HEMATOLOGICALSTUDY OF THE EFFECT OF TITANIUM DIOXIDE NANOPARTICLES USED IN COSMETICS IN LIVER OF MICE

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***Abstract*: Nanoparticles have many characteristics that make them suitable for biological and medical applications. (Farthkooni et al., 2016). Nanotoxicology is a branch of bionanoscience which deals with the study and application of the toxicity of nanomaterials. (Buzea *et al*., 2007) Titanium dioxide nanoparticles can be used in paint production, cosmetics, ceramic production and numerous other applications like in water and sewage industries and many other industries because of its unique properties.(Mahdieh *et al*., 2015). A dose of 0.5 mg/cm^2 and 2.0 mg/cm^{2}was applied on 2 cm^2 area of skin for 15 and 30 days. The result of present study indicate a significant hemoglobin levels, Hematocrit values, Total erythrocyte (RBC) and total leukocyte (WBC) counts, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC).MCV, MCH and MCHC percentage increased inhigh dose group only at 30 days of treatment periodHemoglobin levels, hematocrit values, RBC and WBC decreased in high dose group only at 30 days of treatment period. Platelet count increased in high dose group for 30 days treatment period. Thus the result of the study suggest dermal administration of titanium dioxide nanoparticles have adverse effect on the hematological parameters of mice. And biochemical changes of liver Serum Glutamic Oxaloacetic Transaminase (SGOT), Serum Glutamate Pyruvate Transaminase (SGPT), and Alkaline Phosphatase (ALP) increased in high dose group for 30 days treatment period.**

***Keywords*:-Liver, Blood parameters, Titanium dioxide, Dermal Exposure, Serum Biochemical Test.**

Introduction

Titanium Dioxide Nanoparticles (TiO2-NPs) applications are widely used in the daily life and their possible toxicity to the living organism is necessary to be insured.It may produce health risk when contact with humans and animals because it has unique physical and chemical properties(Daly *et al.*,2017).

Titanium dioxide is a molecule composed of one atom of titanium and two atoms of oxygen and absorbs ultraviolet light this property makes titanium dioxide useful in sunscreens. Titanium dioxide nanoparticles are photocatalytic which means that they have the capability to use energy in light to catalyze reactions with other molecules at reduced temperatures. (Boysan *et al*2011).

TiO_2 NPs have been widely used in many products, such as toothpastes, sunscreens, cosmetics, food products, pharmaceuticals, and nanomedical reagents. (Long et al 2007).TiO_2particles have been considered as nanotoxic mineral particles and traditionally used in the fields of cosmetics, food and drugs.(Zhao *et al*., 2011).

TiO_2 may possess higher toxicity potential than their bulk materials.Long *et al* 2007 found that TiO_2 NPs caused higher cytotoxicity than fine particles in cell culture. Due to their very small size, NPs can penetrate basic biological structures, which may, in turn, disrupt their normal function. (Buzea et al 2007).Recent research evidence shows that TiO_2 NPs may induce cellular toxicity effects in cardiac tissue. (Jawad et al 2011).The toxicity effects of TiO_2 particles were also observed in cells of the circulatory system.(Zhao *et al*., 2011)

Titanium dioxide reflects all colors in the visible light spectrum therefore the light reflected from titanium dioxide are white. This characteristic makes it useful as a white pigment in paints and may make for white residue on the skin. The titanium dioxide nanoparticlesuse the energy from the light to add an electron to oxygen molecules, whichproceed to destroy cancer cells. (Boysan *et al* 2011). It has unique characteristics such as small size, large surface per unit mass and high reactivity that NPs can quickly enter the human body and then imposes potential health risk on human. (Warheit *et al*., 2007 and Oberdorster*et al*.,2005).

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 *adlibitum*. Each group consisted of 8 animals. The dose was mixed with petroleum jelly and applied on a small area of 2 cm^2. Control group was applied petroleum jelly only. Behaviour and mortality were monitored.

Drug:-

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

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

Autopsy

At the end of the respective experimental period, animals were sacrificed under mild ether anesthesia.The blood samples were collected through cardiac puncture in EDTA vials from mice of all the groups.

Clinical hematological variables

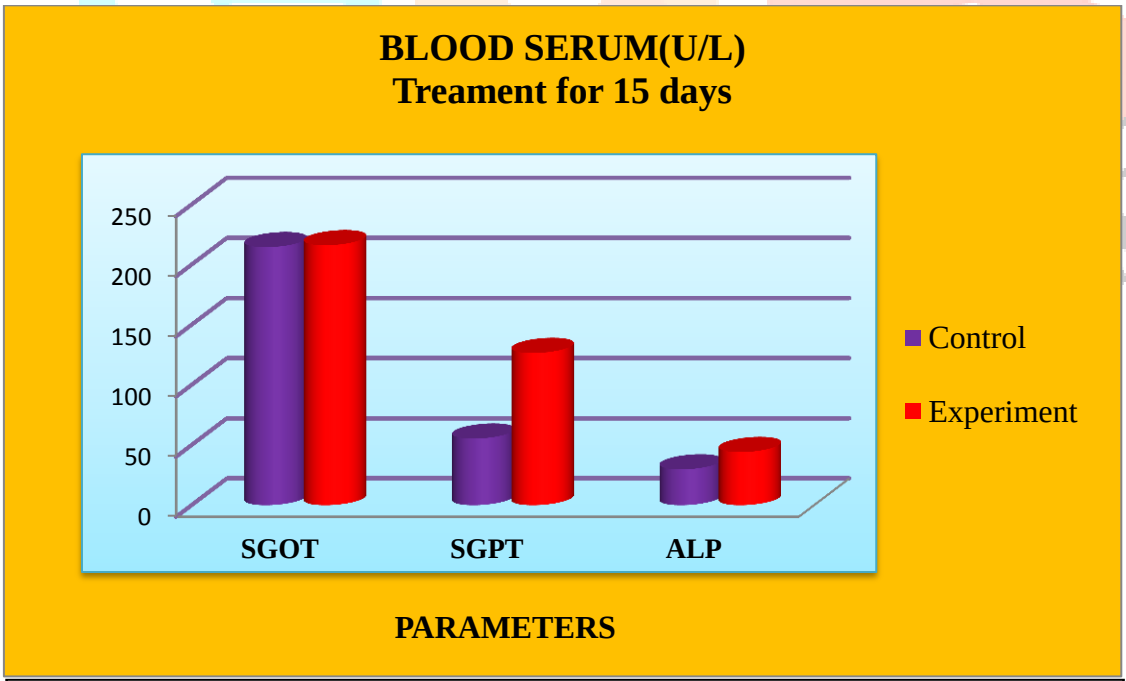
Level of mean cell volume (MCV), Hematocrit (HCT), Hemoglobin (HGB), mean cell hemoglobin (MCH), mean cell hemoglobin concentration (MCHC), platelets count (PLT), red blood cell (RBCs) count and white blood cell (WBCs) count were measured using a Neubar Chamber Method.

Clinical serum parameters

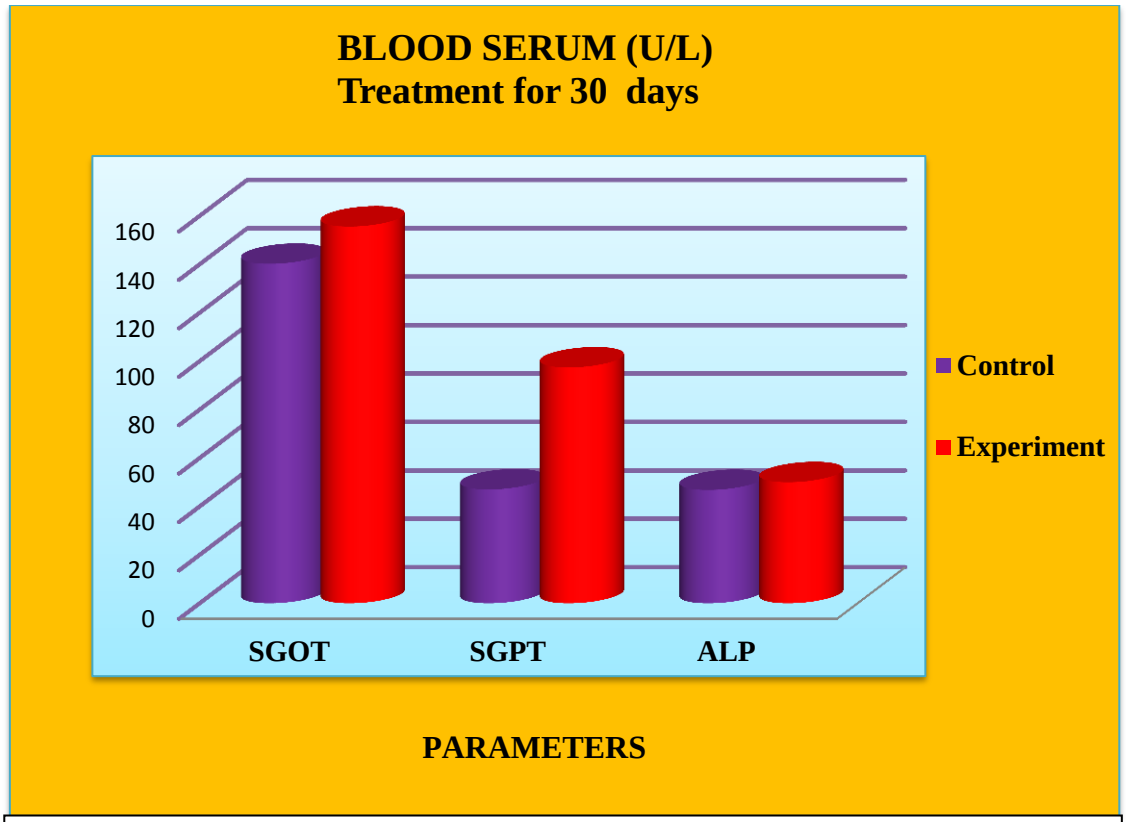
Serum Glutamic Oxaloacetic Transaminase (SGOT), Serum Glutamate Pyruvte Transaminase (SGPT), and Alkaline Phosphatase (ALP) were measured in serum using Beckman counter spectrophotometer (Model AU680).

Target Organs (Liver)

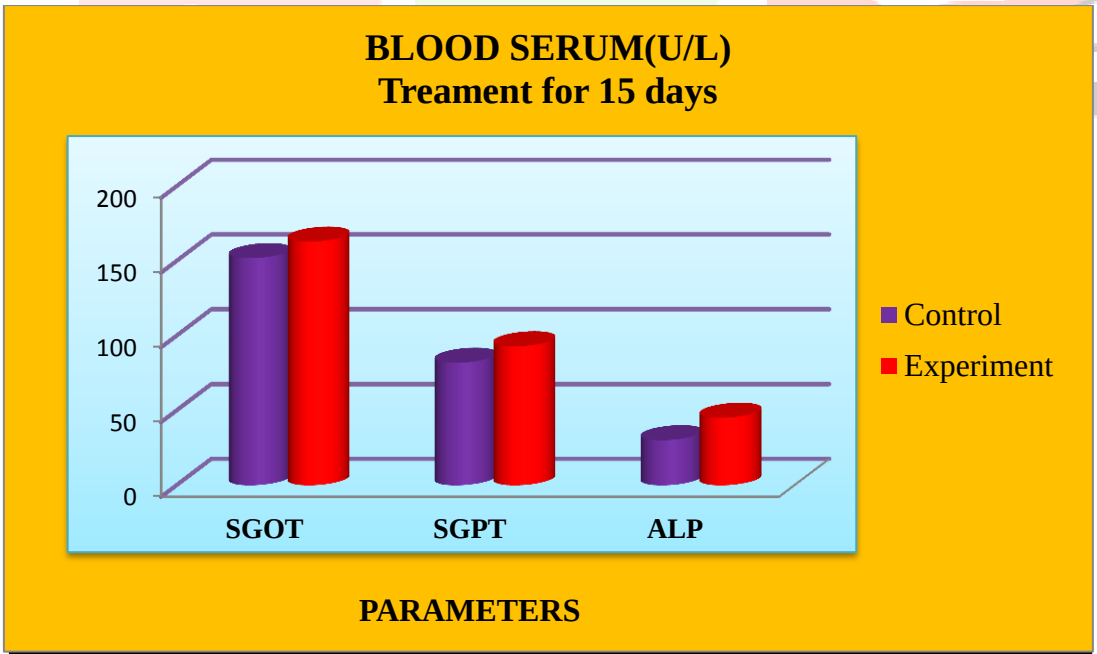
Liver is one of the vital organs and is involved in the regulation of many physiological activities. Any abnormal liver function creates a set of disorders that can cause irreparable damage to this organ. (Yoosefis *et al.*,2016).The goal of this study was to investigate the effects of titanium dioxide nanoparticles on liver function of laboratory mice through its biochemical parameters.



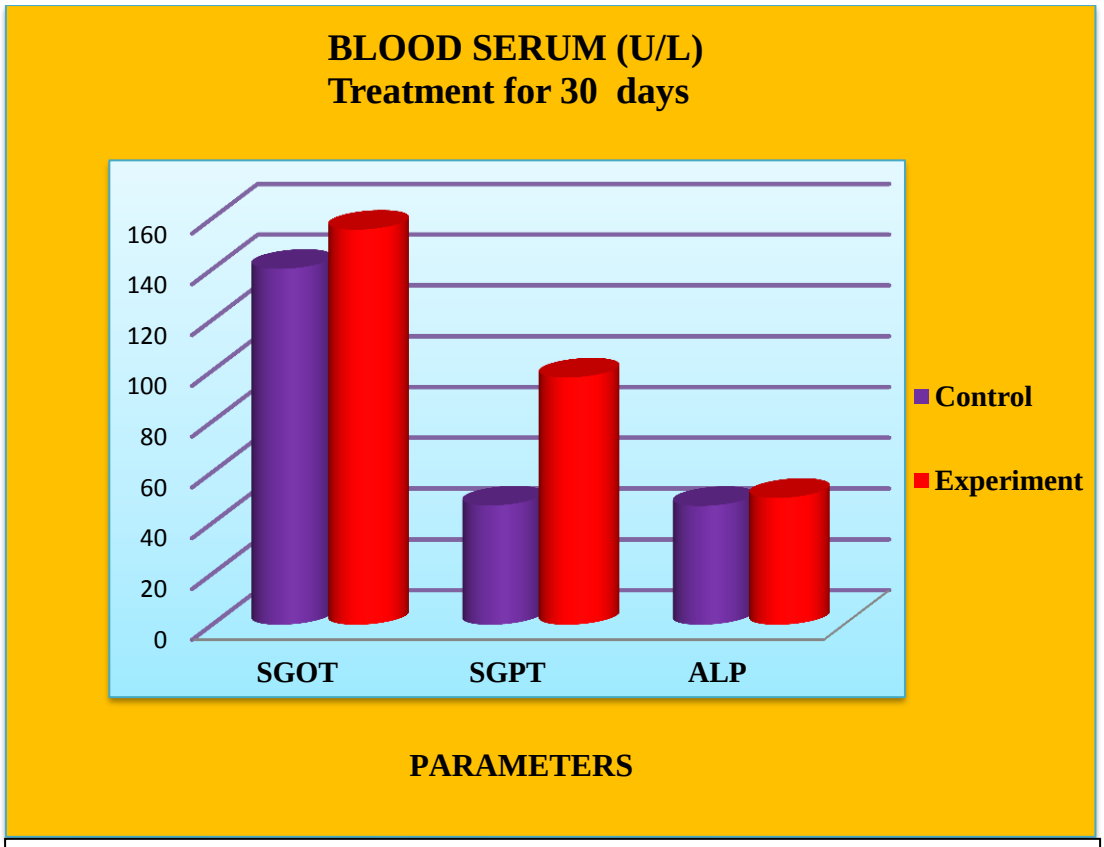
Effect on SGOT, SGPTand ALP concentration in serum of male Swiss albino mice administered with titanium dioxide nanoparticle at dose 0.5 mg/cm^2 for 15 days. A marked increase in SGPT and slight increase in ALP as compared to control was observed



Effect on SGOT, SGPT and ALP concentration in serum of male Swiss albino mice administered with titanium dioxide nanoparticle at dose 0.5 mg/cm^2 for 30 days. Increase in SGOT and SGPT as compared to control is observed.



Effect on SGOT, SGPT and ALP concentration in serum of male swiss albino mice administered with titanium dioxide nanoparticle at dose 2.0 mg/cm^2 for 15 days. Slight increase in SGOT, SGPT and ALP as compared to control is observed.



Effect on SGOT, SGPT and ALP concentration in serum of male Swiss albino mice administered with titanium dioxide nanoparticle at dose 2.0 mg/cm^2 for 30 days. SGOT, SGPT levels increase while ALP remains unchanged as compared to control.

Table 1.Hematological parameters of control and Titanium Dioxide administered mice at different doses and durations.

Values represent mean ± standard error mean (n = 5). A value in a row with different letter in superscript indicatessignificant

	15 days			30 days		
		Titanium Dioxide			Titanium Dioxide	
Parameters	**Control**	**0.5mg/cm^2**	**2.0mg/cm^2**	**Control**	**0.5mg/cm^2**	**2.0mg/cm^2**
RBC (million/mm^3)	1.40 ± 0.05	1.36 ± 0.04	2.06±0.07	6.20±0.33	5.50±0.26	4.13±0.15
WBC(thousand/mm^3)	4.3± 0.05	5.04 ± 0.26	6.05±0.27	3.82±0.44	5.62±0.64	5.10±0.25
Hemoglobin (g/dl)	8.48 ±0.82	8.58 ±0.08	9.60±0.09	10.8±0.33	10.1± 0.35	9.36±0.09
Hematocrit (%)	5.74±0.17	8.28 ±0.11	9.29±0.12	31.6 ±0.48	29.2±0.91	20.30±0.07
MCV (fL)	56.6 ±1.96	60.6±1.29	65.7±1.97	46.6 ±0.51	44.8±1.16	57.00±0.71
MCH(pg)	58.7 ±1.07	67.3±0.07	69.6±1.09	15.6± 0.22	15.3±0.26	25.44±0.10
MCHC(%)	158.28± 17.2	106.4±0.11	109.4±0.12	34.14±0.22	33.94±0.21	45.30±0.07
PLT(/ml)	335±6.4	315.4±18.0	385.8±92.9	312.0±0.71	354±12.0	564 ± 1.8

difference according to Graph Pad Software.

Results and discussion

The result of present study indicates a significant difference in values of Hematocrit ,Total Leukocyte (WBC) counts, Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH) and Mean Corpuscular Hemoglobin Concentration (MCHC) even at low dose; whileMCV, MCH and MCHC percentage increased in high dose group only at 30 days of treatment period. Hemoglobin levels, hematocrit values, RBC and WBC decreased in high dose group only at 30 days of treatment period. Thus the result of our study suggest that dermal exposure of titanium dioxide nanoparticles have adverse effect on the hematological parameters of mice and biochemical changes of liver Serum Glutamic Oxaloacetic Transaminase (SGOT), Serum Glutamate Pyruvate Transaminase (SGPT), and Alkaline Phosphatase (ALP) increased in high dose group for 30 days treatment period. Possibly,titanium dioxide nanoparticles have affected white blood cells therefore, titanium dioxide can also affect defense potential of blood(Yoosefi*et al.*,2015).Also, results suggest that the liver function alteration observed in mice is likely to

be associated with the damage of haemostasis of blood system and immune response. However, low dose nanoparticulate anatase TiO2 has little influences on haemostasis ofs blood system and immune response in mice.(Yanmei *et al*., 2009).

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