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Effect of titanium dioxide nanoparticles on biochemical variance in animal model

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Abstract
This study focused on the determination of toxicity of TiO2 on hepatocyte and the effect of it on liver function. The results indicate that there is no significant difference between the enzymes level in study groups with respect to that of control while there is an increase in serum direct bilirubin and decrease in albumin concentration in study group with respect to control group, while total bilirubin was nearly the same in both groups, in the same time Ca+2 shows a significant increasing in injected groups with respect to that in control group.

Keywords: TiO2 nanoparticles, GOT, GPT, Ca2+, total bilirubin, and direct bilirubin

Introduction

Nanoparticle (NP) is Associate in an object with the diameter of fewer than 100 nm. Because of their tiny size, giant extent, and specific chemical/physical characteristics, NPs nowadays is widely investigated, and are the attention of the many research laboratories across the globe (Dimitrijevic and Pantic, 2016) [15].

There are many alternative classifications of NPs, based on their structure, Methods of synthesis, chemical structure, or its morphology.

Nanoparticles may be organic or inorganic molecules depending on manufacturing process (Pantic et al., 2016) [15]. Today, probably best investigated and applied inorganic nanomaterials are a unit those that incorporate, or made from various metals, such as iron, silver, gold or titanium.

Metallic nanoparticles (MNPs) are a unit thought about as doubtless necessary a part of numerous drug delivery systems applicable in internal medicine, neurology and cancer research (Sintov et al., 2016) [18]. Some MNPs, such as the ones made from silver area unit famous for his or her antibacterial drug properties, and area unit employed in trade and engineering. Some MNPs now a day are part of many products like dietary supplements, cosmetics and Paint materials (Paunovic et al., 2017) [16].

This compendious article focuses on recent analysis on the results of bimetal NPs liver function with stress on their potential hepatotoxicity in Humans and experimental animal models (McGillicuddy et al., 2017) [13]. TiO2 NPs or (Nano-T iO2) are amongst the most commonly used NPs in consumer products. They are included as pigments in paints and as reflecting agents in sunscreens (Weir et al., 2012) [19]. T iO2 particles have long been used for whiteners in products designed for direct exposure of humans, such as toothpastes or foods such as confectionery, sauces or creamers (Lomer et al., 2000) [12].

In the 1990s the T iO2 intake in the average daily diet was estimated to be 5.4 mg per person per day (Lomer et al., 2000) [12], which corresponds to approximately 1012 particles per person per day, of which some part is expected to be in the nano-range of 100 nm and smaller (Kermanizadeh et al., 2013) [6]. These data were recently updated by (Weir et al., 2012) [19]. listing average exposures of 1-2 mg/kg bodyweight of T iO2 for children and of 0.2-0.7 mg/kg bodyweight for adults, mainly depending on dietary habits.

The mean diameter of T iO2 in food colourants such as E171 was measured at 200 nm and 110 nm (Weir et al., 2012) [19], respectively, and Weir et al. report that 36% of particles were in the range of 100 nm and below (Weir et al., 2012) [19]. Therefore, dietary exposure to nano T iO2 is a realistic and everyday scenario. Exposure to nano T iO2 by inhalation can also happen, for example during the production of paints containing T iO2, most commonly used pigments, or during sanding and polishing of surfaces to which these paints have been applied (Van Broekhuizen et al., 2012) [2]. Finally, there has been some concern about absorption of NPs such as ZnO through the skin after application of sunscreens and cosmetics (Gulson et al., 2012) [5]. While NP uptake through intact skin show that either not take place, or be very low, there is still some concern about potential uptake of NPs or dissolved ions through damaged skin (Osmond and McCall, 2010) [14], many others claimed that T iO2 NPs can inter the blood stream after the exposure or inhalation (Kreyling, 2013) [7]. Inhaled Nano-T iO2 have distal effects on antioxidant levels in the liver (Gosens et al., manuscript in preparation). Indeed, the liver frequently acts as a sink for NPs after their translocation into the bloodstream (Kreyling et al. 2009; Schleh et al., 2012) [8, 17]. Therefore, even though direct application of T iO2 NPs into the bloodstream is an unlikely scenario, it is important to test effects of these particles on the liver, since translocation may occur. Other studies show that TiO2 NPs may cause gene mutations, chromosomal damage, or nucleic acid damage (Langie et al., 2015, Li et al., 2013) [9, 11]. (Gordon, Resio and Pellman, 2012) study the relationships between TiO2 and DNA damage.

To further understand TiO2 nanoparticles toxicity in vivo, (Langie et al., 2017) [10] studied effect of TiO2 nanoparticles exposure on genotoxicity, DNA damage, and inflammation in mice.

Experimental part

This study done in University of Babylon / College of Pharmacy during the period from October to February 2018- 2019. Nanoparticles were prepared by other group in the same college (TiO_2 nanoparticle measure according to the weight of animal then dissolved in Distilled water to be administered to the animals). White rat was used for this study its weight was ranged from 250 to 500 mg, the study includes two groups, first group as study group include 14 rats, and the second one includes 5 rats as a control group. The dose of TiO_2 nanoparticles injected for each rat depends on rat weight (400mg nanoparticles / Kg body weight of the animal dissolved in distilled water).

The dose was given to the animals by two methods by divided the study groups into two parts the first group was given the TiO_2 nanoparticles solution orally, the second groups was given the same sample by injection intra-peritoneal, while the control group was given the same volume of distilled water only. The dose was taken three times weekly for one month, 5 ml blood samples were taken from each animal after each experiment, centrifuged to get the serum to be used for measuring the biochemical variance includes in this study.

To estimate the LD50 for the prepared solution the dose was increased gradually until half of the experimental animals was died, the dose was equal to 500 mg / Kg body weight of the animals, so the dose must be not acceding this weight of the prepared nanoparticles. To detect the effect of TiO_2 nanoparticles on the liver of the rats, the parameters which is used for liver function test (GPT, GOT, Total Bilirubin, and Direct Bilirubin) were measured using ready for use kit manufactured in biomatrix Company, the measuring procedures were perfumed according to manufacturer protocols which attached with the kit.

Results and Discussion

The results of liver enzymes concentration in both groups (study group and control) were shown in table-1. These results indicate that there is no significant difference between the enzymes level in study groups with respect to that of control, these results mean that the TiO_2 nanoparticles did not cause any damage or effect on the hepatic cells in the range of the dose used in this study. In case of bilirubin and albumin, the results show an increase in serum direct bilirubin and decrease in albumin concentration in study group with respect to control group, while total bilirubin was nearly the same in both groups (table-2). Calcium ions seems to be increased in study group compared to that in control group as in table-3. Table -4 show the correlation between study biochemical variables, the results show weak negative correlation between GOT and serum direct bilirubin (r= -0.348) and calcium (r= -0.273), also GPT give a significant negative correlation with serum direct bilirubin (r= - 0.644) and a significant positive correlation with albumin (r= 0.643), in the same time albumin show a highly negative significant correlation with serum direct bilirubin (r= -0.856) and moderately negative correlation with total serum bilirubin (r= - 0.517), while there is no any correlation between calcium ion with all biochemical variance used in this study.

Conclusion

Titanium dioxide nanoparticles can be used as diagnostic or therapeutic drug for liver diseases without any side effects in the dose range (400mg/kg)

Similarly, in a study using CaCO cells it was found that there was no cytotoxicity following 24 h exposure to TiO_2 NPs (Kermanizadeh *et al.*, 2013) [6] (Xia *et al.*, 2006). Discovered that TiO_2 nanoparticles did cross the epithelial lining of the intestinal model by transcytosis, albeit at low levels. TiO_2 was able to penetrate into and through the cells without disrupting junctional complexes. It is also interesting to note that a recent study suggests that TiO_2 NM exposure did not result in any toxicological effects to mammalian cells under dark conditions (This lower toxicity of TiO_2 in dose range used because TiO_2 that taken orally were not metabolized ,low absorption , high percentage of titanium dioxide excreted from the body in feces.

In some cosmetic and other product, the TiO_2 used is not pure titanium dioxide but covered by phosphate or silicon species or aluminum species, which modify the surface chemistry of these particles that may increase toxicity. In case of GOT &GPT the result shows a decrease in Serum level of this enzymes in study group in respect to control group. In case of calcium, the result shows an increase in Serum level of calcium in study group in respect to control group, in case of albumin the result shows a decrease in Serum level in study group in respect to control group.

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