

Biophysical Effects of Zinc Oxide Nanoparticles in Alleviate Lipid and Serum Glucose

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Abstract

A crucial cell signaling molecule, zinc is a metal ion. Zinc is an insulin mimic, highlighting this by stimulating cellular pathways that control cellular homeostasis and physiological reactions. Numerous disease states, including cancer, obesity, cardiovascular disease, and diabetes. This study examined the effects of oral administration of ZnO NPs at various concentrations of 20, 40, 60, and 80 mg/kg/rat/day on groups of obese rats fed a high-fat diet. Rat groups that were obese had their lipid profiles, serum glucose levels, liver functions, and antioxidant enzymes assessed. These results were compared to healthy rats in the negative group. Biological investigation observed that in the different rats' groups taken orally ZnO NPs, the lipid profile analysis and glucose of serum were significantly decreased in the obese rat groups and nearly control negative. Meanwhile, high-density lipoprotein cholesterol was significantly increased, and low-density lipoprotein cholesterol was significantly decreased. The results from liver functions showed that in the groups that were given taken orally at 80.0 mg/kg rat/ day from ZnO NPs and fed high-fat, the ALT, AST, and ALK were significantly decreased by 27.84, 9.97, and 38.0 mg/dl, respectively. The results from antioxidant enzymes such as GSH, SOD, and CAT as well as MDA from the obesity rats group confirmed the above results. The current study recommends adding ZnO-NPs to the food of obese rats to improve the state of their liver function, lipid profile, and antioxidant enzymes as well as prevent further weight gain. This amount of ZnO-NPs, specifically 80 mg/kg, is suggested.

Keywords: Zinc oxide, Nanoparticles, Overweight, Rats obesity, Antioxidant enzymes, Lipid profile

Introduction

In addition to increasing the formation of ROS in the liver and producing significant alterations in mitochondrial lipids, a high-fat diet (HFD) is linked to metabolic syndrome, which leads to obesity (Vial *et al.*, 2011). Therefore, according to El-Shiekh *et al.* (2019), obesity is a factor in both morbidity and death.

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The biggest risks to human health are obesity and diseases that are related to it. Nanoparticles (NPs) help in bioactivity, targeting, and toxicity reduction (Mahmoud *et al.*, 2022).

Adipocytes secrete leptin, a metabolic hormone, in proportion to the body fat content. In the high-fat diet (HFD), leptin levels increase as a result of leptin resistance brought on by rising oxidative stress and inflammation (Leon-Cabrera *et al.*, 2013). One of the uses for nanotechnology is in medicine, and one of the more well-known NPs frequently utilized in medicine is zinc oxide nanoparticles (ZnO NPS) (Alotaibi, 2021)s. It can overcome several obstacles to the efficient targeting of molecules and cells in various disorders due to its amazing biological features and minimal toxicity (Rasmussen *et al.*, 2010).

Micronutrient zinc is necessary for many metabolic activities (Shetty *et al.*, 2022). According to Reed *et al.* (2014), it is utilized in roughly 300 biochemical and enzymatic processes in the body. Enzymes like denaturizes and elongases contain zinc (Chimhashu *et al.*, 2018). The connection between zinc and the metabolism of fatty acids (FA) has been supported by numerous studies. As a result, conflicting findings point to zinc's impact on the human body, particularly in pathological situations (Yuvaraj *et al.*, 2023). Zinc's application in nanomedicine is quite intriguing (AlHussain *et al.*, 2022). Numerous disorders can benefit from the use of nanoparticles in treatment (Skrajnowska & Bobrowska-Korczak, 2019).

It can argue that "Skin is considered a mirror of health" since a balanced physique, free of sagging and excess weight, is suggestive of youth and health. Fitness and skin care were therefore among the most crucial research areas about both health and financial benefits (Gaikwad & Choudhari, 2022). In addition to being able to disintegrate and burn fat and prevent obesity, zinc oxide (ZnO) is resistant to these two traits (Nilesh *et al.*, 2021). It may be stated that zinc oxide keeps you young because of this. Moreover, characteristics of zinc oxide A non-toxic semiconductor from the second group is zinc oxide (ZnO). Due to its chemical makeup, it is highly soluble in human plasma influencing neurotransmitters and the central nervous system (Alkattaby, 2022).

The impact of adding zinc sulfate that has undergone hot-melt extrusion (HME) processing on growth performance was examined by Lee *et al.* (2022). The findings showed that Zn NPs' large surface area and high catalytic efficiency enable minerals to be absorbed easily and distributed to the organs and that the pancreatic digestive enzymes, nutrient digestibility enzymes, and the

superoxide dismutase enzyme one of the main antioxidant enzymes increased as a result.

Obesity is a chronic, lifelong condition that greatly worsens health and shortens lifespan (by at least 10 years). Due to the numerous anomalies that would manifest with the development of obesity, proper treatment of obesity needs a lifetime of effort. Large specific surface areas, potent absorptive and high bioavailability of nanomaterials, as well as effective targeting capabilities and adjustable release rates, make them particularly useful for the detection and management of obesity and obesity-related metabolic disorders (Tran *et al.*, 2023). Targeting and correcting functional cell abnormalities, regulating redox homeostasis, and eliminating free lipoprotein from the blood are just a few of the treatments for obesity that nanomaterials can be used for. The treatment of metabolic illnesses linked to obesity would benefit from a diagnosis (Polevoy *et al.*, 2022). According to Li *et al.* (2019), the development of nanomaterials will support the diagnosis and treatment of metabolic illnesses linked to obesity and obesity.

Due to its biological characteristics, nanotechnology is being employed more and more for a variety of purposes, including nanomedicine (Harish *et al.*, 2022). Due to their extremely small size and ability to quickly pass across biological membranes, nanoparticles (NPs) possess discriminating features that make them appropriate for oral application (Virgen-Ortiz *et al.*, 2020).

According to Bhandana *et al.* (2020), humans need to absorb about 2 to 3 g of the 12 mg of zinc they need each day. Zinc oxide nanoparticles play a role in regulating physiological processes in the body, and because of their small size, zinc is easily absorbed from them (Siddiqui *et al.*, 2020). Research has been done on the use of zinc oxide in nanoscale formulations for biomedical purposes (Alhujaily *et al.*, 2022). Additionally, according to recent studies, zinc oxide nanoparticles may be crucial for the delivery of drugs and genes (Alhujaily *et al.*, 2021).

The purpose of this study was to examine the anti-overweight implications of ZnO NPs in obese rats. Rats have taken orally ZnO NPs and antioxidant status, lipid profile, and liver function enzymes were determined.

Materials and Methods

Materials

Zinc oxide nanoparticles (ZnO NPs) were suspended in 0.9% NaCl to prevent particle aggregations; the suspension was syndicated for 20 minutes in a vibration water bath. It was then combined for one minute in a vortex mixer before being swallowed.

At Cairo University, Egypt, the Faculty of Veterinary Medicine's major animal house provided male adult albino rats weighing 150–160 g. They had undergone a two-week conditioning period in a typical laboratory setting. They had a 12-hour light-dark cycle, were kept at a comfortable temperature of 20 to 25 °C, and had free access to food and drink.

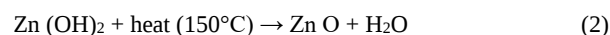
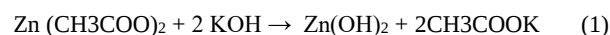
A 65% baseline diet and a 35% butter-fat oil mixture were used to create the high-fat diet (HFD) (Chung *et al.*, 2018).

Kits for determination of the parameters were purchased from Sigma-Aldrich Corp., MO, USA,

Methods

Preparation of Zinc Oxide Nanoparticles (ZnO NPs)

Precipitation was used to create zinc oxide nanoparticles (Kumar *et al.*, 2013). Zinc sulfate heptahydrate solution (431.31 g dissolved in 1500 ml of deionized water) was added dropwise while being magnetically stirred, and the addition was then followed by 12 hours of stirring. Sodium hydroxide solution (122.40 g dissolved in 1500 ml of deionized water) was then added. After filtering, washing with pure water several times, drying at 100 °C for 30 min., and calcining at 150 °C for 6 h., the precipitates were then used to create Zn (OH)₂ NPs. The following equations describe how ZnO NPs are formed:



Biological Experimental

Six groups of six rats each were randomly assigned to experimental rats that were fed a fat and basic diet for seven days. The first major group, which was treated as control-negative rats, received a basic diet for an additional four weeks.

The five rat groups were fed a high-fat diet to induce obesity. The rats from the third, fourth, fifth, and sixth groups were given oral doses of 20, 40, 60, and 80 mg/kg rat/day for a four-week storage period. These groups were then classed as control positive +(ve) as a group (2).

For four weeks, the body weight and food intake were tracked every three days. After the experiment, blood samples were collected from the orbital plexus and centrifuged at 3000 rpm to separate the serum. The sera were then stored at -20°C in a deep freezer until they were analyzed.

According to the methods of Fossati and Principe (1982), Allain *et al.* (1974), Lopes-Virella *et al.* (1977), and Steinberg (1981), respectively, triglycerides, total cholesterol, HDL, and (LDL) were measured, and serum glucose was measured following Tietz (1986).

Using the method outlined by Reitman and Frankel (1957), liver function was assessed using the enzymes ALT and AST transaminoferase. The modified kinetic approach of Belfied and Goldberg (1971) was used to calculate alkaline phosphates activity (ALP).

Malondialdehyde (MDA), a calorimetrically measured indicator of serum lipid peroxidation, was discovered by Yoshioka *et al.* (1979). Additionally, superoxide dismutase (SOD) activity and non-enzyme glutathione (GSH) concentrations in serum were determined by Sairam *et al.* (2003) and Habig *et al.* (1974),

respectively. The catalase enzyme (CAT) was also tested following recommendations.

Statistical Analysis

Data means test was performed to examine the difference between the samples in all analyses after ANOVA was used to evaluate the data and a significant difference ($p \leq 0.05$) was discovered in all variables. The results were assessed using SAS System for Windows, according to SAS (2008).

Results and Discussion

Effect of ZnO NPs on Body Weight in the Obesity Rat Groups

Table 1 observed the effect of ZnO NPs taken orally at levels 20.0, 40.0, 60.0, and 80.0 mg/kg/day on the body weight gain in the obese rat groups fed on a high-fat diet. From the results it could be noticed that the gain in body weight was increased in the control positive (167.6g) compared with the control negative 105.4 g who fed on the basal diet this may be due to the control positive was fed on high- fat basal diet, whilst control negative was fed on basal diet only.

Moreover, the different obesity rat groups 3^{ed}, 4th, and 5th were decreased by 140.5, 125.6, and 110.9 g, respectively than control positive and nearly from control negative. According to these findings, ZnO NPs given orally daily by the rats' group may assist to avoid obesity, maintain a healthy weight, and regulate adipocyte metabolism to stop the accumulation of adipose tissue (Badimon *et al.*, 2010). According to Shirvani *et al.* (2014), ZnO NPs may cause an imbalance in lipid metabolism those results in either an increase or a decrease in body weight.

By drastically reducing leptin levels or increasing adiponectin concentrations, ZnO-NPs may be to blame for better anthropometric measurements or maintaining the appropriate body weight. Leptin resistance and increased leptin levels have been found in obese individuals. Leptin reduces appetite and increases energy utilization by influencing hypothalamic pathways (Berger & Polotsky, 2018). Adiponectin therapy led to weight loss and an

increase in muscle fatty acid oxidation in mice fed a high fat/sucrose diet. Additionally, reducing calorie intake while boosting energy waste is how body weight is controlled (Chong *et al.*, 2014). Another study by Ko *et al.* (2015) found that experimental groups given Nano ZnO at doses (500, 1000, and 2000 mg/kg) for 14 days lost weight. Rats were treated with ZnO NPs (5.0, 50.0, and 300.0 mg/kg, respectively) for 14 days at a concentration of 5 mg/kg, and Mansouri *et al.* (2015) demonstrated a significant decrease in body weight. This decrease in body weight was due to both a direct effect of ZnO NPs and a decrease in food consumption following administration.

Effect of ZnO NPs on Glucose and Lipid Profile in the Obesity Rat Group

To produce energy, regulate appetite, and control adipokines (risk factors for obesity), zinc is essential. Additionally, it has an impact on the hormones leptin, insulin, and adiponectin, which control adiposity and fat mass (Hashemipour *et al.*, 2009).

Glucose and lipid profiles as triglycerides, total cholesterol, LDL, and HDL were determined in the obesity different rat groups fed on a high-fat diet and taken orally at 20, 40, 60, and 80 mg/kg rat/day from ZnO NPs and the results are reported in **Table 2**. The results showed that the highest control positives in glucose, triglycerides, total cholesterol, and LDL were 235.0, 240.3, 220.0, and 140.49mg/dl, respectively. These findings demonstrated a relationship between blood glucose levels above normal and anomalies in lipid metabolism, which are often characterized by an increase in serum lipid levels (Abdulmalek & Balbaa, 2019). Additionally, according to Petrick *et al.* (2016), nano-silica can alter the function of a crucial enzyme and the activity of lipid metabolism through oxidative stress, leading to the buildup of TG and disruption of lipid metabolism. The fact that the control negative was fed a basal diet-free high-fat diet may explain why the lowest values in the control negative were 90.0, 107.6, 100.0, and 20.59 mg/dl, respectively. The HDL levels were highest in the control negative at 60.26 mg/dl and lowest in the control positive at 25.14 mg/dl, respectively.

Table 1. Effect of ZnO NPs on body weight gain in the obesity rat groups during the experimental period.

Groups	Initial (g)	Final (g)	Gain (g)	Daily gain(g)
Negative control	155.7± 5.14 ^a	261.1 ± 11.25 ^d	105.4 ± 2.71 ^b	3.76± 0.05 ^b
Positive control	150.0 ±5.26 ^a	317.6 ± 13.14 ^a	167.6 ± 5.64 ^a	5.99± 0.06 ^a
Group 3 (20 mg/kg/ rat)	160.4 ± 5.71 ^a	300.9 ± 12.86 ^b	140.5 ± 4.94 ^c	5.01 ± 0.05 ^c
Group 4 (40 mg/kg/ rat)	158.6 ±5.83 ^a	296.3 ± 12.57 ^c	137.7 ± 4.56 ^d	4.92 ± 0.06 ^d
Group 5 (60 mg/kg/ rat)	159.7±5.94 ^a	285.3±12.62 ^c	125.6±3.48 ^e	4.48±0.07 ^d
Group 6 (80 mg/kg/ rat)	160.3±5.86 ^a	271.2±11.87 ^d	110.9±2.14 ^c	3.96±0.04 ^b

Values (means ±SD) in the columns are statistically significantly different at ($P \leq 0.05$).

Moreover, the results from obesity in different rat groups observed that the rat groups were taking ZnO PNs orally at 20.0, 40.0, 60.0, and 80.0 mg/kg rat/ day giving the best results and nearly control

negative. These best results were gradually from group 3^{ed} to 6th in glucose, triglycerides, total cholesterol, and LDL from 195.2, 176.2, 184.0, and 11024 mg/dl to 100.0, 112.3, 105.0, and 24.36

mg/dl, respectively. Meanwhile, HDL was increased from 32.74 to 61.98 mg/dl. These findings showed that ZnO NPs may be crucial in promoting health benefits such as lowering blood sugar and LDL cholesterol levels, triglyceride levels, and the risk of cardiovascular diseases. According to Al-Daraji and Amen (2011), the zinc incorporation in the structure of metalloenzymes linked to lipid metabolism may be the cause of ZnO-NPs' hypolipidemic impact. Over 300 enzymes in the body must be activated for which zinc is crucial. Zinc is involved in insulin production, storage, and secretion from the pancreatic cells, as well as inhibiting glucagon secretion, which lowers gluconeogenesis and glycogenolysis (Norouzi *et al.*, 2018). Additionally, ZnONPs showed a remarkable recovery in TG and TC levels, according to Balbaa *et al.* (2017).

These anti-hyperlipidemic ZnONP effects may be related to the nanoparticles' ability to stimulate insulin-like pancreatic -cells (Omarov *et al.*, 2023). Recent findings validated ZnONPs' particular function as a regulator of lipid profile. In comparison to other groups, including the control, only the highest dose of ZnO-NPs (60 mg/kg food) was able to cause a substantial drop in the concentration of TC in the serum of Japanese quail. Higher doses of ZnO-NPs (100 and 200 mg/kg food) have been shown to significantly lower TC concentrations in the plasma of laying hens (Zhao *et al.*, 2016). Regarding treatment, now a day there is an increasing interest toward the potential health benefits of nano-ZnO particles.

Table 2. Levels of some serum lipid patterns and glucose of negative control and obesity rats group after being treated by ZnO NPs at the end of the study

Groups	Triglycerides (mg/dl)	T. cholesterol (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	Glucose (mg/dl)
Negative control	107.6±5.74 ^e	100.0±7.25 ^e	60.26±4.25 ^a	20.59±2.56 ^e	90.00± 6.48 ^e
Positive control	240.3±12.38 ^a	220.0±11.34 ^a	25.14±1.64 ^e	140.49±10.2 ^a	235.00± 15.23 ^a
Group 3 (20 mg/kg/ rat)	176.2±10.21 ^b	184.0±10.38 ^b	32.74±2.18 ^d	110.24±8.10 ^b	195.2± 11.28 ^b
Group 4 (40 mg/kg/ rat)	155.4±8.66 ^c	158.0±9.64 ^c	41.36±2.86 ^c	82.49±3.79 ^c	165.0 ±9.35 ^c
Group 5 (60 mg/kg/ rat)	135.2±9.54 ^d	125.0±8.27 ^d	52.54±3.12 ^b	50.28± 4.03 ^d	133.0± 8.26 ^d
Group 6 (80 mg/kg/ rat)	112.3±5.35 ^e	105.0± 7.67 ^e	61.98±4.21 ^a	24.36±2.82 ^e	100.0± 5.37 ^e

Values (means ±SD) in the columns are statistically significantly different at ($P \leq 0.05$).

Effect of ZnO NPs on Liver Function in the Obesity Rat Group

Liver aminotransferases are very sensitive indicators of hepatic injury and toxicity.

Liver functions as alanine (ALT) and aspartate (AST) transaminiferase, and alkaline phosphates (ALP) were determined in rat groups fed on different diets and the results are reported in **Table 3**. The results illustrated that the highest activity in the enzyme ALT, AST, and ALP in control positive were 60.21, 17.25, and 70.0 mg/dl, respectively while the control negative was the lowest by 25.11, 9.0, and 30.25 mg/dl, respectively. The reason for this large increase is hepatic injury, which caused these marker enzymes to leak out of the cytosol of the hepatocytes and into the bloodstream. This finding agrees with that made by Ghanbari *et al.* (2016). The accumulation of fat within the liver cells, which is detrimental, and the excessive storage of glucose as glycogen can both be caused by hyperglycemia. Julián *et al.* (2015) claimed that this buildup harms the body's organs and tissues, primarily the liver and kidneys, which causes liver enzyme levels to increase.

Whereas, the groups given taken orally 80.0 mg/kg rat/ day from ZnO NPs and fed high-fat were lower by 27.84, 9.97, and 38.0 mg/dl, respectively. According to unchanged values for the activities of AST and ALT and concentrations of total proteins, albumin, and globulin in the serum of Japanese quail fed all examined doses of ZnO-NPs compared to the control, ZnO-NPs were safe in terms of liver function. The results of past studies on ZnO-NPs in broilers (Ahmadi *et al.*, 2014) and weaned piglets (Wang *et al.*, 2018) were supported by this discovery.

According to Potphode *et al.* (2018), treatment alternatives, particularly 80 mg/kg ZnONPs, effectively restored pancreatic and hepatic antioxidant enzyme activity while lowering the oxidative stress indicators MDA and NO in both hepatic and pancreatic tissues. Importantly, it increases islet viability, reduces ROS production, and increases body antioxidant activity to regenerate pancreatic islets.

Table 3. Liver function parameters of negative control and different experimental obesity rats group at the end of the study

Groups	ALT (mg/dl)	AST (mg/dl)	ALP (mg/dl)
Negative control	25.11± 1.24 ^e	9.0± 0.21 ^e	30.25±1.59 ^e
Positive control	60.21 ± 2.39 ^a	17.25 ± 0.85 ^a	70.0±4.35 ^a
Group 3 (20 mg/kg/ rat)	52.34 ±1.91 ^a	15.46 ± 0.76 ^b	62.0±4.15 ^b
Group 4 (40 mg/kg/ rat)	44.24 ± 1.25 ^c	13.37 ± 0.64 ^c	56.0±3.28 ^c
Group 5 (60 mg/kg/ rat)	36.16 ± 1.39 ^d	11.49 ± 0.57 ^d	48.0±3.19 ^d
Group 6 (80 mg/kg/ rat)	27.84 ± 1.28 ^e	9.97± 0.35 ^e	38.0±2.27 ^e

Alanine (ALT) and Aspartate (AST) transaminiferase, Alkaline phosphates (ALP),

Values (means ±SD) in the columns are statistically significantly different at ($P \leq 0.05$).

Effect of ZnO NPs on Oxidative Stress of Obesity Rats

The antioxidant enzymes and the malondialdehyde (MDA) were determined in different rat groups treated with ZnO NPs, fed on a high-fat diet, and compared with the control rats group, and the results are reported in **Table 4**. The results showed that the rats' group control positive was the lowest in GSH, SOD, and CAT by 8.86, 5.26, and 5.98 U/L, respectively, as well as MDA, was the highest by 320.75 nmol/ml, respectively. Rats' group control negative was the highest in all antioxidant enzymes (23.35, 16.21, and 10.15 U/L) also, and the lipid peroxidation as malondialdehyde

(MDA) was the lowest by 155.63 nmol/ml. These results support the hypothesis put forth by Chen *et al.* (2017) that free oxygen radicals lower antioxidant enzymes like superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) proteins, and that a decline in antioxidant factors may be to blame for the pulmonary damage brought on by a high level of lipid peroxidation. Afsar *et al.* (2018) observed that malondialdehyde (MDA) levels in rat lungs were greater than expected, which led to reduced levels of both enzymatic and non-enzymatic antioxidants as well as severe DNA damage.

Table 4. Influence of cupcakes and their formula fat replacer on oxidative stress of rats

Groups	GSH (U/L)	SOD (U/L)	CAT (U/L)	MDA (nmol/ml)
Control negative	23.35 ^a ±0.71	16.21 ^a ±0.35	10.15 ^a ±0.52	155.63 ^e ± 12.36
Control positive	8.86 ^c ±0.08	5.26 ^e ±0.04	5.98 ^e ±0.05	320.75 ^a ± 18.58
Group 3 (20 mg/kg/ rat)	12.45 ^c ±0.16	8.84 ^d ±0.05	6.53 ^d ±0.03	276.34 ^b ±14.56
Group 4 (40 mg/kg/ rat)	15.63 ^b ±0.48	10.41 ^c ±0.31	7.61 ^c ±0.04	224.62 ^c ±12.69
Group 5 (60 mg/kg/ rat)	18.72 ^{ab} ±0.58	13.69 ^b ±0.34	8.59 ^b ±0.11	192.74 ^d ±12.43
Group 6 (80 mg/kg/ rat)	22.24 ^a ±0.69	15.31 ^a ±0.25	9.91 ^a ±0.15	160.81 ^e ±10.86

Values (means ±SD) in the columns are statistically significantly different at ($P \leq 0.05$).

The rats' groups fed high-fat and taken orally ZnO-NPs at levels 20, 40, 60, and 80mg/kg rat/day gradually increased the antioxidant defense, that is, enzymes glutathione (GSH) from 12.45 to 22.24 U/L, superoxide dismutase (SOD) from 8.84 to 15.31 U/L, and catalase (CAT) from 6.35 to 9.91 U/L, respectively, whereas, a significant decrease in lipid peroxidation as malondialdehyde (MDA) from 276.34 to 160.81 nmol/ml. These results showed a significant decrease in MDA concentrations in the rat group when ZnO-NPs were administered at various doses in comparison to the control group. This could be because zinc is the primary component of this antioxidant action and MDA is a well-known indicator of lipid peroxidation (Wasowicz *et al.*, 2003). Hyperglycemia, increased cholesterol levels, chronic inflammation, and hyperleptinemia are some of the factors that may contribute to oxidative stress in obese people (Berger & Polotsky, 2018). ZnO-NPs may reduce oxidative stress in obese rats either directly through their antioxidant characteristics or indirectly by regulating hyperglycemia, dyslipidemia, hyperleptinemia, and inflammation (Li & Shen, 2019). The ability of ZnONPs to scavenge free radicals by interacting with the oxidative cascade to reduce oxidative enzymes, restore the antioxidant status, and chelate metal ions; thus avoiding the Fenton reaction was linked to the ameliorative effect of ZnONPs on hepatic GSH levels (Wei *et al.*, 2006). According to a previous study, adding zinc to the diet of obese rats could boost their catalase and GPx activities as well as GSH levels in the liver, which would reduce the effects of oxidative stress (Ukperoro *et al.*, 2010).

Conclusion

A vital metal ion involved in numerous biological processes is zinc. Therefore, it is possible to infer from earlier findings that zinc

oxide nanoparticles aid in the generation of hormones that control the function of the pancreas and sebaceous glands. It raises insulin levels, which lower blood sugar. Leptin is produced by intestinal fat cells as a result, which promotes the feeling of fullness. It also causes an increase in the concentration of proteins. Thus, zinc oxide nanoparticles help people lose weight and stay healthy since ZnO NPs are a potent metal that boosts metabolism through its potent effects on lipid profile.

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References

- Abdulmalek, S. A., & Balbaa, M. (2019). Synergistic effect of nano-selenium and metformin on type 2 diabetic rat model: Diabetic complications alleviation through insulin sensitivity, oxidative mediators and inflammatory markers. *PLoS ONE*, 14(8), e0220779.
- Afsar, T., Razak, S., Almajwal, A., & Khan, M. R. (2018). Acacia hydasppica R. Parker ameliorates cisplatin induced oxidative stress, DNA damage and morphological alterations in rat pulmonary tissue. *BMC Complementary and Alternative Medicine*, 18, 1-13.
- Ahmadi, F., Ebrahimnejad, Y., Ghalehkandi, J. G., & Sis, N. M. (2014). The effect of dietary zinc oxide nanoparticles on the antioxidant state and serum enzymes activity in broiler

- chickens during starter stage. In *International Conference on Biological, Civil and Environmental Engineering. Dubai* (pp. 26-28). doi:10.15242/iicbe.c0314120
- Al-Daraji, H. J., & Amen, M. H. (2011). Effect of dietary zinc on certain blood traits of broiler breeder chickens. *International Journal of Poultry Science*, 10(10), 807-813.
- Alhujaily, M., Albukhaty, S., Yusuf, M., Mohammed, M. K., Sulaiman, G. M., Al-Karagoly, H., Alyamani, A. A., Albaqami, J., & AlMalki, F. A. (2022). Recent advances in plant-mediated zinc oxide nanoparticles with their significant biomedical properties. *Bioengineering*, 9(10), 541. doi:10.3390/bioengineering9100541
- AlHussain, B. S., AlGhairy, L. A., AlRizqi, A. H., AlHarbi, F. N. O., Ali, A., AlRizqi, H. B. A., AlAssiri, S. N. A., & AlOmran, H. M. (2022). Effect of nano-filled glass ionomer cement on the remineralization of caries lesion: A literature review. *Annals of Dental Specialty*, 10(3), 99-102.
- Alkattaby, L. A. (2022). Zinc oxide nanoparticles keep you younger. Conference: Materials Science, Engineering & Technology International Conference at: U A E, Dubai 21-24 Dec 2022.
- Allain, C. C., Poor, L. S., & Chan, S. O. (1974). Enzymatic determination of total serum cholesterol. *Clinical Chemistry*, 20(4), 470-475.
- Alotaibi, N. S. (2021). Targeting tumor microenvironment-associated immune cells with nanoparticles-based strategies. *Pharmacophore*, 12(4), 1-10.
- Badimon, L., Vilahur, G., & Padro, T. (2010). Nutraceuticals and atherosclerosis: Human trials. *Cardiovascular Therapeutics*, 28(4), 202-215.
- Balbaa, M., El-Zeftawy, M., Taha, N., & Mandour, A. W. (2017). Zinc and curcumin lower arylsulfates and some metabolic parameters in streptozotocin-induced diabetes. *Journal of Diabetes & Metabolic Disorders*, 16, 1-3. doi:10.1186/s40200-017-0293-7
- Belfield, A., & Golobkrg, D. M. (1971). Human serum glucose-6-phosphatase activity: Confirmation of its presence and lack of diagnostic value. *Enzyme*, 12, 561-265.
- Berger, S., & Polotsky, V. Y. (2018). Leptin and leptin resistance in the pathogenesis of obstructive sleep apnea: A possible link to oxidative stress and cardiovascular complications. *Oxidative Medicine and Cellular Longevity*, 2018, 5137947.
- Bhantana, P., Timlin, D., Rana, M. S., Moussa, M. G., Zhihao, D., Sun, X., Tan, Q., & Xiao, H. C. (2020). How to cut down the gap between the Zn requirement and supply of food chain and crop growth: A critical review. *International Journal of Plant, Animal and Environmental Sciences*, 10(1), 1-26.
- Chen, X., Liu, Z., Meng, R., Shi, C., & Guo, N. (2017). Antioxidative and anticancer properties of Licochalcone A from licorice. *Journal of Ethnopharmacology*, 198, 331-337.
- Chimhashu, T., Malan, L., Baumgartner, J., van Jaarsveld, P. J., Galetti, V., Moretti, D., Smuts, C. M., & Zimmermann, M. B. (2018). Sensitivity of fatty acid desaturation and elongation to plasma zinc concentration: A randomised controlled trial in Beninese children. *British Journal of Nutrition*, 119(6), 610-619.
- Chong, P. W., Beah, Z. M., Grube, B., & Riede, L. (2014). IQP-GC-101 reduces body weight and body fat mass: A randomized, double-blind, placebo-controlled study. *Phytotherapy Research*, 28(10), 1520-1526. doi:10.1002/ptr.5158
- Chung, A. P. Y., Gurtu, S., Chakravarthi, S., Moorthy, M., & Palanisamy, U. D. (2018). Geraniin protects high-fat diet-induced oxidative stress in Sprague Dawley rats. *Frontiers in Nutrition*, 5, 17. doi:10.3389/fnut.2018.00017
- El-Shiekh, R. A., Al-Mahdy, D. A., Mouneir, S. M., Hifnawy, M. S., & Abdel-Sattar, E. A. (2019). Anti-obesity effect of argel (Solenostemma argel) on obese rats fed a high fat diet. *Journal of Ethnopharmacology*, 238, 111893. doi:10.1016/j.jep.2019.111893
- Fossati, P., & Prencipe, L. (1982). The determination of triglyceride using enzymatic methods. *Clinical Chemistry*, 28, 2077-2080.
- Gaikwad, S. S., & Choudhari, V. P. (2022). Efficacy and safety of combination therapy of zinc and silver oxide nanoparticles in streptozotocin-induced diabetic rats. *International Journal of Pharmaceutical Research & Allied Sciences*, 11(3), 1-10.
- Ghanbari, E., Nejati, V., & Khazaei, M. (2016). Improvement in serum biochemical alterations and oxidative stress of liver and pancreas following use of royal jelly in streptozotocin-induced diabetic rats. *Cell Journal (Yakhteh)*, 18(3), 362-370.
- Habig, W. H., Pabst M. J., & Jacoby, W. B. (1974). Glutathione S-transferases: The first enzymatic step in mercapturic acid formation. *Journal Biological Chemistry*, 249, 7130-7139.
- Harish, V., Ansari, M. M., Tewari, D., Gaur, M., Yadav, A. B., García-Betancourt, M. L., Abdel-Haleem, F. M., Bechelany, M., & Barhoum, A. (2022). Nanoparticle and nanostructure synthesis and controlled growth methods. *Nanomaterials*, 12(18), 3226. doi:10.3390/nano12183226
- Hashemipour, M., Kelishadi, R., Shapouri, J., Sarrafzadegan, N., Amini, M., Tavakoli, N., Movahedian-Attar, A., Mirmoghtadaee, P., & Poursafa, P. (2009). Effect of zinc supplementation on insulin resistance and components of the metabolic syndrome in prepubertal obese children. *Hormones*, 8(4), 279-285.
- Julián, M. T., Alonso, N., Ojanguren, I., Pizarro, E., Ballestar, E., & Puig-Domingo, M. (2015). Hepatic glycogenosis: An underdiagnosed complication of diabetes mellitus? *World Journal of Diabetes*, 6(2), 321-325.
- Ko, J. W., Hong, E. T., Lee, I. C., Park, S. H., Park, J. I., Seong, N. W., Hong, J. S., Yun, H. I., & Kim, J. C. (2015). Evaluation of 2-week repeated oral dose toxicity of 100 nm zinc oxide nanoparticles in rats. *Laboratory Animal Research*, 31, 139-147.
- Kumar, S. S., Venkateswarlu, P., Rao, V. R., & Rao, G. N. (2013). Synthesis, characterization and optical properties of zinc oxide nanoparticles. *International Nano Letters*, 3, 1-6.
- Lee, J., Hosseindoust, A., Kim, K., Kim, T., Mun, J., Chae, B., & Kim, M. (2022). Improved growth performance, antioxidant status, digestive enzymes, nutrient digestibility and zinc bioavailability of broiler chickens with nano-sized hot-melt

- extruded zinc sulfate. *Biological Trace Element Research*, 200(3), 1321-1330. doi:10.1007/s12011-021-02747-6
- Leon-Cabrera, S., Solís-Lozano, L., Suárez-Álvarez, K., González-Chávez, A., Béjar, Y. L., Robles-Díaz, G., & Escobedo, G. (2013). Hyperleptinemia is associated with parameters of low-grade systemic inflammation and metabolic dysfunction in obese human beings. *Frontiers in Integrative Neuroscience*, 7, 62. doi:10.3389/fnint.2013.00062
- Li, J., & Shen, X. (2019). Oxidative stress and adipokine levels were significantly correlated in diabetic patients with hyperglycemic crises. *Diabetology & Metabolic Syndrome*, 11(1), 1-8. doi:10.1186/s13098-019-0410-5
- Li, J., Cha, R., Luo, H., Hao, W., Zhang, Y., & Jiang, X. (2019). Nanomaterials for the theranostics of obesity. *Biomaterials*, 223, 119474-119488.
- Lopes-Virella, M. F., Stone, P., Ellis, S., & Colwell, J. A. (1977). Cholesterol determination in high-density lipoproteins separated by three different methods. *Clinical Chemistry*, 23(5), 882-884.
- Mahmoud, A. H., AbdElMonem, H. A., & Abbas, M. M. (2022). The role of selenium and zinc oxide nanoparticles on mitigating side effects of obesity in rats. *Brazilian Journal of Biology*, 84, e264004. doi:10.1590/1519-6984.264004
- Mansouri, E., Khorsandi, L., Orazizadeh, M., & Jozi, Z. (2015). Dose-dependent hepatotoxicity effects of zinc oxide nanoparticles. *Nanomedicine Journal*, 2(4), 2015, 273-282.
- Nilesh, K., Dadhich, A., Saluja, H., Patil, D., & Vande, A. (2021). Treatment of oral submucous fibrosis with lycopene, beta-carotene, zinc, selenium, copper, alpha-lipoic acid, and alpha-tocopheryl acetate. *Annals of Dental Specialty*, 9(2), 1-6.
- Norouzi, S., Adulcikas, J., Sohal, S. S., & Myers, S. (2018). Zinc stimulates glucose oxidation and glycemic control by modulating the insulin signaling pathway in human and mouse skeletal muscle cell lines. *Plos One*, 13(1), e0191727. doi:10.1371/journal.pone.0191727
- Omarov, U. G., Nikiforov, I. A., Alibekov, M. A., Kadakoeva, D. A., Makarenko, N. V., & Starodubtsev, A. I. (2023). Effect of drugs based on silver, copper, and zinc nanoparticles on skin wound healing in rats. *Archives of Pharmacy Practice*, 14(2), 66-69.
- Petrick, L., Rosenblat, M., Paland, N., & Aviram, M. (2016). Silicon dioxide nanoparticles increase macrophage atherogenicity: Stimulation of cellular cytotoxicity, oxidative stress, and triglycerides accumulation. *Environmental Toxicology*, 31(6), 713-723.
- Polevoy, G. G., Sablin, A. B., & Chernishev, S. V. (2022). Development of equilibrium in dynamic and static conditions in children aged 8-9 years using standard classics. *Journal of Organizational Behavior Research*, 7(2), 310-316.
- Potphode, N. D., Daunde, J. A., Desai, S. S., & Walvekar, M. V. (2018). Nano-curcumin: A potent enhancer of body antioxidant system in diabetic mice. *International Journal of Phytomedicine*, 10(3), 162-167.
- Rasmussen, J. W., Martinez, E., Louka, P., & Wingett, D. G. (2010). Zinc oxide nanoparticles for selective destruction of tumor cells and potential for drug delivery applications. *Expert Opinion on Drug Delivery*, 7(9), 1063-1077.
- Reed, S., Qin, X., Ran-Ressler, R., Brenna, J. T., Glahn, R. P., & Tako, E. (2014). Dietary zinc deficiency affects blood linoleic acid: Dihomo- γ -linolenic acid (LA: DGLA) ratio; a sensitive physiological marker of zinc status in vivo (Gallus gallus). *Nutrients*, 6(3), 1164-1180.
- Reitman, S., & Frankel, S. (1957). A colorimetric method for the determination of serum glutamic oxalacetic and glutamic pyruvic transaminases. *American Journal of Clinical Pathology*, 28(1), 56-63.
- Sairam, K., Priyambada, S., Aryya, N. C., & Goel, R. K. (2003). Gastroduodenal ulcer protective activity of *Asparagus racemosus*: An experimental, biochemical and histological study. *Journal of Ethnopharmacology*, 86(1), 1-10.
- SAS System for Windows (Statistical Analysis System) (2008). Version 9.2. Cary, USA: SAS Institute.
- Shetty, B., Chauhan, R. S., Vishwas, P., Rath, N., Krishnapriya, N., & Tirupathi, S. (2022). Antimicrobial efficacy of curcumin modified zinc oxide eugenol against endodontic pathogens. *Annals of Dental Specialty*, 10(1), 47-51.
- Shirvani, H., Noori, A., & Mashayekh, A. M. (2014). The effect of ZnO nanoparticles on the growth and puberty of newborn male Wistar rats. *International Journal of Basic Sciences & Applied Research*, 3, 180-185.
- Siddiqui, S. A., Or Rashid, M. M., Uddin, M. G., Robel, F. N., Hossain, M. S., Haque, M. A., & Jakaria, M. (2020). Biological efficacy of zinc oxide nanoparticles against diabetes: A preliminary study conducted in mice. *Bioscience Reports*, 40(4), BSR20193972. doi:10.1042/BSR20193972
- Skrajnowska, D., & Bobrowska-Korczak, B. (2019). Role of zinc in immune system and anti-cancer defense mechanisms. *Nutrients*, 11(10), 2273.
- Steinberg, D. (1981). Metabolism of lipoproteins at the cellular level about atherogenesis. *Lipoproteins, Atherosclerosis and Coronary Heart Disease*, 1(2), 31-48.
- Tietz, N. W. (1986). Text Book of Clinical Chemistry. P.796. Saunders, W. B. Co., London-Philadelphia.
- Tran, A. D., Do, L. H., & Lai, L. T. T. (2023). The impact of monetary policy on environmental pollution in a transition country: The case of Vietnam. *Journal of Organizational Behavior Research*, 8(2), 54-65.
- Uyoyo Ukperoro, J., Offiah, N., Idris, T., & Awogoke, D. (2010). Antioxidant effect of zinc, selenium and their combination on the liver and kidney of alloxan-induced diabetes in rats. *Mediterranean Journal of Nutrition and Metabolism*, 3, 25-30.
- Vial, G., Dubouchaud, H., Couturier, K., Cottet-Rousselle, C., Taleux, N., & Athias, A. (2011). Effects of a high-fat diet on energy metabolism and ROS production in rat liver. *Journal of Hepatology*, 54(2), 348-356. doi:10.1016/j.jhep.2010.06.044
- Virgen-Ortiz, A., Apolinar-Irribé, A., Díaz-Reval, I., Parra-Delgado, H., Limón-Miranda, S., Sánchez-Pastor, E. A., Castro-Sánchez, L., Jesús Castillo, S., Dagnino-Acosta, A., Bonales-Alatorre, E., et al. (2020). Zinc oxide nanoparticles induce an adverse effect on blood glucose levels depending

- on the dose and route of administration in healthy and diabetic rats. *Nanomaterials*, 10(10), 2005. doi:10.3390/nano10102005
- Wang, C., Zhang, L., Ying, Z., He, J., Zhou, L., Zhang, L., Zhong, X., & Wang, T. (2018). Effects of dietary zinc oxide nanoparticles on growth, diarrhea, mineral deposition, intestinal morphology, and barrier of weaned piglets. *Biological Trace Element Research*, 2, 1-11.
- Wasowicz, W., Reszka, E., Gromadzinska, J., & Rydzynski, K. (2003). The role of essential elements in oxidative stress. *Comments on Toxicology*, 9(1), 39-48.
- Wei, Q. Y., Chen, W. F., Zhou, B., Yang, L., & Liu, Z. L. (2006). Inhibition of lipid peroxidation and protein oxidation in rat liver mitochondria by curcumin and its analogues. *Biochimica et Biophysica Acta (BBA)-General Subjects*, 1760(1), 70-77.
- Yoshioka, T., Kawada, K., Shimada, T., & Mori, M. (1979). Lipid peroxidation in maternal and cord blood and protective mechanism against activated-oxygen toxicity in the blood. *American Journal of Obstetrics and Gynecology*, 135(3), 372-376.
- Yuvaraj, A., Priyadharshini, R., Kumar, R., & Sinduja, P. (2023). Anti-inflammatory and antifungal activity of zinc oxide nanoparticle using red sandalwood extract. *Pharmacophore*, 14(1), 25-31.
- Zhao, Y., Li, L., Zhang, P. F., Liu, X. Q., Zhang, W. D., Ding, Z. P., Wang, S. W., Shen, W., Min, L. J., & Hao, Z. H. (2016). Regulation of egg quality and lipids metabolism by Zinc Oxide Nanoparticles. *Poultry Science*, 95(4), 920-933.