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Evaluation of Nephrotoxic Effect of Endosulfan on kidney of *Cavia porcellus*

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ABSTRACT

Exposure to pesticides both occupationally and environmentally causes a range of human health problems. A vast majority of the population in India are engaged in agriculture and are therefore exposed to the pesticides used in agriculture. Endosulfan formulations are used in commercial agriculture and home gardening. Endosulfan causes degeneration of spermatozoa of mice as well as declined testosterone level. Endosulfan exposure lead to ovarian nuclear degeneration. It also causes altered liver function and hepatomegaly. Thus present study is designed to evaluate nephrotoxic effect of on biochemical and histological parameters of kidney of mice. The 'treatment' groups received Endosulfan 2 mg/kg b.w daily by gavage method for four and eight weeks. Animals were sacrificed after the scheduled treatment. Urea, uric acid and creatinine was increased many folds in endosulfan administered group of guinea pig. Degeneration was observed in glomerulus and bowmen's capsule. Tubular system of nephron show more degenerative changes. It is evident from study that endosulfan exposure causes elevated biochemical parameters of kidney and degenerative changes in tubular system of nephrons of guinea pig leading impaired nephrotoxicity in kidney.

Key words: Nephron, Hepatomegly, Glomerulus, Bowmen's Capsule

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INTRODUCTION

The countervailing risks in terms of the health and environmental effects of the pesticide alternatives as well as the economic effects on farmers, rural communities, nutrition, food security, developing countries, and foreign constituencies could be so large that they outweigh the direct effects. Exposure to pesticides both occupationally and environmentally causes a range of human health problems. It is estimated that nearly 10,000 deaths annually to use of chemical pesticide worldwide, with about three-fourths of these occurring in developing countries [1]. A vast majority of the population in India are engaged in agriculture and are therefore exposed to the pesticides used in agriculture. Pesticide is used to control sucking, chewing, and boring insects on a wide variety of vegetables, fruits, grains, cotton, and tea, as well as ornamental shrubs, vines, trees [2]. Endosulfan formulations are used in commercial agriculture and home gardening [3]. Endosulfan causes spermatozoa degeneration [4] as well as declined testosterone level. Endosulfan exposure lead to ovarian nuclear degeneration [5]. Marked hyperplasia and hypertrophy of tubuler cells in kidney are seen as a result of the effect of chronic exposure some pesticides such as malathion. Besides, an increase in excretion of potassium was significant [6]. The alterations in liver tissue such as the increase in vacuolation, sinusoidal dialation and formation of bile plugs, has been also reported by [7] in fish. Sinusoidal dialation in the liver is attributed to the impairment of outflow of the hepatic veins [8]. The mainly effected organ in endosulfan toxicity is liver. Swollen and pale livers commonly seen in this toxicity at the gross examination even in sub-acute poisoning [9, 10]. Very least work was reported on nephrotoxic potential of endosulfan on guinea pig (*Cavia porcellus*). Thus present study is designed to evaluate nephrotoxic effect of on biochemical and histological parameters of kidney of mice.

MATERIALS AND METHODS

Animals:

The guinea pigs (***Cavia porcellus***) were reared in our laboratory. The age group of guinea pig selected for the study was 12 weeks old with 600±50 gm. b.w.

Chemicals:

Organochlorine Pesticide Endosulfan, manufactured by Excel India Pvt. Ltd., Mumbai with EC 35% was utilized for the experiment. Endosulfan were dissolved in distilled water and administered 2 mg/kg b.w to test animal.

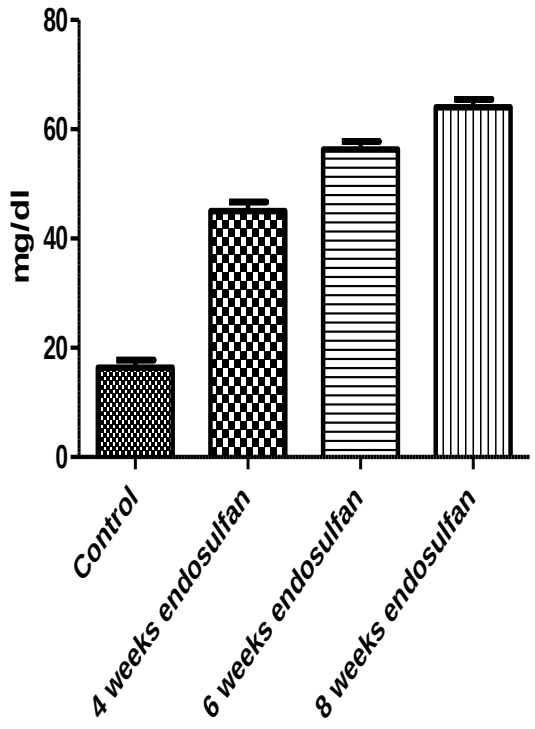
Study groups & sampling:

The animal were kept in 12 hour light and 12 hour dark at 25^{o}C temperature. The control group of

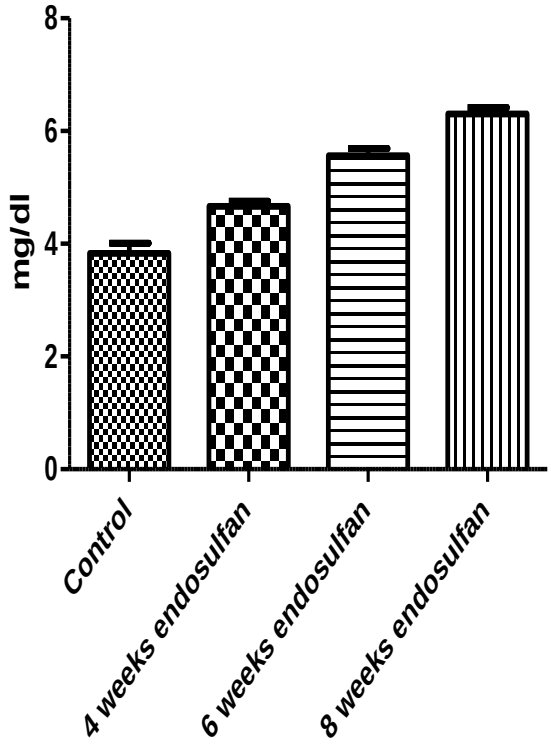
10 guinea pig received distilled water as drinking water. While the treatment groups (n=10) received Endosulfan 2 mg/kg b.w daily by gavage method for four, six and eight weeks. Animals were sacrificed after the scheduled treatment. Serum was collected for urea, uric acid and creatinine estimation, The kidney from all the animals were removed and washed three times in isotonic saline (0.85 v/w%) and fixed in neutral formaline for Light Microscope (LM) study.

RESULTS AND DISCUSSIONS

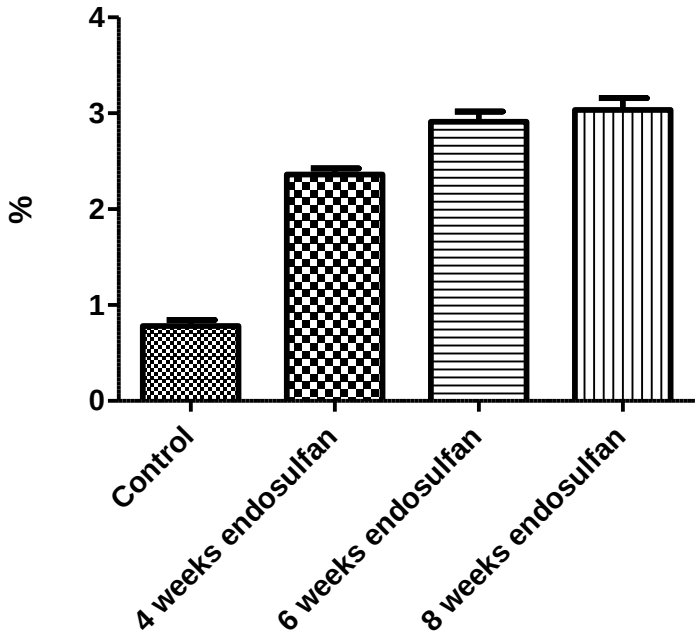
In control group urea level were 16.33 ± 1.45 mg/dl while after four weeks, six weeks and eight weeks endosulfan administration it become 45.00 ± 1.73 mg/dl, 56.33 ± 1.45 mg/dl and 64.00 ± 1.52 mg/dl respectively (Text Figure: I). In control group uric acid level were 3.833 ± 0.17 mg/dl while after four weeks, six weeks and eight weeks endosulfan administration it become 4.667 ± 0.08 mg/dl, 5.567 ± 0.12 mg/dl and 6.300 ± 0.11 mg/dl respectively (Text Figure: II). In control group creatinine level were 0.7833 ± 0.06 percent while after four weeks, six weeks and eight weeks endosulfan administration it become 2.360 ± 0.06 percent, 2.910 ± 0.10 percent and 3.037 ± 0.12 percent respectively (Text Figure: III).



Text Figure- I: Urea Level in Different Groups of Guinea Pig



Text Figure- II: Uric acid Level in Different Groups of Guinea Pig



Text Figure- III: Creatinine Level in Different Groups of Guinea Pig

Kidney of control guinea pig show well defined glomerulus and bowmen's capsule. Proximal Convoluted Tubules (PCT) and Distal Convoluted Tubules (DCT) are also normal in structure (Figure: 1). Collicting ducts were distinct with well defined nucleus and cytoplasmic materials in it (Figure: 2).

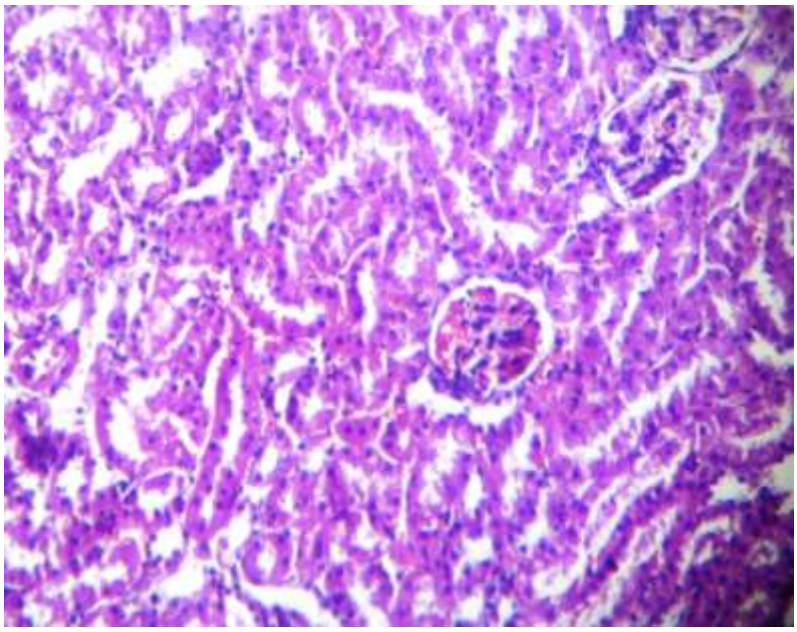


Figure- 1: show kidney of control guinea pig with well defined Glomerulus and bowmen's capsule. Proximal Convoluted Tubules and Distal Convoluted Tubules are also normal in structure.

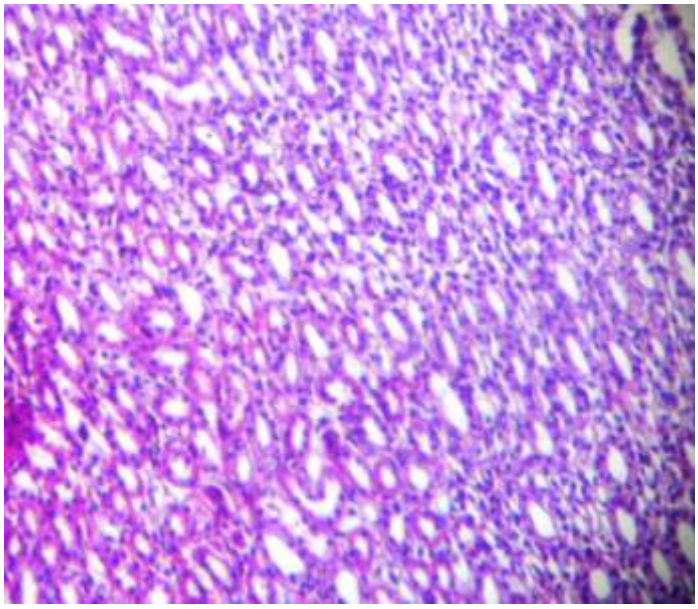


Figure- 2: show kidney of control guinea pig with well defined collecting ducts. Nucleus and cytoplasmic materials of collecting ducts are well organized

Kidney of four weeks endosulfan administered guinea pig show degeneration in glomerulus and dilated bowmen's capsule. Scattered cytoplasm was observed in Proximal Convoluted Tubules. Clustered nuclei were observed in Distal Convoluted Tubules (Figure: 3). Collecting ducts become dilated. Clustered and binuclear structure of nucleus was frequently observed. Degenerated cytoplasmic materials of collecting ducts were observed (Figure: 4).

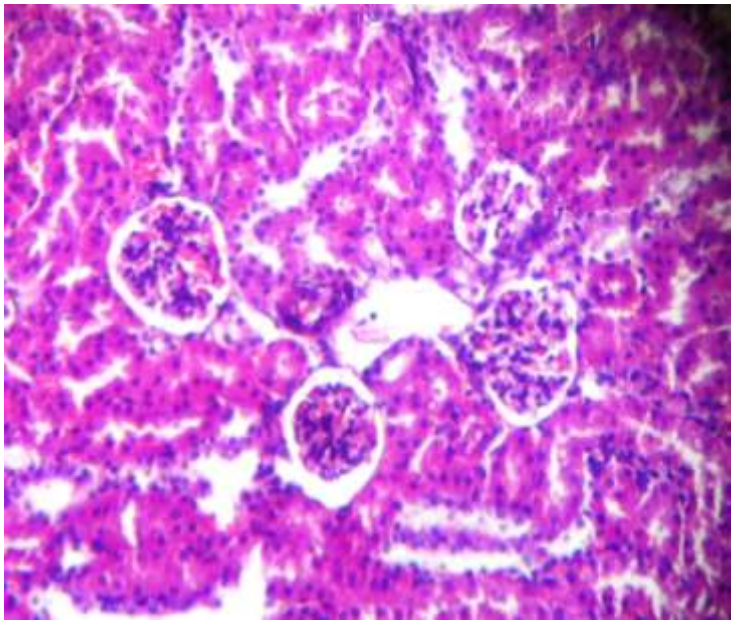


Figure- 3: show kidney of four weeks endosulfan administered guinea pig with degeneration in glomerulus and dilated bowmen's capsule. Scattered cytoplasm were observed in Proximal Convoluted Tubules. Clustered nuclei were observed in Distal Convoluted Tubules.

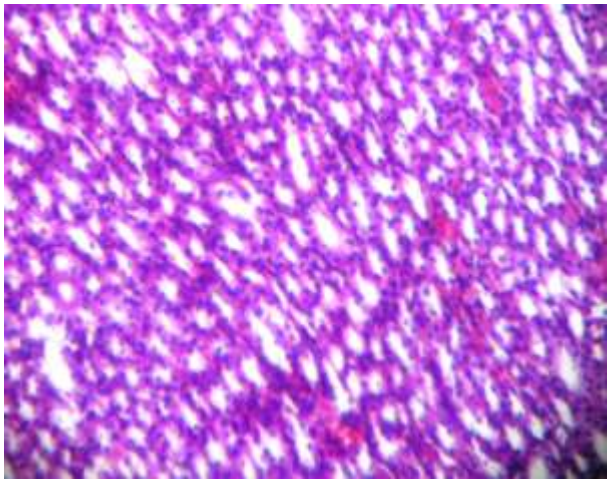


Figure- 4: show kidney of four weeks endosulfan administered guinea pig with dilated collecting ducts. Clustered and binuclear structures of nucleus were frequently observed. Degenerated cytoplasmic materials of collecting ducts were observed

Kidney of eight weeks endosulfan administered guinea pig show degenerated glomerulus, vacuolization is also observed in glomerulus with degenerated cytoplasmic materials and clustered nuclei. Bowmen's capsule is degenerated to greater extent only its rudimentary boundary was observed. Degenerated cytoplasm were observed in Proximal Convoluted Tubules, lumen of tubules is decreased. Clustered nuclei were observed in Distal Convoluted Tubules with scattered cytoplasm. Lumen of DCT is filled with cytoplasmic materials (Figure: 5). Vacuolization was observed in cortex of kidney. Bowmen's capsule is degenerated to greater extent. Lumen of PCT and DCT were decreased to greater extent. Clustered cytoplasmic materials and nuclei were observed in both PCT and DCT (Figure: 6).

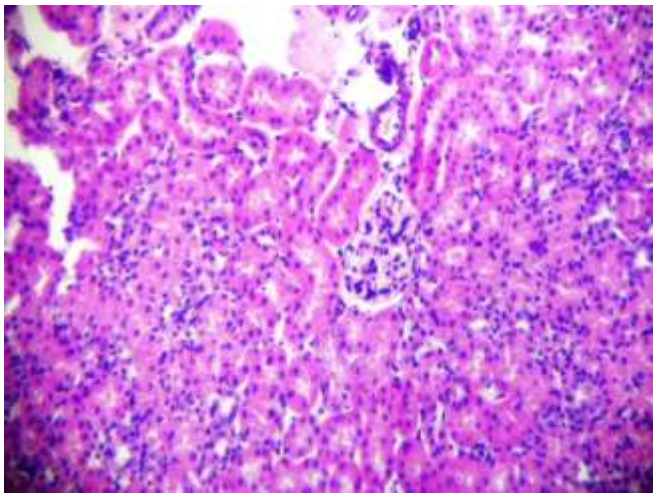


Figure- 5: show kidney of eight weeks endosulfan administered guinea pig with degenerated glomerulus, vacuolization is also observed in glomerulus with degenerated cytoplasmic

materials and clustered nuclei. Bowmen's capsule is degenerated to greater extent only its rudimentary boundry was observed. degenerated cytoplasm were observed in Proximal Convoluted Tubules, lumen of tubules is decreased. Clustered nuclei were observed in Distal Convoluted Tubules with scattered cytoplasm. Lumen of DCT is filled with cytoplasmic materials.

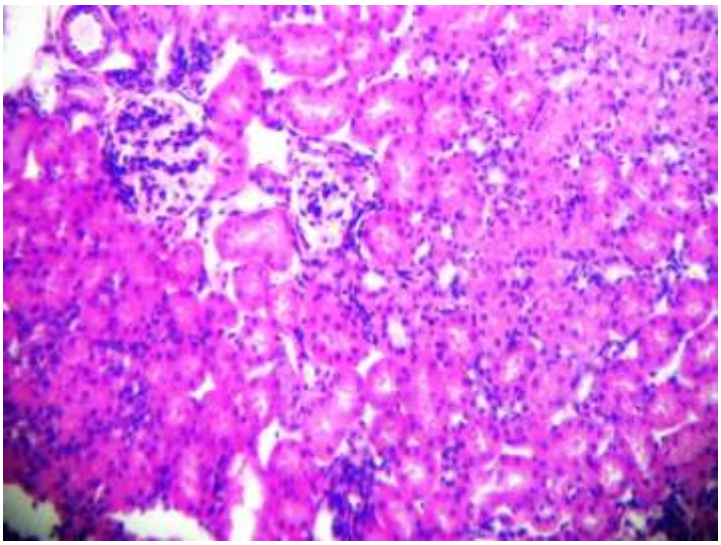


Figure- 6: show kidney of eight weeks endosulfan administered guinea pig with vacuolization in glomerulus, clustered nucleus were observed in glomerulus. Vacuolization is also observed in cortex of kidney. Bowmen's capsule is degenerated to greater extent. Lumen of PCT and DCT were decreased to greater extent. Clustered cytoplasmic materials and nuclei were observed in both PCT and DCT.

The presence of chemicals in the environment that have antiandrogenic activity and thus the ability to disrupt the endocrine system is a source of concern [11], as androgens are critical for male sexual differentiation [12]. Endoosulfan exposure for prolong duration causes decrease in the level of protein in the liver of female and male mice. Significant decrease in total protein level might be due to catabolism of protein and/ or malfunction of liver [13]. Exposure to malathion and other pesticides led to induce severe physiological and biochemical disturbances in experimental animals, buffalo calves [14], goats [15], mice[16]. In present study Urea, Uric acid and creatinine were increased many fold with increased duration of exposure of endosulfan.

The parenchymatous cells appeared large-sized with cytoplasmic vacuolization and condensed nuclei. Also, disruption of hepatic architecture, dilated congested blood vessels with proliferative lining epithelia and lymphocytes infiltration were observed. However, co-treatment of Dimethoate administrated animals with vitamins C and E showed little pathological alterations when compared with those of Dimethoate alone [17]. It has been also reported that the exposure of pregnant mice to

mancozeb inhibits Implantation [18]. Bowman's capsules round the glomeruli seemed to be lined with swollen cells which look like cubiodal cells that is showing hyperplasia instead of normal liner squamous cells as in the control Sections **[19].** A 14-day ad libitum administration of lindane in feed to Wistar rats gave a LOAEL of 72 mg/kg-day for increased kidney weight **[20].** In present study we also observe degeneration in bowmen's capsule and glomerulus of kidney. Tubular systems of kidney were also observed in more degenerated stage. Degeneration were increases with increased duration of endosulfan exposure.

CONCLUSION

Thus it is concluded from study that endosulfan exposure causes elevated level of urea, uric acid and creatinine. It causes degeneration of Glomerulus and Bowmens capsule. More degeneration was observed in tubular system of nephron of kidney. It is evident from study that endosulfan exposure causes elevated biochemical parameters of kidney and degenerative changes in tubular system of nephrons of guinea pig leading impaired nephrotoxicity in kidney.

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