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Effect of acute and chronic administration of gold nanospheres on behavioral changes and body weight in male albino rats

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A B S T R A C T

Objectives: This work was conducted to investigate the acute and chronic effects of gold nanoparticles on animal observation, bodyweight and different organ weight in male rats. Methods: Experiment I: 54 adult male rats were randomly assigned into three equal groups (18 per group). Group 1 (control group): Rats were received intramuscular (i.m) injection of 1 ml normal saline 0.9%. Group II (50nm GNSs) and Group III (10nm GNSs): Rats were i.m injected with a single dose of 75µg GNSs/kg/bwt. xperiment II: 18 adult male rats were randomly divided into three equal groups (6 per group). Group I: Rats were i.m injected with 1 ml normal saline 0.9% for 5 weeks once/week. Group II (50nm GNSs) and Group III (10nm GNSs): Rats were i.m. injected with repeated doses of 75µg GNSs/kg/bwt for 5 weeks once/week followed by 3 weeks washout period. Rats were observed daily for behavioral changes, weighed weekly and scarified by head dislocation at days 3, 7 and 60 days of 1st experiment and at day 60 of 2nd experiment for organ weight measurements.Results: Acute and chronic administration of GNPs (10 or 50nm size) in male albino rats caused no significant variations on animal observation, body weight gain and various organ weights between the gold nanoparticle-treated rats and control rats and also caused no any symptoms of toxicity as well as had no mortalities.

Conclusion: Acute and chronic administration of AuNSs (10 and 50nm size) are safe, induced no significance difference on daily animal observation, body and different organ weights.

Keywords: Male Albino rats, Gold nanospheres, Acute or chronic injection, body weight.

1. Introduction

Nanotechnology provides attractive biocompatibility, high surface and catalytic activities which making nanoparticle (NPs) suitable for a wide range of biomedical uses (Satvekar et al., 2014). NPs can be classified into two types; organic and inorganic. The most prominent inorganic nanoparticles are gold nanoparticles (AuNPs), (Abdo, et al., 2016).

Recently, AuNPs are a major science advance in nanotechnology used in multiple fields of medicine and various industries including farming, livestock, home equipment, food packaging, cosmetics, DNA detection and disease therapy (Balasubramanian et al., 2010) due to their unique surface chemistry, electronic, and optical properties (Zhang et al., 2011).

Nanoparticles may simultaneously be useful or harmful (Fiorito et al., 2006). Several studies have demonstrated that GNPs are toxic which showed the toxicity of gold NPs (Sung et al., 2011), although other studies have found otherwise that AuNPs are not toxic (Patra et al., 2007 and Peng et al., 2009). Nanotoxicology is a branch of bionanoscience that is developed to assess the risks and safety patterns of nanomaterials, which can play an important role in developing sustainable and safe nanotechnology (Drobne, 2007).

Here we focus our attention on studying the acute and chronic effects of AuNPs on animal observation, bodyweight and different organ weight in male albino rats.

2. Materials and Methods

2.1. Chemicals:

AuNPs (10nm size) were purchased from Sigma-Aldrich Com., Germany (PCode: 4100798324), while AuNPs (50nm size) were prepared according to Turkevich method (Turkevich et al., 1951).

Animals and experimental design:

In the current study, 72 adult male Albino Wister rats (110-150 g/bwt) were collected from AL-Zyade Experimental Animals Production Center, Giza, Egypt. They were left for two weeks to be adjusted. The feed of balanced ration and water were added ad libitum. They were randomly separated into 2 experiments.

Experiment I: Effect of acute i.m. administration of 10nm and 50nm gold nanospheres (GNSs) on animal observation, bodyweight and different organ weight in male rats, 54 adult male rats were randomly distributed into three equal groups:

Group I (control group): 18 rats were received i.m. injection of 1 ml normal saline 0.9%.

Group II (50nmGNSs): 18 rats were received a single dose of 75µg 50nm GNPs/kg/bwt, i.m. according to Abdoon et al. (2016).

Group III (10nm GNSs): Eighteen rats were i.m. injected single dose of 75µg GNSs/kg/bwt (Abdoon et al., 2016) at size 10nm, were diluted using physiological saline solution.

Experiment II: Effect of chronic i.m. administration of 10nm and 50nm gold nanospheres on animal observation, bodyweight and different organ weight in male rats, 18 adult male rats were randomly split into three equal groups:

Group I (control group): 6 rats were received i.m. injection of 1 ml normal saline 0.9%.

Group II (50nm GNSs): 6 rats were administered 75µg 50nm GNPs/kg/bwt once weekly for consecutive five weeks then 21-days washout period (Abdoon et al., 2016).

Group III (10nm GNSs): 6 rats were i.m. injected 75µg 10nm GNPs/kg/bwt once weekly for consecutive five weeks, then 21-days washout period (Abdoon et al., 2016).

Animal observation and measurements of body& organ weight:

Rats were observed daily for behavioral changes and body weights of rats in different groups were recorded weekly from 1W to 8W. The weights of liver, kidney, spleen, heart, lung, epididymis and testes were recorded after scarification by head dislocation at days 3, 7 and 60 days of 1st experiment and at day 60 of 2nd experiment.

3. Results

Effect of GNSs on animal observation, body and organ weights:

Data illustrated in tables 1, 2 and 3 represent the acute and chronic effects of i.m. injection of 75µg GNSs/kg/bwt on body and different organ weights as liver, kidney, spleen, heart, lung, epididymis and testes. Results indicated that i.m. injection of either single dose of GNSs at size 10 nm or 50 nm and scarifying after 3, 7 and 60 days or repeated doses for 60 days induced no statistically significant differences in body weight gain and various organ weights between the gold nanoparticle-treated rats and control rats and also cause no any symptoms of toxicity such as exhaustion, loss of appetite and change in fur color as well as had no mortalities and no any abnormalities throughout the study period.

4. Discussion

AuNPs are the most effective inorganic nanoparticles used in a number of biomedical applications including nanomedicine considered to be an emerging method for cancer treatment. The nontoxic effect of GNSs remains unclear, so this study aimed to investigate the acute and chronic effect of GNSs at size 10nm and 50nm on observation of animal behavior and measurement of body and various organ weights in different groups of rats.

During the present study, the acute and chronic administration of GNSs at size 10nm and 50nm induced no any symptoms of toxicity such as no variation in daily animal observation as well as no change in body weight gain between the gold nanoparticle-treated rats and control rats. Necropsy at any point of the experiment did not show any apparent gross lesions and no changes in different organ weights compared to the control group.

Our results are in accordance with the findings of BarathManiKanth et al. (2010) reported that intraperitoneal (IP) injection of AuNPs did not cause any variations within the morphology or behaviour of AuNPs treated mice and there were no any symptoms of toxicity like fatigue, loss of appetence, change in fur color and weight loss compared to control mice. Additionally, Chen et al. (2013) showed that IP injection of mice of spherical AuNPs caused no distinction in weight and organ mass at 1 h and 72 h compared to the control animals. Also, Sung et al. (2011) reported that there was no variation in various organ weights between male or female rats treated with AuNPs (4-5 nm) at different doses for 6 hours/day, 5 days/week, for 90-days in a whole body inhalation chamber and control rats.

5. Conclusion:

Single or repeated i.m injection of 10nm or 50nm AuNSs is safe, induced no alterations on daily animal observation, body and different organ weights compared to the control rats.

Ethical approval:

All animal-handling procedures as well as samples' collection and disposal were according to the regulations of Institutional Animal Care and Use Committee (IACUC), Faculty of Veterinary Medicine, University of Sadat City (Approval number: VUSC-006-1-19).

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Table 1. Effect of acute administration of GNSs on body weight (g) from 1W to 8W in different groups of rats

Time	G1 Control group	G2 GNSs (50nm)	G3 GNSs (10nm)
1W	216.21±9.45	205.02±8.28	219.01±6.65
2W	225.01±4.18	217.51±4.96	224.17±5.96
3W	229.57±5.75	223.88±4.85	226.50±6.24
4W	243.01±5.69	240.50±4.51	243.13±7.43
5W	253.88±4.39	252.38±5.17	255.50±9.11
6W	265.78±5.95	262.91±8.19	268.22±8.13
7W	283.75±5.95	281.75±7.40	285.13±9.51
8W	290.41±6.79	287.40±7.28	291.02±9.79

Table 2. Effect of chronic administration of GNSs on bodyweight (g) from 1W to 8W in different groups of rats

Time	G1 Control group	G2 GNSs (50nm)	G3 GNSs (10nm)
1W	223.75±8.55	214.86±6.01	218.67±5.69
2W	227.51±4.33	217.25±5.76	222.13±4.14
3W	232.33±5.91	232.63±4.49	236.11±4.05
4W	245.57±5.83	250.22±5.86	248.78±5.57
5W	256.58±4.01	263.78±6.58	261.33±5.84
6W	279.57±4.89	276.38±5.17	272.12±6.45
7W	285.51±6.07	278.11±7.64	285.25±8.15
8W	291.64±5.78	286.41±6.84	289.67±4.78

-Mean value ± SE of body weight (g), number of rat= 6

-The mean difference is significant at $P < 0.05$.

Table 3. Effect of acute and chronic administration of GNSs on organ weights (g) in different groups of rats

Treatment	Time	Group	Liver	Kidney	Spleen	Heart	Lung	Epididymis	Testes
Acute	Day -3	G1	7.58 ±0.61	1.34 ±0.05	0.64 ±0.05	0.74 ±0.05	1.52 ±0.05	0.84 ±0.05	2.53 ±0.11
		G2	7.44 ±0.46	1.36 ±0.07	0.68 ±0.05	0.74 ±0.06	1.39 ±0.02	0.76 ±0.07	2.25 ±0.05
		G3	8.11 ±0.46	1.47 ±0.03	0.64 ±0.05	0.79 ±0.04	1.47 ±0.09	0.89 ±0.06	2.51 ±0.09
	Day -7	G1	8.73 ±0.36	1.47 ±0.07	0.62 ±0.08	0.87 ±0.04	1.52 ±0.06	1.01 ±0.06	2.46 ±0.15
		G2	8.39 ±0.29	1.49 ±0.04	0.61 ±0.04	0.83 ±0.03	1.59 ±0.08	0.93 ±0.05	2.59 ±0.12
		G3	8.41 ±0.44	1.45 ±0.11	0.66 ±0.04	0.77 ±0.03	1.58 ±0.11	1.01 ±0.03	2.58 ±0.08
	Day -60	G1	8.43 ±0.27	1.71 ±0.09	0.58 ±0.05	0.87 ±0.04	1.88 ±0.19	1.42 ±0.09	2.66 ±0.11
		G2	8.14 ±0.29	1.61 ±0.05	0.67 ±0.04	0.84 ±0.04	1.72 ±0.11	1.31 ±0.05	2.79 ±0.13
		G3	7.79 ±0.61	1.69 ±0.11	0.63 ±0.08	0.83 ±0.06	1.51 ±0.08	1.21 ±0.05	2.96 ±0.23
Chronic	Day -60	G1	8.43 ±0.27	1.71 ±0.09	0.58 ±0.05	0.87 ±0.04	1.88 ±0.19	1.42 ±0.09	2.66 ±0.11
		G2	9.44 ±0.61	1.78 ±0.09	0.71 ±0.11	0.86 ±0.08	1.77 ±0.09	1.36 ±0.08	3.02 ±0.15
		G3	9.31 ±0.82	1.58 ±0.11	0.61 ±0.09	0.92 ±0.05	1.79 ±0.15	1.34 ±0.16	3.13 ±0.17

-Mean value ± SE of organ weight (g), number of rat= 6
-The mean difference is significant at $P < 0.05$.