شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم

بسم الله الرحمن الرحيم

MONA MAGHRABY

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جامعة عين شمس

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Chronic toxicity of silver nanoparticles on fertility of male rat and atrial for protection by using zinc oxide nanoparticles

Thesis presented by

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For master Degree in
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Approval Sheet

This thesis entitled **"Chronic toxicity of silver nanoparticles on fertility of male rat and atrial for protection by using zinc oxide nanoparticles"** prepared and submitted by **Asmaa Mohamed Shehata** in partial fulfillment of the requirements for **master degree** in **Toxicology and Forensic Medicine** has been examined and hereby recommended for approval and acceptance.

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Abstract

Silver nanoparticles (Ag-NPs) are among the most used nanoparticles. They are included in drug delivery, feed additives, wastewater purification, and many medical applications. Zinc nanoparticles (Zn-NPs) are known as strong antioxidants. This study was conducted to investigate the possible adverse effects of Ag-NPs especially, on the male reproductive system and liver and kidney function and the protective effect of Zn-NPs against these harmful effects. Forty adult male Sprague Dawley rats were used in this study. Animals were randomly divided into four equal groups and treated orally for 90 days as follows, group1: control, group2: received 50 mg/kg body weight of Ag-NPs, group3: received 30mg/kg body weight of Zn-NPs, group4: received Ag-NPs and Zn-NPs at previously mentioned doses.

The results revealed that the administration of Ag-NPs adversely affected male fertility as evidenced by a reduction in sperms concentration, motility, and viability percentages. Besides, sperms abnormalities were increased (coiled and curved tails, detached and deformed heads). Also, exposure to Ag-NPs lowered serum levels of testosterone, FSH, and LH. Additionally, the adverse effect of Ag-NPs on the liver and kidney were evidenced by increased serum ALT, AST, urea, and creatinine. Moreover, Ag-NPs induced DNA damage as showed in comet assay conducted in testicular tissues, and inflammation was observed in increased inflammatory cytokines in hepatic and renal tissues. Apoptosis was also observed in hepatic and renal tissues as a positive expression of caspase-3. Histological examination of testicular, renal, and hepatic tissues revealed inflammation, necrosis, and apoptosis. Furthermore, exposure to Ag-NPs resulted in oxidative stress and lipid peroxidation represented by decreased CAT and GSH and increased MDA in testicular, hepatic, and renal tissues. On the other hand, co-administration of Zn-NPs improved most of these adverse effects thanks to their antioxidant capacity.

Keywords: Ag-NPs, Zn-NPs, oxidative stress, apoptosis, inflammation, DNA damage, reproductive toxicity, liver function, kidney function.

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Asmaa Mohamed Shehata

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$AgNo_3$	Silver nitrate
Ag-NPs	Silver Nanoparticles
ALT	Alanine amino-transferase
ANOVA	Analysis of variance
AST	Aspartate amino-transferase
CAT	Catalase
DMSO	Dimethyl sulfoxide
DNA	Deoxyribonucleic acid
EDTA	Ethylene diamine tetra-acetic acid
ELISA	Enzyme linked immune-sorbant assay
FSH	Follicle stimulating hormone
GnRH	Gonadotropin releasing hormone
GOT	Glutamic oxalo-acetic trans-aminase
GPT	Glutamic pyruvic trans-aminase
GSH	Reduced glutathione
H&E	Haematoxylin and eosin
H_2O_2	Hydrogen peroxide
IFN-β	Interferon- β
IL	Interleukine
LH	Luteinizing hormone
LOAEL	Lowest observable adverse effect level
MDA	Malondialdehyde
NIH	National institute of health
NOAEL	Non observable adverse effect level
NPs	Nanoparticles
PVP	Poly vinyl pyrolidone
RBCs	Red blood cells
ROS	Reactive oxygen species

SD	Standard deviation
SH group	Thiol group
SOD	Superoxide dismutase
SPSS	Statistical package for social sciences
TEM	Transmission electron microscope
TGF-β	Transforming growth factor- β
TNF	Tumor necrosis factor
Zn-NPs	Zinc Nanoparticles

Chapter (1)

INTRODUCTION

<u>INTRODUCTION</u>

Nanoparticles have triggered researchers' interest in the previous few decades due to their widespread use in a variety of applications. Because of their unique physicochemical properties, nanoparticles can adversely affect different organs and tissues. These harmful effects are increased as particle size decreases. NPs may also react with proteins and enzymes within mammalian cells, causing the production of reactive oxygen species, activation of inflammation, and mitochondrial disturbance and damage, resulting in cell death. As a result, there are several issues to resolve before assessing if the advantages outweigh the costs **(Amanda *et al.*, 2010).** Concerning exposure to nanomaterials, they can be consumed through food and water or if used in cosmetics or as drugs. Nano-materials-containing products are available in the market and most of them are used orally **(Chen *et al.*, 2006).**

Silver nanoparticles (Ag-NPs) are among the most commonly used metal nanoparticles. They have been known for a wide range of applications including, chemical catalysts and antimicrobial agents. Ag-NPs act as bacteriostatic and bactericidal as well as fungi-static effects. Additionally, they are used in many feed additives and children's products. They are incorporated into medical products like bandages as well as textiles and household items **(Chen and Schluesener, 2008** and **Marambio and Hoek, 2010).**

Zinc nanoparticles (Zn-NPs) are very common nanoparticles. They showed effective adsorbing action for pesticides in a water system, and the amount of reduction is related to pesticide concentration **(Shahram *et al.*, 2014).** Besides, studies published by **Singh *et al.* (2014); Das *et al.* (2013)**, and **Tura *et al.* (2018)** stated that zinc nanoparticles showed antioxidant ability in many- body systems. Additionally, Zn-NPs are used as anticancer, anti-inflammatory, and antimicrobial agents. Moreover, they are known for their androgenic effects (**El-Maddawy and Abd El Naby, 2019)**.

There is little information about the adverse effect of silver nanoparticles after oral exposure, especially on the male reproductive system. Also, the liver and kidney are the principal organs of detoxification and excretion respectively. Therefore, this