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Research Article

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The effects of titanium dioxide nanoparticles on liver histology in mice

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ABSTRACT

Liver is one the vital organs and is involved in the regulation of many physiological activities. Any abnormal liver function creates a set of disorders that can cause irreparable damage to this organ. The goal of this study was investigating the effects of titanium dioxide nanoparticles on liver histology of little laboratory mice. Forty mice were divided into four groups: control group did not receive anything, placebo group, and two experimental groups which received 10 and 100ppm of nanoparticles via gavage. At the end of period liver was colored using hematoxylin eosin method and studied using light microscopy. Obtained data were analyzed using SPSS software. According to results, both 10 ppm and 100 ppm groups caused significant liver pathological which changes were in necrosis form in 100 ppm group. Results showed dose dependent toxicity of titanium oxide nanoparticles.

Keywords: titanium dioxide, nanoparticles, liver tissue, mice

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INTRODUCTION

Liver as the largest gland of body can be considered as a chemical factory which makes, stores, alters and releases a large number of substances involved in metabolism [1]. It may have up to 100 various tasks which most of them are done by hepatocytes. Also, every of liver cells not only produce exocrine bile but also are in charge of endocrine secretions. Liver cells are probably the most skilled body cells [2]. Different liver tasks are blood filtration and storing, metabolism of carbohydrates, fats, foreign chemicals, and hormones and storing vitamins and iron, making bile and the clotting factors [1].

Although liver is a vital organ factors such as oxidative stress, free radicals, chemical matters, white alcohol, viruses, bacteria and drugs can damage liver tissue [3]. Nanotechnology is the newest technology which provides many opportunities for producing new tools and systems in atomic scale and making structures with brand new molecular order. Therefore Nano biotechnology is applied highly to converge basic sciences, agriculture, food resources, biotechnology and medicine [4].

By converting micro particles to nanoparticles, we face with changing some physical properties such as increase in surface volume ratio, decreasing the size and changes of energy structure by entering into the realm of quantum effects. Increase in surface to volume ratio which occurs gradually by size reduction causes dominance of surface atoms' behavior to internal atoms behavior that this phenomenon affects the physical and chemical properties of the particle. As soon as particles become small enough new quantum behavior and properties appear [5]. By progress in technology and reaching new methods to use natural resources, plus huge effects in human life many negative effects will be experienced [4].

These matters are distributed in organs and tissues rapidly after injection and are absorbed by cells highly. Nowadays, different coatings such as albumin, polyethylene glycol, aspartic acid, etc. are used to increase stability of nanoparticles in biological solutions, blood cycle and tissue distribution. It also facilitates entering these substances into cells and reducing the toxic effects of them [5].

Titanium dioxide nanoparticles (TiO2) are used widely to control microorganisms and microbial factors in sanitary products and wide range of business or applied plans. There is many evidences about potential dangers of titanium dioxide for human health and environment because of its unique physicochemical properties such as small size, increase in surface per mass, chemical composition, surface structure, form and accumulation, and high reactivity. Titanium dioxide nanoparticles can be used in paint production, cosmetics, ceramic production, photocalysts production, water and sewage and many other industries because of its unique properties [4].

These materials exist in three crystalline phases of anatase, rutile and brookite. TiO2 nanoparticles can be used for protection against ultraviolet radiation due to the high reflectivity. Many of these nanoparticles are used in sunscreen creams that are colorless and reflect UV rays more efficiently than larger particles. An important feature of these nano inorganic solids is photo-catalytic activity from the antimicrobial coating to photocatalytic reactions.

On the whole, considering the wide use of nanoparticles in various industries and extant theories about destructive effects of these matters, this study was carried out to study histological, morphological and pathological effects of titanium dioxide nanoparticles on liver of Syrian mice.

EXPERIMENTAL SECTION

Titanium dioxide nanoparticles were prepared from Nano Sunny Company (Iran Nanotechnology). Forty male mature mice from the age of 4-5 weeks and weight range of 25-30g were used. Samples were kept in animal nest of *Ostad Taher Research Center (Shahreza- Iran)* with free access to standard food, water and room situation (12:12 photo period, 25-28$^{°C}$ temperature and 25-30% humidity). Mice were kept for 7 days to adapt to environment.

Treatment groups were control group did not receive anything, placebo group, and two experimental groups which received 10 and 100ppm of nanoparticles via gavage. Liver tissue was kept in formalin 10% and tissue was divided into segments with 5micro meter thickness. Segments were colored were colored using hematoxylin-eosin method and studied using light microscopy.

Obtained data were analyzed using one way analysis of variance and Duncan test (95%) was used to compare means. Mean weights of mice were compared using paired t-test. All analysis were done using SPSS program.

RESULTS AND DISCUSSION

According to histological studies, any pathological effect was not observed and liver tissue had normal appearance. Liver tissue of 10 ppm groups was normal but 100 ppm group showed hyperemia in central veins. Nuclear accumulation of basophils can be seen that is caused by the destruction of liver cells. Also, tissue necrosis was observed which was due to toxicity of 100 ppm dose (Figure 1, 2 and 3).

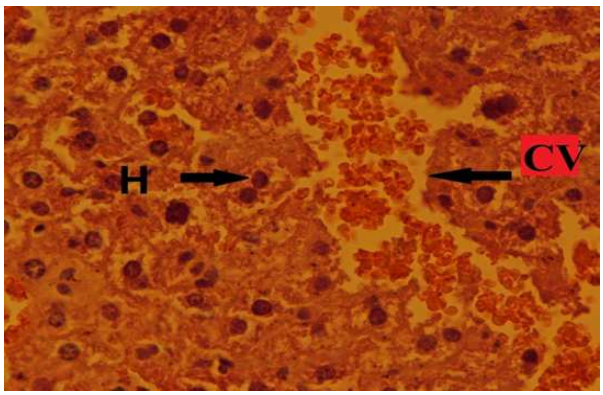

Figure 1. Photomicrograph of liver tissue in the control group
CV: Central Vein H: Hepatocyte

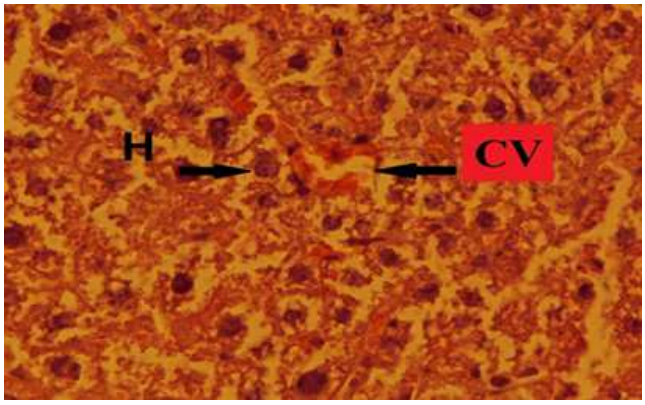

Figure 2. Photomicrograph of liver tissue in the 10 ppm group
CV: Central Vein H: Hepatocyte

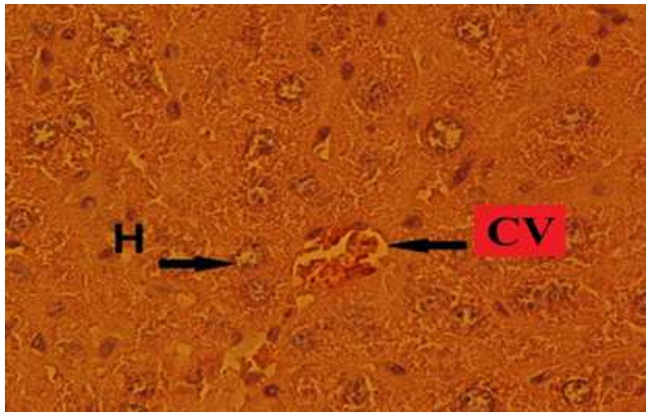

Figure 3. Photomicrograph of liver tissue in the 100 ppm group
CV: Central Vein H: Hepatocyte

Nanoparticles pollution is proposed as a new problem lately [5]. Stability of dioxide metallic nanoparticles is very high in environment and food chain which causes continuance of their toxicity [6]. In current study, toxicity of titanium dioxide nanoparticles was investigated because of their frequent application in industries [4].

Various chemical matters, ammonia, drugs, alcohol, and viruses are from factors which can damage liver tissue and cause liver diseases. Viral hepatitis and serious alcohol hepatitis are from those diseases which can cause liver cirrhosis, but most of the time cirrhosis is due to chronic hepatitis. One the other hand, using these nanoparticles in drugs and edible pigments has exposed people, especially children, to them [7].

From liver enzymes, ALT, AST, GGT, and ALP enzymes that show necrosis of cholestasis liver hepatocytes and are used in diagnosis of severe liver diseases such as inflammation. Nanoparticles cause toxicity by interfering in membrane structure, oxidative stress, binding protein or DNA, producing active oxygen and cell death or apoptosis [8].

In this study, ALT AST, and ALP were measured among various liver enzymes. Increase in nanoparticles concentration increased these enzymes' concentration in blood which is because of cells destruction. Liver histology studies in short time have shown tissue damages in 200 and 300 mg/kg groups of zinc oxide nanoparticles, so that liver hepatocytes have been inflated and therefore sinusoid became very narrow and limited which is accompanied by hypertrophy of Rimac ropes. Also port space was not obvious and bleeding was observed in central veins [9].

Jiangxue et al. studied sharp toxicity and biological distribution of particles and reported that suspension via gavage for 14 days did not show sharp toxicity. Changes of biochemical parameters of serum (AST, ALT and LPH) and liver pathology showed that these particles caused liver injuries significantly which is the sign of myocardial damages [9]

Liang et al. (2009) studied the effects of titanium dioxide nanoparticles on liver and kidney performance and the relationship between oxidative stress changes in Sprague-Dawley rats under two different surface area of (TiO2(2-

S50): 50m(2)/g, TiO(2-S210): 210 m(2)/g) and two dose of 0.5, 5, or 50 mg/kg (by inhalation). After 7 days, any sharp toxicity was not observed in both organs. Also pathological changes were observed in tissues. Inhaling the nanoparticles cause oxidative stress in liver and kidney [10].

Toxicity of nanoparticles can be an effective way for curing cancer but affecting non-cancerous cells is inevitable. Late researches have shown that nanoparticles can cause gene change which is itself a stimulator for cancer growth [9]. High concentrations of iron nanoparticles showed negative effects on liver, damaged liver tissue and increased liver enzymes [10]. Microscopic observations showed that nanoparticles bind to cell surface and some of them entered the cells. This pattern depends on type of metallic nanoparticles [9].

In general, toxicity of titanium dioxide nanoparticles is confirmed in this study and more studies are proposed.

CONCLUSION

According to results of this study, liver tissue was damaged in 100ppm group which showed dose dependent toxic effect of titanium dioxide nanoparticles.

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