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Research Paper

Harmal nanoparticles as potential antiobese , promises for natural control of obesity

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ABSTRACT *:**The current investigation looked at how changes in serum glucose and liver enzymes in rats given a high-calorie diet (HCD) to make them fat were affected by a methanolic extract of P. harmala/ nanopartical (H/ZnONP) extract. Half of the rats became obese after being given HCD for a month. The 36 male rats were split into two groups (normal and obese), each of which had three subgroups.For a month, the main group received H/ZnONP 200 and 400 mg/kg BW/day orally, while the control group of people continued to be overweight and normal. Blood was drawn and tested at a lab for glucose levels and liver enzymes after 4 weeks of treatment. The collected results showed that giving obese rats H/ZnONP considerably reduced serum glucose levels as well as ALT and AST enzymes. According to the data, supplementing rats with H/ZnONP has a powerful anti-obesity effect via elevating glucose levels, especially at high doses. From the data, we may infer that high-dose H/ZnONP supplementation has effective anti-obesity effects in rats through enhancing glucose levels and liver function.***

Keywords: ***Obesity; Methanolic extract of P. harmala / ZnO nanoparticles***

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I. INTRODUCTION

Increased free fatty acid (FFA) concentrations restrict insulin signalling and GLUT-4-stimulated muscle glucose uptake, which in turn suppresses glycogen synthesis and glycolysis (10).As a result, obesity is associated with an increased risk of insulin resistance and type II diabetes.In North Africa and the Middle East, P. harmala, a white blooming plant also known as wild rue (Harmal), is a member of the Zygophyllaceae family, which has about 250 species and roughly 22 genera (**3**).P. harmala, also referred to as "Harmal," is a herbaceous plant of the Zygophyllaceae family that is native to countries bordering the Mediterranean and the central Sahara.

Traditional medicine has used plants from the Middle East, India, Pakistan, south Australia, and western United States to treat a variety of illnesses, such as cancer, depression, leishmaniasis, aggravation, jungle fever, and as an emmenagogue and abortifacient(**5**).In order to develop clinical research on P.harmala that will yield a natural metabolic medication to treat obesity, diabetes, and insulin resistance, novel methodologies have been developed (**9**). This P.harmala can be used to treat a wide range of conditions, including cancer, inflammation, depression, diabetes, obesity, liver damage, stomach pain, bronchitis, and tumors(**11**).

Biosynthesis is the term used to describe the natural process of producing ZnO Nps, and it involves the use of microorganisms as the decreasing specialist, including parasites, yeast, bacteria, and plant extracts(**19**). It has been shown that adopting a nano-based delivery system to improve therapeutic targeting is one of the primary ways to increase the safety and effectiveness of medications (**8**).

Objective

The goal of the current investigation was to determine if a high-fat diet-induced obesity might be treated with P. harmala/zinc oxide nanoparticles.

II.Materials and Methods

In the current investigation, 36 mature male Rattus norvigicus rats weighing 200–250 g were used. They were acquired from the Faculty of Veterinary Medicine's Animal House at Mansoura University in Egypt. The animals were kept in conventional settings, 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 four weeks getting used to the lab environment ZU-IACUC/1/F/81/2022.

2.1.According to NRC (1995), a high-fat diet containing 20% fat was used to cause obesity in half the experimental rats for a period of four weeks.

2.2 Preparation of P. harmala/Zinc Oxide Nanoparticles: P. harmala seeds were bought from a nearby herb shop with a decent amount of quality assurance. According to the procedures outlined in (**7**), it was extracted and produced using zinc nanoparticles.

2.3 The morphology, shape, and size of H/ZnO-NPs were studied by scanning and transmission electron microscopy (TEM; JEM 1400 plus, JEOL Ltd., Japan) and transmission electron microscopy (SEM; JCM 5700, JEOL Ltd., Japan). After the appropriate dilutions of the sample, the zeta potential (surface charge; mV) of the H/ZnO-NPs was measured using the zeta-potential analyzer ELSZ-2000, Otsuka Electronics, Japan.

Experimental Design:

A total of 36 male rats were split into two primary groups, each with 18 rats: Obese and non-obese individuals are divided into 3 subgroups and given a basic diet along with the following treatment regimen.

Non-obese group:

G1: (Control-negative group): standard diet.
G2: Negative group +*P. harmala* / ZnO nanoparticles (200 mg/kg/day) ***(16).***
G3 : Negative group +*P. harmala* /ZnO nanoparticles (400 mg/kg/day) ***(16)***.

Obese group divided into:

G4: **(Control-positive)**: high-fat diet **(15).**
G5: Obese+ *P. harmala* /ZnO nanoparticles (200 mg/kg/day) ***(16).***
G6::Obese+ *P. harmala* /ZnO nanoparticles (400 mg/kg/day) ***(16)***.

Sampling:

Determination of serum glucose levels:

Serum glucose was determined according to **(17).**

Determination of serum aminotransferases

Activities of AST and ALT in the serum were determined colorimetrically by using spectrum kit (Egyptian Company for Biotechnology,Obour city, Cairo, Egypt), according to **(12).**

Statistical Analysis: The results of the trials on animals were presented as mean and standard error (SEM). Using the SPSS software, version 19, one-way ANOVA and Tukey's post hoc tests were used to assess the statistical differences between the experimental groups. Significant differences in the mean values were defined as $p < 0.05$ (**18**).

III.RESLUTS AND DISCUSSIONS

3.1 Table 1 shows the impact of H/ZnONPs therapy on blood glucose levels in rats:

As a result of receiving treatment with H/ZnO NPs (200 mg/kg/day), the percentage of obese rats in groups (G4–G6) that showed significant increases as compared to non-obese groups ranged from 37% in the control obese group (G4) to 16% in group (G5). Nevertheless, treatment with H/ZnO NPs (400 mg/kg/day) in G6 demonstrated a considerable reduction in serum glucose levels as compared to the untreated control group (G1). Data from obese rats treated with H/ZnO NPs (400 mg/kg/day) showed that Serum Glucose levels gradually decreased to a low value of 5% in G6.

Since P.harmala does not secrete insulin, it is thought that its hypoglycemic impact has nothing to do with the pancreas and instead may apply to how glucose is used or absorbed (**6**).

Our findings concur with those of (**1**), who discovered ZnO NPS described as anti-diabetic drugs. They explained that ZnO NPS are more effective in lowering blood sugar and increasing insulin level and expression.

The decline in hepatic ATP observed in obese rats, which may be attributed to the impact of reactive oxygen species on mitochondrial function, was avoided by ZnO-NPs' antioxidant capabilities (**4**).

3.2Table (2) displays the impact of H/ZnONP therapy on the levels of liver enzymes in rats:

The results showed that, as compared to non-obese groups, obese rats in groups (G4–G6) showed substantial increases. The percentages increased from 96.4% in the control obese group (G4) to 48.6% in G5 due to treatment with H/ZnO NPS (200 mg/kg/day). Although the H/ZnO NPS therapy (400 mg/kg/day) in group G6 significantly increased serum enzymes ALT levels as compared to group G1, the control group, there was no treatment. Data from obese rats indicated that ALT gradually dropped to a low value in G6 after treatment with H/ZnO NPS (400 mg/kg/day).

As a result of receiving treatment with H/ZnO NPS (200 mg/kg/day), it was evident that obese rats in groups (G4–G6) displayed increases that were statistically significant when compared to non-obese groups. These increases ranged from 135% in the control obese group (G4) to 67.1% in the group (G5). Although the H/ZnO NPS therapy (400 mg/kg/day) in group G6 significantly increased serum enzymes AST levels as compared to group G1, the control group, there was no treatment. The AST levels of obese rats gradually dropped until they reached the lowest value in G6 after treatment with H/ZnO NPS (400 mg/kg/day).P. harmala have hepato defensive properties(**2**) Our results agree with Protein from P. harmala at the two doses has decreasing effect on the serum ALT, AST and ALP (**14**). Liver enzymes, parameters related to inflammation and adipokines could add information to the evaluation and monitoring in children with obesity **(13).**

Table (1): Comparison of control and variously treated animal groups' serum glucose levels:

Parameters / Animal groups	Glucose (mg/dl)
G1	99 ±2.646
G2	84.33 ±5.239 -14.818*
G3	82.67 ±1.856 -16.495*
G4	136 ±7.627 37.374*
G5	115 ±8.803 16.162* -15.441**
G6	104.3 ±7.319 5.354* -23.309**

Results are presented as means ±SE and % of change for 6 rats in each group.

G1: Non obese (Control-negative group): standard diet. G2: Non obese +H /ZnO NPS (200 mg/kg/day) , G3: Non obese + H /ZnO NPS (400 mg/kg/day) , G4: Obese (Control-positive group): high-fat diet. G5: Obese+ H/ZnO NPS (200 mg/kg/day) ,G6: Obese+ H/ZnO NPS (400 mg/kg/day) .

(*): % of change related to control group. (**): % of change related to:Obese(high-fat diet) .

Table 2 shows the serum ALT and AST enzyme levels of the control and variously treated animal groups.

Parameters / Animal groups	ALT (U/L)	AST (U/L)
G1	57 ±5.292	140 ±4.726
G2	55.33 ±4.978 -2.930*	113.3 ±11.67 -19.071*
G3	47.33 ±2.333 -16.965*	97.33 ±8.95 -30.479*
G4	112 ±7.176 96.491*	329 ±14.59 135*
G5	84.75 ±3.092 48.684* -24.330**	234 ±13.96 67.143* -28.875**
G6	81.25 ±3.326 42.544* -27.455**	208.5 ±11.39 48.929* -36.626**

Results are presented as means ±SE and % of change for 6 rats in each group.

G1: Non obese (Control-negative group): standard diet. G2: Non obese +H /ZnO NPS (200 mg/kg/day) , G3: Non obese + H /ZnO NPS (400 mg/kg/day) , G4: Obese (Control-positive group): high-fat diet. G5: Obese+ H/ZnO NPS (200 mg/kg/day) ,G6: Obese+ H/ZnO NPS (400 mg/kg/day) .
(*): % of change related to control group. (**): % of change related to:Obese(high-fat diet) .

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