

Acute toxicity of two different types of the nanoparticles quantum dots suggested for biomedical applications: an *in vivo* experimental study

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Abstract: Nanoparticles are a promising evolution in this era. Toxicities of nanoparticles are not well known yet. Quantum dots (QDs) are nanoparticles that could be used in biomedical field. Quantum dots containing cadmium are good semiconductors and could play an important role for biomedical applications. *In vivo* toxicity studies are still not sufficient to evaluate Cd containing QDs for biomedical applications. Two types of 'aqueous QDs included CdSe/ZnS and CdTe, with green emission color and 520-550 emission peak, were used. Acute toxicity was studied by injecting single mounting high doses "5, 50, 500 µg/ kg" intravenously in the tails of mice and samples were collected 14 days after injection. Cadmium "Cd", selenium "Se", and tellurium "Te" levels were measured in animals' blood using Energy Dispersive X-ray Fluorescence (EDXRF), a highly sensitive multi-elemental method of micro-analysis. Complete blood picture, liver function and kidney function tests were measured. Histopathological examination was performed for samples from the liver, kidney, lung, spleen and heart. Heavy metals were distributed to all of the studied organs with higher levels than the control group. Intravenous cadmium nanoparticles were distributed to all organs including the lung. Cadmium could cause lung toxicity due to the developed chemical pneumonitis. Tellurium containing QD could be more nephrotoxic. The results revealed variant degrees of pathological changes in the organs and elevated normal levels of the laboratory investigations. The studied QDs were unstable *in vivo* and were still existed in the body 14 days following intravenous administration. No dose related toxicity was noticed. Histopathological changes could be reversible and could not hinder the use of the studied QDs for biomedical applications. Further studies are recommended for longer period for detection of excretion time and long sequel toxicity, and for evaluation of the QDs stability few hours after injection to assess its *in vivo* usage.

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Key words: quantum dots, acute toxicity, semiconductors nanoparticles

1. Introduction

Firstly, quantum dots (QDs) had been discovered by Ekimov, a Russian physicist, who found it in glass crystals in 1980.¹ The advancement of QDs structure has been performed after 1984 by its installation in a spherical shape which related to the wave function that could be used in bulk semiconductors. This technology has been invented by Luis Brus who found a relation between the size of QDs and the band gap for semiconductor nanoparticles.^{2, 3} Murray *et al.* nearly a decade after, synthesized Colloidal structure of QD composed of a core of semiconductor which consisted of cadmium conjugated with another element (CdX) where X could be Selenium (se), Sulphur (s) or Tellurium (Te) with size-tunable band-edge adsorption and emission.⁴ The current typical composition of QDs is usually nanocrystals composed of a core of an element belongs to group II bound to another element belongs to group IV such as CdSe and CdTe or an element belongs to group III and

conjugated to another element belongs to group V such as InP. The core is surrounded by a shell with a higher band gap material like ZnS.⁵ Quantum dots have very different photo-physical characters. They can emit lights with variant wavelengths starting from visible to infrared light according to their sizes and chemical structures. Comparing with the common organic dyes, QDs have larger absorption coefficients, size-tunable light emission, superior signal brightness, resistance to photo-bleaching and simultaneous excitation of multiple fluorescence colors.^{6, 7} The common diameter range of QDs is 1- 10 nm.⁸ Quantum dots are nanocrystals semiconductors which are promising to be used in production of transistors, quantum computing, solar cells, diode lasers, second-harmonic generation and light emission diode "LED".⁹ Current and suggested use of QDs in biomedical field included labeling of reticuloendothelial system¹⁰ and lymph nodes¹¹, cellular sensor¹² and cancer cells' imaging¹³. Polymer coated QDs may be

beneficial as long-circulating vascular probes.¹⁴ Bio-conjugated QDs could be also used as diagnostic targeted cancer and deep-tissue imaging agents¹⁵, photodynamic therapy sensitizers (PDT)^{16,17}, vehicles for gene therapy^{18,19}, and magnetic resonance imaging contrast agents.¹⁵ Traditionally synthesis of QDs has been carried out in organic solvents such as toluene or chloroform at high temperatures in the presence of surfactants. To make it available for biomedical field, QDs should have water soluble surface with maintenance of their optical characters i.e. to functionalize QDs.²⁰ The outer coating layer increases the surface area of the QDs and makes it recognized in order to link to the biomolecules like peptides, antibodies, nucleic acids and small-molecule ligands for further application. The most applicable and known QDs are those with Cadmium containing cores.²¹ Degradation of QDs *in vivo* causes release of cadmium and other heavy metals introduced in its structure. As known, cadmium has toxic effects on the human liver, kidney, nerves and genes.^{21,22} Toxicity of the nanoparticles QDs used for biological application may be a strong reason for restricting its usage *in vivo*, as it contains toxic metals which may produce serious effects in case of degradation of the nanoparticles and its storage in the cell or induction of immunotoxicity.²³ Synthesis of *in vivo* stable QDs which retain their photo-physical properties is a must for its use in biomedical field. Evaluation of systemic toxic effects of QDs is crucial before their biomedical applications.²⁴ Regarding toxicity of quantum dots, most of studies were performed *in vitro* and concluded their chemical stability. However, *in vivo* studies may not produce the same effects as *in vitro* researches.²⁵ *In vivo* toxicity researches are still not sufficient to evaluate the toxicity of the suggested QDs for biomedical applications.

2. Aim of the work

The study aimed to investigate and compare two different types of quantum dots regarding their *in vivo* acute toxicity and distribution to be used for biomedical applications.

3. Experimental

Materials:

Quantum dots, CdSe/ZnS, stabilized by mercaptoundecanionic acid "MUA" (MUA in H₂O and functionalized with a coat of carboxylic acid "COOH" and amine ligands, has green color emission, and approximately 3.60 nm diameter with emission peak 520-550 nm), bought from MK Impex Corp, 6382 Lisgar Drive, Mississauga, Ontario L5N 6x1, Canada. The other QD was CdTe "core type" which was COOH functionalized, has emission fluorescence

color, peak 520 nm and bought from sigma Aldrich, number 777935-10MG.

Animals:

Adult male Swiss albino mice "18–20 g, 8 weeks of age" were purchased from the National Cancer Institute, at Cairo University in Egypt and maintained under standard laboratory conditions "25°C, 5% relative humidity, 12-h light/dark cycle". All mice had *ad libitum* access to standard mouse chow and water, and were acclimated for at least 1 week prior to experiment initiation. The study was performed in accordance with the guidelines for the care and use of laboratory animals approved by Research Ethical Committee of Faculty of pharmacy of Tanta University in Egypt. Mice were randomly assigned into 7 groups "n=8", including one control group "mice received distilled water instead of QDs", three experimental groups were intravenously injected once with higher doses than the used before²⁵, via the tail vein, with three different doses of CdSe/ZnS QD "groups Se5 received 5µg/kg, Se50 received 50 µg/kg, and Se500 received 500 µg/kg" and another three experimental groups that were intravenously injected with the same previously mentioned three different doses but of CdTe QDs "groups Te5 received 5 µg/kg, Te50 received 50 µg/kg, and Te500 received 500 µg/kg". After 14 days, animals were sacrificed by cervical dislocation after anesthesia. Blood samples were collected for measurement of hematological parameters and biochemical markers relevant to liver and kidney functions. Organs including heart, liver, spleen, lung and kidney were harvested and kept frozen at -80°C for measurement of tissue distribution of QDs among the collected tissues. The histopathological sections of various organs were made after being fixed in 4% paraformaldehyde and stained with hematoxylin-eosin "H&E". The pathologist was completely blinded about the experimental groups.

Heavy metal analysis:

Cadmium, selenium and tellurium quantitative analysis was performed by means of microanalysis using Energy Dispersive X-ray Fluorescence "EDXRF", a highly sensitive multi-elemental method. Samples "0.5g" from the liver, spleen, kidney and lung of all test animals were dissected and had been rinsed with normal saline to clear it from any blood remnants. Samples were soaked in nitric acid "67%" in a glass container and left for 24 h for digestion. Then, a mixture of nitric acid and water was prepared "4:1 volume ratio" and added to the samples. Samples were heated up to 110-120°C until clearness of the solution. Hydrogen peroxide was added to the solutions to eliminate nitrogen oxide vapors. Finally, the prepared solutions were fixed by adding 2ml of 2% nitric acid followed by filtration.²⁵ Samples solutions

were dried as powder being placed on KIMPOL polycarbonate film as a backing material previously mounted on polyethylene target frame and fixed by 1% polystyrene in benzene. The samples collected by deposition on a filter paper and were put in an electric oven at 80°C for 4 days until dryness. The samples were grinded for full homogenization and very fine powder formation until analysis with Tube Excited X-ray Fluorescence Analysis apparatus.²⁶

Laboratory analysis:

Using routine lab analysis, the following parameters were measured; hemoglobin level “Hb”, red blood cells count “RBC”, hematocrit percentage “Ht%”, mean corpuscular hemoglobin concentration “MCHC”, platelets count, white blood cells count “WBCs”, kidney function tests including urea, creatinine and blood urea nitrogen “BUN” levels, liver function tests including alanine aminotransferase “ALT”, aspartate aminotransferase “AST”, Total bilirubin “Bt”, total protein “TPR” levels.

Histopathological examination:

Biopsies, three millimeters each one, were taken from the liver, spleen, kidney, lung and heart of each mouse. Formalin fixed paraffin embedded blocks were done for all the 56 samples. Routine H&E staining was performed for samples on mounted glass slide, then histopathological examination was performed to confirm laboratory investigations.

Statistical analysis:

Results were expressed as mean \pm SD. Comparisons between different groups was carried out by one-way analysis of variance “ANOVA” followed by a Tukey- Kramer post-hoc test. The level of significance was set at $p \leq 0.05$. Minitab computer software “Version 16; Minitab Inc., State College, PA” was used to carry out all statistical analyses.

4. Result and Discussion

Routine laboratory:

Comparing with the control group, there was significant increase in Hb level in all groups and the most affected group was Se500 followed by Te50 “ $p = 0.004$ and 0.003 respectively” (Fig.1). Red blood cells count and Ht % were also significantly increased in all groups comparing with the control group with the highest values were noticed in Se500 group “ $p = 0.000$ ” (Fig. 2), whereas MCHC level was significantly decrease in Se5, Se50, Se500 and Te 5 groups and non-significantly decreased in the remaining groups (Figs. 3 & 4). Non-significant decrease in platelets count was noticed in all groups (Fig. 5). White blood cells count was significantly decreased in all groups with the maximum reduction in Te5 and Se5 groups (Fig. 6). Regarding kidneys function; urea level was significantly increased in the all animals (Fig. 7) whereas creatinine level increased

in CdTe QD receiving animals with maximum elevation in Te500 group. Non-significant increase was noticed in BUN in all animals (Fig. 9). Liver functions concerning Bt showed; significant elevation in Te50 group (Fig. 10), significant elevation of ALT in all animals but those received CdSe QD with 5 & 50 $\mu\text{g}/\text{kg}$ doses (Fig. 11), significant elevation of AST in all animals with the highest increase in those receiving the highest doses (Fig. 12), TPR was significantly increase in Se500 group (Fig. 13) and A/G ratio was elevated in all animals received CdTe QD and the elevation was directly proportional to the dose whereas, lower elevation was noticed in Se5 group (Fig. 14). Comparing with the reference values the elevations of the laboratory investigations were within normal ranges.

Quantitative heavy metals results:

In the control group, Cadmium (Cd) was not detected in the spleen, lung, heart but was detected in the liver and kidney. Comparing with the control, Cd, Te and Se levels were highly elevated in all the studied organs (Figs.15, 16 & 17). Cadmium level was higher in the lung, heart and spleen than kidney and liver (Fig. 15). Tellurium’s highest level was in the kidneys (Fig. 16). Liver was the highest of all the studied organs regarding selenium level (Fig. 17). No apparent correlation was noticed between metals concentrations and the type of QDs or the injected doses.

Histopathological examination:

On microscopic examination; it was found that tissues of the studied organs of the control group revealed no pathological changes (Fig. 18), while exposed animals to different doses of the two types of QDs showed different pathological changes. The most common affected organ was the lung, followed by the liver and kidney. The least common affected organ was the spleen, while the hearts were not affected. On lung examination; interstitial pneumonia was seen in most of the cases in the form of polymorphic and lymphocytic inflammatory cellular infiltration and edema of bronchial epithelium with presence of inflammatory exudates. Proliferation and hyperplasia of lymphoid tissue of the lungs were seen as well (Fig. 19). Liver changes were noted in most of the groups as chemical toxicity in the form of monomorphic inflammatory cellular infiltration and fibrosis of portal tracts, and ranged from minimal to moderate hepatitis with congestion of central veins; however, preservation of the liver architecture was noted in all of the studied samples without liver cirrhosis (Fig. 20). In the kidney; signs of toxicity were seen in the form of cloudy swelling of the lining epithelium of proximal and distal renal tubules with obliterations of their lumens. In Te500 group, apical vacuolations denoting hydropic degeneration were noticed. Renal

glomeruli were normal in all cases with preserve Bowman's capsule and space (Fig. 21). Spleen was rarely affected, there was congestive spleen in the form of proliferation of the white pulp and congestion of blood vessels of the red pulp (Fig. 22). Hearts were not affected in all of the studied cases (Fig. 23). Results were tabulated (Table 1).

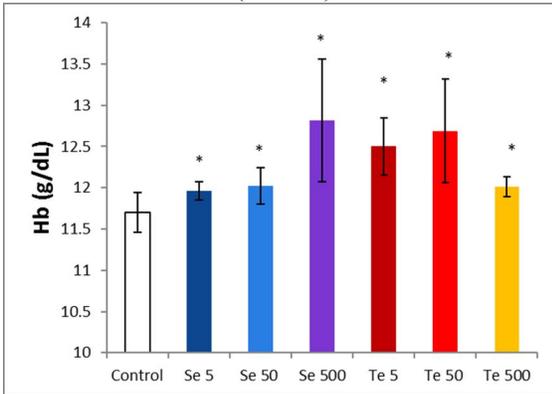


Figure 1: comparison between Se and Te containing QDs regarding hemoglobin. Levels (Hb).

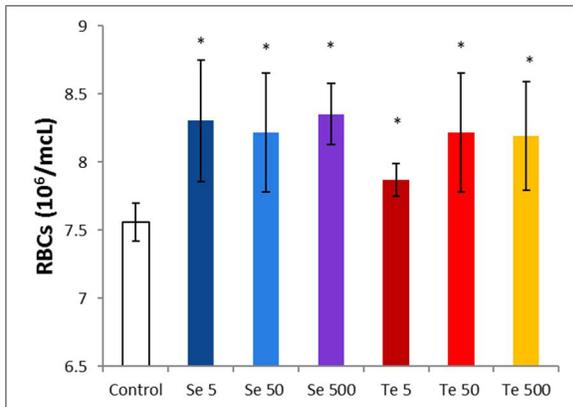


Figure 2: comparison between Se and Te containing QDs regarding red blood cells (RBCs).

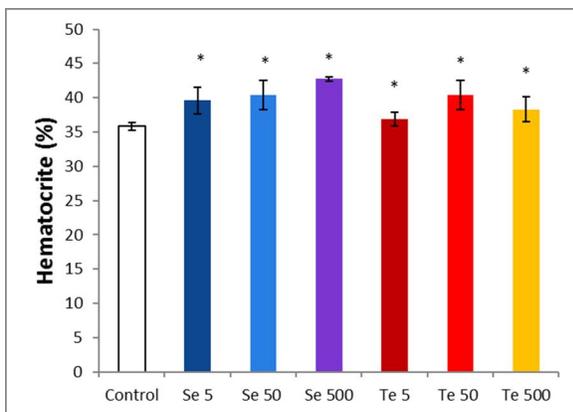


Figure 3: comparison between Se and Te containing QDs regarding hematocrite percentage (Ht %).

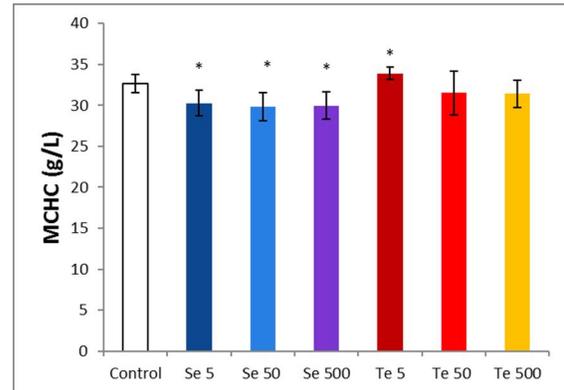


Figure 4: comparison between Se and Te containing QDs regarding mean corpuscular hemoglobin concentration (MCHC).

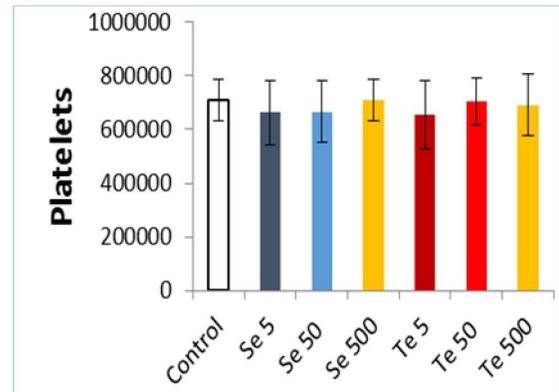


Figure 5: comparison between Se and Te containing QDs regarding platelets number.

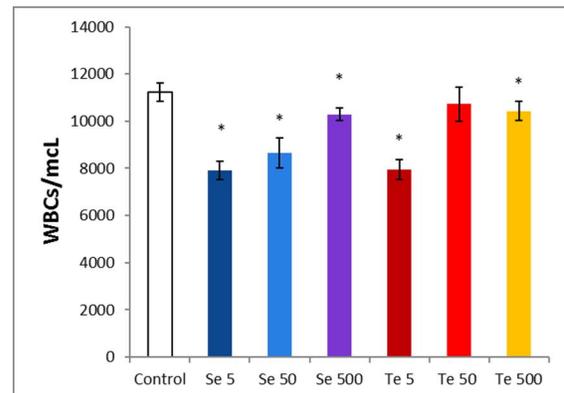


Figure 6: comparison between Se and Te containing QDs regarding white blood cells.

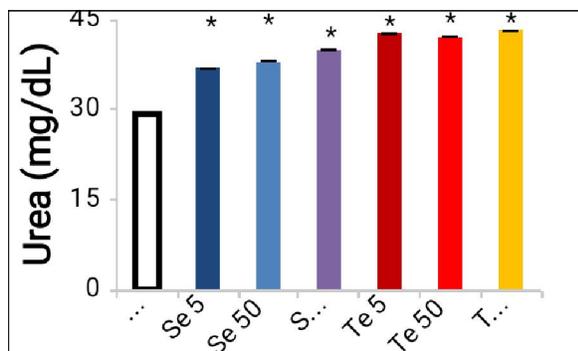


Figure 7: comparison between Se and Te containing QDs regarding urea levels.

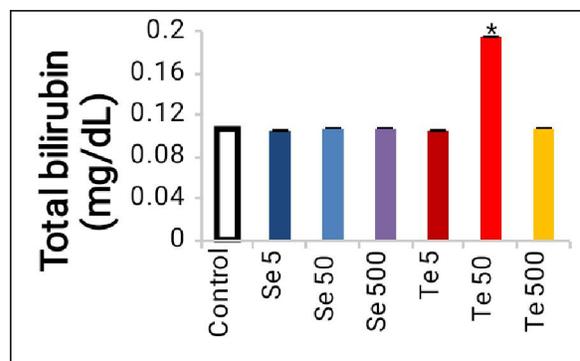


Figure 10: comparison between Se and Te containing QDs regarding total bilirubin.

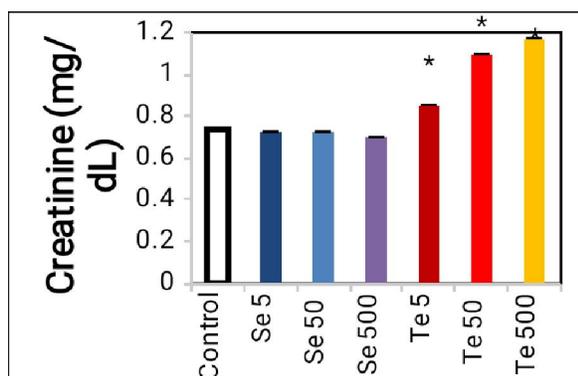


Figure 8: comparison between Se and Te containing QDs regarding creatinine level.

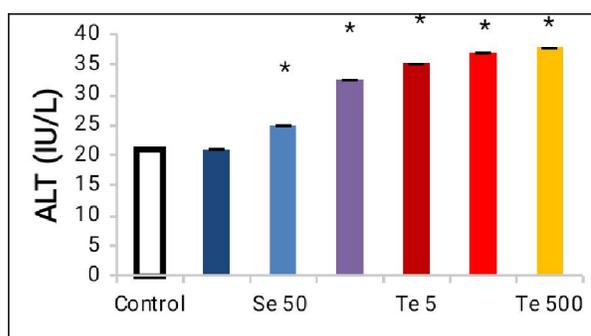


Figure 11: comparison between Se and Te containing QDs regarding Alanine transaminase (ALT).

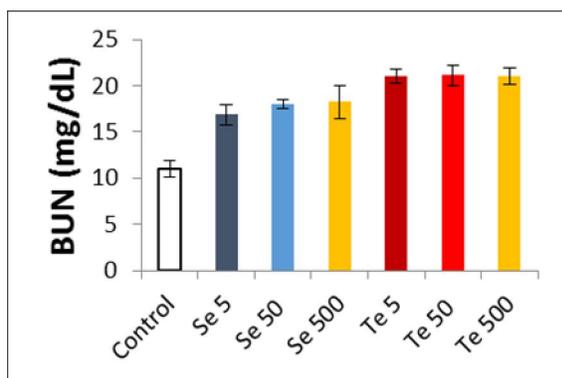


Figure 9: comparison between Se and Te containing QDs regarding blood urea nitrogen (BUN).

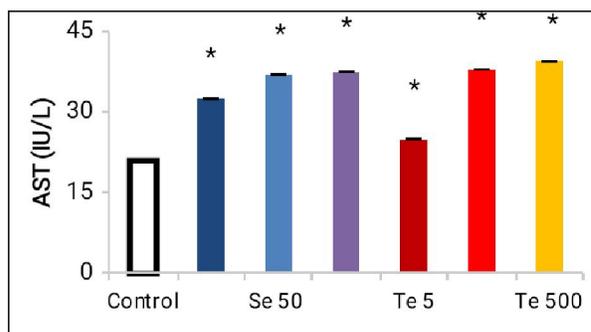


Figure 12: Comparison between Se and Te containing QD regarding aspartate aminotransferase (AST).

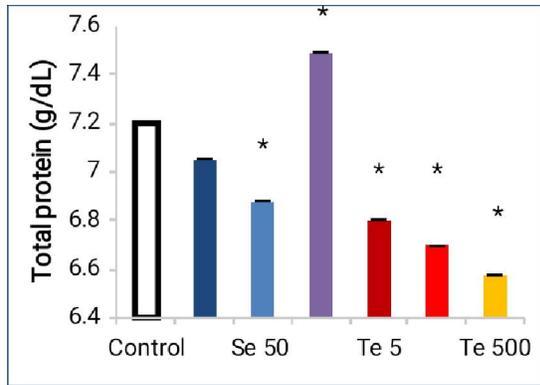


Figure 13: comparison between Se and Te containing QDs regarding total protein.

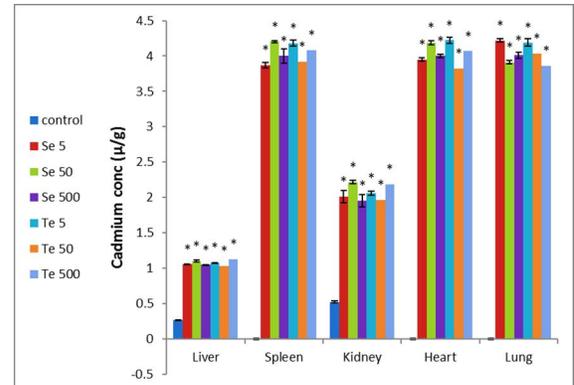


Figure 15: comparison between cadmium concentration in the animals' studied organs.

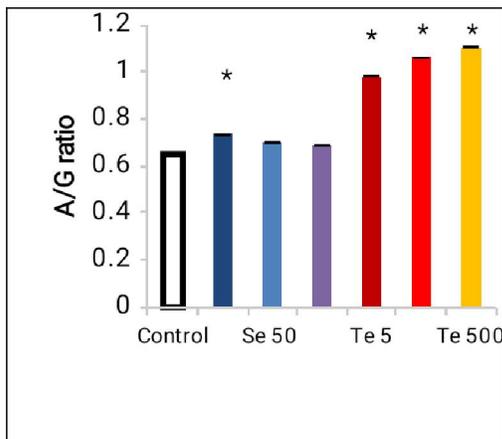


Figure 14: comparison between Se and Te containing QDs regarding albumin/globulin ratio (A/G).

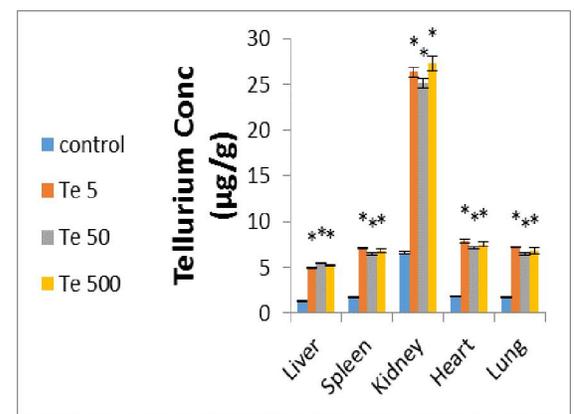


Figure 16: comparison between tellurium concentration in the animals' studied organs.

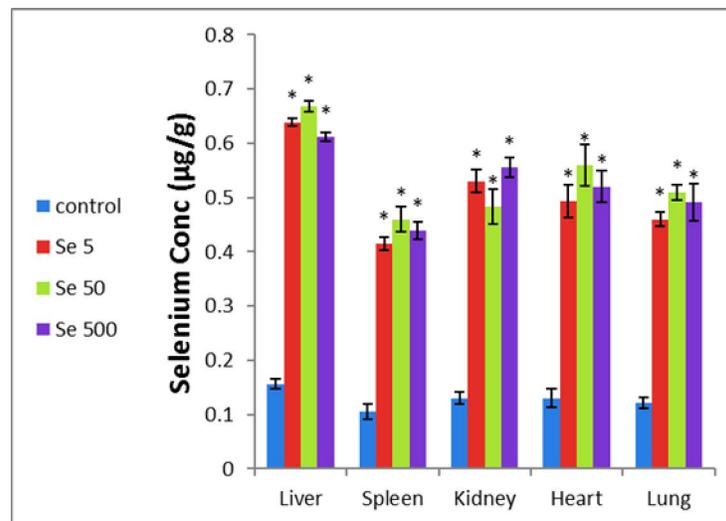


Figure 17: comparison between selenium concentration in the animals' studied organs.

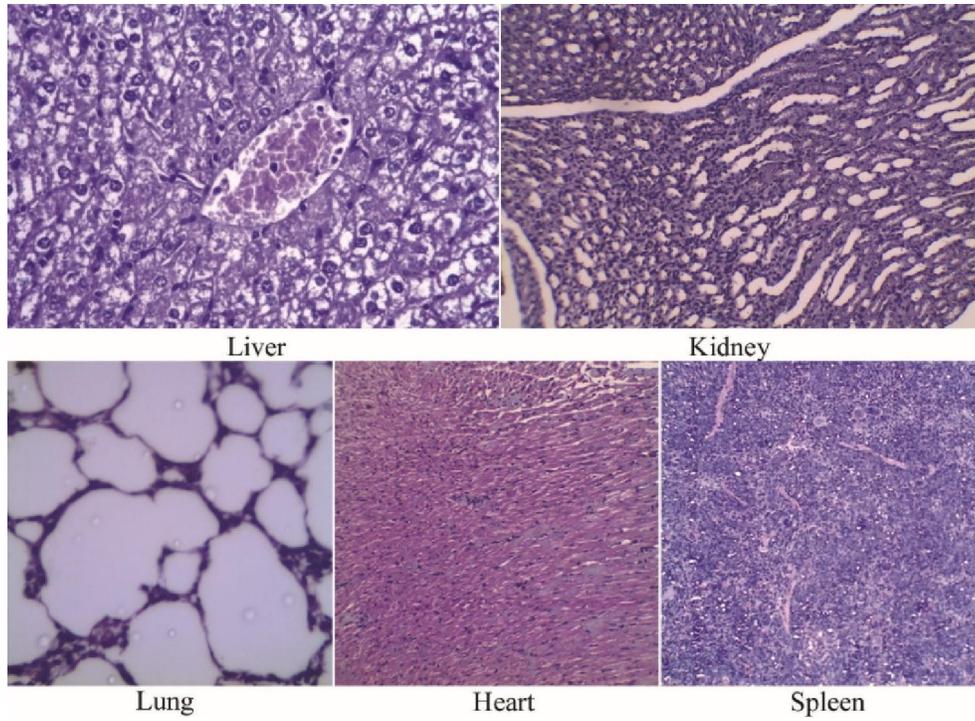


Fig. 18: Normal organs in control group with no pathological changes.

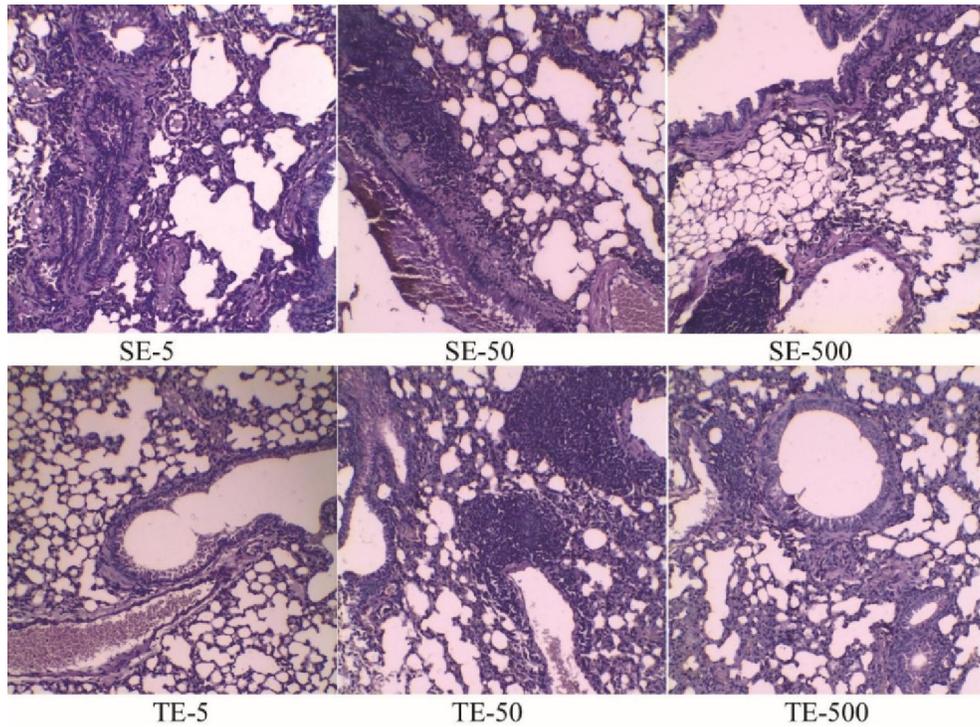


Fig. 19: Lung changes show Interstitial inflammation and edema with presence of inflammatory exudates. Hyperplastic lymphoid follicles are seen in SE-500 and TE-50.

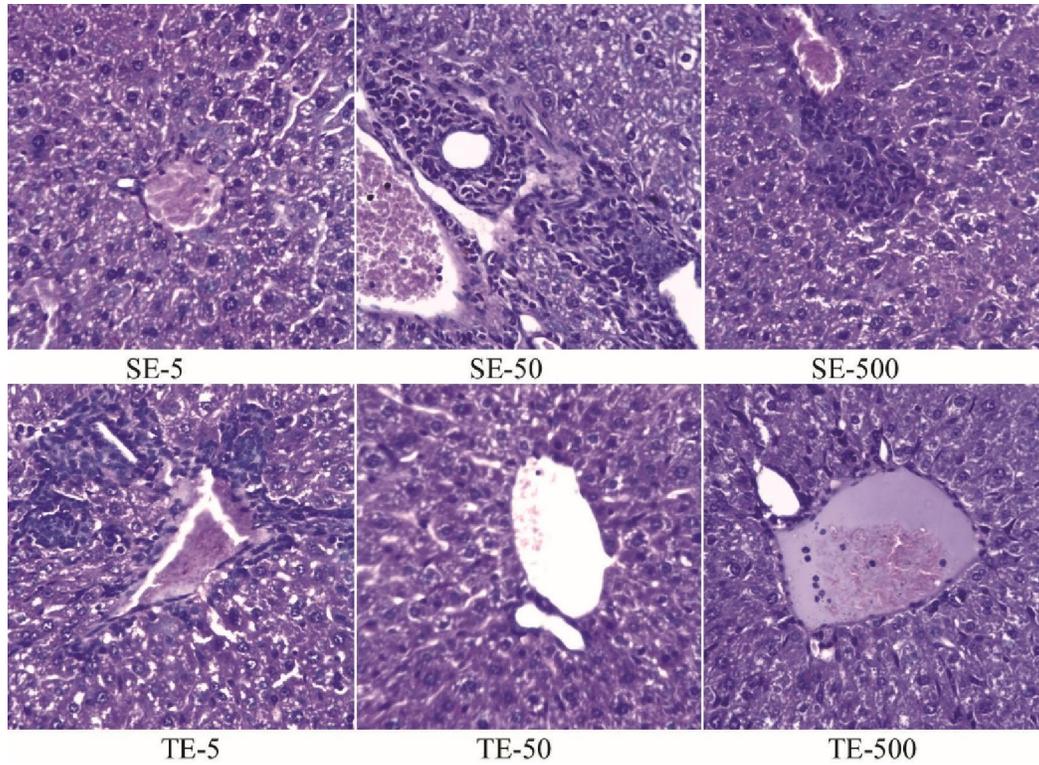


Fig. 20: Normal liver with SE-5, minimal hepatitis with SE-500, TE-50 and TE-500, Moderate hepatitis with fibrosis in SE-50 and TE-5.

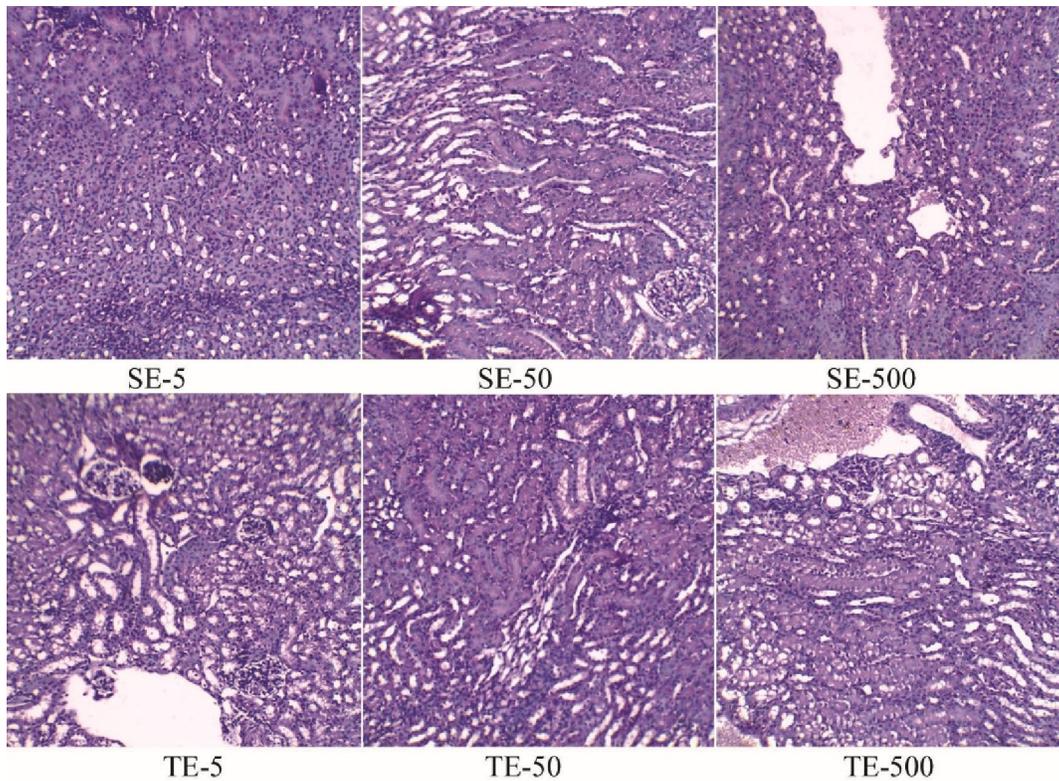


Fig. 21: Kidney changes show tubular lumen obliterations, cloudy swelling of the lining epithelium. Hydropic degeneration is noted with TE-50 and TE-500. Glomeruli showed no changes.

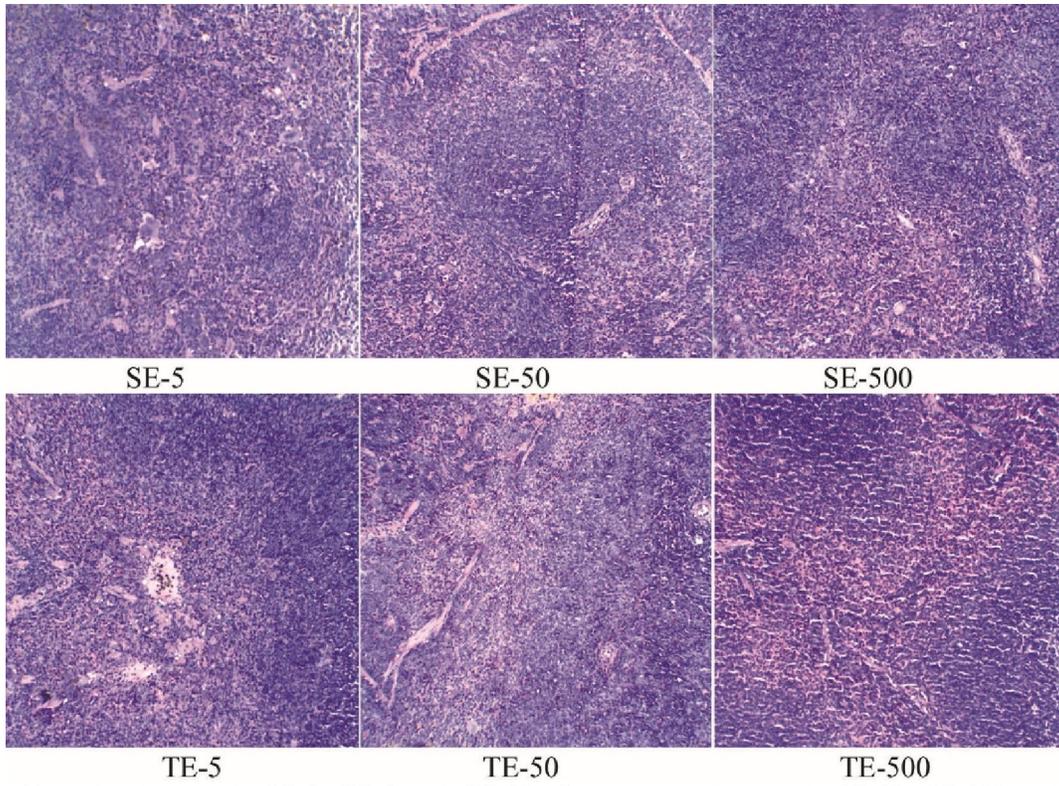


Fig. 22: Normal spleen with SE-5, TE-5 and TE-50. Congestive spleen with SE-50, SE-500 and TE-500 (hyperplastic white pulp and congestion of red pulp).

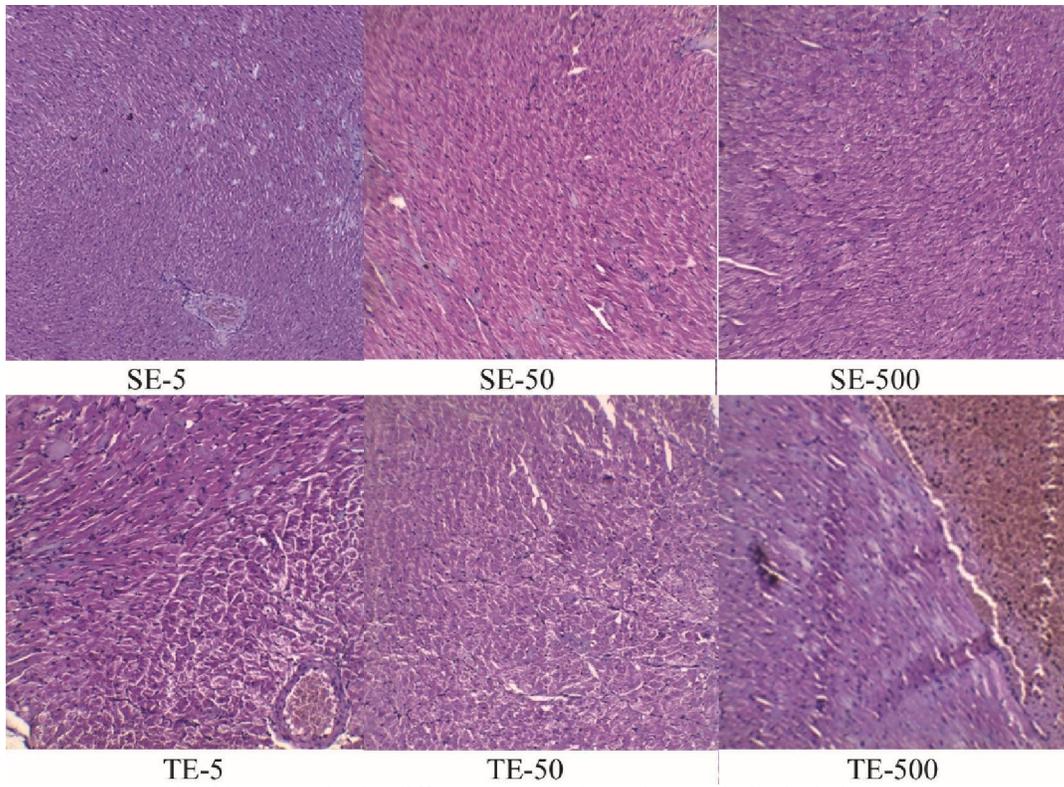


Fig. 23: Hearts in the different groups showed no pathological changes.

Table 1: Histopathological results of the studied organs in the control and the studied QDs treated groups.

Studied Organ	Control (N=8)	Se5 (N=8)	Se50 (N=8)	Se500 (N=8)	Te5 (N=8)	Te50 (N=8)	Te500 (N=8)
Lung							
Normal	8 Cases (100%)	3 Cases (37.5%)	1 Case (12.5%)	0	2 Cases (25%)	0	0
Edema	0	2 Cases (25%)	3 Cases (37.5%)	3 Cases (37.5%)	3 Cases (37.5%)	5 Cases (62.5%)	7 Cases (87.5%)
Inflammation	0	5 Cases (62.5%)	7 Cases (87.5%)	8 Cases (100%)	6 Cases (75%)	8 Cases (100%)	8 Cases (100%)
Exudation	0	1 Case (12.5%)	3 Cases (37.5%)	3 Cases (37.5%)	5 Cases (62.5%)	5 Cases (62.5%)	7 Cases (87.5%)
Liver							
Normal	8 (100%)	4 Cases (50%)	1 Case (12.5%)	0	1 Case (12.5%)	0	0
Minimal Hepatitis	0	2 Cases (25%)	4 Cases (50%)	1 Case (12.5%)	6 Cases (75%)	6 Cases (75%)	1 Case (12.5%)
Moderate Hepatitis	0	2 Cases (25%)	3 Cases (37.5%)	7 Cases (87.5%)	1 Case (12.5%)	2 Cases (25%)	7 Cases (87.5%)
Portal Fibrosis	0	2 Cases (25%)	2 Cases (25%)	4 Cases (50%)	3 Cases (37.5%)	5 Cases (62.5%)	5 Cases (62.5%)
Kidney							
Normal	8 (100%)	5 Cases (62.5%)	4 Cases (50%)	1 Case (12.5%)	3 Cases (37.5%)	0	0
Cloudy Swelling	0	3 Cases (37.5%)	4 Cases (50%)	7 Cases (87.5%)	4 Cases (50%)	5 Cases (62.5%)	4 Cases (50%)
Lumen Obliteration	0	1 Case (12.5%)	2 Cases (25%)	5 Cases (62.5%)	4 Cases (50%)	6 Cases (75%)	7 Cases (87.5%)
Hydropic Deg.	0	0	0	1 Case (12.5%)	1 Case (12.5%)	2 Cases (25%)	4 Cases (50%)
Glomeruli	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Spleen							
Normal	8 (100%)	8 (100%)	8 (100%)	7 Cases (87.5%)	5 Cases (62.5%)	5 Cases (62.5%)	
Congestive	0	0	0	1 Case (12.5%)	3 Cases (37.5%)	3 Cases (37.5%)	
Heart							
Normal	8 (100%)	8 (100%)	8 (100%)	8 (100%)	8 (100%)	8 (100%)	8 (100%)

Primarily before using the nanoparticle QDs as a very promising probe in biomedical applications, studying its toxicity is a stone corner to establish this purpose. Two types of QDs have been investigated. Their choice depended on; first, their commercial marketing as being suggested for biomedical applications; and second, their possessing nearly the same coat in order to fix the cause of their stability in vivo and being different in the core heavy metal component. So, we can conclude which type of the core of QD is not toxic and safe or even both are the same. Single high mounting doses of CdSe/ZnSQD “stabilized by mercaptoundecanionic acid and functionalized with a coat of carboxylic acid and amine ligands, has green color emission, and approximately 3.60 nm diameter with emission peak

520-550 nm” and CdTe QD core type “carboxylic acid functionalized, fluorescence color emission, and emission peak 520 nm” were used in this study. The emission peak and color of both types of the used QDs were nearly the same so they can be used for the same purposes e.g. for cells imaging. Regarding heavy metals’ concentration introduced in the structure of the core, cadmium was only detected in the liver and kidney of the control group which was logic because as known, Cd is normally absent from mammalians’ bodies and accumulates in the liver and kidneys by the time.²⁷ Current results showed that cadmium was in higher concentrations in lung, heart and spleen than liver and kidneys of QDs’ treated animals. Tellurium was detected with nearly concentrations of close in the studied organs but the kidney of the control and

treated groups. It was noticed to be with the highest concentration in the kidney. This is supporting the result of Liu *et al.* (2013) who studied the degradation of CdTe/ZnS quantum dots in mice and concluded that Te distribution was primarily to the kidneys.²⁵ Tellurium was distributed to all the studied organs. Tellurium is a chemical with a structural relation to selenium and sulfur. It is a good electrical conductor.²⁸ Humans exposed to Tellurium in workplace by inhalation, ingestion, skin contact, and eye contact. It has no biological function²⁹, there is lack of literature regarding the toxic effect of tellurium or its air born form 'tellurium hexafluoride'³⁰. Selenium also was detected in all of the studied organs of the control group. Selenium normally exists in mice as a trace element and acts as a cofactor for many enzymes.³¹ Its release from QDs is confirmed too by increased its concentration in the treated animals comparing with the control with the highest concentration was in the liver. It could pass through the liver, pancreas and peripheral tissues several times before excretion.³² It was obvious that QDs used in the present study were unstable *in vivo* because of the release of their heavy metals components including Cd, Se, and Te which were significantly higher in the treated animals comparing with the control group. Complete blood picture as well as biochemistry of blood samples were performed. Interestingly, hemoglobin level, RBCS count, Ht % were increased in all animals treated with both QDs by all doses and MCHC level was increase in selenium containing QD comparing with the control and Te containing QD. Previous studies concluded that selenium could be positively affecting hemoglobin synthesis and erythropoiesis.^{33, 34} Tellurium, the chemical which is related structurally to selenium and its metabolism still not known, could resemble selenium, as it has similar methylated compound end products as selenium.³⁵ Besides that, all the previously mentioned lab hematological parameters were within the normal values. Reduction of WBCS with using both types of QDs was also within the normal values and indicating no immune function effect. Regarding kidney function; urea level was increased on administration of both of the used QDs, it was higher in Te than Se containing QD and directly proportional with the dose. Also, creatinine level increased in Te containing QD treated animals and it was related to the dose also. It seemed that despite of the normal values of the lab results, there were variant pathological changes in the studied organs. On microscopic examination animals exposed to the highest dose of Te containing QD i.e. 500 µg/kg showed the most nephrotoxic effect in the form of hydropic degeneration. Comparing the studied two types of QDs, Te containing QD could have nephrotoxic effect that was concluded by the high

level of Te in the kidney, the elevated urea and creatinine levels and the noticed pathological changes in the kidneys. The lung was the most affected organ. The noticed chemical pneumonitis due to distribution of heavy metals to the lung could occurred and it could be also caused by the chemicals components of the coat i.e. MUA and carboxylic acid. The probability of induction of toxicity could be caused by the capping substances exists.³⁶ Cadmium existed in both types of the investigated QDs and its level was noticed to be high in the lung comparing with the control despite of being injected intravenously. Lung toxicity due to exposure to cadmium fumes is common²⁷, however following intravenous administration is not common. In the current study, distribution of nanoparticles of cadmium to the lung could produce the noticed lung toxicity due to direct toxic chemical pneumonitis. Regarding liver function tests, variable affections were noticed in animals received both types of QDs with elevation of A/G ratio with Te containing QD and TPR associated with the highest dose of Se containing QD. However, all liver function parameters were within normal ranges.³⁷ Histopathological examination revealed chemical toxicity in the liver of all animals with variable degrees with preservation of liver architecture. Liver cells were more affected than kidney cells. This could be explained by being the site of metabolism. The exact human toxicokinetics and toxicodynamics of QDs still not well defined.^{38, 39} QDs may carry positive charges or negative charges and could be bonded to biomolecules through electrostatic integration.⁴⁰ Reduction of toxic degrades occurs through nanoparticles oxidation which leads to liberation of the cadmium core and the other cadmium conjugated heavy metal introduced in the components of QD, which will negatively affect cell function.¹⁶ Toxicity also could occurs as a result of production of reactive oxygen intermediates due to photosensitization of QD results in cell damage.⁴¹ In a study conducted in arsenic containing dots, toxicity was expecting to be minute due to the small size of the dots.⁴² In the present study QD's heavy metals contents still existed for 14 days following single IV administration of it. Storage of QDs in the body could occurs for long time⁴³, especially large QDs, within the reticuloendothelial system like the spleen, liver and lymphatic system. Whereas, smaller QDs could be rapidly excreted via the kidneys.⁴⁴ It means that, to reduce toxicity of the QDs, smaller one could be designed to hasten their excretion.⁴⁵ The current studied CdSe/ZnS was nearly 3.6 nm in diameter whereas CdTe was not measured by the productive company. So, reduction of the size of the used QDs could decrease its retention in the body. In a study conducted in mice, it has been found that CdTe/ZnS core/shell, water soluble QDs were not enough stable

or save to be used *in vivo* without producing toxicity in spite of being inert *in vitro*.²⁵

Conclusions

The used nanoparticles QDs had been degraded *in vivo* and its heavy metals contents had been distributed to the liver, kidneys, lungs, spleen and heart and were still existed within the studied organs after 14 days of intravenous injection. Cadmium nanoparticles were distributed to the lung and could cause chemical pneumonitis. Tellurium containing CdTe QD could had more toxic effect on the kidney. Histopathological examination of the liver, kidney and lung indicated toxic effect with preservation of their function. Histopathological changes could be reversible which could not hinder the use of the studied QDs for biomedical applications.

Recommendations

Further studies are recommended for longer period following administration to study the reversibility of the histopathological changes and long sequel toxicity. Further studies are needed to evaluate the stability of the studied QDs few hours after administration to assess the benefit of its usage in biomedical fields.

Conflict of interest

No potential conflict of interest was reported by the authors.

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