Effect of *BergeniaLigulata* on Metabolic Enzymes of Glucose Homeostasis and Its Correlation With Antioxidant Activity in Streptozotocin Induced Diabetic Rats

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***Abstract: Diabetes mellitus is characterized by loss of glucose homeostasis as a result of impaired secretion and function of insulin. The present study was designed to evaluate the role of flower extractof* Bergenialigulataagainst diabetesin Streptozotocin induced diabetic rats. Albino Wistar rats weighing 120-150g of either sex were selected for the study.*After a week of acclimatization, the rats were subjected to overnight fasting. Diabeteswas induced by intraperitoneal injection of Streptozotocin, freshly dissolved in citrate bufferpH 4.5.In the present study the STZ control animals showed enhanced gluconeogenic enzymes and diminished glycolytic enzymes there by it disturb the glucose homeostasis and diminished insulin production leads increased serum glucose levels. Treatment with flower extract of*Bergenialigulata(AFBL) *showed significant balancing of glucose homeostasis through reduction in gluconeogenic enzymes and elevation of glycolytic enzymes.The selected flower extract of*Bergenialigulata(AFBL) showed in vivo antioxidant activity, antihyperglycemic activity, hepatoprotective activity, nephroprotective activity and finally glucose homeostatic activity might be due to the potent phytoconstituents present in the selected flower extract.**

Keywords: **Bergenialigulata;** ***Streptozotocin; wistarrats; diabetes mellitus***

1. INTRODUCTION

Diabetes mellitus is characterized by loss of glucose homeostasis as a result of impaired secretion and function of insulin. Insulin deficiency causes an imbalance in glucose metabolism and other sources of energy such as lipids and proteins[1] and varies from type 1, type 2 and other types of diabetes. With type 2 diabetes, insulin instability and deficiency lead to a decrease in glucose intake in the liver, tissues and adipose tissue, therefore, the contributing action of insulin directly affects glucose production and utilization in the liver. Glucose is the most common substrate for energy metabolism. Indeed, under normal circumstances glucose is the only energy source that can be used by the brain and the central nervous system[2]. The amount of glucose in a cycle depends on the ratio of the amount of glucose entering the cycle (the appearance of sugar) and the rate of removal of glucose from the circulation (disappearance of sugar).

Plasma glucose concentration is maintained through intestinal absorption, glycogenolysis, glycogen depletion, which is a form of sugar storage, and gluconeogeneis, glucose formation mainly from lactate, glycerol and amino acids during fasting[3]. Maintenance of normal

glycemia requires parallel glucose utilization and endogenous production. This can be achieved with the combined instructions of several metabolic pathways; glycolysis, gluconeogenesis, glycogenolysis, and glycogeneis[4]. Studies have shown that disruption of carbohydrate metabolism has a significant effect on glucose homeostasis. Insulin deficiency impairs carbohydrate metabolism by suppressing the activity of glycolytic and glycogenic enzymes while stimulating gluconeogenic and glycogenolytic enzymes such as glucokinase, phosphofructokinase, pyruvate kinase, glucose 6 -phosphatase, fructose 1, 6-biphosphatase, glycogen syntase, glycogen phosphorylase[5].These enzymes were found to be affected by oxidative stress produced during metabolic dysfunction. Improper glucose can lead to the development of type 2 diabetes mellitus associated with increased oxidative stress and chronic clinical damage[6]. Oxidative stress leads to a depletion of proteins or enzymes such as SOD, GPX, CAT and a decrease in glutathione.

Medicinal plants are traditionally used in many countries to control sugar. As a result, many medicinal plants have been investigated for the purpose of detecting hypoglycemic agents[7]. Because of its efficacy, non-toxic, and minimal or no side effects, the World Health Organization (WHO) has recommended that traditional plants be the most effective component in the treatment of diabetes[8]. Herbs used in traditional medicine to treat diabetes show another important way to control the disease.

It has been reported that the antidiabetic activity of medicinal plants depends on a variety of mechanisms including: promoting insulin secretion, inhibiting insulin secretion processes and reducing insulin resistance, regenerating or repairing pancreatic β cells and preventing β-cell destruction, promoting glycogeneis and hepatic glycolysis, inhibition of α-amylase / α-glucosidase enzymes, inhibition of gluconeogeneis and inhibition of oxidative stress in the breakdown of pancreatic β-cell dysfunction[9]. In recent years, some researchers have focused their attention on the role that botanicals play in the inhibition of gluconeogeneis.

The activity of medicinal plants depends largely on the type of phytochemicals present. The flowers are reported to have a wide range of flavonols including quercetin, kaempferol, isorhamnetin, and myricetin as well as their extracts from rose, chrysanthemum, roselle, watermelon, Xibei tree peony, magnolia flower, fragrant osmanthus, honeysuckle, and cactus etc. Variation of major flavonons in phenolic flavonoids, kaempferol and quercetin derivatives are flavonols, quercitrin, myricetin, quercetin-3-galactoside, quercetin-3-glucoside, luteolin, luteolin-7-glucoside, epratechingallate. sambubioside, cyanidin-3-sambubioside, peonidin, pelargonidin, cyanidin, peonidin-3,5-di-O-glucoside, Caffeic acid, Chlorogenic acid and apigenin[10].Therefore, in order to meet the need, the present study was designed to examine flower extract for their function in glucose homeostasis (enzymes involved in glycolysis, gluconeogenesis, glycogenolysis and glycogeneis) in diabetic rats.

Bergenialigulata belonging to family Saxifragaceae is popularly known as a ‘stone flower/stone breaker’.*Bergenia*has many bioactive compound in its rhizomes, including paashaanolactonearbutin, bergenin, catechin and gallic acid etc. starch (19%), minerals, vitamins, albumin (7.75%), glucose (5.5%), mucilage, ash (mostly calcium oxalate). Seeds of *Bergenialigulata* contain coumarin (bergenin), tannic acid, gallic acid, minerals and wax. The result of the preliminary investigation revealed the presence of alkaloids, steroids, flavonoids, terpenoids, tannins, glycosides, carbohydrates and saponins[11].

There are several studies done on ethnopharmacological activities of *Bergenialigulata* such as The Hydroalcoholic release of B. ligulata was released for direct measurement by antitumor activity and showed cytotoxic activity[12]. The rhizome and root extract of *Bergenialigulata*is used for the treatment of kidney and bladder stones[13]. *Bergenialigulata*root extract had shown significant action intreating urinary problems[14]. As there was no evidence reported on antidiabetic activity, hence, the present study was designed

to evaluate the role of flower extractof *Bergenialigulata*against diabetesin Streptozotocin induced diabetic rats.

2. MATERIALS AND METHODS

Experimental Animals
Albino Wistar rats weighing 120-150g of either sex were selected for the study. They were fed with a standard rat pellet and water. Research on animals was conducted in accordance with guidelines of the committee for the purpose of control and supervision of experiments on animals (CPCSEA) as the institute has CPCSEA registration (516/01/A/CPCSEA).

Acute toxicity study
Acute toxicity study was carried out for *B. liguleta*by adaptingfixed dose method of CPCSEA, OECD guidelines no 423. Thirty fasted male albino rats were weighed (120-150g, 8 weeks old), grouped into I, II, III, IV and V with six animals each. Group I served as control and received distilled water, while groups II, III, IV and V were orally administered 500, 1000, 1500 and 2000 mg/kg body weight of Aqueous flower extract of *B. liguleta* (AFBL) in distilled water, respectively, using oral needle. The animals were observed at 2, 4, 6, 8, 24 and 48 hr after administration of extract to detect changes in somatic, autonomic or behavioral responses. Mortality was observed for 24hrs[15].

Induction of diabetes
After a week of acclimatization, the rats were subjected to overnight fasting. Diabeteswas induced by intraperitoneal injection of Streptozotocin, freshly dissolved in citrate bufferpH 4.5. The control rats received the vehicle alone. The animals were allowed to drink water 5% glucose solution overnight to overcomethe drug induced hypoglycemia due to massive release of insulin from β-cells[16]. After 1 week time for the development of diabetes, the rats with moderate diabetes having glycosuria and hyperglycemia (blood glucose range of above 250mg/dl) were considered as diabetic rats and used for the experiment.

Experimental Design
The fasting glucose and body weight of all animals were recorded at the beginning of the study. The blood glucose was checked by one – touch glucometer throughout the study, in the experiments, 24 rats were divided into 4 groups of six rats each.
GROUP 1: Normal control rats, received distilled water.
GROUP 2: STZ induced diabetic rats received distilled water and served as diabetic control for 8 weeks.
GROUP 3: STZ induced diabetic rats received standard drug Gliclazide (1mg/kg BW p.o) for 8 weeks.
GROUP 4: STZ induced diabetic rats received the AFBL (150mg/kg BW p.o) for 8 weeks.
GROUP 5: STZ induced diabetic rats received the AFBL(300 mg/kg BW p.o) for 8 weeks.

Biochemical estimations
The fasting blood glucose was measured on 0^{th}, 28^{th} and 56^{th} day by GOD-POD estimation kit. Body weight, HbA1c and Insulin after 8 weeks study period in STZ induced diabetic rats. After 8 weeks of treatment, the rats were fasted for 16h. The blood was collected from retro orbital route and liver enzymes (SGOT, SGPT, ALP), bilurubin, renal enzymes (urea, uric acid and creatinine), protein content in pancreas and liver , superoxide Dismutase of pancreas and liver, Catalase, Malondialdehyde (MDA), reduced gluthatione, glycogen, glucose

homeostasis enzymes (Hexokinase, Glucokinase and Pyruvate kinase, Glucose-6-phosphatase, Fructose-1-6-bisphosphatase).

Statistical Analysis

The results were expressed as mean±S.E.M. Statistical difference was tested by using one-way analysis of variance (ANOVA) followed by Dunnette's multiple comparison test. A difference in the mean p value <0.05 was considered as statistically significant.

3. RESULTS AND DISCUSSION

The treatment groups showed significant reduction of blood glucose levels, glycated haemoglobin (HbA1c) and also significantly elevated insulin levels at p<0.05* when compared with diabetic control

Table 1: Effect of AFBL on blood glucose, HbA1c and Insulin after 8 weeks study period in STZ induced diabetic rats.

Groups	Blood glucose(mg/dL)	HbA1c (%)	Insulin (µIU/ml)
Control	91.33±4.30*	4.61±0.20*	8.46±0.27*
D.Control	321.16±8.11#	11.57±0.21#	4.20±0.16#
Gliclazide	110.66±5.88*	5.46±0.17*	8.80±0.17*
AFBL (150mg/kg)	135.16±4.04*	6.95±0.22*	7.55±0.17*
AFBL (300mg/kg)	115.50±3.94*	6.22±0.09*	8.32±0.06*

All values are expressed as Mean ± S.E.M. Statistical comparisons were made by using One way ANOVA followed by Dunnett' s multiple comparison test and found significantly different at *P<0.05 when compared to Disease Control and #p<0.001 when disease control is compared with control group

The treatment groups showed significant reduction of liver enzymes and Bilirubin levels at p<0.05* when compared with diabetic control

Table 2: Effect of AFBL on Liver enzymes and Bilirubin after 8 weeks study period in STZ induced diabetic rats

Groups	SGOT (IU/dL)	SGPT (IU/dL)	ALP (IU/dL)	Bilirubin (mg/dL)
Control	70.6±2.10*	40.00±2.11*	3.59±0.14*	0.74±0.02*
D.Control	131.00±2.76#	77.50±1.87#	7.32±0.20#	1.75±0.05#
Gliclazide	75.00±3.81*	42.83±2.30*	4.04±0.20*	0.72±0.02*
AFBL (150mg/kg)	99.06±4.46*	58.16±3.26*	4.16±0.05*	0.87±0.02*
AFBL (300mg/kg)	88.83±3.15*	50.50±2.84*	4.02±0.14*	0.82±0.01*

All values are expressed as Mean ± S.E.M. Statistical comparisons were made by using One way ANOVA followed by Dunnett' s multiple comparison test and found significantly

different at *P<0.05 when compared to Disease Control and #p<0.001 when disease control is compared with control group

The treatment groups showed significant reduction in levels of kidney parameters at p<0.05* when compared with diabetic control

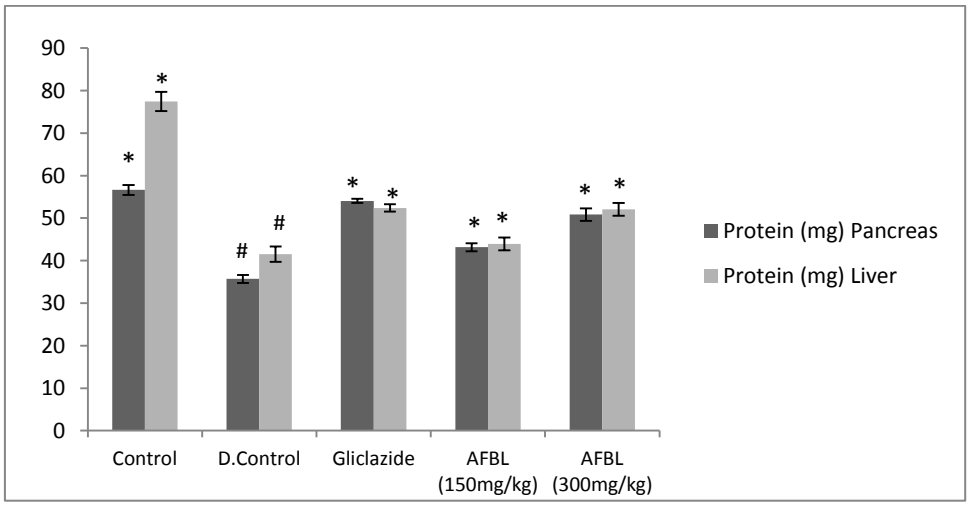
Table 3: Effect of AFBL on kidney parameters after 8 weeks study period in STZ induced diabetic rats

Groups	Urea (mg/dL)	Uric Acid (mg/dL)	Creatinine (mg/dL)
Control	22.32±0.55*	3.52±0.15*	0.68±0.02*
D.Control	35.52±0.61#	8.09±0.17#	1.90±0.04#
Gliclazide	22.68±0.35*	4.16±0.14*	0.78±0.02*
AFBL (150mg/kg)	28.01±0.67*	5.12±0.19*	1.03±0.04*
AFBL (300mg/kg)	24.58±0.23*	4.15±0.04*	0.84±0.04*

All values are expressed as Mean ± S.E.M. Statistical comparisons were made by using One way ANOVA followed by Dunnett' s multiple comparison test and found significantly different at *P<0.05 when compared to Disease Control and #p<0.001 when disease control is compared with control group.

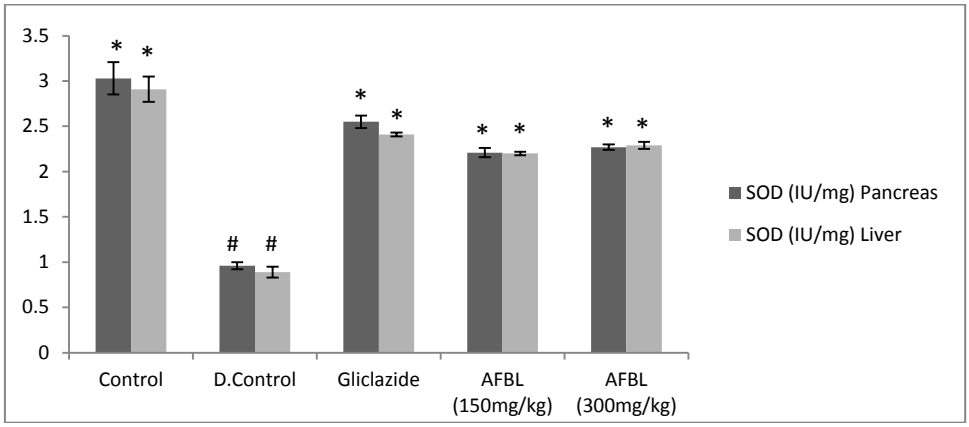
The treatment groups showed significant elevation of pancreatic and hepatic protien levels at p<0.05* when compared with diabetic control

Fig 1: Effect of AFBL on protein after 8 weeks study period in STZ induced diabetic rats



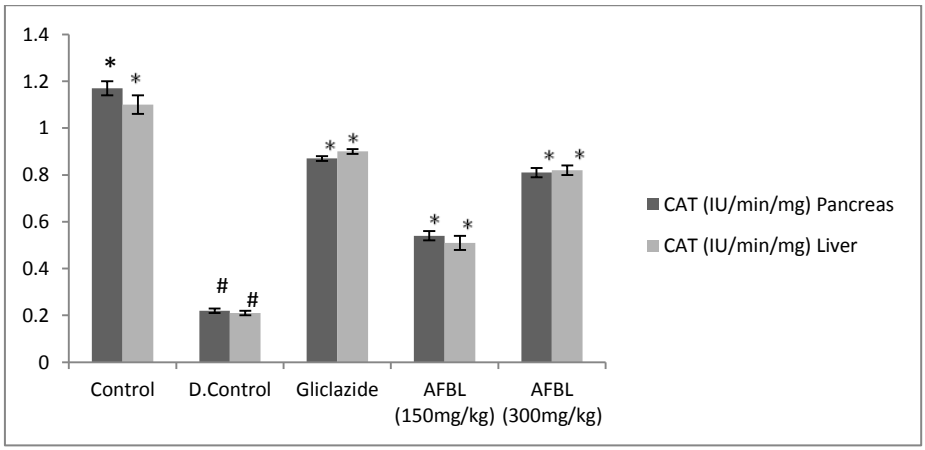
The treatment groups showed significant elevation of pancreatic and hepatic superoxide dismutase (SOD) levels at p<0.05* when compared with diabetic control

Fig 2: Effect of AFBL on superoxide dismutase after 8 weeks study period in STZ induced diabetic rats



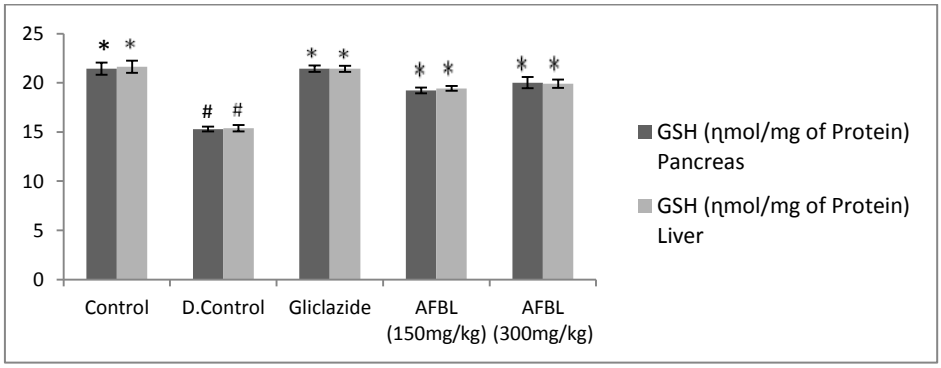
The treatment groups showed significant elevation of pancreatic and liver protien levels at p<0.05* when compared with diabetic control

Fig 3: Effect of AFBL on Catalase after 8 weeks study period in STZ induced diabetic rats



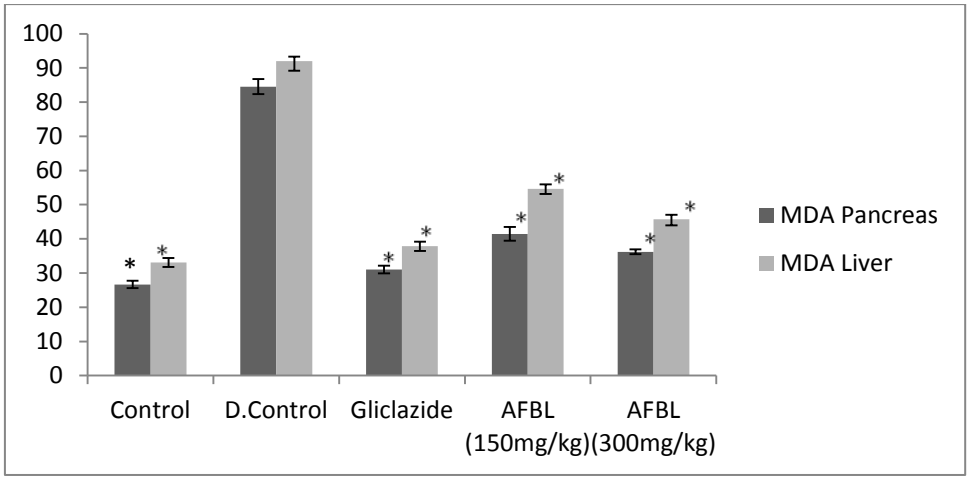
The treatment groups showed significant elevation of pancreatic and hepatic glutathione levels at p<0.05* when compared with diabetic control

Fig 4:Effect of AFBL on reduced glutathione after 8 weeks study period in STZ induced diabetic rats



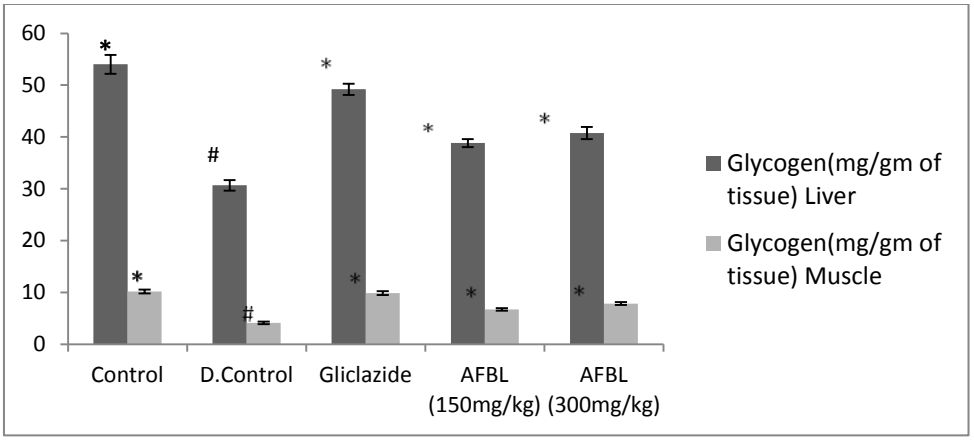
The treatment groups showed significant reduced of pancreatic and hepatic Malondialdehyde (MDA) levels at p<0.05* when compared with diabetic control

Fig 5: Effect of AFBL on MDA after 8 weeks study period in STZ induced diabetic rats



The treatment groups showed significant reduced of pancreatic and hepatic glycogen levels at p<0.05* when compared with diabetic control

Fig 6: Effect of AFBL on glycogen after 8 weeks study period in STZ induced diabetic rats



The treatment groups showed significant elevation of enzymes involved in glucose homeostasis levels at p<0.05* when compared with diabetic control

Table 4: Effect of AFBL on glucose homeostasis enzymes in liver homogenates after 8 weeks study period in STZ induced diabetic rats

Groups	Hexokinase[a]	Lactate dehydrogenase[b]	Pyruvate Kinase[c]
Control	4.93±0.05*	3.52±0.06*	9.72±0.21*
D.Control	1.70±0.04#	5.59±0.05#	4.09±0.313#

Gliclazide	4.77±0.09*	3.64±0.06*	9.33±0.15*
AFBL (150mg/kg)	3.13±0.11*	4.33±0.04*	6.48±0.06*
AFBL (300mg/kg)	4.32±0.10*	4.11±0.04*	7.87±0.08*

[a]µmoles of G-6-P liberated/min/mg of protein; [b]µmolesof formazan formed/min/mg of protein; [c] µmoles of Pyruvate formed/min/mg of protein

All values are expressed as Mean ± S.E.M. Statistical comparisons were made by using One way ANOVA followed by Dunnett' s multiple comparison test and found significantly different at *P<0.05 when compared to Disease Control and #p<0.001 when disease control is compared with control group

The treatment groups showed significant reduction of enzymes involved in glucose homeostasis levels at p<0.05* when compared with diabetic control

Table 5: Effect of AFBL on glucose homeostasis enzymes in liver homogenates after 8 weeks study period in STZ induced diabetic rats

Groups	Glucose-6-phosphatase[a]	Fructose-1,6-bisphosphatase[b]
Control	0.15±0.015*	0.33±0.009*
D.Control	0.29±0.08#	0.58±0.011#
Gliclazide	0.17±0.011*	0.34±0.007*
AFBL (150mg/kg)	0.23±0.009*	0.44±0.010*
AFBL (300mg/kg)	0.21±0.008*	0.42±0.016*

[a]µmoles of inorganic phosphate liberated/min/mg of protein; [b]µmoles of inorganic phosphate liberated/hr/mg of protein.

All values are expressed as Mean ± S.E.M. Statistical comparisons were made by using One way ANOVA followed by Dunnett' s multiple comparison test and found significantly different at *P<0.05 when compared to Disease Control and #p<0.001 when disease control is compared with control group

Histopathological study of pancreas and liver

Figure 7: Histopathology of pancreas in normal control (vehicle control)

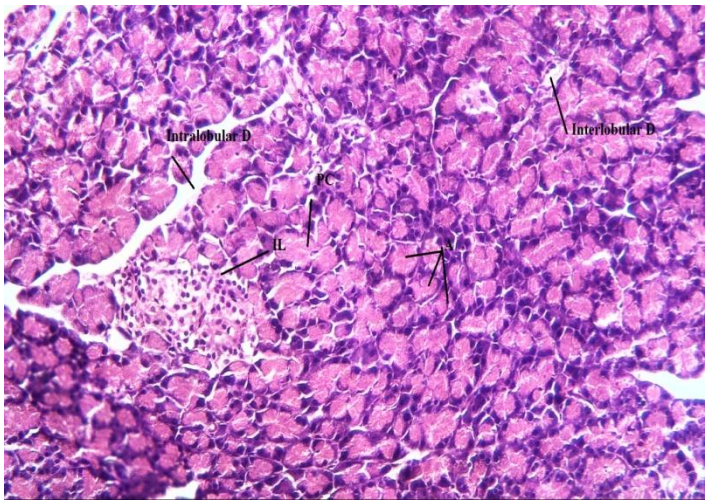


Figure 7 representing the histopathology of pancreas of control rats. It showed normal pancreatic tissue with islets of Langerhans, exocrine portion filled with acini which are in pyramidal shape. The intralobular and interlobular ducts were found to be normal.

Figure 8: Histopathology of diabetic control pancreas in STZ induced diabetic rats

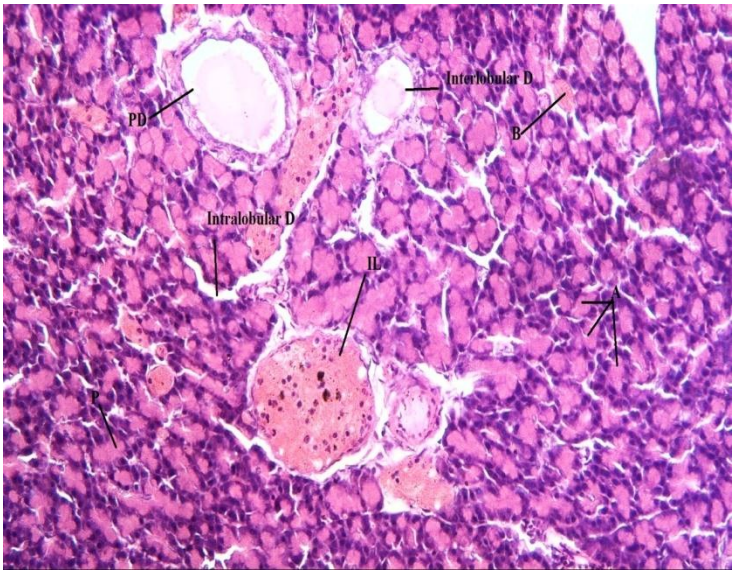
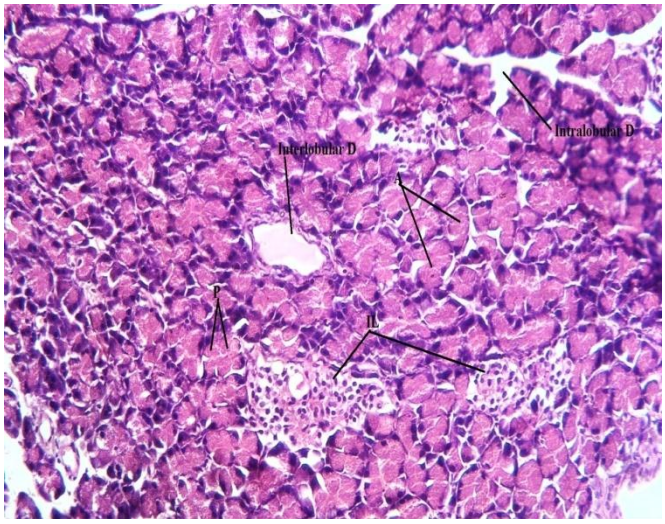


Figure 8 represents the histopathology of pancreas in diabetic control rats and the severity of the damage evidenced with presence of cellular infiltration and damaged islets. Vacuolated pancreatic duct and interlobular ducts were observed. The acini the pyramidal shape was disturbed. Some parts of tissue contain damaged blood vessels.

Figure 9: Histopathology of pancreas in gliclazide treated rats in STZ induced diabetic rats



The figure 9 showed marked amelioration of damage to the islets. It was also observed that the mild ballooning of interlobular duct was observed. Acinus was packed closely with pyramidal shape.

Figure 10: Histopathology of pancreas in AFBL treated rats in STZ induced diabetic rats

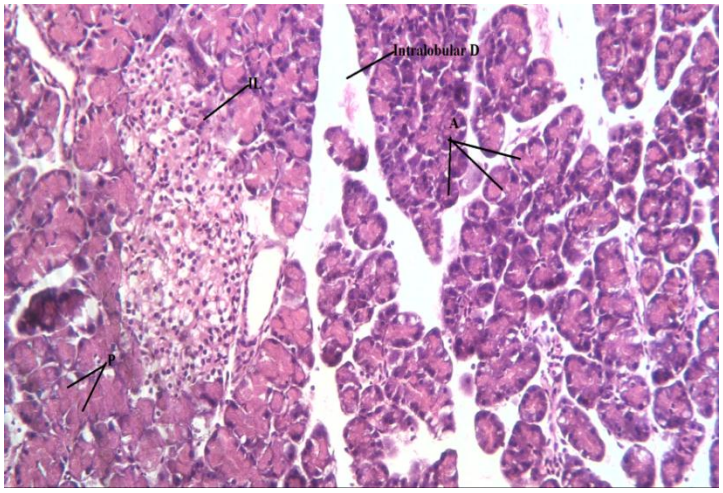


Figure 10 showed mild distention of pancreatic acini and islets. The pyramidal shape was maintained well.

Figure 11: Histopathology of liver in normal control (vehicle control)

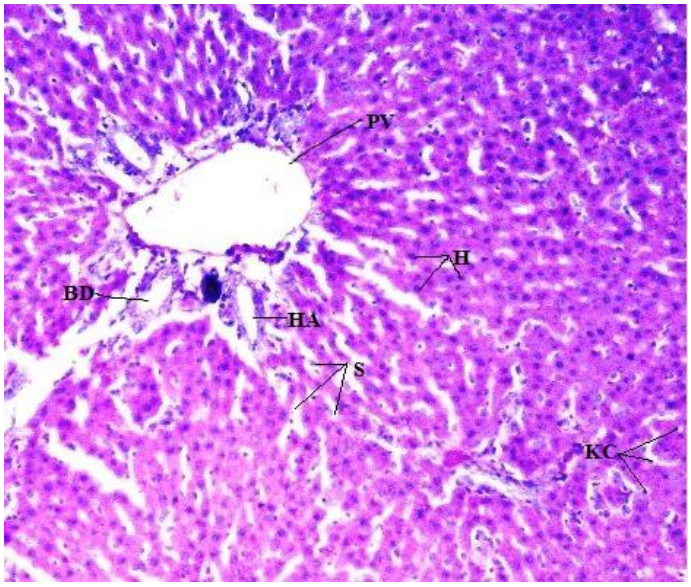


Figure 11: Histopathology of liver tissue in normal control rats showed normal architecture of liver with prominent hepatocytes embedded in hepatic plates separated by sinusoids. The portal triad showed portal vein with bile duct and hepatic artery without evidence of damage. The kupffer cells present on the epithelium of the sinusoids are normal.

Figure 12: Histopathology of diabetic control liver in STZ induced diabetic rats

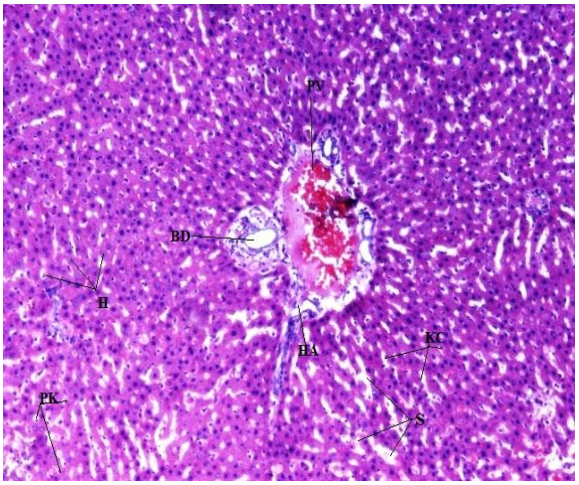


Figure 12 represents histopathology of liver in diabetic control i.e Streptozotocin induced rats. The entire picture evidenced marked destruction of liver structure. The portal vein were found to be completely necrotized with cellular infiltrates and inflammation. The bile duct was found to be distended and also hepatic tissue was damaged. Expanded sinusoids with pynkotic hepatocytes due to activated Kupffer cells.

Figure 13: Histopathology of liver in gliclazide treated rats in STZ induced diabetic rats

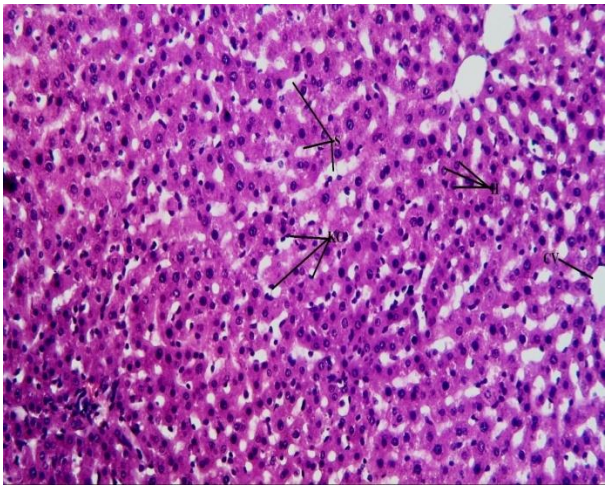


Figure 13 represented the hepatic tissue of gliclazide showed normal histological architecture of liver with well arranged hepatocytes and embedded as plates. The hepatic plates are separated by thin walled sinusoids lined with endothelial cells. Central vein and Kupffer cells were observed prominently without any damage.

Figure 14: Histopathology of AFBL treated liver in STZ induced diabetic rats

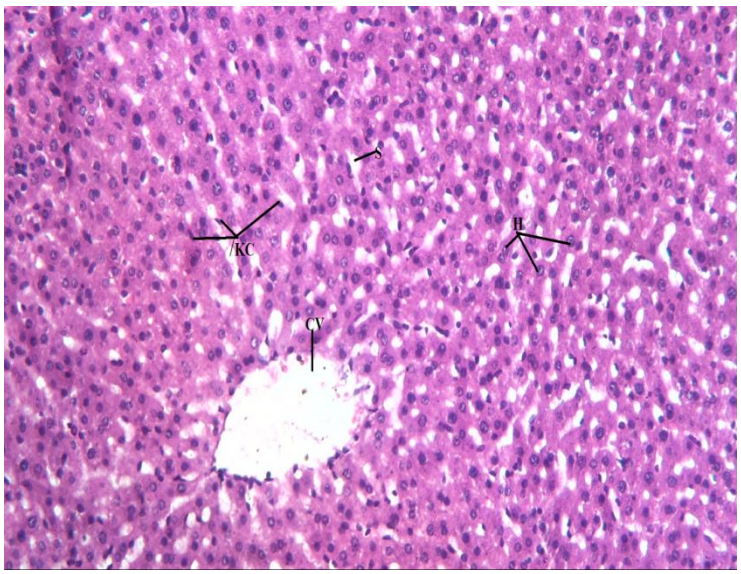


Figure 14 representing the hepatic section of AFBL treated rats. The liver section showed marked regeneration damaged central vein. The hepatocytes were found to be normal with any shrinkage. The sinusoids are covered with epithelium and kupffer cells.

4. DISCUSSION

Diabetes mellitus is a metabolic disorder, characterized by chronic hyperglycemia with disturbance of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both. Recently, interests in finding naturalhypoglycemic agents from plant materials to replace synthetic ones to combat diabeticcomplications are going on relentlessly[17].

In our study the aqueous flower extract of *B. liguleta* chemical constituents such as alkaloids, steroids, flavonoids, terpenoids, tannins, glycosides, carbohydrates and saponins were present[18].

Acute toxicity study revealed that the aqueous flower extract of *B. liguleta*wasrelatively nontoxic upto 2000mg/kg/bwp.o indirectly pronouncing safety profile of theextract.

STZ, an antibiotic produced by S. achromogenes, is widely used for inducing diabetes in the experimental animals as it produces toxic effects on pancreatic β-cells[19]. This cytotoxic action of STZ causes degranulation and reduction of insulin secretion leading to hyperglycemia.

In the present study, diabetic rats had shown significant elevation of fasting blood glucose accompanied with diminished serum insulin levels. It was observed that the levels of HbA1c in diabetic rats have been increased and is due to the presence of excessive amounts of blood glucose. During diabetes, the excess of glucose present in blood reacts with hemoglobin to form glycosylated hemoglobin[20]. HbA1c levels were particularly estimated to monitor the effectiveness of AFBL in treatment of diabetes[21]. Decreased levels of fasting blood glucose and HbA1c accompanying with increased the level of plasma insulin in diabetic rats had shown dose-dependent manner. Based on the results obtained from the study, it can be concluded that the elevated levels of plasma insulin may have improved the utilization of glucose by peripheral either by promoting glucose uptake and metabolism or by inhibiting hepatic gluconeogenesis and decreased blood glucose levels.

Increased gluconeogenesis and ketogenesis observed in diabetic may be due to the high level in the activities of the transaminases like SGOT, SGPT and Alkaline Phosphatase enzymes[22]. In this study, the diabetic control showed elevated liver enzymes and restoration of SGOT, SGPT, ALP and bilirubin are seen in AFBL treated rats. Increased serum creatinine, urea and uric acid are indicators of the development of diabetic nephropathy[23]. The AFBL exhibited the potential action in protecting the kidney by decreasing the creatinine, urea and uric acid and also the non toxic effect of the extract.

During diabetes, there is increased protein catabolism with flow of amino acids into the liver, which feeds gluconeogenesis[24].Administration of AFBL to diabetic rats significantly increased plasma proteins by inhibiting proteolysis caused by insulin deficiency.

Superoxide dismutase is an antioxidant enzyme which reduces superoxide radical to water and oxygen. Two other enzymes, catalase and glutathione peroxidase, are considered biologically essential in reduction of hydrogen peroxide[25].Decreased levels of these enzymes were observed in diabetic control. The administration of AFBL has elevated the levels of both enzymic and non enzymic antioxidants which indicates the protective nature of the extract. Malondialdehyde (MDA) is degradative product of peroxidation of polyunsaturated fatty acids in the cells membrane. Presence of higher MDA in the serum is an indication of induced lipid peroxidation and of oxidative stress of which has been reported as one of the underlying cause of diabetes mellitus[26]. Elevated levels of MDA were seen in diabetic control rats. The administration of AFBL decreased the MDA levels indicating the protective nature of the tissue.

The liver is an important organ that plays a pivotal role in glycolysis and gluconeogenesis. A partial or total deficiency of insulin causes derangement in carbohydrate metabolism that decreases activity of several key enzymes including glucokinase, (hexokinase) phosphofructokinase, and pyruvate kinase[27], resulting in impaired peripheral glucose utilization and augmented hepatic glucose production. The hexokinase is involved in the phosphorylation step of glucose in glycolysis. Hepatic hexokinase is the most sensitive and its increased level can increase the utilization of blood glucose for glycogen storage in liver.

Glucose-6-phosphate dehydrogenase activity was decreased in diabetic mellitus, resulting in diminished functioning of HMP pathway and there by the production of reducing equivalent such as NADH and NADPH[28].In the present study, hexokinase activity was decreasedin diabetic control rats and the treatment with AFBL has increased hexokinase and glucose-6-phosphate levels thereby increasing the utilization of glucose and promotes overall glucose homeostatisis. Lactate dehydrogenase (LDH) is a cytosolic enzyme that catalyzes the conversion of pyruvate to lactate in anaerobic glycolysis, which is subsequently converted to glucose in glucogenic flux. Increased activity of lactate dehydrogenase interferes with normal glucose metabolism and insulin secretion secretary defects in diabetes[29]. In the present study, the LDH activity was significantly elevated in diabetic control group. In the AFBLextract treated group, the LDH activity was suppressed significantly.The decrease in the activity of pyruvate kinase accounts for the decreased utilization of glucose (glycolysis) and increased production of glucose (gluconeogenesis) by liver and kidney indicating that these two pathways are altered in diabetes[30].The treatment with AFBL to diabetic rats showed a notable increase in plasma insulin that induces a decrease in ATP, a known allosteric inhibitor of Pyruvate kinase, thereby increases the pyruvate kinase activity to nearly normal.Normally, insulin inhibits the hepatic glucose production by suppressing fructose 1,6-bisphosphatase activity[31]. The fructose 1,6-bisphosphatase level are elevated in diabetic control rats and when treated with AFBL extract activity of fructose 1,6-bisphosphatase was reduced and by decreasing gluconeogenisis.

Histopathology of pancreas and liver were tested at the end of 8 weeks study period. The pancreas of the normal rats showed normal architecture evidenced with endocrine pancreas with islets of langerhans, compact acini, intra and interlobular ducts, but the induction of streptozotocin showed marked destruction of pancreatic tissue with damaged islets, cellular necrosis, extension of intra and intercellular pancreatic duct damage. Treatment with gliclazide and AFBL showed significant protection over STZ induced damage through regeneration of damaged islets and acinar cells.

5. CONCLUSION

Diabetes is characterized by an increase in blood sugar and reduction in insulin levels, which might be due to β cell to produce insufficient amount of insulin to lowers blood sugar levels and is responsible for the development of persistent hyperglycemia as seen in diabetic patients.The antidiabetic properties of many herbal medicines are due to presenceflavanoids, phenols, tannins, and andrographolids, terpenoids, alkaloids and glycosides. The current study focused on flowers as experimental drugs due to the high availability and richness of phytoconstituents and most of them reported for strong antidiabetic activity.*Bergenialigulata*contains Coumarins: bergenin; Flavonoids: (+) afzelechin and Benzenoids: arbutin.Based on this view supported for antidiabetic claims on flower, the present study was attempted to enlighten the mechanism of action and possible effects of selected flower extract on diabetic rats.The process of keeping blood glucose at a stable level is called "glucose homeostasis".Gluconeogenic enzymes and glycolytic enzymes have played a major role in maintaining glucose homeostasis.In the present study the STZ control animals showed enhanced gluconeogenic enzymes and diminished glycolytic enzymes there by it disturb the glucose homeostasis and diminished insulin production leads increased serum glucose levels. Treatment with AFBL showed significant balancing of glucose homeostasis through reduction in gluconeogenic enzymes and elevation of glycolytic enzymes.The selected flower extract of*Bergenialigulata(AFBL)* showed in vivo antioxidant activity, antihyperglycemic activity, hepatoprotective activity, nephroprotective activity and finally glucose homeostatic activity might be due to the potent phytoconstituents present in the selected flower extract.

6. REFERENCES

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