

Biochemical and morphological changes in rats exposed to platinum nanoparticles

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Received: 29 April 2015 / Accepted: 27 April 2016
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Abstract This study evaluated the toxicity potential of platinum (Pt) nanoparticles in Wistar rats. Wistar rats weighing between 180 and 193 g were randomly assigned into four groups. Animals in group 1 served as the control and received distilled water. Those in groups 2, 3, and 4 were administered with 10, 50, and 100 mg/kg body weight of Pt nanoparticles, respectively. At the end of treatments, the rats were fasted for 24 h and sacrificed under mild anesthesia. The blood and vital organs were collected and used for the biochemical and histopathological examinations. Pt nanoparticles caused significant alterations to the rat organ weights relative to the control. Also, the Pt nanoparticles altered the rat level of lipid profile and significantly elevated the atherogenic index relative to the control. The total protein level was increased in the tissues while the albumin decreased following nanoparticle treatment. Also, the nanoparticles inconsistently altered the level of serum urea and creatinine while the serum bilirubin level was raised. The activities of aspartate transaminase and alkaline phosphatase were reduced by nanoparticle treatments. However, the level of alanine aminotransferase (ALT) was inconsistently altered in serum and tissues by nanoparticle treatment with a significant elevation in the liver. Furthermore, nanoparticle exposure in rats caused several

morphological lesions including inflammation and cellular degeneration, all of which were conspicuously absent in the control group. We show evidence that Pt nanoparticles potentiated alteration of rat biochemical and morphological indices in manners reminiscent of early cellular injury.

Keywords Nanotoxicology · Lipid profile · Safety evaluation

Introduction

In recent years, the biomedical applications of metal nanoparticles have expanded. These nanoparticles or nanomaterials are used in diagnosis and therapeutics due to their unique properties which include high reactivity to the living cells, stability over high temperatures, and translocation into the cells amongst others (Adeyemi and Sulaiman 2015).

Of special interest is the platinum nanoparticles (PtNPs) which have been shown to possess antioxidant capacity (Onizawa et al. 2009). The Pt nanoparticles have been implicated as a mimetic of superoxide dismutase (SOD)/catalase. Particularly, the Pt nanoparticle has been reported with capacity to protect against drug-induced oxidative stress and was implicated for extension of lifespan (Kim et al. 2006).

However, the small size in addition to the novel physico-chemical properties of nanoparticles is cause for concern as these unique properties may predispose to adverse biological effects (Adeyemi et al. 2014). Consequently, over the last 4 years, the health and environmental safety of nanomaterials has drawn increasing attention, with the first report published in 2004 by the Royal Society and Royal Academy of Engineering highlighting the distinct lack of information on human health and environmental impacts of nanomaterials (Royal Society and Royal Academy of Engineering Report 2004). Several other governmental reports have since emerged

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(Department for Environment, Food and Rural Affairs Report 2007; European Scientific Committee on Emerging and Newly Identified Health Risks 2006, 2009), but currently, the safety considerations have certainly not paralleled the growth of the material development side of the nanotechnology industry. Furthermore, the limited information that is slowly emerging does indicate that these substances induce cytotoxicity, oxidative stress, and inflammatory responses (Nel et al. 2006; Sayes et al. 2007; Stone et al. 2007; Xia et al. 2006; Adeyemi and Faniyan 2014). This underscores concern of uncertainty about the safety of nanomaterials. It is therefore imperative that we understand and are able to minimize any potential toxicological hazards associated with the use of nanomaterials or nanoparticles, not only to protect human health and the environment, but also to avoid damaging the nanotechnology industry in the longer term.

In the light of the foregoing, the present study evaluated the biochemical and morphological changes in Wistar rats following oral and daily exposure to PtNPs.

Material and methods

Preparation of PtNPs

The PtNPs were synthesized based on established protocols with little modification. Briefly, the Pt nanoparticles were made by adding 100 mM platinum salt (chloroplatinic acid (H_2PtCl_6)) to a 1 % (w/v) tannic acid solution (pH adjusted to 8 by adding 150 mM potassium carbonate) of polyvinylpyrrolidone (PVP) with stirring (Sivaraman et al. 2009). The solution turned pale yellow to deep brown revealing the presence of Pt nanoparticles. The Pt nanoparticles were filtered using the 0.22- μM filter and characterized by UV/vis spectrophotometry (Biotek Epoch, USA), inductively coupled plasma optical emission spectrometry (ICP-OES, Cambridge, UK), and transmission electron microscopy (TEM, Brno, Czech Republic).

Experimental animals

Wistar rats with an average weight between 180 and 193 g were obtained from the small animal unit of the Department of Biochemistry, University of Ilorin, Nigeria.

Chemicals and reagents

The assay kits for creatinine (CREA), urea, bilirubin (BIL) and albumin (ALB), total cholesterol (TC), triacylglycerol (TAG), high-density lipoprotein cholesterol (HDL-C), free glycerol (FG), alkaline phosphatase (ALP), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) were products of Randox Laboratory Limited, Cumlin, UK. All

other reagents used were of analytical grade and supplied by Sigma-Aldrich Inc., St. Louis, USA.

Animal groupings and treatments

The animals were housed in standard plastic cages and were acclimatized for 2 weeks. They were maintained under standard conditions of 12-h light and dark cycle and were given free access to standard rat chow and clean water ad libitum. Handling of animals was humane and consistent with relevant guidelines (National Research Council 2011) as approved by the institutional ethics committee on scientific study. The details of animal groupings are as shown below:

Group 1 served as control and was administered distilled water.

Group 2 was administered 10 mg/kg body weight of Pt nanoparticles.

Group 3 was administered 50 mg/kg body weight of Pt nanoparticles.

Group 4 was administered 100 mg/kg body weight of Pt nanoparticles.

The nanoparticle treatment was administered by means of an oral gavage. The treatments lasted for 30 days. Selection of dosages was premised on previous studies (Adeyemi and Faniyan 2014; Adeyemi and Adewumi 2014; Adeyemi et al. 2014).

Preparation of serum and tissue homogenates

At the end of treatments, animals were fasted for 24 h and thereafter sacrificed under anesthesia. The blood was collected into clean and sterile sample bottles. The blood was centrifuged at 3000g for 15 min using a Uniscope Laboratory Centrifuge (model SM800B) to yield the serum, which was stored frozen until required for analyses. The tissue (liver, kidney, and heart) samples were removed, blotted, weighed, and homogenized in ice-cold 0.25-M sucrose solution (1:5 w/v). The homogenates were used for biochemical analyses. Sections of the excised tissue were fixed in buffered neutral formalin and used for the histopathological examination.

Determination of biochemical parameters

All biochemical measurements were done using Spectronic 21 spectrophotometer (Bausch and Lomb, NY). The activities of aspartate transaminase (AST) (E.C. 2.6.1.1), alanine transaminase (ALT) (E.C. 2.6.1.2), alkaline phosphatase (ALP) (E.C.3.1.3.1), albumin (ALB), bilirubin (BIL), CREA, urea, serum total cholesterol (TC) concentration, high-density lipoprotein cholesterol (HDL-C), and triacylglycerol (TAG) were assayed using the Randox assay kits (Crumlin, UK). The

concentration of serum low-density lipoprotein (LDL-C) was estimated using the Friedewald formula (Warnick et al. 1990) while the atherogenic index (AI) was estimated by finding the ratio of the TC to HDL-C concentration. The protein content of the serum and homogenates was determined using the Biuret method as previously described by Sulaiman and Adeyemi (2010).

Histological examination

The tissue sections were prepared for histological examination as previously described by Adeyemi and Akanji (2010). The photomicrographs were captured at $\times 100$ using the software, *Presto! Image Folio package*.

Statistical analysis

The data are expressed as mean $\pm$ standard error of the mean. Statistical analysis was performed using analysis of variance (ANOVA) and Duncan multiple range test at 5 % level of confidence ($p < 0.05$).

Results

Synthesis and characterization PtNPs

Figure 1 shows UV absorption spectrum for Pt nanoparticles at between 200 and 800 nm. The TEM images revealed spherical nanoparticle diameter size range of between 12 and 19 nm.

Average weight of animals

The daily exposure of rats to Pt nanoparticles did not appreciably affect average rat weights (Fig. 2). Also, the rat organ (heart, kidney, and liver) weights were significantly altered by the nanoparticle exposure (Table 1). The Pt nanoparticles

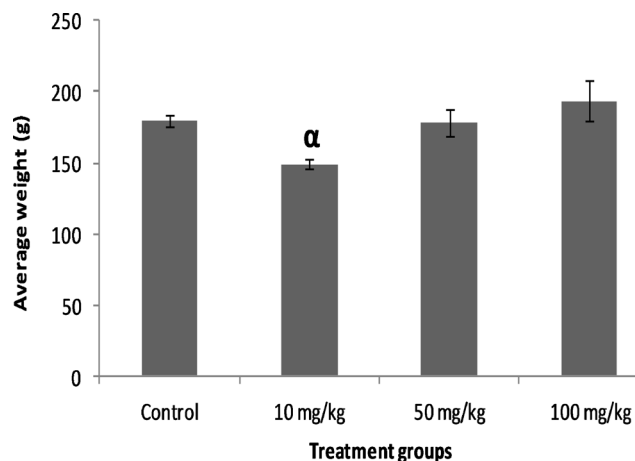
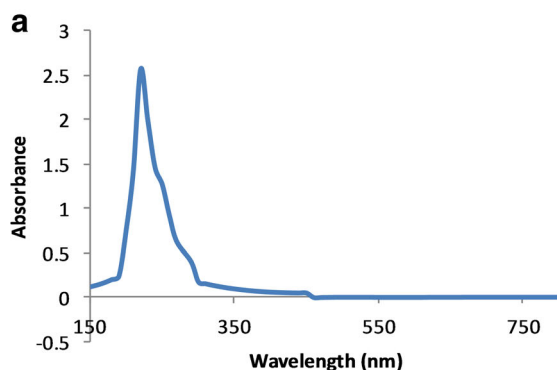


Fig. 2 Average weight of rat following oral exposure to platinum nanoparticles at different dosages. Data are expressed as mean $\pm$ SEM ($n = 3$). α is significant at $p < 0.05$ relative to the control

caused an average of 13 % reduction in the heart and liver to body weight ratios (Table 2) while the kidney to body weight ratio was decreased by an average of 36 %.

Lipid profile

The rat lipid profile is as shown in Table 3. The Pt nanoparticles caused inconsistent elevation to the level of serum TC, TAG, and FG relative to the control group. Furthermore, Pt nanoparticles inconsistently altered the level of serum HDL-C and LDL-C when compared to the control group (Table 4). To further determine the atherogenic property of Pt nanoparticles, the atherogenic index (AI) was estimated. Pt nanoparticles at 10 and 50 mg/kg elevated the rat serum AI significantly.

Total protein

The Pt nanoparticles caused significant increases in the level of heart, kidney, and liver total protein relative to the control group (Table 5). In contrast, the serum total protein was inconsistently altered by the Pt nanoparticles.

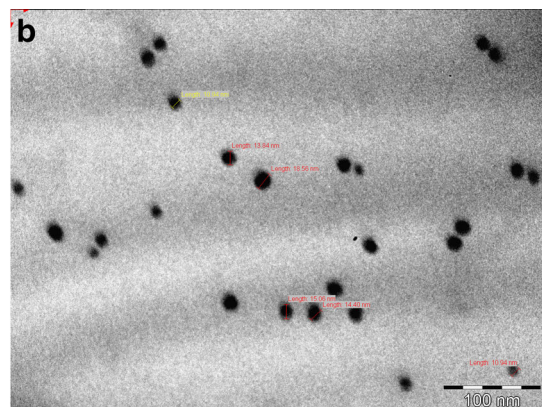


Fig. 1 **a** UV/vis absorption spectrum (200–800 nm). **b** Transmission electron microscopy (TEM) images of platinum nanoparticles

Table 1 Rat organ weights following oral exposure to platinum nanoparticles

Group	Organ weight of rats (g)		
	Heart	Liver	Kidney
Control	1.56 ± 0.00 a	9.01 ± 0.09 a	2.57 ± 0.12 a
Pt 10 mg/kg	1.33 ± 0.09 d	6.77 ± 0.30 d	1.43 ± 0.24 c
Pt 50 mg/kg	1.47 ± 0.07 b	7.77 ± 0.68 b	2.07 ± 0.18 a
Pt 100 mg/kg	1.37 ± 0.09 c	7.30 ± 0.10 d	1.73 ± 0.19 b

Values are expressed as mean ± SEM ($n = 3$). Values in each column with different letters are significantly different ($p < 0.05$)

Pt platinum

Serum metabolites

The serum ALB was significantly lowered by Pt nanoparticles (Table 6). On the other hand, Pt nanoparticles at 50 and 100 mg/kg raised the serum BIL level relative to the control group. In order to determine the effect of Pt nanoparticles on kidney function, the serum level of urea and CREA was estimated. The level of serum urea was inconsistently altered by Pt nanoparticles while the level of serum CREA was significantly elevated.

Other biochemical indices

In order to evaluate the effect of Pt nanoparticles on vital organs, the serum and tissue levels of AST, ALT, and ALP were determined. The oral administration of Pt nanoparticles caused a significant reduction in the level of serum, liver, kidney, and heart AST (Table 7). The level of liver and heart ALT was significantly elevated by Pt nanoparticles while serum and kidney ALT was inconsistently altered relative to the control group (Table 8). Furthermore, the level of serum, liver, kidney, and heart ALP was significantly elevated when compared to the control group (Table 9).

Table 2 Organ to body weight ratios of Wistar rats orally administered with platinum nanoparticles

Group	Percentage organ/body weight ratios		
	Heart	Liver	Kidney
Control	0.93 ± 0.04 a	4.89 ± 0.26 a	1.60 ± 0.12 a
Pt 10 mg/kg	0.89 ± 0.08 b	4.54 ± 0.31 b	0.97 ± 0.18 c
Pt 50 mg/kg	0.83 ± 0.09 c	4.41 ± 0.64 b	1.18 ± 0.17 b
Pt 100 mg/kg	0.71 ± 0.03 d	3.80 ± 0.25 c	0.89 ± 0.03 d

Values are expressed as mean ± SEM ($n = 3$). Values in each column with different letters are significantly different ($p < 0.05$)

Pt platinum

Table 3 Effect of platinum nanoparticles on the level of rat serum total cholesterol, triacylglyceride and free glycerol

Group	TC (mmol/l)	TAG (mmol/l)	FG (mmol/l)
Control	0.21 ± 0.05 a	0.43 ± 0.03 a	0.33 ± 0.03 a
Pt 10 mg/kg	2.34 ± 0.25 b	0.92 ± 0.07 b	0.81 ± 0.037 b
Pt 50 mg/kg	1.91 ± 0.09 b	0.73 ± 0.07 c	0.62 ± 0.07 c
Pt 100 mg/kg	0.52 ± 0.15 c	0.33 ± 0.01 d	0.22 ± 0.01 d

Values are expressed as mean ± SEM ($n = 3$). Values in each column with different letters are significantly different ($p < 0.05$)

Pt platinum

Histopathology examination

Histological examination of rat heart following oral exposure to Pt nanoparticles showed mild degeneration of cardiac tissue as well as presence of inflammation (Fig. 3). The control group showed intact cellular architecture. Also, the histological examination of rat renal sections revealed mild glomeruli degeneration and inflammation caused by the administration of Pt nanoparticles (Fig. 4). The control group showed no incidence of cellular lesion. On the other hand, rat hepatic tissue was mildly inflamed after oral exposure to Pt nanoparticles (Fig. 5). The control group showed no visible hepatocellular alteration.

Discussion

Nanoparticles are increasingly being applied for biomedical purposes (Adeyemi and Faniyan 2014; Adeyemi and Sulaiman 2015), yet our understanding of the toxic effect on living cells remains limited. Also, the small size in addition to the novel physicochemical properties of nanoparticles is cause for concern as these unique properties may predispose to adverse biological effects (Adeyemi et al. 2014). These factors underscore the safety evaluations of nanoparticles.

Table 4 Effect of platinum nanoparticles on the level of rat serum high-density lipoprotein, low-density lipoprotein, and atherogenic index

Group	HDL-C (mmol/l)	LDL-C (mmol/l)	Atherogenic index
Control	0.52 ± 0.04 a	0.07 ± 0.03 a	1.10 ± 0.08 a
Pt 10 mg/kg	0.47 ± 0.02 a	0.18 ± 0.04 b	12.19 ± 1.54 c
Pt 50 mg/kg	0.64 ± 0.09 c	0.14 ± 0.04 c	7.18 ± 0.92 b
Pt 100 mg/kg	1.31 ± 0.12 b	0.07 ± 0.02 a	0.34 ± 0.01 a

Values are expressed as mean ± SEM ($n = 3$). Values in each column with different letters are significantly different ($p < 0.05$)

Pt platinum

Table 5 Effect of platinum nanoparticles on the level of rat serum and tissue total protein

Group	Total protein concentration (g/dl)			
	Serum	Heart	Kidney	Liver
Control	2.39±0.51 a	5.21±1.47 a	7.52±1.94 a	6.89±2.34 a
Pt 10 mg/kg	2.05±0.40 a	22.12±5.17 d	10.97±3.64 d	11.82±3.24 c
Pt 50 mg/kg	4.78±1.15 a	50.18±2.92 b	45.25±0.57 b	23.05±0.53 b
Pt 100 mg/kg	1.93±0.31 b	27.26±1.87 c	21.80±1.67 c	23.86±3.14 b

Values are expressed as mean±SEM ($n=3$). Values in each column with different letters are significantly different ($p<0.05$)

Pt platinum

The UV spectrum and TEM images are consistent with literatures (Hikosaka et al. 2008) and confirmed the successful synthesis of Pt nanoparticles. The daily administration of Pt nanoparticles to rats caused significant reduction in the weight of vital organs including the heart, kidney, and liver relative to the control. Furthermore, reductions of >13 % in organ (heart, kidney, and liver) to body weight ratio were caused by Pt nanoparticles. Although the Pt nanoparticles did not affect the average rat weights appreciably, the significant effect it had on the organ weights may implicate early toxic potential of the nanoparticles. According to Adeyemi and Adewumi (2014), alteration to the average body or organ weight by an administered chemical or drug is indicative of ensuing toxic event.

The Pt nanoparticles significantly altered the level of serum TC, TAG, and FG relative to the control. Though, the lowest concentration increased the serum TC sharply and this elevation gradually depressed with increasing concentration of Pt nanoparticles. The reason for this is unclear; however, the data suggest Pt nanoparticle-induced influence on lipid metabolism or, to a large extent, the energy metabolism. This is more plausible considering the fact that a separate study by Przybytkowski et al. (2009) has previously revealed the capacity of nanoparticles to affect lipid metabolism. Meanwhile, studies have shown that serum lipid profile could be used as indices of atherosclerosis and other cardiac disorders (Ruidavets et al. 2000; Maghrani et al. 2004). Therefore, any alteration to the serum lipid profile is expected to impact the cardiac system positively or negatively. In the present study, Pt nanoparticle effect on the serum TC, TAG, FG, HDL, and

LDL did not follow a definite trend. However, an estimation of atherogenic index (AI) revealed that Pt nanoparticles at lower to medium concentration significantly raised the serum AI relative to control group, even though the rat serum HDL rose with increasing dosages of nanoparticles. This may indicate the potential of Pt nanoparticles to predispose to the development of atherosclerosis or other related conditions (Adeyemi and Akanji 2011a; Olukanni et al. 2013).

The level of total protein increased in the heart, kidney, and liver relative to the control. This may be due to increased synthesis and/or decreased catabolism consequent upon the administration of the nanoparticles (Guyton and Hall 2000). Previous findings have shown that stress imposed by a drug or chemical administered could stimulate de novo synthesis of total protein (Adeyemi et al. 2012). The ALB is an essential transport component of blood synthesized by the liver. The level of serum ALB could be used to evaluate the synthetic function of the liver. The reduction in ALB may be an indication of decreased synthesis by the liver. The level of serum ALB has been associated with the synthetic function of the liver (Adeyemi et al. 2010, 2012). Previously, decrease in serum ALB has been associated with tissue inflammation and damages (Gabay and Kushner 1999). This may suggest that the liver of the experimental rats might have been injured following administration of the Pt nanoparticles.

On the other hand, the elevated level of rat serum BIL following oral exposure to Pt nanoparticles may be attributed to increased red blood cell hemolysis leading to formation of BIL beyond the hepatic function capacity (Adeyemi et al.

Table 6 Effect of platinum nanoparticle on the level of rat serum metabolites

Group	ALB (g/dl)	BIL (mmol/l)	UREA (mmol/l)	CREA (μmol/l)
Control	2.56±0.25 a	3.03±0.32 a	38.98±0.00 a	15.22±1.71 a
Pt 10 mg/kg	0.35±0.05 c	1.31±0.06 d	63.96±3.24 b	15.40±0.50 a
Pt 50 mg/kg	0.58±0.02 b	15.57±0.27 b	36.48±0.48 c	19.87±2.71 b
Pt 100 mg/kg	0.34±0.01 c	19.48±0.26 b	18.51±1.45 d	19.38±1.26 c

Values are expressed as mean±SEM ($n=3$). Values in each column with different letters are significantly different ($p<0.05$)

Pt platinum

Table 7 Effect of platinum nanoparticles on the activity of aspartate transaminase in rat serum and tissues

Group	AST (U/l)			
	Serum	Liver	Kidney	Heart
Control	54.11 ± 5.78 a	55.85 ± 4.44 a	55.21 ± 3.24 a	52.01 ± 9.49 a
Pt 10 mg/kg	14.83 ± 2.24 d	43.00 ± 4.54 b	26.33 ± 7.10 c	40.50 ± 3.01 c
Pt 50 mg/kg	22.00 ± 6.00 c	23.83 ± 1.86 c	37.50 ± 9.01 b	25.50 ± 9.39 d
Pt 100 mg/kg	40.00 ± 7.52 b	23.33 ± 7.53 c	39.00 ± 2.2 b	55.83 ± 3.42 b

Values are expressed as mean ± SEM ($n = 3$). Values in each column with different letters are significantly different ($p < 0.05$)

Pt platinum

2012). BIL is formed as a by-product of hemoglobin degradation following red blood hemolysis. The liver metabolizes BIL making it more polar to be easily excreted in the urine or feces. However, when the formation of BIL far outweighs its detoxification by the liver, the level rises in the extracellular fluid such as the serum or plasma.

In order to evaluate effect of the exposure of Pt nanoparticles on kidney function, the serum urea and CREA levels were determined. Serum urea and CREA have been indicated as useful indices for evaluating the status of renal functions (Gross et al. 2005). Urea is formed by the liver and excreted in the urine by the kidney. Therefore, a rise in the level of serum urea may imply impaired renal excretion (Adeyemi and Akanji 2010). However, in the present study, serum urea decreased. The decrease in the concentration of serum urea after the administration of the Pt nanoparticles might be attributable to decreased protein turn over. This is more plausible considering the fact that the exposure to Pt nanoparticles also caused increased level of tissue total protein. In a separate study, silver nanoparticles have been shown to cause reduction in the level of serum urea (Adeyemi et al. 2014). CREA is a product resulting from muscle metabolism. The amount of CREA excreted is constant and shows correlation with body mass. Using the proportional relationship between CREA and muscle mass, serum CREA level has been advanced to assess renal glomerular filtration (Gross et al. 2005). The exposure of rats to Pt nanoparticles elevated the level of serum CREA though not statistically significant when compared to the

control group. The elevated level of rat serum CREA may suggest reduced glomerular clearance or enhanced muscle metabolism.

To further determine whether exposure to Pt nanoparticles has the capacity to cause tissue toxicity, the measurement of the activity of some enzyme markers including ALT, AST, and ALP was determined. The enzymes measured have been implicated for the evaluation of liver injury arising from exposure to chemical compounds including drugs amongst others (Adeyemi and Akanji 2011b; Adeyemi and Sulaiman 2014). The decrease in the activities of AST and ALP in rat serum, heart, kidney, and liver following exposure to Pt nanoparticles may be due to inactivation of the enzyme molecules by the nanoparticles or their metabolites. Recent findings have demonstrated the potential of metal nanoparticles to inhibit enzyme activity (Adeyemi and Whiteley 2013a, b). In contrast, the elevated activity of rat ALT in the serum, liver, and heart after exposure to Pt nanoparticles may represent adaptive mechanism by the rats in order to offset stress imposed by the nanoparticles. Living cells have been reported to increase the de novo synthesis of proteins in response to stressors such as drugs or chemical agents (Adeyemi and Sulaiman 2012). The elevation of ALT activity may also be an early indicator for hepatotoxicity consequent upon exposure to Pt nanoparticles (Adeyemi and Akanji 2011b; Sulaiman et al. 2014). The present findings on ALT and AST activities following exposure to Pt nanoparticles are consistent with earlier reports (Salma et al. 2011; Adeyemi and Adewumi 2014), which

Table 8 Effect of platinum nanoparticles on the activity of alanine transaminase in rat serum and tissues

Group	ALT (U/l)			
	Serum	Liver	Kidney	Heart
Control	52.94 ± 2.52 a	25.96 ± 1.20 a	89.12 ± 3.84 a	16.83 ± 1.45 a
Pt 10 mg/kg	76.00 ± 2.08 b	72.70 ± 6.06 b	35.70 ± 4.70 c	21.30 ± 1.86 a
Pt 50 mg/kg	42.30 ± 6.36 c	35.70 ± 6.17 c	32.30 ± 1.45 c	29.30 ± 1.45 c
Pt 100 mg/kg	48.00 ± 5.03 a	73.00 ± 2.00 b	46.30 ± 0.88 b	46.00 ± 5.57 b

Values are expressed as mean ± SEM ($n = 3$). Values in each column with different letters are significantly different ($p < 0.05$)

Pt platinum

Table 9 Effect of platinum nanoparticles on the activity of alkaline phosphatase in rat serum and tissues

Group	ALP (U/l)			
	Serum	Liver	Kidney	Heart
Control	122.80 ± 7.21 a	111.91 ± 9.74 a	165.32 ± 6.61 a	167.69 ± 8.95 a
Pt 10 mg/kg	57.32 ± 4.66 b	56.40 ± 1.29 b	46.31 ± 0.61 c	34.96 ± 2.90 c
Pt 50 mg/kg	30.08 ± 2.09 d	46.00 ± 2.77 c	63.20 ± 3.20 b	50.32 ± 10.33 b
Pt 100 mg/kg	43.52 ± 8.66 c	42.32 ± 9.20 d	60.08 ± 10.97 b	45.36 ± 6.56 b

Values are expressed as mean ± SEM ($n = 3$). Values in each column with different letters are significantly different ($p < 0.05$)

Pt platinum

demonstrated the potential of metal nanoparticles to alter the activity of transaminases.

The examination of tissue sections for histological changes may serve as complementary evidence to the biochemical evaluation. The incidence of inflammation and cellular degeneration which were precipitated by the Pt nanoparticle treatments may indicate likely cellular toxicity. The cellular lesions caused by exposure to the Pt nanoparticle were conspicuously absent in the control group, thus implicating the potential of Pt nanoparticles to cause cellular damage. These cellular lesions may represent evidence of the likely toxic potential of Pt nanoparticles. Meanwhile, separate studies have demonstrated that nanoparticles could sequester and bio-accumulate in

tissues (Yang et al. 2009), thereby causing cellular damage (Adeyemi et al. 2014).

Conclusion

There is increasing usage of nanoparticles for biomedical purposes, but available data on safety/toxicity profile are insufficient. Thus, studies which evaluate nanoparticles for safety or toxicity profile are needed. The present data reveal the status of some cellular biochemistry and morphological indices in rat following oral exposure to Pt nanoparticles and contribute to aid our understanding of the toxic potential of nanoparticles. To our knowledge,

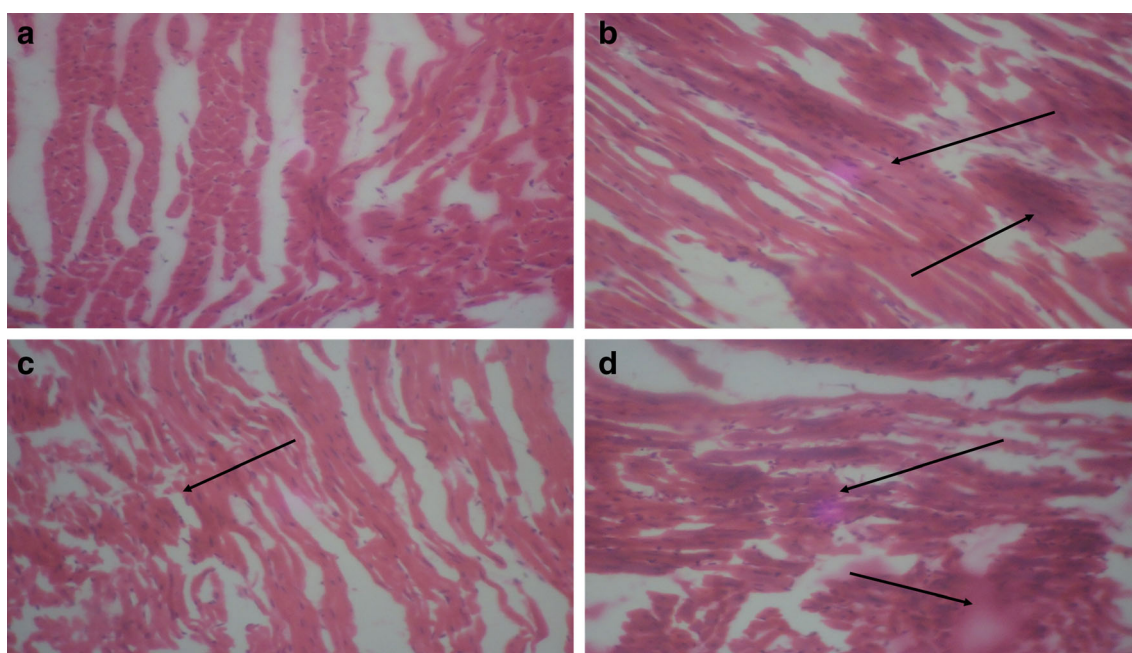


Fig. 3 Photomicrographs of rat heart following subchronic exposure to platinum nanoparticles at different dosages. **a** Control group given distilled water showing intact cellular morphology. **b** Group given platinum nanoparticles at 10 mg/kg body weight showing mild inflammation and cellular degeneration. **c** Group given platinum

nanoparticles at 50 mg/kg body weight showing inflammation and cellular degeneration. **d** Group given platinum nanoparticles at 100 mg/kg body weight showing inflammation and cellular degeneration. H&E staining ($\times 100$)

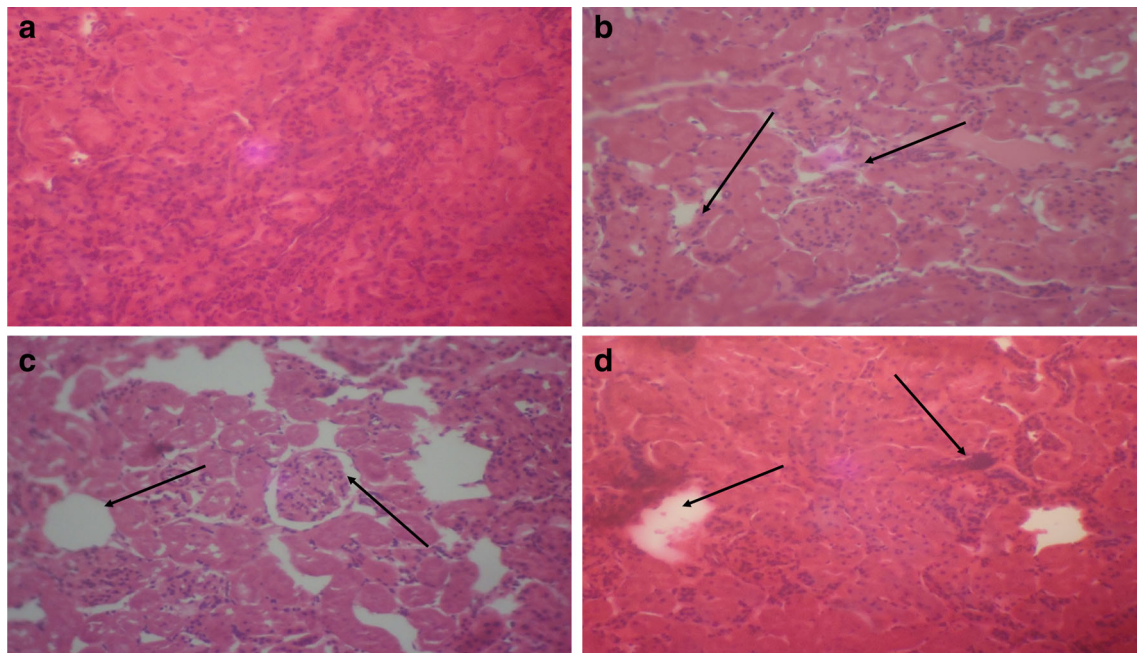


Fig. 4 Photomicrographs of rat kidney following subchronic exposure to platinum nanoparticles at different dosages. **a** Control group given distilled water showing intact cellular morphology. **b** Group given platinum nanoparticles at 10 mg/kg body weight showing mild

inflammation and ballooning. **c** Group given platinum nanoparticles at 50 mg/kg body weight showing ballooning and cellular degeneration. **d** Group given platinum nanoparticles at 100 mg/kg body weight showing ballooning and cellular degeneration. H&E staining ($\times 100$)

this is the first report showing evidence that Pt nanoparticles elevated the atherogenic index as well as potentiated

biochemical and morphological parameters in manners reminiscent of cellular injury.

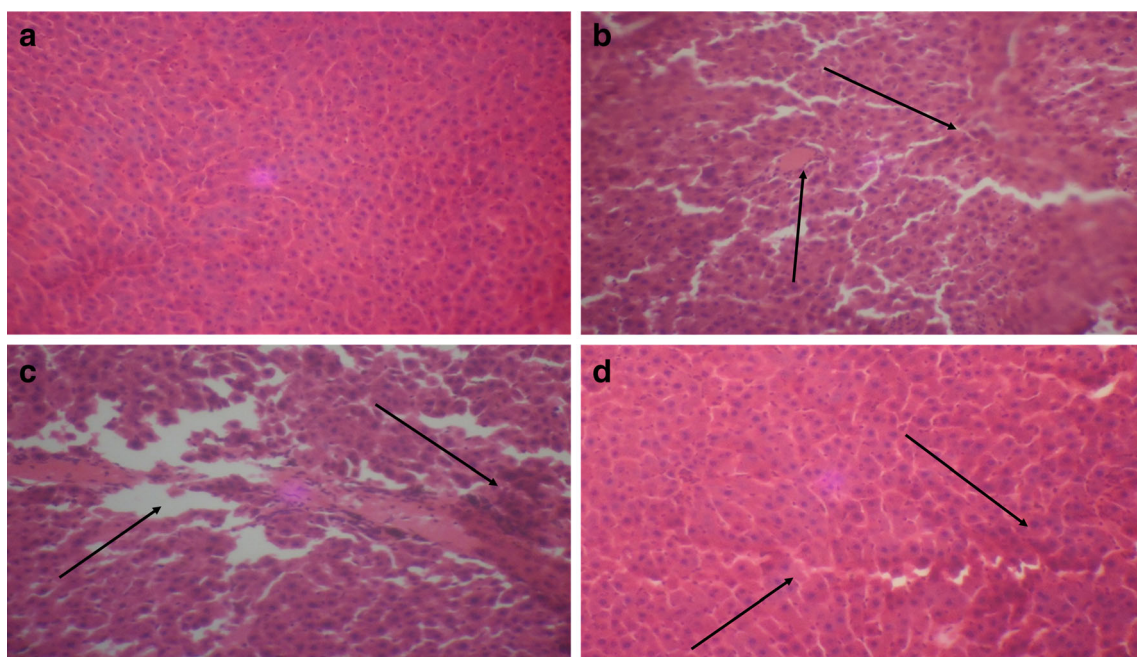


Fig. 5 Photomicrographs of rat liver following subchronic exposure to platinum nanoparticles at different dosages. **a** Control group given distilled water showing intact cellular morphology. **b** Group given platinum nanoparticles at 10 mg/kg body weight showing mild inflammation and intercellular cracking. **c** Group given platinum

nanoparticles at 50 mg/kg body weight showing inflammation and cellular degeneration. **d** Group given platinum nanoparticles at 100 mg/kg body weight showing inflammation and cellular degeneration. H&E staining ($\times 100$)

Acknowledgments The authors acknowledge the International Foundation for Science (IFS) Grant F/5672 to Dr OS ADEYEMI.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

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