



## Investigation the Zinc Oxide Nanoparticle's Effect on Sex Hormones and Cholesterol in Rat

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### Abstract

Nowadays nanoparticles have widespread application in various industries and medicine because of their special and unique futures. Zinc oxide nanoparticles have increased production and widespread application in biological systems, but there are limited studies in side effects of these nanoparticles. This study done by 48 wistar rats with daily injection of different doses of zinc oxide nanoparticles intraperitoneally (5, 10, 20 and 40 mg / kg). After a 21 –day period, threats were bled and serum level of LH, FSH and testosterone hormones were measured, blood cholesterol level measured also. The results showed a significant effect of zinc oxide nanoparticles on testosterone and cholesterol level of blood. The results indicate in the dose of 40mg / kg, FSH significantly decreased, but no significant change in LH levels was observed at the doses administered. It's may be LH and FSH decreased by negative feedback of increased TSH. This study revealed presence of nanoparticle cause decreased FSH and increased TSH and cholesterol and not significant decreased in LH level.

**Keywords:** Cholesterol level, sex hormones, nano zinc oxide, wistar rats.

### Introduction

Nanoparticles based on physical and chemical properties and special shape, size and surface area to volume ratio are unique for biological, medical and industrial applications.

Unfortunately the dose of nanoparticles had been used in vitro and in vivo researches was high dose in comparison with doses that usually used. Although in some cases the lowest dose was used, but it was so low that it was negligible.

The term of nanotechnology first applied by Norio Taniguchi, the professor of Tokyo University. He used this word for describing the instruments in nanoscale. Scientific societies associated to nanotechnology defined nanoparticles as particles with 1 to 100 nm dimensions<sup>1</sup>.

In general, nanotechnology is production of new materials, instruments and systems and taking their control in molecular and atomic level<sup>2</sup>.

Nowadays because of widespread application of nanoparticles there is increasing concern about the effects of these substances like reactive oxygen (ROS) on human health and environment<sup>3</sup>. It also causes toxicity in lab environment<sup>4</sup>. Nanoparticles can pass through cell membrane easily and even pass through blood-brain barrier and blood-testes barrier<sup>5</sup>, so it can affect all of the body.

Toxicity of nanoparticles and other cell response are dependent on nature of material and doses have been used. This proved that liver parenchymal cells have a major role in the removal of nanoparticles from blood<sup>6</sup>.

There are many studies that proved application of high dose of nanoparticles (fine or big) is dangerous for human health.

Zinc oxide nanoparticles have widespread application such as prevent sunburn, biosensor, food additives, pigments, resin production and electronic materials<sup>7</sup>. There are many researches on benefits and toxicity of nanoparticles recently<sup>8</sup>. Zinc oxide nanoparticles have negative effects on bacterial growth like staphylococcus and streptococcus, so they can prevent spreading of epidemic diseases as an etiological agent<sup>9,10</sup>.

In experiment some of injected nanoparticles are excluded from blood circulation rapidly so they can't penetrate to body and they have negligible side effect<sup>11</sup>. Because of antibacterial effects of zinc oxide nanoparticles, they can be used in infectious related disease<sup>12</sup>.

Recent studies on zinc oxide nanoparticles showed these nanoparticles can inhibit *E.coli* growth in vivo<sup>13</sup>, so they can protect intestine cells against damages of *E.coli* toxicity<sup>11</sup>.

This study investigates the effects of different doses of zinc oxide nanoparticle on TSH, FSH and LH sex hormones level and cholesterol level in animal blood.

## Material and Methods

This study is an experimental effort that carried out on animals and we used adult male Wistar rats weighing 250-300 gr were estimated from the animal house of martyr portal was developed. Animals with average age of 3-5/2 months selected. Testing carried out at temperature of 20-25 centigrade degree that day duration was 12 hours and 12 hours dark lighting. Municipal tap water was used adjusted drinking water and eating animals for food by rats (feed compression) that the company prepared feed was barking in this study. Experimental animals were randomly divided to six groups as follows: first control group feed by usual water and food. Second control group injected by 1 ml distilled water every other day intraperitoneally for equivalency of shock that obtained by intraperitoneally injection. Other groups from 3<sup>rd</sup> to 6<sup>th</sup> injected by 1 ml zinc oxide nanoparticles in 5, 10, 20 and 40 mg/kg doses, injection repeated every other day intraperitoneally. This continued until 21 day.

One day after the last injection, blood sample of all animals prepared from neck veins. After clotting, samples were centrifuged at 3000 rpm for 15 minutes. After separating the serum from the clot by Smplr, serums frozen at temperature of -20°C and stored, then used for hormones measurement. LH and FSH hormones measured by Immuno radiometric assay. Cholesterol level of serum measured also.

The results (hormone and cholesterol levels) analyzed based on the statistical program SPSS and analyzed by ANOVA and Tukey test was the difference in the  $P < 0.05$  was considered significant.

## Results and Discussion

Comparison of LH, FSH and TSH hormone concentrations in animals that threatened by zinc oxide nanoparticles and controls were done. Statistical analysis was done also in this study. Asterisks\* indicate significant differences at  $P < 0.05$  for each test group rather than the control group. Results showed injection of zinc oxide nanoparticles don't have a significant effect on LH hormone level (figure 1).

Injection of medium and trace dose of zinc oxide nanoparticles don't show significant effect on FSH hormone level but groups that received high dose of nanoparticles show decreasing in FSH concentration rather than controls (figure 2).

Animals that treated by high dose of zinc oxide nanoparticle showed significant increase in TSH hormone level but those who treated by 5, 10, 20 mg/kg don't show this effect (figure 3).

Figure 4 show zinc oxide nanoparticle effect on cholesterol level of animal blood that indicates nanoparticles only in high concentration (40 mg/kg) increased cholesterol level and in medium and trace concentrations don't have significant effect.

The results of this experimental study indicated the zinc oxide nanoparticles in mentioned concentrations have different effect on sex hormones and cholesterol in serum. Pituitary hormones (LH and FSH) that have protein structure decreased by nanoparticle injection and this reduction was more significant for FSH. Its possible nanoparticles inhibit function of endocrine system by blocking of pituitary-hypothalamus axis and it's may be because of reduction in GnRH level. Since FSH and LH are pituitary hormones, therefore this decrease can be considered as a result of penetration of nanoparticle from blood-brain barrier<sup>5</sup>.

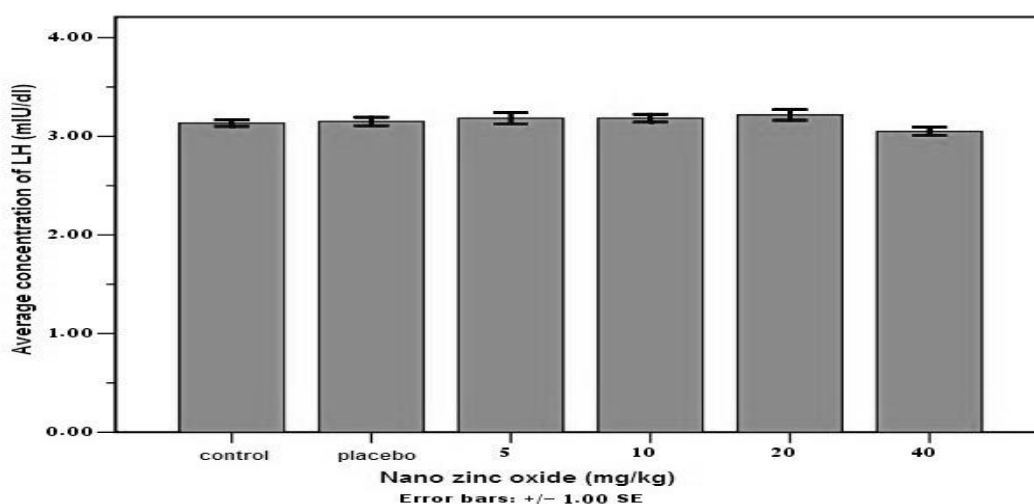
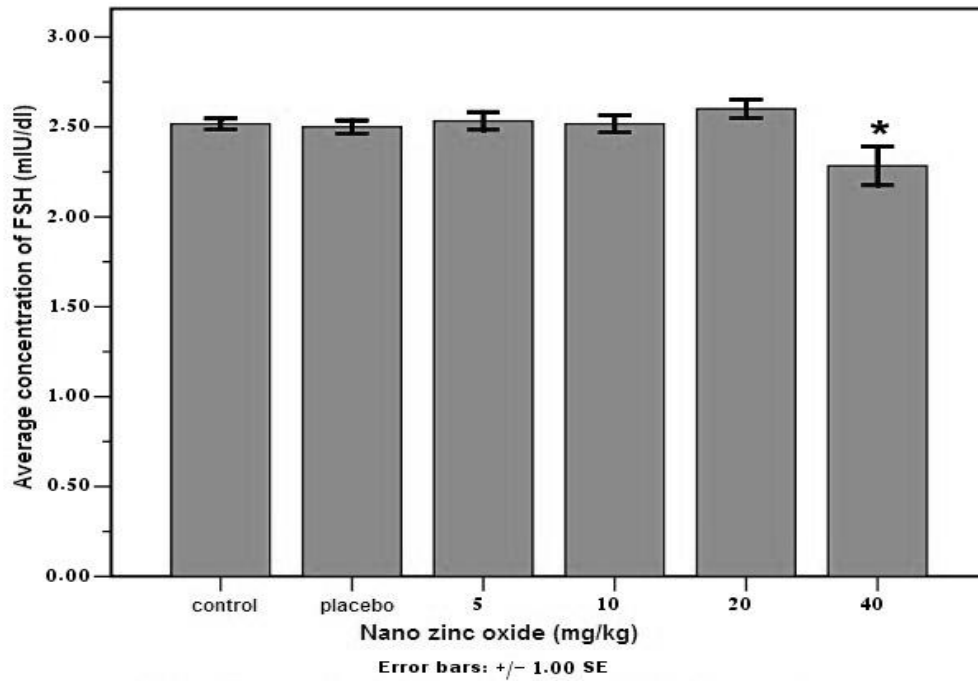


Figure-1

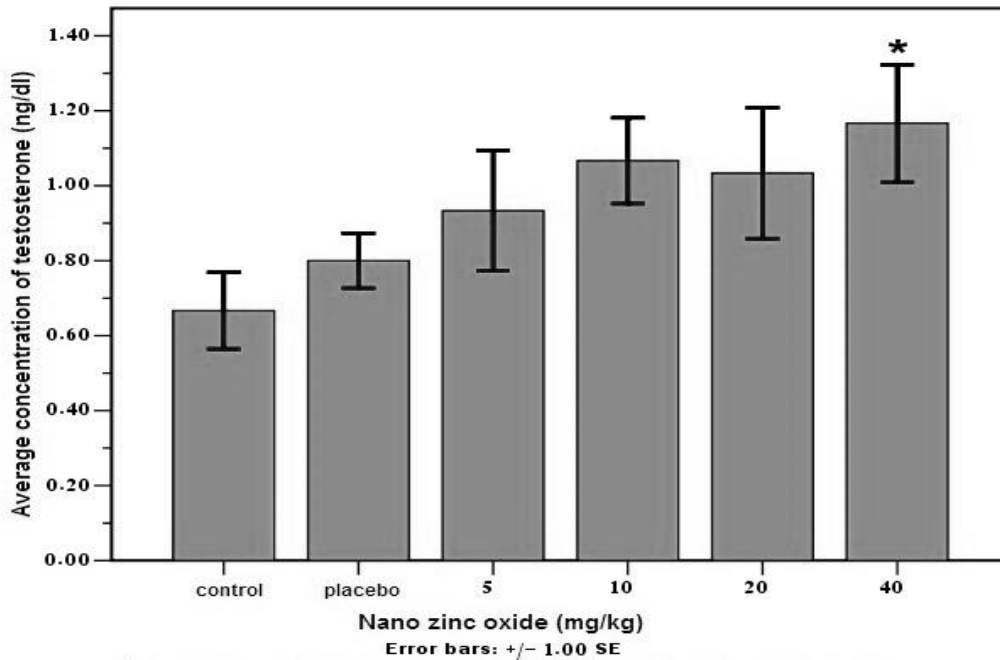
The effect of different concentration of zinc oxide nanoparticle on LH level of blood, As showed there are no significant changes in LH level in different doses of nanoparticle



\*:The difference is significant in compared with the control group

Figure-2

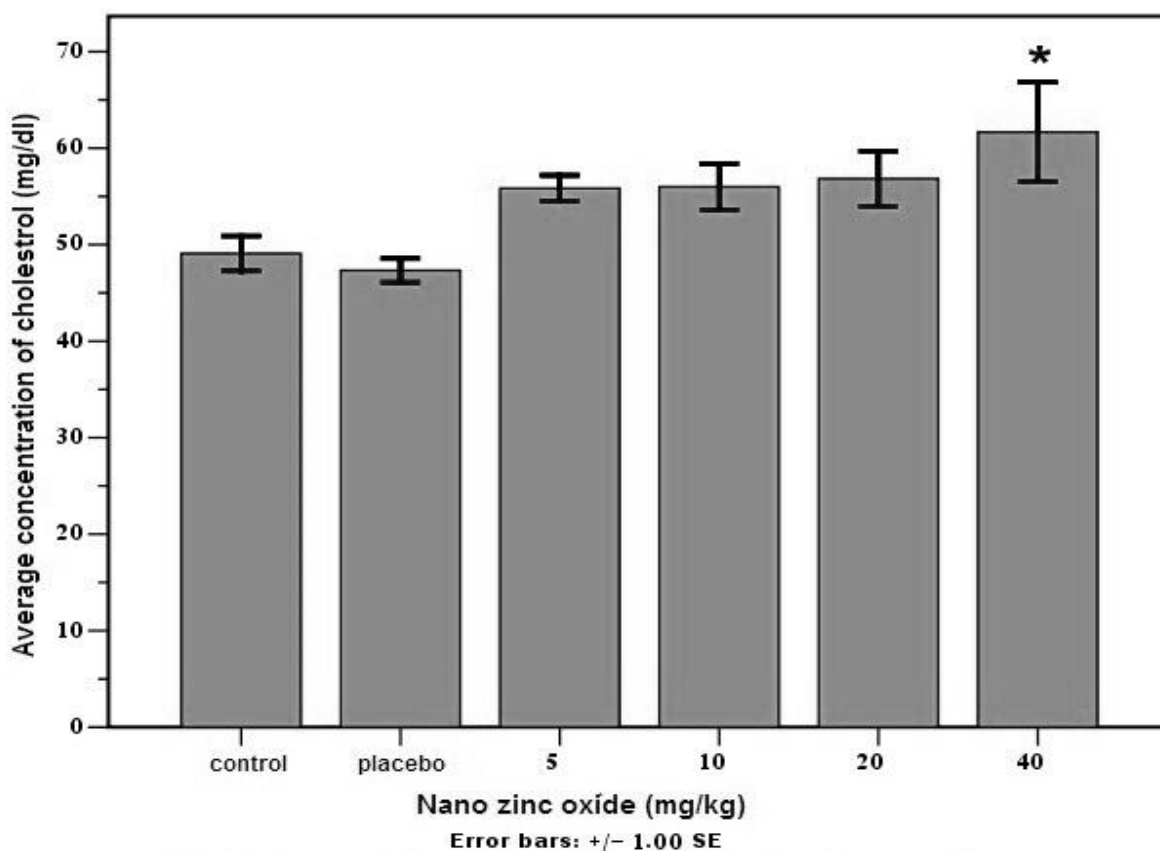
The effect of different concentration of zinc oxide nanoparticle on FSH level of blood, Results showed decrease in FSH level in 40 mg/kg concentration of nano zinc oxide



\*:The difference is significant in compared with the control group

Figure-3

The effect of different concentration of zinc oxide nanoparticle on TSH level of blood, As showed in high concentration of nano zinc oxide TSH level significantly differed



\*: The difference is significant in compared with the control group

Figure-4

The effect of different concentration of zinc oxide nanoparticle on cholesterol level of blood, High concentration of nano zinc oxide cause decreasing of cholesterol

## Conclusion

It's possible increasing in TSH level, that caused by nanoparticle, decreased GnRH secretion by negative feedback inhibition and it caused LH and FSH reduction. Inhibin hormone that released from sertoli cells can be affect FSH hormone level.

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