Original Article

Zahedan Journal of Research in Medical Sciences

Journal homepage: www.zjrms.ir

Comparing Poisonous Effects of Thioacetamide and Silver Nanoparticles on Enzymic Changes and Liver Tissue in Mice

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Article information

Article history:
Received: 13 Dec 2012
Accepted: 17 Feb 2013
Available online: 12 Mar 2013
ZJRMS 2014; 16(2): 54-57

Keywords:
Thioacetamide
Silver nanoparticles
SGOT
SGPT
Liver damage

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Abstract

***Background*:** Nanoparticles are small particles which can destroy many diseases resulting from microorganisms. Due to very small size, these particles can penetrate various tissues easily like liver and many side effects. This study has compared poisonous effects of thioacetamide with silver nanoparticles on amino transferase enzymes and liver tissue in male mice.

***Materials and Methods*:** In this study, mice were divided to four groups. First group or control was received food and water, second group received thioacetamide 50 mg/kg, third group received 3000 ppm silver nanoparticles and fourth group received a compound of silver nanoparticles 3000 ppm and thioacetamide (50 mg/kg). Then, blood from mice hearts was collected and liver tissue was separated for measuring, SGPT and SGOT enzymes, and also for tissue studies.

***Results*:** Injection thioacetamide increased SGOT and SGPT enzymes in second group more significantly than group. However, nanosilver injection only increased SGPT enzyme significantly (p=0.02).

***Conclusion*:** According to the results of this study, silver nanoparticles and thioacetamide can damage liver cells. But destruction of hepatocytes resulting from oxidative pressure of combination silver nanoparticles and thioacetamide was more than the other groups.

Introduction

Recently, various substances have emerged with size less than 100 nanometers which are called nanoparticles. While a microscopic substances change to nanoparticles size. Their chemical and physical features are changed in comparison with their initial state [1].

Silver is a white and shining element which can destroy 650 diseases resulting from microorganisms [2]. Nowadays, silver has been created as particles with size of 10–100 nanometers which are called silver nanoparticles or nanosilver [3]. Silver nanoparticles have important features such as: high resistance, much effect in short time, stability against temperature (heat) and lack of compatibility in microorganism [4].

Applying antimicrobial effects of silver has been usual in different societies during many years. But today Research has demonstrated its effect on disinfecting and removing microbes [3, 5]. Silver nanoparticles influence on metabolism and bacteria reproduction. Also, they penetrate respiratory system of bacteria and control this system [5]. These antibacterial effects of nanosilver are because of some biological events such as: linking to cells membrane, superficial absorption, negative charge of bacterium in cell wall, changes of membranous permeability, creating oxidative stress and inactivation of cell enzymes [6]. So, these effects have negative effects on the health and environment and cause poisonous properties of nanosilver. Silver nanoparticles are able to remove much kind of bacteria, viruses and fungi. Therefore, they can be used for treatment of specific virus diseases in animals. Although, like the other drugs, they can have side effects especially for liver tissue. On the other hand, absorbed nutrients by digestion system have been processed in the liver and stored for using in the other parts of body, so liver is an organ between circulation and digestion system. Also, drugs which enter the body can be metabolized in the liver and then they pass from kidneys. Therefore, liver is damaged more than tissues during using special drugs with side effects [6].

Recently it has been reported nanoparticles and nanomaterials make free radicals with oxidation pressure. According to results of different studies, silver nanopartides can damage different organs especially liver tissues [6, 7].

Thioacetamide is a powerful hepatic poison which acts as many materials like acetaminophen, some antibiotics, and ethanol and tetrachloride carbon. It is metabolized by enzymes of toxin destruction system (cytochrome P-450) [8, 9]. Thioacetamide metabolism results in production of thioacetamide s-oxide, oxide and other metabolites [10, 11]. So, thioacetamide oxide is a medium compound in oxidation stages of thioacetamide by mono oxigenases whit mixed operation (such as cytochrome P-4502B1) which causes oxidative stress in liver cells [12, 13]. Studies have been shown that thioacetamide causes cell death, necrosis and apoptosis in liver cells [14].

Liver damage causes by thioacetamide shows liver toxicity resulting from xenobiotics, which it is used as a suitable model for studying effects of anti toxicity or protective effects in drugs and different compounds [15, 16].

Serum glutamic oxaloacetic transaminases (SGOT) and serum glutamic pyruvic transaminase (SGPT) are two amino transferase enzymes which play key role for identifying liver function. Concentrations of these two enzymes increase significantly in the blood plasma by liver damage. So, evaluating changes of these enzymes can provide useful information about the dim of this study in comparison of SGPT and SGOT levels and tissue changes in liver of male mice by doing bio chemical tests and microscopic studies on tissues for comparing toxic effects of silver nanoparticles and thio acetamide in liver and the manner of their influence on liver, simultaneously. Since thioacetamide has toxic effects on liver, it has been considered as a positive sample in this study [17].

Materials and Methods

Laboratory animals: In this study, male mouse with the weight of 28–30 gr was used, these mice were prepared from Islamic Azad University of Shahr-e-Kord district, they were kept in animal house with standard conditions (12 hour darkness, 12 hour lightness, temperature of 25ºC and suitable humidity). Animals were fed by standard food without limitation.

Animals' treatment: The mice were divided to four groups (8 mice in each group) randomly. And each group was kept in separate cage. First group as control group just received water and food. Second group received thioacetamide (with dose of 50 mg/kg) as intraperitoneum in 3 successive days. Third group received a solution from nanosilver every other day as 20 intraperitoneum injections with dose of 3000 ppm [18]. Fourth group received nanosilver with the above dose as 20 intraperitoneum injections every other day and then they received 3 injections of thioacetamide with dose of 50 mg/kg in there successive days. After wands, mice were anaesthetized by chloroform and blood sampling was done from heart of mice. Blood was collected in laboratory tubes carefully and kept for 45 minutes in the laboratory temperature. After coagulating the blood, serum was separated by centrifuge. For evaluating and comparing liver function in various groups, serum transaminases including SGPT and SGOT were measured by auto analyzer BT3000.

Histology studies: After blood-sampling from mice, their livers were separated carefully. Then the samples were fixed and kept in solution of 10% formalin .Then stained by hematoxilin and eosin for histological studies.

Data analysis: SPSS-15 software was used for data analysis. After applying one way variance analysis ANOVA and LSD tests were used for studying significance or insignificance of differences. Significance of means difference was studied at the level of p=0.02, p=0.05.

Results

Results obtained from measuring SGPT and SGOT enzymes show that mean of SGOT enzymes was 128.66±5.1, 262±26.4, 138.33±333.9, 265.2±37.1 U/L in first, second, third and fourth groups, respectively (Fig.1). Also, SGPT mean in the above groups has been 41.7±6.7, 64±714.1, 51.7±15 and 75.2±2.8 U/L, respectively (Fig. 2).

Comparing mean of SGOT and SGPT enzymes by LSD test shows that level of these enzymes in those groups receiving thioacetamide or thioacetamide and nanosilver has changed more significantly than the control (p=0.02).

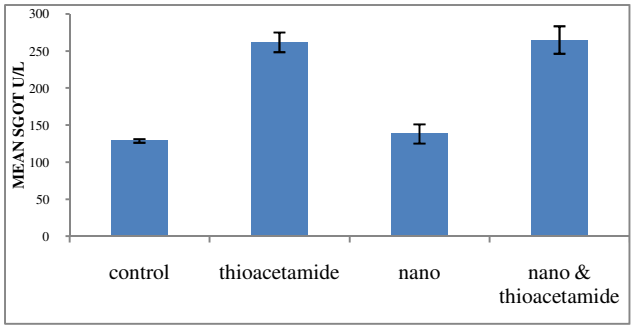

Figure 1. Comparing mean of SGOT enzyme activity in different groups

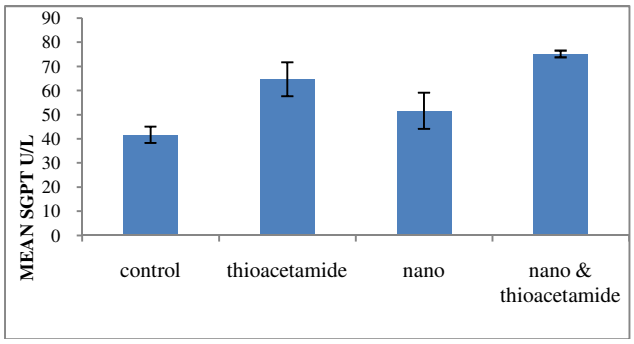

Figure 2. Comparing mean of SGPT enzyme activity in different groups

Histology results: Microscopic studies of slices from group receiving thioacetamide show vacuolar degeneration or white and void vacuoles inside the hepatocytes cytoplasm and hepatocytes damage were considered very much in these tissues (Fig. 4). These changes were observed in tissues of group receiving silver nanoparticles, as well (Fig. 5). But more liver damage was observed in slices from treated groups with silver nanoparticles and thioacetamide, so that hepatocytes necrosis was more than group receiving thioacetamide. Vascular degeneration was more than the other 3 groups and the cells were disordered and seen disorderly. In this group, a collection of inflammatory cells was seen in the portal space and around central vein. Generally, observed losses in this group were more than the second group (Fig. 6, 7).

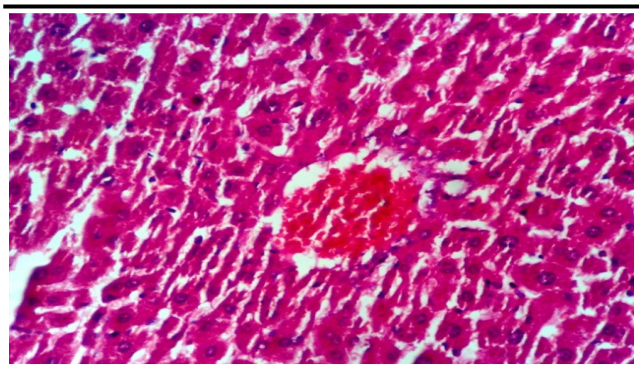

Figure 3. Liver tissue in control group shows normal tissue of liver

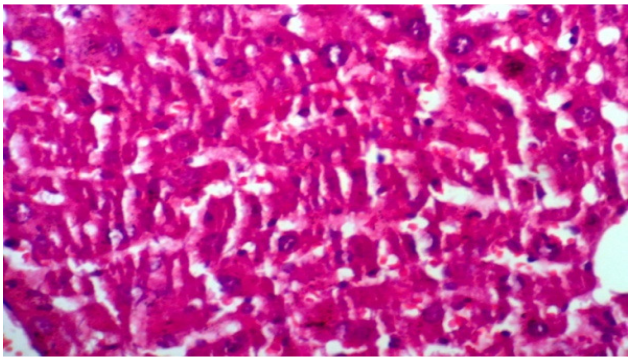

Figure 4. Liver tissue in group receiving thioacetamide. Arrangment of normal cells in this group has been disturbed and vacuolar degeneration is observable in the hepatocytes

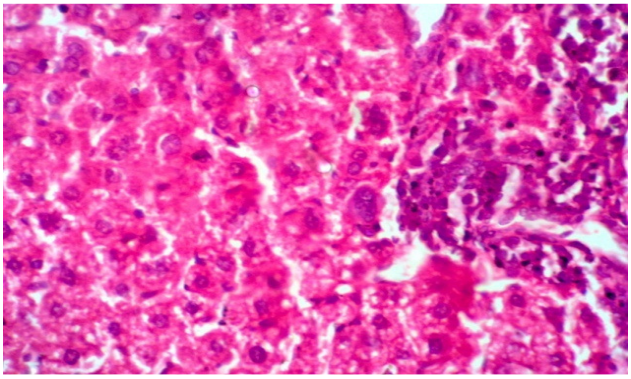

Figure 5. Liver tissue in group receiving nanosilver shows hepatocytes necrosis and vacuolar degeneration in the cells

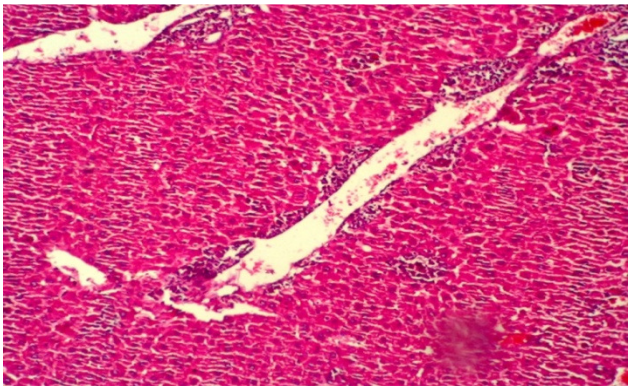

Figure 6. Liver tissue in group receiving silver nanoparticles and thioacetamide shows a collection of inflammatory cells in the portal space around central vein

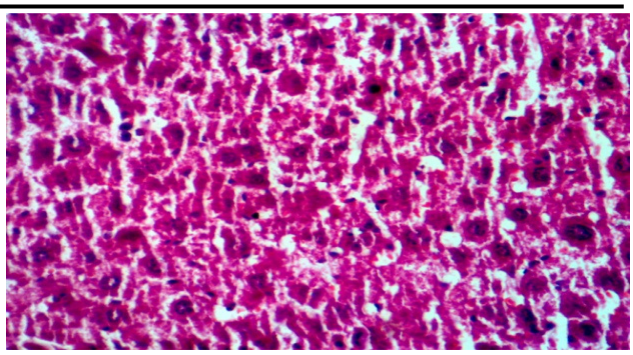

Figure 7. Liver tissue in group receiving silver nanoparticles and thioacetamide shows the most damage in appearance of cells and disorder in cells arrangement vacuolar degeneration is more than the other groups, and hepatocytes necrosis is more severe than the other groups

Discussion

Results obtained from this study show that SGOT and SGPT enzymes in three treated groups have increased in compare with the control group. Since these enzymes are in liver cells in normal conditions, when the cell damage and they go into the serum, we can conclude that thioacetamide and silver nanoparticles can damage liver cells [19]. Moudgi et al. showed that nanoparticles effects on cells of living beings depend on diameter, size and shape of particles [5].

In this study, spheral silver nanoparticles in the 3000 ppm concentration influenced on liver tissue destructively. On the other hand, thioacetamide damaged liver cells and caused necrosis in these cells. Also, with regard thioacetamide caused severe damage of tissue in this group. So, we can conclude that these two materials have synergistic effect on the liver cells and cause more damage to these cells.

Silver nanoparticles have more contact area with outer space due to their small size and have more effect on cell membranes [20]. Silver nanoparticles damage respiratory system of microorganisms for encountering so they disturb their metabolism and prevent their growth [20].

Absorbed nanosilver link to plasma proteins in some organs such as liver, destroy it or damage mitochondria and reduce glutathione level [6, 22].

Troup et al. showed that absorbed nanosilver from stomach duct enter the portal vein, then enter liver and influence on liver cells. In addition, they concluded that liver can collect some compounds from the blood actively and chemical forms for excretion. These particles can be observed in urine clearly [23].

In another study by Xia and Hussain, toxicity of silver nanoparticles in liver cell of mouse was studied results showed that mitochondria have abnormal size in the liver tissue. Cell cleavages and their irregular shape were observed, too [21, 24].

In conclusion, with regard to different studies in this domain and available documents, one can conclude that silver nanoparticles can release free radicals and reactive oxygen (Ros); excessive accumulation of Ros, can trigger inflammatory responses and destroy mitochondria. GSH

level reduces due to this inflammation; therefore, Apoptogenic factors (like cytochrome c) are released and cell death occurs.

With regards to vast applications of silver nanoparticles in our country and lack of enough information about exact physiological mechanism of these nanoparticles on the liver, researches must be done for find toxic dose of silver nanoparticles based on the change of their shape.

Acknowledgements

The efforts of all staff of research laboratory of Islamic Azad University of Shahr-e-Kord, will be highly appreciated.

Authors' Contributions

All authors had equal role in design, work, statistical analysis and manuscript writing.

Conflict of Interest

The authors declare no conflict of interest.

Funding/Support

Islamic Azad University, Felavarjan District.

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Please cite this article as: Zamani N, Naghsh N, Fathpour H. Comparing poisonous effects of thioacetamide and silver nanoparticles on enzymic changes and liver tissue in mice. Zahedan J Res Med Sci (ZJRMS) 2014; 16(2): 54-57.