Lanthanum Zirconate Nanoparticles, used in Blades of Gas Turbine Engines, Can Disturb Behavior, Leukocyte Count and Antioxidant Metabolites from Vital Organs of Albino Mice

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ABSTRACT

Lanthanum Zirconate ($La_2Zr_2O_7$) nanoparticles (NPs) are generally used in blades of gas turbine engines to thermally insulate them and to protect them against hot and corrosive gas streams. The present research experiment was aimed to determine the effect of Lanthanum Zirconate NPs on selected aspects of behavior, serum biochemistry, complete blood count and antioxidant metabolites from vital organs of albino mice in a gender specific manner. Seven weeks old mice were administered orally with 25mg/ml solvent/Kg body weight of Lanthanum Zirconate nanoparticles for consecutive 22 days. Saline treated control groups were maintained in parallel. It was observed that neuromuscular coordination was significantly improved (P = 0.01) in NPs treated female mice while rearing frequency was significantly decreased (P = 0.004) in NPs treated male mice than their respective controls. Complete blood count analysis revelaed that NPs treated female mice had significantly reduced white blood cell (P = 0.04) and lymphocyte count (P = 0.02) than control group. It was observed that Superoxide dismutase concentrations in kidney (P = 0.04), Malonaldehyde concentrations in brain (P = 0.002), heart (P = 0.001), liver (P = 0.05) of male and in kidney (P = 0.001) of NPs treated female mice were significantly higher than their respective control groups. In conclusion, we are reporting that oral supplementation with 25mg/ml solvent/Kg body weight of Lanthanum Zirconate nanoparticles is affecting neuromuscular coordination, exploratory behavior, leukocyte count and antioxidant metabolites from vital organs in a gender specific manner with more pronounced effects in male.

Key Words: Lanthanum Zirconate, behavior, serum biochemistry, complete blood count, antioxidant metabolites

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Introduction

Nanotechnology has become the forefront of research in the past decade. With the advent of this field wide varieties of nanoparticles with exciting characteristics are manufactured and are used for broad range of applications (Balasubramanyam *et al.,* 2009; Zhao and Castranova, 2011). Use of metal oxide nanoparticles are becoming quite common because they are more stable and generally considered as safe for humans (Syama *et al.,* 2013).

Lanthanum zirconate ($La_2Zr_2O_7$) is a typical pyrochlore structure ceramic material (Zhang *et al.,* 2016) with many interesting industrial) applications including thermal barrier coating (TBC) (Cao *et al.,*

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2003) i.e., multi-layered material systems deposited on blades of gas turbine engines that thermally insulate them and to protect them against hot and corrosive gas streams (Weber *et al.,* 2013). All those people that are exposed to workplace where Lanthanum Zirconate is used as surface coating material are at a potential risk that these NPs may enter in human body as it has been an established fact that NPs can enter the living systems through various routes like ingestion, inhalation, injection, and dermal penetration and can induce toxicity on environment and human either deliberately or accidently (Oberdorster *et al.,* 2005; Pasupuleti *et al.,* 2012). Currently, Lanthanum zirconate NPs have not been comprehensively assed in regard to the potential effect on the human health, due to exposure (accidental or otherwise) in the workplace during the production of nanoparticles or exposure through the use in commercial products. Present study was designed to report the effects of oral supplementation of 25mg/ml solvent/Kg body weight of Lanthanum Zirconate NPs on selective aspects of behavior, blood chemistry and antioxidant metabolites from vital organs of albino mice in a gender specific manner.

Materials and Methods

Synthesis of Lanthanum Zirconate nanoparticles

Lanthanum Zirconate NPs were kindly provided by Dr. Muhammad Naeem Ashiq, Associate Professor at Institute of Chemical Sciences, Bahauddin Zakariya University, Multan. Pakistan. NPs were synthesized by the hydrothermal method as described previously (Farid *et al.,* 2014).

Experimental animals

7 weeks old, male and female albino mice were used as experimental animals. Animals were housed in locally manufactured rodent cages filled with wooden chips with air temperature maintained at 22 ± 1^0C with 12-hours light-dark cycle Subjects had access to standard rodent diet and water *ad libitum*. All the experimental protocol and animal handling procedures were approved by the ethical committee of Institute of Pure and Applied Biology at Bahauddin Zakariya University, Multan, Pakistan.

Experimental Design

Following weaning, male and female mice were separated from their parents and were kept individually in cages until they were seven weeks old. At this point, mice of both genders were divided into two groups. Treated group (N = 10 for each gender) orally received 25 mg/ml solvent/Kg body weight of Lanthanum Zirconate NPs for 22 consecutive days. While control mice (N = 10 for each gender) orally received saline (0.9 % NaCl) solution for the same duration. A series of neurological (Rota rod, light and dark, open field and Morris water maize) test performance, complete blood count, serum biochemical parameters and antioxidant metabolites from vital organs were analyzed in both experimental treatments. Dose was supplemented 30 minutes before the conduction of each test. Throughout the experiment the changes in weight for each mouse was recorded.

Rota Rod Test

Rota Rod apparatus is used to test the balance and neuromuscular coordination of an animal. Rota Rod test was performed by using a locally manufactured apparatus comprising of rotating drum with acceleration of 40 rpm. During experimentation, each mouse received three training trials followed by three experimental trials. Mean time spent on rotating drum was compared between the control and Lanthanum Zirconate nanoparticles treated groups following Allahyar *et al.* (2016).

Open Field Test

Open field test is used to assess locomotory and exploratory behavior of an animal (Iqbal *et al.,* 2015). A computational tracking system, Any-Maze (Stoeling Co, USA) connected with video camera (XPod-058, China) was employed to detect the behavior of mice in the open field chamber (40 cm x 40 cm x 70 cm). Each mouse was released in the corner of the open field box for ten minutes of test duration. Maximum speed (m), Means speed (m/s), Time mobile and Time immobile (seconds), Mobile episodes, immobile episodes, Rotations: Clockwise and anticlockwise, defecation, urination, were noted following Allahyar *et al.* (2016).

Light Dark Box Test

The light/dark box test equipment was having an area of (45 x 27 x 27 cm) made up of plywood and consisted of one third dark safe chamber (18 x 27 cm) and two third light aversive chamber (27 x 27 cm) with light intensity of 200 Watt. The two chambers were connected by an opening (7.5 x 7.5 cm) located in the center of the dividing wall adjacent to floor. The floor was divided into 9 x 9 cm squares and was covered with Plexiglas. A mouse was placed in the centre of light chamber keeping its snout towards

opening in the wall. Time spent in each chamber, transition frequency, rearing, stretch attended, defecation and urination were counted over a five minutes' test following Zahra *et al.* (2015).

Morris Water Maze (MWM)

MWM consists of a circular pool of diameter of 122cm and depth of 76cm. In the pool mice were trained to swim to find a platform concealed (1.5 cm) under water surface. In order to identify the position of concealed platform, distal extra-maze cues of different colors and dimensions were attached to the room walls. During the whole experiment both colors and dimension of visual cues were kept constant. Water temperature was maintained at 21 ± 1°C. The circular pool was partitioned into four quadrants (compass locations: NE, NW, SW and SE) by a computerised tracking/image analyzer system (video camcorder Add link Software Scientific, Barcelona) coupled to computational tracking system: Any Maze (Stoeling Co, USA). The middle of the South-East quadrant was selected as a place for concealed platform where it remained during the whole experiment.

In the spatial acquisition phase, mice were subjected to 16 training trials: 4 training trials per day and 4 training days with an inter-trial interval of 30 min. Mice were released (randomly) in the circular pool from the four compass locations for swimming. For 120 Sec mice were allowed to search the platform by swimming. Then the mice were allowed to stay on the platform for another 30 Sec after failure of subject to find the concealed platform within 120 Sec.

In acclimatization training session of first training day in the MWM each mouse was manually placed on the platform, and was subsequently guided back to the platform after swimming of 30 Sec. Parameters like distance travelled to reach the hidden platform, latency to reach platform, mean speed, platform entries, platform latency to first entry and platform max visit was recorded.

Hematology and serum biochemistry

At the end of oral supplementation experiment, mice were anaesthetized with chloroform and blood was collected either from retro-orbital sinus or through direct cardiac puncture and divided into two parts. One part was used to determine the complete blood count parameters red blood cells, white blood cells, hemoglobin concentration, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, platelet, lymphocyte, red cell distribution width, Platelet crit, platelet distribution width and mean platelet volume by using haematology analyzer (SYSMEX 21, Japan). The remaining blood sample was centrifuged at 10,000 rpm for 10 minutes and the extracted serum was used for the estimation of cholesterol, triglycerides, creatinine, urea, albumin and total protein by using diagnostic kits following the protocol mentioned by the manufacturers.

Determination of antioxidant metabolites in vital organs

Following sacrifice, vital organs (brain, liver, heart, lungs and kidney) were surgically removed, rinsed in isotonic saline solution and stored immediately at -20°C. In all organs, concentrations of superoxide dismutase were determined following Chidambara et al. (2002), estimation of lipid peroxidation was carried out as described by Haider *et al.* (2015) and catalase activity were determined following Lateef and Qureshi. (2013).

Statistical analysis

All the data was expressed as mean ± standard error of mean and analyzed by using statistical package Minitab (version 16, Pennsylvania). Significance level was set at $P < 0.05$. Two sample student's t-test was applied to compare all studied parameters of behavior, complete blood count, serum and antioxidant profile between Lanthanum Zirconate nanoparticles treated and untreated albino mice of both genders.

Results

Body Weight Analysis

Analysis of results revealed that body weight varied non significant ($P > 0.05$) at all studied time points when compared between 25mg/ml solvent/ Kg body weight of Lanthanum Zirconate NPs treated and untreated albino mice of both genders (Supplementary Fig.1).

Rota Rod

Statistical analysis of results indicated that NPs treated female albino mice had significantly improved rota rod test performance ($P = 0.01$) than control group. While rota rod test performance remained unaffected ($P > 0.05$) when compared between NP treated and untreated male mice (Fig. 1).

Open Field Test

Analysis of open field results indicated that all the studied parameters varied non significant ($P > 0.05$)

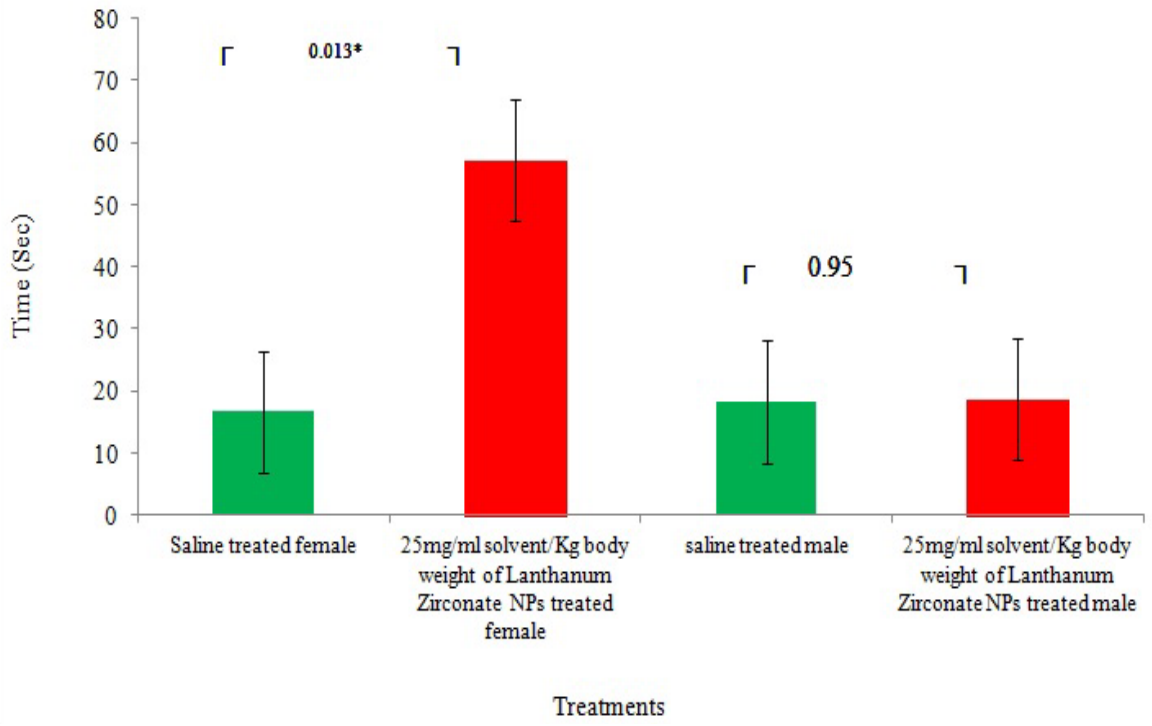
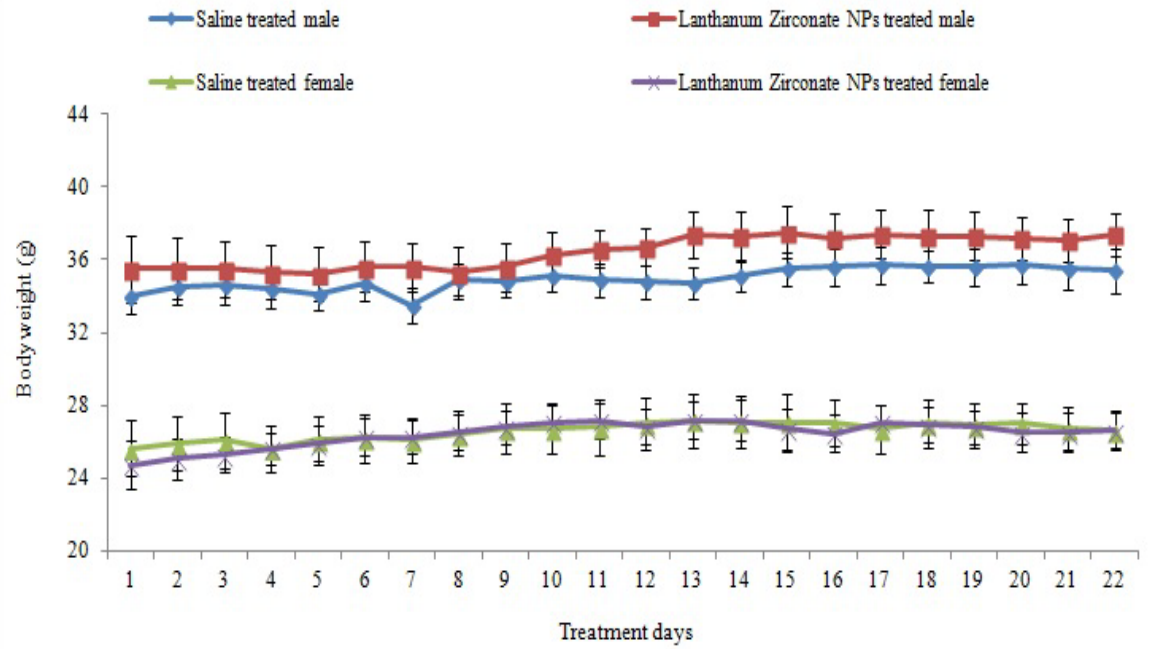


Figure 1. Comparison of Rota rod test performance between Lanthnum Zirconate nanoparticle treated (25mg/ ml of solvent/ Kg body weight) and untreated adult albino mice of both genders after 22 days of treatment. N = 10 for each treatment. Data is expressed as mean ± standard error of mean. P > 0.05 = Least significant for female mice (Two sample t test).



Supplementary Figure 1. Comparison of gain in body weight for 22 days on daily basis between Lanthnum Zirconate nanoparticles treated (25mg/ ml of solvent/ Kg body weight) and untreated adult albino mice of both genders. N = 10 for each treatment. Data is expressed as mean ± standard error of mean. P > 0.05 = Non significant for all each day (Two sample t test).

when compared between Lanthanum Zirconate NPs treated and untreated animals of both genders (Data not shown here).

Light Dark Box Test

Student t test data analysis revealed that all the studied parameters of light dark box test varied non-significant (P > 0.05) when compared between Lanthanum Zirconate NPs treated and untreated animals of both gender except rearing frequency that was significantly reduced (P = 0.004) in NPs treated male albino mice than their saline treated control (Table 1).

Table 1. Comparison of various studied parameters of light dark box test between 25mg/ml saline/Kg body weight of Lanthanum Zirconate (nanoparticles) and saline treated adult albino mice of both genders. N = 10 for each treatment. Data is expressed as mean ± standard deviation. P- value represents the results for two sample t – test calculated for each parameter.

Studied parameters	Female mice			Male mice		
	Saline treated	25mg Lanthanum Zirconate treatment	P-value	Saline treated	25mg Lanthanum Zirconate treatment	P-value
Transition frequency	16.82 ± 2.1	19.00 ± 1.7	0.4	15.50 ± 2.0	17.50 ± 1.7	0.5
Rearing frequency	6.27 ± 3	3.91 ± 1.1	0.5	5.20 ± 0.74	2.10 ± 0.59	0.004**
Stretch attend frequency	43.5 ± 6.2	48.4 ± 4.9	0.6	36.40 ± 3.0	41.8 ± 3.6	0.3
Time in dark (sec)	171.5 ± 16	168.4 ± 13	0.9	173.6 ± 12	148.0 ± 15	0.2
Time in light (sec)	128.5 ± 16	131.6 ± 13	0.9	126.4 ± 12	153.0 ± 15	0.2
Line cross	19.45 ± 2.2	22.09 ± 1.7	0.4	18 ± 2.2	18.40 ± 1.8	0.9
Defecation	1.91 ± 0.51	4.09 ± 0.95	0.06	4.80 ± 1.1	3.60 ± 1.0	0.4

P > 0.05 = Non significant; P < 0.01 = Significant (**)

Morris Water Maze Test

Analysis of data from acquisition phase revealed that Lanthanum Zirconate nanoparticles treated male had significantly more latency to reach platform (P = 0.0057), (P = 0.057), (P = 0.03) and mean speed (P = 0.0019), (P = 0.0022), (P = 0.0034) during training day 1, 3,4 and latency to first entery (P = 0.21) during training day 1 than control group. While all studied parameters varied non significantly (P > 0.05) when compared between Lanthnum Zirocnate NPs treated and control male albino mice (Data not shown here).

For female mice, it was observed that Lanthnum Zirconate NPs treated mice were significantly less motile on training day 1 (P = 0.033) than control. While all studied parameters varied non significantly (P > 0.05) when compared between Lanthnum Zirconate NPs treated and control female albino mice (Data not shown here).

Analysis of results indicated that all studied parameters during probe trials varied non-significantly (P > 0.05) when compared between 25 mg/ml solvent/kg body weight Lanthanum Zircoante nanoparticles and untreated albino mice (Data not shown here).

Complete blood count analysis

Analysis of results revealed that all studied complete blood count parameters varied non significant (P > 0.05) when compared between the two experimental treatments except white blood cells ((P = 0.04) and lymphocyte count (P = 0.02) that were significantly reduced and in NPs treated female albino mice than their control (Table 2)

Serum biochemical parameters analysis

When the studied serum parameters were compared between Lanthanum Zirconate nano-particles treated and untreated mice, it was observed that all the parameters varied non significantly (P > 0.05) between the two treatments for both genders (Data not shown here).

Analysis of antioxidant metabolites in vital organs

Analysis of the results revealed that Superoxide dismutase concentrations were significantly higher in the kidney (P = 0.04) of Lanthnum Zirconate NPs treated male albino mice than control group. It was observed that Lanthnum Zirconate NPs treated male mice had significantly higher Malodialdehyde levels in brain (P = 0.0002), liver (P = 0.05), kidney (P < 0.001) and heart (P < 0.001) than control group. For female mice, Malondialdehyde concentrations were significantly elevated in heart (P = 0.002) than control group (Table 3).

Discussion

Nanoparticles are known to cross the physiological barriers and have the ability to enter, translocate, generate oxidative stress and can cause significant damage to the cell or tissue (Li *et al.,* 2003). Pathways by which nanoparticles uptake may occur include hemolysis and thrombogenicity. These pathways include numerous activities like reduced number of blood cells, anti-mitotic properties and increasing the number of cells involved in the immune processes (Lian *et al.,* 2004). They also lead to the formation of free radicals due to oxidative stress. These free radicals interact with lipids, proteins, and nucleic acids changing the cell signalling and transcription

Table 2. Comparison of various studied parameters of complete blood count between 25mg/ml saline/Kg body weight of Lanthanum Zirconate (nanoparticles) and saline treated adult albino mice of both genders. N = 10 for each treatment. Data is expressed as mean ± standard deviation. P- value represents the results for two sample t – test calculated for each parameter.

Parameters	Female mice			Male mice		
	Saline treatment	25mg Lanthanum Zirconate treatment	P - value	Saline treatment	25mg Lanthanum Zirconate treatment	P – value
WBC (x 10^3 μL^{-1})	6.32 ± 1.2	3.32 ± 0.6	0.04*	4.66 ± 0.78	5.75 ± 1.6	0.6
Monocytes (x 10^3 μL^{-1})	0.09 ± 0.05	0.018 ± 0.01	0.2	0.030 ± 0.015	0.050 ± 0.022	0.5
Lymphocytes (x 10^3 μL^{-1})	5.41 ± 0.81	2.93 ± 0.5	0.02*	4.13 ± 0.61	5.20 ± 1.4	0.5
Granulocytes (x 10^3 μL^{-1})	0.98 ± 0.41	0.345 ± 0.12	0.2	0.510 ± 0.21	0.470 ± 0.18	0.9
Lymphocytes (%)	86.52 ± 2.9	90.00 ± 1.9	0.3	90.54 ± 2.3	91.95 ± 1.4	0.6
Monocytes (%)	1.120 ± 0.3	0.936 ± 0.18	0.6	0.920 ± 0.15	0.820 ± 0.15	0.7
Granulocytes (%)	12.36 ± 2.6	9.06 ± 1.8	0.3	8.54 ± 2.3	7.23 ± 1.3	0.6
RBC (x 10^6 μL^{-1})	6.77 ± 0.49	6.82 ± 0.43	0.9	7.741 ± 0.20	7.558 ± 0.31	0.6
Hemoglobin (gdL^{-1})	11.77 ± 0.83	11.77 ± 0.48	1.0	13.04 ± 0.35	12.85 ± 0.53	0.8
Hematocrit (%)	34.06 ± 2.9	33.55 ± 3	0.9	39.50 ± 2.6	40.2 ± 3.2	0.9
MCV (µmˆ3)	50.30 ± 2.5	48.66 ± 2.2	0.6	50.90 ± 2.8	53.1 ± 3.3	0.6
MCH (pg)	17.48 ± 0.33	17.51 ± 0.53	1.0	16.90 ± 0.42	17.020 ± 0.28	0.8
MCHC (gdL^{-1})	35.78 ± 2.1	36.71 ± 2	0.8	34.47 ± 2.6	33.64 ± 2.5	0.8
RDW(%)	21.66 ± 0.83	22.25 ± 1.1	0.7	20.72 ± 1.5	20.86 ± 1.0	0.9
RDW-SD(µmˆ3)	37.04 ± 2.5	37.76 ± 2.2	0.8	37.02 ± 2.1	39.0 ± 3.6	0.6
Platelets (x 10^3 μL^{-1})	363 ± 34	383 ± 59	0.8	414 ± 65	446 ± 61	0.7
PCT(%)	0.267±0.077	0.2791±0.032	0.9	0.293 ± 0.048	0.303 ± 0.047	0.9
PDW(%)	19.98 ± 1.5	21.15 ± 2.5	0.7	21.68 ± 1.1	18.45 ± 2.6	0.3
MPV (µmˆ3)	7.118 ± 0.15	7.455 ± 0.25	0.3	7.050 ± 0.13	6.67 ± 0.83	0.7

P> 0.05 = Non significant; P < 0.05 = Least significant (*)
RBC: red blood cell, WBC: white blood cell, HGB: hemoglobin concentration, HCT: hematocrit, MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin, MCHC: mean corpuscular hemoglobin concentration, PLT: Platelet, LYM: Lymphocyte, LYM: Lymphocytes, RDW: Red cell distribution width, PCT: Platelet Crit PDW: Platelet distribution width, MPV: Mean platelet volume.

(Monteiller *et al.,* 2007). Despite industrial use of Lanthanum Zirconate NPs, no information is available in literature regarding their biocompatibility in living systems. Hence, the present study was designed to report the effects of oral supplementation of Lanthanum Zirconate NPs on mice behavior, blood chemistry and antioxidant metabolites from vital organs.

Analysis of body weight during present research indicated that Lanthnum Zirconate NPs treatment did not affected the body weight gain in both genders (Supplementary Fig. 1). Our results are in agreement with (Hu *et al.,* 2010; Briner *et al.,* 2000) who had reported no significant effect of Titanium dioxide (TiO_2) and lanthnum on body weight of mice respectively.

Analysis of neurological test results indicated that oral supplementation of Lanthanum Zirconate NPs (25mg/ml solvent/Kg body weight) resulted in decreased rearing frequency in male mice (Table 2) while it resulted in improved neuromuscular coordination in female mice (Fig. 1). These gender specific differences are probably due to the Lanthnum part of NPs as it is well known to interfere with neurotransmitter release and their response and both of these phenomenon are necessary for normal neural functioning (Briner *et al.,* 2000).

Our complete blood count results revealed that Lanthanum Zirconate NPs treatment resulted in reduced white blood cells (WBCs) and lymphocyte count in female albino mice (Table.3). This decrease in WBCs count indicating decrease in the immune system, and therefore the organism becomes susceptible to any infection or dangerous external agent (Abdelhalim and Moussa, 2012). Our results are in agreement with (Duan *et al.,* 2009) who also reported decrease number of white blood cells and lymphocytes in Titanium dioxide (TiO_2) treated mice. (Tabish *et al.,* 2016) had also reported decreased white blood cells, lymphocytes concentration in rabbits following a 10 mg/ Kg body weight implantation of cobalt iron oxide and suggested that metal oxide nanoparticles at high doses can disturb the immune system in animals by affecting white blood cell production.

Nanoparticles induces oxidative stress that leads to the formation of reactive oxygen species

Table 3. Comparison of various studied antioxidant parameters between 25mg/ml saline/Kg body weight of Lanthanum Zirconate (nanoparticles) and saline treated adult albino mice of both genders.. (N = 10 for each treatment). All values are expressed as mean ± standard deviation. P-value presents the results of 2 sample t-test conducted for each parameter between the two treated groups.

Gender	Metabolites	Brain			Heart			Liver			Lungs			Kidney		
		Saline treated Control	25mg Lanthanum Zirconate Treatment	P-value	Saline treated Control	25mg Lanthanum Zirconate Treatment	P- value	Saline treated Control	25mg Lanthanum Zirconate Treatment	P- value	Saline treated Control	25mg Lanthanum Zirconate Treatment	P- value	Saline treated Control	25mg Lanthanum Zirconate Treatment	P value
Female Mice	Superoxide dismutase (unit/min/mg protein)	15.0 ± 5.2	7.79 ± 3.8	0.3	0.471 ± 0.097	0.699 ± 0.094	0.1	0.316 ± 0. 063	0.447 ± 0.12	0.3	0.630 ± 0.11	0.782 ± 0.17	0.4	0.440 ± 0.090	0.670 ± 0.27	0.4
	Malonaldehyde (picomol/gm)	34.27 ± 2.9	58.5 ± 5.5	0.002**	34.27 ± 2.9	58.5 ± 5.5	0.002**	35.98 ± 2.5	36.60 ± 1.9	0.8	35.4 ± 3.5	34.85 ± 2.1	0.9	59.8 ± 4.3	57.4 ± 7.1	0.7
	Catalase (mg/ dL)	31.74± 0.42	32.74 ± 0.44	0.1	31.74 ± 0.42	32.74 ± 0.44	0.1	2.37 ± 0.41	3.47 ± 0.51	0.1	31.58 ± 0.45	31.92 ± 0.77	0.7	30.64 ± 0.94	31.33 ± 1.3	0.6
Male Mice	Superoxide dismutase (unit/min/mg protein)	0.928 ± 0.31	1.98 ± 1.6	0.6	0.478 ± 0.11	1.01 ± 0.32	0.1	0.574 ± 0.088	1.22 ± 0.37	0.1	0.519 ± 0.11	0.341 ± 0.097	0.2	0.659 ± 0.069	1.60 ± 0.38	0. 036*
	Malonaldehyde (picomol/gm)	34.8 ± 6.9	194.3 ± 15	0.0002**	53.1 ± 5.1	86.5 ± 3.3	P < 0.001***	52.4 ± 4.2	63.54 ± 2.9	0.05*	65.1 ± 3.9	57.5 ± 4.9	0.2	36.73 ± 1.7	80.45 ± 2.6	P < 0.001***
	Catalase (mg/ dL)	46.01 ± 1.9	42.30± 1.1	0.10	26.97 ± 1.7	30.06 ± 1.7	0.2	5.92 ± 0.44	17.12± 1.2	0.4	28.65 ± 1.4	32.22 ± 1.4	0.09	31.93 ± 1.9	28.22 ± 2.0	0.2

P > 0.05 = Non significant; P < 0.05 = least significant (*); P < 0.05 = least significant (**); P < 0.001 = highly significant (***)

that can disturb the antioxidant defense system which consists of enzymes superoxide dismutase (SOD), catalase and non enzymes like vitamins E, C and glutathione (Shohami *et al.,* 1997). Superoxide dismutase generates H_2O_2 from super oxide free radicals that are more toxic than oxygen derived free radicals and are detoxify by catalase and reduced glutathione (Blake *et al.,* 1987). Increased free radicals could activate and induce the biosynthesis of antioxidant enzymes because of the compensative response in the body (Miyasaka *et al.,* 1998). Our results indicated that concentration of SOD in kidney increased significantly in NP treated male mice than untreated control group indicating disturbed H_2O_2 associated metabolism in male mouse kidney.

Reactive oxygen species (ROS) attack polyunsaturated fats of cell membranes and produces lipid peroxide that are toxic to the cells (Okolie *et al.,* 2007). Under normal condition lipid peroxidation is a natural metabolic process (Shewfelt and Purvis, 1995) having three steps Initiation, propagation and termination (Blokhina *et al.,* 2003). ROS that are initiator of lipid peroxidation are used in signal transduction (Tarchevskii, 1992), control cell proliferation, initiation of cell differentiation, maturation and apoptosis (Cejas *et al.,* 2004). Malondialdehyde (MDA) is the toxic by product of lipid peroxidation (Del-Rio *et al.,* 2005). In human cells they can interacting with DNA and produces compound that cause genetic mutation so, MDA is genotoxic (Del- Rio *et al.,* 2005). Malondialdehyde concentrations were significantly elevated in brain, heart, liver, kidney of NPs treated male mice and heart of female mice than control group indicating disturbed lipid peroxidation due to exposure to Lanthnum Zirconate nanoparticles.

In conclusion, our results indicated that oral treatment with 25mg/ ml solvent/Kg body weight of Lanthanum Zirconate NPs for 22 days has improved the neuromuscular coordination in female mice but it has drastically affected their leukocyte count and antioxidant metabolites in heart. While male suffered more adverse effects of NPs treatment as they had poor rearing frequency during light dark box test and significantly elevated Malondialdehyde concentrations in brain, heart, liver and kidney indicating compromised antioxidant profile in vital organs As these nanomaterials are part of our everyday life, so it is recommended that their effects in living systems should be explored under variable dose and exposure time conditions to get a broader vision regarding their biocompatibility.

Conflict of Interest

Authors declare that they do not have conflict of interest of any sort with anyone.

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