epithelium of lining tubules in kidneys of rats was reported by Heikal et al., (2012). The appearance of degenerative changes in imidacloprid intoxicated kidneys in the present study confirm that of Somia and Madiha (2012) who also found tubular vascular degeneration and lumen dilation in the kidneys of mice treated with dichlorvos and fenitrothion. El-Gerberd (2012) reported mild necrotic changes in rats treated with deltamethrin. Tubular degeneration, glomerular atrophy, leucocytic infiltrations and congestion of renal blood vessels were noticed during deltamethrin - intoxication in kidneys of male wistar rats (Sakr and Al-Amoudi, 2012). Kammon et al., (2010) found haemorrhages, vacuolar degeneration of tubular epithelial cells in chlorpyrifos treated and sub-capsular haemorrhages, coagulative necrosis of tubular epithelium in imidacloprid intoxicated kidneys of layer chickens. The appearance of rudimentary glomerulus, degenerated bowman's capsules, degenerated cytoplasm in convoluted tubules, haemorrhages, necrosis and vacuolization in all groups of mice (on day 4, 16 &

30) confirm that of Kumar et al., (2011) in kidneys of mice treated with chlorpyrifos and Khseerasagar et al., (2011) in kidneys of mice treated with carbosulfan and of wistar rats treated with acrylamide. Al-Sarar (2012) observed dose-related degenerative changes in kidneys of male mice intoxicated by lambda-cyhalothrin. Al-Sharqi et al., (2012) noticed large haemorrhagic areas, lobulated glomeruli, congested blood vessels, degenerative changes and infiltration of inflammatory cells in kidneys of insecticide (actara) treated mice.



**Figure 1:** Effect of different doses of imidacloprid on the kidney of male Swiss albino mice (400x). **a**, control; **b**, 0.4 mg/kg (day 4); **c**, 0.4 mg/kg (day 16); **d**, 0.4 mg/kg (day 30); **e**, 0.8 mg/kg (day 4); **f**, 0.8 mg/kg (day 16); **g**, 0.8 mg/kg (day 30); **h**, 1.6 mg/kg (day 4); **i**, 1.6 mg/kg (day 16); **j**, 1.6 mg/kg (day 30).

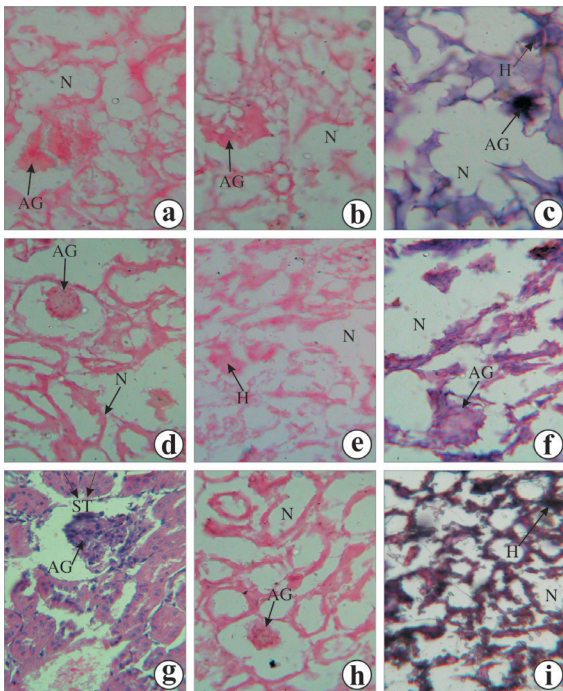
#### Figure 1

- a :** T.S. of the control mouse kidney showing glomeruli bowman's capsules and renal tubules (400x).
- b :** T.S. of the kidney of mouse (treated with 0.4 mg/kg bw) at day 4 of treatment showing normal glomeruli, bowman's capsules, slight tubular atrophy and hyperplasia (400x).
- c :** T.S. of the kidney of mouse (treated with 0.4 mg/kg bw) at day 16 of treatment showing glomerular atrophy, degenerated bowman's capsules and associated tubular structure, haemorrhages, necrotic and vacuolated tubules (400x).
- d :** T.S. of the kidney of mouse (treated with 0.4 mg/kg bw) at day 30 of treatment showing atrophied glomeruli, necrotized bowman's capsules and degeneration in tubules (400x).
- e :** T.S. of the kidney of mouse (treated with 0.8 mg/kg bw) at day 4 of treatment showing rudimentary glomeruli, degeneration of bowman's capsules, necrosis, vacuoliza-

tion and atrophy in tubules and hyperplasia (400x).

- f : T.S. of the kidney of mouse (treated with 0.8 mg/kg bw) at day 16 of treatment showing shrunken glomeruli necrotised bowman's capsules, necrosis and tubular degeneration at certain places (400x).
- g : T.S. of the kidney of mouse (treated with 0.8 mg/kg bw) at day 30 of treatment showing atrophied glomerulus, degenerated bowman's capsules, necrosis and severe tubular atrophy (400x).
- h : T.S. of the kidney of mouse (treated with 1.6 mg/kg bw) at day 4 of treatment showing glomerular atrophy, necrosis and destructed renal tubular structure (400x).
- i : T.S. of the kidney of mouse (treated with 1.6 mg/kg bw) at day 16 of treatment showing degeneration of glomeruli, and destructed bowman's capsules, necrosis, vacuolization and flattened tubular cells (400x).
- j : T.S. of the kidney of mouse (treated with 1.6 mg/kg bw) at day 30 of treatment showing shrunken glomeruli, destructed bowman's capsules and necrotic renal tubules and (400x).

(G, glomerulus; BC, bowman's capsule; CT, convoluted tubules; AG, atrophied glomerulus; Hy: hyperplasia; TA, tubular atrophy; N, necrosis; H, haemorrhage).



**Figure 2:** Effect of different doses of imidacloprid on the kidney male Swiss albino mice (400x). **a**, 3.2 mg/kg (day 4); **b**, 3.2 mg/kg (day 16); **c**, 3.2 mg/kg (day 30); **d**, 4.0 mg/kg (day 4); **e**, 4.0 mg/kg (day 16); **f**, 4.0 mg/kg (day 30); **g**, 8.0 mg/kg (day 4); **h**, 8.0 mg/kg (day 16); **i**, 8.0 mg/kg (day 30).

#### Figure 2

- a : T.S. of the kidney of mouse (treated with 3.2 mg/kg bw) at day 4 of treatment showing atrophied glomeruli, necrosis and destruction in convoluted tubules (400 x).
- b : T.S. of the kidney of mouse (treated with 3.2 mg/kg bw) at day 16 of treatment showing glomerular atrophy, mild necrosis in renal tubular structure, vacuolization and haemorrhages (400x).
- c : T.S. of the kidney of mouse (treated with 3.2 mg/kg bw) at

day 30 of treatment showing shrunken glomeruli, severe destruction and loss of texture of bowman's capsules and associated renal tubules and haemorrhages(400x).

- d : T.S. of the kidney of mouse (treated with 4.0 mg/kg bw) at day 4 of treatment showing glomerular atrophy, destructed bowman's capsules and parenchymatous degeneration of cells of renal tubules, necrosis and haemorrhages (400x).
- e : T.S. of the kidney of mouse (treated with 4.0 mg/kg bw) at day 16 of treatment showing atrophied glomeruli found in bowman's capsules, degenerated convoluted tubules and haemorrhages (400x).
- f : T.S. of the kidney of mouse (treated with 4.0 mg/kg bw) at day 30 of treatment showing atrophied glomeruli, destructed bowman's capsules and heavy degeneration of parenchymatous cells of renal tubules, necrosis and haemorrhages (400x).
- g : T.S. of the kidney of mouse (treated with 8.0 mg/kg bw) at day 4 showing glomerular atrophy, destructed bowman's capsular epithelium and swollen renal tubules (400x).
- h : T.S. of the kidney of mouse (treated with 8.0 mg/kg bw) at day 16 is showing atrophied glomeruli, destructed bowman's capsules and necrotised renal tubules, vacuolization, necrosis and haemorrhages (400x).
- i : T.S. of the kidney of mouse (treated with 8.0 mg/kg bw) at day 30 showing highly degeneration of glomeruli and bowman's capsules, necrosis, dilation of renal blood vessel and haemorrhages at many places (400x).

(AG, atrophied glomerulus; N, necrosis; H, haemorrhage; ST, swollen tubules).

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