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Research Article

Impact of *Peganum harmala*/Zinc Oxide Nanoparticles on Thyroid and Pancreatic Function in Obese Rats: A Biochemical and Physiological Analysis

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Abstract

Background and Objective: Obesity is widespread in both developed and developing nations and it is one of the major risk factors for diseases like diabetes mellitus type II, hypertension and atherosclerosis. *Peganum harmala* (*P. harmala*) is considered as an effective anti-cancer, anti-inflammatory and hypolipidemic agent. This study examined how the methanolic extract of harmala nanoparticle extract affects the alterations in diabetic state and thyroid hormone levels in obese rats induced by a high-calorie diet.

Materials and Methods: A total of 36 male rats were divided into two groups (obese and normal), each of which was further divided into 3 sub-groups. Obesity was induced with a high-calorie diet for one month. Harmal zinc oxide nanoparticles (H/ZnO NPs) 200 and 400 mg/kg b.wt/day were administered orally for one month. After 4 weeks of treatment, blood and tissue samples were collected and analyzed for glucose and insulin levels, lipid profile, thyroid hormones and pancreas histology. **Results:** It showed that the treatment with H/ZnO NPs in obese rats significantly reduced blood glucose and increased insulin levels, suggesting improved insulin sensitivity and decreased cholesterol, triglycerides and LDL, indicating a better lipid profile. Additionally, H/ZnO NPs partially corrected hypothyroidism by increasing T3 and T4 levels and even improved pancreatic islet morphology compared to untreated rats.

Conclusion: The supplementation of H/ZnO NPs has a strong anti-obesity effect in rats by improving glucose utilization and enhancing the secretion of thyroid and pancreatic hormones.

Key words: Obesity, diabetes mellitus, *Peganum harmala*, insulin, thyroid hormones

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Over the past 50 years, many countries have significantly improved life expectancy and overall health. However, the obesity epidemic has emerged as a persistent problem with 42% of United States adults and 20% of children and adolescents being classified as obese in 2017¹. However, recent investigations suggest that the prevalence of obesity has ceased to increase in certain countries². Obesity can cause the release of pro-inflammatory chemicals, cytokines and hormones from fat cells due to increased free fatty acids (FFA). This can lead to reduced sensitivity to insulin in the body, causing cells to be unresponsive to insulin. This, in turn, can contribute to the development of insulin resistance and dysfunction of pancreatic islet beta-cells that produce insulin, ultimately leading to uncontrolled blood glucose levels³.

Obesity is a significant risk factor for several health conditions, including type II diabetes, cancer and cardiovascular diseases⁴. Obesity and hypothyroidism are two clinical conditions that are closely linked. Hypothyroidism has been linked to lower thermogenesis and metabolic rate, as well as a higher BMI and obesity prevalence. This link has become more significant due to the increasing prevalence of obesity globally⁵. Insulin resistance is often suggested as the primary causative factor for the metabolic syndrome and its associated conditions, such as Type 2 Diabetes (T2D) related to obesity⁶.

Thyroid hormones play a pivotal role in regulating body metabolism and maintaining energy balance. Hyperthyroidism has been associated with promoting high blood sugar levels, leading to poor glycemic control in diabetic patients and an increased risk of diabetic ketoacidosis⁷. However, clinical and subclinical hypothyroidism have been recognized as risk factors for metabolic syndrome. Several research have explored the association between thyroid hormone levels and insulin resistance; however the findings are conflicting. Overall, thyroid dysfunction is believed to be linked to insulin resistance, but further research is needed to fully understand this relationship⁸. Insulin resistance has been linked to both hypo- and hyperthyroidism, although the underlying mechanisms may differ for each condition and are not well understood⁹.

Peganum harmala, which is a member of the Zygophyllaceae family, is used in traditional medicinal practices in Pakistan, China, Morocco, Algeria and Spain to address various chronic health conditions¹⁰. The extracts derived from *Peganum harmala* have been found to possess a wide range of biological activities, such as anti-inflammatory,

antimicrobial, fungicidal, antiviral, antioxidant, pain reliver, cardio-protective, antitumor, antidiabetic, histo-functional, cerebral protective, anti-proliferative and cancer-preventing properties¹¹⁻¹⁶. Recent research found that the methanol extract of *P. harmala* leaves had antioxidant properties similar to those of the conventional chemicals quercetin and rutoside¹⁷. The observed effects of *Peganum harmala* are primarily attributed to its alkaloid components, such as harmaline, harmine and harman¹⁸.

Elevated insulin levels in type 2 diabetic rats are often linked to the development of insulin resistance. Nevertheless, administration of *P. harmala* led to decreased insulin levels in diabetic rats, suggesting its potential efficacy in mitigating insulin resistance. According to the findings, the extract from *P. harmala* seeds does not directly trigger the release of insulin. This implies that the extract from *P. harmala* seeds could potentially lower blood sugar levels may be achieved via affecting the absorption and utilization of glucose¹⁹.

Therapy with *P. harmala* was found to lower plasma glucose levels and increase plasma insulin levels. The seed extract of *P. harmala* was shown to be more effective than its active component, harmine, in preventing diabetes-related apoptosis. This may be due to the extract's high concentration of antioxidants and β -carboline chemicals²⁰.

The aim of the present study was to evaluate the therapeutic effect of *Peganum harmala*/zinc oxide nanoparticles (H/ZnO NPs) on obesity induced by a high-fat diet (HFD).

MATERIALS AND METHODS

Study area: The experiment took place at the Faculty of Veterinary Medicine at Mansoura University in Egypt. The experiment ran from August, 2022 to May, 2023.

Animals: While 36 mature male *Rattus norvegicus* rats weighing 200-250 g were used. The animals were achieved from the Faculty of Veterinary Medicine's Animal House at Mansoura University, Egypt. The animals were kept in conventional conditions, with aeration and a room temperature of approximately 25 °C. The animals were housed in metal cages with bedding made of wood shavings. The animals had unlimited access to their regular meals and water. Before being subjected to an experiment, the animals spent two weeks in the lab environment for adaptation. Obesity was conducted in half the number of animals through a fat-rich diet containing 20% fat based on NRC *et al.*²¹, the animal could be free access to diet for 4 weeks.

Ethical approval: All the experiment is approved by the Institutional Animal Care and Use Committee at Zagazig University, Egypt, (ZU-IACUC), with the approval number ZU-IACUC/1/F/81/2022.

***Peganum harmala*/zinc oxide nanoparticles preparation:**

Harmal zinc oxide nanoparticles were prepared after harmal seed extract according to the method mentioned by Ismail *et al.*²². The structure, form and dimensions of H/ZnO NPs were examined using scanning and transmission electron microscopy (TEM; JEM 1400 plus, JEOL Ltd., Japan) and transmission electron microscopy (SEM; JCM 5700, JEOL Ltd., Japan). Following suitable sample dilutions, the zeta potential (surface charge; mV) of the H/ZnO-NPs was determined using the zeta-potential analyzer ELSZ-2000, Otsuka Electronics, Japan.

Experimental design: The rats were divided into two main groups, with 18 rats in each group. Each of the three subgroups of obese and non-obese rats is provided with a basal diet and subjected to the following specified treatment protocol.

Non-obese group divided into:

- **G1:** Control-fed basal diets
- **G2:** Basal diets+*Peganum harmala*/ZnO nanoparticles (200 mg/kg/day) orally by orogastric tube²³
- **G3:** Basal diets+*Peganum harmala*/ZnO nanoparticles (400 mg/kg/day) orally by orogastric tube²³

Obese group is divided into:

- **G4:** High-fat diet²⁴
- **G5:** High-fat diet+*Peganum harmala*/ZnO nanoparticles (200 mg/kg/day) orally by orogastric tube²³
- **G6:** High-fat diet+*Peganum harmala*/ZnO nanoparticles (400 mg/kg/day) orally by orogastric tube²³

Sampling: After the 4-week of treatment, the animals were anesthetized and blood was drawn from the retro-orbital venous plexus into a clean tub and allowed to coagulate to collect serum, which was then stored frozen at -20°C until biochemical and hormonal assay.

Determination of serum glucose: Serum glucose was determined using commercially available kits according to manufacturer instructions.

Determination of hormones: A solid phase enzyme amplified sensitivity immunoassay for insulin was conducted on microtiter plates. This assay utilizes monoclonal antibodies (MABs) targeted against specific epitopes of insulin. The utilization of multiple distinct (MABs) enables highly sensitive assays with an expanded standard range and short incubation time²⁵. For thyroid gland hormones, commercial ELISA kits supplied by Abcam Co. (United States) were used for the quantitative determination of thyroid hormones (T3) according to Braverman *et al.*²⁶ and T4 according to Ormston *et al.*²⁷.

Determination of serum triglycerides (TG) and total cholesterol (TC) concentration: Serum triglycerides and cholesterol levels were measured using a colorimetric method with a spectrum kit (Egyptian Company for Biotechnology, Obour City, Cairo, Egypt), following the manufacturer's instructions.

Determination of High and Low-Density Lipoproteins (HDL and LDL): Serum HDL-cholesterol and LDL was determined according to Fotschki *et al.*²⁸ and Friedewald *et al.*²⁹, respectively.

Histopathological and scoring systems: The pancreatic tissue samples were fixed in 10% neutral buffered formalin for 48 hrs to ensure proper preservation. Subsequently, they were washed eight times under running water, dehydrated using increasing concentrations of alcohol and embedded in paraffin wax. Following this, the samples were sectioned into four µm-thick slices using a rotary microtome and deparaffinized using xylene. Finally, the sections were stained with Hematoxylin and Eosin (H&E) in a routine manner³⁰. The sections were examined using light microscopy and images were captured at X: 100 and X: 400 magnifications to detect any pathological changes. Semi-quantitative scoring of pancreatic damage was assessed using histological grading, ranging from 0 to 3 as follows: 0 = no damage, 1 = mild damage (less than 33%), 2 = moderate damage (more than 33% and less than 66%) and 3 = severe damage (more than 66%). Additionally, the diameter of pancreatic islets was measured using ImageJ software (v 1.53, National Institutes of Health, USA).

Statistical analysis: The data obtained from the experiments were presented as Mean ± Standard Deviation (±SD). Statistical differences in measured biochemical parameters among experimental groups were assessed using one-way

ANOVA and Tukey's *post hoc* tests with SPSS computer software program version 19. A mean difference was considered significant when $p < 0.05$. The histopathological damage score (non-parametric data) was analyzed using Kruskal-Wallis test followed by Dunn's test for comparing all means. The diameter of islets (parametric data) was analyzed using one-way ANOVA and Tukey's *post hoc* tests with SPSS computer software program version 19.

RESULTS

Effects of treatment of rats with H/ZnO NPs on serum glucose levels:

Serum glucose levels showed significant increases in obese rats compared to non-obese normal rats ($p = 0.0091$) and normal rats receiving 200 mg H/ZnO ($p = 0.0004$) and 400 mg H/ZnO ($p = 0.0003$). However, treatment of obese rats with H/ZnO nanoparticles at the doses of 200mg and 400 mg significantly reduced the elevated serum glucose ($p = 0.0162$ and 0.0204 , respectively) with no statistical difference between both groups and either of them or the control non obese rats (Fig. 1a).

Effects of treatment of rats with H/ZnO NPs on serum insulin:

The results showed that treatment with H/ZnO nanoparticle in a dose of 200mg non-significantly increased serum insulin ($p = 0.227$) but 400 mg H/ZnO nanoparticle significantly increased serum insulin ($p = 0.0052$) when compared to the control non obese rats. Moreover, the rats of the obese groups showed significant increases when

compared with nonobese control rats or rats receiving H/ZnO nanoparticle in both doses ($p < 0.0001$ except when comparing group 3 with group 4 $p = 0.0003$). The increased dose of H/ZnO nanoparticles significantly increase serum insulin when compared to the HFD obese rats ($p = 0.043$). There was non-statistically significant difference when comparing the non-obese control and nonobese control receiving low dose ($p = 0.227$) or when comparing nonobese control receiving low versus high dose ($p = 0.263$), similar finding when comparing obese rats and obese rats treated with the low dose or when comparing obese rats receiving low versus high dose ($p = 0.493$ and 0.595 , respectively) (Fig. 1b).

Effects of H/ZnO NPs treatment on thyroid hormones (T3 and T4):

Regarding T3 and T4, there was no statistical difference between control nonobese rats and nonobese rats receiving low dose, on the other hand there was significant increase when comparing the nonobese control rats and the nonobese rats receiving high dose ($p = 0.0014$ and 0.0001 , respectively). The result showed that obese rats showed significant decreases in serum T3 and T4 when compared with nonobese control rats, nonobese and obese rats receiving H/ZnO nanoparticles in low and high doses ($p < 0.0001$). Obese rats treated with H/ZnO nanoparticles significantly increase the serum T3 levels when compared with obese non treated rats ($p < 0.0001$). High dose H/ZnO nanoparticles significantly increase T3 and T4 when compared to low dose ($p < 0.0001$) (Fig. 2).

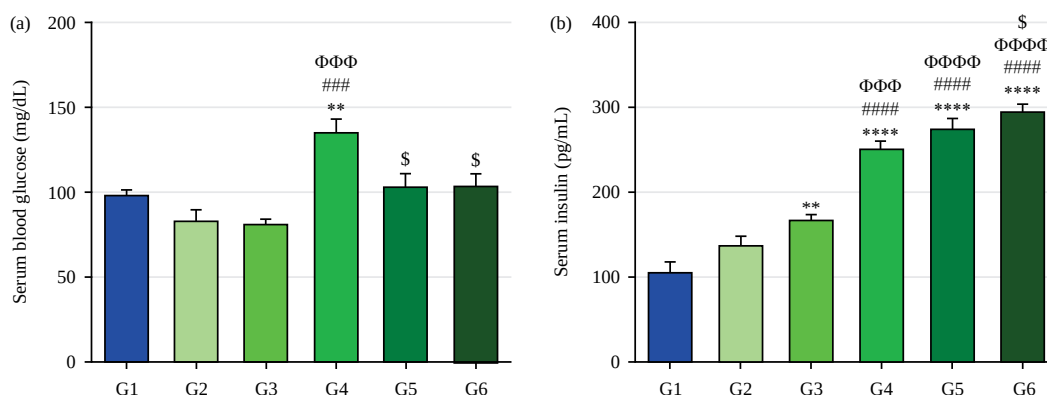


Fig. 1(a-b): Histogram showing the H/ZnO NPs treatment on (a) Serum concentration of glucose and (b) Insulin

G1: Consists of nonobese rats on a standard diet (control-negative group), G2: Includes nonobese rats receiving H/ZnO nanoparticles at a dosage of 200 mg/kg/day, G3: Comprises nonobese rats on a standard diet treated with H/ZnO nanoparticles at a dosage of 400 mg/kg/day, G4: Composed of obese rats on a high-fat diet (control-positive group), G5: Involves obese rats receiving H/ZnO nanoparticles at a dosage of 200 mg/kg/day, G6: Consists of obese rats receiving H/ZnO nanoparticles at a dosage of 400 mg/kg/day, *Significance vs G1, #Significance vs G2, ΦSignificance vs G3 and \$Significance vs G4

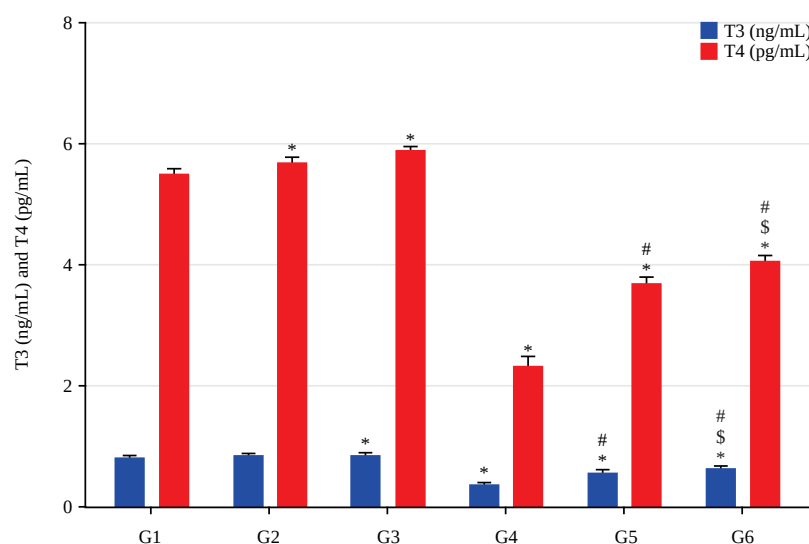


Fig. 2: Histogram showing the effects of H/ZnO NPs treatment on thyroid hormones (T3 and T4)

G1: Consists of nonobese rats on a standard diet (control-negative group), G2: Includes nonobese rats receiving H/ZnO nanoparticles at a dosage of 200 mg/kg/day, G3: Comprises nonobese rats on a standard diet treated with H/ZnO nanoparticles at a dosage of 400 mg/kg/day, G4: Composed of obese rats on a high-fat diet (control-positive group), G5: Involves obese rats receiving H/ZnO nanoparticles at a dosage of 200 mg/kg/day, G6: Consists of obese rats receiving H/ZnO nanoparticles at a dosage of 400 mg/kg/day, *Significance vs G1, #Significance vs G4 and \$Significance vs G5

Table 1: Effects of H/ZnO NPs treatment on the lipid profile of rats in the studied groups (TG, TC, LDL and HDL)

	TG (mg/dL)	TC (mg/dL)	LDL (mg/dL)	HDL (mg/dL)
G1	101.2±10.06	85.18±5.7	13.92±1.32	50.69±6.31
G2	94.81±7.87	79.13±3.16	10.35±1.45	49.08±5.73
G3	83.64±8.26	77.56±2.11	8.780±1.36	50.01±7.61
G4	175.2±13.9*	147.5±8.36*	68.33±5.51*	44.79±5.65
G5	151.3±12.5**	129.4±9.04**	53.59±4.19**	44.94±4.42
G6	130.4±9.10**\$	111.7±6.15**\$	37.52±3.87**\$	47.31±4.95

G1: Consists of nonobese rats on a standard diet (control-negative group), G2: Includes nonobese rats receiving H/ZnO nanoparticles at a dosage of 200 mg/kg/day, G3: Comprises nonobese rats on a standard diet treated with H/ZnO nanoparticles at a dosage of 400 mg/kg/day, G4: Composed of obese rats on a high-fat diet (control-positive group), G5: Involves obese rats receiving H/ZnO nanoparticles at a dosage of 200 mg/kg/day, G6: Consists of obese rats receiving H/ZnO nanoparticles at a dosage of 400 mg/kg/day, *Significance vs G1, #Significance vs G4 and \$Significance vs G5

Effects of H/ZnO NPs treatment on lipid profile (TG, TC, LDL and HDL): The results showed significant increase in TG, TC and LDL in the obese rats when compared to the control nonobese rats or nonobese rats receiving H/ZnO NPs in low or high dose. Additionally, obese rats treated with H/ZnO NPs showed significant decrease in TG, TC and LDL when compared to obese non treated rats. The high dose (400 mg/kg/day) treated rats showed significant decrease when compared to low dose (200 mg/kg/day). Regarding the HDL, there were non statistically significant changes among the studied groups (T1) (Table 1).

Effects of H/ZnO NPs treatment of rats on the histology of the pancreas: Normal and intact Langerhans islands and exocrine pancreas in the control group and non-obese groups G1-G3 (Fig. 3a-c and Fig. 4a-c). Marked shrinkage and damage

of Langerhans islands and exocrine pancreas was detected in obese group G4 (Fig. 3d and Fig. 4d-e). Moderate improvement of histology of Langerhans islands and exocrine pancreas were observed in G5 (Fig. 3e and Fig. 4f-g), while marked improvement of histology of Langerhans islands and exocrine pancreas were observed in G6 (Fig. 3f and Fig. 4h-i).

DISCUSSION

The present study was an attempt to evaluate the protective effect of *P. harmala* extract/ZnO NPs on thyroid and pancreatic hormones and metabolites related to them in experimental obese rats. The results proved that treatment of rats with H/ZnO NPs could improve the negative impact of obesity on glucose and insulin levels. The H/ZnO NPs significantly decrease serum levels of glucose in treated rats,

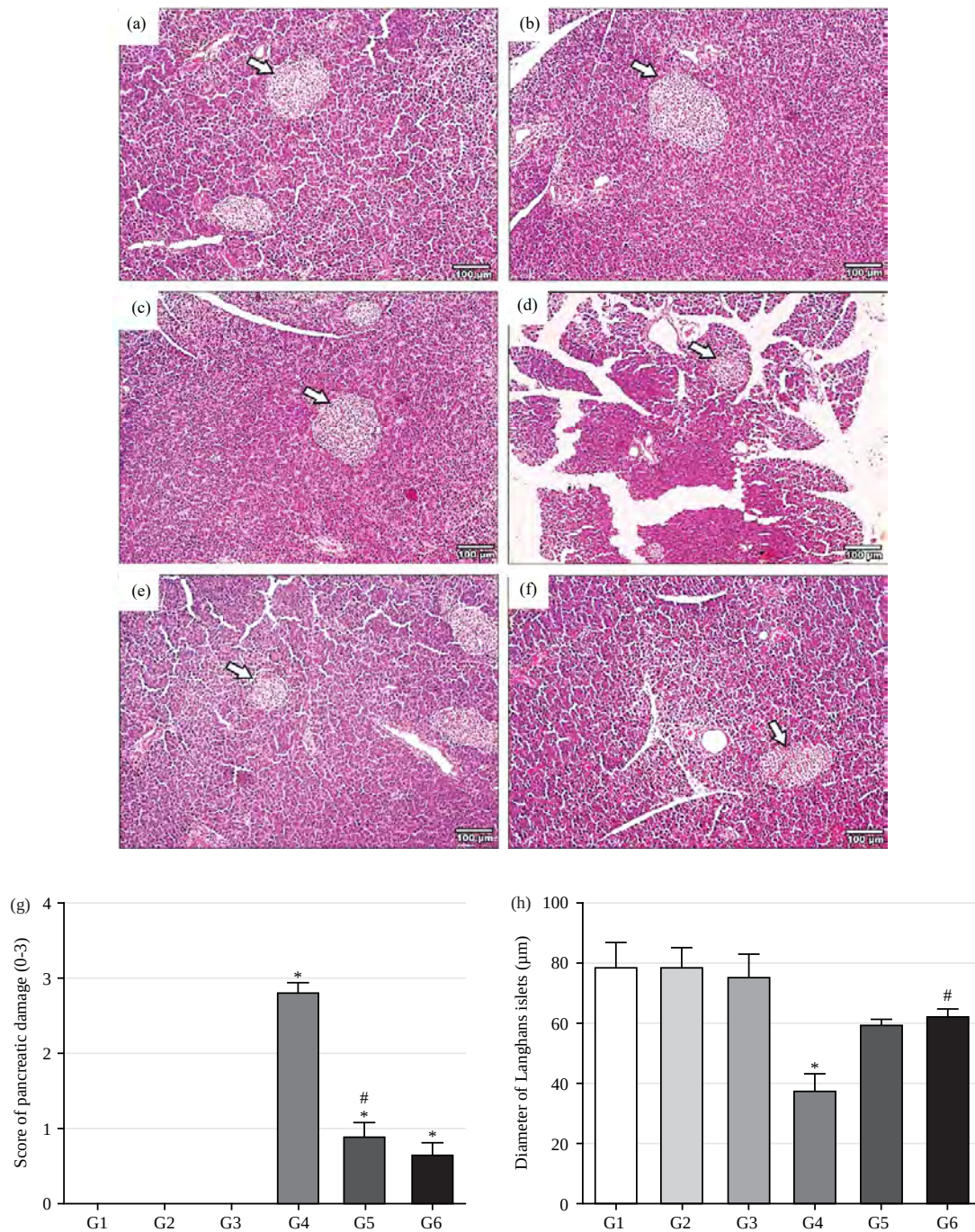


Fig. 3(a-h): (a-c) Microscopic pictures of pancreatic sections showing normal and intact Langerhans islands (thick arrows) and exocrine pancreas in the control group and non-obese groups G1-G3, (d) Pancreatic sections from obese group G4 showed marked shrinkage of Langerhans islands (thick arrows) and exocrine pancreas and distorted normal pancreatic architecture, (e,f) Treated groups show retaining of the normal pancreatic architecture, (g) Damage score showed a significant decrease in damage scores is seen in treated group G6 when compared with G4, but still higher than that of control group G1 and (h) Langham's islets diameter showed a significant decrease in G4 which was significantly increased in G6 treated rats when compared to diabetic rats G4

Data in bars represent Means $\pm$ SD of lesional scores in H&E stained pictures picked up at X: 100 from all groups analyzed by Kruskal-Wallis followed by Dunn's test to compare all means, *Means significant compared to non-obese groups G1-G3 and #Means significant compared to obese group G4

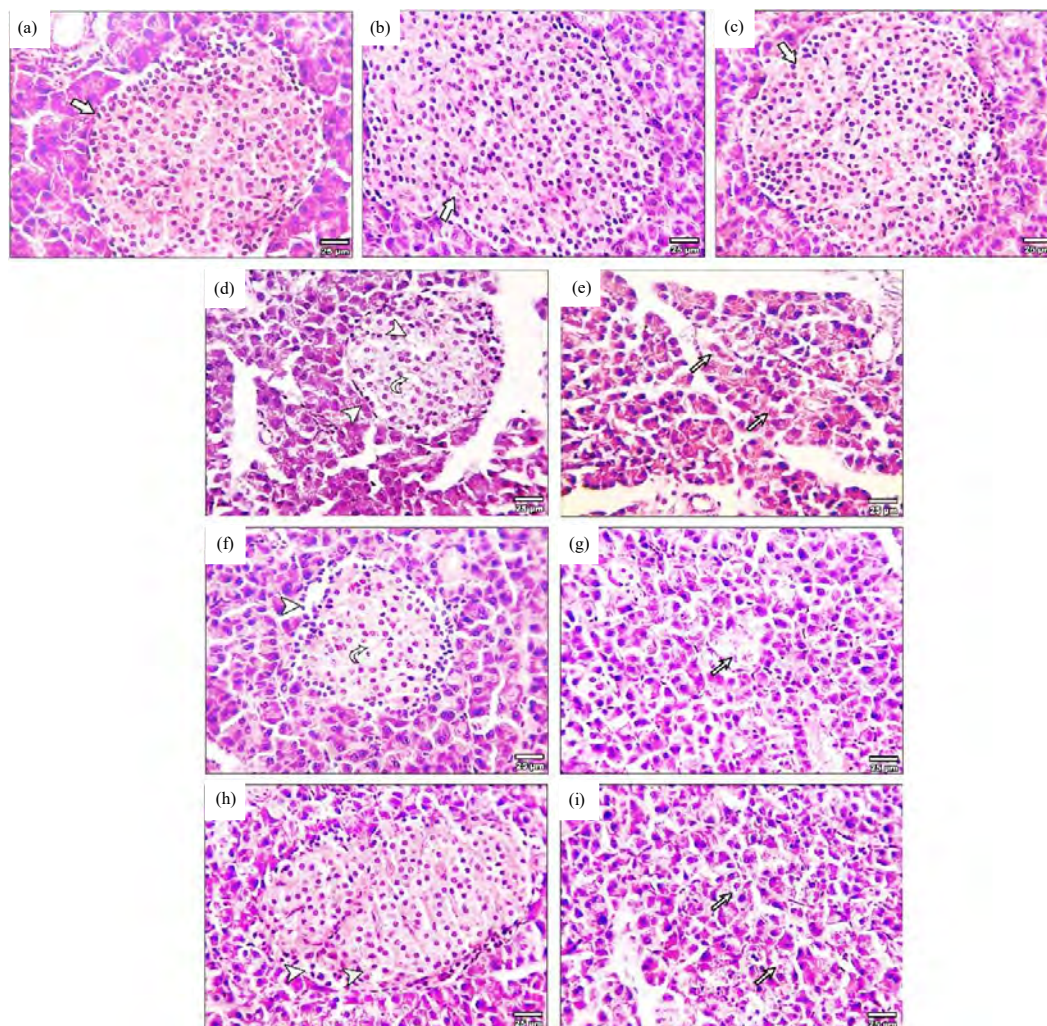


Fig. 4(a-i): (a-c) Microscopic pictures of pancreatic sections showing normal and intact Langerhans Islands (thick arrows) and exocrine pancreas in the control group and non-obese groups G1-G3, Alpha and beta cells were distributed normally, (d-e) Pancreatic sections from obese group G4 showed marked shrinkage of Langerhans islands (thick arrows) and exocrine pancreas, apoptosis of alpha and beta cells (arrowheads), vacuolation of beta cells (curved arrows), besides prominent hydropic degeneration in epithelial cells lining exocrine acini (thin arrows). (f-g) Pancreatic sections from treated obese group G5 showed marked apoptosis of alpha cells (arrowheads), mild vacuolation of beta cells (curved arrows), besides mild hydropic degeneration in epithelial cells lining exocrine acini (thin arrows) and (h-i) Pancreatic sections from treated obese group G6 showed mild apoptosis of alpha cells (arrowheads), besides moderate hydropic degeneration in epithelial cells lining exocrine acini (thin arrows)

moreover treated rats showed significant increases in insulin levels when compared with control groups. Current results agreed with Safamanesh *et al.*²⁰, who found that *P. harmala* treatment decreased plasma glucose levels while increasing plasma insulin levels.

The antidiabetic effects of harmin may be related to high concentrations of antioxidants and carboline chemicals as previously cited by Singh *et al.*¹⁸. Alternatively, it has been documented that *P. harmala* seed extract has no impact on

insulin secretion. Therefore, its potential hypoglycemic effect may be attributed to its influence on glucose absorption and utilization¹⁹. Moreover, Alkaladi *et al.*³¹ found that ZnO NPs potentiates insulin expression and lowers blood glucose significantly. These data could explain the results obtained in this study, especially in H/ZnO NPs-treated groups. In the same respect hyperinsulinemia and hyperglycemia were associated with obesity³². They referred to these effects as developing insulin resistance associated

with obesity. These results could explain the elevated insulin and hyperglycemic data reported in obese rats in this study.

On the other side, *P. harmala* seed extract is more potent at preventing diabetes-related apoptosis, this property appears to be brought about by a high concentration of antioxidants and carboline chemicals¹⁸. Ethanolic extract of *P. harmala* seed significantly reduced blood glucose levels in healthy and diabetic rats.

Regarding data on thyroids hormones, the results showed that obese rats showed significant decreases when compared with nonobese groups. Treatment of obese rats with H/ZnO nanoparticles significantly improved serum levels of T3 and T4 when compared with control obese groups but did not return to the levels of normal rats. The relationship between the thyroid gland and obesity is complex and bidirectional as many studies have shown that obesity can occur accompanied with change or without change in the thyroid hormones in obese individuals³³. In the same respect, changes in thyroid activities accompanied with obesity not established until now whether are primary or secondary effect³⁴. The previous data may explain the obtained results in this study where the obese group showed a condition of significant hypothyroidism when compared with the normal control one. Contrary to our results, obese individuals showed significant increases in serum TSH and T3 levels³⁵. Similarly, a moderate increase in T3 or free T3 (fT3) levels has been reported in obese subjects³⁶. The mechanism explaining the change in the thyroid level is still unclear. However several mechanisms have been reported including that related to adaptive mechanisms to increase energy expenditure or the effect of leptin or insulin resistance accompanied by obesity³⁷.

In the present study, it is reported that treatment of rats with H/ZnO NPs could improve the level of thyroids hormones as compared with control non-treated groups. Short-term treatment with zinc oxide will reduce T3 and medium and long-term administration will increase T3 and T4 as zinc oxide documented to increase TSH³⁸. This could explain the increased levels of thyroid hormones in H/ZnO NPs-treated groups.

Harmala is a potent inhibitor of the hypothalamus-pituitary-thyroid axis as it inhibits TSH and consequently T3 and T4³⁹. These data are opposite to the obtained results and this controversy resulted from our study including zinc oxide in the experimental design with harmala, but previous studies considered only harmala.

The lipid profile data from the current study indicated a significant increase in hyperlipidemia, as evidenced by elevated serum levels of TC, TG and LDL in the obese groups compared to the normal group. However, in the groups

treated with H/ZnO NPs, the serum lipid parameters showed a significant decrease compared to the obese non-treated group. These results agreed with Hayet *et al.*⁴⁰, who found The extract of *P. harmala* seeds led to notable reductions in total cholesterol, triglycerides and LDL, along with significant increases in HDL when compared to untreated obese diabetic rats. *Peganum harmala* is a natural plant containing significant amounts of β -carboline and quinazoline alkaloids, which are found in high concentrations in various parts of the plant such as capsules, fruits and seeds⁴¹. The reduction in body weight after treatment with *P. harmala* (1000, 2000 and 3000) mg/kg, the activity to lower cholesterol, TG and LDL cholesterol and the mechanism efficacy of various medicinal herbs to lower serum cholesterol levels. This is because *P. harmala* contains various quantities of the alkaloid harmine, harmaline and harmol⁴². *Peganum harmala* has an effect on lipid metabolism in rats, lowering total cholesterol and low-density cholesterol in the blood⁴³. The presence of flavonoids, which have anti-hypercholesterolemic and anti-diabetic effects, is a factor in lowering blood glucose^{44,45}. The use of *P. harmala* can lead to a reduction in total cholesterol, along with minimized oxidative stress and a strong ability to deactivate lipid peroxidation⁴⁶. These data were inconsistent with the results obtained in this study where H/ZnO NPs treatment resulted in hypolipidemia with significant decreases in TC, TG and LDL of obese rats.

CONCLUSION

The study assessed the protective effects of *P. harmala* extract/ZnO NPs on thyroid and pancreatic hormones, as well as related metabolites in obese rats. Treatment with H/ZnO NPs improved the negative impact of obesity on glucose and insulin levels, consistent with previous research on *P. harmala*'s potential antidiabetic effects. Additionally, improvements in thyroid hormone levels were observed in treated obese rats. The study suggests that treatment with *P. harmala* extract/ZnO NPs may offer potential benefits in improving glucose and insulin levels, thyroid hormone levels and lipid profiles in obese rats. However, further research is needed to fully understand the mechanisms and potential interactions between *P. harmala* and zinc oxide in influencing these physiological parameters.

SIGNIFICANCE STATEMENT

Obesity is a major concern, leading to insulin resistance, potentially type 2 diabetes and associated with hypothyroidism with decreased metabolism and a higher BMI. The current study aimed to determine the effects of

Peganum harmala extract combined with zinc oxide nanoparticles (H/ZnO NPs) on thyroid and pancreatic function in obese rats. The H/ZnO NPs lowered blood glucose and boosted insulin levels in obese rats, indicating better insulin sensitivity. Furthermore, H/ZnO NPs dramatically reduced serum TC, TG and LDL in obese rats, improving their lipid profile. The H/ZnO NPs enhanced pancreatic islet shape compared to untreated obese rats. The H/ZnO NPs considerably enhanced serum levels of T3 and T4. Further studies are needed to understand their mechanisms and maximize their use in therapeutic applications.

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