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PROTECTIVE ROLE OF ETHANOLIC EXTRACT OF *ALOE VERA* ANTIOXIDANT PROPERTIES ON LIVER AND KIDNEY OF STREPTOZOTOCIN-INDUCED DIABETIC RATS

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Our investigations explore that herbal medicine ethanolic extract of *Aloe vera* exibits antihyperglycemic, and antioxidant effects in streptozotocin (STZ) induced diabetic rats. *Aloe vera* (AV) leaf gel extract administered orally to different groups of rat at a dose of 300 mg/kg body weight. Five groups (n = 6) follows, control rats, control + *Aloe vera,* diabetic rats (STZ 40 mg/kg body weight), diabetic + *Aloe vera,* diabetic + glibenclamide. The experimental period was 30 days. In diabetic rats body weights were decreased and blood glucose levels were increased when compared to control rats. The diabetic rats exhibited lower activity levels of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GP_X) and glutathione reductase (GR) in hepatic and renal tissues as compared with normal rats. The activities of SOD, CAT, GPx and GR were increased in hepatic and renal tissue of AV extract treated diabetic rats. The increased level of lipid peroxidation in diabetic rats was also found to be decreased and regenerative liver and kidney histological changes were observed in the AV extract treated rats. In conclusion the *Aloe vera* extract exhibits the potent antidiabetic property by decreasing the body weights, antioxidative enzymes and histology of liver and kidney of diabetes rats.

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Keywords: Diabetes; *Aloe vera*; hyperglycemia; oxidative stress; Streptozotocin; rats.

1. Introduction

According to world health organization, diabetes mellitus (DM) is one of the most common metabolic disorders all over the world [1, 2]. DM is a group of metabolic disorders characterized by hyperglycemia, where alterations in the carbohydrate, fat and protein metabolisms accompanied by absolute or relative deficiencies in insulin secretion and /or its action. Moreover, basal hyperglycemia occurs irrespective of whether insulin deficiency or insulin resistance is the dominant defect [33]. It has been well known that suffering from diabetes for long time may cause many complications such as diabetic nephropathy, retinopathy, neuropathy and cardiomyopathy and hyperglycemia [3, 4]. Many studies indicated that oxidative stress is also one of the major route pathophysiological condition during DM. Persistent hyperglycemia causes increased production of free radicals especially reactive oxygen species (ROS), in tissues from glucose auto-oxidation and protein glycosylation [3, 7, 44]. Several reports suggested that increased free-radical mediated oxidative stress is involved in diabetic complications [5],which includes primarily the ROS generated due to the increased free fatty acids (FFA) levels in the cells [5-8]. Increased levels of FFAs are positively correlated with both insulin resistance [5, 6] and the deterioration of cell function in the context of concomitant hyperglycemia [7, 8].

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The liver is the important insulin-dependent organ, which plays a vital role in glucose and lipid homeostasis and it is severely affected during diabetes [9]. The kidney was also affected by diabetes which leading to the cause of diabetic nephropathy (DN). DN is characteristic dysfunction of kidney by specific renal morphological and functional alterations. ROS play an important role in signaling molecules to activate a number of cellular stress-sensitive pathways which leads to the high glucose induced renal injury [11]. In addition to that oxidative stress has also been proposed to play a role in the pathogenesis of renal and hepatic tissues damage [12-14]. However, during pathological conditions, the decline free radical production and the protective antioxidant defense system may causes ROS-induced tissue damage including renal and hepatic injury [8-10].

Earlier, hormone therapy using insulin is one of the classical approaches to treat diabetes. Though it is promising, the ineffectiveness of oral insulin therapy against diabetes limits the insulin therapy, moreover, the insulin formulations including biguanides, sulfonylureas, glinides, glitazones [15, 6, 17] causes side effects like hematological and gastrointestinal reactions, brain damage and disturbances of liver and kidney functions [18].

Recent scientific investigations explore on traditional medicinal plants plays significant importance in the last few decades in the treatment of diabetes in worldwide [19, 20]. World Health Organization has recommended that the evaluation of traditional medicinal plants treatment for diabetes were effective, non-toxic, with less or no side effects and is considered being excellent candidates for oral therapy [21]. *Aloe vera L*. (Syn: Aloe barbadensis Miller; Hindi: Ghikanvar) is one of the medicinal plants which is a traditionally well acknowledged plant in the management of diabetes. It belongs to family Liliaceae (sub-family of the Asphodelaceae). Many studies claims that the high contents of phenolic compounds, glycosides (aloins), 1,8-dihydroxyanthraquinone derivatives, β-1,4 acetylated mannan, mannose-phosphate and alprogen glucoprotein [22] in the *A. vera* is important for its biological action. Earlier it has been suggested that *Aloe vera* leaf contain anticancer [23], antioxidant [24], gastric ulceration [25], cytoprotective, cardiac stimulatory and immunomodulatory activities [26].

During past two decades, *Aloe vera* used as beneficial therapeutic agent which protectively act as a free radical scavenging and other antioxidant properties on diabetic patients [27, 28], by controlling elevated anions in an alloxan or STZ-induced diabetic animal models [29, 30]. The objective of the present study was 2 fold: a) to know the anti-hyperglycemic affect of plant extarct and b) to evaluate the protective role of *Aloe vera* on antioxidant status in liver and kidney in STZ induced diabetes in rats as animal models.

2. Materials and methods

2.1. Preparation of *Aloe vera* extract

Aloe vera solid gel in the center of the leaf was collected and homogenized resulting mucilaginous, thick and straw colored homogenate was obtained and lyophilized. Then the lyophilized sample was extracted using 95% ethanol. The filtrate was collected and evaporated to dryness under reduced pressure in a rotary evaporator at 60°C. The residue was stored in dry sterilized small containers at 4°C until further use. An suspension which is the form customarily used in folk medicine was prepared by dissolving suitable amount of ethanol free extract of *Aloe vera* leaf gel to get the desired concentration. The drug solutions were prepared freshly each time. The dosing schedule used was once per day. The extracts were administered orally daily to different groups of rat at a dose of 300 mg/kg body weight.

2.2. Selection of animals

Male albino Wistar rats (180 ± 20 g) were obtained from the Indian Institute of Science, Bangalore, India. Animals were housed in clean polypropylene cages maintained under a 12 h:12 h schedule of light:dark cycle at 25 ± 2ºC with a relative humidity of 50 ± 5 % at the Department of Zoology, Sri Venkateswara University, Tirupati, India. The animals were fed on pellet diet (manufactured by Hindustan Lever Ltd., Bangalore, India) and water *ad libitum*. This study was carried out according to guidelines for the care and use of laboratory animals [31] and approved by

the Institutional Animal Ethical Committee at Sri Venkateswara university, Tirupati, India (No. 01/2011-2012/(i)/a/CPCSEA/IAEC/SVU/MB-SSR/Dt 20/06/2011).

2.3. Induction of experimental diabetes

After fasting, diabetes was induced by intraperitoneal injection of single dose STZ (Sigma, St. Louis, Mo., USA) freshly dissolved in 0.1 M cold sodium citrate buffer, (pH 4.5) at a dose of 40 mg/kg body weight [32]. After injection, they had a free access to food and water was given 5% glucose solution to drink overnight to counter hypoglycemic shock.

The animals were considered as diabetic, if their blood glucose (Accu chek sensor comfort glucometer (manufacture - Johnson and Johnson) levels were above 250 mg/dl on the 4^{th} day after STZ injection.

2.4. Experimental design

Rats were randomly divided into five groups of six animals in each group.

Group -I **:** Control rats.
Group- II **:** Control + *Aloe vera* (300 mg/kg body weight of *Aloe vera*).
Group –III **:** Diabetic control rats (40mg/kg body weight of STZ)
Group –IV **:** Diabetic + *Aloe vera* extract (300 mg/kg body weight in ethanol solution daily once in a day by an intragastric tube for 30 days).
Group–V **:** Diabetic + Glibenclamide (600 µg/kg body weight in ethanol solution daily an intragastric tube for 30 days).

The body weights of control and experimental groups were recorded at an interval of one week till the completion of the experimental period (30 days). The blood glucose levels were carried out by using Accu Chek glucometer (Manufacture: Johnson and Johnson) every week during experimental period.

The animals were sacrificed after 24 hrs of the last treatment (30^{th} day) by cervical dislocation and the liver and kidney tissues were isolated. The tissues were washed with ice-cold saline, and immediately stored in deep freeze at -80^0C for biochemical analysis and enzymatic assays. A part of the tissue was processed for histological studies.

2.5. Assay of lipid peroxidation and antioxidant enzymes

Lipid peroxidation levels were determined in kidney and liver by the method of Hiroshi et al., [33]. The activities of SOD (EC 1.15.1.1) and CAT (EC 1.11.1.6) were determined in the mitochondrial fraction of kidney and liver by the method of Misra and Fridovich, [34] and Chance and Machly [35] respectively. Also the activites of GPx (EC 1.11.1.9) and GR (EC 1.6.4.2) were determined by the method of Flohe and Gunzler [36] and Carlberg and Mannervik [37] respectively.

2.6. Estimation of protein in enzyme source

Protein content in the enzyme source was estimated by the method of Lowry et al., [38] using bovine serum albumin as standard.

2.7. Histopathological Studies

A small portion of liver and kidney was fixed in 10% formalin for histopathological studies. Liver and kidney sections were taken with 5µm thick, and stained with hemotoxylin and eosin (Culling 1974) [39]. Sections were observed under microscope for histopathological changes.

2.8. Statistical analysis

The data were statistically analyzed using One-way Analysis of Variance (ANOVA) followed by Dunnet's *t*-test and 'p' value <0.05 was considered significant. The data were presented as mean ± S.D. and analysis was carried out by using SPSS 16.0.1 program

3. Results

3.1. Effect of *Aloe vera* extract on the body weights and blood glucose levels

The body weights of normal and experimental animals in each group change were observed in *Aloe vera* treated group with mean value of (4.32) when compared with the diabetic group (-1.51) (Table 1).

Table 1: Effect of Aloe vera extract on body weights in control and experimental group rats.

Weeks	Normal control	Control + *Aloe vera*	Diabetic control	Diabetic + *Aloe vera*	Diabetic + Glibenclamide
I	$183.25^{a} \pm 5.47$	$181.42^{a} \pm 3.52$ (-0.99)	$180.48^{a} \pm 6.52$ (-1.51)	$191.18^{a} \pm 4.32$ (4.32)	$186.19^{a} \pm 9.82$ (1.6)
II	$195.32^{a} \pm 7.56$	$193.19^{a} \pm 5.19$ (-1.09)	$171.17^{b} \pm 7.66$ (-12.36)	$192.26^{a} \pm 6.16$ (-1.56)	$189.45^{a} \pm 10.14$ (-3)
III	$218.12^{a} \pm 9.23$	$214.27^{a} \pm 8.18$ (-1.76)	$162.28^{b} \pm 10.11$ (-25.6)	$198.17^{c} \pm 7.18$ (-9.15)	$182.19^{d} \pm 11.23$ (-16.47)
IV	$234.19^{a} \pm 1.42$	$232.11^{a} \pm 9.45$ (-0.88)	$155.19^{b} \pm 11.15$ (-33.73)	$210.25^{c} \pm 10.22$ (-10.22)	$189.48^{d} \pm 11.76$ (-19.9)

Values are mean ± S.D. of 6 individuals
Values in the parentheses are percent change from the control.
Mean values in a row that do not share the same superscript differ significantly at $p<0.05$.

There was a significant ($p<0.05$) reduction in body weight of the diabetic rats compared with normal control rats. After ethanolic extract of *Aloe vera* supplementation for 30 days there was a significant increase ($p<0.05$) in the body weight of diabetic rats were observed.

3.2. Effects of *Aloe vera* extract on the blood glucose levels

Effect of *Aloe vera* on blood glucose levels of normal diabetic (478.31) and *Aloe vera* treated group (391.52) is shown in (Table 2).

Table 2: Effect of Aloe vera extract on blood glucose levels in control and experimental group rats.

Weeks	Normal control	Control + *Aloe vera*	Diabetic control	Diabetic + *Aloe vera*	Diabetic + Glibenclamide
I	$82.33^{a} \pm 9.93$	$80.83^{a} \pm 7.9$ (-1.82)	$476.12^{b} \pm 10.17$ (478.31)	$404.67^{c} \pm 12.12$ (391.52)	$356.97^{d} \pm 13.65$ (333.58)
II	$70.67^{a} \pm 7.76$	$74.25^{a} \pm 5.36$ (5.06)	$388.17^{b} \pm 7.87$ (449.27)	$165.83^{c} \pm 9.88$ (134.65)	$154.67^{cd} \pm 8.07$ (118.86)
III	$65.5^{a} \pm 7.02$	$69.5^{a} \pm 6.5$ (6.11)	$273.67^{b} \pm 4.05$ (317.81)	$82.33^{c} \pm 6.5$ (25.69)	$110.6^{d} \pm 3.63$ (68.85)
IV	$81.83^{a} \pm 8.85$	$79.64^{a} \pm 4.15$ (-2.67)	$303.56^{b} \pm 3.48$ (270.96)	$92.5^{c} \pm 3.02$ (13.03)	$102.7^{d} \pm 3.91$ (25.5)

Values are mean ± S.D. of 6 individuals
Values in the parentheses are percent change from the control.
Mean values in a row that do not share the same superscript differ significantly at $p<0.05$.

Significant ($p<0.05$) *Aloe vera* extract produced a reduction in the blood glucose levels were observed in diabetic rats when compared with diabetic control.

3.3. Effect of *Aloe vera* extract on lipid peroxidation and antioxidant enzymes in

control and diabetic rats

The levels of lipid peroxidation and activities of antioxidant enzymes in the liver and kidney of control and experimental rats were shown in table 3 and 4. A significant increase ($p<0.05$) in lipid peroxidation was observed in the liver and kidney of diabetic rats when compared to controls. The activity levels of SOD, CAT, GPx and GR significantly ($p< 0.05$) decreased in the liver and kidney of diabetic rats when compared to control rats. Whereas in *Aloe vera* extract treated diabetic rats lipid peroxidation levels were significantly ($p<0.05$) decreased and antioxidant enzymes like SOD, CAT, GPx and GR activity levels were significantly ($p<0.05$) increased in the liver and kidney when compared to diabetic rats (Table 3 and 4).

Table 3: Effect of Aloe vera on lipid peroxidation and antioxidant enzymes activity levels in liver of in control and experimental group rats.

	Normal control	**Control + *Aloe vera***	**Diabetic control**	**Diabetic + *Aloe vera***	**Diabetic + Glibenclamide**
Lipid peroxidation (μ moles of malondialdehyde formed/g wet wt/h	$43.21^{a} \pm 9.42$	$37.08^{a} \pm 8.23$ (-14.19)	$78.02^{b} \pm 9.07$ (80.56)	$39.02^{a} \pm 4.09$ (-9.69)	$38.92^{a} \pm 3.98$ (-9.93)
Superoxide dismutase (Units/mg protein/min)	$10.12^{a} \pm 1.05$	$11.03^{a} \pm 1.08$ (8.99)	$5.02^{b} \pm 0.62$ (-50.39)	$8.45^{c} \pm 0.71$ (-16.5)	$7.02^{d} \pm 0.42$ (-30.63)
Catalase (μ moles of H_2O_2 metabolised/mg protein/min)	$78.62^{a} \pm 9.73$	$79.63^{a} \pm 8.33$ (1.28)	$58.02^{b} \pm 6.81$ (-26.2)	$69.92^{a,b} \pm 4.28$ (-11.06)	$62.10^{b} \pm 5.61$ (-21.01)
Glutathione peroxidase (μ moles of NADPH oxidized / mg protein/ min)	$10.12^{a} \pm 1.05$	$11.07^{a} \pm 1.08$ (9.39)	$6.18^{b} \pm 0.76$ (-38.93)	$9.16^{c} \pm 0.98$ (-9.49)	$8.14^{c,d} \pm 0.83$ (-19.56)
Glutathione reductase (μ moles of NADPH oxidized / mg protein/ min)	$4.08^{a} \pm 0.61$	$4.9^{a} \pm 0.58$ (20.09)	$2.14^{b} \pm 0.18$ (-47.55)	$3.29^{c} \pm 0.13$ (-19.36)	$2.91^{d} \pm 0.21$ (-28.68)

Values are mean ± S.D. of 6 individuals
Values in the parentheses are percent change from the control.
Mean values in a row that do not share the same superscript differ significantly at $p<0.05$.

Table 4: Effect of Aloe vera on lipid peroxidation and antioxidant enzymes activity levels in kidney of diabetic rats.

	Normal control	**Control + *Aloe vera***	**Diabetic control**	**Diabetic + *Aloe vera***	**Diabetic + Glibenclamide**
Lipid peroxidation (μ moles of malondialdehyde formed/g wet wt/h)	$40.02^{a} \pm 10.24$	$37.25^{a} \pm 9.27$ (-6.92)	$60.82^{b} \pm 8.79$ (51.97)	$32.97^{a} \pm 6.47$ (-17.61)	$30.21^{a} \pm 5.42$ (-24.51)
Superoxide dismutase (Units/mg protein/min)	$15.11^{a} \pm 3.54$	$16.01^{a} \pm 3.89$ (5.96)	$8.13^{b} \pm 0.73$ (46.19)	$13.78^{a} \pm 2.42$ (8.8)	$12.13^{a,b} \pm 2.13$ (-19.72)
Catalase	$38.01^{a} \pm 2.04$	$39.28^{a} \pm 2.08$	$28.15^{b} \pm 4.29$	$35.81^{b} \pm 2.82$	$32.66^{b} \pm 2.13$

(μ moles of H_2O_2 metabolised/mg protein/min)		(3.34)	(-25.94)	(-5.79)	(-14.07)
Glutathione peroxidase (μ moles of NADPH oxidized/ mg protein / min)	$9.13^{a} \pm 0.89$	$9.45^{a} \pm 0.99$ (3.5)	$6.86^{b} \pm 0.51$ (-24.86)	$8.42^{b} \pm 0.42$ (-7.78)	$7.99^{b} \pm 0.15$ (-12.49)
Glutathione reductase (μ moles of NADPH oxidized/ mg protein / min)	$1.15^{a} \pm 0.07$	$1.32^{a} \pm 0.03$ (14.78)	$0.82^{b} \pm 0.04$ (-28.69)	$0.98^{c} \pm 0.06$ (-14.78)	$0.92^{c} \pm 0.03$ (-20)

Values are mean ± S.D. of 6 individuals
Values in the parentheses are percent change from the control.
Mean values in a row that do not share the same superscript differ significantly at $p<0.05$.

3.4. Effect of *Aloe vera* on histopathological changes in liver and kidney of diabetic rats

In control rat liver contain hexagonal lobules contain number of hepatocytes with central vein. Whereas in diabetic rats lumen of central vein extensively filled with fibrous tissue. However, in diabetic rats treated with *Aloe vera* extract the liver looked almost normal (Figure 1).In diabetic rat kidney contain severe tubular degeneration of glomeruli, focal necrosis of tubules was observed. Whereas in *Aloe vera* extract treated diabetic rats above the pathological changes were decreased (Figure 2).

Figure-1

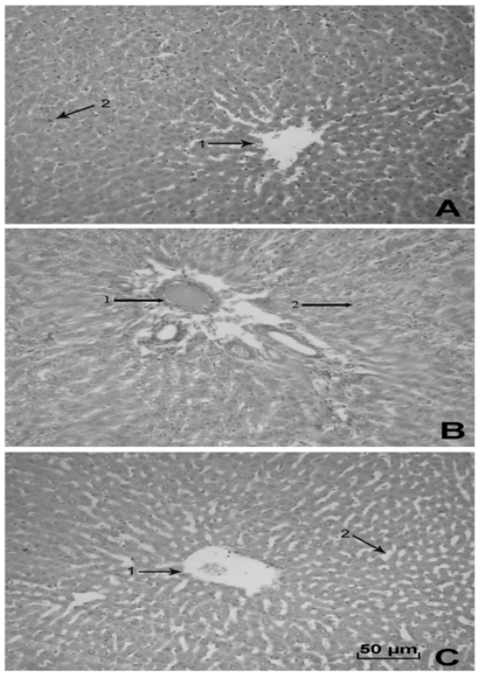

Fig. 1. Histological observations of liver of normal control rats, diabetic and Aloe vera extract treated diabetic rats (Scale Bar: 50μm)
A. Normal central vein and normal hepatic cells were observed in liver of control rats.
B. Central vein with high hemarage (1) and dense kupper cells (2) were observed in liver of diabetic control rats.
C. Normal central vein mild degenerative changes (1) and vacuolization (2) was observed in liver of Aloe vera extract treated diabetic rats.

Figure-2

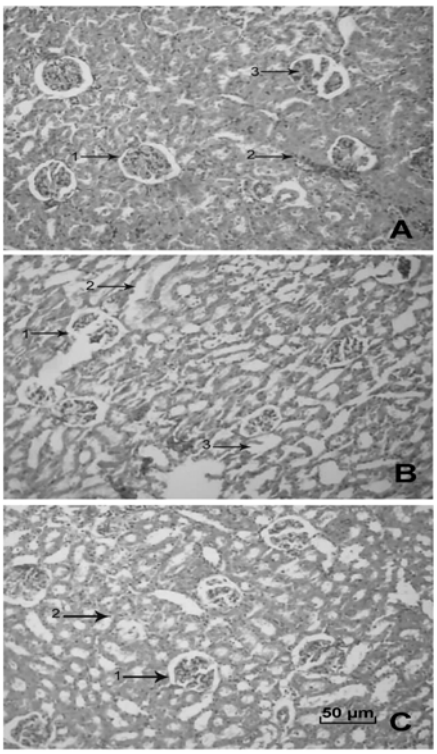

Fig. 2. Histological observations of kidney of control, diabetic and Aloe vera extract treated diabetic rats (Scale Bar: 50µm)
A. Normal glomeruli (1), tubular epithelial cells (2) and Bowman's capsule (3) were observed in kidney of control rats.
B. Complete degeneration of glomeruli (1), enlarged tubules (2) and Intouchbular vacuolization (3) were observed in kidney of diabetic rats.
C. Atropic glomeruli (1) and regeneration of tubular epithelial cells (2) were observed in kidney of Aloe vera extract treated diabetic rats.

4. Discussion

In the present study, administration of *Aloe vera* leaf extract ameliorated the liver and kidney damage in STZ-induced diabetic rats as evidenced by a) decrease in the levels of lipid peroxidation products and b) enhanced activity levels of antioxidant enzymes.

In the present study, the body weights in STZ-induced diabetic rats were increased when compared to the *Aloe vera* treated rats. The *Aloe vera* extract have been ability to protect weight loss by regaining the tissue damage of liver and kidney caused by the free radical exposure due to its antidiabetic activity. The decrease in glucose level was observed in *Aloe vera* treated rats indicated that the *Aloe vera* extract stimulates insulin secretion from the remnant β-cells and/or from regenerated β- cells. Our results are in consonance with earlier reports [46]. It has been suggested that antihyperglycaemic activity of *Aloe vera* could be due to an insulinogenic activity of the leaf extract. Moreover, the hypoglycemic polysaccharides, arboran A and arboran B, isolated from *Aloe arbor-escens* [40], a 'bitter principle' isolated from the exudates of *Aloe vera* [41] (Ajabnoor, 1990), and phytosterols isolated from the gel of *Aloe vera* [41] have been shown to have antidiabetic activity.

Liver and kidney are the two important organs which play important role in physiological aspects. Thus, any damage in these tissues, may lead to alterations in metabolic activities including cellular antioxidant status. It is well known that increased reactive oxygen species (ROS) have been implicated in diabetes and its complications [47] and to overcome increased ROS, an intrinsic scavenging system, including antioxidants and antioxidant enzymes plays a vital role. In the

present study, there was a significant increase in the levels of lipid peroxidation products in liver and kidney of STZ-induced diabetic rats when compared to controls. It has been reported that hyperglycemia leads to generation of ROS in tissues from glucose auto-oxidation and protein glycosylation [3, 7, 44] thereby alters normal cellular defense mechanisms and eventually leads to increased oxidative stress. The increased levels of ROS in diabetes due to their increased production and/ or decreased destruction of free radical scavenger enzymes function has been linked to altered activity of nonenzymatic and enzymatic which includes antioxidant enzymes are glutathione reductase (GR) and catalase (CAT), glutathione peroxidase (GPx), superoxide dismutase (SOD) antioxidants. Several reports suggested that increased free-radical mediated oxidative stress is involved in diabetic complications [5]. On the other hand, administration of ethanolic extract of *Aloe vera* leaves reduces the levels of lipid peroxidation products in STZ induced diabetic rats over controls. The results are in consonance with earlier reports [48].

It is well-known that tissues of diabetic animal exhibit increased oxidative stress and disturbances in antioxidant defense system [51]. The increased lipid peroxidation in the tissues of diabetic animals may be due to the remarkable increase in the concentration of TBARS and hydroperoxides in the liver and kidney of diabetic rats [52]**.** *Aloe* leaf extract oral administration (at a doses of 300 mg/kg body weight) significantly ($P<0.05$) decreased the level of LPx. Our result shows that, oral administration of *Aloe vera* gel extract at a concentration of 300 mg/kg body weight to diabetic rats significantly decreased the levels of LPx [29].

Reduced activities of SOD and CAT in liver and kidney tissues have been observed in diabetes rats. The enzyme SOD catalyzes the dismutation reaction $2O_2^- + 2H^+$ ---> $H_2O_2 + O_2$ [53]. Catalase is heme protein enzyme, catalyses the dismutation of hydrogen peroxide into water and oxygen ($H_2O_2 + H_2O_2$ ---------> $2\ H_2O + O_2$) [54]. Similar to our studies lower levels of SOD and CAT was observed in diabetic rats [29]. The reduced activities of SOD and CAT in the liver and kidney during diabetes may result in a number of deleterious effects due to the accumulation of superoxide radicals and hydrogen peroxides. Administration of *Aloe vera* leaf extract increases the activities of SOD and CAT in diabetic rats. The result of the SOD and CAT activity clearly shows that *Aloe vera* contains a free radical scavenging activity, which could beneficial action against pathological alteration caused by ROS.

The decreased activities of GPx and GR in liver and kidney result in the involvement of deleterious oxidative changes and also insufficient availability of reduced glutathione (GR) also number of deleterious effects due to the accumulation of toxic products. In *Aloe vera* leaf extract treated rats elevation of GPx and GR enzyme levels were observed.

In this context, other researchers also reported a decreased activities of these antioxidant enzymes (SOD, CAT, GPx and GR) in the liver and kidney of diabetic rats [54]. In diabetic rats treated with the ethanolic extract of *Aloe vera* a significant increase in activity of these enzymes was observed. This might reflect the antioxidant potency of the ethanolic extract of *Aloe vera*, which by reducing blood glucose levels prevented glycation and inactivation of enzymes.

From the results, it is clear that *Aloe vera* extract not only decreases the blood glucose levels, but also reverses the damage of liver and kidney in diabetic animals when compared to controls. This may be attributed to the fact that administration of *Aloe vera* extract may provide antioxidant activity, which may lead to its protective action on LPx and to the enhancing effect on cellular antioxidant defense, indicating antioxidant property. The extract was also more effective than glibenclamide, standard drug, in restoring the selected biochemical variables.

5. Conclusions

In conclusion, that *Aloe vera* exhibits potential characteristic feature on the glucose lowering activity observed in the diabetic animals due to the stimulation of the β- cells of the pancreatic islets, we strongly report that the body weights of diabetic treated with *Aloe vera* group were significantly recovered when compared to the diabetic control and diabetic treated with glibenclamide groups. At the same time decreased blood glucose levels were observed by the stimulation of the β- cells of the pancreatic islets naturally in diabetic group followed by increased oxidative levels were experimentally proved and no tissue damage were observed by the activity of *Aloe vera* in STZ treated animals. It has been found that only 300 mg/kg body weight of *Aloe*

leaf extract has a protective effect comparable to glibenclamide against hepato and renal toxicity produced by diabetes, and that *Aloe vera* could have a beneficial effect on liver and kidney if used as a hypoglycemic agent in the treatment of type-II diabetes.

References

[1] Thorsby P, Undlien DE, Berg JP, Thorsby E, Birkeland KI. Tidsskr Nor Laegeforen., **118,** 2519-24 (1998).
[2] Wild S, Roglic G, Green A, Sicree R, King H. Diabetes Care **27,** 1047-53 (2004).
[3] Asbun J, Villarreal FJ. J Am Coll Cardiol., **47,** 693-700 (2006).
[4] Oluleye TS. Afr J Med Med Sci; **39,** 199-206 (2010).
[5] McGarry JD: Diabetes **51,**7–18, (2002).
[6] Boden G: Diabetes **46**, 3–10, (1997).
[7] Poitout V, Robertson RP. Endocrinology **143**,339–342, (2002).
[8] Harmon JS, Catherine E. Gleason, Yoshito Tanaka, Vincent Poitout, and R. Paul Robertson Diabetes **50,**2481–2486, (2001).
[9] Whaley-Connell A, McCullough PA, Sowers JR. Rev Cardiovasc Med; **12**, 21-9 (2011).
[10] Lacraz G, Figeac F, Movassat J, Kassis N, Coulaud J, Galinier A, Leloup C, Bailbé D,Homo-Delarche F, Portha B. PLoS One; **4**, e6500 (2009).
[11] Acharya JD, Ghaskadbi SS. Islets; **2,** 225-35 (2010).
[12] Ha H, Lee HB. Curr Diab Rep; **1,** 282-7(2001).
[13] Amarapurkar D, Das HS. Trop Gastroenterol; **23,** 3-5(2002).
[14] Kashihara N, Haruna Y, Kondeti VK, Kanwar YS. Curr Med Chem; **17,** 4256-69(2010).
[15] Iglesias-De La Cruz MC, Ruiz-Torres P, Alcamí J, Díez-Marqués L, Ortega-Velázquez R, Chen S, *et al*. Kidney International, **59**, no. 1, pp. 87-95, (2001).
[16] Choudhury D, Tuncel M, Levi M. Discov Med; **10,** 406-15 (2010).
[17] Lorenzi R, Andrades ME, Bortolin RC, Nagai R, Dal-Pizzol F, Moreira JC. Int J Toxicol; **30,** 253-8(2011).
[18] Singh DK, Winocour P, Farrington K. Nat Rev Endocrinol; **7**,176-84 (2011).
[19] Anuradha K, Hota D, Pandhi P. Indian J Exp Biol ; **42**, 368-72 (2004).
[20] Schwab S, Diem P. Ther Umsch; **66**, 677-84 (2009).
[21] Takamoto I, Kadowaki T. Nippon Rinsho; **69**,563-72 (2011).
[22] Alarcon-Aguilar FJ, Jimenez-Estrada M, Reyes-Chilpa R, Roman-Ramos R.J Ethnopharmacol; **72,** 21-7 (2000).
[23] Li Y, Huang TH, Yamahara J. Life Sci; **82,** 1045-9(2008).
[24] Nakamura S, Matsuda H, Yoshikawa M. Yakugaku Zasshi; **131**, 909-15 (2011).
[25] Day C. Br J Nutr; **80**, 203-8 (1998).
[26] Abd-Alla HI, Shaaban M, Shaaban KA, Abu-Gabal NS, Shalaby NM, Laatsch H. Nat Prod Res ; **23**, 1035-49 (2009).
[27] Tabolacci C, Lentini A, Mattioli P, Provenzano B, Oliverio S, Carlomosti F,Life Sci; **87**, 316-24 (2010).
[28] Saada HN, Ussama ZS, Mahdy AM. Pharmazie; **58**, 929-31(2003).
[29] Borrelli F, Izzo AA. Phytother Res; **14**, 581-91(2000).
[30] Im SA, Lee YR, Lee YH, Lee MK, Park YI, Lee S, Arch Pharm Res; **33**, 451-6 (2010).
[31] Ajabnoor MA. J Ethnopharmacol ; **28**, 215-20 (1990).
[32] Bunyapraphatsara N, Yongchaiyudha S, Rungpitarangsi V, Chokechaijaroenporn O. Phytomedicine; **3**, 245-8 (1996).
[33] Rajasekaran S, Sivagnanam K, Subramanian S. Pharmacol Rep; **57**, 90-6 (2005).
[34] Beppu H, Shimpo K, Chihara T, Kaneko T, Tamai I, Yamaji S, J Ethnopharmacol; **103**, 468-77 (2006).
[35] NRC. Guide for the Care and Use of Laboratory Animals. Institute of Laboratory Animal Resources (ILAR), Commission on Life Sciences, Washington DC, National Academy Press; p.125 (1996).

[36] Carlsson PO, Flodström M, Sandler S. Endocrinology; **141**, 2752-7 (2000).
[37] Hiroshi O, Habuko D, Yagi K. Anal Biochem; **95**, 351-8 (1979).
[38] Misra HP, Fridovich I. J Biol Chem; **247**, 3170-5 (1972).
[39] Chance B, Maehley A. Methods Enzymol; **2**,764-75 (1955).
[40] Flohé L, Günzler WA. Methods Enzymol; **105,** 114-21 (1984).
[41] Carlberg I, Mannervik B. Methods Enzymol; **113**, 484-90 (1985).
[42] Lowry H, Rosebrough NI, Far AL, Ranall RJ. J Biol Chem; **193**, 265-75 (1951).
[43] Hikino, H., Takahashi, M., Murakami, M., Konno, C., Mirin, Y.,.Int. J.CrudeDrugRes. **24**, 183-186 (1986).
[44] Ajabnoor MA. J Ethnopharmacol; **28**, 215-20 (1990).
[45] Tanaka M, Misawa E, Ito Y, Habara N, Nomaguchi K, Yamada M, Biol Pharm Bull; **29**, 1418-22 (2006).
[46] Solomon G, Raosaheb KK, Najma ZB. Indian J Exp Biol; **37**, 200-2 (1999).
[47] Vats V, Yadav SP, Grover JK. J Ethnopharmacol **90**, 155-60 (2004).
[48] Shokeen P, Anand P, Murali Y. K, Tandon V. Food Chem Toxicol; **46**, 3458-66 (2008).
[49] Kesari AN, Gupta RK, Watal G. J Ethnopharmacol; **97**, 247-51 (2005).
[50] Baynes JW, Thorpe SR. Diabetes; **48**, 1-9 (1999).
[51] Rajasekaran S, Ravi K, Sivagnanam K, Subramanian S. Clin Exp Pharmacol Physiol; **33**, 232-7 (2006).
[52] Can A, Akev N, Ozsoy N, Bolkvent S, Arda BP, Yanardag R, Okyar A. Biol Pharm Bull;**27**,694-8(2004).
[53] Parinandi NL, Thompson EW, Schmid HH. Biochim Biophys Acta ; **1047**, 63-9 (1990).
[53] Rauscher FM, Sanders RA, Watkins JB 3rd. J Biochem Mol Toxicol; **14**, 329-34 (2000).