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# The Effect of Copper Nanoparticles on Liver Function and Some Hematological Parameters in Rat

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**Abstract:** ***The objective of the present study was to evaluate the effect of copper nanoparticles (CuNPs) on liver function enzymes (ALT, AST and ALP) and some hematological parameters (RBCs, Hb, PCV and WBCs). The study included the use of 54 white male rats, which were divided into three groups. Rats in The first and second groups were injected intraperitoneally with 0.5 ml of copper nanoparticles at a dose of 20 and 40 mg/kg body weight for 3, 6 and 9 days. Rats in the control group were injected intraperitoneally with 0.5 ml of distilled water only. The blood samples were collected by heart puncture. The results revealed a significant elevation in liver function enzyme levels and significant decrease in RBCs, Hb and PCV especially at high dose with significant increase in WBC count. All results showed dose-and time-dependent.***

**Keywords:** Copper Nanoparticles, Liver Function, Hematological Parameters

## 1. Introduction

Metal nanoparticles, are widely used in important applications such as optical, magnetic, thermal, electrical, sensor devices and cosmetics [1]. Unfortunately these particles can potentially cause adverse effects on organ, tissue, cellular, subcellular and protein levels due to their unusual physiochemical properties [2]. Copper nanoparticles are one of the first engineered nanoparticles which are used in industrial applications [3]. These particles have attracted the biologists because of their significant and broad-spectrum bioactivity. Additionally, they have been used as a potential antimicrobial agent in many biomedical applications due to the large surface area to volume ratio. However, the excess use of any metal nanoparticles increases the chance of toxic effect of these particles on human, other living beings, and environment [4], [5].Ibrahim *et al*. [6] reported that excessive accumulation of CuNPs in the liver caused several adverse effects including changes in liver enzymes activities, generation of reactive oxygen species (ROS), marked pathological changes, DNA damage, and apoptosis. In fish, Jahanbakhshi *et al* [7] found that copper oxide nanoparticles lead to a reduction in RBC count, Hb amount and PCV, this associated with elevation in the WBC count. Khabbazi *et al* [8] showed that a 96 hours exposure to copper oxide nanoparticles stimulated WBCs, lymphocytes, eosinophils, neutrophils, PCV, and there was no effect on monocytes and Hb level. The present study was carried out to investigate the effect of dose and exposure duration of CuNPs on the liver function enzyme levels and some hematological parameters in rats.

## 2. Materials and Methods

### 2.1 Copper Nanoparticles Preparation

Copper nanopowder with a particle size of (20-30) nm and purity of 99.99% was purchased from Xuzhou Hongwu Nanomaterial Co. China. CuNPs suspension was prepared by dispersing CuNPs powder in distilled water then stirred overnight using magnetic stirrer followed by sonication for 30 min, prior to each use the solution was vortexed to ensure proper particle suspension.

### 2.2 Experimental Animals

Fifty four male albino rats (weighing 200 ± 10 g) were randomly assigned to cages (6 rats per cage), acclimatize for 14 days at a temperature of 25 ± 2 and accessed libitum to fresh water and rodent pelleted diet.

Rats were divided into 3 groups, each group included 18 rats:
Group1: (Control) rats intraperitoneally received 0.5 ml of distilled water for 3, 6 and 9 days (6 rats for each duration).
Group 2: Rats treated intraperitoneally with 0.5 ml of 20 mg/kg CuNPs for 3, 6 and 9 days (6 rats for each duration).
Group 3: Rats treated intraperitoneally with 0.5 ml of 40 mg/kg CuNPs for 3, 6 and 9 days (6 rats for each duration).

### 2.3 Blood Sampling

At the end of treatments, the rats were anaesthetized with diethyl ether, and blood samples obtained by cardiac puncture were collected into gel/clot activator tube for 30 min to accelerate clotting, then centrifuged at 3000 rpm for 10 min in order to separate serum. Blood samples for hematological analysis were collected into EDTA tube.

### 2.4 Serum Liver Function Analysis

Liver function enzyme analysis was carried out with a Cobas c111 Automated Analyzer, (Roche. Germany) using appropriate kits. The following parameters were tested: alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP).

### 2.5 Hematological Analysis

Red blood cell (RBC) count, Hemoglobin (Hb), packed cell volume (PCV), and total white blood cell (WBC) count were estimated by Mindary BC-3000 Automated Analyzer. China.

### 2.6 Statistical Analysis

All data were analyzed using the SPSS software, version 24. The data were expressed as mean ± standard error of mean (SEM) and statistical analysis were carried out using the F-test and analysis of Variance (ANOVA). Differences were considered statistically significant at $p \leq 0.05$.

## 3. Results and Discussion

### 3.1 Liver Function

Depending on the dosage, and the duration of exposure, The results of the present study showed a significant increase ($P \leq 0.05$) in the level of liver enzymes AST, ALT, and ALP in rats treated with both doses of CuNPs compared to control group for a periods of 3, 6 and 9 days. The results also revealed a significant increase in the level of liver enzymes in rats injected with 40 mg/kg compared to those injected with 20 mg/kg for all three periods. The level of these enzymes were significantly increased in injected rats for 9 days compared to those injected for 3 and 6 days for both doses (Fig. 1, 2 and 3).

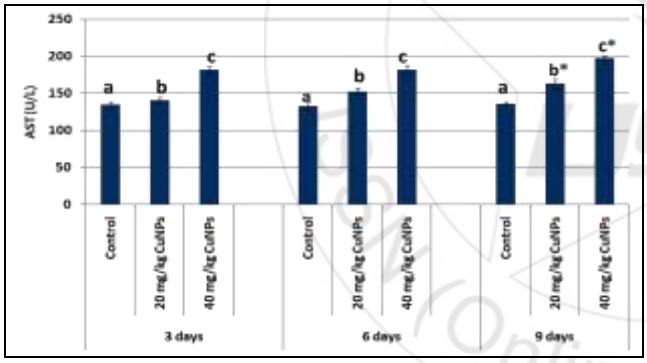


**Figure 1:** Changes in AST in rats injected with 20 and 40 mg/kg of CuNPs for 3, 6 and 9 days. Values are expressed as means ± SEM. Different letters show significant differences ($P \leq 0.05$) among exposure doses.* shows significant differences ($P \leq 0.05$) among duration of exposure.

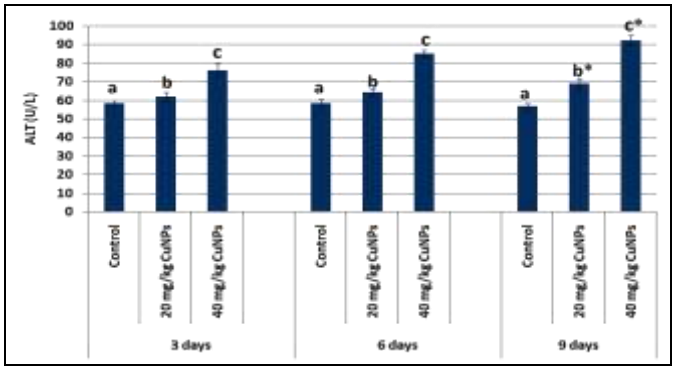


**Figure 2:** Changes in ALT in rats injected with 20 and 40 mg/kg of CuNPs for 3, 6 and 9 days. Values are expressed as means ± SEM. Different letters show significant differences ($P \leq 0.05$) among exposure doses.
* shows significant differences ($P \leq 0.05$) among duration of exposure.

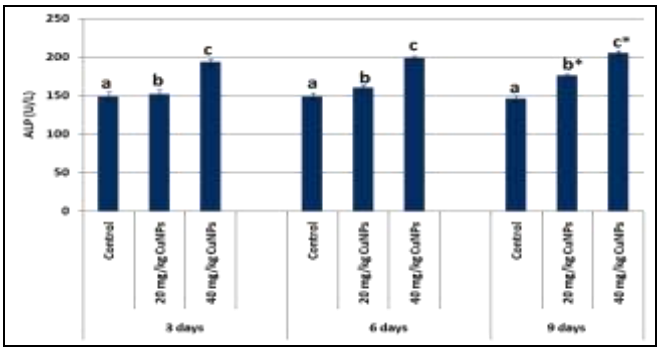


**Figure 3:** Changes in ALP in rats injected with 20 and 40 mg/kg of CuNPs for 3, 6 and 9 days. Values are expressed as means ± SEM. Different letters show significant differences ($P \leq 0.05$) among exposure doses. * shows significant differences ($P \leq 0.05$) among duration of exposure

Copper nanoparticles induced a dose-dependent increase in liver function enzymes ALT, AST, and ALP. This observation is consistent with the data obtained by Ibrahim et al. [6], who found that a 5 days/week for 2 months oral exposure to CuNPs at a dose of 40 mg/kg, caused a significant elevation in ALT and AST activity. A significant and dose-dependent increase of ALP was also reported in a study by Chen et al.[9], these authors observed a significant increase in blood serum ALP in mice following a single oral exposure to CuNPs at a dose of 501 and 736 mg/kg . The toxic effect of nanoparticles leads to increase production of free radicals and beginning of ROS reactions, that causes damage to liver hepatocytes, and increase the level of liver enzymes due to tissue destruction and releasing these enzymes into the blood stream [10], [11].

### 3.2 Hematological Parameters

The results showed that RBC count, Hb and PCV levels decreased significantly ($P \leq 0.05$) in group receiving 40 mg/kg of CuNPs for 6 and 9 days, while these parameters were decreased significantly ($P \leq 0.05$) in group receiving 20 mg/kg of CuNPs for 9 days only (Fig. 4, 5 and 6). The level of WBC count increased significantly ($P \leq 0.05$) in all groups except that received 20 mg/kg of CuNPs for 3 days (Fig. 7). These observations is agree with Jahanbakhshi et al. [7]. The decrease in RBC count, Hb and PCV levels observed in this study may be due to the dysfunction of hematopoietic system induced by nanoparticles [12] or due to the hemolytic effect induced by the release of oxidative stress products following the exposure to CuNPs [13], [14] . The elevation of WBC count in the present study may be due to the interaction between CuNPs and the immune system which can stimulates inflammatory or allergic reactions [15].

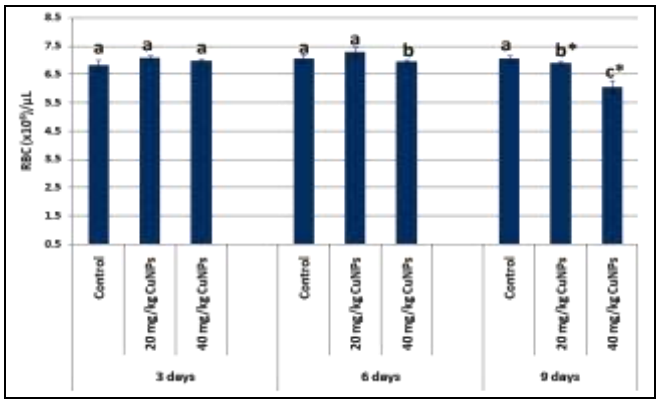


**Figure 4:** Changes in RBC count in rats injected with 20 and 40 mg/kg of CuNPs for 3, 6 and 9 days. Values are expressed as means ± SEM. Different letters show significant differences ($P \leq 0.05$) among exposure doses. * shows significant differences ($P \leq 0.05$) among duration of exposure.

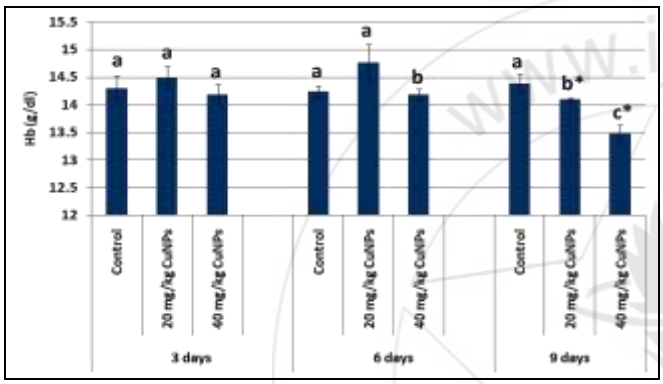


**Figure 5:** Changes in Hb amount in rats injected with 20 and 40 mg/kg of CuNPs for 3, 6 and 9 days. Values are expressed as means ± SEM. Different letters show significant differences ($P \leq 0.05$) among exposure doses. * shows significant differences ($P \leq 0.05$) among duration of exposure.

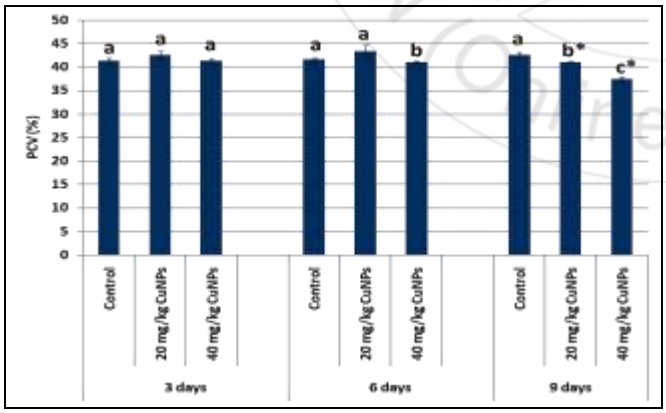


**Figure 6:** Changes in PCV in rats injected with 20 and 40 mg/kg of CuNPs for 3, 6 and 9 days. Values are expressed as means ± SEM. Different letters show significant differences ($P \leq 0.05$) among exposure doses. * shows significant differences ($P \leq 0.05$) among duration of exposure.

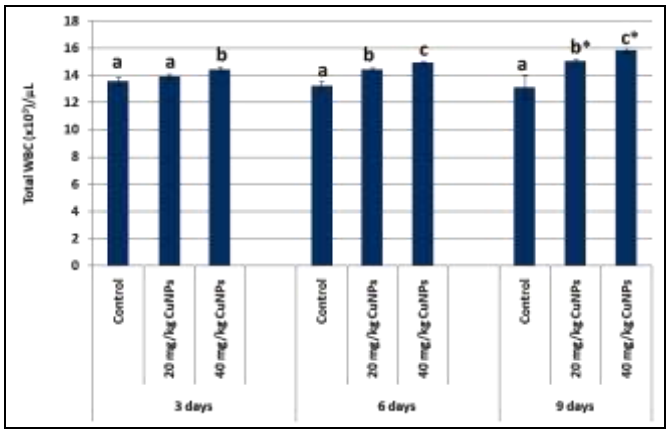


**Figure 7:** Changes in total WBC count in rats injected with 20 and 40 mg/kg of CuNPs for 3, 6 and 9 days. Values are expressed as means ± SEM. Different letters show significant differences ($P \leq 0.05$) among exposure doses. * shows significant differences ($P \leq 0.05$) among duration of exposure.

## 4. Conclusion

In conclusion, the present study showed that CuNPs had dose - and time - dependent toxic effect on liver function and some hematological parameters in rats.

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