



HISTOLOGICAL STUDY OF THE EFFECT OF TITANIUM DIOXIDE USED IN COSMETICS IN MICE

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ABSTRACT

The rapid advancement of nanotechnology has prompted the necessity to investigate the health effects of nanoparticles and nanomaterials which are frequently used in products like sunscreen, lotions, talcs, perfume, cream etc. Titanium dioxide is a molecule composed of one atom of titanium and two atoms of oxygen. (Liu *et a.*,2013). Titanium dioxide absorbs ultraviolet light; this property makes titanium dioxide useful in sunscreens. In cosmetic and skin care products titanium dioxide is one of the main constituents which are used as pigment and a thickener. Titanium dioxide the main constituent is produced in varying particle sizes and is oil and water dispersible. (Liu *et a.*,2013). It is due to this feature of Titanium dioxide it can penetrate the skin, reaches the blood and different organs. The present study was planned to find out any toxicological effect of this nanoparticle on vital organs of body when applied on mice skin. The kidney maintains the vital functions of clearing excess body fluid and removing metabolic and exogenous toxins from the blood. The kidney is particularly vulnerable to drugs and other agents that cause renal damage. The heart pumps approximately 25% of cardiac output into the kidneys any drug in the blood will eventually reach the highly vascularized kidneys may potentially cause drug-induced renal failure. (Zhang *et al.*, 2012). The sections of kidney were studied at 5 μ . The histological study of kidney does not reveals any major change in its structure when experimental group of Swiss Albino mice was applied with a dose of 0.5mg/cm² on 2cm² area of skin twice a day for 15 days. But the same dose applied for 45 days showed changes in the section of

kidney such as glomerular enlargement, tubular degeneration and swelling and dilatation of Bowman's capsule, while some disruption was observed in the liver tissue.

KEYWORDS: Histopathological Study, Kidney, Titanium dioxide, Dermal Exposure.

INTRODUCTION

Nanoparticles are particles between 1and100 nanometers in size. In nanotechnology a particle is defined as a small object that behaves as a whole unit with respect to its transport and properties. (Liu *et a.*,2013). Nanoparticles like titanium dioxide and zinc oxide have new properties such as chemical reactivity and optical behavior because of which they are used in many commercially available products like sunscreens, cosmetics, textiles, paints and even are used as catalysts. (Liu *et a.*,2013). They have also found a role in drug delivery where they could be used to deliver drugs to a specific site in the body. (Ambalavanan *et al.*, 2013). Nanoparticles have many characteristics that make them suitable for biological and medical applications. Despite the widespread use of titanium dioxide nanoparticles, studies are being conducted on the toxicity of these nanoparticles in biological systems (Fartkhooni *et al.*, 2016).

Titanium dioxide is used in cosmetics, skin care products, as a tattoo pigment and in styptic pencils. Titanium dioxide is found in the majority of physical sunscreens because of its high refractive index, its strong UV light absorbing capabilities and its resistance to discoloration under ultraviolet light. (Winkler, 2003). Now a day Nano-scaled titanium dioxide particles are more used in sun screen lotion because they scatter visible light less than titanium dioxide pigments while still providing UV protection. Sunscreens designed for infants

or people with sensitive skin are often based on titanium dioxide or zinc oxide, as these mineral UV blockers are believed to cause less skin irritation than other UV absorbing chemicals. (Winkler, 2003)

METHODOLOGY

Experimental Animal:

Three groups of Swiss Albino Male Mice 6-8 weeks old were housed in cages in a ventilated animal room of the University. Room temperature was maintained at 20⁺°C water and food given ad libitum. The animals were divided into three groups each consisting of 8 animals. The dose was mixed with petroleum jelly and applied on a small area of 2 cm². Control group was applied on a petroleum jelly only. Behaviour and mortality were monitored.

Drug:-

Pure Powered Emplura Titanium (IV) Oxide from Merck Specialities Private Limited was administered.

Dose:-

Dose for dermal administration:- 0.5 mg/ cm² Titanium Dioxide with Petroleum Jelly (applied to a small area of shaved skin for 15 days and 45 days to a 2 cm² area of the experimental animal. And 0.5 mg/ cm² and 2.0 mg/ cm² Titanium Dioxide with Petroleum Jelly (applied to a small area of shaved skin for 15 days and 30 days to a 2 cm² area of the experimental animal.

Target Organs (Kidney): Major Detoxifying Organs of the Body

The kidney maintains the vital functions of clearing excess body fluid and removing metabolic and exogenous toxins from the blood. The kidney is particularly vulnerable to drugs and other agents that cause renal damage. If the drug is primarily cleared by the kidney, the drug will become increasingly concentrated as it moves from the renal artery into the smaller vasculature of the kidney. The drug may be filtered or secreted into the lumen of the renal tubules, the concentrated drug exposes the kidney tissue to far greater drug concentration per surface area. (Zhang et al, 2012).

Target Organs (Liver):

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. Yoosefis *et a.*, (2016). The goal of this study was investigating the effects of titanium dioxide nanoparticles on liver histology of the laboratory mice. Yoosefis *et al* (2016).

Histological Procedure:

The fixed tissues were embedded in paraffin- bee wax blocks and 5 μ thick sections were stained with haematoxylin and Eosin (H&E). Histopathological morphology was studied under the camera fitted Nikon microscope at 10x.

OBSERVATION

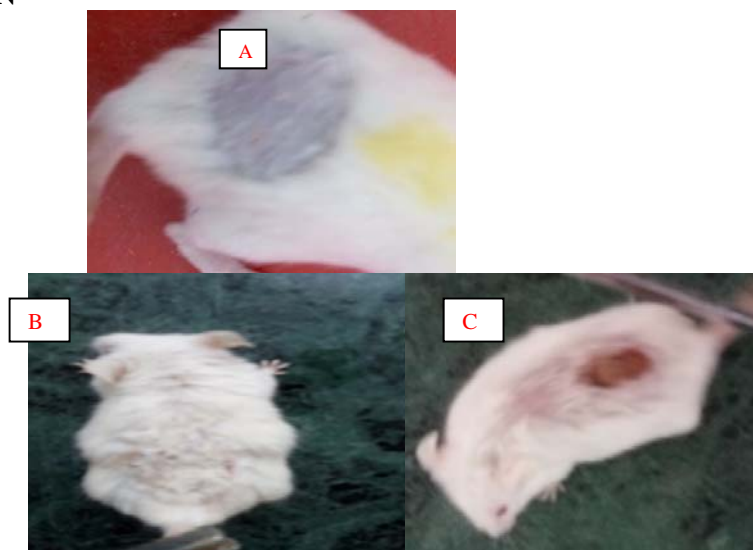
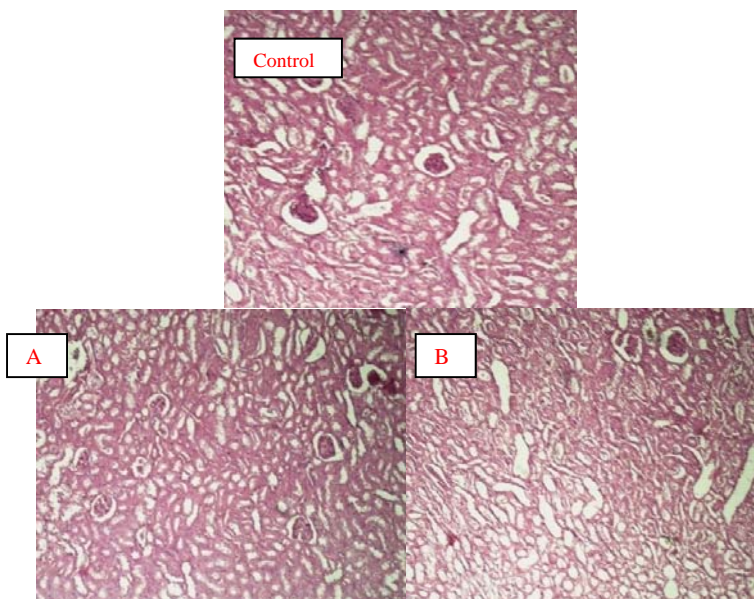
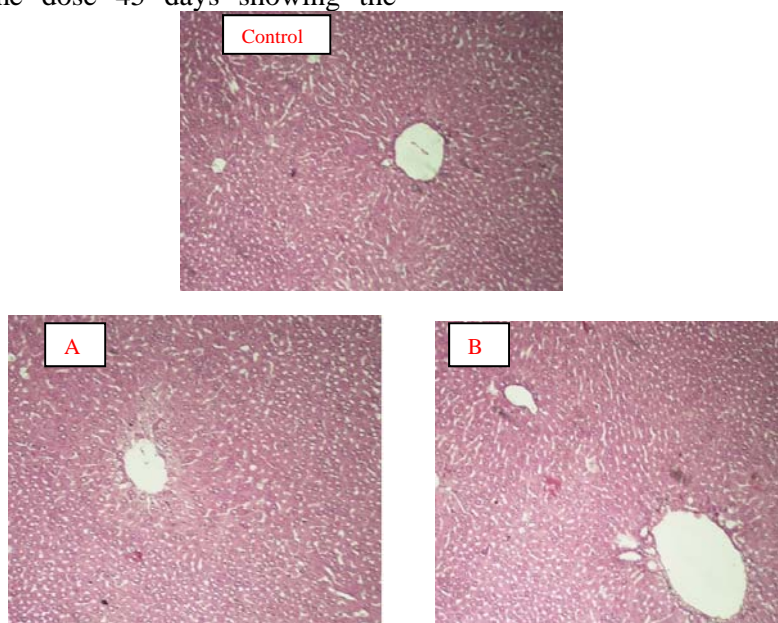


Figure: A skin of a normal mouse. Figure B & C lesion on skin of mice treated with TiO₂ with dose 0.5 mg/cm² for 15 days and 45 days respectively



Section of kidney (10x) of control mice showing normal glomerulus. Treated A dose 0.5mg/cm²15 days showing major changes and Treated B same dose 45 days showing the glomerular enlargement, tubular degeneration and swelling and dilatation of Bowman's capsule.



Section of Liver (10x) of control mice showing normal histo-architecture. Fig A and B of treated animals at dose 0.5mg/cm²for 15 days showing changes like shrinkage of central vein and enlarged central vein when treated for 45 days respectively.

RESULT

In the section of a control animal there was normal arrangement of renal corpuscle, proximal and distal convoluted tubules, Henle's loop and collecting duct. The histo-architectural changes observed in the Titanium Dioxide treated mice

were lesions and blocking of blood vessels at some places. The luminal space of the Bowman's capsule and proximal tubule diameter seemed to be reduced. Minor histopathological changes of liver, including congestion of vasculum, prominent vasodilatation and vacuolization leads to the damage of liver function, thus leading to its instability.

DISCUSSION

Accumulation of Titanium Dioxide has been observed in liver, kidney, and lung after dermal administration (Wu *et al* 2009). However no

remarkable toxic effects were observed in the histological structure of kidney except a swelling in the renal glomerulus and Bowman's capsule at 15 days treated animals indicating some degree of toxic insult to it, while at 45 days treated animals lesions and blocking of blood vessels at some places and reduction of the luminal space of the Bowman's capsule and proximal tubule diameter was observed. Hydropic degeneration around the central vein was prominent and the spotty necrosis of hepatocytes was prominent. The present study indicates that penetration of Titanium dioxide has triggered some histopathological resulting in disruption of liver tissue and apoptosis at few places. Although it is known that nano-TiO₂ or other nanoparticles can induce serious liver toxicities, the mechanisms and the molecular pathogenesis are still unclear. Fartkhoni *et al* 2016 who administered TiO₂ intraperitoneally for 21 days an alternate (11 days). Similar results were also reported by Wang *et al* 2007. Our finding can be explained by the result of Borm *et al* 2006 who reported that histopathological changes observed in kidney may be due to the reason that kidney is major organ which remove toxic products from the body.

CONCLUSION

The histological study of changes in the section of kidney at 5 μ such as glomerular enlargement, tubular degeneration and lumen up space reduction indication abnormal view of kidney and some disruption of liver tissue. Further evaluation for chronic toxicity is still needed.

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