have differential impact on yield. However, it is not possible to study this effect under standardized conditions and therefore, further analysis along this line was not pursued.

Our study showed that addition of neem cake was an economical and acceptable way of reducing fertilizer application. However, it also showed higher growth of vegetative than reproductive tissue, although both were higher than the control. Better controlled conditions would allow determination of the impact of such treatments on paddy yield. Also, an additional control where only neem cake is applied, would have allowed us to further clarify its role.

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ACKNOWLEDGEMENTS. This study was funded by the Department of Science and Technology, New Delhi, under the Science and Society Programme. We acknowledge useful comments by an anonymous referee.

Received 17 September 2007; revised accepted 13 March 2008

Antidiabetic activity of *Aloe vera* and histology of organs in streptozotocin-induced diabetic rats

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An attempt was made to study the beneficial effects of *Aloe vera* (L.) Burm. fil. in streptozotocin-induced diabetic rats. In diabetic induced rats fed with *A. vera* (300 mg/kg body wt), the fasting plasma glucose levels were reduced to normal and body weight was found to be increased. In the pancreatic sections of diabetic rats fed with *A. vera*, the islets were comparable to normal rats. In liver, the changes caused after induction of diabetes are granular cytoplasm, dilated sinusoids, shrunken nuclei and inflammation, which was re-

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duced after feeding with *A. vera*. Excess proliferation of epithelium in the small intestine was observed in diabetic rats, which was reduced after *A. vera* feeding. In diabetic rats and diabetic rats fed with *A. vera*, no change was noticed in the kidney and stomach.

Keywords: *Aloe vera*, antidiabetic activity, blood glucose, pancreas, streptozotocin-induced diabetes.

DIABETES is a complex and multifarious group of disorders characterized by hyperglycaemia, that has reached epidemic proportions in the present century. Several drugs such as biguanides and sulfonylureas are presently available to reduce hyperglycaemia in diabetes mellitus. These drugs have side effects and thus searching for a new class of compounds is essential to overcome these problems[1]. Management of diabetes without any side effects is still a challenge to the medical community. There is continuous search for alternative drugs. Therefore, it is prudent to look for options in herbal medicine for diabetes as well.

Traditional antidiabetic plants might provide new oral hypoglycaemic compounds, which can counter the high cost and poor availability of the current medicines/ present day drugs for many rural populations in developing countries. India is well known for its herbal wealth. Medicinal plants like *Trigonella foenum graecum*, *Allium sativum*, *Gymnema slyvestre* and *Syzigium cumini* have been studied[2] for treatment of diabetes mellitus. However, detailed studies on the efficacy, mechanism of action and safety of plant extracts are needed.

Aloe vera (L.) Burm. fil. (synonym *A. barbadensis* Miller) (Tamil – Southakathalai, Hindi – Ghikanvar), is a cactus-like plant with green, dagger-shaped leaves that are fleshy, tapering, spiny, marginated and filled with a clear viscous gel. The name was derived from the Arabic 'alloeh' meaning 'bitter', because of the bitter liquid found in the leaves. It is also known as 'lily of the desert', the 'plant of immortality', and the 'medicine plant' with qualities to serve as alternate medicine.

A. vera is as old as civilization and throughout history it has been used as a popular folk medicine. It is present in the arid regions of India, and is believed to be effective treating in treating stomach ailments, gastrointestinal problems, skin diseases, constipation, for radiation injury[3], for its anti-inflammatory effect[4], for wound healing[5,6] and burns, as an anti-ulcer[7] and diabetes[8–11]. Currently, the plant is widely used in skin care, cosmetics and as nutraceuticals. The use and research on this plant have been described in two well-referenced reviews[12,13].

There have been several reports on the hypoglycaemic activity of *Aloe*, which vary in regard to the plant species, the part of the plant used, and in the preparation of extracts as well as the animal models. The present work was undertaken to study the antidiabetic effect of *A. vera* extract and its effect on the pancreas, liver, kidney, stomach and small intestine on healthy and diabetic rat models.

Three-month-old male albino Wistar rats weighing 150–200 g were used. Rats were maintained under good laboratory conditions and were allowed free access of food and water *ad libitum*. Animal feed was obtained from Sai Durga, Bangalore. Experiments were conducted according to the ethical norms approved by the Institutional Animal Ethics Committee guidelines of Christian Medical College, Vellore.

Streptozotocin (STZ) was purchased from Sigma (USA), glucose oxidase/peroxidase (GOD/POD) reagent glucose kits were obtained from Randox Laboratories Ltd (UK) and keto-diastix reagent strips for urinalysis were from Bayer Diagnostics India Ltd, Baroda. All other chemicals used were of analytical grade.

After fasting, diabetes mellitus was induced by intraperitoneal injection of STZ dissolved in 0.1 M cold sodium citrate buffer (pH 4.4) at a dose of 30 mg/kg body wt. STZ-treated animals were considered as diabetic when the fasting plasma levels were observed above 250 mg/dl with glucosuria.

After standardizing the dose of STZ, the experiments were conducted on animal groups to see the effect of *A. vera* on diabetic rats. In the experiments, six rats were used in each group. The rats were divided into four main groups:

Group-I: Healthy rats (vehicle).
Group-II: Healthy rats fed with *A. vera* extract (300 mg/kg body wt).
Group-III: Diabetic rats (induced with 30 mg/kg body wt of STZ).
Group-IV: Diabetic rats fed with *A. vera* extract (300 mg/kg body wt.).

The sample was prepared as follows. Fresh leaves of *A. vera* (L.) Burm. fil. were collected from the Vellore Institute of Technology (VIT), Vellore between March and April 2005. The leaves were identified by the authorized staff at VIT, as *A. vera* (*A. barbadensis* Miller), a member of the lily family. A voucher specimen has been deposited in the university's herbarium.

A. vera powder was prepared from *A. vera* gel according to published procedures[14], with slight modifications. Four different extracts were standardized (data not shown). The method of preparation of extract-2 is given below. Mature fresh leaves of *A. vera* were washed with water. The leaves were cut transversely into pieces. The thick epidermis was selectively removed and fleshy solid gel was cut into small pieces. The gel was refluxed with absolute ethanol and dried in a rotary vacuum evaporator at 80°C. A crude extract of *A. vera* was obtained as greenish-brown powder. The dried powder was stored at 4°C until further use. The extract was standardized by various physico-chemical methods for moisture, ash mineral content and antioxidant properties.

Table 1. Physico-chemical and biochemical data of *Aloe vera* extracts

Physico-chemical and biochemical analysis	*Aloe vera*			
	Extract-1	Extract-2	Extract-3	Extract-4
Moisture content (%)	16.5	9.2	8.5	5.8
Ash conten (%)	31.7	18.9	26.15	22.58
Mineral content (ppm)				
Cr^{+++}	1.12	1.37	1.61	1.36
Fe^{++}	3.9	3.58	3.46	3.54
Pb^{++}	0.23	0.20	0.21	0.21
Hg^{++}	1.6	1.0	1.4	1.3
Cd^{++}	0.07	0.0	0.2	0.0
Reducing sugars (mg/g)	19.5 ± 0.16	40.9 ± 0.74	35.5 ± 0.3	42.6 ± 3.3
Protein (mg/g)	3.95 ± 0.05	9.2 ± 0.04	4.7 ± 0.08	6.75 ± 0.04
Cellulose (mg/g)	1.2 ± 0.08	0.85 ± 0.01	0.93 ± 0.03	0.86 ± 0.01
Total antioxidants (mg/g)	3.7 ± 0.2	16.9 ± 0.05	4.11 ± 0.25	13.3 ± 0.5

ppm, Parts per million.
Results are expressed as mean ± SD of triplicate measurements.

For the administration of the sample, a suspension was prepared by mixing 300 mg of *A. vera* extract powder in 5 ml water. Rats of group-II and group-IV were fed with 300 mg/kg body wt of *A. vera* approximately every day in single dose for three weeks.

Rat fasting plasma glucose (FPG) levels were estimated after an overnight fasting with free access to water. Blood was collected from the tail vein. The tip of the tail was cut carefully by one stroke with a sharp sterile blade. Blood was collected in a test tube containing anticoagulant. The blood was centrifuged at 2500 rpm for 15 min and the plasma was separated. Glucose concentration in the plasma was estimated using GOD/POD kit and measured at 500 nm using Spectronic UVD spectrophotometer (Milton Roy, New York).

Fresh urine was collected by slightly pressing the tail and back of the rat. Glucose and ketone in urine was checked using keto-diastix strips.

All animals were sacrificed after the third week by thiopentone sodium (40 mg/kg body wt, i.p.). The pancreas, stomach, liver, kidney and small intestine were dissected and fixed in 10% buffered formalin. The organs were processed in graded series of alcohol and embedded in paraffin wax. Serial sections of 5 μm were cut using a microtome American Optical, Model 82, mounted on glass slides and stained with hematoxylin-eosin.

Data were statistically analysed using ANOVA for repeated measurements to compare glycaemic levels from day 0 till the third week. Kruskal–Wallis and Whitney *U* test were also used. Statistical analysis was done using SPSS 11.5. For all the tests, results with P values < 0.05 were taken to imply statistical significance. Data are expressed as mean values ± standard deviation (mean ± SD) for groups of six animals.

The physico-chemical and biochemical data of *A. vera* extracts are summarized in Table 1. Significant differences between extracts 1 and 2 in terms of their reducing sugars, protein and antioxidant contents were observed. Extracts 2–4 showed somewhat similar composition. Nevertheless, antioxidant content of extract-2 was high. Based on this extract-2 was chosen for animal studies.

There was no change in FPG levels in group-II rats and they were comparable to group-I rats (vehicle). From the results it is evident that *A. vera* did not produce any significant change in FPG values in normal rats (Table 2).

FPG levels were estimated every week for three weeks. Diabetic rats fed with *A. vera* showed normal FPG levels compared to the untreated diabetic group of rats (group-III). The observed FPG value of 256.3 mg/dl (after confirmation of diabetes), subsequently dropped down to 130 mg/dl in the first week, which further reduced to the normal level in the second and third weeks (Table 2). In group-III rats, the diabetic state was maintained for three weeks (Table 2).

Urine analysis was done every week for three weeks. Glucose and ketone were absent in urine during all the weeks in group-I and group-II rats (Table 3). In group-III rats, glucose and trace amount of ketone were present during all the weeks. In group-IV, initially urine analysis showed the presence of glucose and trace amount of ketone, which were completely absent after feeding with *A. vera*. Body weight was checked every week for three weeks. In groups I, II and IV rats increase in body weight was noticed and in group-III rats body weight decreased (Table 4).

In the pancreas of group-I and group-II rats (figure not shown), many round (Figure 1 *a*) and elongated islets (Figure 1 *b*) were evenly distributed throughout the cytoplasm, with their nucleus lightly stained than the surrounding acinar cells. In group-III rats, the islets were damaged, shrunken in size (Figure 1 *c*) and infiltration of lymphocytes (Figure 1 *d*) was observed. In group-IV rats, islets were comparable to normal rats (Figure 2 *e*) and one islet was enlarged (Figure 1 *f*).

Table 2. Effect of *A. vera* (300 mg/kg) on fasting plasma glucose levels in normal and streptozotocin-induced diabetic rats (30 mg/kg)

Group treatment	Fasting plasma glucose levels (mg/dl)			
	Day 0	First week	Second week	Third week
Group-I[a] (vehicle)	100.3 ± 3.2	103.7 ± 3.2	104.0 ± 3.3	99.0 ± 3.3
Group-II[b] (normal + *Aloe*)	99.7 ± 2.9	102.7 ± 6.8	105.0 ± 7.6	103.3 ± 5.3
Group-III[c] (diabetic control)	283.3 ± 24.3	305.3 ± 19.9	294.3 ± 21.5	280.8 ± 16.2
Group-IV[d] (diabetic + *Aloe*)	256.3 ± 15.2	130.0 ± 18.5	103.7 ± 16.5	101.7 ± 3.7

[a,b]Statistically significant compared with vehicle and normal rats fed with *A. vera* ($P < 0.05$).
[c,d]Statistically significant decrease compared with diabetic control (group-III) and diabetic rats fed with *A. vera* (group-IV; $P < 0.001$).
Day 0, Corresponds to the start of *A. vera* feeding with confirmation of diabetes in diabetic-induced rats.

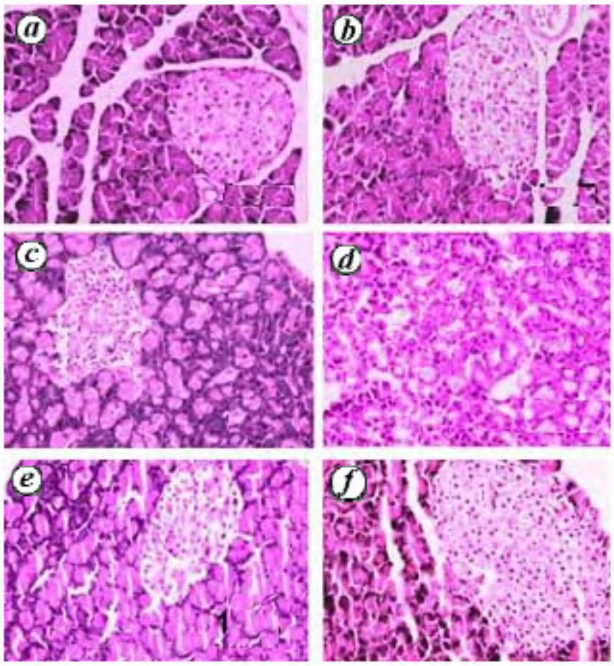

Figure 1. Photomicrograph of pancreas stained with haemotoxylin and Eosin (H & E) (magnification × 200). ***a***, ***b***, Group-I (vehicle) islets with normal round (***a***) and elongated (***b***) structural intactness with their nucleus. ***c***, ***d***, Group-III (diabetic rats) islets damaged and shrunken in size (***c***) with infiltration of lymphocytes (***d***). ***e***, ***f***, Group-IV (diabetic rats fed with *Aloe vera*) islets resemble normal rat islets (***e***), with one islet enlarged in size (***f***).

The liver (Figure 2 *a*), small intestine (Figure 3 *a*), kidney and stomach (figure not shown) of group-I rats had normal histological appearances. In the hepatocytes of group-III, shrunken nuclei, granular cytoplasm, dilatation in the sinusoids and inflammation were observed (Figure 2 *b* and *c*). In the hepatocytes of group-IV, these degenerative changes were partly reduced, although there were individual differences (Figure 2 *d*).

In small intestine of group-III (Figure 3 *b*), excess proliferation of epithelium was noticed, which was reduced in group-IV (Figure 3 *c*). No changes were noticed in the kidney and stomach sections of group-III and group-IV rats.

In the present study, we investigated the antidiabetic effect of *A. vera* extract in STZ-induced diabetic rats. Diabetes can be induced in animals by injection of STZ, a glucose analogue (2-deoxy-2-(3-methyl-3-nitrosuuredio)-D-glucopyranose), which is stable at pH 4.5 and degrades rapidly in alkaline solution, forming diazomethane, an alkylating agent[15]. STZ is taken up by pancreatic β-cells via the glucose transporter (GLUT2) and causes alkylation of DNA, thereby damaging the pancreatic β-cells[16].

A dose of 30 mg/kg of STZ gave rise to a pronounced diabetic state (mean FPG above 250 mg/dl) and this was maintained for three weeks. We chose this dose level for further studies to check the effect of *A. vera* on diabetes.

Ghannam *et al.*[17] reported the antidiabetic effect of *A. vera* in alloxan-induced mice. A significant reduction in FPG levels was observed for a week after oral feeding of dried sap of *A. vera* 500 mg/kg body wt, twice daily. In alloxanized mice, chronic administration of crystalline mass of *A. vera* 500 mg/kg, twice a day significantly reduced the FPG with the reduction being 30.7, 32.1 and 37.7% on the third, fourth and fifth day respectively[18]. In our studies, oral feeding of *A. vera* extract-2 (300 mg/kg body wt) daily to diabetic rats (30 mg/kg STZ) reduced the FPG levels by 50.7%. This could be due to better extraction of blood sugar-lowering active principles by ethanol.

Helal *et al.*[19] reported a decrease in FPG in alloxan-treated albino rats after *A. vera* was orally administered for 30 days. The FPG level decreased to 139.2 mg/dl compared with that of diabetic rats (mean FPG 266 mg/dl) after 30 days. Rajasekaran *et al.*[14] reported that after 21 days of oral feeding of *A. vera* extract 300 mg/kg body wt, FPG levels decreased to 102.5 mg/dl compared to the diabetic group (270 mg/dl). In our study, we estimated FPG levels every week for three weeks after confirmation of diabetes (Table 2). Reduction in FPG levels to normal was noticed in the second week and third week compared to diabetic rats (mean FPG 280.3 mg/dl). The results indicate that the *A. vera* extract was effective in lowering hypergly-

Table 3. Effect of *A. vera* on urine glucose and ketone in normal and streptozotocin-induced diabetic rats (30 mg/kg)

Group treatment	Glucose and ketone levels in urine							
	Day 0		First week		Second week		Third week	
	Glucose	Ketone	Glucose	Ketone	Glucose	Ketone	Glucose	Ketone
Group-I (vehicle)	–	–	–	–	–	–	–	–
Group-II (normal + *Aloe*)	–	–	–	–	–	–	–	–
Group-III (diabetic control)	+++	Trace	+++	Trace	+++	Trace	+++	Trace
Group-IV (diabetic + *Aloe*)	+++	Trace	–	–	–	–	–	–

Glucose: Trace, 100 mg/dl; +++, 1 g/dl; –, Absence of glucose.
Ketone: Trace, 5 mg/dl; –, Absence of ketone.
Day 0, Corresponds to start of *A. vera* feeding with confirmation of diabetes in diabetic-induced rats.

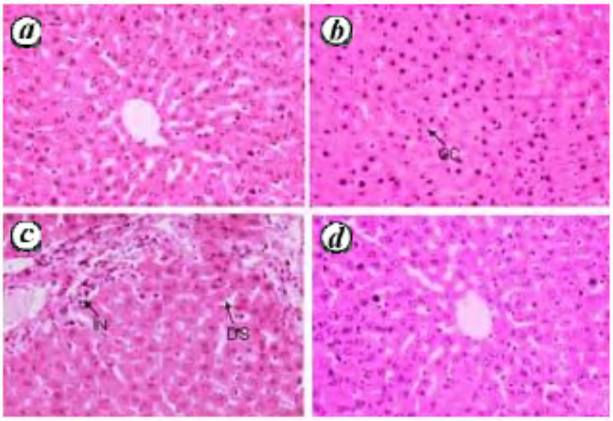

Figure 2. Photomicrograph of liver stained with H & E (magnification × 200). ***a***, Group-I (vehicle) control rats. ***b***, ***c***, Group-III (diabetic rats) with shrunken nuclei, granular cytoplasm (→ GC) (***b***), dilated sinusoids (→ DS), and inflammation (→ IN) (***c***) observed. (***d***), Group-IV (diabetic rats fed with *A. vera)* with degenerative changes partly reduced in comparison to group-III.

caemia in STZ-induced rats. Besides, no significant decrease in FPG levels was observed in untreated diabetic rats for the same period of time. There are two possible explanations for this finding. First, *A. vera* may exert its effect by preventing the death of β-cells and/or second, it may permit recovery of partially destroyed β-cells. Like *Momordica charantia*[20], *A. vera* may also have initiated cell proliferation. Hypoglycaemic effects have been reported with other plants, such as *Azadirachta indica*[21], *Ocimum sanctum*[22], *Coccinia indica*[23] and *Pterocarpus marsupium*[24], well known for their antidiabetic activities.

FPG levels were normal in healthy rats fed with *A. vera* (group-II). Table 1 shows that the FPG levels were comparable to healthy rats fed with water (group-I). This result corroborates the observation made by Rajasekaran *et al*[14]. The behaviour of normal rats fed with *A. vera* (group-II) appeared normal. They were healthy, fed well and no mortality was observed, indicating that there was no acute toxic effect of *A. vera* feeding.

In our study we checked the presence of glucose and ketone in urine in the first, second and third week after confirmation of diabetes. Presence of glucose and trace amounts of ketone was noticed in urine of untreated diabetic rats during all the weeks (group-III). In diabetic rats fed with *A. vera* (group-IV), there was absence of glucose and ketone in urine during all the weeks compared to untreated diabetic rats (Table 3). Weight gain was noticed in *A. vera*-fed diabetic rats compared to diabetic rats (Table 4). The normoglycaemia has helped to gain body weight in *A. vera*-fed rats. No mortality was observed in *A. vera*-fed diabetic rats.

The histological sections of the pancreas, liver, kidney, stomach and small intestine tissues were observed to know the effect of *A. vera* fed in non-diabetic and diabetic rats. This was done to observe any protective or harmful effect of *A. vera* extract on non-diabetic and diabetic rats.

In pancreatic sections of diabetic rats (group-III), the islets were less and their shape was destroyed compared to group-I with infiltration of lymphocytes (Figure 1 *c* and *d*). In *A. vera*-fed diabetic rats (Figure 1 *e* and *f*), there were more islets and they were comparable to normal rat islets, although there were individual differences. One enlarged islet was observed. The relative distribution of pancreatic islet cells was similar to control rats.

The liver (Figure 2 *a*), small intestine (Figure 3 *a*), kidney and stomach of group-I rats had normal histological appearance.

In the liver of diabetic rats (group-III) shrunken nuclei, granular cytoplasm (Figure 2 *b*), dilatation in the sinusoids and inflammation were noticed (Figure 2 *c*). These changes were reduced in *A. vera*-fed rats of group-IV (Figure 2 *d*). This may be due to beneficial and protective effect of *A. vera* extract on liver tissues of diabetic rats. Our histological findings are in agreement with the degenerative structural changes reported in liver tissues as result of insulin depletion[25] in neonatal STZ (100 mg/kg)-induced type-II diabetic rat models. Can *et al.*[25] observed an increase in degeneration in central veins to portal veins, excess vacuolization, granular appearance in the cytoplasm, dilations in the sinusoids and moderate hyperemia.

In a study reported by Bolkent[26] in the neonatal STZ (100 mg/kg STZ)-induced type-II diabetes, alteration in

Table 4. Effect of *A. vera* on body weight in normal and streptozotocin-induced diabetic rats (30 mg/kg)

Group treatment	Body weight (g)			
	Day 0	First week	Second week	Third week
Group-I[a] (vehicle)	160.8 ± 7.3	168.3 ± 9.8	175.8 ± 9.7	181.7 ± 9.3
Group-II[b] (normal + *Aloe*)	153.3 ± 2.6	161.7 ± 2.6	165.8 ± 2.0	173.3 ± 4.1
Group-III[c] (diabetic control)	169.2 ± 3.8	160.0 ± 3.2	154.2 ± 3.8	151.7 ± 2.6
Group-IV[d] (diabetic + *Aloe*)	172.5 ± 4.2	172.5 ± 5.2	179.2 ± 5.8	187.5 ± 7.6

Comparisons were made between groups. I[a], II[b] and IV[d]. They are statistically not significant. But group-III[c] and group-IV[d] are statistically significant ($P < 0.05$).
Day 0, Corresponds to start of *A. vera* feeding with confirmation of diabetes in diabetic-induced rats.

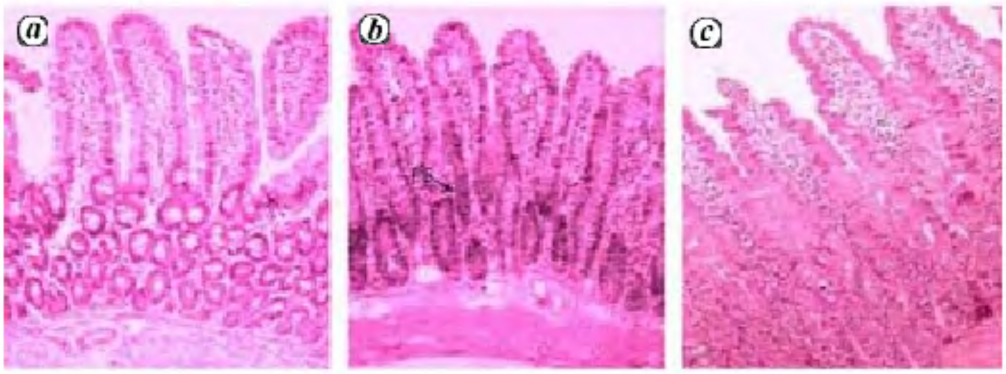

Figure 3. Photomicrograph of small intestine stained with H & E (magnification × 200). ***a***, group-I (vehicle) control rats. ***b***, group-III (diabetic rats) with excess proliferation of epithelium (→ PE). ***c***, group-IV (diabetic rats fed with *A. vera*) with excess proliferation of epithelium, reduced in comparison to group-III.

the structural integrity of the apical membrane of proximal tubules of the kidney tissue in the diabetic rats was observed. In our study, there were no notable changes in the histology of kidney and stomach sections after feeding with *A. vera* extract to diabetic rats. Nevertheless, the extract used by Bolkent[26] was an aqueous liquid extract.

In our study, excess proliferation of epithelium was noticed in the small intestine of diabetic rats (group-III; Figure 3 *b*), which was reduced after feeding with *A. vera* extract to diabetic rats (group-IV; Figure 3 *c*). *A. vera* has protective effect on the small intestine tissues of diabetic rats.

In conclusion, the results of the present study show that *A. vera* extract brings back the FPG levels to normal in diabetes-induced rats, i.e. shows hypoglycaemic activity. Although the exact chemical compound/s responsible for the hypoglycaemic effects of *A. vera* extract still remain speculative, experimental evidence obtained in the present laboratory animal study indicates that *A. vera* extract possesses antidiabetic property. In histology, *Aloe* showed protective effect on the organ tissues. More detailed studies on *A. vera* using different doses and covering longer periods of observation are needed before reaching a clear-cut conclusion. Future research to refine the extraction procedure of *A. vera* could lead to improved pharmaceutical products.

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ACKNOWLEDGEMENTS. We thank Dr Anna B. Pulimood, Department of Pathology, Christian Medical College and Hospital, for help with using light microscopy and R. Srinivasan for help in processing the tissues for histological studies. We also thank Visalakshi for statistical analysis, Y. Samuel for the maintenance of rats and Dr K. Gunasekaran, VIT, for help in manuscript preparation.

Received 19 March 2007; revised accepted 19 February 2008

Expert system for prediction of avalanches

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Many statistical as well as classical methods have been developed as guidance tools for forecasting avalanches. Statistical methods are based on strict mathematical procedures (i.e. mathematical expression used to build the system) and classical methods are mainly based on reasoning and lack in analytical explanation. To overcome the problems posed by both the methods, a data-based expert system has been developed for the Chowkibal–Tangdhar road axis in Pir Panjal range of NW Himalaya. The expert system has been developed using situation-based rules which make it highly flexible and compact. In addition, an inductive incremental learning feature has been included in the model. The developed expert system predicts a day as avalanche day, with degree of avalanche danger as practised for operational avalanche forecasting in NW Himalaya, or as a non-avalanche day. It has been tested independently with two types of avalanche occurrence namely, actual avalanche occurrence reports available and these reports combined with the expert forecaster's assessment of the situation. This is mainly to overcome the loss of avalanche occurrence information due to bad weather conditions during winter. Independent testing of the expert system with actual avalanche occurrence reports available combined with the expert forecaster's assessment of the situation may help largely to ensure whether the system is in agreement or disagreement with the assessment of the expert avalanche forecasters. The developed expert system was tested independently for the past five winters. The independent test results show that the expert system predicts more than 80% days correctly for both types of avalanche occurrence information. The results are encouraging and the expert system is in good agreement with the assessment of expert avalanche forecasters.

Keywords: Avalanche, avalanche prediction, expert system.

TWO predominant methods for forecasting avalanche danger are the conventional and statistical methods[1,2]. Conventional avalanche forecasting is practised as a mix of deterministic treatment for snow and weather parameters and inductive logic to reach an actual forecast decision[1]. The statistical methods utilize past measured data of snow, weather and avalanche occurrence to distinguish avalanche days from non-avalanche days. The statistical

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