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Research Article

Comparing the effects of silver nanoparticles as well as Roaccutane on lipids and plasma lipoprotein of Wistar male rats

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ABSTRACT

Silver nanoparticles are known as valuable products of nanotechnology which has wide applications, especially in medical sciences. For example, the medical uses of silver nanoparticles include their incorporation into wound dressing, supplying surgical tools and bone as well as dental prostheses. Silver nanoparticles are able to enter cell nucleus, cause DNA damage, inhibit cellular processes, and consequently lead to the formation of mutant cells. Moreover, accutane is an oral drug primarily applied to treat severe acne and it is also used to prevent certain skin cancers. On the other hand, nanoparticles can cause cardiac necrosis.Therefore, this study was done to assess the association of silver nanoparticles and roaccutane with lipids, and lipoproteins. The data for the current study came from 7 treatment groups included: three groups treated with nanosilver particles at concentrations of 250 ppm, 500 ppm, and 1000 ppm, three groups treated with roaccutane at concentrations of 13.6 mg/kg, 26.6 mg/kg, and 53.3 mg/kg, and the seventh group received both roaccutane and silver nanoparticles.The other two groups received solvent (edible oil) and the control group was under natural condition and received food and water. At the end of the experiment, the level of lipids and lipoproteins were measured.The results showed no significant difference between the concentration means of lipids in any of the treatments ($p < 0.05$); however, significant differences were found between combination group and treatment groups ($p < 0.00$).As a result, treatments and Accutane and silver nanoparticles were toxic at the used concentrations, for biological systems.

Keywords: Lipids, Roaccutane, Silver Nanoparticles

INTRODUCTION

Recently, nanostructures have a braod application in different sciences such as medicine, africulture, pharamcology and etc [1-6]. Silver nanoparticles are known as valuable products of nanotechnology which has wide applications in medical sciences. For example, the medical uses of silver nanoparticles include their incorporation into wound dressing, supplying surgical tools and bone as well as dental prostheses. Industrial applications of silver nanoparticles are as follows : antimicrobial and anti-odor fibers, use in medicine, wound treating and healing, in hygiene products such as soap, toothpaste, toothbrush, in the production of household appliances such as refrigerators, washing machines, packing food, plastic containers, and its use in agriculture [7-9]. Along with all the useful mentioned applications of this nanoparticle, the toxicity of silver nanoparticles such as anemia, induced sarcoma, and enlargement of cardiac is a major concern [10-12]. Today, the possible side effects of silver nanoparticles on workers and consumers who are

exposed to these products have attracted the attention of the public and scientists [5, 6,13,14]. Therefore, the assessment of the potential risks of silver nanoparticles, especially their impact on biological systems, can facilitate the design of safer and more effective antimicrobial products in future [15, 16]. Silver nanoparticles are increasingly used in various products in which the release of silver nanoparticles can pollute the environment and harm wildlife [17]. Accutane is a drug for the treatment of severe acne. This drug can prevent certain skin cancers as well as cancers of brain, pancreas, and etc. This drug is available in capsules for oral administration and marketed with the brand names of roaccutane and accutane. Isotretinoin is a natural vitamin A derivative and is found in small quantities naturally in the body. Serious complications of accutane include fetal malformations, depressed mood, difficulty concentrating, hallucinations, sudden severe headache, severe pain in the upper abdomen, increased cardiac rate, and vision as well as hearing problems. Less serious side effects of accutane include feeling dizziness, joint pain, dry lips, mouth, and nose, skin cracking, itching, rash, and changes in the nails of hands and feet [18, 19]. Since roaccutane is prescribed for the treatment of severe acne during a period of treatment, it can have wide side effects on different organs including lungs, spleen, testes, cardiac, and liver. It will even cause fetal malformations and dry eye [20]. The medical use of roaccutane and silver nanoparticles on the one hand and lack of precise investigation about thier effects on lipids, and lipoproteins on the ther hand, this study attempted to compare the effects of silver nanoparticles with roaccutane at different concentrations on male Wistar rats.

MATERIALS AND METHOD

This study was conducted on 54 male Wistar rats. The study subjects (rats) were collected and kept in accordance with Institute of National Animals Health laboratory and all the ethics of working with animals were observed in all stages of the experiment. Before the experiment, all the animals were weighed and the weight range of them was 225 ± 25 g. The subjects were randomly divided into 9 groups including 6 rats in each group: Group 1, 2, and 3 received 13/6, 26/6, and 53/3 mg / kg roaccutane, respectively. Group 4, 5, and 6 received 1000, 500, and received 250 ppm nanosilver. Combined group (group 7) received a capsule of roaccutane and nanosilver at the concentration of 250 ppm. Group 8 received 0.5 ml of oil and Control group received no treatment and were under natural condition. Considering body weight, the dose of roaccutane and silver nanoparticles were administered. The weights of rats were measured on the first and last day of the experiment. At the end of the treatment period, Blood samples were taken for the measurements of blood glucose, triglycerides, LDL, and HDL. In order to measure all aforementioned factors, Pars Azmoon laboratory kit was used.

Data Analysis

All data analysis was done by SPSS software (version 22).

RESULTS

Comparing the mean of cholesterol plasma concentration

The concentration of cholesterol in the blood samples was shown in tests. The results showed the lowest level of plasma cholesterol in roaccutane group (53.3 mg / kg) that was 44/4 ± 4/44 and the highest level of plasma cholesterol in the combination group (128.8 ± 17/ 73). The combination group had a statistically significant increase of 54.60 ± 16/69 compared to the control group.According to the results, the combination group had a significant difference with other groups in terms of cholesterol concentration (Figure 1).

Comparing the mean of HDL plasma concentration

The concentration of HDL in the blood samples are demonstrated in Figures of 2. The results showed the highest concentration of plasma HDL in the 1000 ppm group (32.6± 2/79 ng / ml) and

the lowest concentration in the combination group (12±5/7).

Comparing the mean of LDL plasma concentration

According to the results, combination group allocated the highest plasma LDL level to itself (28.± 5.94 ng/ml); at the opposite, there was the control group (12 ± 1 ng/ml). The result of this section for all concentrations was summarized Figure 3.

Comparing the mean of TG plasma concentration

Maximum plasma TG level was seen in the combination group (339.8±24/03 ng/ml) and minimum plasma TG level was observed in the control group (41.4 ± 5/02 ng/ml). the data of all groups was shown in Figure 4.

DISCUSSION

As it is clear from Tukey test (analysis of variance), the only significant difference among group means was observed in the groups treated with 500 ppm of silver nanoparticles, 53/3 mg / kg, and 26/6 mg / kg of roaccutane. Although, differences were observed in other groups, they were not statistically significant. Moreover, the combined treatment (nanoparticles and roaccutane combination) had a synergistic effect on reducing the concentration of HDL in treatment. This negative synergistic effect was approximately 200% (2 times) compared to single treatments.

The results regarding LDL level revealed that the lowest and highest levels of LDL were seen in untreated and treated groups, respectively.Based on Tukey test (analysis of variance), a significant difference was found comparing the combination group with other groups. On the other hand, roaccutane along with silver nanoparticles exacerbate these effects.In the combination group (containing both roaccutane and silver nanoparticles treatments), a great difference was found in terms of TG concentration.

This means that combination group had most TG concentration comparing other groups.The combined treatment group was significantly able to alter concentration of TG in the blood. This significant change can be definitely attributed to oxidative potential tension of silver nanoparticles that was intensified by the presence of roaccutane. This argument that nanoparticles damage tissue was also supported in the current study since silver nanoparticles could damage cells,and connective tissue. Thus silver nanoparticles were recognized harmful for living organisms (tissue) and their extensive use in biological systems should be prevented. Nanoparticles can bind to cells and also to macromolecules such as proteins and DNA [21], lead to the activation of the cell signaling processes, produce reactive oxygen species and inflammation, and consequently stop cell cycle and lead to cell [22].Silver nanoparticles caused Apoptosis and / or necrosis [12, 23]. In another study [24] about the assessment of triglyceride level in the rats, it was revealed that dose significantly lowered blood triglyceride levels. These results demonstrated the reduction of TG levels in the injection control group; however, it is incompatible compared to control group.The level of cholesterol in the combination groups had highest concentration compared to other groups. The average of cholesterol in the control groups was lower than treatment groups' average. Moreover, it was found that combination treatment of nanoparticles and had the synergistic effect on increasing the concentration of cholesterol.

According to researchs, the effects of silver treatment on the body reported as silver anemia, induced sarcoma, enlargement of cardiac, a dose-dependent toxicity in the fetus [25-28]. In the current study, changes in the concentration of triglycerides, cholesterol, and LDL and HDL, their production and processing directly related to cellular enzymes, can be due to inactivation of cell metabolism enzymes in line with previous reported studies [11, 29]. Based on research conducted by Sikka et al [30] and Warren et al [31], silver nanoparticles lead to premature death of cells and also lead to oxidative effects which eventually is associated with the normal function

of the cells. These results were also consistent with this study. Silver nanoparticles can be introduced as potential oxidative stressors which are able to damage cells at high concentration. In a research done by Soriano et al [32], in patients treated with isotretinoin, the increase in the concentration of fat, triglycerides, and liver enzymes have been reported. Therefore, it can be concluded that roaccutane can increase triglyceride and fat levels. At this experiment, the effects of increased LDL were also observed in roaccutane and silver nanoparticles treatment groups.

Therefore, this harmful function of each roaccutane and silver nanoparticles can be considered as a proportion of LDL increase. All the results reported from other studies and current research present evidence that silver nanoparticles enter to tissue and bring about damaging consequences. The silver nanoparticles can be described as potential oxidative stressors that can damage cells in high concentrations. The results observed from this study were consistent with Ahamed et al [22], and Razavian et al [24].

They reported that silver nanoparticles accumulate in various tissues of mammals and lead to cell damage. According to this study, almost all of the treatments brought about changes in the concentration of plasma lipids and lipoproteins. Furthermore, it was seen that the observed damage and destruction in cells was non-negligible. Based on the results of the present study, both silver nanoparticles and roaccutane in used concentrations had side effects such as changes in plasma lipids and lipoproteins, and in general had the ability to interfere with biological systems.

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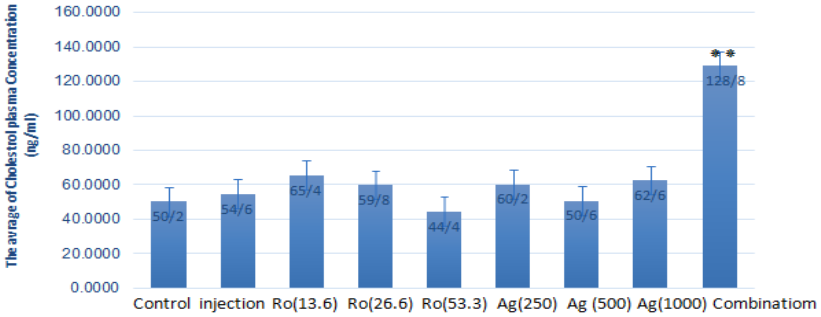

Figure1. The comparison of Cholestrole levels in control and treatment groups

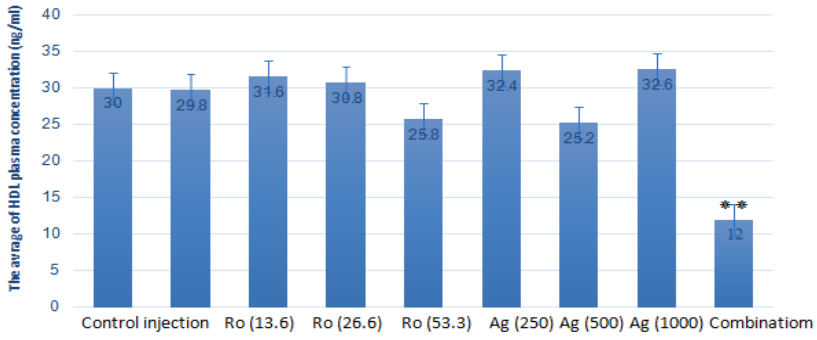

Figure2. The comparison of HDL levels in control and treatment groups

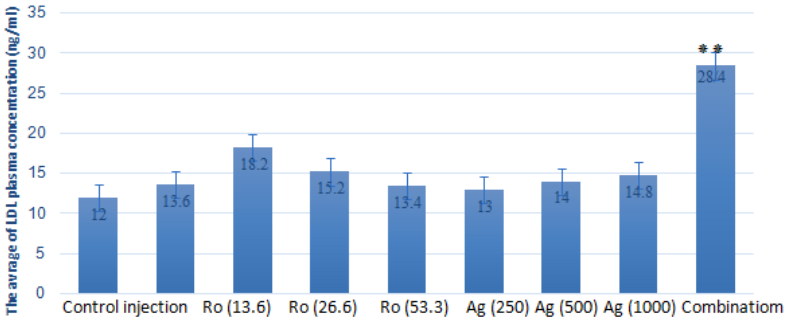

Figure 3. The comparison of LDL levels in control and treatment groups

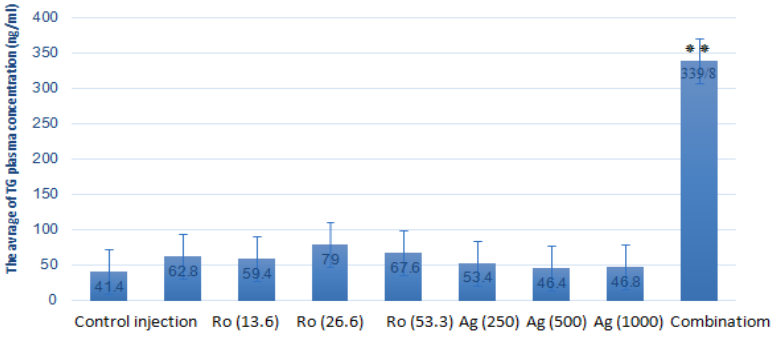

Figure 4. The comparison of TG levels in control and treatment groups