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The weight changes in bodies and some organs system of albino mice treated with silver nanoparticles

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ABSTRACT

This study was conducted to determine the weight changes in their bodies and some organs system of albino mice that orally administrated with silver nanoparticles (Ag-NPs). Use 20 mice were divided into two groups: the first group as a control (5 animals) and the second group administrated with 200 mg/kg BW of Ag-NPs for 5, 10, and 15 days. Each period involved 5 animals. The animals weighted before and after the end of the treatment period and dissected to collect the organs (liver, spleen, kidney, gastrointestinal tract (GIT), heart and seminal vesicle) for weighting. Results indicated to obtain significant decrease ($P<0.05$) in the average body weights of animals after the end of each treatment period compared to the period before treatment. The results also showed a significant decrease ($P<0.05$) in the average coefficient relative weight of the spleen after 5 days of treatment compared to the control group. Whereas, there was a significantly increase ($P<0.05$) in the average coefficient relative weight of the kidneys, GIT, lung and heart after 10 days of treatment compared with the control groups. So, it seems that Ag-NPs have a negative effect on the animals' body weights and the internal organs system. Therefore more studies are necessary to evaluate the effects of this material on the histology structure of these organs.

الخلاصة

أجريت الدراسة لمعرفة التغيرات الوزنية في اجسام وبعض اعضاء اجهزة الفئران البيض المجرعة فموياً بجسيمات الفضة النانوية. استخدم ٢٠ فاراً وقسمت الى مجموعتين الاولى كسيطرة (٥ حيوان) والمجموعة الثانية جرعت بـ ٢٠٠ ملغم/كم من جسيمات الفضة النانوية ولفترات زمنية ٥ و ١٠ و ١٥ يوم. وكل فترة تضمنت ٥ حيوانات. وزنت الحيوانات قبل وبعد نهاية فترة المعاملة وشرحت الفئران لجمع الاعضاء وهي الكبد والطحال والكلية والمجرى المعوي المعدي والقلب والحويصلة المنوية ثم وزنها. اشارت النتائج الى حصول انخفاض معنوي ($P<0.05$) في معدل اوزان اجسام الحيوانات بعد نهاية فترة كل معاملة مقارنة بمجموعة السيطرة. كما اظهرت النتائج حصول انخفاض معنوي ($P<0.05$) في معدل المعامل النسبي لوزن الطحال بعد فترة ٥ يوم من المعاملة مقارنة بمجموعة السيطرة. في حين حدثت زيادة معنوية ($P<0.05$) في معدل المعامل النسبي لأوزان الكلى والمجرى االمعدي المعوي والرئة والقلب بعد ١٠ ايام من المعاملة مقارنة مع مجاميع السيطرة. وهكذا يبدو ان جسيمات الفضة النانوية لها تأثير سلبي على معدل أوزان اجسام الحيوانات وأعضاء أجهزتها الداخلية. ان المزيد من الدراسات ضرورية لتقييم اثار هذه المواد على البنية النسجية لهذه الاعضاء.

INTRODUCTION

Nanoparticles (NP) are defined as substances made within the nanoscale between 1–100 nm in diameter that show exclusive new properties of the structural integrity as well as chemical and physical properties [1]. Silver nanoparticles (Ag NPs) is considered as a one of the most commonly used metal based nanoparticles, which are widely used in consumer products and medical uses [2 and 3]. Ag NPs have also abilities for inhibitory and bactericidal effects as well as a slow down the growth of mold, harmful spores and germs [2]. Due to increased uses of Ag-NPs, human exposure to these materials has been increased. Limited information have been recounted for silver nanoparticles by oral routes of exposure. Oral exposure to Ag-NPs (56 nm) over a period of 90 days in male rats caused a significant decrease ($P < 0.05$) in the body weight of animals after 4 weeks of exposure [4]. Whereas [5] found that intragastric administration of 2.5,5, and 10 mg/kg TiO_2 NPs in mice caused decreased body weight, elevation kidney indices, unbalance of element distribution, creation of reactive oxygen species and peroxidation of lipid, protein and DNA in mouse kidney tissue after 90 days of exposure. The main objective of this study was to investigate the effect of Ag NPs on body weight and some organs in the mice body during different time of exposure.

Material and methods

Preparation and characterization of Ag NPs

The Ag-NPs used were purchased from Sigma Aldrich company and had (manufacturer's information) a

spherical configuration with an average particle size >80 nm and 99.9 % purity. The powder had a dark gray color. The 200 mg/kg Ag NPs solutions or 50 mg /1 ml were prepared by diluted 750 mg of Ag NPs with 15 ml of distilled water and then put it overnight on magnetic stirrer to dissolve.

Animal treatments

All laboratory mice were purchased from the Health Center for Control and Pharmaceutical Research. Twenty male ICR mice (10–13 weeks old, 29–33 g body weight) were used in oral administration test. The experimental mice were housed in plastic cages in a ventilated animal room under 12:12 hr light dark cycle, and temperature of 25 ^{o}C. They were provided with pelleted commercial food and tap water *ad libitum* all over the experiment. Animals were randomly divided into 2 groups: one control group and one experimental group (200 mg/kg BW of Ag NPs). The experimental groups divided into 3 groups depend on the period of exposure (5, 10, and 15 days). Each group had 5 animals and each treated animal received 0.1 ml from stock Ag-NPs solution daily. The remaining 5 mice were used as the positive control group. The mice received Ag-NPs at the limited dose of 200 mg/kg orally using a suitable intubation cannula at each period of exposure. At 5, 10 and 15 days after gavage, five mice in each group were sacrificed. Whole body weight was recorded before and after one day of the end of the dose. Various organs such as gastrointestinal tract (GIT), liver, spleen, lung, kidney, seminal vesicles and heart were also collected from mice and then weight recorded (Figure 1). The organ weight/body weight (BW) coefficients of GIT, liver, spleen, lung, kidney, seminal vesicles and heart, were calculated as organ weight (wet weight, g)/BW (g) x 100%.

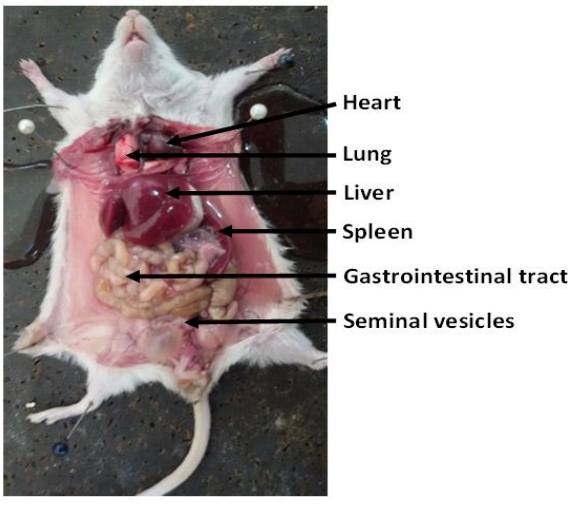

Figure 1 shows the organs position which are collected from mice.

Statistical analysis

The results of this experiment were expressed as means (Mean ± S.E.). Data were analyzed by using the SPSS statistical software (ver. 20, SPSS Inc., Chicago, IL). All data were analyzed by using one-way analysis of variance followed by t test. A value of ($P< 0.05$) was considered statistically significant.

Result and Discussion

Animal observation

The general behavior of animals belonging to the all experimental mice that orally administrated with 200 mg/kg of silver nanoparticles (Ag-NPs) were similar. During the experiment, several stress symptoms such as reduced appetite and elevated aggression were seen in all Ag-NPs treated groups. The current results is agreement with [6] that found the treatment of anemia progression by magnetite and folate nanoparticles in rats caused vomiting, loss of appetite, and severe lethargy demonstrate and the author suggest that magnetite and folate-coated magnetite nanoparticles have severe toxicological effects *in vivo*.

Body weight

The results showed significantly decrease ($P<0.05$) in the average weight of animals body after 5, 10 and 15 days of exposure to Ag-NPs compared to the same animals groups before treated. The body weight decrease was about 3–4 g. While the animals of control group exhibit a statistically significant increased ($P<0.05$) in the average of body weight after gavage with distill water compare to the same animal group before treated (Figure 2). The body weight increase was 4 g.

Decreases in the average body weight reported in the current study are consistent with literature showing that oral exposure to 30, 125, and 500 mg/kg of Ag-NPs for 13 weeks in male rats caused a significant decrease ($P< 0.05$) in the body weight after 4 weeks of exposure [4]. Another study found also that oral administration of 1100 µg/kg gold nanoparticles over 28 days caused a decrease in the body weight [7]. [7] suggest that oral exposure to NPs could produce some effects on the digestive system.

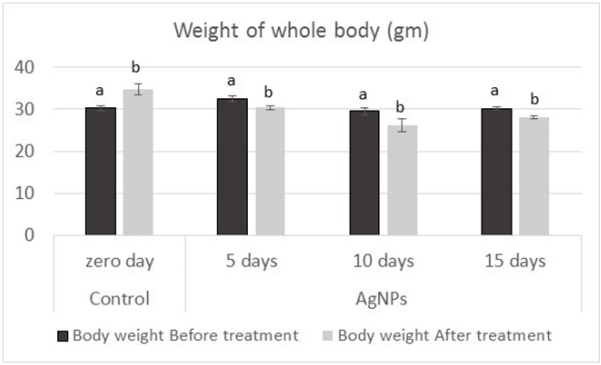

Figure 2 shows the whole body weight of albino mice before and after orally administration with 200 mg/kg body weight of Ag NPs for 5, 10, and 15 days. Data are means ±S.E.M. (n = 5). Different letters denote significant difference between treatment groups ($P<0.05$). Similar letters denote no significant difference between treatment groups ($P>0.05$).

Organs weight

The coefficient-relative of some organs weights in all treatments during different time of exposure, relative to the control are shown in Table 1. The present study exhibit a statistically significant decrease ($P<0.05$) in the coefficient of spleen weight after 5 days of exposure to 200 mg/kg Ag-NPs compared to control groups (Figure 3 and Table 1). Whereas other period time (10 and 15 days) of treated animals does not show any significant difference when compared to the control. This may indicate that the oral administration can disturb the gastrointestinal system and then can damage the immune system [8]. In addition, the spleen is one of the target organs for nanoparticles (TiO_2 NPs) accumulation [9]. The current results is agreement with [8] That found the oral administration of gold nanoparticles(550-2200 µg/kg) for14 days in mice caused significant decreases in body weight, spleen index, and red blood cells.

The coefficient-relative of kidney, GIT, lung and heart weight in the present study showed statistically significant increase after 10 days of orally administrated with 200 mg/kg Ag-NPs compared to group mice (Figure 4). While other period time (5 and 15 days) does not show any significant difference when compared to control animal.

Absorption of silver after oral administration has been revealed to be first-pass through the liver, resulting in elimination into the bile duct [10]. Un-cleared silver has been revealed to be deposited in the basement membrane of renal glomerular [11-13], mesangium [14], Kupffer cells and endothelium cells in the sinusoid of the liver [15].

In previous study, the target organs for Ag-NPs were revealed to be the liver after 28 days of oral administration [16] and the liver and lungs after 90 days of inhalation exposure [17]. The alteration that observed in the coefficient-relative of kidney, GIT, lung, heart weight could be due to the injuries that occurred in these organs. Study by [5] found that intragastric administration of 2.5, 5, and 10 mg/kg body weight of TiO_2 NPs for 90 days in mice induced body weight reduction, increased kidney indices, histopathological alteration, apoptosis, oxidative stress, and deterioration of element balance in kidney with elevation of TiO_2 NPs doses. The increased coefficients lung weight suggested that the inflammation may be made and kept in the pulmonary tissues for one week after rat exposure of TiO_2 NPs [18].Study by [17] showed that inhalation of Ag-NPs in rats for 90 days caused chronic alveolar inflammation, accumulation of alveolar macrophages, and a mixed cell perivascular in lungs.

In this study, oral administration of Ag-NPs had effect on coefficient weight of the heart. This may occurred due to the pathological effects. This was relatively in agreement with previous reports. [19] found that oral administration of ZnO NPs caused pathological effects (mild hyaline degeneration of the heart muscle tissue with severe anemia and high condensation of nuclei as well as bleeding) on the heart of rats.

The coefficient-relative of liver and seminal vesicle weight does not shown any statistically significant difference ($P>0.05$) as compared to control groups (Figure 4 and Table 1). This may indicate that the liver work to detoxify the blood to rid it of harmful substances (Ag-NPs). The current result is agreement with [4] that found the oral administration of Ag-NPs over 90 days in rats did not caused alteration in the weight of liver and seminal vesicles.

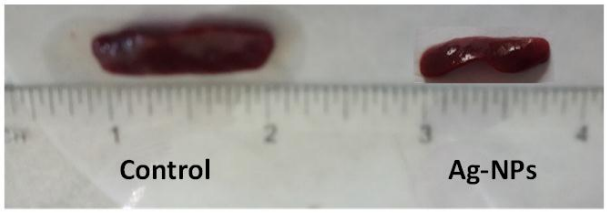

Figure 3 Show the spleen of control groups and treated animal with Ag-NPs.

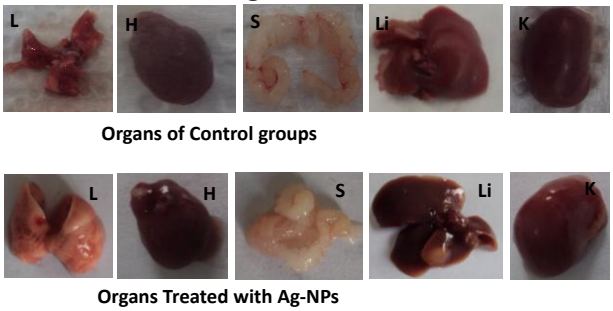

Figure 4 Show the shape of some organs of control groups and treated animal with 200 mg/kg of Ag-NPs after 10 days of treatment. Note: the symbol indicate L (lung), H (heart), S (seminal vesicle), Li (liver), K (kidney).

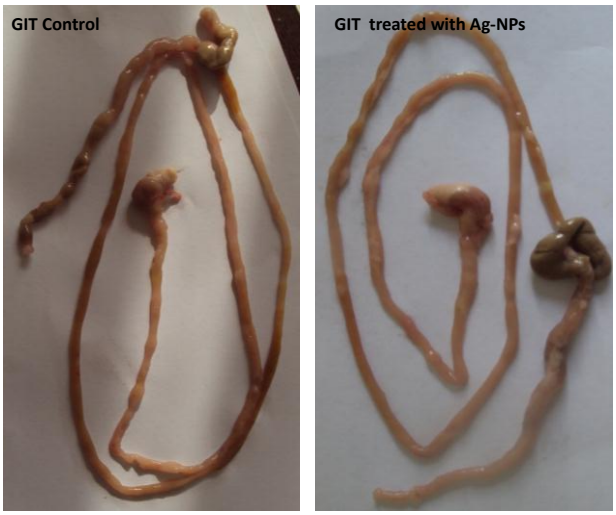

Figure 5 Show the shape of GIT of control groups and treated animal with 200 mg/kg of Ag-NPs after 10 days of treatment

Conclusion

An animal toxicity study using 200 mg/kg silver nanoparticles in mice was carried out. Animal observation, body weight, and coefficient organs weight were detected over 15 days. The results show that Ag-

NPs at 200 mg/kg induce significant decrease in body weight. Obvious effects on coefficient organs weight have been revealed that spleen, kidney, GIT, lung and heart is considered as a target organs to Ag-NPs toxicity.

Table (1) shows a coefficient-relative organs weight in albino mice treated with 200 mg/kg of Ag NPs for 5, 10 and 15 days.

Treatment	Time/ Day	N	The coefficient weight of						
			Liver	Spleen	Kidney	GIT	Lung	Heart	Seminal vesicle
Control	zero	5	6.49 ± 0.35	0.66 ± 0.07 a	0.68 ± 0.04 a	12.69 ± 0.45 a	0.81 ± 0.02 a	0.49 ± 0.01 a	0.46 ± 0.03
200 mg/kg AgNPs	5	5	5.82 ± 0.25	0.44 ± 0.06 b	0.68 ± 0.05 a	14.52 ± 0.72 a	0.76 ± 0.05 a	0.52 ± 0.02 a	0.54 ± 0.13
	10	5	5.56 ± 0.42	0.66 ± 0.03 ac	0.86 ± 0.04 bc	15.88 ± 1.80 b	1.14 ± 0.04 bc	0.66 ± 0.03 bc	0.57 ± 0.08
	15	5	6.15 ± 0.22	0.60 ± 0.03 ac	0.76 ± 0.06 a	15.52 ± 0.48 a	0.83 ± 0.04 ac	0.55 ± 0.02 d	0.45 ± 0.13

Data are means ±S.E.M. Different letters denote significant difference between treatment groups (P<0.05). Similar letters denote no significant difference between treatment groups (P>0.05).

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