

# Studying the Effect of Zinc Oxide Nanoparticles, Banana Peel Aqueous Extract and Metformin on The Level of Glucose and Liver Enzymes in Male Rats Infected Experimentally with Diabetes

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## Conclusion

The current study aimed to evaluate the effectiveness of the extract of zinc oxide nanoparticles and the aqueous extract of banana peels, the drug Metformin, in reducing glucose levels and liver enzymes ALT and AST in male rats with experimental diabetes. The study included bio-preparation of zinc oxide nanoparticles from banana peel extract and confirmation of their formation the nanomaterial By conducting several tests, namely, UV-vis, XRD, SEM, and preparing an aqueous extract of banana peels. The study included 25 male Albino white rats, whose weights reached (180-250) and their age ranged between (2-3) months. rats to 5 Groups and each group included 5 males, the first group was given water and diet only and the negative control group returned, the second group was injected subcutaneously with alloxan at a concentration of (100 mg/kg), and the third group was injected with alloxan and then dosed orally with an extract of zinc oxide nanoparticles at concentrations (10 mg/kg). ) respectively, and the fourth group was injected with alloxan and then dosed with an extract aqueous solution of banana peels at a concentration of (500 mg / kg), and the fifth group was injected with Oxan and then dosed orally with Metformin at a concentration of (0.1 mg / kg), noting that the injection process took place for 3 days, followed by the dosing process for a period of 30 days, once a day, where the results showed that there was A therapeutic effect of zinc oxide nanoparticles and aqueous extract of banana peels in lowering glucose levels and liver enzymes ALT and AST better than metformin in diabetic male rats.

**Keywords:** Green synthesis, ZnONPs, Diabetes, Milletus, Metformin, Banana Peel

## 1. Introduction

Diabetes mellitus causes an imbalance in the process of sugar metabolism, which in turn leads to an increase in the leve Abnormal glucose in the blood for various reasons that may be psychological or organic, or excessive intake of sugars, or due to genetic factors. It may occur as a result of a defect in the secretion of insulin by the pancreas, where the amount of insulin secreted is less than required (El-Missiry et al., 2015; Genuth et al., 2021) Diabetes occurs as a result of not converting glucose into a sourceEnergy, and therefore it will accumulate in the bloodstream in large quantities, while the cells of the body remain without energy. Over the years, hyperglycemia increases and results in great damage to blood vessels and nerves, and causes diseases including gingivitis, diabetic neuropathy, kidney disease, heart, blindness, Diabetic foot, which may lead to amputation (Cheng et al., 2021),

Nanotechnology means engineering, science and technology that uses nanoscale dimensions At a level ranging from (1-100) nanometers, and is concerned with studying the applications of materials whose dimensions are infinitesimally small, and is used in several scientific fields that include biology, physics, chemistry, materials science and engineering (Chan et al., 2018), a lot of interest has emerged.

nanoparticles as a result of the large number Its use

in various fields such as nanomedicine, as well as as a result of its distinct characteristics that lead to the production of simple techniques for the synthesis of metallic particles of nano-sizes. Plaza et al., 2014), a technique is implemented Nanomaterials affect a wide range of medical conditions such as Alzheimer's disease, diabetes, tuberculosis and cancer (Nikalje, 2015), among nanomaterials zinc oxide, which has gained great interest in medical and scientific directions as a result of its chemical and physical properties and its biological and antibacterial applications (Noor et al., 2017), ZnO nanoparticles is a semiconducting material that possesses molasses The chemical ZnO, which is an inorganic compound, has a white color that tends to yellow when heated. ZnO is considered a non-toxic substance (Ahemed, 2018). Zinc oxide nanoparticles are widely added to a number of products that include plastics, ointments, glass, batteries, cement, and sometimes adhesives. ZnO is used for commercial purposes synthetically (Osmond and McCall, 2010) and zinc oxide nanoparticles are synthesized by plant extracts, instead of Physical and chemical types, by using different plant parts such as roots, leaves, seeds, fruits, which are not toxic chemicals, that natural extracts of plant parts are environmentally friendly and cheap, and form a product of high purity and impurities (Heinlaan et al., 2008).

About 80% of medicinal plants and herbs have been used in developed countries to treat many diseases, including diabetes (Patel et al., 2012), and large amounts of phenolic compounds in banana peel have a role in the synthesis of metallic nanoparticles (Bankar et al., 2010). The researchers (2015) Pereira and Maraschin stated that banana peel contains a number of compounds with biological activity, which include glycosides, anthocyanins, alkaloids, flavonoids, terpenoid, tannin, and Phlobatannins, which have proven to have different pharmacological and biological effects, as they are antibacterial and Hypotensive, anti-inflammatory, and diabetic activities.

## 2. Materials and Methods of Work

### Preparation of aqueous extract of banana peels

Add 10g of banana peel powder to 100ml of distilled water in a glass beaker and put it in a water bath at a temperature of 80°C for two hours and leave the solution Cool and filter using filter paper, then centrifuge at 4500 cycles for 10 minutes. The extract is collected in clean containers and kept in the refrigerator until use (Irshad et al., 2020).

### Preparation of zinc oxide nanoparticles

The method of preparation was followed according to (Irshad et al., 2020) with some modifications to it, by adding zinc acetate ( $\text{CH}_3\text{COO})_2\text{Zn}\cdot 2\text{H}_2\text{O}$ ) at a concentration of 0.2L / mol to 100 ml of plant extract at room temperature, and the pH was equalized by Adding sodium hydroxide NaOH down to PH = 7, then the mixture is placed on the plate device Hot plate for three hours at a temperature of 60 °C until the color change of the solution is evidence of the formation of zinc oxide nanoparticles, after which it is filtered by a centrifuge at 4500 cycles for 15 minutes, and the precipitate is taken and washed three times, and dried in the electric oven at a temperature of 40-45 °C and ground By manual mill, and kept in clean boxes until use.

### Characterization of zinc oxide nanoparticles

UV-vis spectrophotometer analyzes zinc oxide particles from banana peel extract. This test is done by adding 1 ml of nanomaterials in a UV-vis spectrophotometer, and the wavelength range ranges from (200-800) nanometers, and this test was conducted at the Research Center - University of Tehran - Iran (Duan et al., 2015), and X-Ray Diffraction (XRD) is used in the analysis of crystalline and molecular bodies, and it also measures the degrees of crystallization , particle sizes, qualitative knowledge In compounds, zinc oxide nanoparticles prepared from banana peel extract were sent to the Research Center - University of Tehran - Iran (Zhang et al., 2016), and analysis by scanning electron microscope (SEM) was used to characterize the morphology And the sizes of zinc oxide

nanoparticles prepared from banana peel extract, and the material was prepared by adding a few drops on a silicon wafer, left to dry, and then analyzed by a scanning electron microscope, where the material was examined at the Research Center - University of Tehran - Iran (Caroling et al., 2013) .

### Diabetes mellitus induction

Male rats were injected with alloxan at a concentration of (100 mg/kg) of body weight in a single dose subcutaneously to induce experimental diabetes mellitus (Owoyele et al., 2005), using a 1 ml insulin syringe, and they were starved in the past 24 hours before injection, and after alloxan injection during For the next 24 hours, I was given a 5% glucose solution, which was mixed with drinking water, and during the next three days, the blood sugar level was measured from the vein in the tail with test strips Monitoring for blood sugar analysis, the rats that showed a level of more than (200 mg / dl) were considered to have diabetes (Teixeira et al., 2002).

### Experimental design

**The first group:** a group of rats that were given regular water and normal diet and left without dose for 30 days, and a negative control group.

**The second group:** a group of rats injected with alloxan at a concentration of 100 mg / kg of animal body weight, and a positive control group (Owoyele et al., 2005).

**The third group:** a group of diabetic rats dosed daily orally with zinc oxide nanoparticles extract at a concentration of (10 mg / kg) of the animal's body weight for a period of 30 days (Reza et al., 2014).

**The fourth group:** a group of rats with diabetes was dosed daily orally with an aqueous extract of banana peels at a concentration of (500 mg / kg) of the animal's body weight for a period of 30 days (Mokuna et al., 2014).

**The fifth group:** a group of diabetic rats dosed daily orally with Metformin at a concentration of (0.1 mg / kg) of the animal's body weight for a period of 30 days.

### Biochemical parameters

At the end of the experiment for a period of 30 days, the rats fasted for 24 hours, and they were anesthetized with chloroform and sacrificed, and blood was drawn from the heart through what is known as a heart puncture to obtain an adequate amount of blood by means of a plastic medical syringe with a capacity of 5 ml The blood is in gel tubes and left for half an hour until it coagulates, then it is taken to a centrifuge at a speed of 3000 revolutions per minute for a quarter of an hour to separate the serum, which is kept in tubes for freezing at -20 degrees for the purpose of conducting biochemical tests, which include estimating the level of glucose in blood. blood, and estimation of the activity of liver enzymes (ALT, AST).

### 3. Results and Discussion

#### Characterization of ZnONPs

A UV-vis spectrophotometer was analyzed to confirm the green synthesis of the ZnONPs extract, and the test was carried out between wavelengths ranging from 190-900 nm, and the appearance of the highest peak at the wavelength of 370 nm, as in Figure (1) It is an evidence for the formation of bio-synthesized zinc oxide nanoparticles from the aqueous extract of banana peels, and as a result of the presence of the surface plasmon resonance (SPR) effect, where the conductive electrons begin to vibrate in a specific wavelength range, and the spectral resonance feature that confirmed the decrease of the zinc metal ion and the formation of nanoparticles where they were. The absorption peak is at the wavelength of 370 nm. Which indicates the presence of zinc oxide nanoparticles in the reaction solution, the obtained result is consistent with the study of Rad *et al.*, (2019) who prepared zinc oxide nanoparticles from catnip leaf extract and the absorption range was 370 nm as agreed with what he found Researchers Mohammad and Ghasemi (2018) who used cherry plant extract to prepare zinc oxide nanoparticles and the absorption peak was 378 nm.

The results of the X-ray diffraction (XRD) examination showed the presence of diffraction peaks at  $\theta = 31.2^\circ$ ,  $34.0^\circ$ ,  $36.1^\circ$ ,  $48.0^\circ$ ,  $56.4^\circ$ ,  $62.6^\circ$ ,  $68.3^\circ$  and  $75.0^\circ$  which correspond to the indicators Miller (100, 002, 101, 102, 110, 103, 112 and 202) respectively as in Figure (3) and these levels are consistent with the standard international card file (JCPDS: 80-0075 card) to calculate the rate. The particulate size, depending on the Debye-Scherrer equation, found that the particulate size is between (19-66) nm, and the average diameter is (41.15) nm. This result is consistent with Siripireddy and Mandal, 2017, and also with the study of (Talam *et al.* , 2012).

SEM analysis was used to verify the nanoparticle sizes and structural shape and between green and environmentally friendly manufacturing. The ZnONP extract has a spherical shape and the nanoparticles have a homogeneous distribution and have a nanosize range of less than 100 nanometers as in Figure (4), and as a result of using Zinc acetate In the preparation process, the zinc oxide particles grow slowly and have small spherical structures and accumulate in the form of aggregations, and the spherical nanoparticles have more desirable characteristics and characteristics than the rest of the nanoparticles, and the result was similar to what Vijayakumar *et al.* (2016) on the preparation of zinc oxide nanoparticles by an extract Leaves of *Laurus nobilis* where the nanoparticles were characterized by a spherical shape and the diameters of the sizes were less than 100 nm.

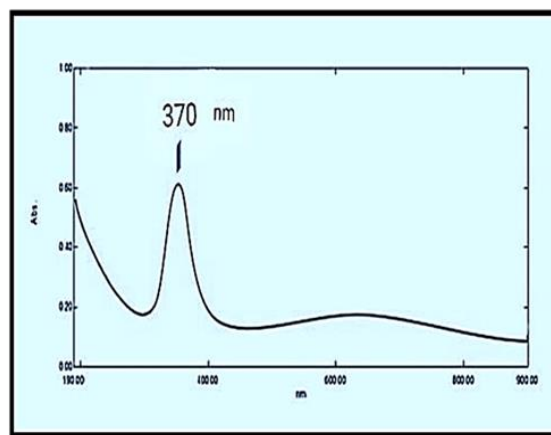


Figure (1) Vis-UV spectrum analysis of zinc oxide nanoparticles biosynthesized from banana peel extract

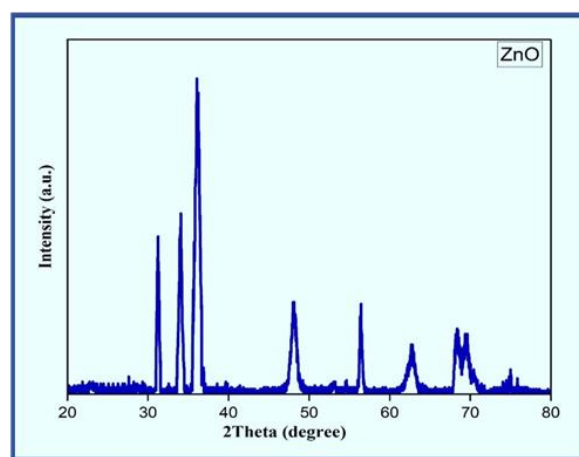


Figure (2) X-ray diffraction (XRD) of zinc oxide nanoparticles biosynthesized from banana peel extract

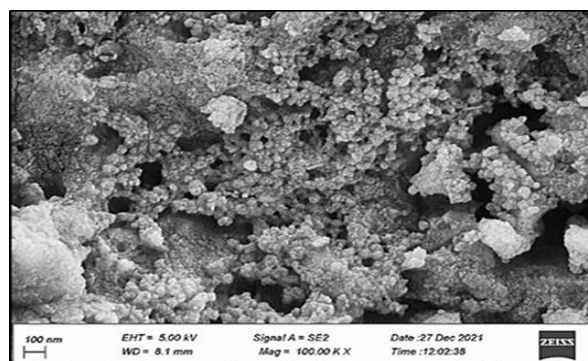


Figure (3) a scanning electron microscope image showing the shape and size of ZnO nanoparticles

#### Effect of treatment with alloxan, zinc oxide nanoparticles extract, aqueous extract of banana peels and metformin drug on glucose level.

The results showed that the use of alloxan to induce diabetes led to a significant increase ( $P < 0.05$ ) in the level of glucose in the blood of rats with neodiabetes and untreated throughout the experiment period compared with the healthy control group. Our results agreed with what it indicated (Samoo *et al.*, 2018), and a study., Naim *et al.* (2012) showed that alloxan is a highly toxic chemical drug that partially destroys pancreatic cells and then leads to an increase in blood sugar levels and a decrease in insulin

secretion.

The results showed that there was a significant decrease ( $P < 0.05$ ) in the level of glucose in diabetic rats treated with zinc oxide nanoparticles extract at concentrations (10 mg / kg) compared with the experimental diabetic group, and the result agreed with (Bhuyan, et al., 2010; Siddiqui et al., 2014 )

where it was shown that the use of prepared zinc oxide nanoparticles Bioavailable from *Syzygium cumini* at a concentration of (10 mg/kg) led to a significant decrease in the level of blood sugar, due to the fact that zinc has an insulin-like property Also, the similarity of the results obtained with what was found Ball et al., (2015) When treating diabetic rats with zinc oxide nanoparticles prepared biologically from *Hibiscus subdariffa* leaf extract at a concentration of (8 mg/kg), a decrease in the blood sugar level was mainly caused by the effect of both the plant extract and zinc, which acts as insulin in the body, as it contains Abstract on a number of Bioactive compounds such as flavonoids, anthocyanins, and phenolic acids that have strong antioxidant properties work to stop various metabolic disorders (Ayya et al., 2015).

Also, the results of the current study indicated a significant decrease ( $P < 0.05$ ) in the level of glucose in a group of diabetic rats treated with an aqueous extract of banana peels. The reason may be

attributed to the fact that banana peels contain effective compounds that include pectin, lignin, cellulose, and Hemicellulose (Oyeyinka and Afolayan, 2019). Banana peel also contains compounds Effective as flavonoids, terpenoids, tannins, alkaloids, raising the activity of Glucokinase has Glycolysis also lowers the level of glucose in the blood through the flow of glucose into the process glycolysis as such In muscle and liver glycogen increases (Indriawati, 2020; Ahmed et al., 2021) , and it works Flavonoids increase the binding activity of free radicals that have the ability as antioxidants (Martins et al., 2019; Indriawati et al., 2021), and this may be due to the content of the extracts on substances with great activity such as vitamin E, polyunsaturated fatty acids and acid ester ( Kumar et al., 2010).

The results also indicated that there was a significant decrease ( $P < 0.05$ ) in glucose levels in diabetic rats that were given Metformin compared to the Alloxan group Reducing glycemia and increasing insulin sensitivity thus likely increases peripheral glucose uptake, inhibits gluconeogenesis, and then reduces hepatic gluconeogenesis ( Grieb, 2016; Sharma, 2018), and this result agreed with Konopka et al., (2019), which showed that the drug is able to lower the blood sugar level in patients with type 2 diabetes.

Table (1) the effect of treatment with alloxan, zinc oxide nanoparticles extract, aqueous extract of banana peels and metformin drug on glucose level

The group	Glucose Level (mg/dl)
Control	91.4±4.03 E
Alloxan (ml /kg 100(	423±7.44 A
Alloxan+ Extract ZnONPs10) ml/kg(	118±1.87 C
Alloxan + Aqueous extract of banana peels) ml/kg ( 500	120.2±2.38 C
Alloxan +Metformin ml/kg) 0.1(	178.4±5.45 B
LSD( $P < 0.05$ )	5.02

### The effect of treatment with alloxan, extracts of oxide nanoparticles, aqueous extracts of banana peels, and drug Metformin on the activity of liver enzymes (AST, ALT)

A significant increase ( $P < 0.05$ ) was observed in the activity of liver enzymes (AST, ALT) in the group with alloxan-induced diabetes, compared with the control group. Alloxan leads to an increase in the level of glucose in the blood and then increases the level of ROS formation and oxidative stress, and thus will lead to the occurrence of lipid oxidation in the hepatocyte membranes in addition to the occurrence of necrosis in them, and finally it will lead to an increase in the activity of these enzymes in the liver (Hanan and Alharbi, 2017).

Contrary to the above, an extract of zinc oxide nanoparticles was shown in concentrations (10 mg / kg) Compared with the alloxan treatment group, there was a significant decrease ( $P < 0.05$ ) in the activity of enzymes (AST, ALT), and the reason is attributed to the ability of zinc oxide nanoparticles to reduce oxidative stress and inflammation Diabetic

mice, which indicates its therapeutic and preventive effects through strong anti-inflammatory and antioxidant activities. These results indicated the possibility of nanoparticles to reduce or treat diabetes complications (Ghosh et al., 2015; Ahmed et al., 2020).

The group with diabetes mellitus caused by alloxan and treated with aqueous extract of banana peels showed a significant decrease ( $P < 0.05$ ) in the activity of liver enzymes (AST, ALT) compared with the group treated with alloxan alone. This is due to the fact that banana peel extract contains minerals, vitamins, proteins and antioxidants that can regulate These enzymes (Mosa and Khalil, 2015; Meliala et al., 2020), antioxidants work to stop the oxidation of Other molecules where free radicals are produced during oxidative reactions, which can cause damage to liver cells. The antioxidants in banana peel extract represent pectin, saponins, vitamin C, and tannins, which represent the largest content in the extract (Meliala et al., 2020), as well as serotonin is a precursor of melatonin that reduces inflammation, cirrhosis, and tissue injury in diabetic rats (Colares et al., 2016).

The current study also indicated a significant decrease in the activity of enzymes (AST, ALT) in the diabetic group treated with Metformin, and this result agreed with what was reached by (Khadre et al, 2011; Albasher et al., 2020) in rats with diabetes induced by STZ, where the drug led to a significant

decrease in the activity of enzymes The drug works to restore enzyme activity to normal levels, and the reason may be attributed to the important role of the drug in protecting the integrity of liver functions, in addition to the effectiveness of radical scavenging (Al-Quraishy et al., 2015).

Table (2) the effect of treatment with alloxan, zinc oxide nanoparticles extract, an aqueous extract of banana peels, and metformin drug on the activity of liver enzymes (ALT, AST)

The group	AST(U/L)	ALT(U/L)
Control	41.4±3.91 D	25±4 E
Alloxan (ml /kg 100(	118.8±2.16 A	135.2±7.25 A
Alloxan+ Extract ZnONPs 10) ml/kg(	45±4.74 CD	32.4±5.85 CD
Alloxan +Aqueous extract of banana peels) ml/kg (500	42±6.08 D	27.4±4.56 DE
Alloxan + Metformin ml/kg ) 0.1(	60.2±6.76 B	53±5.09 B
LSD(P<0.05)	5.42	6.36

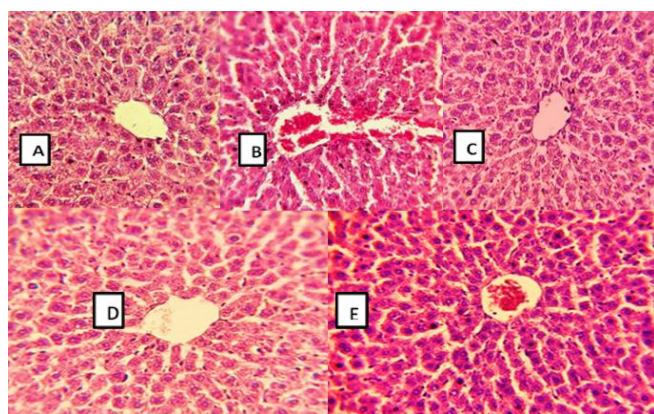


Figure (1) shows histological sections in experimental aggregates

(A) shows the negative control group Central vein and normal hepatocytes (B) The infected group shows damage and congestion of the central vein with the interstitial connective tissue of the liver (C) The infected group treated with zinc oxide nanoparticles extract shows a central vein and normal hepatocytes (D) The infected group treated with aqueous extract of banana peels shows a vein Central and normal hepatocytes (E) A group infected and treated with Metformin shows congestion in the central vein and normal hepatocytes.

#### 4. Conclusions

The extract of zinc oxide nanoparticles and the aqueous extract of banana peels showed a decrease in the level of glucose glucose and liver enzymes (AST, ALT) and a good improvement in liver tissue better than the drug Metformin in male rats with type II diabetes.

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