JPP
Journal of
Pharmacy and Pharmacology

JPP 2010, 62: 115–123

Received March 3, 2009
Accepted October 14, 2009
DOI 10.1211/jpp/62.01.0013
ISSN 0022-3573

Research Paper

Aloe vera gel alleviates cardiotoxicity in streptozocin-induced diabetes in rats

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Abstract

Objectives Persistent hyperglycaemia results in oxidative stress along with the generation of oxygen free radicals and appears to be an important factor in the production of secondary complications in diabetes. The aim of this work was to evaluate markers of oxidative stress in heart tissue along with the protective, antioxidant and antidiabetic activity of 30% *Aloe vera* gel in diabetic rats.

Methods Streptozocin was given as a single intravenous injection and 30% *Aloe vera* gel was given in two doses for 20 days, orally. Blood glucose, glycosylated haemoglobin, blood reduced glutathione, serum lactate dehydrogenase and serum creatine kinase levels were measured on day 21 after drug treatment. Heart rate and mean blood pressure were recorded at the end of the study. Different biochemical variables were evaluated in the heart tissue, including thiobarbituric acid reactive substance (TBARS), reduced glutathione, superoxide dismutase and catalase in diabetic and in *Aloe vera*-treated diabetic rats.

Key findings In streptozocin diabetic rats, the TBARS level was increased significantly, superoxide dismutase and reduced glutathione significantly decreased, and the catalase level was significantly increased. *Aloe vera* 30% gel (200 mg/kg) treatment in diabetic rats reduced the increased TBARS and maintained the superoxide dismutase and catalase activity up to the normal level. *Aloe vera* gel increased reduced glutathione by four times in diabetic rats.

Conclusions *Aloe vera* gel at 200 mg/kg had significant antidiabetic and cardioprotective activity.

Keywords *Aloe vera* gel; antidiabetic; cardioprotection; streptozocin

Introduction

Active oxygen metabolism plays an important role in the normal functioning of cells. Blood glucose level, free oxygen radicals and oxidative stress appear to be important factors in the production of secondary complications in diabetes.[1,2] Hyperglycaemia generates abnormally high levels of free radicals by autoxidation of glucose and protein glycation. The goal of treatment should be glycaemic control and oxidative stress reduction to control the risk of complications.[3,4] It is well established that the major reason for mortality occurring in diabetic patients is cardiovascular disease, because reactive oxygen species (ROS) are increased in various tissues which are involved in the development of diabetic complications.[5,6] Lipid peroxidation is a free radical mediated event. The primary products of such damage are complex mixtures of peroxides that break down to produce carbonyl compounds, e.g. malondialdehyde. There is evidence that acute elevation in the blood glucose level destroys the body's natural antioxidant defence such as superoxide dismutase (SOD), catalase and reduced glutathione, which results in reduced protection against the damaging effect of free radicals. The circulating level of malondialdehyde is higher in plasma of diabetic patients as compared with those in nondiabetic individuals.[7]

Modern drugs, including insulin and other oral hypoglycaemic agents such as sulfonylureas and biguanides, control blood glucose level but they also produce side effects.[8] Recently there has been renewed interest in natural products as potential therapeutic agents. Many plants synthesize a variety of phenolic compounds with antioxidant

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activity that can play a role in protection against molecular damage induced by ROS.[9] In traditional medicine, several medicinal plants or their extracts are widely used in many countries for the prevention and treatment of a variety of diseases including diabetes.[10] Aloe plants have been used medicinally for centuries. There are more than 200 verities of *Aloe vera* found worldwide. Among them, we have used *Aloe barbadensis*, commonly called *Aloe vera*. It belongs to the family Liliaceae and is one of the most widely used healing plants in the history of mankind.[11]

The plant has stiff gray-green lance-shaped leaves containing a clear gel in a central mucilaginous pulp. Two distinct preparations of Aloe plants are mostly used medicinally. The leaf exudates (aloe) are used as a laxative and the mucilaginous gel (*Aloe vera*) is used as a remedy against a variety of skin disorders.[12] Aloe leaf exudates also possess antidiabetic properties.[13]

Countless studies have demonstrated the healing power of *Aloe vera* gel. Acemannan, the major carbohydrate fraction in the gel, is a water-soluble long chain mannose polymer which accelerates wound healing, modulates immune function (particularly macrophage activation and production of cytokines) and demonstrates antineoplastic and antiviral effects.[14–16] The gel also contains bradykininase, an anti-inflammatory component, magnesium lactate, which helps in the prevention of itching, and salicylic acid and other anti-prostaglandin compounds which relieve inflammation.[17]

There have been several reports on the hypoglycaemic and antioxidant activity of *Aloe*. The effect varies with regard to the plant species, the part of the plant used, and in the preparation of extracts as well as the animal models.[18–20] However, the antioxidant and cardioprotective activities in diabetic patients have not yet been reported. This work was undertaken to study the cardioprotective effect of *A. vera* gel in diabetic rats.

Materials and Methods

Chemicals

Streptozocin and bovine serum albumin (BSA) were obtained from Sigma Chemicals (St Louis, MO, USA). All other chemicals used in the study were from Merck, (India). Commercially available kits were used for lactate dehydrogenase (LDH) and creatine kinase assay (Ecoline, Merck, India).

Plant material

Aloe vera was collected from the botanical garden of Jamia Hamdard and authenticated by Dr M. P. Sharma (Professor and taxonomist, Department of Botany, Jamia Hamdard, New Delhi, India). A specimen was retained in the Department of Pharmacognosy and Phytochemistry, Faculty of Pharmacy, Jamia Hamdard (voucher no. PRL/JH/06/19). Mucilage of *Aloe vera (Aloe vera* gel*)* was obtained by incision on the leaves. It was stored at 4°C under refrigeration. For preparing the 30% gel, leaf mucilage was homogenized in distilled water freshly before use.

For experimental study, doses of 100 and 200 mg/kg of each were calculated and the weighed amount of residue was dissolved in distilled water.

Experimental animals

Male Wistar albino rats (150–200 g) were procured from the Central Animal House Facility, DRDE, Gwalior, India. The animals were kept in polypropylene cages (three in each cage) under standard laboratory conditions. They had free access to a pellet diet (Ashirwad feed, India) and water was freely available. The animal house temperature was maintained at 25 ± 2°C and relative humidity maintained at 50 ± 15%. The study was approved by Animal Ethics Committee (IAEC) of the institute.

Experimental induction of diabetes

After 18-h fasting, the rats were injected intravenously through the tail vein with a single dose of 40 mg/kg streptozocin, freshly dissolved in 0.1 M citrate buffer (pH 4.5). Streptozocin-treated animals were allowed to drink 5% glucose solution overnight to overcome hypoglycaemic shock. Diabetes in rats was observed by moderate polydipsia and marked polyurea. Three days after streptozocin injection, blood glucose level was estimated by the orthotoludine method.[21] Animals having a blood glucose level of more than 200 mg/dl were selected for study. These rats were observed daily for any mortality or morbidity.

Treatment protocol

The animals were randomly divided into five groups of six animals each. Group I received distilled water, 1 ml/kg (healthy rats); group II, the streptozocin group, received distilled water (1 ml/kg); group III, the streptozocin-diabetic animals, received 30% *Aloe vera* gel (100 mg/kg); group IV, the streptozocin-diabetic animals, received 30% *Aloe vera* gel (200 mg/kg); and group V, the streptozocin-diabetic animals, received gliclazide (25 mg/kg). The drugs were administered to all rats by oral gavage, once a day for 20 days.

Blood collection and biochemical studies in serum

On day 21, fasting blood samples were collected from the retro-orbital plexus of all rat groups. Blood was used for assay of blood glucose, glycosylated haemoglobin (HbA1c), and reduced glutathione levels.[21–23]

Serum was separated for assay of specific serum marker enzymes, namely lactate dehydrogenase (LDH) and creatine kinase.[24–26] Assays were performed using commercial kits (Ecoline, Merck, India), as per the manufacturer's instructions.

Study of cardioprotective activity

Heart rate and blood pressure was measured by using a plethysmograph (Letica Scientific Instrument, USA). Animals were trained for one week in a restrainer before taking heart rate and blood pressure.

With this method rats were placed in a constant temperature (32°C) chamber for 90 min and were then put into a rat holder. The tail-cuff and piezoelectric pulse sensor

were placed at the base of the tail and were connected to a fully automatic blood pressure analyser (Letica Scientific Instruments, USA). The tail-cuff was inflated and deflated automatically at 1 min intervals. The pressure in the cuff was displayed on the screen of the plethysmograph. For each rat, eight individual readings were obtained. The highest and the lowest measurement were discarded, and the average of the remaining six readings was taken as the individual mean blood pressure (MBP). Heart rate was calculated in the same way.

All the animals were killed by decapitation under ether anaesthesia on day 21 post *Aloe vera* treatment and hearts were dissected out. Heart tissues were washed with ice-cold normal saline for biochemical assay and histopathological evaluation.

Biochemical studies

The thiobarbituric acid reactive substance assay was used to measure lipid peroxidation. A 10% suspension of homogenized myocardial tissue was prepared in 0.15 M KCl, pH 7.4, and a sample was used for the assay according to the method by Ohkawa *et al.*[27] In brief, to 1 ml suspension, 0.2 ml SDS, 1.5 ml 20% acetic acid followed by 0.5 ml 0.8% thiobarbituric acid were added. The absorbance of supernatants was read at 540 nm at room temperature against an appropriate blank.

Heart tissues were homogenized in 50 mM potassium phosphate buffer (1 : 10) and homogenate was used for assay of superoxide dismutase (SOD) activity by following the inhibition of pyrogallol autoxidation at 420 nm according to the method of Marklund.[28] For catalase assay, 50 μl supernatant was added to 19 mM H_2O_2. Disappearance of H_2O_2 was monitored at 240 nm for 3 min at 1-min intervals.[29]

For the reduced glutathione assay, heart homogenate was prepared separately in 0.02 M EDTA solution. Total glutathione was measured according to modified methods of Sedlak and Lindsay[30] and Ellman[31] at 410 nm.

Histopathological studies

Rat heart tissue was removed, washed with normal saline and fixed in 10% natural buffered formalin solution (pH 7.0–7.2). After proper fixation, tissue was processed for dehydration in ascending grades of ethanol, clearing with toluene, followed by impregnation in paraffin wax; 5-μm sections thick were cut with the help of a semiautomatic rotary microtome. Sections were stained with haematoxylin and eosin. Stained paraffin sections of heart were examined under a light microscope (Leica DMLB, Leica Microsystems Ltd, Germany) and photomicrographs were taken. Representative areas in the images were captured and analysed with the help of a Leica Qwin V3 digital image processing and analysis system.

HPTLC analysis

Aloe vera gel was dissolved in 100% methanol and sonicated for 20 min. The solution was filtered to obtain a clear solution and enough volume of the solution was spotted on the TLC with an auto-spotting machine. The mobile phase used for the development of the chromatogram was ethyl acetate : methanol : water (10 : 1.7 : 1.3).

The plate was developed on a CAMAG HPTLC Scorin Unit and dried. A CAMAG HPTLC plate scanner was used to record the chromatograms on the plates. The plates were scanned at 254 nm.

Statistical analysis

Statistical analysis was carried out using Sigma Stat 2.03 (Sigma Stat software, USA). All data were expressed as mean ± SEM. Groups of data were compared with analysis of variance followed by Dunnett's *t*-test. Values were considered statistically significant when $P < 0.05$.

Results

Effect of *Aloe vera* gel on haemodynamic changes in diabetic rats

Figure 1 represents the effect of *Aloe vera* gel on the haemodynamic parameters of diabetic rats. The heart rate of rats fed on a normal diet was 395 beats/min. Conversely, in the streptozocin-treated groups, no significant change was observed in heart rate. The mean blood pressure of the healthy group was 137 mmHg. Streptozocin treatment resulted in a significant increase ($P < 0.01$) in mean blood pressure as compared with the healthy group. Treatment with 30% *Aloe vera* gel (100 and 200 mg/kg) in streptozocin-treated animals maintained the mean blood pressure at the normal level. Gliclazide treatment also maintained the mean blood pressure in diabetic animals.

Effect of *Aloe vera* gel on biochemical parameters in blood of diabetic rats

Table 1 shows the blood glucose, %HbA1c and blood reduced glutathione, serum LDH and serum creatine kinase levels in various groups. Streptozocin-treated animals showed a significant rise ($P < 0.01$) in blood glucose level, serum LDH and creatine kinase levels compared with healthy rats. The streptozocin-treated group showed a threefold increase in the glycosylated haemoglobin level. Streptozocin treatment significantly reduced ($P < 0.01$) the blood reduced glutathione level. Treatment with 30% *Aloe vera* gel 200 mg/kg showed a significant reduction in blood glucose, glycosylated haemoglobin, serum LDH and serum creatine kinase levels, with an increase in the blood reduced glutathione level. Gliclazide treatment for 20 days showed a significant recovery of reduced glutathione as compared with streptozocin rats.

Effect of *Aloe vera gel* on endogenous antioxidants and TBARS in heart of diabetic rats

Table 2 shows the activity of SOD, catalase, reduced glutathione and level of TBARS in rat heart tissue of all the test groups. In this study, streptozocin administration resulted in significant depletion in the cardiac SOD and reduced glutathione level in the heart homogenate. Treatment with 200 mg/kg *Aloe vera* gel significantly increased SOD and reduced glutathione levels in heart tissue as compared with the pathogenic group rats ($P < 0.01$). There was a sharp rise in the cardiac catalase level in diabetic heart tissue compared with the healthy rats ($P < 0.01$) but treatment with

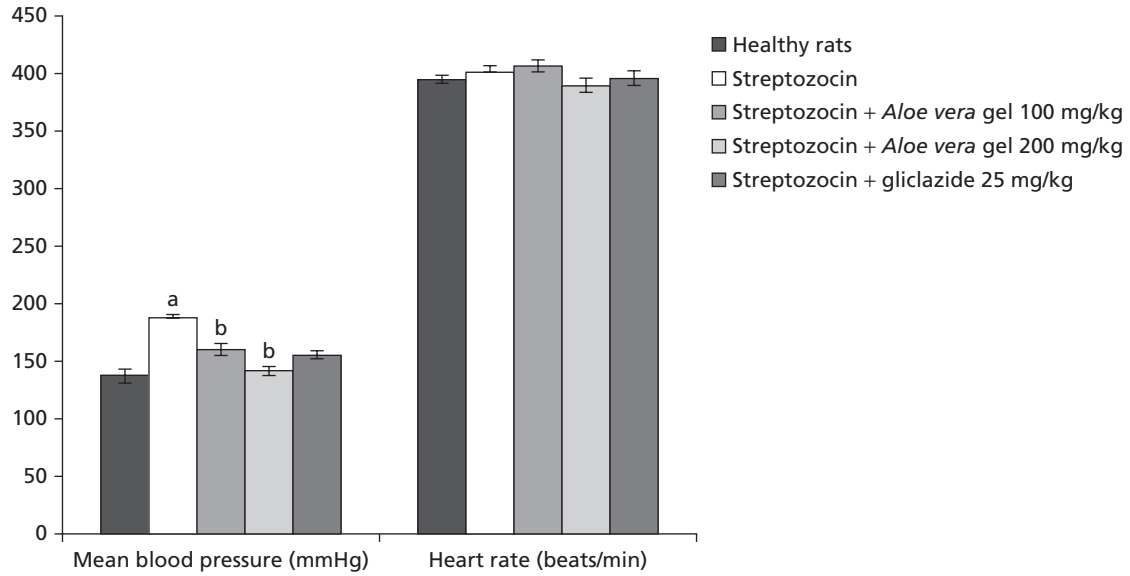

Figure 1 Effect of 30% *Aloe vera* gel on mean blood pressure and heart rate in diabetic rats. [a]$P < 0.01$ as compared with group I (analysis of variance followed by Dunnett's *t*-test). [b]$P < 0.01$ as compared with group II (analysis of variance followed by Dunnett's *t*-test).

Table 1 Effect of 30% *Aloe vera* gel on biochemical variables of diabetic rats

Groups	Blood glucose (mg/dl)	Blood HbA1c (%)	Blood reduced glutathione (mg/dl)	Serum LDH (IU/l)	Serum creatine kinase (IU/l)
Healthy rats	69.3 ± 0.78	5.05 ± 0.2	3.8 ± 0.07	159.2 ± 4.9	82.2 ± 2.1
Streptozocin treated	324.1 ± 11.3[a]	10.5 ± 0.6[a]	1.1 ± 0.05[a]	366.8 ± 6.3[a]	159.5 ± 11.9[a]
Streptozocin + *Aloe vera* gel 100 mg/kg	104.7 ± 1.8[a,b]	7.9 ± 0.9[b]	2.3 ± 0.22[a,b]	217.8 ± 3.9[a,b]	123.7 ± 9.5[a]
Streptozocin + *Aloe vera* gel 200 mg/kg	81.7 ± 1.6[b]	6.2 ± 0.5[b]	3.6 ± 0.12[b]	187.7 ± 5.2[b]	101.6 ± 7.1[b]
Streptozocin + gliclazide 25 mg/kg	79.0 ± 1.3[b]	5.9 ± 0.6[b]	2.0 ± 0.30[a,b]	213.5 ± 6.1[a,b]	136.8 ± 6.9[a,b]

Diabetes was induced by administration of streptozocin. Values given are mean ± SEM. HbA1c, blood glycosylated haemoglobin; LDH, serum lactate dehydrogenase. [a]$P < 0.01$ as compared with group I (analysis of variance followed by Dunnett's *t*-test). [b]$P < 0.01$ as compared with group II (analysis of variance followed by Dunnett's *t*-test).

Table 2 Effect of *Aloe vera* gel on the antioxidant system of heart tissue in diabetic rats

Group	TBARS	Reduced glutathione	Catalase	SOD
Healthy rats	0.52 ± 0.04	99.6 ± 6.0	2.1 ± 0.4	1.61 ± 0.03
Streptozocin treated	1.73 ± 0.32[a]	34.5 ± 3.3[a]	134.9 ± 6.3[a]	0.79 ± 0.06[a]
Streptozocin + *Aloe vera* gel 100 mg/kg	0.95 ± 0.23[b]	61.1 ± 4.1[b]	5.5 ± 0.5[b]	1.04 ± 0.04[a]
Streptozocin + *Aloe vera* gel 200 mg/kg	0.41 ± 0.02[b]	79.8 ± 3.9[b]	4.9 ± 0.6[b]	1.71 ± 0.21[b]
Streptozocin + gliclazide 25 mg/kg	0.89 ± 0.12	40.5 ± 3.1[a]	16.9 ± 0.5[b]	0.89 ± 0.10[a]

Values given are mean ± SEM. TBARS, thiobarbituric acid reactive substance (nmol malondialdehyde/mg protein); reduced glutathione (μg/mg protein); catalase (nmol phosphorus liberated/min per mg protein); SOD, superoxide dismutase (IU/mg protein). [a]$P < 0.01$ as compared with group I (analysis of variance followed by Dunnett's *t*-test). [b]$P < 0.01$ as compared with group II (analysis of variance followed by Dunnett's *t*-test).

either dose of *Aloe vera* gel prevented this rise in the cardiac catalase level.

The myocardial lipid peroxidation marker TBARS was significantly elevated in diabetic rat heart tissue ($P < 0.01$). *Aloe vera* gel (200 mg/kg) treatment significantly reduced the activity of lipid peroxides as compared with diabetic rats ($P < 0.01$). Gliclazide treatment did not show any significant reduction in lipid peroxide levels in streptozocin rats after 20 days treatment.

Histopathological observations

Heart sections of healthy rats showed normal cardiac muscle bundles and normal myocardium (Figure 2a). The diabetic rat heart showed marked congestion and haemorrhage

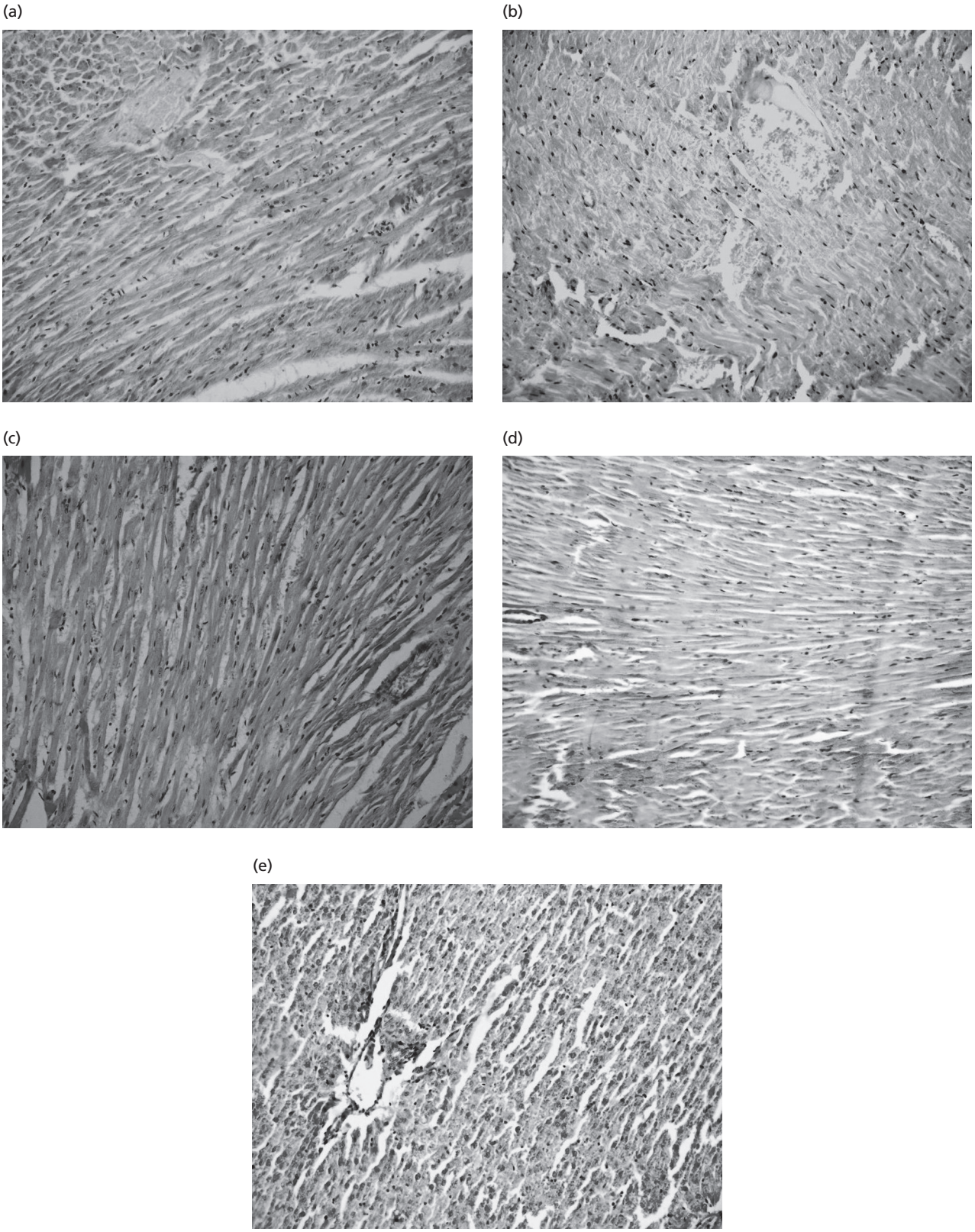

Figure 2 Typical photomicrographs of the normal rat heart and diabetic rat heart after treatment with and without *Aloe vera*. The heart tissue was stained with haematoxylin and eosin. (a) Normal control rats. (b) Diabetic rats treated with streptozocin only. (c) Diabetic rats treated with *Aloe vera* gel 100 mg/kg. (d) Diabetic rats treated with *Aloe vera* gel 200 mg/kg. (e) Diabetic rats treated with gliclazide 25 mg/kg. Magnification ×20.

(Figure 2b). The heart section of diabetic rats treated with 30% *Aloe vera* gel (100 mg/kg) showed congested blood vessels with mild haemorrhage (Figure 2c). Administration of 200 mg/kg 30% gel to diabetic rats resulted in heart sections showing normal myocardium (Figure 2d). Heart sections of diabetic rats treated with gliclazide showed congestion with patchy haemorrhage (Figure 2e).

Discussion

Diabetes mellitus is one of the most common chronic diseases and is associated with hyperglycaemia and comorbidities such as obesity and hypertension. The use of a lower dose of streptozocin (40 mg/kg) produced a partial destruction of β-cells, but the rats become permanently diabetic.[32] Since the β-cells are not completely destroyed the rats do not require insulin to survive.[33] In diabetes, hyperglycaemia-induced oxidative stress is caused by free radical generation or by overproduction of superoxide anion. Hyperglycaemia can simply inactivate existing enzymes by glycating their protein, leading to DNA cleavage.[34]

The increased level of blood glucose in streptozocin-induced diabetic rats was lowered by both doses of 30% *Aloe vera* gel (100 and 200 mg/kg). Aloe has long been used all over the world for its various medicinal properties. Reports are available regarding the antidiabetic activity of different extracts of *Aloe vera* gel. Okyar *et al*.[35] reported the hypoglycaemic activity of the alcoholic extract of *Aloe vera* leaf pulp and gel on diabetic rats. Our findings matched those of Can *et al.,*[36] who reported the antidiabetic, antioxidant and hepatoprotective activity of *Aloe vera* leaf pulp and gel extract in type 2 diabetic rats. Glycosylated haemoglobin (HbA1c) indicates the percentage of haemoglobin bound to glucose. It is used as a measurement of the mean blood glucose level over a period of six to eight weeks i.e. during the life span of red blood cells.[37] This glycation itself gives rise to oxygen free radical formation, which leads to peroxidation of lipids and further generation of free radicals.[38,39] The measurement of glycosylated haemoglobin is supposed to be a very sensitive index for glycaemic control. In our short study we found a significant rise in the level of HbA1c in diabetic control rats. Fuji and Nomoto[40] reported a significant change in the HbA1c level after two weeks of streptozocin administration in rats. Treatment with *Aloe vera* gel significantly reduced the HbA1c level, thus showing regulation of the blood glucose level for 20 days in streptozocin-treated rats. It has been reported that each per cent reduction in the HbA1c level resulted in a 35% reduction in the risk of microvascular complications, including myocardial infarction, in patients with type 2 diabetes.[4,41]

In diabetic patients, uncontrolled elevation in the blood sugar level gives rise to the formation of free radicals. There are many ways by which hyperglycaemia may increase the generation of free radicals, such as glycoxidation, polyol pathway, prostanoid biosynthesis and protein glycation.[42] Reduced glutathione is an important inhibitor of free radical mediated lipid peroxidation and it protects the cellular system against the toxic effects of lipid peroxidation.[43] Hence, a drug that could prevent the generation of free radicals or increase the free radical scavenging enzymes may be effective in streptozocin-induced diabetes.[44] It has been reported that the ethanolic extract of *Aloe vera* gel possesses antioxidant properties.[36] In this study, administration of 30% *Aloe vera* gel at either dose maintained the blood and heart levels of reduced glutathione.

The cytotoxicity of xenobiotics can be evaluated using the serum activity of marker enzymes. Serum LDH and creatine kinase, which are distributed throughout the body, possess isoenzymes that are recognized as markers for liver muscle and heart lesion.[45] Contradictory reports are available in the literature on the relationship between diabetes and creatine kinase activity.[46–50] The quantity of enzyme released from the damaged tissue is a measure of the number of the necrotic cells. Treatment with 30% *Aloe vera* gel reduced the leakage of LDH and creatine kinase from the tissue bed to serum, thus showing muscle integrity and a reduction in cytotoxicity in diabetic rats. *Aloe vera* gel showed a reduction in the leakage of these enzymes in serum, providing the protection against streptozocin-induced muscular damage.[51,52]

Oxidative stress leads to cardiac fibrosis and one of the most important pathogenetic factors of the heart's impaired functional integrity in diabetes.[53] Lipid peroxidation (LPO) is a key marker of oxidative stress. The peroxidation of polyunsaturated fatty acids of the cell membrane may produce tissue damage and finally causes various diabetes-induced complications.[54,55] The heart is a vital organ for diabetes-induced secondary complications, such as diabetes cardiomyopathy, which generally occurs due to hyperglycaemia and oxygen free radicals. Several reports are available stating that cardiomyopathy has resulted due to accumulation of myocardial collagen, and early diastolic and systolic dysfunction.[56–58] Reports are available regarding the antioxidant property of gel extracts along with its antidiabetic activity, and these factors could be responsible for the cardioprotection as shown by histological observation.[20,59] Interestingly, gliclazide (a second generation sulfonylurea derivative) by controlling the blood glucose level showed similar results against oxidative stress.[60]

SOD and catalase are principally antioxidant enzymes that scavenge superoxide anion ($O^{\cdot-}$) formed as the intermediate product of H_2O_2 breakdown and catalysed reduction of H_2O_2, thus protecting tissue from highly reactive hydroxyl radicals.[61–63] However, there is variation on the status of this enzyme in the diabetic state. Some studies have reported decreased SOD and catalase activity in vital organs during diabetes, or increased activity, or no change in the enzyme.[64–70] SOD and catalase play vital roles in cardioprotection and muscular integrity during diabetes. It has been reported that impairment of endothelium-dependent vasodilatation by the coronay bed could be abolished by perfusion with SOD and persistent with α-tocopherol.[71]

In our study, administration of streptozocin decreased the activity of SOD in heart.[72] The observed decrease in SOD activity could result from inactivation of SOD by H_2O_2 or by glycation of the enzyme, which has been reported to occur in diabetes.[73–75] A sharp rise in heart catalase activity was found in diabetic rats that matched the findings of others.[54,76–81] This result suggested a compensatory response to oxidative stress due to an increase in endogenous H_2O_2 production.

Treatment of diabetic rats with 30% *Aloe vera* gel for 20 days increased the activity of non-enzymatic antioxidants such as reduced glutathione in heart and blood. The activity of SOD and catalase in diabetic hearts was retained with this treatment. Thus, the antioxidant activity of *Aloe vera* gel could be either due to inhibition of glycation of these antioxidant enzymes or protection of β-cells from streptozocin-induced damage. Glucose, which forms a Schiff's base with protein, has been reported to have affinity for proteins, especially those containing transition metal ions.[82] This increased level of glucose was maintained by *Aloe vera* gel, thus reducing the glycation of the enzyme. The elevated level of SOD in diabetic rats after treatment with *Aloe vera* gel predicts that *Aloe vera* gel may contain free radical scavenging activity, which could exert a beneficial action against the pathological alteration caused by the presence of $O_2^{\cdot-}$ and $^{\cdot}OH$.[83]

Hypertension is generally believed to be more prevalent among diabetic than nondiabetic subjects, and it is known that hypertension is an independent risk factor for cardiovascular mortality in patients with diabetes.[84–87] In diabetes, it seems that increased oxidative stress due to hyperglycaemia or reduced availability of nitric oxide to vascular tissue leads to hypertension.[88] Consequently, treatment which can reduce oxidative stress may be effective in preventing hypertension observed in diabetes.

In this study, we observed a significant increase in the mean blood pressure and found normal heart rate after 20 days of streptozocin administration. These results were in agreement with the conclusions of studies which have used the direct technique for measurement of blood pressure.[89–91] Gliclazide has been reported also to reduce blood pressure in diabetic rats for a longer duration.[92]

Hamman[93] reported that the mechanism of action of *Aloe vera* extracts to reduce blood glucose levels was by enhancing glucose metabolism. They proposed that the glucose lowering effect could have been due to an antioxidant mechanism.

Aloe vera contains approximately 75 potentially active constituents.[94] It is a rich source of antioxidants such as vitamins A and C, and also contains minerals, sugars, lignin and other chemicals.[95] Tanaka *et al.*[96] have identified five phytosterols from the leaves which are responsible for its antidiabetic activity. HPTLC analysis has shown the presence of two major phytochemicals, which may be phenolic compounds, and polysaccharide, which are reported to have antioxidant and antidiabetic properties.[94,97]

Conclusions

The effect of *Aloe vera* gel on heart antioxidants could have been due to tight regulation of the blood glucose level in diabetic rats, which prevented excessive formation of free radicals through various biochemical pathways and reduced the glycation of potential antioxidant enzymes.

Declarations

Conflict of interest

The Author(s) declare(s) that they have no conflicts of interest to disclose.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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