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Toxipathological Effect of Silver Nanoparticles on The Brain and liver of Albino Rats

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Abstract : Silver nanoparticles have been used extensively in a range of medical setting due to antibacterial properties, Despite the wide used of silver Nps products ,relativity few undertaken to determine the biological effect of nanosilver exposure, the present study objective to investigate the effect of nanosilver on brain and liver, in *vivo* via intravenous injection of silver Nps dose 0.5 ml into rats. Ten female rats aged (9) weeks and weight (180-195) gm were divided equally into (2) groups n=5 , group I: rats served as control ,group II: rats serve as experimental ,after one month the rats were scarified for hitopathological samples ,the result were serve pathological lesion in brain and liver.
Keywords: Nanosilver, brain, liver, histopathological, rats, intravenous injection.

Introduction

Nanoparticles are increasingly used in many applications due to unique physical,chemical and biological properties in compared to bulk materials, silver Nps one of the most nanomaterial's used nowdays for many application in medicine due to strong activity anti bacteria and fungi[1],silver Nps used in both consumer and medical product. It has been used for treatment of burns and some diseases ,food ,drugs delivery devices ,cosmetics, filters, toys, shampoo and tooth paste ,daily exposure to silver Nps may be hazard to environment and human health, many of both in *vivo* and *vitro* studies have shown the negative effect of silver Nps to human health[2,3]. The long skin contact and inhalation of silver Nps may be increased risk of chronic diseases[4], the small size to volume ratio for nanoparticles can be undergo a series of hazard, by the small size nanoparticles can passing through the cellular membranes and interact with biomolecules with DNA and protein casing cell death then organ damage such as liver ,kidney failure or can cross the blood – brain to cause nerotoxity[5].

Despite of widespread application of silver Nps in medicine, there are rare information about the effect on human health and environment we have designed to investigate the negative impact of silver Npson brain of rat during wound healing.

Materials and methods

Silver nitrate ($AgNo_3$) ,was purchased from Reagent World , double –distilled deionized water ,tri sodium citrate.

Preparation of silver Npa:

Chemical reduction methods was used to synthesis Silver Nps by using tri sodium citrate as a reduction agent ,0.001 M of AgNo3 was heated to boil ,then 5 ml of 1 % tri sodium citrate was added to the solution drop by drop ,the solution were heated and mixed until color changed (clear yellow) ,then it removed from heat device and it was stirred until cooled to the room temperature.

Animals and conditions:

A group of (10) Adult albino female rats with average weight of (180-195) g were obtained fromanimal house of Veterinary medicine college / Al-Qasim green university ,the animals were kept at 25 C and fedsstandard diets and filtered water .

Experimental design :

Ten female rats (10) weeks were divided in to equally two groups (n=5).

Group I/ rats served as control, injected 0.5 ml/rat normal saline for one month.

Group II / rats served as experimental and injected 0.5 ml/rat silver Nps for one month.

Histopathological study:

At the end of the experiment ,the rats sacrificed and the brain, liver tissues were separated , the tissues were fixed into 10% formaldehyde solution in order to conduct histopathalogy experiment ,histological section were prepared from brain and liver then examined under light microscope.

Statical analysis :

The data were analyzed one way analysis of variance (ANOVA) to test the data.

Results:

Characterization techniques :

Chemical reduction method has been used in this study for synthesis silver Nps,from fig. (1) ,the colorless solution turned to clear yellow which indicated the formation of silver Npa .

Fig. (1): color of silver Nps solution

UV – Vis spectroscopy :

Uv-vis spectroscopy was used to determine the surface Plasmon resonance (SPR) bands ,,from fig. (2) the SPR bands detected around 430 nm, previous studies shown that the spherical shape of silver Nps

contributed to the absorption bands around 400 nm (*Stamplecoskis K. 2010*), SPR 430 nm strongly suggests that silver Nps were spherical in shape and have been confined by SEM fig .(3)

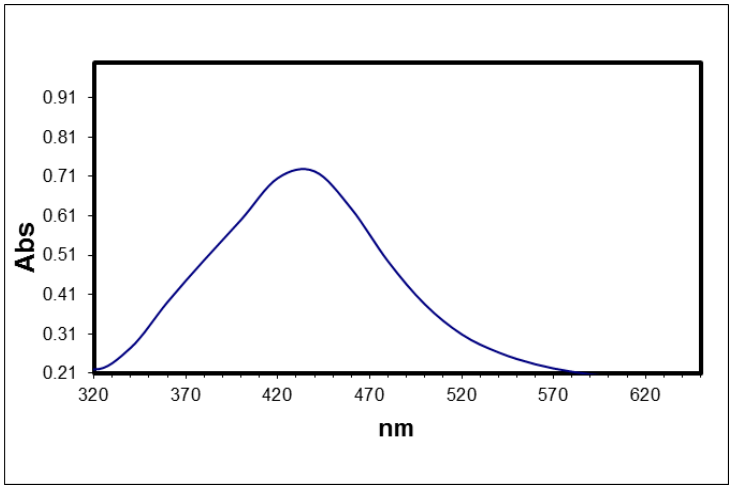

Fig.(2) : Absorbance band of silver Nps

Scanning Electron Microscope (SEM):

Size and morphology of silver Nps were studied by Scanning electron microscope ,the nanoparticles are spherical in shape ,the structure of Nano silver distributed uniformly with range diameter (55-90.5)

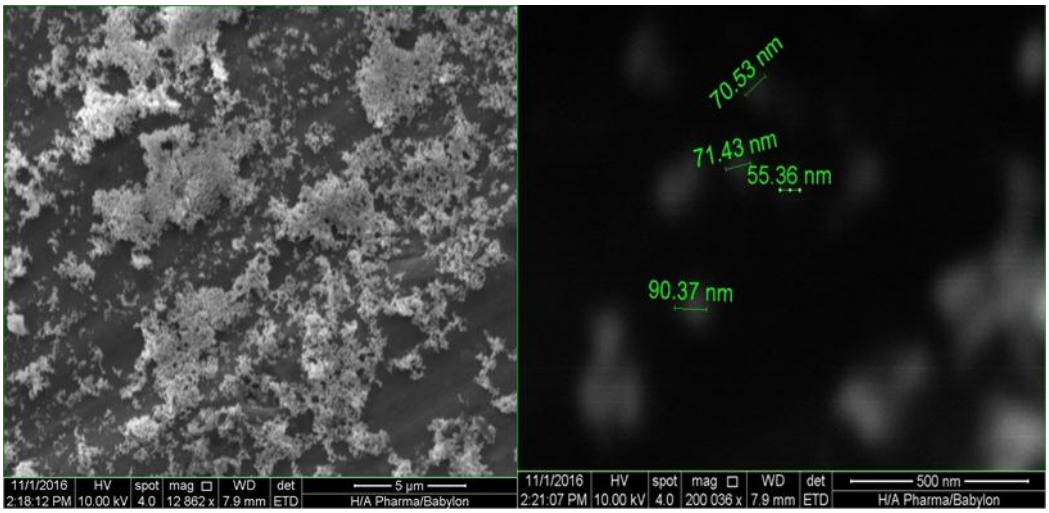

Fig.(3): Scanning Electron Microscope (SEM) of Silver Nps

Histopathologicalstudy :

Control groups : show normal histological structures as in fig.(4)

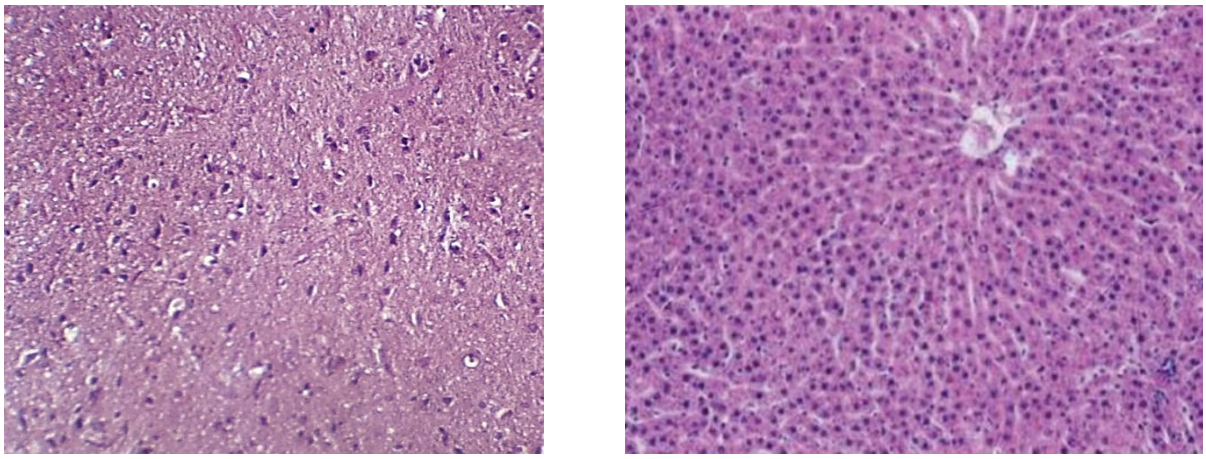

Fig.(4):Histopathological section of brain(A) and liver (B) of rats for control groups showing normal histological structures H&E (400X)

Treated groups :

Brain : The brain show distraction in brain tissue with edema and vacoulation around the neuronal cells and increasing in the number of red neuron fig (5).

Liver : the liver show centrilobular necrosis sever congestion in central veins with vacoulations was also seen fig.(6).

(A) **(B)**

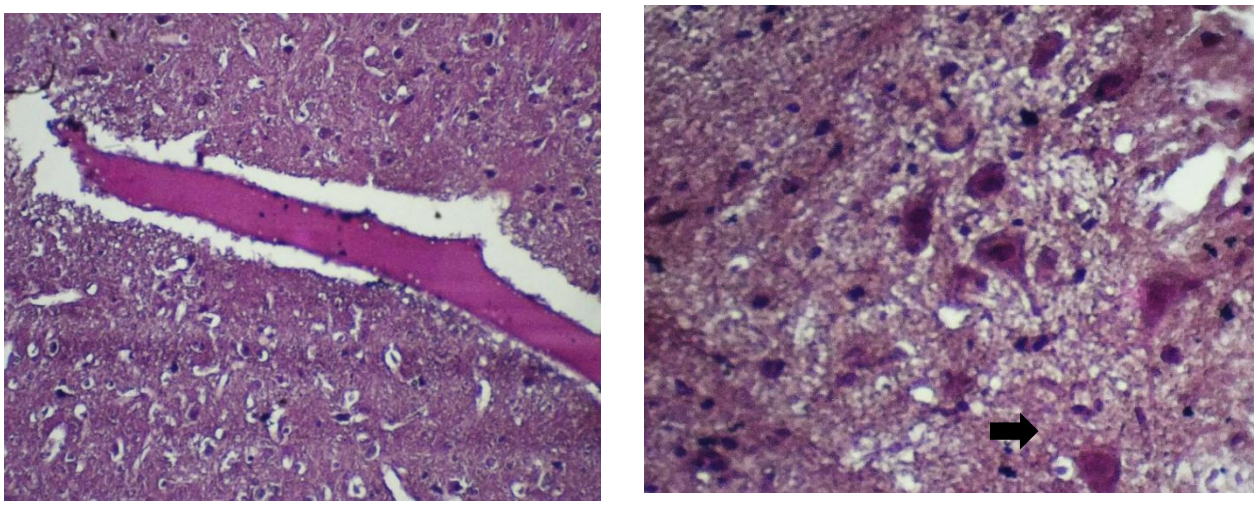

Fig (5):Morphological and pathological changes in section of brain for female rats treated with silver Nps for one month

A: Histopathological section of brain of rats treated with silver Nps for one month showing distraction in brain tissue with edema(⟶) and vacoulation around the neuronal cells (➡)H&E (400X).

B:Histopathological section of brain of rats treated with silver Nps for one month showing increasing in the number of red neuron (⟶) H&E (400X).

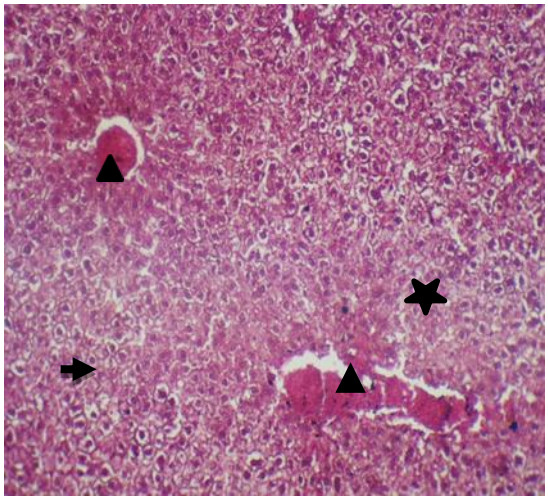

Fig.(6):Morphological and pathological changes in section of liver for female rats treated with silver Nps for one month showing centrilobular necrosis, (★) congestion (▲)and vacoulation (➔) H&E (400X).

Discussion :

At present: silver Nps are widely used in medicine and drug delivery device due to antibacterial properties[1] resulting an increased in human exposure, however the knowledge of the systemic toxicity of nano silver is relativity limited .

Silver nanoparticles are known to be distributed in many tissues after injection. Thus, understanding the tissue clearance of such distributed nanoparticles is very important to understand the behavior of silver nanoparticles in *vivo*. For risk assessment purposes, easy clearance indicates a lower overall cumulative toxicity. Accordingly, to investigate the clearance of tissue silver concentrations following oral silver nanoparticle.

The objective of this study is to evaluate the silver clearance from tissues following the cessation of silver nanoparticle administration. Exposure, the present study clearly showed that Ag-NPs used for injection in adult rats can dependent manner. Section of brain and liver of rats for control groups showing normal histological structures in fig.(4) while fig.(5&6) showing Histopathological section of brain and liver of rats treated with silver Nps for one month showing distraction in brain tissue with edema and vacoulation around the neuronal cells and increasing in the number of red neuron**.**The liver showed centrilobular necrosis with congestion of central vein that demonstrated the liver is the primary target organ for silver Nps toxicity

It is well known that silver ion and silver-based compound are highly toxic effects on the mammalian cells. Due to small size of nanoparticles It could move into the circulatory system by traversing the blood-brain barrier and, thus, distribute the whole body[6]. Therefore, this nanoparticle can affect organs such as heart, Brain, lung and others. In this organ, nanoparticles cause diseases such as cardiovascular disease, pulmonary inflammation, and neural degeneration[7]. The veins injectedsilver Npshas a short circulation time and a broad tissue distribution *in vivo*.

Cytotoxicity is a direct outcome due to oxidation stress caused by silver NPs and release of Ag ions. Silver NPs and silver ions may evoke lipid peroxide and increase the permeation of cell membrane systems.

This study agree with many Studies have shown that nanoparticles may change or damage cellular processes by passing through cellular membranes due to small size and interact with biomolecules leading to DNA and protein damage[5,8] or cross the blood-brain barrier to cause neurotoxicity[9].There are considerable evidences that silver NPs can disrupt the Blood-Brain Barrier (BBB) and induce subsequent brain edema formation. Therefore, it is essential to understand the differential effects of silver NPs on brain cell with especial emphasis on the possible mechanisms of action. An infiltration of the brain with xenobiotics, such as silver NPs, may also lead to inflammation of brain tissues. One study in 2010 has demonstrated that Ag-NPs

accumulate with primary rat brain microvessel endothelial cells (rBMEC) in a size-dependent manner and induce the release of cytokines and other inflammatory me diator s from the r BMEC cell monolayers[10]for the silver Npstoxicity is still question whether the toxity is due to the release of ions or due to nanoparticle themselves? The total toxicity could be described to both of the cytotoxity of silver Npa and ion content[11,12].

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