



## Anti-hyperglycemic, pathogenic and anticancer activities of *Bambusa arundinacea* mediated Zinc Oxide nanoparticles

N. Jayarambabu<sup>a</sup>, T. Venkatappa Rao<sup>a,\*</sup>, R. Rakesh Kumar<sup>a</sup>, A. Akshaykranth<sup>a</sup>, Kalakotla Shanker<sup>b</sup>, Velpula Suresh<sup>c</sup>

<sup>a</sup> Department of Physics, National Institute of Technology Warangal, Telangana, 506004, India

<sup>b</sup> Centre for Pharmaceutical Sciences, Institute of Science and Technology, Jawaharlal Nehru, Technological University Hyderabad, Kukatpally, Telangana, 500085, India

<sup>c</sup> Department of Biochemistry, Osmania University, Hyderabad, Telangana, 500007, India

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### ABSTRACT

Diabetes can be treated effectively by the nanoparticles (NPs), which have been converted into nanomedicine. The present study describes the synthesis of Zinc oxide nanoparticles (ZnO NPs) using *Bambusa arundinacea* (BA), their antidiabetic, antibacterial, and anticancer potential. Histopathological studies of synthesized ZnO NPs and BA extract were carried out on male Wistar rats. The Wistar rats were divided into normal, toxicant, standard, and test groups. It is observed that the ZnO NPs have shown enhanced anti-diabetic potential when compared with BA extract. It is mainly due to the extensive pharmacological and biological properties of ZnO NPs. Further experiments needed to be carried out to confirm the exact mechanism of ZnO NPs for anti-hyperglycemic activity. Good antibacterial efficacy of biosynthesized ZnO NPs against gram-positive organisms was observed. The zone of inhibition values of 14, 16, 17, 19 mm for *Staphylococcus aureus* (*S. aureus*) and 12, 14, 15, 17 mm for *Bacillus subtilis* (*B. Subtilis*) were observed for the concentration of 25, 50, 100, 150  $\mu$ l. Further, ZnO NPs also exhibited anticancer activity against MCF-7 cell lines. These results indicate that bio-synthesized ZnO NPs have prospective pharmaceutical applications.

### 1. Introduction

Diabetes mellitus (DM) has globally depicted as a harmful disease with less awareness and improper treatment procedures. Symptoms of diabetes are enlarged dryness, frequent urination, starvation, weakness, and blurred vision. In a few cases, there might be no symptoms. The remedy of diabetes includes a controlled diet, exercise, and insulin [1,2]. The current situation of an accelerated global increase in diabetes was attributed to an individual's unnatural lifestyle, aging, and urbanization. Worldwide statistics on people with diabetics show a significant expansion from 160 million to 410 million during the last three decades. The commonness of diabetes is evaluated at 420 million individuals in 2019 and is expected to ascend to 690 million by 2040 [3,4]. Therefore, research on the treatment of diabetes with various herbal mediated NPs has attracted much attention since the last decade [5].

Globally the herbal extracts such as *Vaccinium arctostaphylos*, *Momordica charantia*, *Moringa oleifera*, *Morinda citrifolia*, *Gymnema sylvestre*, *Bamboo vulgaris*, *Bambusa arundinacea* have been used for the

treatment of DM since ancient days. These medicinal plants also used for control and treat antibacterial infections, anti-hyperlipidemic, antioxidant, anti-inflammatory and antifungal [6–8]. Among these, *Bambusa arundinacea* is chosen in this study for the preparation of ZnO NPs, its antidiabetic, and antibacterial activity. The utilization of *Bambusa arundinacea* for many ailments was common, especially in Africa and Asia. *Bambusa arundinacea* belongs to a plant of *Graminae* family, and it varies from other branches of the grass family with the availability of sections at the respective node. Bamboo comprises of internodes and a hub, because of which it is strong and gives necessary support to the plant and also contain the excellent mechanical and thermal properties [9]. The BA is used as antipyretic, diuretic, arthritis, hemoptysis, anti-leprotic, counteracting spasmodic disorders, secretion of bleeding, sedative, expectorant, anti-rheumatic, and asthma [10–12].

More diabetic patients choose nano-herbal medicine, which is guided by nanoparticles, inclusive of compliance of the patient, enhanced bio-availability. Nanoparticles exhibit good biomedical applications such as antibacterial, anticancer, anti-diabetics, drug

\* Corresponding author.

E-mail address: [tvraokmm@nitw.ac.in](mailto:tvraokmm@nitw.ac.in) (T. Venkatappa Rao).

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delivery, bioimaging, wound healing, and anti-inflammation [13,14].

Advanced treatment is needed for typical diabetes patients. Various revelations illustrate the use of metals and metal oxides in glucose processing with the association of their deficiency along with diabetes. The silver, zinc oxide, magnesium, vanadium, chromium, and cerium oxide have been used to control the glucose levels and have numerous other pharmacological properties [15,16,17]. Although ZnO is a significant metal oxide in an immense number of metabolic procedures, there are limited reports about the viability of ZnO for the control of glucose levels [18,19].

Most of the physical and chemical synthesis methods of metal oxide NPs require radiation, extremely hazardous reductants, and stabilizing compounds, which are harmful to human life. In comparison, the green synthesis method of metal oxide NPs is a single-step method, bio-reduction process, eco-friendly, cost-effective, and it needs comparatively low energy to begin the reaction process. Among various approaches of ZnO NPs synthesis, the green methods are most favored as they create safe, clean, and homogenous nanoparticles in a simple and reasonable technique during maintenance of biological cooperation. The green approach of preparing nanoparticles using plant extracts provides the bio-functionalization of nanoparticles with the phytochemicals surrounding the ZnO NPs surface. This bi-functionalization of NPs restrict the interaction among them and also the response from the hyperglycemic, anticancer, and bacterial cells for the targeted action [20–22].

In the present study, ZnO NPs are synthesized by a green method using *Bambusa arundinacea* extract. Green synthesis of ZnO NPs has advantages such as inexpensive, eco-friendly, easy to prepare, and safe methods compared to the other synthesis methods. The anti-hyperglycemic, antimicrobial, and anticancer activities of bio-synthesized ZnO NPs and *Bambusa arundinacea* extract were reported. As per the authors' knowledge, this is the first report on the green synthesis of ZnO NPs using *Bambusa arundinacea* extract.

## 2. Details of the experiment

### 2.1. Resources

*Bambusa arundinacea* was collected from the National Institute of Technology, Warangal and ethanol, zinc acetate from Sigma-Aldrich.

### 2.2. Soxhlet extraction process: plant extraction

*Bambusa arundinacea* leaves washed with DI-water multiple times for the removal of struck unwanted impurities. Further plant leaves were air-dried for few days to remove moisture. The leaves were crushed in the powder form, then pass through the 20 mesh sieve. The sieved fine particles were placed in Soxhlet equipment and authorized to hot percolation with 60% ethanol to produce the extract solution. The hydroalcoholic plant extract solution was concentrated by rota-evaporator and placed in desiccator [23].

### 2.3. ZnO NPs synthesis using *Bambusa arundinacea* extract

0.1 M Zinc acetate precursor solution and *Bambusa arundinacea* extract solution were mixed in 1:3 ratios. The resulting solution stirred for 2 h after that incubated at 70 °C for the complete evaporation of the solution. The resulting powder was collected for further studies. In the green synthesis method tannins, flavanoids, phenolic, glycosides and alkaloids compounds react with zinc acetate to form a ZnO NPs. The tannins, flavanoids phenolic and glycosides compound may act as a stabilizing agent for the ZnO NPs. The biological molecules coated on the surface of ZnO NPs makes them biocompatible for anti-hyperglycemic, pathogenic and anticancer activities [24].

### 2.4. Animals & histopathology study

Wistar rats were obtained from the authorized animal supply company, Mahaveer Hyderabad. Institutional Animal Ethical committee Reg. no. 1684/PO/a/13/CPCSEA is the protocol reference number for the conduct of animal study from the Institutional Animal Ethical Committee (IAEC). Histopathology study is initiated by sacrificing the test animals on the end day of the experiment (i.e., 14th day) by separating the organs.

### 2.5. Antimicrobial efficacy of biosynthesized ZnO NPs

The antimicrobial activity of biosynthesized ZnO NPs was performed by the agar disc diffusion technique against gram-positive bacteria. The fresh culture of every strain was swabbed equally on each plate. Different concentrations (25 µl, 50 µl, 100 µl, and 150 µl) of ZnO NPs liquid impregnated in the discs were positioned on to the petriplate were incubated for 24 hrs at 37 °C. After incubation time, the zone of inhibition for all the samples was determined.

### 2.6. Induction of diabetes by toxicant

Preceding to the study, the streptozotocin (toxicant), which is prepared by the addition of 40 mg/kg in 0.1 M citrate buffer, at pH 4.5. The toxicant impregnates interpretable to Wistar rats. Wistar rats that exhibited hyperglycemia of 250 mg/dl glucose levels after the injection were selected for the current experiment.

### 2.7. Hypoglycemic effect on normal Wistar rats

Test animals selected for the study were separated into six groups.

**1st group** (normal control) administered with saline.

**2nd group** (diabetic control) administered with streptozotocin (STZ) at dose 40 mg/kg.

**3rd group** (standard) administered with metformin at dose 200 mg/kg

**4th group** administered with *Bambusa arundinacea* at dose 400 mg/kg.

**5th group** administered with *Bambusa arundinacea* at dose 200 mg/kg.

**6th group** administered with ZnO nanoparticles at dose 200 mg/kg.

**7th group** administered with ZnO nanoparticles at dose 100 mg/kg.

The first group was administered orally with 0.9% w/v vehicle (saline) alone at a dose of 0.5 ml/kg, and this group considered as control. 2nd group was administered with metformin (reference standard) at a dose range of 200 mg/kg. 3rd & fourth groups were administered with *Bambusa arundinacea* (L) at a dose range 200 & 400 mg/kg. 5th and sixth groups were administered with and ZnO NPs at a quantity range of 100 & 200 mg/kg. The samples of rat blood were received from retro-orbital sinus with ether inhalation at 0, 30, 60, and 120 min. The glucose levels were tested by Accu-Chek active device. Blood was again collected by a retro-orbital puncture at the end of the experiment and centrifuged at 5000 rpm. The serum glucose was also estimated using an automatic biochemistry analyzer by Andersen method [25,26].

### 2.8. Assay of MTT

Cell viability (MTT) assay was proceeding on the Breast cancer cell line (MCF-7) was collected from the National Centre for Cell Sciences, India. The cells were developed in Dulbeccos Modified Eagles Medium containing Fetal bovine Serum 10%, Penicillin G 100 units/mL and amphotericin B 5 µg/mL, Streptomycin 1 µg/mL, L-glutamine 2 mM and non-essential amino acids, at 37 °C in humidified 5% CO<sub>2</sub> chamber. Cytotoxicity of the ZnO NPs was analyzed under the conditions of after 80% confluence, cells were trypsinized with 0.1% trypsin-EDTA and were harvested by centrifugation at 500×g. Serial dilutions of cells were

made  $1 \times 10^6$  to  $1 \times 10^3$  cells per mL. The 96 well plates were used for cells seeded in triplicates. The cells suspended were treated with 00-0.5  $\mu\text{g L}^{-1}$  concentrations of NPs, with different dose manner at the time point (24 h). Tamoxifen drug used as positive control and tumor cells without NPs was added served as control. After incubation, MTT (20  $\mu\text{l}$ , 5 mg/mL) solution was poured into very well, and cell viability was identified by measuring the ability of cells to change MTT to a purple color in formazan dye. The measured by ELISA test absorbance of samples at 570 nm, finally check the percent viable cells were calculated with below equation [27].

$$\text{cell viability\%} = \frac{A_{570 \text{ Sample}}}{A_{570 \text{ control}}} \times 100$$

## 2.9. Statistical analysis

Results were asserted as mean  $\pm$  standard error mean. Mean has been correlated with ANOVA oneway analysis followed by Dunnett's test.  $p < 0.001$  was treated to be statistically compelling.

## 3. Results and discussion

### 3.1. ZnO powders characterization

FESEM analysis was employed to check the morphology of the obtained ZnO powder. (Fig. 1a-b) show the FESEM images of the obtained powders at low and higher magnifications and confirmed the formation of ZnO NPs. Due to the high-density growth, the maximum of the ZnO NPs were agglomerated, and most of them are in spherical. However, ZnO NPs reveal soft surfaces because of the biosynthesis process. To obtain finer scale nano-structural information of the size and shape distribution of ZnO NPs TEM investigations were conducted.

Fig. 1c-d shows the TEM images of as-prepared ZnO NPs at different magnifications, and most of the particles were spherical with broad size distribution (See supplementary information (See SI, S1)). From Fig. 1d, the sizes of the particles were observed in the range of  $\sim 7$ -20 nm. The size and shape of synthesized ZnO NPs were based on the extract used in the biosynthesis process, which may be attributed to the antioxidant reduction potential capacity of the extract. The constituents in the

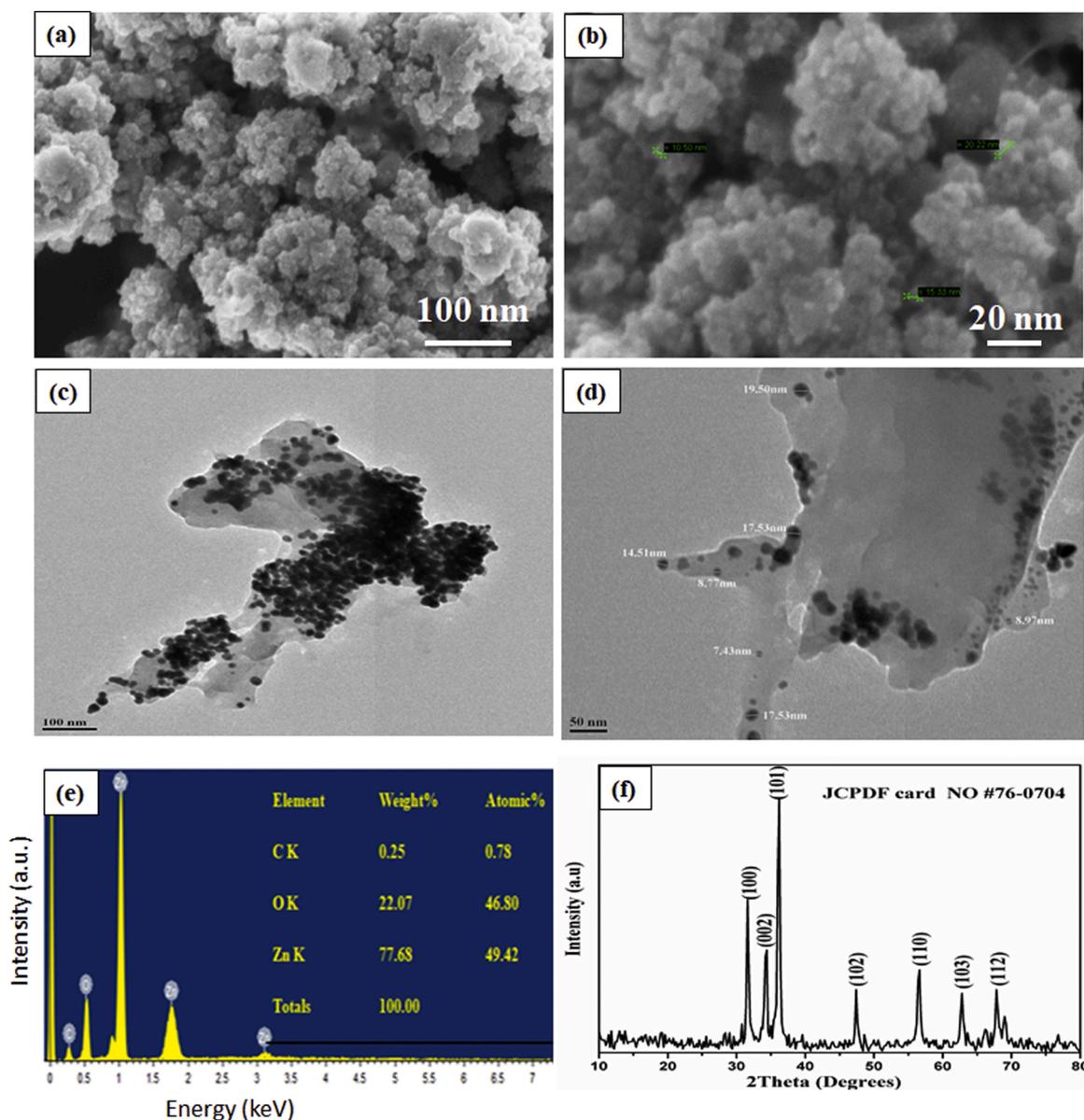


Fig. 1. FESEM images of the ZnO NPs biosynthesized with plant extract (a-b) low and high magnifications. (c-d) TEM images of ZnO NPs at different magnifications, (e) EDS spectrum of ZnO NPs powder, (f) XRD pattern of the obtained ZnO NPs powder.

extract may also contribute as the capping agents. Further compositional analysis of the ZnO NPs was estimated by EDS shown in Fig. 1e. EDS spectrum confirms the presence of zinc and oxygen elements with atmospheric absorbed carbon. Each of the observed peaks is indexed for Zn and O devoid of any unidentified compound signals confirms the purity of ZnO. X-ray diffraction pattern of the prepared ZnO NPs powder is shown in Fig. 1f. The diffraction peaks at  $2\theta = 31.7^\circ$ ,  $34.2^\circ$ ,  $36.1^\circ$ ,  $47.5^\circ$ ,  $56.5^\circ$ ,  $63.9^\circ$ , and  $68.1^\circ$  corresponds to (1 0 0), (0 0 2), (1 0 1), (1 0 2), (1 1 0), (1 0 3) and (1 1 2) planes of the ZnO respectively. Indexed XRD pattern well coinciding with the standard JCPDS card #76-0704. XRD study confirmed the crystalline nature of the nanoparticles.

DLS analysis is a consistent method to evaluate the average particle size and particle distribution of the NPs in the liquid. The DLS analysis shows the average diameter of green synthesized ZnO NPs in the liquid solution  $\sim 29.8$  nm (See SI, S2). Zeta potential distribution (ZPD) of ZnO NPs, as determined by DLS, is around  $-27.4$  mV. The Zeta potential is a significant parameter for predicting the long-term stability of nanoparticles. The observation revealed the net negative charge at the surface of the green synthesized nanoparticles. The negative charge indicates the stability of the ZnO NPs and also evaded the agglomeration of particles. The negative potential charge might be due to the capping

action of biomolecules present in the plant extract.

The UV-visible spectroscopy is an extensively used technique to measure the optical properties of nanosize particles. The peak observed at  $\sim 369$  nm wavelength was attributed to ZnO NPs (See SI, S2).

The FTIR spectrum was recorded in the range from  $500$ – $4000$   $\text{cm}^{-1}$  for the ZnO NPs synthesized through the green method (See SI, S2). Stretching vibrations of Zn–O sharp peaks were observed in the range of  $500$ – $800$   $\text{cm}^{-1}$ . The peak at  $1384$   $\text{cm}^{-1}$  was attributed to C = O stretching mode. The asymmetric and symmetric peaks associated with C–H bonds situated at  $2359$   $\text{cm}^{-1}$  proves the adsorption of surfactant compounds on the surface of ZnO NPs. The broad bands near  $1629$  and  $3421$   $\text{cm}^{-1}$  were recognized as the stretching modes of the hydroxyl group.

### 3.2. Anti-hyperglycemic activity of BA mediated ZnO NPs

The histopathological perception of liver segments from the test rodents delineated that both the leaf extract and ZnO NPs limited the cell harm prompted by STZ were shown in Fig. 2a–e. The histological sections of the control animal group depicted the normal architecture of cells. Congested central veins and peripheral inflammation is seen in the diabetic control group. Common architecture by obstruction of the

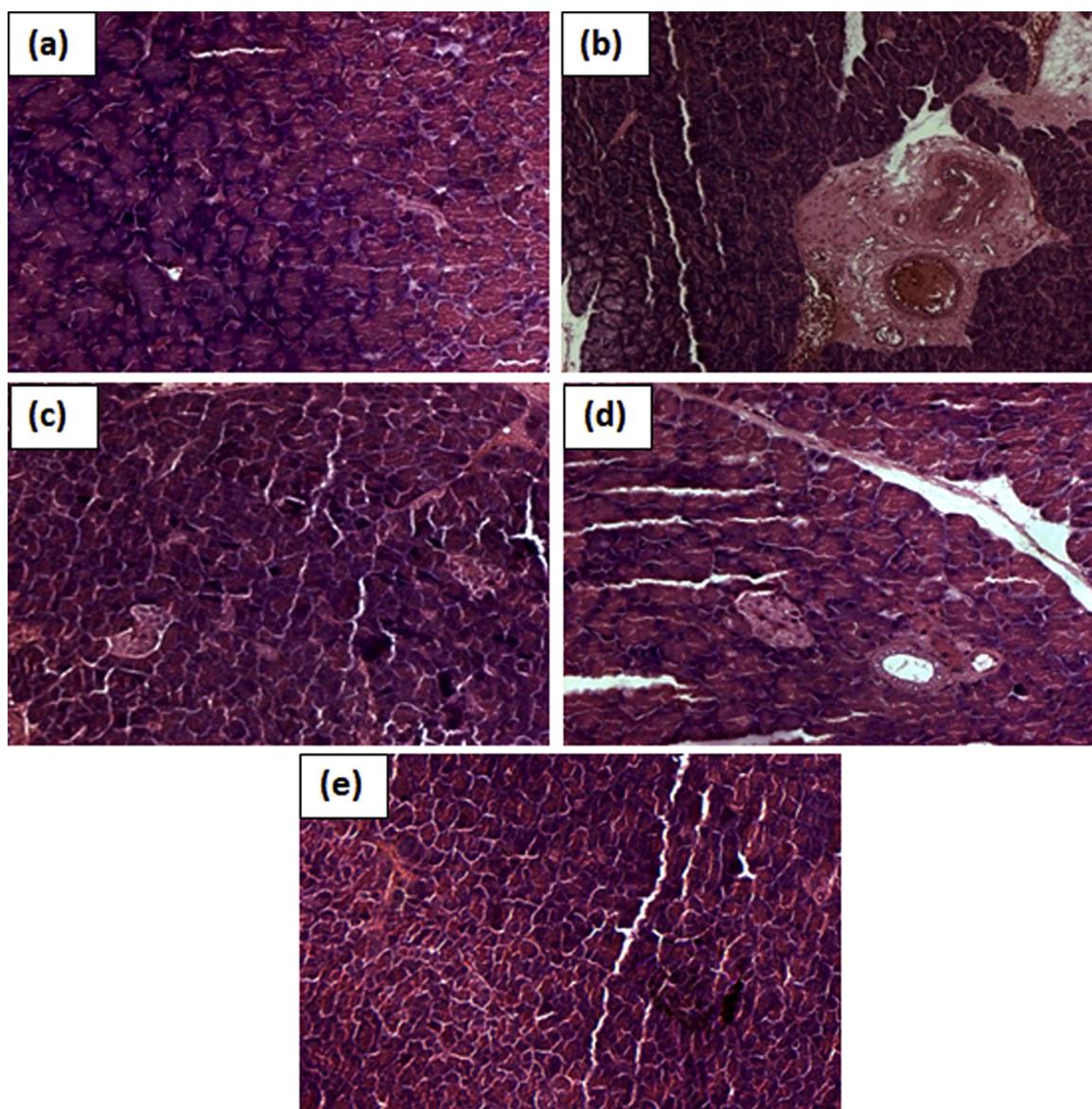


Fig. 2. (a) Normal control, (b) Diabetic control, (c) Metformin standard, (d) *Bambusa arundinacea* group, (e) Zinc oxide nanoparticles group.

portal vessels seen in the standard metformin group. Common architecture and the morphology of the hepatocytes were seen in *Bambusa arundinacea* group. Alike, normal architecture, and the hepatocytes were observed in the ZnO nanoparticles group.

The *Bambusa arundinacea* and ZnO nanoparticles oppressed to hypoglycemic conditions with a dose range of (200, 400) and (100 and 200) mg/kg respectively in the hypoglycemic study. With this study, it is observed that *Bambusa arundinacea* & ZnO NPs did not depict reduction in glucose levels in normal group rats' (Fig. 3a). The promising action by which nanoparticles depicted a hypoglycemic response maybe by the improvement of insulin secretions as of occurring  $\beta$ -cells of Langerhans of islets [28,29].

In Fig. 3b the *Bambusa arundinacea* & ZnO NPs anti-diabetic effects are represented in normal and diabetics groups. The normal control animals depicted normal glucose levels, whereas the diabetic group represented impressively more elevated levels than that of normal group animals. The event of the hyperglycemic condition has been encountered due to uncontrolled glucose levels expedited by a change in cell digestion in diabetic group animals [30,31]. It ought to be observed that diabetic group animals treated with ZnO nanoparticles completely ( $p < 0.001$ ) carries parameters of the biochemical to an ordinary level, depict the advantageous result of ZnO nanoparticles. The blood glucose levels were decreased on a dosage of 200 mg/kg of ZnO nanoparticles fundamentally, though *Bambusa arundinacea* additionally demonstrated hypoglycemic action in STZ incited diabetic animals. Oral organization of ZnO nanoparticles for a time of 14 days delivered a critical decrease in blood glucose levels than that of *Bambusa arundinacea* extract.

Insulin levels restored in ZnO nanoparticles treated group significantly to normal ( $p < 0.001$ ) when collating with diabetic group animals (Fig. 4). The present research work, the streptozotocin greatly enhanced the hyperglycemia. The persuade mechanism by which ZnO nanoparticles arbitrate their anti-hyperglycemic activity would be with the addition of pancreatic insulin emission as of the current  $\beta$ -cells of islets, as was clear by the basic improvement within the degree of insulin of the ZnO nanoparticles group animals.

### 3.3. Antimicrobial activity

The ZnO NPs have revealed the intense antimicrobial action against gram-positive bacteria. Enhanced zone of inhibition was observed with an increase in the concentration of ZnO NPs as shown in Fig. 5. Different concentrations (25  $\mu$ l, 50  $\mu$ l, 100  $\mu$ l, and 150  $\mu$ l) of ZnO NPs prohibited the organism replication and also killed the organisms. The zone of inhibition for *S. aureus* and *B. subtilis* for the concentration of 25, 50, 100, 150  $\mu$ l are 14, 16, 17, 19 mm and 12, 14, 15, 17 mm respectively. The outcome confirms that the biogenic assembly of ZnO NPs performs the effectiveness of an organism's growth hang-up. The outer membrane of the organism cells was surrounded by ZnO NPs by absorption

mechanism and activated the Zn + formation, which leads to the degeneration of the organisms cell membrane. The antimicrobial toxicity mechanism of synthesized ZnO NPs depends on their capability to create intemperance rarer oxygen species (ROS) development such as hydrogen peroxide, hydroxyl radicals, and superoxide anions. ZnO NPs penetrate the organism's cell membrane, which blocks the function of respiratory systems and transport proteins. The antibacterial activity is indomitable by the occurrence of biosynthesized ZnO NPs along with phytochemicals components such as phenolic and flavonoids. The ZnO NPs interaction between *S. aureus* and *B. Subtilis* was studied by SEM to observe the morphology changes of bacteria and under ZnO NPs treatment. In this study we collected the treated samples along with control separately, suspended in saline for centrifugation 10,000 rpm for 10 min, and collected pellet after the pellet was fixed overnight (4 °C) with glutaraldehyde. After that dehydrated through a series of graded ethanol 50, 70, 90, 100% for 15 min for each. The pellet was suspended in hexamethyldisilazane, finally suspension was air dried and coated with gold for SEM analysis. The normal *S. aureus* and *B. subtilis* shows spherical and rod shape with smooth surface area, but the morphology of bacteria treated by ZnO NPs appears the changes. The ZnO NPs treated bacteria shows the irregular morphology and change the bacterial cell walls. The results indicated that there is an interaction between bacteria and ZnO NPs, which lead to the demolition of bacterial cells.

### 3.4. Cytotoxicity study of ZnO NPs

Anticancer activity of *Bambusa arundinacea* mediated ZnO NPs against the MCF-7 cell lines are shown in Fig. 6. The ZnO NPs employed at different concentrations (0, 20, 40, 60, 80 and 100  $\mu$ L). It was observed that with an increase in ZnO NPs concentration the cell viability levels decreased. These results indicate that biosynthesized ZnO NPs exhibit good anticancer activity [32].

## 4. Conclusion

The current study involves the appraisal of the anti-diabetic activity of *Bambusa arundinacea* and its mediated ZnO NPs on a selected animal model. The ZnO nanoparticles have been synthesized using a green method and characterized. The results show that the dosing of the green synthesized ZnO nanoparticles has depicted the compelling anti-hyperglycemic effect than *Bambusa arundinacea*. In addition to the above, the theory for the biosynthesis of these nanoparticles is to explore biosynthesis as improved pharmacological & therapeutic features by a herbal extract, which is safe to the human body. The *Bambusa arundinacea* mediated ZnO nanoparticles have shown enhanced effects on diabetes mellitus compared to other test sample drugs, which shows that ZnO nanoparticles may substitute the harmful compound medications

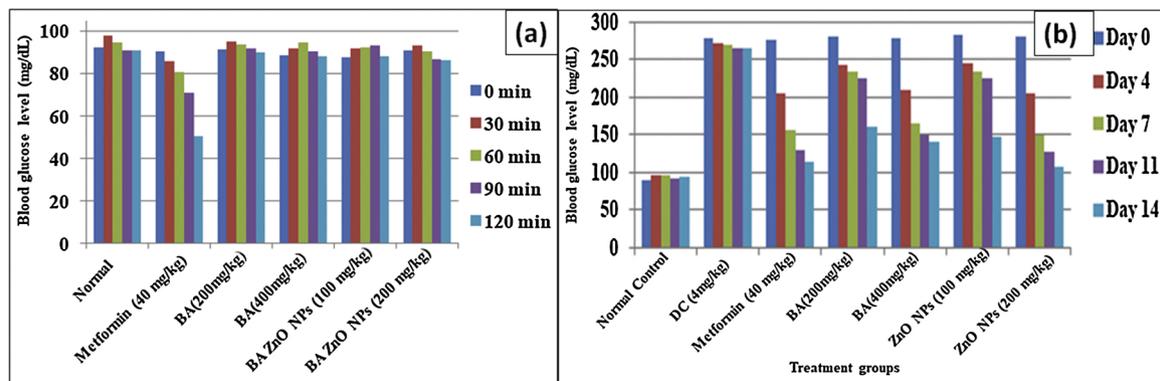


Fig. 3. (a) Effect of *Bambusa arundinacea* and ZnO NPs on fasted normal Wister rats, (b) Effect of *Bambusa arundinacea* and ZnO NPs on blood glucose levels in STZ induced diabetic Wister rats.

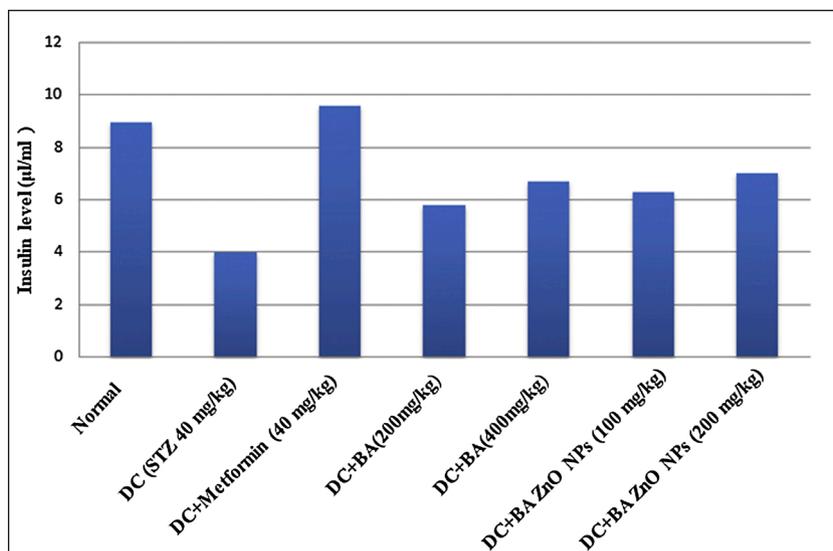


Fig. 4. Result of *Bambusa arundinacea* and ZnO NPs on serum insulin levels in diabetic rats.

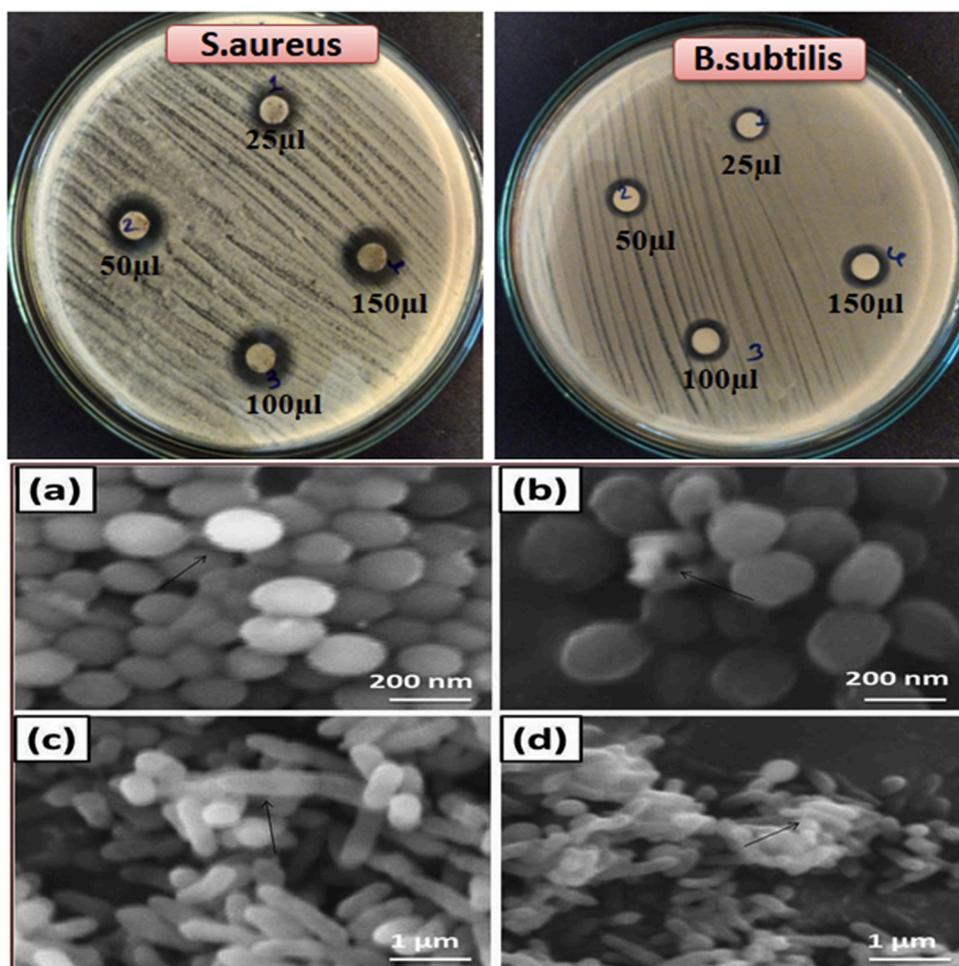


Fig. 5. Antimicrobial activity of *Bambusa Arundinacea* mediated ZnO NPs against *S. aureus* and *B. subtilis* and SEM images of a) Control *S. aureus* b) ZnO NPs treated Control *B. subtilis* and d) ZnO NPs treated.

and an alternate to unrefined extracts. The biosynthesized ZnO NPs were exhibiting strong antibacterial activity against pathogenic bacteria and anticancer activity. The current investigations have been helpful and supportive of the applications in nano-drugs formation, food, cosmetic

and pharmaceutical industries. Additional examinations will be conducted on biosynthesized ZnO NPs for the other medical applications.

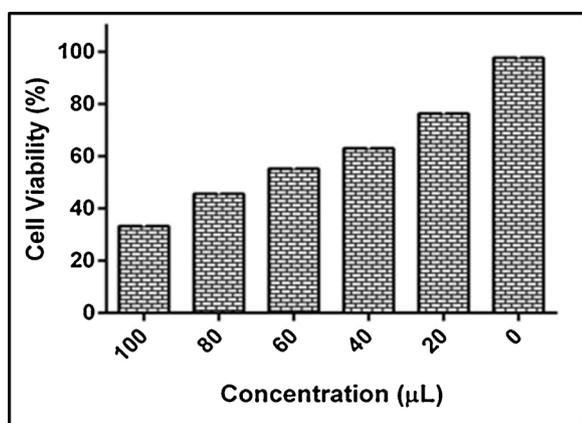


Fig. 6. Anticancer activity of *Bambusa arundinacea* mediated ZnO NPs.

### Declaration of Competing Interest

None.

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### Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.mtcomm.2020.101688>.

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