Histological effects of gold nanoparticles on kidneys of male albino rats

Abstract

Objective: Gold nanoparticles (GNPs) have important application for cell labeling and imaging, drug delivery, diagnostic and therapeutic purposes mainly in cancer. Nanoparticles (NPs) are being increasingly exploited for medical applications. The aim of the present study was to investigate the effects of gold nanoparticles on renal tisues. **Materials and methods:** Fifteen male adult albino rats aged 10-12 week old with 210-240 body weight , they were randomly divided into three groups as follows: Group I: given distilled water. Group II: given 50mg/kg body weight of gold nanoparticles . Group III: given 100 mg/kg body weight of gold nanoparticles for 60 days. Kidneys and bloods were retrieved for histological and biochemical examination .**Results:** Results explained significant increase in blood levels of urea and uric acid among the treated groups comparing with control group, and a significant increase in creatinine levels in group 100 mg /kg than control and 50 mg/kg group with and a significant increase in albumin levels in group 50 mg /kg than control and 100 mg/kg group. Histological evaluation exhibited hemorrhage and necrosis in different degrees according to NPS concentration with monocyte infiltration. **Conclusion:** Our data show that GNPs Could cause an impairment at the biochemical and histological alterations that were present after the 60th day of GNP administration.

Key words: Gold nanoparticles , renal tissue, kidney, biochemical parameters, histology,rat

Introduction

Gold nanoparticles used in many important applications, including industrial purposes, medical diagnosis and therapeutic purposes mainly in cancer , cell labeling , photodynamic therapy, biological detectors and imaging . This particle is an intermediate state of matter between the molecular and volumetric levels [1-8] . These tiny particles are biologically active due to their unique properties as they accumulate in vital organs such as liver, spleen, lungs, aorta, esophagus and olfactory bulb [9-12] . Moreover, Nanoparticles are more biologically reactive than their bulk counter parts and they have toxic effects due to their small size and larger surface area to volume ratio ,As smaller particles are more toxic than the larger ones [13-16]. Gold is considered a metal that has no effect and is noble and has many benefits, including diagnostic and medical, but later researchs showed that oxidative stress and the molecular interaction of gold lead to histo-cytotoxicity [17-20]. In addition, Experiments have proven that gold nanoparticles produce toxicity to some cells and

not to others, as particles whose size ranges from 5 to 20 nanometers are more toxic and accumulate for a long time in organs, including the kidneys. And that this toxicity produced by these particles may be a result of interference with chemical stereoisomers and differences in the innate response to types of cells, and this is a sign that must be paid attention to when gold nanoparticles are used to deliver drugs and genes[21-25] . In this experiment, we will learn about the changes that occur in tissues due to nanoparticles, and whether the particle size has an effect on the toxicity that occurs in tissues.

Materials and Methods

In this experiment was used 15 healthy male adult albino rat Rattus norvegicus aged 10-12 week old with 210-240 body weight . These rats were placed throughout the experiment period in the Animal house of University of Babylon in large cages with ventilation, humidity, and appropriate temperature. After ensuring that the rats were acclimatized in cages, they were randomly divided into three groups as follows: Group I: given distilled water. Group II: given 50mg/kg body weight of gold nanoparticles . Group III: given 100 mg/kg body weight of gold nanoparticles .

The dose was given to rats orally for 60 days .After 24 hour of last administration , the rats were sacrificed , blood was drawn by heart puncture, and kidney biopsies were taken for each rat and fixed in formalin 10% then processed for light microscope histologic examination . Plasma albumin, creatinine, urea, and uric acid were measured using enzymatic test kits (Sigma Chemical Co., St. Louis, MO).

Results and discussion

Biochemical Findings

Renal impairment was indicated by an increase in creatinine at higher GNP dose 100 mg/kg in rats along with less similar impairment in the lower dose 50 mg/kg . Urea was increased in all rats treated with GNPs, and uric acid showed a higher plasma level at 50 and 100 mg/kg GNPs. Large amounts of uric acid can be produced from tissue injury and the promoted immune responses.[26] Microscopic observations demonstrated that the hyperuricemic rats developed renal disease with inflammatory cell infiltration [27,28]

Parameters / Groups	control	50 mg/kg	100 mg/kg	P value
albumin (μM)	521±3.1	572.5±18.1*	533.2±11.2	P < 0.01
urea (mg/dL)	20.7±1.5	82.3±4.1*	73.6±2.2*	P < 0.01
creatinine (mg/dL)	1.4±0.2	3.8±0.4*	5.1±0.3*	P < 0.01

uric acid (mg/dL)	6.2±0.3	5.2±0.4	11.3±0.7	P < 0.01

Values are presented as mean ± SD

Histological Findings

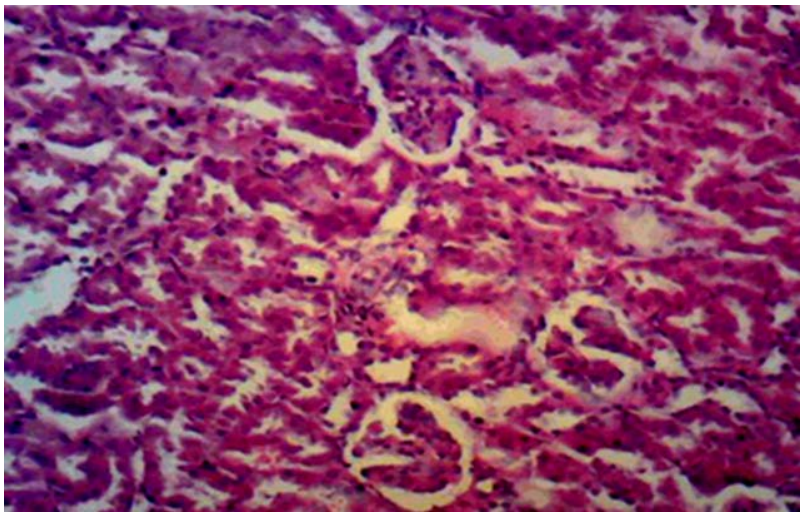

Figure 1: Cross section of renal cortex of male rat from control group explained the normal renal architecture . (40X ,H&E stain)

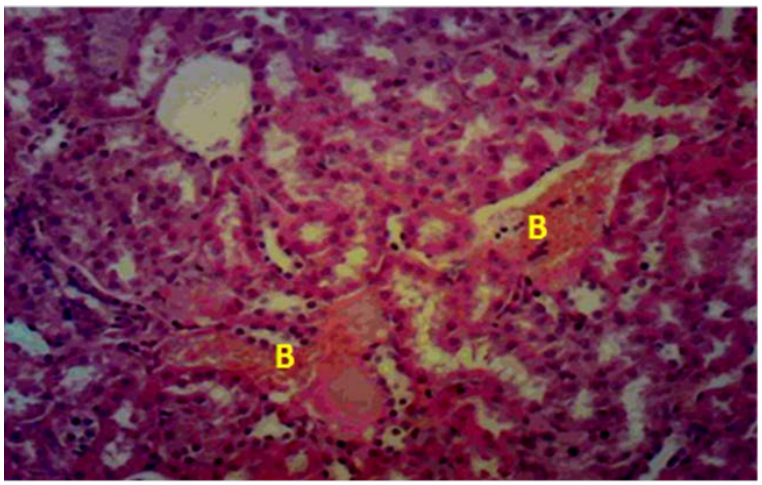

Figure 2: Cross section of renal cortex of male rat from 50mg/kg body weight of gold nanoparticles explained the presence of hemorrhage B with some cellular necrosis (40 X, H&E stain)

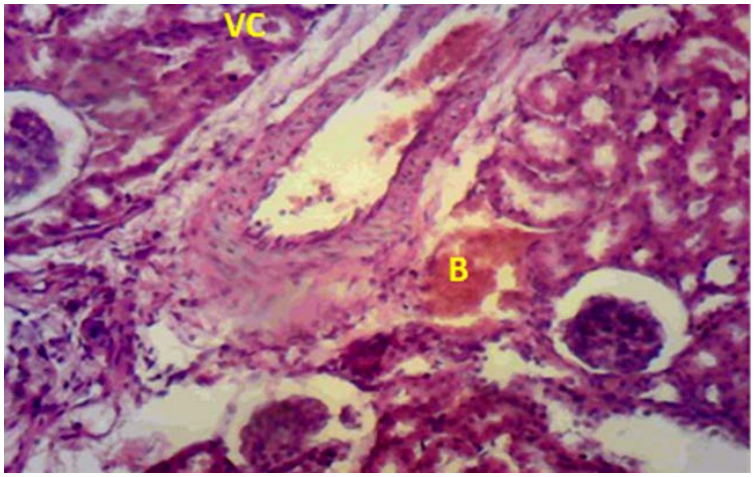

Figure 3: Cross section of renal cortex of male rat from 100 mg/kg body weight of gold nanoparticles explained the presence of hemorrhage B and vascular congestion and disintegration of Bowman capsule and necrosis with immune cell infiltration (40X, H&E stain).

In this experiment, no deaths occurred for the rats that were used, but histological changes were detected in the tissues of the kidney due to the gold nanoparticles administration . The results of previous studies were revealed that gold nanoparticles have great risks on the microstructure and functional structure of the kidney [29] . The results showed the renal cortex were more affected than the medulla and the reason of this may related to gold nanoparticles reach the cortex via the blood stream . On examination, there was a cloudy swelling, as the epithelial lining of the renal tubules is exposed to this swelling, with pale cytoplasm and displaced nuclei , The reason for the swelling of the cytoplasm was as a result of the disturbance in the function of the membranes, as it led to the flow of quantities of water due to the effects of gold nanoparticles . This change is accompanied by the leakage of somatic glycolytic enzymes and consequently the crowding of macromolecules [30] . Also, vacuolar degeneration appeared in the cells of the kidney. The reason for this may be that the proximal tubules are the primary sites for reabsorption, and therefore a greater concentration of gold nanoparticles. This vacuolar degeneration is the result of ions and fluids thus increasing intracellular water [31]. Hyaline droplets were detected in the renal epithelium of rats, and these droplets appear due to the disturbance in protein metabolism. A change in the sizes of the nuclei was also observed in some cells of the kidney, and research indicates that the change in size is a cancerous lesion [32] . Some epithelial cells lining the proximal tubules are shown nuclear pyknosis , This was due to the condensation of chromatin around the nucleus with irregular nuclear membranes . Karyopyknosis It is an irreversible condensation of chromatin in the cell nucleus, which leads to necrosis and death of the cell [33] . A disappearance of the nucleus was

also detected in some rat kidney cells , Karyorrhexis It is a kind of continuing destructive fragmentation of the nucleus [34]. And one of the changes that appeared is karyolysis It is the complete dissolution of the chromatin of the cell [35] .

Conclusion

The results of this study reveal the impact of gold nanoparticle doses on renal tissues. Our data show that GNPs Could cause an impairment at the biochemical and histological alterations that were present after the 60th day of GNP administration. These are significant at 100 mg/kg but minimal at the lower doses of 50.

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