

# Effect of Titanium Dioxide Nanoparticles on the Histology of Liver of White Male Rats

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## ABSTRACT

**Background:** Nanotechnology or nanoscience considers as a new field of science which has an effective role in the day to day life aspects. This field deals with the production, processing, and use of materials ranging in nanometers. Recently, this field becomes a confederate science that is usually used in other fields of science, like electronics, physics, and engineering.

**Materials and methods:** Study design starts with the choice of nanoparticles (NPs) [titanium dioxide nanoparticles (TiO<sub>2</sub>)]. Eighteen white male rats were used in this research. Study groups classified into six groups (each group includes three animals): two control groups (for oral and i.p. administration) and four treatment groups (group I: treated with 400 mg/kg orally and i.p., group II: treated with 150 mg/kg orally and i.p.).

**Results and discussion:** Results of this research include the presence of some inflammatory cells infiltration (lymphocyte infiltration), as it showed in the figures of the histological sections of the treated groups compared with the control group. These results were found to be different than studies of other researches that refer to the presence of many undesired hepatic histological and biochemical changes, such as, the effects on membrane structure, oxidative stress, binding protein, or DNA, cell death or apoptosis, and hepatocytes necrosis.

**Conclusion:** In conclusion, TiO<sub>2</sub> induce lymphocyte infiltration, but there are no additional deleterious histological changes in the liver tissue.

**Keywords:** Liver histology, Nanoparticles, Rat, TiO<sub>2</sub>.

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**Conflict of interest:** None

## INTRODUCTION

Nanotechnology term comes from two words combination: the first Greek numerical part nano, which refers to the billionth and the second-word technology.<sup>1</sup> Nanotechnology is considered as a new field of science, which has an effective role in the day to day life aspects. This field deals with producing, manipulating, processing, and using different materials in the nanometers range. It deals with various materials that approximately have dimensions of 1 to 100 nm that are used in different modern technologies for their unique physical features. So, nanoparticles represent materials that commonly have a size of less than 100 nm. These materials or particles can be tubular, spherical, or may irregular shape.<sup>2,3</sup> Now, nanotechnologies become a principled science that is usually used in other branches of sciences, such as, the science of physics, engineering, and electronic fields,<sup>4,5</sup> with many

variant advantages.<sup>6,7</sup> It represents processes of manipulation of different matters on the scale of the atom, molecule, and supramolecular scale, including the very small materials production, design, effective characterization, and application in various areas of science and providing novel technological approaches mainly in the field of medicine.<sup>1,8,9</sup>

According to many previous studies designed on both the toxic and biological effects of nanoparticles, it was found that there is a significant relationship between the exposure to nanoparticles and the appearance of many pulmonary diseases, cardiovascular complications, and events of mortality. However, adequate information on the primary mechanisms, which lead to nanomaterial toxicity is not well understood. For example, penetration of nanoparticles to different cellular parts (intracellular and extracellular parts), like the cytoplasm of lung cells (both mesothelial and epithelial cells), it was

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confirmed by electron microscopy. Therefore, it is so essential to identify the potential dangers of new enhancements using nanoparticles for avoiding human harms.<sup>10</sup>

TiO<sub>2</sub> represent one of the well-known, widely produced NPs in the world because of their great physicochemical properties, like biocompatibility, stability against corrosion, have low cost, whitening, photocatalysis, and its easy to be prepared at nano sizes. They are considered one of the most famous NPs used in industry with several useful uses in different branches of sciences, like medicine, pharmaceuticals, cosmetics, neutralization, and the destruction of the cancer cells, gases purification, and filtration, especially air, treatment of water, and processes of decolorization.<sup>11-13</sup> TiO<sub>2</sub> photocatalyst may destroy the cell membrane; solid the proteins of many viruses, reduce, and restrain virus activation. It also kills bacteria up to 99.97%. TiO<sub>2</sub> was found to kill golden grape cocci, coliform, and green suppuration bacilli, in addition to mildew and suppuration fungus.<sup>14</sup>

However, TiO<sub>2</sub> has high redox activity, and a large surface area to weight ratio. These specific properties are common causes of adverse effects on human health and the environment, and intrinsic toxicity to them.<sup>12,15</sup> Besides, a previous study showed that zinc oxide and TiO<sub>2</sub> NPs may cause the production of free radicals in the skin, may cause damage in the DNA, and can cause alteration of protein structure that may be an important reason for types of cancers and tumors.<sup>16</sup>

## MATERIALS AND METHODS

The study design starts with the choice of NPs (TiO<sub>2</sub>, size 21 nm) which was prepared previously. The solvent used in the study was dimethyl sulfoxide, which was associated with mortality, so the solvent was replaced by distilled water to complete the experiment.

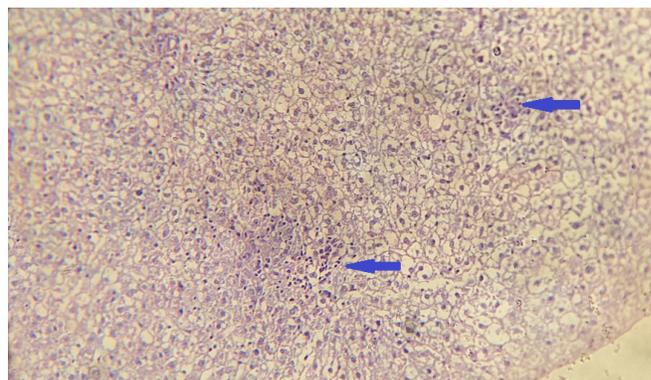
Eighteen white male rats were used in this research. Study groups classified into six groups (each group includes three animals): two control groups (for oral and i.p. administration) and four treatment groups (group I: treated with 400 mg/kg orally and i.p., group II: treated with 150 mg/kg orally and i.p.). The period of study was 1-month with a 48 hours treatment interval. The dose was prepared immediately according to body weight. Oral dosage was performed by using an oral tube (gavage method), while an insulin syringe was used in the i.p. dosage. Finally, animals were sacrificed at the end of the research for histological study.

## RESULTS AND DISCUSSION

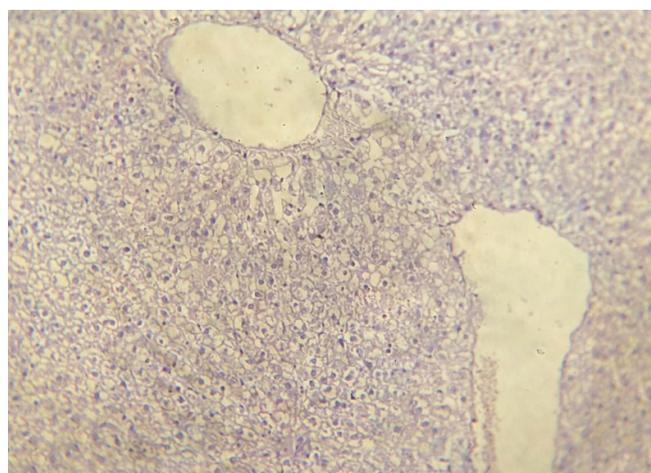
The results of this research include the presence of some inflammatory cells infiltration (lymphocyte infiltration), as it showed in the figures of the histological sections of the treated groups compared with the control group (Figures 1 to 5).

Different research was performed on the effects of TiO<sub>2</sub> NPs.<sup>3,7</sup> The TiO<sub>2</sub> which is considered one of the most produced NPs in the world, has attracted particular technological and scientific interest because of their specific and unique physical and chemical properties in addition to their different effects on

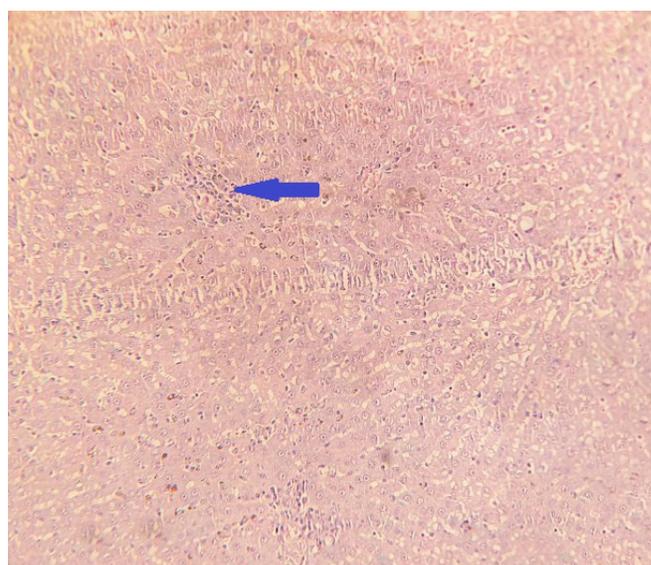
human health.<sup>17</sup> However, there is an obvious increase in the researches performed on the toxicities of many NPs, both in



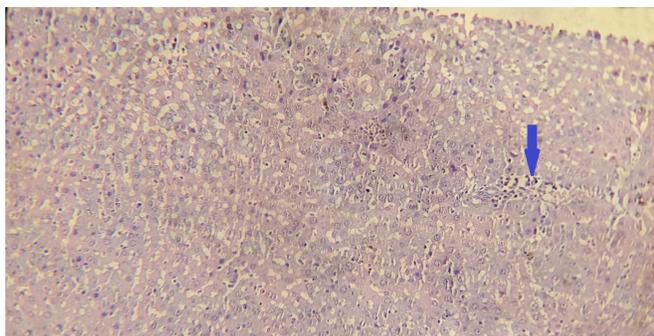
**Figure 2:** Cross histological section of the liver of rat treated with 150 mg of TiO<sub>2</sub> (oral dose) showing the presence of lymphocyte infiltration (blue arrows); 200x



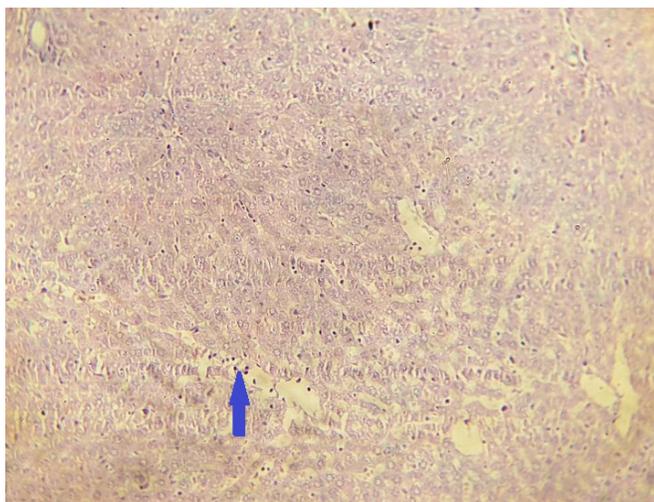
**Figure 1:** Cross histological section of the liver of normal rat (control group) showing normal histology



**Figure 3:** Cross histological section of the liver of rat treated with 150 mg of TiO<sub>2</sub> (i.p. dose) showing the presence of lymphocyte infiltration (blue arrow); 200x



**Figure 4:** Cross histological section of the liver of rat treated with 400 mg of TiO<sub>2</sub> (oral dose) showing the presence of lymphocyte infiltration (blue arrow); 200x



**Figure 5:** Cross histological section of the liver of rat treated with 400 mg of TiO<sub>2</sub> (i.p. dose) showing the presence of lymphocyte infiltration (blue arrow); 200x

naturally occurring particles and in engineered nanomaterials.<sup>18</sup> TiO<sub>2</sub> have the ability to cross the plasma membrane of the lung cells (air born) and have direct access to intracellular proteins, organelles, and DNA, which may greatly increase their toxic potential,<sup>19,20</sup> and different undesired effects on the histology of kidneys, including exfoliation of some lining epithelial cells, degenerative changes, interstitial hemorrhage, mononuclear cell infiltration and increase in collagen fibers around degenerated convoluted tubules and glomeruli.<sup>21</sup> Our results showed no deleterious effects of TiO<sub>2</sub> on the histology of the liver of all study groups. There was only lymphocytic infiltration which may refer to the direct effect of TiO<sub>2</sub> on the inflammatory mechanisms in the body or it may be correlated to another factor that may induce the infiltration within the liver of the treated animals. These results were found to be different than other researches that refer to the presence of many undesired hepatic histological and biochemical changes, such as, the effects on membrane structural components, oxidative stress, binding and altering protein or DNA, affecting cell death or apoptosis, and hepatocytes necrosis, which also may be indicated by the increased serum liver enzymes (AST, ALT, and ALP).<sup>22-24</sup>

The absence of deleterious changes (like carcinogenic effects, types of degenerations, and necrosis effects), may reflect important sides of the safety of these NPs in the field of this research.

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