

RENAL-TOXICITY OF CYLINDROSPERMOPSIN IN WISTAR RATS

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A naturally-derived cyanotoxin, Cylindrospermopsin (CYN), has a wide spectrum of toxicity on biological activity in animals and humans. Hepatotoxicity, genotoxicity, cytotoxicity and carcinogenic effects on animals and humans have been recorded. The present study aimed to determine the possible toxic effects of CYN on mammalian kidneys using male Wistar rats as an animal model. Thirty-five Wistar rats were randomly divided into five groups ($n = 7$), and rats were orally treated with different concentrations of cyanotoxin; CYN (0.175 $\mu\text{g}/\text{kg}$, 0.140 $\mu\text{g}/\text{kg}$ and 0.105 $\mu\text{g}/\text{kg}$) with a control group treated with distilled water for 90 days. The fifth group received water contaminated with Cylindrospermopsin at 0.161 $\mu\text{g}/\text{kg}$, collected from a well from Padaviya. Blood samples were collected from the lateral tail veins at 0, 7, 14, 28, 42, 60, 90 days, and serum creatinine was analyzed. Urine was collected from each rat at 0, 7, 14, 28, 42, 60, and 90 days using the individual metabolic cages and urine creatinine was analyzed. Kidney Injury Molecule-1 (KIM-1) level was quantified using the ELISA weekly. After 90 days, the kidney of each exposed rat was taken and fixed for histological evaluation. The results showed that the mean body weight of treated and control group rats gradually increased until the 90th day. The absolute and relative weights of kidneys of the treated groups were significantly less ($p < 0.05$) than the control group. A significant ($p < 0.05$) increase of serum creatinine concentration from 0.62 ± 0.01 to 0.89 ± 0.03 mg/dL, 0.64 ± 0.02 to 0.86 ± 0.01 mg/dL, 0.64 ± 0.02 to 0.85 ± 0.02 mg/dL, 0.61 ± 0.02 to 0.83 ± 0.01 mg/dL were detected for 0.175 $\mu\text{g}/\text{kg}$, 0.140 $\mu\text{g}/\text{kg}$, 0.105 $\mu\text{g}/\text{kg}$, 0.161 $\mu\text{g}/\text{kg}$ doses of the CYN treated compare to the control (0.60 ± 0.01 to 0.70 ± 0.01 mg/dL) at 90 days of exposure. Decrease of urine creatinine level from 55 ± 1 to 33 ± 1 mg/dL, 54 ± 1 to 35 ± 2 mg/dL, 54 ± 2 to 38 ± 1 mg/dL, 53 ± 1 to 32 ± 2 mg/dL were recorded for CYN exposed rat groups of 0.175 $\mu\text{g}/\text{kg}$, 0.140 $\mu\text{g}/\text{kg}$, 0.105 $\mu\text{g}/\text{kg}$, 0.161 $\mu\text{g}/\text{kg}$ respectively compare to the control (54 ± 1 to 47 ± 1 mg/dL). The highest KIM-1 concentrations were recorded in the 0.175 $\mu\text{g}/\text{kg}$ treatment dose. Histologically, kidney changes included luminal protein, focal nuclear pyknosis and a single case of glomerular collapse. Thus, the study showed the prolonged exposure to CYN contaminated water leads to kidney injuries.

Keywords: Cylindrospermopsin (CYN), KIM-1, Serum Creatinine, Urine Creatinine, Wistar Rats