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PJBS

ISSN 1028-8880

Pakistan Journal of Biological Sciences

ANSInet
Asian Network for Scientific Information
308 Lasani Town, Sargodha Road, Faisalabad - Pakistan

OPEN ACCESS Pakistan Journal of Biological Sciences

ISSN 1028-8880
DOI: 10.3923/pjbs.2020.959.967

Research Article
Effects of Gold and Cerium Oxide Nanoparticles on Type 1 Diabetes in Experimental Mice

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Abstract

Background and Objective: Diabetes mellitus (DM) has appeared as an epidemic disease globally in the last few years. The nanotechnology has providing management, treatment and insulin delivery modalities which potential to improve quality of life for diabetics. Recent development in the field of diabetic treatment research at its line with nanotechnology is great attention to explore their benefits. **Materials and Methods:** In this study, experimental mice are induce with type 1 diabetes after streptozotocin (STZ) inoculation of 60 mg kg^{-1} of body weight for 5 days. Then, the diabetes-induced mice were divided into different groups: (1) treated with insulin as a traditional treatment, (2) treated with gold nanoparticles (AuNP) 1.5 mg kg^{-1} b.wt./day and (3) treated with nanoceria 50 mg kg^{-1} b.wt. by intraperitoneal inoculation for 25 days. **Results:** Our data clearly showed a hypoglycemic effect, by which blood glucose level (BGL) decreased to 140±6.84 and 140.90±6.74 from 236.60±16.48 mg dL^{-1} in groups treated with AuNP and nanoceria, respectively. Moreover, a significant improvement observed in serum liver enzymes and insulin level with a marked decrease in the pancreatic level of inflammatory cytokines, interferon gamma (IFN-γ) and interleukin-beta 1 (IL-1β). Confirming the previous results showed a marked improvement in pancreatic islet cells, with a lower percentage of apoptosis in groups treated with AuNP and nanoceria. **Conclusion:** AuNPs and nanoceria have a distinct and effective role in lowering glucose levels, with a marked improvement in blood insulin level. In addition, a marked improvement in pancreatic islet cells observed and confirmed by diminishing percentage of apoptosis in the treated groups. This role has a potential therapeutic use for humans in the future.

Key words: Diabetes, gold and cerium oxide, nanoparticles, cytokines, apoptosis

Citation: Jameel Alghamdi and Mohamed F. El-Refaei, 2020. Effects of gold and cerium oxide nanoparticles on type 1 diabetes in experimental mice. Pak. J. Biol. Sci., 23: 959-967.

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Competing Interest: The authors have declared that no competing interest exists.

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

INTRODUCTION

Diabetes mellitus (DM) is a disease manifested by an incomplete or occasionally severe deficiency in the insulin excretion level, consequently increase of the glucose level in blood. Scientific surveys in low and poor-income countries have established that there are approximately 366 million people confirmed to be diabetic, possibly increasing to more[1] than 500 million by 2030. In developed countries, diabetes has increased rapidly in the last decade. This disease may become a pandemic and threaten the lives and livelihood of individuals in many parts of the world, including Asia, South America, the Middle East, Africa and Latin America[2]. The symptoms of diabetes include life-threatening weight loss, polyuria, polydipsia and polyphagia[3].

Diabetes categorized into type 1 and type 2. Type 1 diabetes is very dependent on insulin secreted from the pancreatic beta cells, which is the basis of the excretion of insulin from the islets of Langerhans by the autoimmune system in the pancreas. Type 2 diabetes results from defects in insulin receptors on cells, followed by a deficit in insulin secretion[4]. In addition to the two primary types of diabetes, gestational diabetes is a type of diabetes that occurs in some pregnant women because of excess hormonal change during this period and it is relate to insulin sensitivity followed by excess glucose level[5].

DM is a disease that requires careful and continuous follow-up, in addition to the necessity of adjusted diet, lifestyle and regular exercise. Insulin (subcutaneous management) is a unique solution to address hyperglycemia[6]. However, low blood glucose (hypoglycemia) is a disadvantage of insulin therapy[7] as are peripheral hyperinsulinemia[8], lipoatrophy, lipohyperatrophy[9], obesity owing to severe therapy[10], insulin neuropathy and insulin presbyopia. Daily injections are necessary to maintain an adequate glucose level in blood[11], sometimes causing psychological stress for the patient and leading to poor patient compliance.

Accordingly, different routes of administration, such as oral and inhaled, is developed to overcome the flaws and complications of conventional insulin therapy[12].

As a solution to these challenges, nanocarriers have considered the best-suited vehicle for insulin as they taken by mouth[13]. Lately, nanotechnology found to be useful in general medicine and in the control of diabetes in particular[14]. In general, small nanoparticles used especially fine gold nanoparticles (AuNPs), because of their biochemical and biological properties[15], to resolve many complications of treatment. Techniques such as biosynthesis used to prepare AuNPs that have special abilities in the treatment of diabetes[16]. Because a nanoparticle contains compounds with multiple activities, it can treat blood sugar at different levels[17,18].

Recently, AuNPs has studied extensively because of their inert nature and on the grounds that they can be potential and influential carriers for drugs[19]. Moreover, their ability to bind to many biomolecules such as amino acids, proteins and DNA as well as adjusting their sizes and shapes and simply the ability to change and modify their surface are features unique to AuNPs[20,21].

The AuNPs used in many investigations as treatment for DM are in the form of an insulin-AuNP composite, in which insulin is condensed on the AuNP exterior either alone or combined with an alternative molecule that plugs the AuNP nanosphere. Most AuNPs prepared by the chemical decrease of tetrachloroauric acid (HAuCl4) to obtain the metal nanosphere[22].

Moreover, cerium oxide nanoparticles (nanoceria) have oxygen flaws in their matrix construction that recreate a free radical and scavenger in a physiological environment[23]. Many past research studies have shown how nanoceria have improved the level of antioxidants in addition to their capability to eliminate toxins and free radicals in both the liver and brain[24]. The present study was conducted to find the effects of management with AuNPs and nanoceria on glucose level. The effects of nanoparticles in mice with induced type 1 diabetes, in the presence of certain inflammatory mediators, biochemical, cytokines and apoptotic effects, were evaluated

MATERIALS AND METHODS

Experimental animals: This research was conducted on 100 adult male albino mice (50 mice were used to check toxicity and dosage), 6-8 weeks of age, weighing 25-30 g. The animals received from the University of King Abdulaziz, Saudi Arabia. All the animals housed in steel wire cages (5/cage) in the Laboratory of Biochemistry, Faculty of Medicine, Al Baha University Saudi Arabia, under sterile conditions. The mice fed a normal commercial laboratory diet with free access to water and chow supplied in clean dishware. The animals housed at room temperature with a 12 h light/dark cycle. To avoid the effect of different food elements on the experiments, all mice fed a similar type of food[25]. The mice allowed acclimating for 1 week before the experiments.

Study area: In this study, experiments carried out at biochemistry laboratory from (February-November, 2019) at Faculty of Medicine, Al Baha University, Saudi Arabia.

All procedures in this research work approved by the ethical committee of the Faculty of Medicine of Al Baha University. The mice divided into the following groups: Group 1: (Normal group, n = 10), they received a normal diet. Group 2: [Streptozotocin (STZ)-induced diabetic group, n = 40], they received an intraperitoneal (IP) injection of 60 mg kg^{-1} of body weight (b.wt.) of newly organized STZ solution at pH 4.5 liquefied in 0.2 mmol L^{-1} sodium citrate to develop type 1 diabetes[26,27]. Verification of induced diabetes done after 4 days by measuring the blood level of glucose in tail vein blood with the Ultra 2 Glucometer One Touch. Diabetic mice (blood glucose level (BGL) >200 mg dL^{-1}) selected for experiments. Then, the diabetic mice divided into three groups as follows: Group 2a: Diabetic insulin-treated group, 0.3 U/100 g of Lantus daily for 25 days (DI, n = 10), representing traditional treatment. Group 2b: Diabetic AuNPs-treated group (DG, n = 10), in which diabetes-induced mice were treated with AuNPs (6 nm) (1.5 mg kg^{-1} b.wt./day) for 25 days. Group 2c: Diabetic nanoceria-treated group (DC, n = 10), in which diabetes-induced mice were treated with a selected nanoceria dose (50 mg kg^{-1} b.wt. IP) for 25 days[28,29]. The group 2a received only saline[30]. At the end of experiments on day 26, blood was drawn with heart puncher under anesthesia, all groups experienced euthanized and organs were sliced and kept frozen for further analysis.

Determination of serum liver enzymes: In accordance with the procedure of Young[27], the level of alanine transaminase (ALT) determined by lactate dehydrogenase (LDH)-reduced nicotinamide adenine dinucleotide (NADH) kinetic ultra-violet reaction. The aspartate transaminase (AST) level was assessed using multi-dehydrogenase (MDH)-NADH kinetic ultra-violet reaction, in accordance with the procedure designated by Tietz *et al.*[28] and Murray *et al.*[30]. Using the p-nitrophenylphosphate kinetic reaction defined by Tietz *et al.*[28] and Wenger *et al.*[29], the alkaline phosphatase (ALP) level was determined.

Determination of glucose and insulin levels in mouse serum: The same blood samples size drawn from all groups through a heart perforation at the end of the study on day 26. Using an Ultra 2 glucometer and well-matched blood glucose strip, the glucose concentration was determined (Lifescance chesterbrook, PA, USA)[31]. Using the microparticle enzyme immunoassay (MEIA), Abbott AxSYM® system, the insulin level was determined.

Measurement of serum creatinine and serum blood urea nitrogen (BUN) level: The serum creatinine level was assessed with creatinine kits provided by Spinreact, according to Murray *et al.*[30]. The BUN level was determined using Spinreact urea kits.

Determination of the IFN-γ and IL-1β (pg mL^{-1}) content in pancreatic tissue: The pancreatic levels of interferon gamma (IFN-γ) and interleukin-beta 1 (IL-1β) were analyzed using the enzyme-linked immunosorbent assay (ELISA) technique, with monoclonal antibodies specific for IFN-γ and IL-1β, respectively. Using regular curves, concentrations will define. Samples were tested in duplicate according to the manufacturer's directions.

Determination of DNA fragmentation flow cytometry: The samples defrosted and pulverized with a scalpel in an ice-cold phosphate-buffered saline (PBS) solution. Then, the samples clarified through a 70 m nylon mesh. After washing in the PBS solution and centrifugation, the cells chosen for analysis were collected and incubated with a solution containing propidium iodide (PI) (10 g mL^{-1}, Sigma) and RNA-ase (1 mg mL^{-1}, Sigma). The tubes placed at 4°C in the dark for at least 30 min before analyzing by flow cytometry. The PI fluorescence of individual nuclei measured using a Coulter Epics XL. At least 5×10^3 cells for each sample were measure. Apoptotic cells signify by a subdiploid peak of cells that can be simply distinguished from the peak of cells with the diploid DNA in the red fluorescence passage. The ratio of apoptosis was designate by the fraction of cells with subdiploid DNA content[32].

Statistical analysis: The data analyzed using Statistical Package for Social Science software computer program version 15 (SPSS, Inc., Chicago, IL, USA). The data were parametric and presented in the mean and standard deviation. A one-way analysis of variance (ANOVA) followed by Tukey test used for comparing parametric data. The pearson correlation used to correlate different parameters. The $p<0.05$ were consider statistically significant

RESULTS

Serum liver enzymes (ALT, AST and ALP): As shown in Table 1, the mean values of serum liver enzymes in the diabetic untreated group (group 2) were significantly high

Table 1: Levels of ALT, AST and ALP in control normal mice, diabetic mice and diabetic treated mice group with insulin, AuNPs and nanoceria

Liver enzymes parameters (IU L^{-1})	Control normal mice (group 1)	Diabetic mice (group 2)	Insulin treated mice (group 2a)	AuNPs treated mice (group 2b)	Nanoceria treated mice (group 2c)	p-value
ALT	64.05±2.78	150.40±7.18***	95.32±3.86***,###,¶¶¶	84.67±3.33***,###,¶¶¶	94.04±3.49***,###,¤¤¤	<0.001*
AST	80.91±2.70	164.30±4.34***	99.25±4.07***,###	88.60±3.83***,###,¶¶¶	97.41±4.02***,###,¤¤¤	<0.001*
ALP	201.20±6.41	374.80±5.93***	226.30±8.10***,###	213.20±5.88***,###,¶¶¶	227.70±6.14***,###,¤¤¤	<0.001*

*p<0.05,***p<0.001 vs. control normal mice group, #p<0.05, vs. diabetic mice group, ¶¶¶p<0.001 vs. Insulin treated mice group, ¤¤¤p<0.001 vs. Au/NPs treated mice group

Table 2: Levels of insulin, glucose, BUN and creatinine in control normal mice, diabetic mice group and diabetic treated mice group with insulin, AuNPs and nanoceria

Biochemical parameters	Control normal mice (group 1)	Diabetic mice (group 2)	Insulin treated mice (group 2a)	AuNPs treated mice (group 2b)	Nanoceria treated mice (group 2c)	p-value
Insulin level (μIU mL^{-1})	11.00±0.99	4.69±0.36***	7.42±0.56***,###	9.71±0.93***,###,¶¶¶	10.70±0.72###,¶¶¶,¤¤¤	<0.001*
Glucose level (mg dL^{-1})	97.02±5.77	236.60±16.48***	125.10±9.56***,###	140.00±6.84***,###,¶¶¶	140.90±6.74***,###,¶¶¶	<0.001*
BUN level (mg dL^{-1})	13.39±1.10	38.75±3.22***	19.61±1.10***,###	20.65±1.63***,###	19.22±1.44***,###	<0.001*
Creatinine level (mg dL^{-1})	0.91±0.09	1.59±0.13***	1.02±0.09*,###	0.99±0.14###	0.99±0.11###	<0.001*

One way ANOVA followed by *post hoc* tukey, *p<0.05,***p<0.001 vs. control normal mice group, ###p<0.001 vs. diabetic mice group, ¶¶¶p<0.001 vs. insulin treated mice group, ¤¤¤p<0.001 vs. Au/NPs treated mice group

Table 3: Levels of IFN-γ and IL-1β in control normal mice, diabetic mice group and diabetic treated mice group with insulin, AuNPs and nanoceria

Cytokines parameters (pg mL^{-1})	Control normal mice (group 1)	Diabetic mice (group 2)	Insulin treated mice (group 2a)	AuNPs treated mice (group 2b)	Nanoceria treated mice (group 2c)	p-value
IFN-γ	10.87±0.53	27.85±0.44***	22.71±0.71***,###	14.13±0.68***,###,¶¶¶	17.99±0.49***,###,¶¶¶,¤¤¤	<0.001*
IL-1β	128.40±3.35	249.50±3.59***	146.80±3.34***,###	135.50±3.88***,###,¶¶¶	149.40±2.94***,###,¤¤¤	<0.001*

*p<0.05,***p<0.001 vs. control normal mice group, ###p<0.001 vs. diabetic mice group, ¶¶¶p<0.001 vs. insulin treated mice group, ¤¤¤p<0.001 vs. Au/NPs treated mice group

150.40±7.18, 164.30±4.34 and 374.80±5.93 for ALT, AST and ALP respectively, compared with normal mice. These results were decreased significantly in groups treated with insulin 0.3 U/100 g, AuNPs 1.5 mg kg^{-1} b.wt./day IP and nanoceria 50 mg kg^{-1} b.wt. IP, respectively.

Effect of AuNPs and nanoceria on serum blood glucose and insulin levels: The treatment of diabetic mice with AuNPs (1.5 mg kg^{-1} b.wt./day) showed a time-dependent decrease in BGL. The reduction in BGL started to be significant by day 15 of treatment compared with the level before treatment (236.60±16.48 mg dL^{-1}) (Fig. 1). By day 25, the BGL decreased to 140±6.84 mg dL^{-1}, treated with AuNPs 1.5 mg kg^{-1} b.wt./day IP, which was non-significantly different from the value in the normal group 1. The diabetic mice treated with nanoceria (50 mg kg^{-1} b.wt. IP) for 25 days showed significant decreases in BGL 140.90±6.74 compared with the diabetic saline group 2 ($p>0.05$, ANOVA) (Table 2). The insulin-treated group 2b kept as a positive control throughout the experiment and showed significant effect for all parameters analyzed. Conversely, the BGL of diabetic mice group 2, which treated with saline, increased during the treatment period time-dependently. The normal mice that treated with insulin for lethality, dose selection, AuNPs and nanoceria did not show any changes at the beginning and during the experiment period (data not shown). Moreover, diabetic mice that treated with both

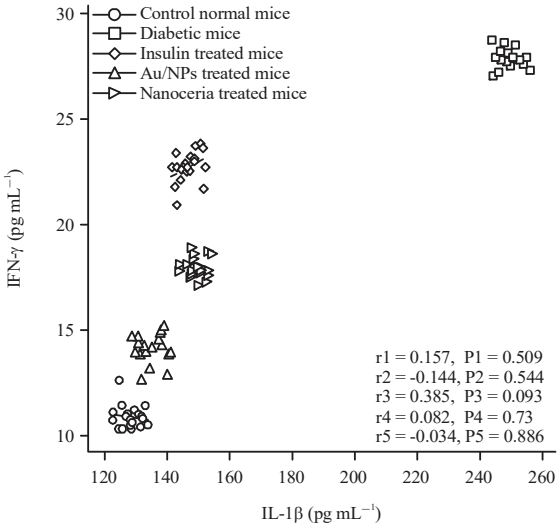

Fig. 1: Correlation between investigated cytokines parameters and control normal mice, diabetic mice, insulin, AuNPs and nanoceria diabetic treated mice groups

nanoparticles for 25 days showed significant increases in the serum insulin level compared with the diabetic group 2 and almost the same as normal levels. Furthermore, creatinine and BUN levels for group 2b and c resulted in significant decreases compared with the diabetic group (Table 2).

Effect of AuNPs and nanoceria on the IFN-γ and IL-1β (pg mL^{-1}) content in pancreatic tissue: The diabetic mice group 2 kept without treatment throughout the experiment for 25 days showed a significant increase in the pancreatic level of IFN-γ and IL-1β (27.85±0.44, 249.50±3.59, respectively), compared with the normal group. On the other hand, treatment of diabetic mice with insulin 0.3 U/100 g, AuNPs 1.5 mg kg^{-1} b.wt./day and nanoceria 50 mg kg^{-1} b.wt. IP, respectively, for 25 days resulted in a significant decrease in the pancreatic level of IFN-γ and IL-1β (Table 3) compared with the diabetic group 2 without treatment. However, normal mice treated with insulin 0.3 U/100 g, AuNPs 1.5 mg kg^{-1} b.wt./day and nanoceria 50 mg kg^{-1} b.wt. IP for 25 days showed a non-significant change in pancreatic IFN-γ and IL-1β (data not shown).

Flow cytometry for cell apoptosis: The percentage of apoptotic cells with hypodiploid DNA content in pancreatic tissues was determined from DNA histograms. Figure 2a showed a normal pattern with 7.6% of apoptotic cells for the normal mice group 1. Untreated diabetic group 2 mice showed a peak pattern that represented proliferative and high percent of apoptotic activity (62.9%) (Fig. 2b). However, the mice that treated with insulin 0.3 U/100 g, Au/NPs 1.5 mg kg^{-1} b.wt./day and nanoceria 50 mg kg^{-1} b.wt. IP respectively for 25 days resulted in a significant decreased size of the peak and a shift to the lowest intense parallel and significant fluorescence area. This decrease in the intensity and shift may be termed reduced nuclear apoptosis and fragmentation (Fig. 2c-e).

DISCUSSION

Presently, nanotechnology is rapidly evolving in the medical field. It has beneficial roles in diagnosis, therapeutics and prophylaxis. Modern medicines based on nanotechnology considered the best available medical tools in the 21th century to correspond to traditional drugs. Nanotechnology has created new and diverse avenues for improvement of new medication transport systems[33]. Another advantage of nanotechnology is decreased safety issues compared with all newer medication pathways[34].

In the current study, the anti-diabetic effect of using AuNP and nanoceria agents has received much attention from researchers and investigators in treating diabetes mellitus. The chief purpose of the present research study was to endorse the anti-hyperglycemic effects and mechanism of action of AuNP of 1.5 mg kg^{-1} b.wt./day and nanoceria 50 mg kg^{-1} b.wt./day on in experimental male Swiss albino mice induced diabetes type 1. This was recognize with the main decrease of blood levels that emphasizes the anti-diabetic effect of AuNP and nanoceria[35,36].

The results of this study exhibit a significant increase in the mean glucose level, while the mean insulin level significantly diminished in the diabetic group 2 of mice in compare to the normal group. The intraperitoneal injection of AuNP at a dosage 1.5 mg kg^{-1} b.wt./day and nanoceria 50 mg kg^{-1} b.wt./day for 25 days, illustrate that the blood glucose level for group 2b and c were significantly decreased. The insulin injection considered as base and control group for traditional ways in diabetes treatment, whereas, the serum insulin level was significantly improved compared to diabetic group 2 for both treatment. Contrariwise, the blood glucose level was not away from the normal level of glucose and near to the traditional insulin treatment group 2a. These findings are in a harmony with the earlier study designated by Barathmanikanth *et al.*[37]. Their results clearly showed a decrease in glucose level clearly after the specified treatment period with AuNPs compared to diabetic group 2. Moreover, Jahani *et al.*[38] has shown that nanoceria may be used as a distinct and complementary treatment for the treatment of glucose elevation and has an effective role in preventing complications as a result of hyperglycemia. While another study directed by Selim *et al.*[39] did not find any obvious differences in glucose level either before or after treatment. Furthermore, Karthick *et al.*[40], showed a significant decrease in blood glucose level and effective increase in blood insulin level when AuNP used on experimental rats treatment groups. In parallel to this study, they noticed a reduction in blood glucose levels after treatment as well as, insulin, where it seemed at the normal level.

Metabolic enzymes AST (aspartate transaminase), ALT (alanine transaminase) and ALP (alkaline phosphatase) are well-known to outflow and escape to the blood in several cases, including high blood sugar level and some times in the case of damage to liver tissue and other cases, this is scientifically confirmed. In this study on mice experiments STZ-induced type I, the results showed that after the incidence of diabetes, the mean of serum levels of liver enzymes ALT, AST and ALP, in addition to creatinine and nitrogen urea increases significantly compared with normal group ($p<0.001$). At the selected concentration 1.5 mg kg^{-1} b.wt./day and 50 mg kg^{-1}b.wt./day for 25 days respectively, the levels of both enzymes and kidney function significantly decreases ($p<0.001$) in compare to diabetic group 2, which is an amazing result of the effects of both AuNP and nanoceria for protective liver and kidney tissues from damage. These comparing results obtained from this study in similarity with the results of

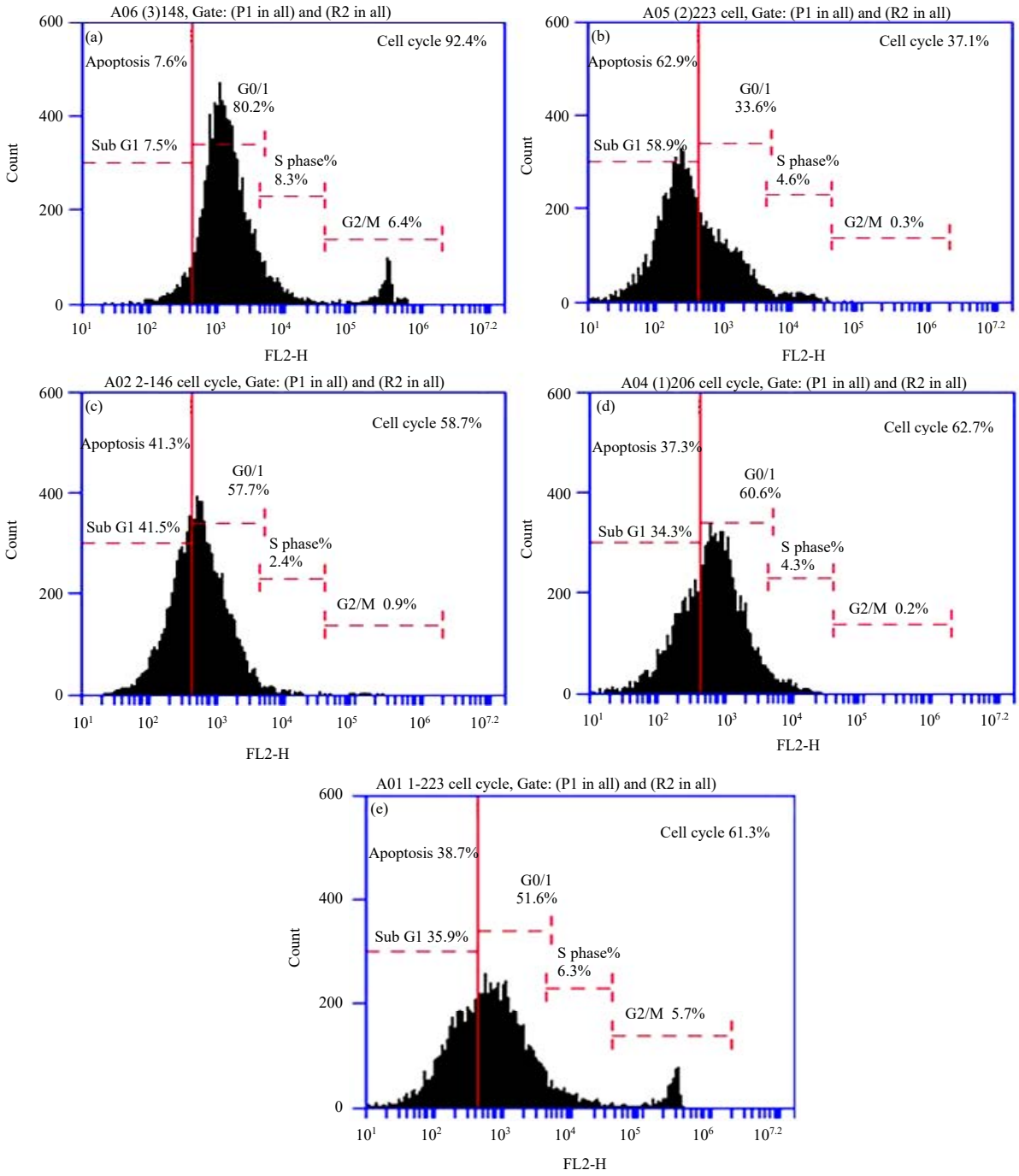

Fig. 2(a-e): DNA histograms (a) Showed normal pattern 7.6% apoptotic cell for normal mice group 1, (b) Untreated diabetic group 2 mice showed a peak pattern which represented proliferative and high percent of apoptotic activity 62.9%, (c) Represent treatment with insulin, (d) AuNPs and (e) Nanoceria, respectively

Barathmanikanth *et al.*[37]. Where their study proved the potential effect of AuNPs in treatment of mice induced diabetes and a marked decrease and certain and led to a decrease in the level of enzyme and kidney function compared to non-treatment in the group, close to the normal levels. Furthermore, Selim *et al.*[39] studied the effect of the AuNP treated diabetic mice and showed that the level of liver enzymes as well as the level of creatine improved significantly, return to normal level, which are key indicators for both the liver and kidneys when compared with the mice diabetic

group 2. In contrast to the results of the current study, Doudi and Setorki[41] and Abdelhalim and Moussa[42] demonstrated have been shown that there is no change in the level of creatinine and urea even after treatment with AuNP and when compared to the untreated group. This may accredited to the use of non-significant concentrations with 10 nm and 50 nm nanoparticles or short treatment period.

Cytokines, such as IL-1, TNF and IFN-γ have been known leading to type 1 diabetes motivate inducible nitric oxide synthase (iNOS) appearance in islets and the resulting increased production of nitric oxide (NO) causes islet cell destruction or cytokines that then stimulate NO production by β-cells. The anti-inflammatory activity and immune modulatory effects of gold nanoparticles and nanoceria are associated with an extracellular interaction with many cytokines, thus opening hypothetically innovative choices for additional therapeutic claims. This may take for chronic cases as an effective treatment.

Results showed that the nanoparticles used as treatment of diabetic groups in this research study is significantly inhibit most common immunoregulatory and anti-inflammatory cytokines IFN-γ and IL-1β, which have an effective role in ROS production. The data, exhibit that group 2b and c were showed a decrease in the serum levels of IFN-γ and IL-1β compared to diabetic group 2 ($p<0.001$), Table 3. However, these data not in track with the normal data of group 1 but are mostly improved compared with the insulin-treated group 2a with the consideration that effects are significantly clear. The results gained from this research are well matched with Dhall and Self[43] and Ribera *et al.*[44], who showed that cerium oxide nanoparticles can possibly diminish ROS production in inflammation conditions and consequently, provide an innovative treatment for chronic inflammation. Moreover, the results of Barathmanikanth *et al.*[37] and Kingston *et al.*[45], show that gold nanoparticles have an anti-inflammatory effect, balancing or inhibiting the ROS generation in hyperglycemic conditions, scavenging free radicals and decreasing hyperglycemia. Furthermore, Dkhil *et al.*[46] are in agreement with the results obtained in this study and mention that AuNP amended the inflammatory response by decreasing the mRNA expression of IL-1β and INF-γ. On the other hand, investigated IL-1β and INF-γ correlate with AuNPs and nanoceria treated diabetic mice (Fig. 1).

The toxicity of glucose due to its high and uncontrolled level in diabetes, especially type 1, may have a negative impact on pancreatic islet cells, which causes the programmed death of pancreatic islet cells[47]. Results clearly illustrate the hypoglycemic effects of both AuNP and nanoceria at the selected dose, which considerably improved the apoptotic percent of treated groups (Fig. 2d and e) compared with the untreated group 2 (Fig. 2b), with 62.9% apoptosis. These data show that AuNP and nanoceria may have protective effects in addition to the antidiabetic effects. At the same time, these findings may attribute to the improvement in the level of inflammatory mediators after a nanoparticle, which discussed earlier.

CONCLUSION

This study has summarized that both AuNPs and nanoceria have a distinct and actual effect on lowering the level of glucose in treated mice groups, with a marked improvement in blood insulin level. In addition, the signs of inflammation decreased and the level of liver enzymes and kidneys improved positively. In addition, a marked improvement in pancreatic islet cells observed and confirmed by a diminishing percentage of apoptosis in the treated groups. Taking into account that, these nanoparticles have negative side effects, the effectiveness and cost may have an influential role in the treatment of humans in the near future.

SIGNIFICANCE STATEMENT

This study discovers and gives great attention for applied the nanotechnology in treatment of and improve quality of life for diabetes. Experimental Swiss mice were designate for this research work. The study address the novelty aspect of both AuNP and nanoceria in reducing the glucose level, inhibiting the inflammatory cytokines, improve the biochemical parameters without altering or threatening survival rate. As well, markedly improve in pancreatic islet cells through diminishing percentage of apoptosis. This research work surely, with respect to the existing publications in that field will encourage the use of nanoparticles in treatment of diabetes in the future. Moreover, the traditional drugs will avoid for more safety and can consider as innovative choices for additional therapeutic claims. Finally, this may be effective treatment more generally to the society in the future.

ACKNOWLEDGMENT

The authors would like to express their appreciation to the supportive team of technical specialists in the Deanship of Scientific Research in Al Baha University, Kingdom of Saudi Arabia, for providing necessary guidance Project No. 2/1439-2018.

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