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Sub-acute dermal toxicity of *Jatropha curcas* Linn. leaf extract coated silver nanoparticles (SNPs) in wistar rats

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ABSTRACT

The application of different nanoparticles is underway in the development of phyto-medicines. Silver nanoparticles (AgNPs) are commonly used as coating agents to treat various bacterial and viral diseases. Their safety and potential toxicity necessitate further research to explore the development of nanoparticles coated herbal drugs. The *Azadirachta indica* (neem) 5% leaf extract and silver nitrate was used to prepare the silver nanoparticles (SNPs) with the biological reduction (green synthesis) method [1]. The application of silver nanoparticles (SNPs) coated with *J. carcus* leaf extract (JcLE) on Wistar rats showed no adverse sign of toxicity on hematological parameters except an increase in the neutrophil count and increased in total erythrocyte count (TEC) on 28th day. Similarly, serum biochemical values exhibited an increase in aspartate aminotransferase (AST/SGOT) and alanine transaminase (ALT/SGPT) with JcLE-coated SNPs in treated groups. The histopathology revealed that there was no alteration in skin architecture, however, minimal alteration was observed in the liver and kidney with dilatation of the central vein and sinusoidal space, fatty change in the liver, multifocal necrobiotic changes, cystic degeneration and mild focal glomerular atrophy and hyaline cast in the lumen of tubules of kidney. It indicates the proper absorption and excretion of SNPs from the body. There was no significant effect on hematological parameters in the rats treated with *J. curcas* leaf extract-coated SNP. However, the serum biochemical analysis revealed a toxic effect on the kidney.

Keywords: Histopathology, Hematology, *Jatropha curcas*, Extract, Nanoparticles, Wistar rat.

INTRODUCTION

Nanoparticles are one of the novel drug delivery systems which avoid the physiological barriers and have specificity with the target sites. Nanoparticles can be used therapeutically either as a drug or as a carrier to transport the active substance to the desired site [2]. Because of their unique properties, nowadays, the preparation of drug coated with nanoparticles become very important as compared with the routine bulk materials preparation [3]. There are three methods for the production of nanoparticles viz, chemical, physical, and biological methods. Since noble metal nanoparticles such as gold, silver, and platinum nanoparticles are widely applied to human contacting areas, there is a growing need to develop environmentally friendly processes of nanoparticle synthesis that should be nontoxic. There are many more studies were conducted for synthesis of gold nano-triangles and silver nanoparticles (SNPs) using *Aloe vera* plant extracts with *Azadirachta indica* by biological method [4] and [5]. Even, the Department of Pharmacology and Toxicology, COVAS, Parbhani have synthesized nanoparticles, their coating with herbal extracts, and their efficacy. Gold and silver nanoparticles coated with different herbal extracts were also assessed for their efficacy against diabetes, mammary gland cancer and for antioxidant potency [6].

Jatropha curcas is a well-known plant species for its medicinal importance. Extracts of seeds, leaves, and bark of the plant are commonly used as traditional medicine in the treatment of various diseases of veterinary importance. Various skin diseases and rheumatic pain are generally cured with its oil. Traditionally, the plant is used in the treatment of cough and diarrhea. Antibacterial activity of *J. curcas* against *Staphylococcus aureus* and *Escherichia coli* was also reported [6] while crude extract of stem bark inhibited the development of pathogenic bacteria and fungi [6]. Besides various medicinal properties of *J. curcas* extract coated with SNPs was reported to possess significant anti-cancer properties under *in vitro* and *in vivo* studies on Wistar rats [6]. Keeping this view in mind, the present study was implemented to assess the dermal toxicity of *J. curcas* leaf extract coated with silver nanoparticles in Wistar rats.

MATERIAL AND METHODS

The toxicological effects of SNPs coated with *J. curcas* leaf extract were evaluated in Wistar rats, as per the OECD guideline no. 410 [8].

Silver Nitrate

The compound (Sliver nitrate, AgNO3, mol. Wt. 169.87) was procured from Loba Chemie Pvt. Ltd, Mumbai. It was white colored powder and stored in the refrigerator. Deionized water was used as a vehicle for this compound. By using Azadirachta indica (Neem) leaf extract and silver nitrate, the silver nanoparticles (SNPs) were obtained from the biological reduction method.

Plant material

Jatropha curcas is commonly known as Bagbh erenda, Jangali arandi, or Safed arand in Hindi and belongs to the family Euphobiaceae. Leaf extract was used for the study.

Collection and processing of *J. curcas* Linn.

The fresh leaves of the *J. curcas* plant were collected from the surrounding area of Vasantrao Naik Marathwada Agriculture University, Parbhani. The leaves were shade-dried for 15-20 days till no moisture was contained in the leaves and ground to coarse powder for aqueous cold extraction. 20% of the aqueous extract was prepared by dissolving 200 gm of coarse powder in a mortar mixed with 1000 ml of distilled water and kept for 24 hours. Then the slurries were strained through two layers of muslin cloth and were centrifuged at 4500 rpm for 10 minutes. The supernatant was considered a 20% aqueous extract. By subsequent dilution with distilled water, aqueous extracts of 15%, 10%, and 5% were prepared and kept at 4°C till for further use [9].

Synthesis of Silver nanoparticles

The dried leaves of *Azadirachta indica* (5gm) were cut into small pieces (without grind), dispensed in 100 ml of sterile distilled water, and kept in the water bath for an hour at 80ºC. Then, the *A. indica* leaf extract was collected in a separate conical flask and filtered through Whatmann filter paper no. 42. Silver nitrate solution of 10-3 M was prepared and stored in brown bottles. An amount of 5 ml of *A. indica* leaf extract was poured into the Biological oxygen demand bottle (BOD) and separately added with 95 ml of 10-3 M AgNo3 solution. The BOD bottle was incubated at room temperature for further incubation for 28 h. The colour changed to brown which indicates the synthesis of AgNPs from the leaves. Characterization of the synthesized and purified AgNPs was carried out with the help of Transmission Electron Microscopy (TEM) [10].

Evaluation of extracts for sub-acute dermal toxicity

The present study was conducted on 50 Wistar rats of either sex. The average age of rats was 8-10 weeks and the body weight of 200-300 gm. Animals were selected after physical and behavioral examination with a live body weight range ±20% of the mean body weight at the time of randomization. The Wistar rats were housed under standard laboratory conditions in polypropylene cages, and provided with ad-libitum food and water in the experimental room of the laboratory animal house, Department of Veterinary Pharmacology and Toxicology, College of Veterinary and Animal Sciences, Parbhani. The necessary approval from the Institutional Animals Ethical Committee (IAEC) was accorded as per the guidelines of the Committee For Control and Supervision of Experiments on Animals (CCSEA). The experimental animals were kept for the five-day acclimatization period.

The experimental animals then were divided into 5 groups each containing 10 rats of either sex as detailed below: -

Group I (Healthy control): The animals were provided with an unlimited supply of pure drinking water and were treated with vehicle/deionized water.

Group II (SNPs coated with extract dose-I): The animals were treated with *J. curcas* leaf extract @ 150 mg/kg body weight coated SNPs @ 1 mg/kg body weight.

Group III (SNPs coated with extract dose – II): The animals were treated with extract @ 300 mg/kg body weight coated SNPs @ 2 mg/kg body weight.

Group IV (SNPs coated with extract dose - III): Rats were treated with extract @ 600 mg/kg body weight coated SNPs @ 4 mg/kg body weight.

(Group V) (Satellite group): Rats were treated with extract @ 1200 mg/kg body weight coated SNPs @ 8 mg/kg body weight.

Preparation of site for drug application

The site of drug application was prepared by clipping the fur from the dorsal area of the trunk of rats. The skin hairs of the dorsal thoracic area of the rats were trimmer using an electric trimmer, followed by manual shaving with a razor blade. Repeated the hairs were trimmed approximately on weekly intervals. The dorsal area was applied with the *J. curcas* leaf extract-coated Silver nanoparticles. As per the guideline, the test substance, should ideally on skin for 6 hours a day consecutively for 28 days. After the application period, the treated skin area was washed with normal saline and wiped with a cotton swab [8].

Parameters studied

Serum biochemical estimations and hematological parameters were assessed on the 1st, 14th, and 28th day of the experiment. AST and ALT were determined by the UV kinetic method, BUN by the Berthelot method, creatinine by the alkaline picrate method, and total protein by the biuret method. However, hematological parameters i.e. hemoglobin by acid hematin method, TEC and TLC by hemocytometer, and DLC by Wright's staining method. The pathological observations i.e. gross pathology and histopathology were also studied for the evaluation of sub-acute dermal toxicity *of J. curcas* Linn. leaf extract coated Silver nanoparticles in Wistar rats.

Statistical analysis

The factorial randomized block design (FRBD) and completely randomized block design (CRBD) was implemented to analyzed the received data of treatment groups as per the requirement of the experiment and interpreted [11]. All the data were statistically analyzed and significant differences among different groups were determined by ANOVA.

RESULTS

The present study was conducted to assess the repeated dose dermal toxicity of *J. curcas* Linn. leaf extract-coated SNPs in Wistar rats and the data revealed no significant behavioral changes or any abnormalities in animals of all the treated and control animals. The blood parameters of the animals treated with different doses of JcLE-coated SNPs showed no significant variations in treated groups compared to control animals on the 1st, 14th, and 28th day of the experiment (Table 1). No significant variation in differential percent counts was noticed in all the treated groups compared to the control group (Table 2).

The experimental data of liver and kidney function tests (LFT and KFT) revealed that the AST values in animals of control, groups I, II, and III were recorded as 185.5 ± 19.5, 196.3 ± 20.9, 172.8 ± 20.7; 161.9 ± 14.5, 175.2 ± 13.8, 185.8 ± 13.7 and 143.0 ± 20.6, 169.6 ±

25.8, 222.4 ± 11.5 IU/L on 1st, 14th and 28th day, respectively. The AST values in groups IV and V were determined as 174.0 ± 15.3, 186.4 ± 14.0, 233.4 ± 8.6 and 145.7 ± 15.0, 166.6 ± 18.3, 150.2 ± 15.2 IU/L, respectively, on 1st, 14th and 28th day of the experiment as compared to group I, II and III (Table 3). The total protein content in different treated groups on the 1st, 14th, and 28th day was also found insignificant as compared to the control group revealing that the JcLE-coated extract SNPs did not adversely affect the liver and kidney. The BUN values were also found in the range showing no sign of toxicity. The creatinine values in healthy control group-I animals on days 1st, 14th, and 28th were noticed to be 0.34±0.03, 0.29±0.06, and 0.34±0.06 mg/dl, respectively. However, in groups II, III, IV, and V, it was found to be very close to the control group on the 1st, 14th, and 28th day of the experiment (Table 3).

Table 1: Hemoglobin, Total erythrocyte and Total leucocytes values (Mean ± SE) on different days in experimental rats of different groups with different doses of *J. curcas* leaf extract coated SNPs

Group	Hemoglobin (g/dl)			Total erythrocyte (million/µl)			Total leucocyte (thousand/ml)		
	1st day	14th day	28th day	1st day	14th day	28th day	1st day	14th day	28th day
I*	12.93±0.14^{cp}	13.25±0.30^{abp}	13.25±0.27^{ap}	7.78±0.28^{ap}	7.21±0.20^{ap}	7.98±0.19^{ap}	10.05±1.07^{ap}	7.93±0.81^{bp}	10.11±1.03^{ap}
II	14.20±0.19^{ap}	14.11±0.29^{ap}	14.21±0.16^{ap}	7.80±0.18^{aq}	7.59±0.28^{aq}	7.92±0.18^{ap}	12.51±1.34^{ap}	9.68±0.73^{abp}	12.58±1.35^{ap}
III	13.89±0.46^{abp}	13.70±0.30^{abp}	15.11±1.08^{ap}	7.49±0.26^{aq}	7.42±0.31^{aq}	8.62±0.32^{ap}	14.45±2.00^{ap}	11.08±1.12^{ap}	14.63±2.01^{ap}
IV	13.69±0.26^{bq}	14.00±0.21^{bq}	15.44±0.51^{ap}	6.24±0.60^{aq}	7.37±0.23^{apq}	8.29±0.59^{ap}	10.98±1.49^{ap}	7.81±0.68^{bp}	10.93±1.46^{ap}
V**	13.14±0.33^{bcp}	12.65±0.57^{bp}	15.31±1.34^{ap}	7.03±0.28^{abp}	6.23±0.60^{ap}	8.13±0.79^{ap}	12.27±1.47^{ap}	9.47±0.70^{abp}	12.52±1.58^{ap}

*Health control group; **Satellite control group

Hemoglobin: Superscripts a,b,c,d,e and p,q,r show significant difference within the column and row (between different groups on specific day) (p = 0.05); CD: At 5% 1.03; At 1% 1.37

Total erythrocyte: Superscripts a,b,c,d,e and p,q,r show significant difference within the column and row (between different groups on specific day) (p = 0.05); CD: At 5% 0.97; At 1% 1.31

Total leucocyte: Superscripts a,b,c,d,e and p,q,r show significant difference within the column and row (between different groups on specific day) (p = 0.05); CD: At 5% 2.29; At 1% 3.21

Table 2: Differential Leucocyte Count (Mean ± SE, 10^3/µl) on different days in experimental rats of different groups with different doses of *J. curcas* leaf extract coated SNPs

Group	Lymphocyte count %			Monocyte count %			Neutrophil count %			Eosinophil count %			Basophil count %		
	1st day	14th day	28th day	1st day	14th day	28th day	1st day	14th day	28th day	1st day	14th day	28th day	1st day	14th day	28th day
I*	71.0± 0.9^{ap}	70.4± 1.0^{ap}	70.6± 1.0^{ap}	7.2± 0.3^{ap}	7.0± 0.3^{bp}	6.6± 0.4^{ap}	18.3± 0.9^{ap}	18.6± 0.7^{cp}	19.0± 0.8^{bp}	3.3± 0.3^{ap}	3.78 0.1^{ap}	3.4± 0.4^{ap}	0.2± 0.02^{ap}	0.2± 0.05^{ap}	0.1± 0.03^{ap}
II	70.6± 1.0^{ap}	67.3± 0.4^{bq}	65.5± 0.3^{br}	6.6± 0.4^{aq}	7.8± 0.1^{ap}	7.2± 0.1^{apq}	18.9± 0.8^{ar}	21.8± 0.3^{bq}	23.6± 0.4^{bap}	3.4± 0.4^{ap}	3.3± 0.3^{ap}	3.6± 0.1^{ap}	0.8± 0.05^{ap}	0.2± 0.02^{ap}	0.2± 0.02^{ap}
III	70.3± 1.0^{ap}	67.1± 0.3^{bq}	65.3± 0.5^{bq}	7.1± 0.3^{ap}	7.9± 0.1^{ap}	7.5± 0.2^{ap}	18.7± 0.7^{ar}	22.1± 0.3^{abq}	23.8± 0.5^{ap}	3.7± 0.2^{ap}	3.4± 0.3^{ap}	3.2± 0.2^{ap}	0.2± 0.05^{ap}	0.2± 0.02^{ap}	0.2± 0.02^{ap}
IV	69.8± 0.9^{ap}	64.8± 0.7^{cq}	64.0± 0.7^{bq}	7.1± 0.3^{ap}	8.0± 0.1^{ap}	7.3± 0.2^{ap}	19.3± 0.6^{aq}	24.2± 0.9^{ap}	25.5± 0.7^{ap}	3.6± 0.2^{ap}	3.4± 0.3^{ap}	3.0± 0.1^{ap}	0.2± 0.04^{ap}	0.2± 0.02^{ap}	0.2± 0.02^{ap}
V**	70.4± 1.0^{ap}	70.7± 0.9^{ap}	70.6± 0.9^{ap}	7.0± 0.3^{ap}	7.8± 0.2^{ap}	7.1± 0.3^{ap}	18.6± 0.7^{ap}	18.4± 1.2^{cp}	18.9± 0.9^{bp}	3.8± 0.1^{ap}	3.3± 0.3^{ap}	3.1± 0.1^{ap}	0.2± 0.05^{ap}	0.2± 0.02^{ap}	0.2± 0.02^{ap}

*Health control group; **Satellite control group

Lymphocyte count: Superscripts a,b,c,d,e and p, q, r show significant difference within the column and row (between different groups on specific day) (p = 0.05); CD: At 5% 1.98, At 1% 2.64

Monocyte count: Superscripts a,b,c,d,e and p, q, r show significant difference within the column and row (between different groups on specific day) (p = 0.05); CD: At 5% 0.79, At 1% 1.05

Neutophil count: Superscripts a,b,c,d,e and p, q, r show significant difference within the column and row (between different groups on specific day) (p = 0.05); CD: At 5% 1.77, At 1% 2.36

Eosinophil count: Superscripts a,b,c,d,e and p, q, r show significant difference within the column and row (between different groups on specific day) (p = 0.05); CD: At 5% 0.71, At 1% 0.94

Basophil count: Superscripts a,b,c,d,e and p, q, r show significant difference within the column and row (between different groups on specific day) (p = 0.05); CD: At 5% 0.87; At 1% 1.17

Table 3 Values of liver and kidney function (Mean ± SE, $10^3/\mu l$) on different days in experimental rats of different groups with different doses of *J. curcas* leaf extract coated SNPs

Group	Serum AST/SGOT (IU/L)			Serum ALT / SGPT (IU/L)			Serum TP (g/dl)			Serum BUN (mg/L)			Serum Creatinine (mg/dl)		
	1st day	14th day	28th day	1st day	14th day	28th day	1st day	14th day	28th day	1st day	14th day	28th day	1st day	14th day	28th day
I*	185.5± 19.5^{ap}	196.3± 20.9^{ap}	188.1± 11.5^{bp}	77.4± 7.8^{ap}	77.2± 13.6^{ap}	82.6± 9.3^{ap}	6.2± 0.3^{bq}	6.6± 0.3^{bq}	8.0± 0.7^{ap}	55.8± 4.3^{ap}	64.7± 12.2^{ap}	76.7± 3.4^{bp}	0.34± 0.03^{ap}	0.29± 0.06^{bp}	0.34± 0.06^{bp}
II	161.9± 14.5^{ap}	175.3± 13.8^{ap}	185.8± 13.7^{bp}	74.5± 4.1^{ap}	83.2± 4.5^{ap}	83.6± 3.6^{ap}	6.9± 0.2^{abp}	7.7± 0.4^{ap}	7.4± 0.3^{ap}	57.9± 2.2^{aq}	60.0± 2.6^{aq}	78.7± 0.9^{bp}	0.46± 0.02^{ap}	0.48± 0.03^{ap}	0.47± 0.03^{bp}
III	143.0± 20.6^{aq}	169.6± 25.8^{apq}	222.4± 11.5^{abp}	87.4± 6.7^{ap}	96.4± 8.4^{ap}	74.6± 5.6^{ap}	7.6± 0.3^{ap}	8.4± 0.4^{ap}	10.9± 2.4^{ap}	44.5± 2.5^{bp}	46.6± 4.5^{aq}	82.7± 1.4^{abp}	0.32± 0.04^{ap}	0.32± 0.08^{bp}	0.37± 0.04^{bp}
IV	174.0± 15.3^{aq}	186.4± 14.0^{aq}	233.4± 8.6^{ap}	82.1± 7.1^{ap}	97.4± 12.0^{ap}	88.0± 8.5^{ap}	7.3± 0.3^{aq}	8.7± 0.4^{ap}	8.3± 0.3^{apq}	43.9± 2.5^{bp}	46.3± 3.3^{aq}	87.8± 3.6^{ap}	0.32± 0.04^{bq}	0.30± 0.05^{bq}	0.77± 0.04^{ap}
V**	145.7± 15.0^{ap}	166.6± 18.3^{ap}	150.2± 15.2^{cp}	87.7± 8.6^{ap}	106.5± 8.31^{ap}	87.6± 6.4^{ap}	7.2± 0.3^{aq}	7.9± 0.3^{apq}	8.0± 0.1^{ap}	42.9± 3.0^{bp}	45.7± 2.0^{ap}	40.0± 1.8^{cp}	0.38± 0.04^{ap}	0.42± 0.07^{abp}	0.40± 0.04^{bp}

*Health control group; **Satellite control group

Serum AST: Superscripts a,b,c,d,e and p, q, r show significant difference within the column and row (between different groups on specific day) (p = 0.05); CD: At 5% 43.94; At 1% 58.70

Serum ALT: Superscripts a,b,c,d,e and p, q, r show significant difference within the column and row (between different groups on specific day) (p = 0.05); CD: At 5% 19.95; At 1% 26.64

Total protein: Superscripts a,b,c,d,e and p, q, r show significant difference within the column and row (between different groups on specific day) (p = 0.05); CD: At 5% 0.83; At 1% 1.10

BUN level: Superscripts a,b,c,d,e and p, q, r show significant difference within the column and row (between different groups on specific day) (p = 0.05); CD: At 5% 8.46; At 1% 11.30

Creatinine: Superscripts a,b,c,d,e and p, q, r show significant difference within the column and row (between different groups on specific day) (p = 0.05); CD: At 5% 0.17; At 1% 0.23.

DISCUSSION

Recently, nanotechnology has attracted the attention of researchers to improve their role in human and animal health. The use of biological materials/methods in nanotechnology is a novel and unique environmentally friendly approach that is still insufficiently investigated. The present study used *A. indica* as a bio-mediator for SNPs formation, and *J. curcas* aqueous leaf extract-coated SNPs for the sublethal toxicity in the Wistar rat model. The observed values of hemoglobin, total erythrocyte count (TEC), and total leucocyte count (TLC) in the treatment groups were significantly ($p<0.05$) increased throughout the experimental period as compared to control animals (Table 1) on the 14th and 28th day but, the values were within the standard physiological limits. Some of the reports indicated increased mean values of hemoglobin [12, 13], however, De Jong *et al*. reported a reduction in the mean values of hemoglobin of treated animals [14]. No toxicity sign was noticed in all the animals treated with different doses of *J. curcas* leaf extract-coated SNPs, however, the parameters were found within normal physiological limits.

In differential leucocyte count (DLC), there was a significant ($p<0.05$) decrease in lymphocyte counts on the 14th day onwards in both control and treatment groups, however, the values were within the normal physiological limits (Table 2). Similar observations were recorded indicating a relative decrease in lymphocyte counts due to an increase in neutrophil values after the 14th day of repeated administration of AuNPs to rats [15].

The monocyte, eosinophil, and basophil counts were higher on the 14th day of treatment and were lower on the 28th day of treatment than normal values. Similar findings suggested that it might be due to a decrease in other leucocyte counts and the inflammatory reaction caused by SNPs in the body [15]. The neutrophil values were increased on the 14th and 28th day of treatment compared to the control group which was indicative of reactive response of the immune system to the treatment [15].

The LFT included aspartate aminotransferase (AST/SGOT) and alanine transaminase (ALT/SGPT) and showed an insignificant increase on the 14th and 28th day of the experiment which indicated that *J. curcas* leaf extract-coated SNPs had more interaction and accumulation capacity, so a chance of hepatocyte damage when treatment continued for long term was observed.

The present study correlates and concludes that the SNPs interacted with the liver severely to increase these enzymes [12, 16, 17, 18]. The total protein value was increased throughout the experimental period in the treatment group which confirmed that there was a slightly toxic effect on the immune system for long-term administration of this herbal formulation. The other researcher also recorded the similar observations [18, 19, 20]. The kidney function test, the blood urea nitrogen (BUN), and creatinine values were significantly increased in the treatment groups which confirmed slight kidney affection on long-term application of J. curcas leaf extract-coated SNPs in rats. It was also reported that an increase in BUN values indicated that coated SNPs had more interacting capacity resulting in more toxic effects on kidneys [19].

The histo-architectural observations of kidneys in experimental rats revealed vacuolar degenerative, necrobiotic changes with mild to moderate and local to multifocal hyaline casts located in the lumen of exposed tubules and cystic degeneration with hemorrhages. The kidney tubules exposed to SNPs alone showed congestion, necrosis, and marked cellular swelling. In group II animals, occasional mild focal atrophy of glomeruli was noted. There was severe congestion at cortico-medullary junction observed in group III animals. The severity of affection was more in coated SNPs doses than in SNPs alone. Histopathological studies of all experimental rats did not show any appreciable changes in any of the section of skin examined.

CONCLUSION

It can be concluded from the present data that there was no significant effect on hematological parameters in the rats treated with *J. curcas* leaf extract-coated SNP. However, the serum biochemical analysis revealed a toxic effect on the kidney. The gross and histopathological examination shown the minimal alterations in liver and kidney tissues in a dose dependent manner related to toxicity while the skin tissues showed normal hitsoarchitecture.

List of abbreviations

COVAS: College of Veterinary and Animal Sciences

OECD: Organization for Economic Co-operation and Development

BUN: Blood urea nitrogen

ANOVA: Analysis of Variance

AuNPs: Gold nanoparticles

Conflict of interest

The authors declare that they have no conflict of interest.

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