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Toxicity of some metal oxides nanoparticles on male rats with respect to biochemical and histological changes

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Abstract

Nowadays more than thousands of different nanoparticles are known, though no well-defined guidelines to evaluate their potential toxicity and to control their exposure are fully provided. The present work involved the synthesis of mesoporous alumina sphere (MAS), Mesoporous aluminasilica nanoparticles (MASN) and Mesoporous silica nanoparticles (MSN) to evaluate their toxicity with respect to biochemical and histological changes in male rats to model their safety to human health. The results showed that there are no significant differences in the measured biochemical parameters (GOT, GPT, creatinine and urea) in rats treated with fabricated nanoparticles and untreated rats. Furthermore, the histology test confirmed that there is no significant histological changes either in kidney or liver tissues of rated treated with fabricated nanoparticles relative to untreated rats. Our findings indicated the absence of significant toxic effects on rats treated with the fabricated nanoparticles in terms of the biochemical and histological changes with the untreated controls. Our study demonstrated the possible use of these fabricated nanoparticles in different applications as safe compounds.

Keywords: Toxicity, nanomaterials; rats; fabrication

Introduction

Recent improvements on nanotechnology science, especially in the preparation of arranged nanoparticles with specific size and shape, results in the detection of novel and widespread application of it. The popularity of metallic nanoparticles (NPs) increased nowadays because of their significant properties. Nanomaterials provide a good molecular support in diverse potential applications related to their unique properties, such as geometrical order, tunable size, and high stability under various environment phases (**El-Safty et al., 2008; El-Safty et al., 2012**). Fabrication and design of mesoporous materials, which display order and

connectivity of mesopores and high surface area, may offer potential applications for chemical capture and analysis in environmental and medical fields (**Platschek et al., 2006; El Safty et al., 2010; Khairy and El-Safty, 2014**). However, several questions regarding their safety and toxicity have arisen due to numerous novel properties (**Shin et al., 2015**).

Hence, in this context, inorganic oxide powders may treat well with these demands. The conjunction of aluminium atoms in the framework of mesopore aluminosilica is considered as one of the main reasons for creating acidic active sites; such acidity is considered a major factor in different material applications (**Garcia-Bennett et al., 2006; Wang et al., 2006; El Safty et al., 2013**). Nevertheless, many different applications in our daily lives, such as catalysis processes, sensor design, and membrane filtration, are based on the use of aluminosilica materials (**Climent et al. 1996; El-Safty et al., 2008; Zukal et al., 2010**).

Mesoporous alumina oxide has been greatly considered and extensively used as non-siliceous materials with a broad range of applications (**El-Safty et al., 2013**) Alumina is interesting to researchers because of their strong antimicrobial activity and non-toxic characteristics in appropriate amounts, in addition to their physical and chemical properties and potential biological applications. Alumina nanoparticles have been used in various applications, such as catalysis and water treatment, as well as widespread biological applications, such as protein separation, drug delivery, and biosensors, among others. (**Rajan et al., 2015; Ke et al., 2013**).

Nanoparticles such as silica have widespread applications, i.e., in disease diagnosis and therapy (**Thangam et al., 2014; Yuan et al., 2015; Yao et al., 2016; Xie et al., 2016; Rehman et al., 2016**). Recently, the attention given to mesoporous silica is attributed to their unique characteristics, such as uniformed mesoporous tunnels, narrow pore size distribution, good biocompatibility, low toxicity, and chemical stability. Much effort has been devoted toward the improvement and manipulation of this material for various applications.

While nanotechnology and the production of nanoparticles are growing exponentially, research into the toxicological impact and possible hazard of nanoparticles to human health and the environment is still in its infancy (**Elsaesser and Howard, 2012**). Nanotoxicology has emerged only recently, years after the first boom of nanotechnology, when various nanomaterials had already been introduced into a number of industrial processes and products.

Therefore In this study, we tried to identify the adverse effects of fabricated nanoparticles (MASN, MAS and MSN) that commonly used in wide spread applications using rats treated with oral administration. The toxicity was examined on rats with respect to biochemical and histological changes in the liver and kidney of treated rats compared with untreated rats.

Materials and Methods

Synthesis of the tested nanoparticles

Mesoporous aluminasilica nanoparticles (MASN) were fabricated using simple one-pot microemulsion polymerization technique in conjunction with sol-gel process, according to previous fabrication method reported for HOM silica monoliths (**El-Safty et al., 2012**).

The mesoporous alumina sphere (MAS) nanoparticles were synthesized via quaternary microemulsion in liquid crystalline phases with the surfactant/oil microemulsion phase as described by **Shenashen et al. (2017).**

The one-pot direct template approach was used to synthesize the mesoporous silica nanoparticles (MSN), as previously reported (**El-Safty and Hanaoka 2003, 2004; 2008**).

Toxicity assessment of fabricated nanoparticles

This experiment was carried out on rats to determine the safety of fabricated nanoparticles on rats. Its effect on some biochemical parameters was investigated. Then, the effect was confirmed by checking the histological alterations in kidney and liver tissues compared with the control group. Wistar male rats *(Rattus norvegicus*), 8 weeks old and weighing 80–100 g, were obtained from the Faculty of Medicine, Cairo University. The tested animals were placed in cages under suitable conditions with a connection to water and food (**Romestaing et al., 2007).** The animals were kept 2 weeks before treatment for acclamation. The animals were separated into four sections each consisting of six rats, three for the treatment with MASN, MAS as well as MSN and the forth for control. Rats were orally administered with fabricated nanoparticles (500 mg/kg body weight),

whereas the control group was administrated with water. After 30 days, the blood samples were taken from rats before scarifying. Liver and kidney organs were taken and kept in formalin after scarifying the rats.

Biochemical parameters

Glutamic-pyruvate transaminase (GPT) and glutamic oxaloacetic transaminase (GOT) were estimated in blood serum by centrifugation of blood samples at 4500 rpm for 15 min at 4°C to obtain the blood serum. The colorimetric methods described by **Barham and Trinder (1972)** were used for the determination of GOT and GPT. Serum urea and creatinine level were determined by colorimetric test using DiaSys reagent kits **Fawcet and Scott (1960**) and **Reitman and Frankel (1957)**, respectively.

Histology test

The histological trail was performed in accordance with the method of **Bancroft and Stevens (1996)** in the Department of Histopathology, Faculty of Veterinary Medicine, Cairo University, Egypt.

Statistical analysis

The data were statistically analyzed using one-way analysis of variance. Furthermore, comparison was done by Duncan's multiple range test (**Duncan, 1955**) using SPSS program (Version 6.12, SAS Institute Inc., Cary, USA).

Results

Properties of fabricated nanoparticles

The measured surface area of fabricated metal oxides nanoparticles were 380 m^2/g while the average particle size was 10 nm. The shape of the fabricated nanoparticles was spherical with uniform size.

Toxicity evaluation

This test was performed on rats to assess the safety of fabricated nanoparticles by considering the impact on some biochemical factors. The safety was confirmed by checking the alterations in kidney and liver tissues as compared with the controls.

Biochemical parameters

For liver function biochemical parameters (GPT and GPT), the data in Table 1 showed no significant differences in the activity of GPT and GPT enzymes in rats treated with the fabricated nanoparticles at a given dose relative to untreated rats. Regarding to kidney function parameters (creatinine and urea level), the data in Table (2) showed no significant differences in the measured parameters in rats treated with fabricated nanoparticles and untreated rats.

Table 1: Effect of fabricated nanoparticles on liver function of treated rats

Treatments	SGPT (U/L)	SGOT (U/L)
MAS	58.30±1.76 a	58.95±1.10 a
MASM	57.10±1.45 a	59.52±0.98 a
MSM	58.10±1.12 a	59.22±1.23 a
Control	57.70±2.56 a	60.41±1.52 a

Each value is mean of six replicates.
Mean ± SE followed by same letter in column of each treatment are not significant different at p = 0.05 as determined by Duncan

Table 2: Effect of fabricated nanoparticles on kidney functions of treated rats

Treatments	Urea (mg/dl)	Creatinine (mg/dl)
MAS	23.10± 0.013 a	0.510± 0.013 a
MASN	23.12± 0.011 a	0.512± 0.011 a
MSN	23.09± 0.012 a	0.509± 0.012 a
Control	23.11±0.014 a	0.511±0.014 a

Each value is mean of six replicates.
Mean ± SE followed by same letter in column of each treatment are not significant different at p = 0.05 as determined by Duncan

The histopathological changes in the kidney

The kidney tissues of rats treated with MSN (Fig. 1 D) and MAS (Fig1 C) anoparticles were normal and showed similarities to those in the control group (Fig. 1A). However, for rats treated with MASN, the kidney tissue was normal like control with mild histopathological changes such as slight congestion of glomerular tuft (Fig. 1B).

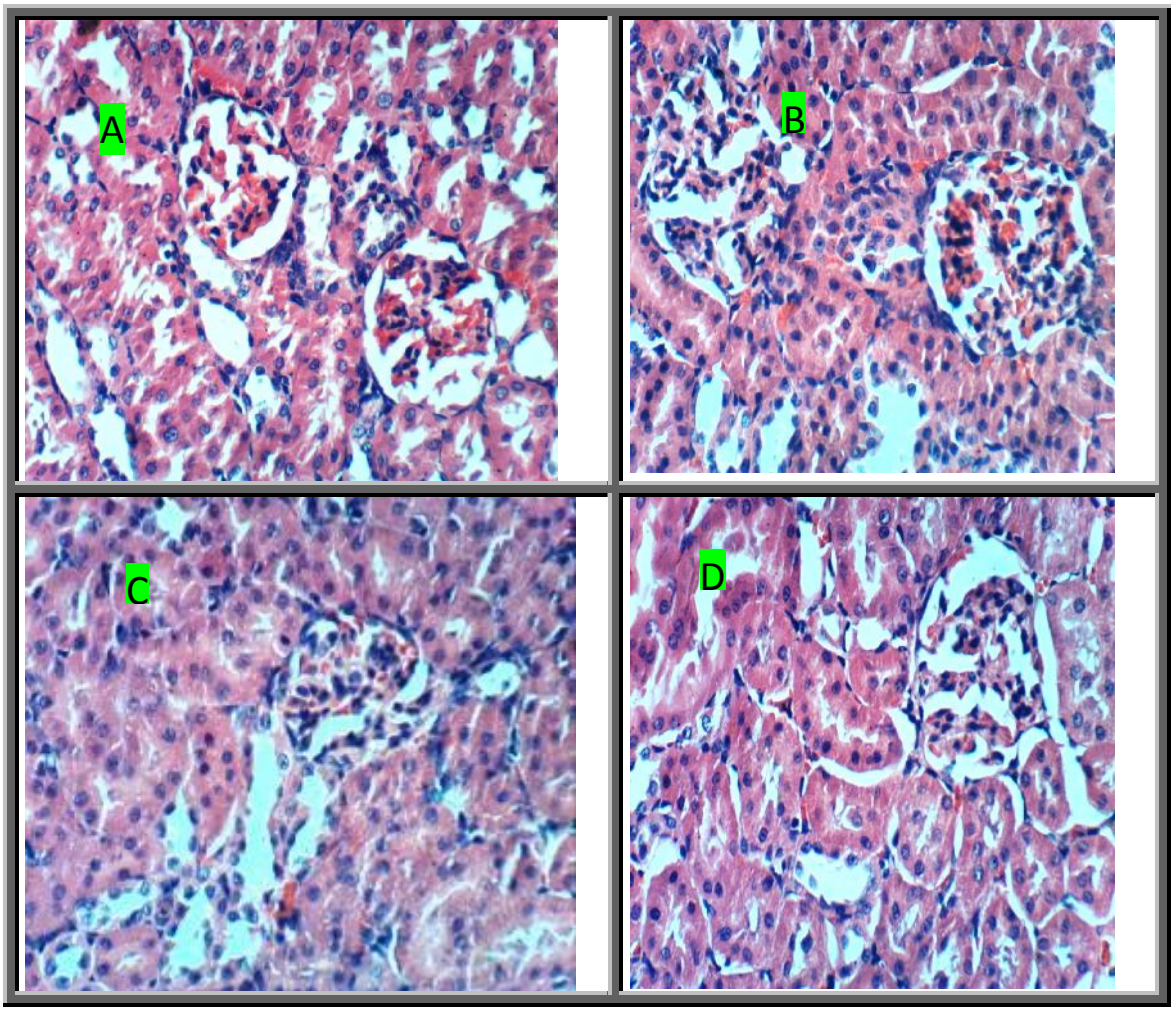

Fig. 1. Sections of the kidney of rats treated with MASM (B), MAS (C) and MSN (D) relative to the control (A).

The histopathological changes in the liver

Liver tissue of the rats treated with fabricated nanoparticles (MASN, MAS and MSN) was normal like those in the control group (Fig. 2A) with mild histopathological changes, such as slight hydropic degeneration of hepatocytes (Fig. 2B, C, D).

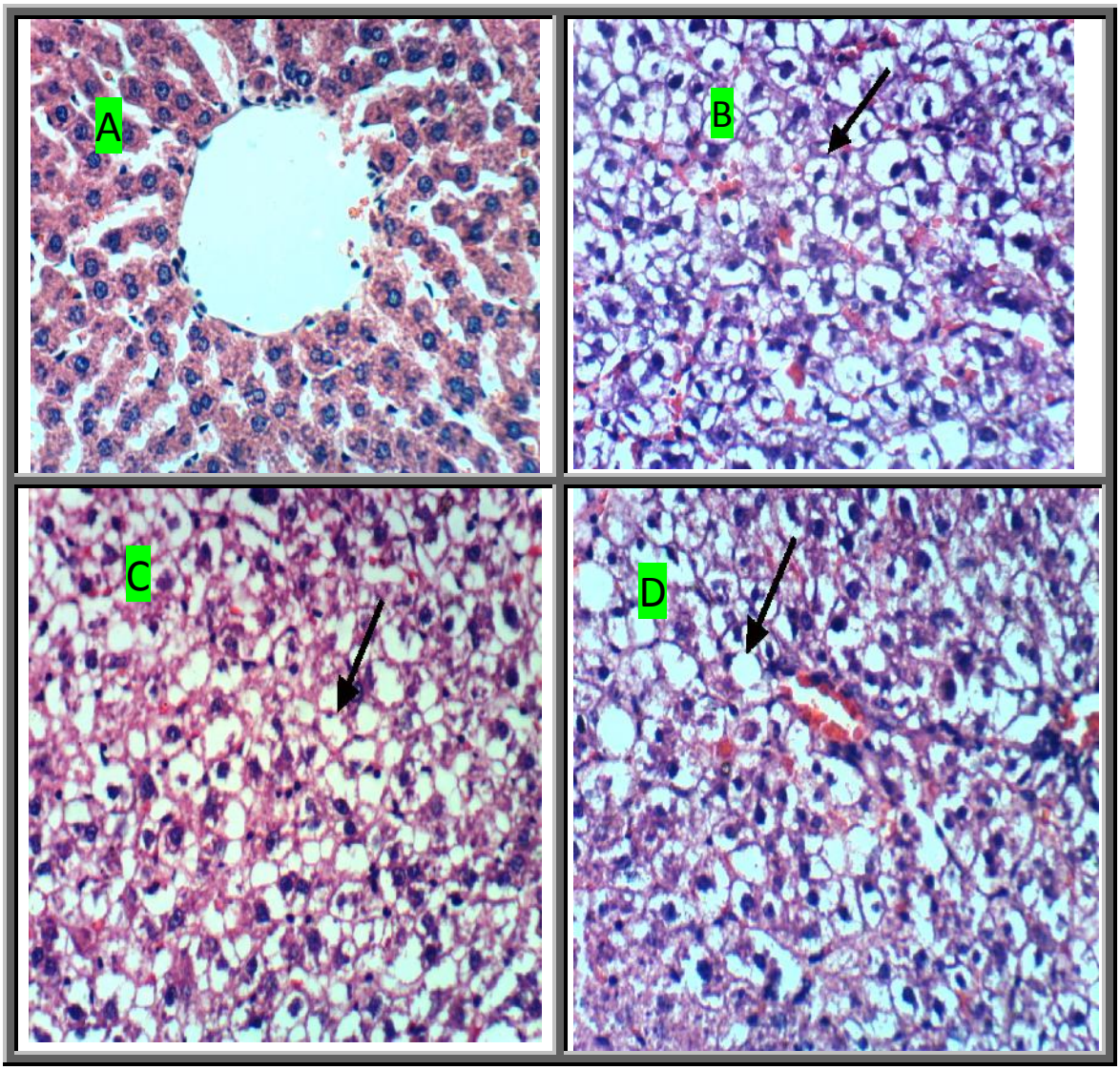

Fig.2. Sections of the liver of rats treated with MASN (B), MAS (C) and MSN (D) relative to the control (A)
*The arrows showed a slight hydropic degeneration of hepatocytes

Discussion

The safety considered one of the key factors for any nanoparticles used in any application. These nanoparticles should not affect the environment and the public health**.** Therefore, when we evaluate any nanoparticles we should considered its safety using several toxicological tests with respect to biochemical and histopathological changes. Currently, the toxicity of engineered NPs is assessed with a number of approaches. Among of these approaches are biochemical and histological tests. GPT and GPT are enzymes usually present in the liver cells, when hepatic tissue is damaged theses enzymes leak out from the cells into blood leading to increased levels and activities in plasma (**Banaee et al., 2009**). Our results revealed that fabricated nanoparticles in water showed no changes in the activities of enzyme such as GOT and GPT in rats. These non-significant alterations in these enzymes are biomarkers of hepatic safety and indicated no hepatic damage caused by water containing fabricated metal oxides nanoparticles.

Serum levels of urea and creatinine were shown to be of clinical value that denotes renal impairment (**Reddy et al., 2012**). Urea is formed by deamination of amino acids in the liver, and then it is transported by blood to the kidneys where it is excreted with urine (**Harvey and Ferrier, 2011**). Creatinine is a waste product that is normally filtered from the blood and excreted with urine. Therefore, creatinine and urea level considered a biomarker of kidney damage (**Yousaf et al., 2003**). Our study revealed non-significant elevation in the level of serum creatinine and urea in rats treated with fabricated nanoparticles relative to untreated rats.

Histological changes provide a rapid method to detect effects of toxicants, especially chronic ones, in various tissues and organs (**Bernet et al., 1999**). The liver is the main organ for detoxification (**Dutta et al., 1993**) that suffers serious morphological alterations as results of exposure to toxic compounds (**Rodrigues and Fanta, 1998**). Alterations in the liver may be useful as markers that indicate prior exposure to environmental stressors. Our study showed no significant alterations in the kidney or liver of rats treated with fabricated nanoparticles compared with untreated one. Besides, the observed mild changes were uncorrelated with the dose given orally to the treated rats. Most likely, a residue of this dose will not reach humans under any conditions, which reflects safety to human health.

Our results confirmed the safety of fabricated nanoparticles to human health based on obtained data. We found that the studied three metal oxides nanoparticles indeed exhibit much low toxicity, and that their low toxicity can be attributed to their tendency to aggregate in solution which results in limited interaction between the nanoparticles and cell walls of the test organisms (**Ching-Ng et al., 2015).** Recently, in two studies, different designs of silica nanoparticles have not damage human cells (**Liong et al., 2009; Song et al., 2013**). Histopathological examination revealed no abnormalities in any tissues (liver, kidney, large intestine, brain, lungs, spleen, heart, stomach and small intestine) after orally exposing silica nanoparticles for 28 days at a daily dose of 2.5 mg. (**Mebert et al., 2017).** Also regarding to alumina oxide nanoparticles the majority of the studies on the toxicity of alumina indicate that it has moderate to low toxicity **(Ching-Ng et al., 2015)**.

Conclusion

Based on our biochemical and histological data, the fabricated nanoparticles may be safe on human health. However, further and extensive studies about toxicity of nanomaterials are in demand because engineered nanoparticles represent a novel toxicological challenge. They are completely novel in evolutionary terms, the evidence shows that they gain can access to the body, particularly through inhalation, and then translocate within the body to distant sites at low doses.

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