GSC Biological and Pharmaceutical Sciences
eISSN: 2581-3250 CODEN (USA): GBPSC2
Cross Ref DOI: 10.30574/gscbps
Journal homepage: https://gsconlinepress.com/journals/gscbps/

(RESEARCH ARTICLE)

Check for updates

Intrarenal injection of silica mesoporous reduced renal toxicity induced by gentamycin in rats

Tahani Younis Omar [1], Sara Bayoumi Ali [2], Rokia Gamal Mohamed [2], Ahmed Osama Abdelaty [2], Liali Yousef Talat [2], Ahmed Mostafa Fahmy [2], Ayman Saber Mohamed [2,*], Sohair Ramadan Fahmy [2] and May Mohamed El Batran [3]

[1] *Department of zoology, Faculty of science, Sirte University. Sirte Libya.*
[2] *Department of Zoology. Faculty of Science, Cairo University, Egypt.*
[3] *Faculty of Pharmacy, Cairo University, Egypt.*

GSC Biological and Pharmaceutical Sciences, 2022, 19(01), 061–065

Publication history: Received on 01 March 2022; revised on 04 April 2022; accepted on 06 April 2022

Article DOI: https://doi.org/10.30574/gscbps.2022.19.1.0138

Abstract

Introduction: Mesoporous silica (MS) has recently used in biomedical applications due to its distinctive physicochemical properties.

Purpose: The study aims to investigate the efficacy of MS to reduce renal toxicity induced by gentamicin in rats.

Methods: The rats were randomly divided into three groups (n=6 per group): Control group (injected with 0.9% saline i.p daily for 8 consecutive), Gentamycin (injected with gentamycin, 100 mg/kg bw i.p. for 8 consecutive days) and MS group (after gentamycin injection, rat injected into left kidney with MS; 70 µg/0.5 ml/ rat).

Results: Ms Treatment caused significant decreases in creatinine, urea, uric acid, and MDA while it increased GSH and catalase levels.

Conclusion: Intrarenal injection of MS improved renal function in rats suffering from acute kidney injury.

Keywords: Acute Kidney Injury; Mesoporous Silica; Intrarenal Injection; Gentamycin

1. Introduction

Acute kidney injury (AKI) is a loss of kidney function that outcomes in increased urea, creatinine, uric acid levels, and dysregulation of extracellular volume and electrolytes [1]. About 15% of patients admitted to hospitals suffer from acute kidney injury with frequency in intensive care over half of the patients [2]. The development of nanoscale materials for multiple applications has become a hot issue in recent years because of their environmental friendliness, low cost, and biocompatibility **[**3,4**].** Mesoporous silica (MS) recently used in biomedical applications due to its distinctive physicochemical properties, such as large surface area and pore volume, tunable pore and particle sizes and biocompatibility, [5]. The biocompatibility and adsorbent activity of MS makes it an excellent choice to remove toxic substances from the biological system. It has been shown that MS can adsorb creatinine and extract it [6]. Furthermore, MS has high efficiency for urea adsorption [7]. Injection of MS of different particle sizes distributes mainly in the liver and spleen [8]. Thus, the intrarenal injection should be used to focus silica into the kidney. The next problem discussed before using MS is the excretion after removing toxic compounds from the blood. Another study found that MS is mainly

* Corresponding author: Ayman Saber Mohamed
Department of Zoology, Faculty of Science, Cairo University, Egypt.

excreted through urine after different administration routes (intravenous, hypodermic, intramuscular injection and oral administration [9]. Thus, the study aims to investigate the efficacy of MS to reduce renal toxicity induced by gentamicin in rats.

2. Material and methods

2.1. Chemicals

Mesoporous silica was purchase from Sigma-Aldrich (St. Louis, MO, USA). Kits were purchased from the Biodiagnistic Company (El Moror St, Dokki, and EGY).

2.2. Transmission electron microscope

TEM were performed on JEOL JEM-2100 high resolution transmission electron microscope at an accelerating voltage of 200 kV, respectively.

2.3. Ethical consideration

All methods used in this experiment were approved by the Cairo University, Faculty of Science, Institutional Animal Care, and Use Committee (IACUC) (Egypt) (CU/I/F/52/18).

2.4. Animals handling

Adult male Wistar rats (Rattus norvegicus) with an average body weight of 150 - 170 gm were purchased from the National Research Center (NRC), Egypt, grouped and housed in polypropylene cages (six animals/cage) in a well-ventilated animal house at a temperature of (23 ± 2 °C) with 12:12 h day/night cycle. They were nourished standard chow pellets and drinking water *ad libitum*.

Rats were acclimatized to animal house conditions for 7 days before starting of the study. The rats were randomly divided into five groups (n=6 per group):

- Group I (Control): injected with 0.9% saline i.p daily for 8 consecutive days. On day 9, the rats were injected by 1ml/rat intravenously of the 0.9% saline.
- Group II (GM): injected with gentamycin (100 mg/kg bw i.p.) dissolved in 0.9% saline for 8 consecutive days [10]. On day 9, the rats were injected by 1ml/rat intravenously of the 0.9% saline.
- Group III (GM+ MS): injected with gentamycin (100 mg/kg bw i.p.) for 8 consecutive days. On day 9, the rats were injected with MS (70 µg/0.5 ml/ rat).
- Intra renal injection of MS was performed according to Quimby with slight modification **[**11]. Rats were anesthetized with sodium pentobarbital (50 mg/kg body weight). The rat surgical area was sterilized with Betadine followed by a single unilateral laparotomy. MS suspended in distilled water were divided into three aliquots 150, 115 and 200 µl and injected using a 25-gauge needle into three sites in the renal cortex. The cortical injection sites were assessed for hemorrhage 1 h and 24 h after injection using ultrasonography.

On day 16, the rats were *anesthetized* by intraperitoneal injection sodium pentobarbital (50 mg/kg body weight). The chest was opened and the blood was collected by cardiac puncture. The blood collected from the rats was separated by centrifugation at 3000 rpm for 15 minutes to obtain sera, which were stored at -80˚C for subsequent biochemical assays. The kidney was removed and immediately blotted using filter paper to remove traces of blood.

2.5. Kidney homogenate

Kidney was weighted and homogenized (10% w/v) in ice-cold 0.1 M Tris-HCl buffers (pH 7.4). The homogenate was centrifuged at 3000 rpm for 15 min. at 4 ^{o}C and the resultant supernatant was used for the biochemical assays.

2.6. Kidney function markers

The collected sera were used for determining creatinine [12], urea [13] and uric acid according to the manufacturer's instructions using Bio-diagnostic kits (Giza, Egypt).

2.7. Oxidative stress markers

The kidney homogenates was used for the measurement of oxidative markers according to the manufacturer's instructions using Bio diagnostic kits (Giza, Egypt). MDA level is an index of lipid peroxidation and it was estimated by colorimetric kit according to Ohkawa *et al* [14], reduced glutathione (GSH) was measured by colorimetric kit glutathione reduced [15] while catalase was estimated by kinetic Kit [16].

2.8. Statistical analysis

All data were expressed as means ± standard error of the mean (SEM). The comparisons within groups were evaluated utilizing one-way analysis of variance (ANOVA) with Duncan post hoc test was used to compare the group means and $p < 0.05$ was considered statistically significant. SPSS statistical software package for Windows (version 21.0) was used for the statistical analysis.

3. Results

As appeared from the Fig. 1 taken by TEM the formed silica particles are semispherical with very small porous with size around 350 nm.

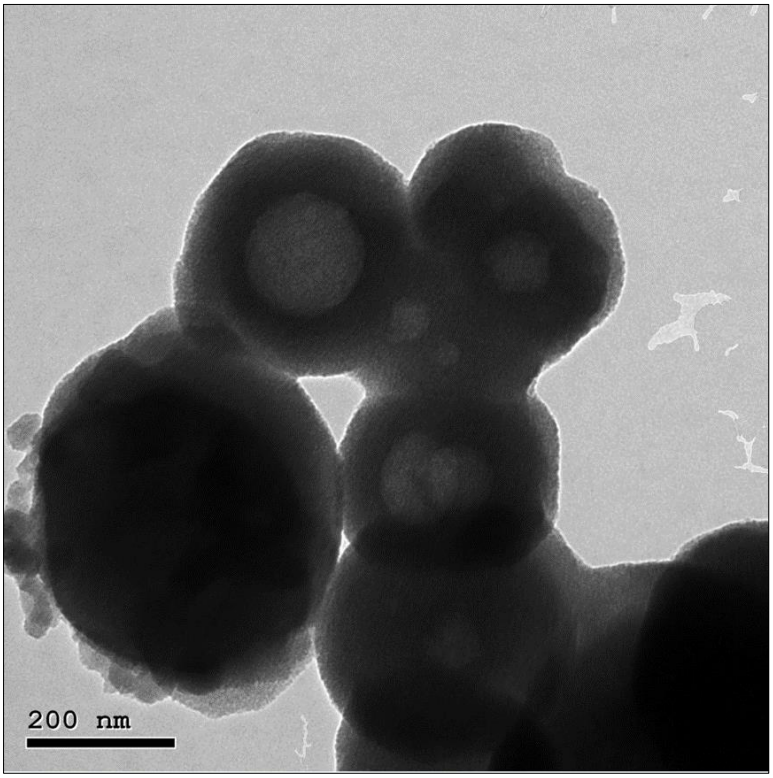

Figure 1 TEM micrographs of silica particles.

Gentamycin induced kidney dysfunction, which confirmed by the significant increase ($p< 0.05$) in urea, creatinine and uric acid (Table 1). While the treatment with MS reduced this elevation in kidney function parameters.

Table 1 Effect of MS on kidney parameters of GM-induced renal toxicity in rats.

Parameters	Control	GM	MS
Creatinine (mg/dL)	0.70 ± 0.03^{a}	1.31 ± 0.21^{c}	0.81 ± 0.03^{b}
Uric Acid (mg/dL)	1.57 ± 0.11^{a}	3.38 ± 0.65^{c}	2.11 ± 0.38^{b}
Urea (mg/dL)	26.35 ± 1.47^{a}	42.37 ± 1.25^{c}	34.82 ± 1.67^{b}

Values are mean ± SEM (n=6). Different letters indicate significant values (P<0.05) while same letters indicate non significant.GM: Gentamicin, MS: Mesoporous Silica.

Compare with the control group, GM caused a significant increase ($p< 0.05$) in tissues MDA concentration while GSH CAT levels decreased significantly. However MS treatment induced a significant increase in antioxidant markers (GSH, and CAT) and reduced lipid peroxidation marker (MDA) (Tables 2).

Table 2 Effect of MS on oxidative stress parameters of GM-induced renal toxicity in rats.

Parameters	Control	GM	MS
MDA (nmol/g. tissue)	3.31 ± 0.07^{a}	5.33 ± 0.44^{c}	4.47 ± 0.15^{b}
GSH (mg/ g. tissue)	24.93 ± 0.58^{c}	17.16 ± 0.46^{a}	19.39 ± 0.29^{b}
Catalase (U/min)	26.35 ± 1.15^{c}	12.92 ± 0.71^{a}	16.01 ± 0.49^{b}

Values are mean ± SEM (n=6). Different letters indicate significant values ($P<0.05$) while same letters indicate non significant.GM: Gentamicin, MS: Mesoporous Silica.

4. Discussion

Gentamycin accumulates in proximal renal convoluted tubules that lead to loss of its brush border integrity and activation of inflammatory processes, diminished glomerular filtration rate (GFR) and renal dysfunction [17,18]. The treatment with MS reduces renal toxicity as a result in form decrease creatinine, urea, and uric acid levels. MS has high efficiency for adsorption of urea [7] and creatinine [6] and extracts them with urine [9].

Gentamycin also acts as an iron chelator and the iron-GM complex is a potent catalyst of radical and reactive oxygen species (ROS) production [19]. Increase ROS leads to oxidative stress that results in elevation MDA and decreases GSH and CAT levels. MS treatment reduces MDA level and increase GSH and Cat which indicator for decrease oxidative stress condition and improve renal functions.

5. Conclusion

Intrarenal injection of silica mesoporous improve renal function in rats suffers from acute kidney injury.

Compliance with ethical standards

Acknowledgments

The authors extend their appreciation to the Faculty of Science, Cairo University for supporting the current work..

Disclosure of conflict of interest

No conflict of interest associated with this work.

Statement of ethical approval

Experimental protocols and procedures in this study were approved by the Cairo University, Faculty of Science, Institutional Animal Care and Use Committee (IACUC) (Egypt) (CU/I/F/52/18). All the experimental procedures were performed according to international guidelines for the care and use of laboratory animals.

References

[1] Zyada AMA, Mohammed HAK, Salah AAE, Elharrisi MAE, Halim SMA. Incidence and risk factors of acute kidney injury in trauma. Research and Opinion in Anesthesia & Intensive Care. 2019; 95-107.

[2] Ronco C, Bellomo R, Kellum JA. Acute kidney injury. Lancet. 2019; 394(10212): 1949-1964.

[3] Farokhzad OC, Langer R. Impact of nanotechnology on drug delivery. ACS Nano. 2009; 3(1): 16-20.

[4] Pu X, Li J, Li M, Wang H, Zong L, Yuan Q, Duan S. Mesoporous Silica Nanoparticles as a Prospective and Promising Approach for Drug Delivery and Biomedical Applications. Curr Cancer Drug Targets. 2019; 19(4): 285-295.

[5] Hoang Thi TT, Cao VD, Nguyen TNQ, Hoang DT, Ngo VC, Nguyen DH. Functionalized mesoporous silica nanoparticles and biomedical applications. Mater Sci Eng C Mater Biol Appl. 2019; 99: 631-656.

[6] Benbakhta G, Mokhtari M, Hamaizi H, Galera MM, García MDG. Extraction of creatinine by adsorption onto pure micro- and mesoporous silica materials. Journal of Biotech Research. 2017; 113-122.

[7] Cheah WK, Sim YL, Yeoh FY. Amine-functionalized mesoporous silica for urea adsorption. Mater. Chemi. Phys. 2016; 175: 151-157.

[8] He Q, Zhang Z, Gao F, Li Y, Shi J. In vivo Biodistribution and Urinary Excretion of Mesoporous Silica Nanoparticles: Effects of Particle Size and PEGylation. Small. 2011; 7(2): 271–280.

[9] Fu C, Liu T, Liu H, Chen D, Tang F. The absorption, distribution, excretion and toxicity of mesoporous silica nanoparticles in mice following different exposure routes. Biomaterials. 2013; 34(10): 2565-2575.

[10] Jabbari M, Rostami Z, Jenabi A, Zahedi-Shoolami L, Mooraki A. Simvastatin Ameliorates Gentamicin-Induced Renal Injury in Rats. Saudi J Kidney Dis Transpl. 2011; 22(6): 1181-1186.

[11] Quimby JM, Webb TL, Gibbons DS, Dow SW. Evaluation of intrarenal mesenchymal stem cell injection for treatment of chronic kidney disease in cats: A pilot study. Journal of Feline Medicine and Surgery. 2011; 13(6): 418-426.

[12] Schirmeister J. Determination of creatinine in serum. Dtsch Med Wschr. 1964; 89: 1940.

[13] Fawcett JK, Soctt JE. A RAPID AND PRECISE METHOD FOR THE DETERMINATION OF UREA. J Clin Pathol. 1960; 13: 156-159.

[14] Ohkawa H, Ohishi N, Yagi K. Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. Anal.Biochem. 1979; 95: 351-358.

[15] Beutler E, Duron O, Kelly MB. Improved method for the determination of blood glutathione. J. Lab. Clin. Med. 1963; 61: 882–888.

[16] Aebi H. Catalase in vitro. Methods enzymol. 1984; 105: 121-126.

[17] Martinez-Salgado C, López-Hernández FJ, Lopez-Novoa JM. Glomerular nephrotoxicity of aminoglycosides. Toxicol Appl Pharmacol. 2007; 223: 86-98.

[18] Lopez-Novoa JM, Quiros Y, Vicente L, Morales AI, Lopez-Hernandez FJ. New insights into the mechanism of aminoglycoside nephrotoxicity: an integrative point of view. Kidney Int. 2011; 79: 33–45.

[19] Chilwant KS, Muglikar AG. Effect of Honey on Gentamicin Induced Nephrotoxicity in Albino Rats. Int J Pharm Bio Sci. 2012; 3(1): 459-464.