International Journal of Pharmaceutical Science and Research
ISSN: 2455-4685, Impact Factor: RJIF 5.28
www.pharmacyresearchjournal.com
Volume 1; Issue 3; March 2016; Page No. 43-45

Effect of silver nanoparticles on carbohydrate and protein biochemical parameters in induced diabetic rats

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Abstract
The objective of this study was to evaluate the antidiabetic activity of silver nanoparticles (SNPs) in a model of dextrose -induced experimental diabetes in rats. Silver nanoparticles were used as reducing agent. In control and hyperglycemic rats was performed the measurement of blood glucose levels and glucose tolerance tests. Hepatic Glycogen Synthase enzymes were decreased from 41.07% to 26.20% when diabetic rats treated with silver nanoparticles. The protein metabolic enzymes includes Total synthesis of –L-Hexoses (5.27 mmol/L to 5.14 mmol/L), Serum Hexosamine (135.13 mg/%) to 132.95 mg/%)) and serum Sialic acids (83.70 mg/%) to73.80 mg/%) were decreased by the silver nanoparticle treatment. Intra peritoneal injection of silver nanoparticles decreased the carbohydrate and protein metabolic enzymes levels. The experiment showed the silver nanoparticles have antidiabetic activity.

Keywords: Glucose, Hexokinase, Hepatic glycogen synthase, Sialic acid, Silver nanoparticles

Introduction

Diabetes is one of the leading cause of deaths in the world. India is the leading country in diabetes. Without enough insulin, the cells of the body cannot absorb sufficient glucose from the blood; hence blood glucose levels increase, which is termed as hyperglycemia. Diabetes is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels. Diabetes mellitus is a chronic metabolic disease with the highest rates of prevalence and mortality worldwide that is caused by an absolute or relative lack of insulin and or reduced insulin activity, which results in hyperglycemy and abnormalities in carbohydrate, protein and fat metabolism [1].

Presently, there are 382 million people living with diabetes. Another 316 million with impaired glucose tolerance are at high risk from the disease – it is an alarming number that is set to reach 471 million by 2035. Diabetes is on the rise all over the world and countries are struggling to keep pace.

The noble metals includes Ag, Pt, Au and Pd. Among these metals, silver (Ag) have potential applications in the field of biological systems, living organisms and medicine [2]. silver nanoparticles (Ag-NPs) may have many applications, includes catalysts in chemical reactions [3] (3), electrical batteries and in spectrally selective coatings for absorption of solar energy [4, 5], as optical elements [6], pharmaceutical components and in chemical sensing and biosensing [7, 8].

Materials and methods

Induction of experimental diabetes

Normal healthy male Wistar albino rats, 9-12 weeks old with an average weight of 200-250 gm were procured from the Mahaveer Enterprises, Bagh Amberpet, Hyderabad. All experimental procedures involving animals were conducted in accordance with the guidelines of Committee for the Purpose of Control and Supervision on Experiments on Animals (CPCSEA).

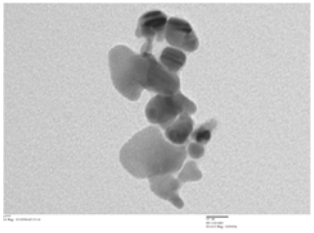
Dextrose was used to induce diabetes mellitus in male albino wistar rats. A freshly prepared dextrose solution was given orally at 6.6 gm/rat/5ml. After 15 days, rats with moderate diabetes having glycosuria and hyperglycemia were selected for the experiment. Synthesized Silver nanoparticles were purchaged from Nano Green Technology LTD, India. The nanoparticles were injected intraperitonial to experimental rats.

Experimental protocol

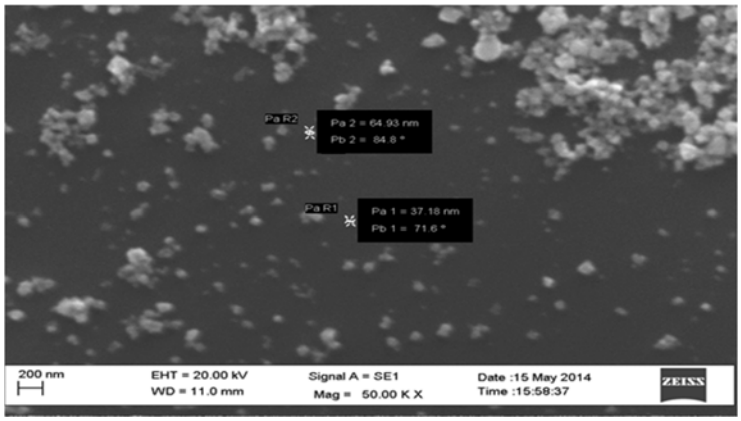
Group1	Normal Rats
Group2	Diabetic controlled Rats
Group3	Diabetic rats treated with Standard drug Glipizide-4 mg/kg body weight
Group4	Diabetic rats treated with Silver nano particles(50 ug)-2 ml/200gms body weight

Results

Below the images of 50u size of silver nanoparticles were given and all the biochemical parameters of the experiment were given.



SEM image of $AgNO_3$ naoparticles



TEM image of $AgNO_3$ naoparticles

Table 1: Changes in the levels of glucose, hexokinase, glucose 6 phasphatase and hepatic gylycogen synthase in control and experimental rats.

	Glucose (mg/dl)	Hexo Kinase(mg/dl)	Glucose 6 phasphatase (Umoles/mg)	Hepatic Glycogen Synthase (%)
Normal	134.50±5.75	91.82±1.68	7.57±0.15	26.97±1.81
Diabetic controlled	428.67±25.97*	212.10±2.07*	12.42±0.71*	41.07±1.94*
Standard Glipizide-4 mg/kg body weight	144.00±12.02	103.22±2.14*	10.69±0.16*	33.40±2.59*
Silver Nano particles(50ug)-2 ml/200gms body weight	193.33±15.42*	125.57±2.66*	11.41±0.26*	26.20±3.18

Table 2: Changes in the levels of plasma glycoproteins in control and experimental animals

	Total Synthesis of The L-Hexoses(mmol/L)	Serum Hexosamine (mg/%)	Serum Sialic Acid (mg/%)
Normal	3.45±0.14	112.62±2.71	69.17±2.48
Diabetic controlled	5.27±0.18*	135.13±1.73*	83.70±2.57*
Standard Glipizide-4 mg/kg body weight	4.57±0.23*	123.68±2.45*	74.28±1.25*
Silver nano particles(50 ug)-2 ml/200gms body weight	5.14±0.14*	132.95±2.09*	73.80±1.91*

Discussion

Anti-diabetic activity of silver nanoparticles were investigated on rats for their potential therapeutic effects against dextrose induced hyperglycemia. In this current study we have investigated anti-diabetic activity of silver nanoparticles size 50u. It was observed there was a signifcant enhancement of blood glucose level in rats induced with dextrose and which was restored by silver nanoparticles treatments. (Table.1). Reduction of blood glucose level in rats treated with silver nanoparticles were significant.

In this study, we have observed altered levels of L- hexose, hexosamine, and sialic acid in plasma and tissues of dextrose - induced diabetic rats. Glycation is a nonenzymatic reaction of glucose and the saccharide derivatives with proteins, nucleotides and lipids [9]. In hyperglycemia, the reactions occur between reducing sugars and amino groups of proteins to yield a Schiff'sbase intermediate. These schiff's base intermediate undergoes rearrangement to form a relatively stable Amadori product. The Amadori product further undergoes a series of reactions through dicarbonyl intermediates to form AGE (advanced glycation endproducts). Glycation occurs inside and outside the cells. Glycation of cellular proteins produces changes in structure and loss of enzymatic activity. These effects are countered by protein degradation and renewal. In extracellular matrix the glycation produces changes in macromolecular structure affecting matrix-matrix and matrix cell interactions associated with decreased elasticity and increased fluid filtration across the arterial wall and endothelial cell adhesion [10]. When the concentration of AGEs increased above a critical level, cell surface AGE receptors become activated. Abnormalities in the metabolism of glycoproteins are observed in both naturally occurring and experimental diabetes [11]. The increases in plasma glycoprotein components have been reported to be associated with the severity and duration of diabetes. Decreased incorporation of the carbohydrate structure and composition to these in circulation. The vascular complications that involve complex of protein-carbohydrate molecules could contribute to an increase in plasma glycoproteins.

The biosynthesis of the carbohydrate moieties of glycoprotein forms the insulin independent pathways for the use of glucose 6-phosphate. But the deficiency of insulin during diabetes produces derangement of glycoprotein metabolism, resulting in the thickening of the basal membrane of pancreatic beta cells. In hyperglycemic state, the excess availability of glucose accelerates the synthesis of glucose basement membrane components i.e, glycoproteins [12].

Treatment with silver nanoparticles decreased the hexokinase from 212.10 mg/dl to 125.57mg/dl. Glucose 6 phosphatase reduced from 12.42 Umoles/mg to 11.41 Umoles/mg when treated with silver nanoparticles in diabetic rats. Hepatic Glycogen Synthase enzymes were decreased from 41.07% to 26.20% when diabetic rats treated with silver nanoparticles. The protein metabolic enzymes includes Total synthesis of –L-

Hexoses (5.27 mmol/L to 5.14 mmol/L), Serum Hexosamine (135.13 mg/%) to 132.95 mg/%)) and serum Sialic acids (83.70 mg/%) to73.80 mg/%) were decreased by the silver nanoparticle treatment.

Conclusion: Intraperitonial administration of Silver nanoparticles exhibits a protective effect on the carbohydrate moieties of glycoproteins in dextrose induced diabetic rats. Treatment with Silver nanoparticles decreased the carbohydrate and protein biochemical parameters. The experiment results showed, silver nanoparticles have the antidiabetic activity.

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