Research Journal of Environmental Sciences

ISSN 1819-3412

Academic
Journals Inc.

www.academicjournals.com

OPEN ACCESS Research Journal of Environmental Sciences

ISSN 1819-3412
DOI: 10.3923/rjes.2018.41.52

Research Article
Comparative Toxicity of Two Nanoparticles and Two Insecticides Against Albino Rats

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Abstract

Background and Objective: Nanotechnology has become one of the most promising new approaches for plant protection in recent years. However, no or very little data was available about its toxicity on non target organisms. Therefore, this study aimed to investigate the comparative toxicity of two nanoparticles (NPs) (nano-silica and nano-copper oxide) with 2 insecticides (methoxyfenozide and profenofos) against albino rats. **Materials and Methods:** The rats were divided into 5 treatments groups (10 rats of each) the 1st and 2nd groups were treated with $^{1}/_{10}$ LD_{50} of nano-silica and nano-copper oxide while, the 3rd and the 4th groups treated by $^{1}/_{10}$ LD_{50} of Profenofos and methoxyfenozide insecticides. Statistical analysis of data collected was carried out using Duncan's multiple range test. **Results:** The results showed that there was a significant difference in body weight between all treatments with each other. Also all tested compounds caused a significant increase in all evaluated parameter (liver and kidney functions) concentrations. The highest activity of these parameters were noticed after 5th dose and decreased gradually after the 10th dose, after recovery periods the activity of these parameters did not return to normal level. Pathological examination showed dilated hepatic sinusoids, some foci of necrotic hepatocytes. Also, necrosis of some cells of the proximal convoluted tubules and the nuclei of these cells are pyknotic was observed. Methoxyfenozide caused the highest effect followed by profenofos while two nanoparticles had a less toxic effect. **Conclusion:** The effect of nanoparticles on the tissues may cause organ toxicity in animals.

Key words: Nanoparticles, insecticides, toxicity, histology, hematological

Citation: Shehata Shalaby, Azza Abdel-Latif and Abdel Razik Farrag, 2018. Comparative toxicity of two nanoparticles and two insecticides against albino rats. Res. J. Environ. Sci., 12: 41-52.

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

The application of chemical pesticides has grown considerably world wide as increased yields are wanted by controlling pests. These compounds assured good agricultural production but can raise serious concerns stemming from poor application events and lack of prudence in usage[1-4]. The overuse of traditional pesticides can cause serious pollution to the agro-ecosystem, mammalian toxicity and threaten non-target organisms that were beneficial to the environment[5]. Throughout the last decade, there has been an explosion in the development and application of engineered nanomaterials (ENM) resulting from a theatrical increase in exposure to humans. Whereas, ENM can give positively to quality of lives by providing improved materials, products, medical devices, drug delivery systems, etc., there is an urgent need to understand the potential health risks related with exposure to such materials[6-9]. Particulate systems like nanoparticles have been used a physical approach to modify and improve the effective to properties of some types of traditional pesticides or in the production of biopesticides directly[10]. Also, nanoparticles help to produce new pesticides and insect repellants[11]. Wan and Gong[12] studied the effect of the action of a mixture of two nanoparticles with 2 insecticides to the pest mite (Epitrimerus pyri). They reported that cypermethrin and alpha terthienyl mixed with nano-zinc oxide and copper oxide was effective on the tested mite. Undesirable effects of nanoparticles are attracting considerable and growing worldwide recognition. Nanoparticles ingested via water, food, cosmetics, drugs, drug delivery devices, etc[13]. Uptake of particles of different dimensions via the gastrointestinal tract induces unlike bad effects[14]. As EPA has cited, "these novel products may furthermore permit for further effective concentrated on of pests, use of smaller quantities of a pesticide and minimizing the frequency of spray-applied floor disinfection. Little research has been carried out to study the toxicity effect of nanoparticles on animals. Therefore, this study aimed to investigate the comparative toxicity of two nanoparticles (Nano-silica and nano-copper oxide) with two insecticides (methoxyfenozide and profenofos) on rats.

MATERIALS AND METHODS

Chemicals used:

- Nano-silica (50-70 nm), LD_{50} = 262.45±33.78 mg kg^{-1} b.w., according to Yu *et al.*[15]
- Nano-copper oxide (50-70 nm), LD_{50} = 100 mg kg^{-1} b.wt., both nanoparticles were obtained from Nanotech Egypt, Company Limited, Cairo, Egypt.
- Profenofos 72% EC (Selecron), LD50 = 358 mg kg^{-1} b.wt., according to Anonymous[16]
- Methoxyfenozide 24% SC (Runner), LD50 = >5000 mg kg^{-1} b.wt., according to Anonymous[16]

Experimental animals: Albino rats (*Rattus norvegicus* var. albus), of 100-110 g were obtained from the Animal Breeding House of the National Research Centre (NRC), Dokki, Cairo, Egypt. The animals were acclimatized under laboratory conditions at room temperature for 1 week. Food and water were provided *ad libitum*. The rats were divided into 5 treatments groups (10 rats of each) the 1st and 2nd groups were treated with $^1/_{10}$ LD_{50} of nano-silica and nano-copper oxide (26.2 and 10.0 mg kg^{-1} b.wt.) while, the 3rd and the 4th groups treated by $^1/_{10}$ LD_{50} of profenofos and methoxyfenozide insecticides (38.5 and 500.0 mg kg^{-1} b.wt. The 5th group controlled. Toxicants were dissolved in corn oil and administered 10 doses by convenient stomach tube a day after day. The tested chemicals were withdrawn for 10 days to allow recovery from toxicity. Animal's body weights were recorded after the treatment of the 5th and the 10th doses and after recovery periods.

Biochemical analysis: At 5th, 10th doses and 2 weeks recovery periods, blood samples were taken from retro-orbital venous plexus, placed into sterile tubes and centrifuged at 3500 rpm for 20 min to separate the serum. Biochemical parameters (AST, ALT, ALP, urea and creatinine concentration) were determined and analyzed spectrophotometrically using kits purchased from BioMarieux Company France. Using automated clinical chemistry analyzed Olympus Au 4oo Analyzer. Blood picture was made on Coulter Counter T890 (Coulter Counter Harpenden, UK).

Histopathological examinations: At the end of the exposure period (10 doses), rats were anesthetized and liver and kidney were quickly removed, cleaned of extraneous tissues, cut into small pieces and put into 10% buffered formalin after 24 h specimens were dehydrated in ascending grades of alcohol and imbedded in paraffin wax. Paraffin sections (5 µm thick) were stained for routine histological study using Hematoxylin and Eosin stain[17].

Histochemical studies

Polysaccharide inclusions: Periodic acid-Schiff method[18] was applied for detection of the polysaccharide materials.

Statistical analysis: The experimental design was a factorial CRD (complete randomized design) with 10 replicates. Statistical analysis of data collected was carried out using a computer program[19], Duncan's multiple range test with a significant difference of $p<0.05$.

RESULTS AND DISCUSSION

During the experiment, animals from all groups were checked daily for any signs of toxicity. Slight choreoathetosis and hypersensitivity were noticed in rats administered with profenofos after 4-5 h of dosing and these signs were gradually declined after next few hours, no visible adverse effects were observed in other groups.

Effect of tested chemicals on rat's body weight: Data in Table 1 revealed insignificant changes in body weight of rats before treatment (the average in weight ranged from 104-105 g). After the 5th dose, the obtained results showed significant increase ($p<0.05$) in body weight in untreated and treated rats, the highest increase was noticed in check rats (124.0 g) followed by methoxyfenozide and nano-copper oxide (116.0 g) while the lowest increase was observed in profenofos treated rats (108.0 g), then nano-silica (112.0 g). The same trend happened after the 10th dose, a significant increase ($p<0.05$) in untreated rats when compared with all treatments was shown, but no significant differences between all treated rats. After recovery periods, the increase in body weight was continuing in all animals and there were significant differences between untreated and treated rats, also there were significant differences ($p<0.05$) between all treatments with each other. The general mean in body weight indicated that the highest increase was noticed in untreated animals (136.9 g), while the lowest was observed in profenofos treated rats (121.5 g) (Table 1). On the contrary, data obtained by Ben-Slama *et al.*[20] indicated that the mean body weight in rats given nano-zinc oxide was similar with control, so no significant differences in the relative organs weight between treated and untreated rats.

Effect of tested chemicals on liver functions of treated rats: Data presented in Table 2 indicated that all tested compounds caused significant increase ($p<0.05$) in aspartate aminotransferase (AST) activity compared with untreated rats. The highest activity of this enzyme was noticed after the 5th dose and decreased gradually after the 10th dose but still above the normal level. After the recovery period, the activity of AST enzyme still high except in the case of nano-copper oxide decreased below normal level (-3.1%). The general mean of AST activity revealed that methoxyfenozide [Insect growth regulators (IGR)] caused the highest effect on this enzyme followed by profenofos, while two nanoparticles had less toxic effect when compared with 2 insecticides. The same effects were observed in the case of alanine aminotransferase (ALT), obtained data revealed that all tested chemicals caused a significant increase in this enzyme activity. The highest effects have happened in methoxyfenozide treated rats followed by profenofos then 2 nanoparticles. The data also reveal that the activity of Alkaline phosphatase (ALP) enzyme reach its peak after the 5th dose and decreased gradually after the 10th dose and recovery period. Also, all chemicals caused a significant increase ($p<0.05$) in this enzyme activity after different periods except in the case of nano-copper oxide after 10th dose. In the same respect, methoxyfenozide caused the highest effect on ALP activity followed by profenofos the nano-silica, while nano-copper had the lowest effect. Data obtained by Doudi and Setorki[21] revealed that the hepatic enzymes showed that the SGOT level in rats treated with 5 and 10 mg kg^{-1} of nano-copper oxide were significantly higher than the control 2 days after the treatment. Also, Yu *et al.*[15] reported that the activities of serum LDH, AST and ALT were all increased in the silica nanoparticles treated mice. On the same trend, Ben-Slama *et al.*[20] reported that exposure rats to nano-zinc oxide induced marked increase in AST and ALT activity.

Effect of tested chemicals on kidney functions of treated rats: There were statistically significant increases in urea concentration in all treated rats (Table 3). The highest effect

Table 1: Effect of tested chemicals on rats body weight

Periods treatments	Pre-treatment	5th dose	10th dose	After recovery days	General mean
Methoxyfenozide	105.0^{a}	116.0^{b}	130.0^{b}	155.0^{c}	126.5
Profenofos	104.0^{a}	108.0^{d}	132.0^{b}	142.5^{d}	121.5
Nano-copper oxide	104.0^{a}	116.0^{b}	132.0^{b}	157.5^{b}	127.25
Nano-silica	104.0^{a}	112.0^{c}	130.0^{b}	157.5^{b}	125.75
Control	104.0^{a}	124.0^{a}	152.0^{a}	167.5^{a}	136.9
LSD 5 (%)	2.86	2.79	2.53	2.1	

The figures superscripted with same alphabets in the same columns do not significantly differ from each other as per Duncan's multiple range tests

Table 2: Effect of tested chemicals on liver functions of treated rats

Parameters	AST (u L^{-1})			ALT (u L^{-1})			ALP (u L^{-1})		
Treatments	5 doses	10doses	After recovery days	5 doses	10 doses	After recovery days	5 doses	10 doses	After recovery days
Methoxyfenozide	227.0^{a} (+56.1)	188.0^{a} (+29.3)	180.4^{a} (+24.1)	52.0^{a} (+39.0)	48.8^{a} (+30.5)	44.8^{b} (+19.8)	312.5^{a} (+78.7)	264.0^{a} (+50.9)	226.4^{a} (+29.4)
Profenofos	215.4^{b} (+48.1)	185.9^{a} (+27.9)	179.2^{a} (+23.2)	45.6^{b} (+21.9)	48.4^{a} (+29.4)	42.1^{c} (+12.6)	297.6^{b} (+70.2)	235.8^{b} (+34.8)	200.9^{b} (+14.9)
Nano-silica	181.3^{c} (+17.8)	163.2^{b} (+12.2)	146.0^{b} (+0.4)	43.3^{c} (+15.8)	38.9^{b} (+4.0)	38.5^{d} (+2.8)	264.0^{c} (+50.9)	180.7^{c} (+3.3)	178.8^{c} (+2.2)
Nano-copper oxide	165.8^{d} (+14.0)	156.6^{c} (+7.7)	140.9^{c} (-3.1)	42.6^{c} (+13.9)	37.9^{b} (+1.3)	46.4^{a} (+24.1)	231.0^{d} (+32.1)	176.1^{d} (+0.7)	177.2^{d} (+1.3)
Control	145.4^{e}	145.4^{d}	145.4^{b}	37.4^{d}	37.4^{b}	37.4^{e}	174.9^{e}	174.9^{d}	174.9^{e}
LSD 5%	2.23	2.45	2.66	1.47	1.58	0.992	1.28	2.48	0.87

(According to Duncan's test) Letters means the significant differences between treatments and control (p<0.05). Each figure between brackets represents the percentage of content as check

was happened after the 5th dose and decreased gradually after the 10th dose and still high at the recovery period. Also, the same trend was noticed in creatinine concentration. Methoxyfenozide had the highest toxic effect followed by profenofos then nano-silica, while nano-copper oxide had the lowest effect on biochemical parameters. On the contrary, Ben-Slama *et al.*[20] found that uric acid, creatinine and glucose levels are not modulated in nano-zinc oxide treated rats.

Effect of tested chemicals on blood picture of treated rats: The obtained results revealed that there was significantly decreased in blood picture parameters of 4 treated groups than in untreated rats ($p<0.05$), except in the case of mean corpuscular volume (MCV) there is a significant increase (Table 4). Also the highest effect of these chemicals was observed after the 5th dose, while the toxic effect decreased after the 10th dose but still below the normal level after recovery days. On the contrary, Ben-Slama *et al.*[20] reported that nano-zinc oxide exposed rats showed normal values for the blood picture.

Histopathological results

Liver: Sections of control liver show the regular architecture of hepatic lobules. The central veins lies at the center of the lobules surrounded by the hepatocytes with strongly eosinophilic granulated cytoplasm and distinct nuclei. Between the strands of hepatocytes, the hepatic sinusoids are shown (Fig. 1a, b). Liver sections of rats given nano-silica showed hydropic degeneration in the hepatocytes (Fig. 1c). In addition, moderate lymphocyte penetration in the portal and periportal tracts with dilated and congested veins and some pyknotic nuclei were noticed (Fig. 1d). Examination of the liver of nano-copper oxide treated rats showed dilated hepatic sinusoids and some foci of necrotic hepatocytes. The normal portal tracts were revealed (Fig. 1e). Histopathological investigation of the liver of rats given methoxyfenozide showed foci of necrotic hepatocytes (Fig. 1f). On the other hand, liver of rats treated by profenofos showed hydropic degeneration in the hepatocytes (Fig. 1g) and mild lymphocyte infiltration in the portal and periportal tracts with dilated and congested veins. Some necrotic hepatocytes were noticed (Fig. 1h). In the same trend Sardari *et al.*[22], reported that inflammation of the parenchymal cells was observed in the liver of rats treated with nano-silver (1 and 2 mg kg^{-1} b.wt) and nuclear duplication of some cells and intercellular space enlargement were noticed in the hepatic lobule. More so, apoptosis around the central vein and blood between some

Table 3: Effect of tested chemicals on kidney functions of treated rats

Parameters	Urea (mol dL^{-1})			Creatinine (mol dL^{-1})		
Treatments	5 doses	10 doses	After recovery days	5 doses	10 doses	After recovery days
Methoxyfenozide	18.8^{a} (+261.5)	13.2^{a} (+153.8)	9.3^{a} (+78.8)	1.08^{a} (+27.0)	1.02^{a} (+19.4)	0.94^{a} (+9.5)
Profenofos	17.6^{b} (+238.5)	13.1^{a} (+151.9)	8.2^{b} (+57.7)	0.96^{b} (+12.3)	0.92^{b} (+7.5)	0.94^{a} (+9.5)
Nano-silica	11.2^{c} (+115.4)	9.1^{b} (+75.0)	7.7^{c} (+48.1)	0.92^{c} (+7.5)	0.9^{c} (+5.0)	0.87^{b} (+2.4)
Nano-copper oxide	10.0^{d} (+92.3)	8.2^{c} (+57.7)	7.0^{d} (+34.6)	0.91^{c} (+6.7)	0.86^{d} (+1.2)	0.84^{c} (-1.2)
Control	5.20^{e}	5.20^{d}	5.2^{e}	0.85^{d}	0.85^{d}	0.85^{c}
LSD 5 %	0.397	0.876	0.4	3.42	1.17	1.30

(According to Duncan's test) Letters means the significant differences between treatments and control ($p<0.05$). Each figure between brackets represents the percentage of content as check

cells were also observed. This study results coincide also with those obtained by Doudi and Setorki[21], who reported that nano-copper oxide induces toxicity and changes of histopathological in liver and lung tissues of treated rats. It is evident that these nanoparticles cannot be used for human purposes because of their toxicity. Also, a pathological damage in the liver was manifested by sinusoidal congestion (SC), RBC deposition in the vein and inflammatory response after oral administration of ZnO-NPs for 5 consecutive days[20]. Data obtained by Farrag and Shalaby[23] revealed that $^{1}/_{10}$ LD_{50} of profenofos induced venous congestion in the liver, focal necrosis of hepatocytes in the portal and periportal areas. Many of the hepatocytes are pale stained and a few display late vacuolation.

Kidney: Sections of control kidney show the normal renal corpuscles and tubules, proximal convoluted tubules and distal convoluted tubules. The glomerului, urinary spaces and Bowman's capsules are shown (Fig. 2a). Light microscopy of the kidney of nano-silica treated rats showed inflammatory infiltration in the interstitial spaces and cellular debris in the lumen of the renal tubules. The cells of the renal tubules showed degenerative changes (Fig. 2b). In case administration of nano-copper oxide, kidney of rats showed necrosis of some cells of the proximal convoluted tubules. The nuclei of these cells are pyknotic. The renal corpuscles exhibited almost normal structures (Fig. 2c). Treated rats by methoxyfenozide showed necrosis of some cells of the proximal convoluted tubules of kidneys. The nuclei of these cells are pyknotic. The renal corpuscles exhibit almost normal structure (Fig. 2e). Kidney of rats received profenofos showed moderate inflammatory infiltration in the interstitial spaces and cellular debris in the lumen of the renal tubules (Fig. 2e). These data was agreement with those reported by Sardari *et al.*[22], who noticed damages in kidney's tissue, including necrosis of glomerular cells, Bowman's capsule, proximal tubular and proteinic sediment was seen in renal tubules. Also, Yu *et al.*[15] reported that treated mice by silica nanoparticles caused lymphocytic infiltration, granuloma formation and hydropic degeneration in liver hepatocytes, megakaryocyte hyperplasia in the spleen and pneumonia and pulmonary interstitial thickening in the lung. In the same trend, the histopathology of kidneys tissues showed intratubular protein deposition and vascular congestion in rats treated with ZnO-NPs[20]. Farrag and Shalaby[23] reported that $^{1}/_{10}$ LD_{50} of caused kidney exhibited inflammatory cell infiltration, congestion and hypercellularity of the glomeruli.

Histochemical examination

Liver: Examination of liver sections of control rat stained according to periodic acid Schiff`s technique (PAS) shows the abundance of polysaccharide materials (glycogen) in the hepatocytes. The nuclei of the hepatocytes give negative periodic acid Schiff`s reaction indicating the absence of polysaccharides. The glycogen particles appear accumulated at one side of the cytoplasm leaving the other side almost devoid of such material (Fig. 3a). Treatment with nano-silica gives faint homogeneous stainability of the polysaccharide inclusions in the hepatocytes of the administrated rats (Fig. 3b). Administration of nano-copper oxide caused diffuse stainability of the positive PAS materials of the hepatocytes of the treated rats. A few number of the hepatocytes displayed dense stainability than the others (Fig. 3c). Administration of methoxyfenozide revealed depletion of the polysaccharide inclusions of the hepatocytes of the treated animals. The cytoplasm of such cells exhibited faint stain ability with periodic acid Schiff's technique (PAS). Nevertheless, strong positive staining of the polysaccharide materials was shown (Fig. 3d). Examination of liver sections of rats received a profenofos showed moderate and weak PAS-positive material in the hepatocytes. Heterogeneous staining was encountered in the liver cells, the degenerated cells were weakly stained while the necrotic cells were devoid of stainable inclusions (Fig. 3e).

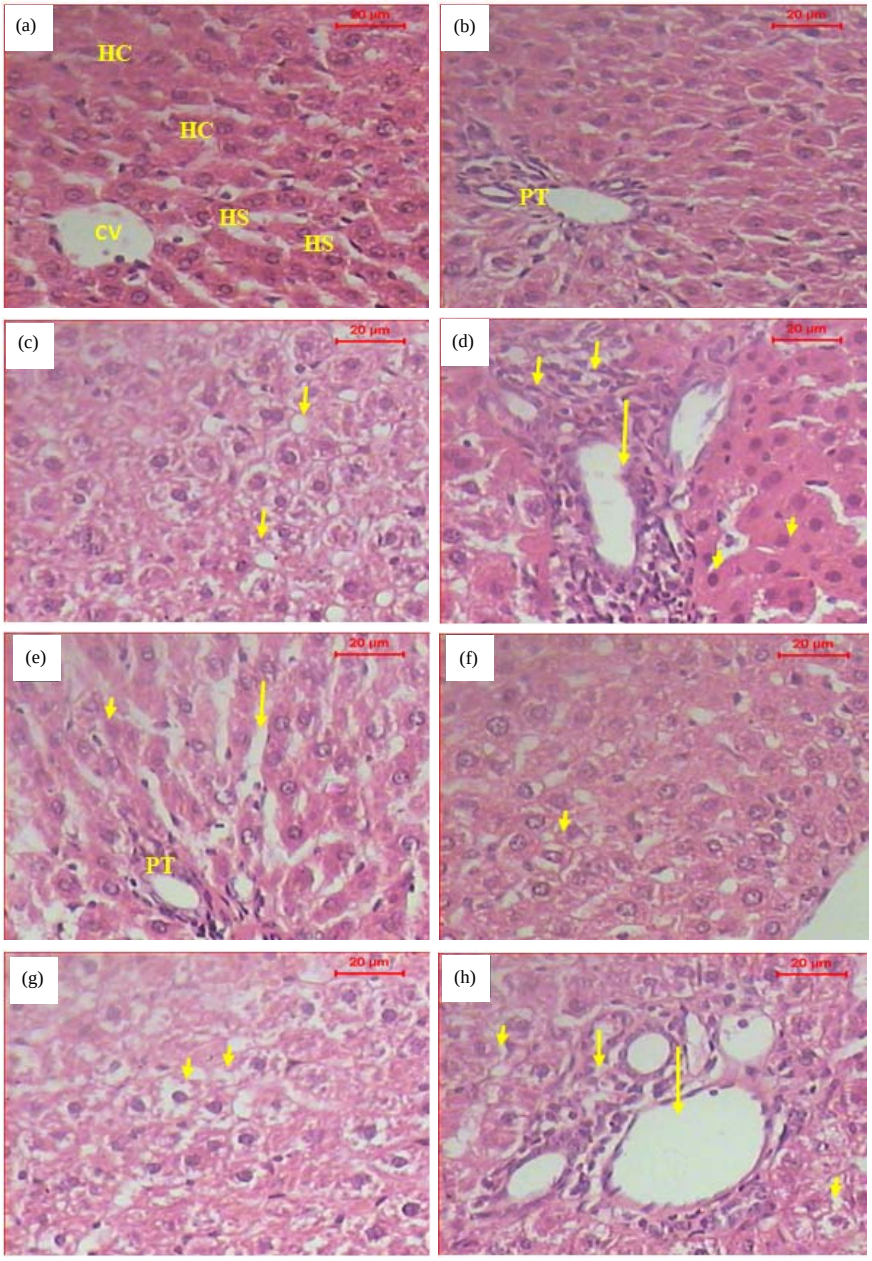

Fig. 1(a-h): A micrograph of sections of (a) Control liver shows the architecture of a hepatic lobule. The central vein (CV) lies at the center of the lobule surrounded by the hepatocytes (HC) with strongly eosinophilic granulated cytoplasm and distinct nuclei. Between the strands of hepatocytes the hepatic sinusoids are shown (HS), (b) Control liver shows portal tract (PT), (c) Liver of rat given nano-silica shows hydropic degeneration in the hepatocytes (arrows), (d) Liver of rat given nano Silicon shows moderate lymphocyte infiltration in the portal and periportal tract (short arrows) with dilated and congested veins (long arrow), (e) Liver of nano copper oxide treated rats shows dilated hepatic sinusoids (arrow) and some foci of necrotic hepatocytes (arrow head). Notice the normal portal tracts (PT), (f) Liver of rat given methoxyfenozide shows foci of necrotic hepatocytes (arrow head), (g) Liver of rat given profenofos shows hydropic degeneration in the hepatocytes (arrow heads), (h) Liver of rat given profenofos shows mild lymphocyte infiltration in the portal and periportal tract (short arrows) with dilated and congested veins (long arrow). Notice, some necrotic hepatocytes (arrow head) (H and E stain, Scale bar: 20 μm)

Table 4: Effect of tested chemicals on blood picture of treated rats

Parameters	RBCs (10^6)			Hb (%)			PLT (10^3)		
Treatments	5 doses	10 doses	After recovery days	5 doses	10 doses	After recovery days	5 doses	10 doses	After recovery days
Methoxyfenozide	6.98^{b} (-6.7)	6.83^{b} (-8.7)	7.18^{a} (-4.0)	12.5^{b} (-12.0)	13.6^{a} (-4.2)	13.9^{ab} (-2.1)	59.0^{e} (-45.4)	68.0e (-37.0)	74.0^{e} (-31.5)
Profenofos	5.42^{d} (-27.5)	5.88^{c} (-21.4)	6.03^{b} (-19.4)	9.1^{d} (-35.9)	10.2^{c} (-28.2)	10.8^{c} (-23.9)	77.0^{d} (-28.7)	79.0^{d} (-26.9)	81.0^{d} (-25.0)
Nano-silica	5.93^{c} (-20.7)	6.01^{c} (-19.7)	6.12^{b} (-18.2)	10.0^{c} (-29.6)	10.1^{c} (-28.9)	11.4^{c} (-19.7)	87.0^{b} (-19.4)	89.0^{c} (-17.6)	89.0^{c} (-17.6)
Nano-copper oxide	6.82^{b} (-8.8)	6.92^{b} (-7.5)	7.15^{a} (-4.4)	12.4^{b} (-12.7)	12.7^{b} (-10.6)	13.2^{b} (-7.0)	86.0^{c} (-20.4)	92.0^{b} (-14.8)	98.0^{b} (-9.3)
Control	7.48^{a}	7.48^{a}	7.48^{a}	14.20^{a}	14.20^{a}	14.20^{a}	108.0^{a}	108.0^{a}	108.0^{a}
LSD 5%	0.347	0.47	0.436	0.71	0.74	0.81	1.2	2.0	2.3
Parameters	MCH (Pg)			MCHC (g dL^{-1})			MCV (fl0)		
Treatments	5 doses	10 doses	After recovery days	5 doses	10 doses	After recovery days	5 doses	10 doses	After recovery days
Methoxyfenozide	14.9^{d} (-27.3)	16.2^{c} (-21.0)	18.3^{b} (-10.7)	29.8^{b} (-14.6)	30.2^{c} (-13.5)	33.5^{ab} (-4.0)	53.1^{c} (+0.95)	53.1^{c} (+0.95)	52.0^{b} (-1.1)
Profenofos	15.7^{c} (-23.4)	16.3^{c} (-20.5)	18.6^{b} (-9.3)	30.2^{bc} (-13.5)	31.1^{bc} (-10.9)	33.1^{b} (-5.2)	59.1^{a} (+12.4)	58.5^{a} (+11.4)	57.6^{a} (+9.5)
Nano-silica	18.2^{b} (-11.2)	17.3^{b} (-15.6)	19.0^{b} (-7.3)	31.2^{bc} (-10.6)	32.2^{bc} (-7.7)	32.5^{b} (-6.9)	58.3^{a} (+10.8)	55.9^{b} (+6.3)	56.5^{a} (+7.4)
Nano-copper oxide	18.6^{b} (-9.3)	18.1^{b} (-11.7)	19.9^{a} (-2.9)	31.8^{b} (-8.9)	32.8^{b} (-6.0)	32.6^{b} (-6.6)	55.9^{b} (+6.3)	54.8^{b} (+4.2)	51.5^{b} (-2.1)
Control	20.50^{a}	20.50^{a}	20.50^{a}	34.90^{a}	34.90^{a}	34.90^{a}	52.60^{c}	52.60^{c}	52.60^{b}
LSD 5 %	0.61	0.78	0.75	1.76	1.91	1.65	2.25	1.57	1.52

(According to Duncan's test) Letters means the significant differences between treatments and control ($p<0.05$). Each figure between brackets represents the percentage of content as check

Kidney: Examination of kidney sections of control rats stained with periodic acid Schiff`s technique (PAS) shows the positive materials in the parietal and visceral walls of the Bowman's capsule and capillaries of the glomeruli, the basement membrane of the proximal and distal convoluted tubules and the brush borders of the proximal convoluted tubules. The glomeruli and the brush borders of the proximal convoluted tubules give more intense magenta color than the other structures (Fig. 4a). Microscopic observations of kidney sections of nano-silica treated rats showed marked diminution in PAS positive materials in the basement membranes of the distal and proximal complicated tubules, the brush borders of the proximal convoluted tubules and glomeruli (Fig. 4b). In rats administrated with nano-copper oxide, the PAS positive materials displayed strong stainability in the parietal and visceral layers of the Bowman's capsules and the glomeruli. The polysaccharide inclusions in the tubules showed heterogeneous stain ability where the degenerated tubule cells were weakly stained while the necrotic ones were devoid of stainable materials. A moderate to a strong reaction in the brush borders of the healthy cells was observed (Fig. 4c). Histochemical examination of kidney sections of methoxyfenozide treated rats showed mild diminution in PAS positive materials in the basement membranes of the distal and proximal convoluted tubules, the brush borders of the proximal convoluted tubules and glomeruli. A moderate to a strong reaction in the brush borders of the healthy cells was observed (Fig. 4d). Examination of kidney sections of rats received a profenofos showed moderate and weak PAS-positive material in the glomeruli and the renal tubules, respectively. Heterogeneous staining was encountered in the cells of the lining of the renal tubules, the degenerated cells were weakly stained while the necrotic cells were devoid of stainable inclusions (Fig. 4e). The above investigations indicated that nano-silica, nano-copper oxide, methoxyfenozide and profenofos caused a reduction in the polysaccharide inclusions of the liver and kidney tissues of the treated rats. It was found that the reduction was relevant in rats given nano-silica or profenofos. On the contrary, data obtained by Kim *et al.*[24] indicating that the high dose of nano silica against rats was 2000 mg kg^{-1}, while middle and low were 1000 and 500 mg kg^{-1} b.wt. They reported that the 90 day toxicity study, there were no animal deaths in relation to the administration of SiO_2 particles of either size. In addition, no treatment-related clinical changes or histopathological findings were observed in any of the experimental groups. These data coincide with those obtained

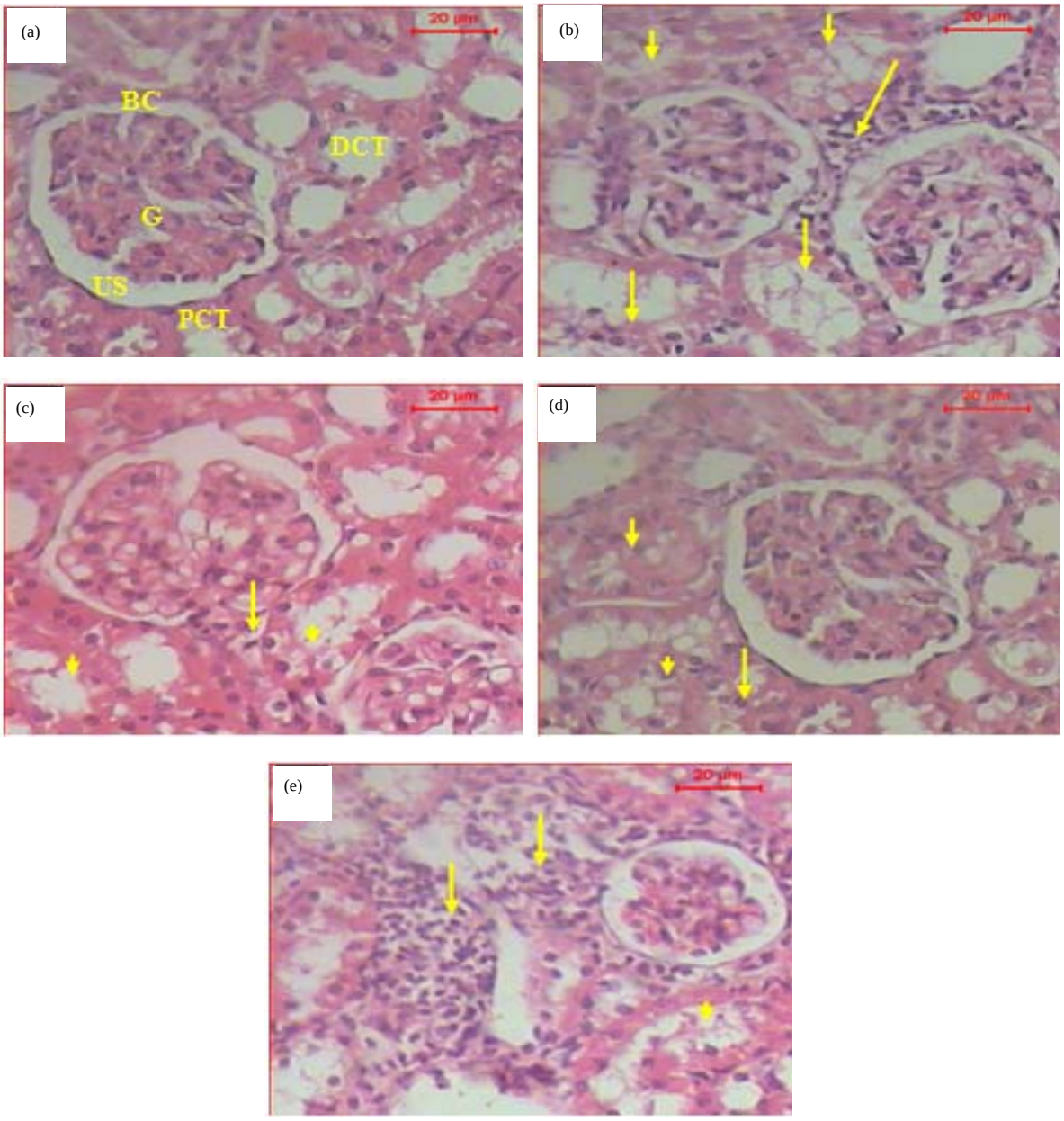

Fig. 2(a-e): A micrograph of sections of (a) Control kidney shows the renal corpuscle and renal tubules, proximal convoluted tubules (PCT) and distal convoluted tubules (DCT). Notice the glomerulus (G), urinary space (US) and Bowman's capsule (BC), (b) Kidney of rat given nanosilica shows inflammatory infiltration in the interstitial space (arrow) and some cellular debris in the lumens of the renal tubules (arrowheads). The cells of the renal tubules show many degenerative changes (short arrows), (c) Kidney of rat given nano CuO shows necrosis of some cells of the proximal convoluted tubules (arrow head). The nuclei of these cells are pyknotic (long arrow). The renal corpuscles exhibit almost normal structures, (d) kidney of rat given methoxyfenozide shows necrosis of some cells of the proximal convoluted tubules (arrow head). The nuclei of these cells are pyknotic (long arrow). The renal corpuscles exhibit almost normal structure, (e) kidney of profenofos treated rats shows moderate inflammatory infiltration in the interstitial space and some cellular debris in the lumens of the renal tubules (H and E stain, Scale bar: 20 µm)

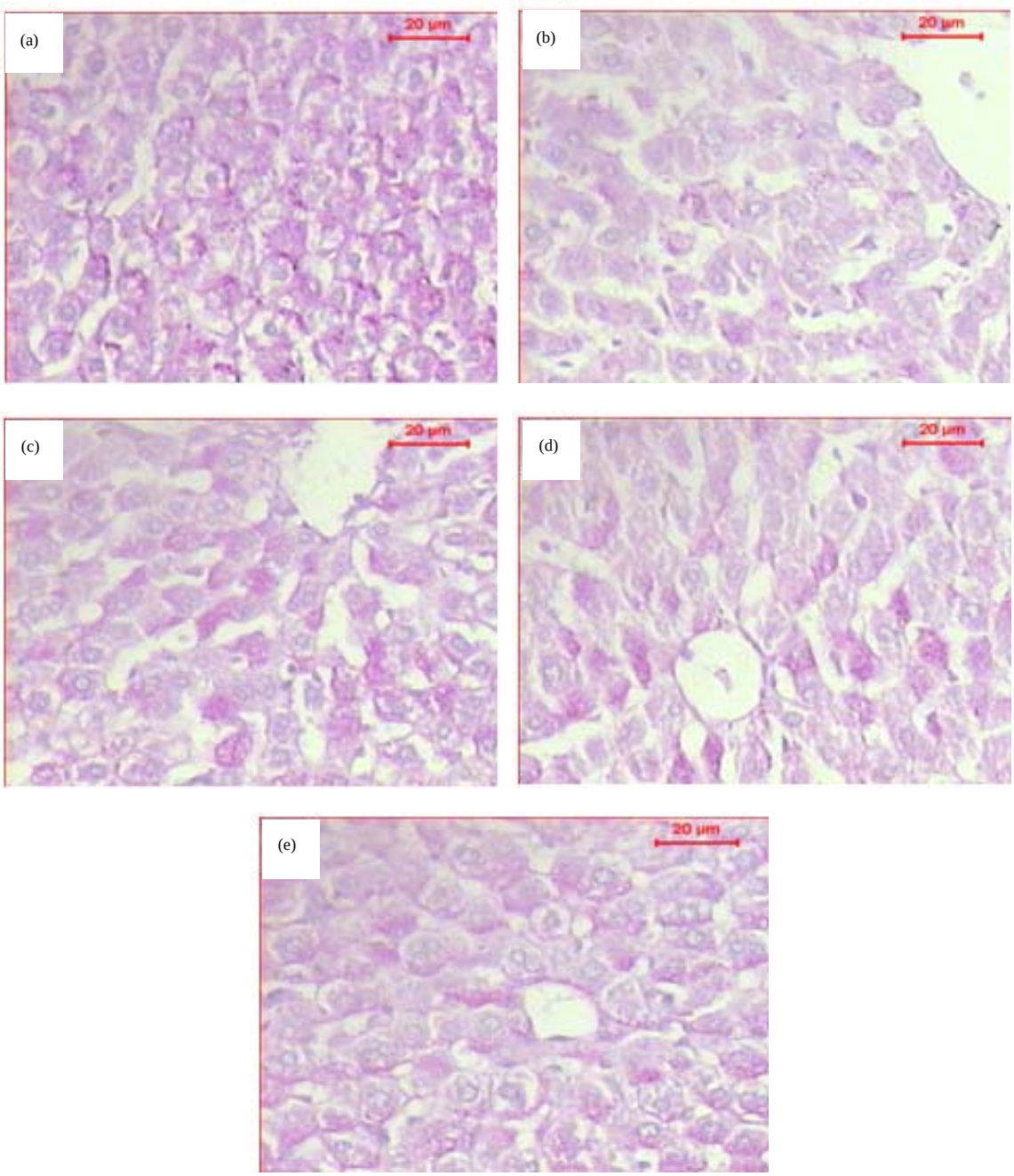

Fig. 3(a-e): A micrograph of sections of (a) Control liver shows the nuclei of the hepatocytes give negative periodic acid Schiff`s reaction indicating the absence of polysaccharides., (b) Liver of nanosilica treated rats shows faint homogeneous stainability of the polysaccharide inclusions in the hepatocytes, (c) Liver of rat given nano-copper oxide shows diffuse stainability of the positive PAS materials of the hepatocytes of the treated rats., (d) Liver of methoxyfenozide treated rats shows depletion of the polysaccharide inclusions of the hepatocytes of the treated animals. Nevertheless, strong positive staining of the polysaccharide materials was shown, (e) Liver of rat received a profenofos showed moderate and weak PAS positive material in the hepatocytes. (PAS stain, Scale bar: 20 µm)

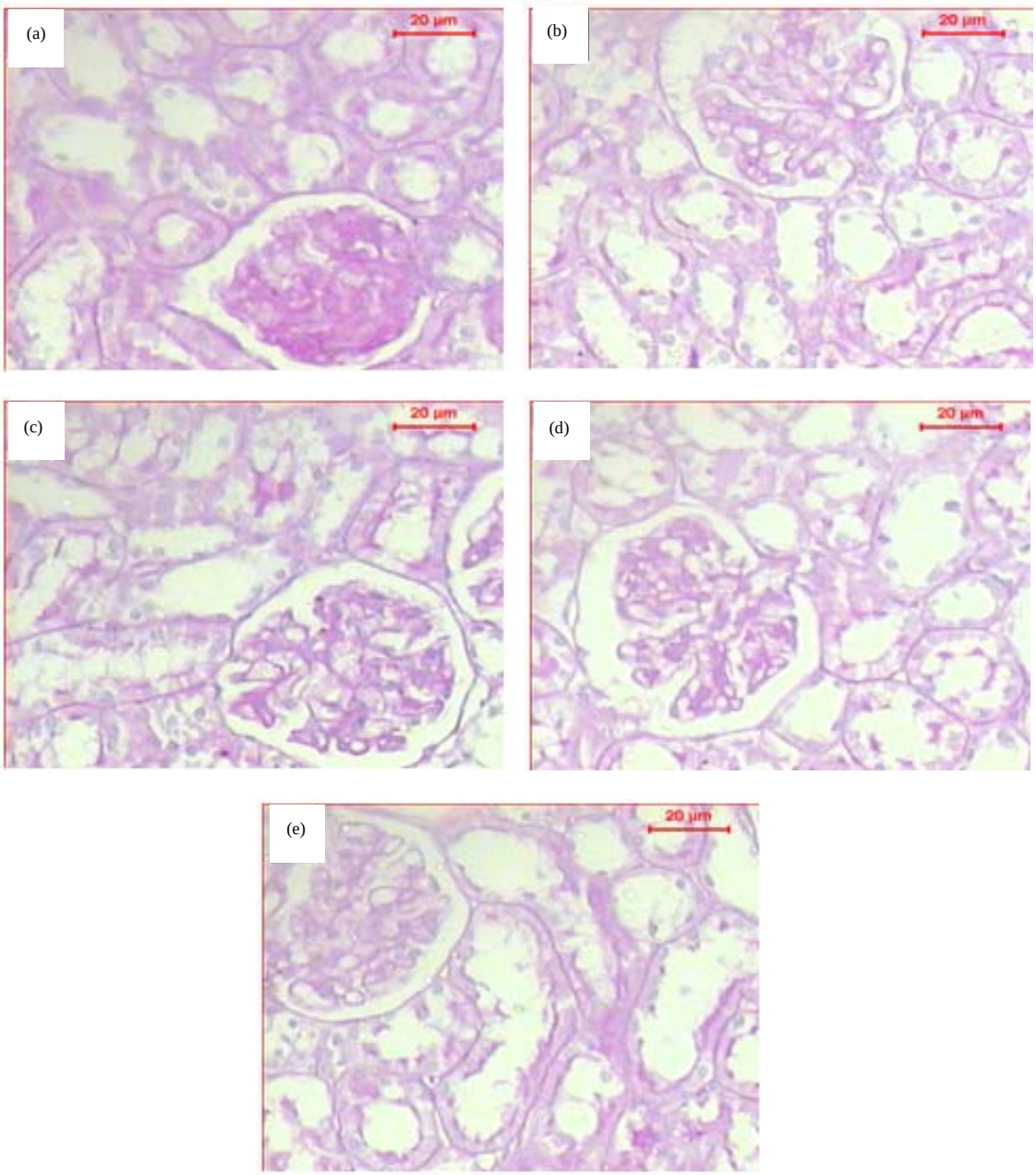

Fig. 4(a-e): A micrograph of sections of (a) Control kidney shows the positive materials of polysaccharides in the parietal and visceral walls of the Bowman's capsule and capillaries of the glomeruli, the basement membrane of the proximal and distal convoluted tubules and the brush borders of the proximal convoluted tubules, (b) Kidney of nanosilica treated rats shows marked diminution in PAS positive materials in the basement membranes of the distal and proximal convoluted tubules, the brush borders of the proximal convoluted tubules and glomeruli, (c) Kidney of rat given nanocopper oxide shows strong stainability in the parietal and visceral layers of the Bowman's capsules and the glomeruli., (d) Kidney of methoxyfenozide treated rats shows mild diminution in PAS positive materials in the basement membranes of the distal and proximal convoluted tubules, the brush borders of the proximal convoluted tubules and glomeruli, (e) Kidney of rat received a profenofos shows moderate and weak PAS positive material in the glomeruli and the renal tubules respectively. (PAS stain, Scale bar: 20 µm)

by Farrag and Shalaby[23], they reported a repeated oral administration of $^{10}/LD_{50}$ doses of lufenuron or profenofos for 2 months showed a severe depletion in the polysaccharides content of the hepatocytes.

CONCLUSION

The increase of modern pesticides, while undeniably a success in science and technology. It has grown to be clear that numerous pesticides have affected the environment negatively. Biodistribution experiments have showed liver, kidney and spleen as the target organs for engineered nanoparticles after uptake by the gastrointestinal tract. Therefore, it is concluded that the effect of NPS on the tissues may cause organ toxicity in animals.

SIGNIFICANCE STATEMENTS

This study revealed that the use of some biologically active chemicals (such as nanoparticles) poses possible problems of toxicity between those who manufacture, prepare or apply these compounds. Ingested NPS may be absorbed through the intestinal lining and translocation into the blood stream where they undergo the first-pass metabolism in the liver. Again, the effects of this translocation are largely unknown. This study data also showed that liver and kidney act as the target organs for engineered nanoparticles after uptake by the gastrointestinal tract.

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