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Antidiabetic activity of *Aloe vera* L. juice II. Clinical trial in diabetes mellitus patients in combination with glibenclamide

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Summary

The effect of *Aloe vera* juice in combination with glibenclamide was investigated in diabetic patients. There was no response to glibenclamide alone but *Aloe vera* juice significantly reduced levels of fasting blood glucose within *two* weeks and of triglycerides within *four* weeks. It showed no effect on cholesterol levels and had no toxic effects on kidney or liver function as assessed by blood chemistry. The results support the use of *Aloe vera* in the treatment of diabetes.

Introduction

Aloe vera is a Thai medicinal plant that is claimed to have antidiabetic activity. Our first clinical study on the antidiabetic effect of *Aloe vera* L. juice in new cases of diabetes mellitus showed convincing results (Yongchaiyudha, et al. 1995). Serum fasting blood glucose levels (FBS) were significantly decreased from day 14 and continued to fall throughout 42 days of treatment.Triglyceride levels also decreased significantly. These results support previous reports on the activity in mice (Beppu et al., 1993; Hikino et al., 1986 b) and in diabetic patients (Agarwal, 1985; Hikino et al., 1986 a, b; Beppu et al., 1993).

The acceptable regimen for new cases of diabetes mellitus is treatment with glibenclamide. This prompted us to study the combined effects of *Aloe vera* L. juice and glibenclamide on new cases of diabetes mellitus.

Materials and Methods

Subjects

Forty-nine men and 23 women were enrolled in the study and divided into equal-sized treatment and control groups with matching sexes, ages and weights. (Each pair are the same sex with 5 kg differences in body weights, and 5 year differences in ages.) The patients were selected from cases of diabetes mellitus at the Soft Drink Center, Infirmary who were treated with glibenclamide using the following inclusion and exclusion criteria.

- Inclusion criteria

1. Aged 35–70 years.
2. High fasting blood sugar levels and a typical diabetic curve of glucose tolerance analysis.
3. Freely consented to participate in the study.

- Exclusion criteria

1. Liver disease as defined by abnormal levels of serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT) and alkaline phosphatase)
2. Kidney disease as defined by abnormal levels of blood urea nitrogen (BUN) or creatinine and urine examination (specific gravity and albumin content).

Samples

Aloe vera Linn. juice (80%) with suitable preservatives and a placebo with the same color, taste and smell as aloe juice were prepared at the Faculty of Pharmacy, Mahidol University. The method of preparation is the same as in the first paper.

Study design

The study was a placebo controlled and single-blind trial.

Procedures

1. The treatment group received *one* tablespoonful of aloe juice twice a day, in the morning and before bed time, and *two* tablets of glibenclamide (5 mg) for 42 days. The control group received glibenclamide (2x5 mg) and the placebo under the same administration protocol as the treatment group.
2. Blood samples were analyzed for alkaline phosphatase, SGOT, SGPT, BUN, creatinine and uric acid before and after treatment.
3. Blood samples were taken weekly for measurement of fasting blood glucose levels, and every two weeks for triglyceride and cholesterol analyses.

Data Analysis

Student's t-test was used to determine the difference in biochemical changes between the aloe juice treated group and the control group. Paired Student's t-test was also used in this study. The 99% confidence limit (p = 0.01) was chosen for statistical significance.

Termination of the study

This occurred when:
1. Subjects experienced serious adverse effects, as determined by physicians.
2. Subjects developed symptoms and signs of acute diabetic complications.
3. Subjects developed an acute illnesses that affected the trial.
4. Subjects elected to terminate their participation in the study.

Results

Levels of fasting blood glucose, cholesterol or triglycerides remained stable in the glibenclamide-treated group (Table 1, Fig. 1). Treatment with aloe juice and glibenclamide produced a significant decrease in blood sugar levels within *two* weeks and in triglyceride levels within *four* weeks; these levels continued to fall throughout the treatment period (Table 1, Fig. 1). Cholesterol levels remained the same as before treatment. There were no differences in blood BUN, SGOT, SGPT, alkaline phosphatase, creatinine or uric acid levels before and after treatment (Table 2, 3).

Discussion

The results of these studies indicated the potential of *Aloe vera* gel in the treatment of diabetes in patients receiving glibenclamide. The patients selected for this study were

Table 1. Blood sugar, cholesterol and triglyceride levels of patients treated with glibenclamide (control) and patients treated with glibenclamide and aloe gel (treated group).

Vaiables	mg% (Mean±SEM)	2-tail	Statistical	
	Control Group	Treated Group	Prob.	results*
Sex f:m	12:24	11:25		
Age (years)	49.28±1.24	49.06±1.30	0.902	NS
Blood Sugar levels				
day 1	289.17±7.11	288.14±8.45	0.926	NS
day 7	285.67±6.60	260.97±8.77	0.028	NS
day 14	279.47±6.17	231.72±8.56	0.000	S
day 21	287.33±8.07	185.42±7.71	0.000	S
day 28	286.58±8.01	167.39±6.37	0.000	S
day 35	289.50±8.70	153.97±5.49	0.000	S
day 42	289.67±8.12	148.03±4.61	0.000	S
Blood Cholesterol Levels				
day 1	235.28±7.83	229.83±8.56	0.640	NS
day 14	236.61±6.83	227.31±6.84	0.339	NS
day 28	243.58±7.09	223.83±6.46	0.043	NS
day 42	243.39±7.02	225.72±5.96	0.059	NS
Blood Triglyceride Levels				
day 1	223.25±12.21	264.67±15.19	0.037	NS
day 14	221.78±13.55	218.53±12.78	0.862	NS
day 28	226.81±13.09	170.31± 9.07	0.001	S
day 42	233.08±13.68	128.28±5 .47	0.000	S

*Significantly different from control at p = 0.01

Table 2. Blood chemistry values of treated group measured at pre and post treatment

Pat.No.	Alk. phosphatase (normal: 30–110 IU/L)		SGOT (normal: <40 units/L)		SGPT (normal: <40 units/L)		BUN (normal: 10–20 mg%)		Creatinine (normal: <1 mg%)		Uric acid (normal: <7 mg%)	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
1	31	27	25	30	19	12	14	14	1.4	1.0	5.8	5.5
2	25	21	19	24	14	15	11	18	1.2	1.0	4.8	4.7
3	24	20	22	18	19	12	12	16	1.0	1.0	6.1	5.7
4	24	32	19	24	19	18	11	15	1.1	1.2	5.7	6.0
5	19	26	15	20	12	14	13	14	1.0	1.0	5.2	5.8
6	20	26	17	20	12	12	14	14	0.8	1.0	5.5	5.6
7	27	26	30	30	21	24	14	14	1.4	1.4	6.0	5.7
8	25	24	25	20	17	20	12	14	0.8	0.8	5.9	5.2
9	29	34	30	36	15	14	15	16	1.6	1.8	6.2	6.4
10	17	24	14	14	5	10	10	10	1.2	1.2	5.6	5.5
11	23	24	18	20	10	16	13	12	1.0	1.0	6.0	6.4
12	30	28	17	24	9	16	12	16	1.4	1.2	5.4	5.9
13	31	27	16	20	21	14	14	22	1.1	1.0	5.2	5.5
14	40	32	15	18	12	20	14	16	1.2	1.2	4.8	5.0
15	37	40	24	22	19	20	17	18	1.4	1.2	5.0	5.0
16	36	24	18	28	12	16	12	12	0.8	1.0	4.1	4.6
17	41	42	20	20	11	16	11	16	0.9	0.8	4.8	4.2
18	47	50	25	24	15	12	13	14	1.2	1.0	5.1	5.6
19	42	40	30	26	14	14	12	18	1.1	1.4	4.8	4.4
20	38	32	20	28	12	18	11	21	1.2	1.2	5.1	5.7
21	44	40	27	26	12	14	11	15	1.1	1.0	4.4	4.8
22	47	48	29	32	15	18	12	14	0.8	0.8	4.7	5.0
23	44	46	31	30	8	16	11	14	0.7	0.8	4.2	4.4
24	35	40	17	18	11	12	14	14	1.2	1.4	4.6	4.6
25	42	38	32	24	37	28	18	22	1.5	1.4	6.8	6.0
26	35	40	29	30	31	28	16	12	1.2	1.2	5.9	5.5
27	21	28	15	26	20	18	11	16	0.9	1.0	4.6	4.8
28	16	27	30	34	30	24	14	24	1.1	1.4	4.7	4.9
29	18	30	25	32	18	20	10	18	1.0	1.2	5.1	5.6
30	27	32	18	18	12	14	12	20	1.2	1.0	5.4	5.4
31	32	32	41	40	32	32	22	24	0.8	1.0	5.0	5.2
32	25	32	34	34	26	26	17	18	1.4	1.2	5.8	5.0
33	34	28	45	40	35	32	15	25	1.4	1.4	6.3	6.4
34	29	35	20	28	14	14	13	20	1.2	1.2	5.6	5.6
35	22	32	18	20	15	16	15	18	0.8	1.0	5.5	5.4
36	28	30	16	24	12	18	12	21	1.0	1.4	5.0	5.2
Mean	30.69	32.14	23.50	25.61	17.11	17.86	13.28	16.81	1.11	1.13	5.30	5.34
SEM	1.48	1.26	1.26	1.07	1.29	0.95	0.42	0.62	0.04	0.04	0.11	0.10

Table 3. Blood chemistry values of treated group measured pre and post treatment.

Blood chemistry	Pretreatment			Post treatment			Normal levels
	Max	Min	Mean ± SEM	Max	Min	Mean±SEM	
Treated							
Alkaline phosphatase (I.U./L)	47	16	30.69±1.48	50	20	32.14±1.26	30–110
SGOT (units/L)	45	14	23.50±1.26	40	14	25.61±1.07	<40
SGPT (units/L)	37	5	17.11±1.29	32	10	17.86±0.95	<40
BUN (mg%)	22	10	13.28±0.42	25	10	16.81±0.62	10–20
Creatinine (mg%)	1.6	0.7	1.11±0.04	1.8	0.8	1.13±0.04	<1
Uric acid (mg%)	4.1	6.8	5.30±0.11	4.2	6.4	5.34± 0.10	<7

SGOT-serum glutamic oxaloacetic transaminase; SGPT-serum glutamic pyruvic transaminase; BUN-blood urea nitrogen

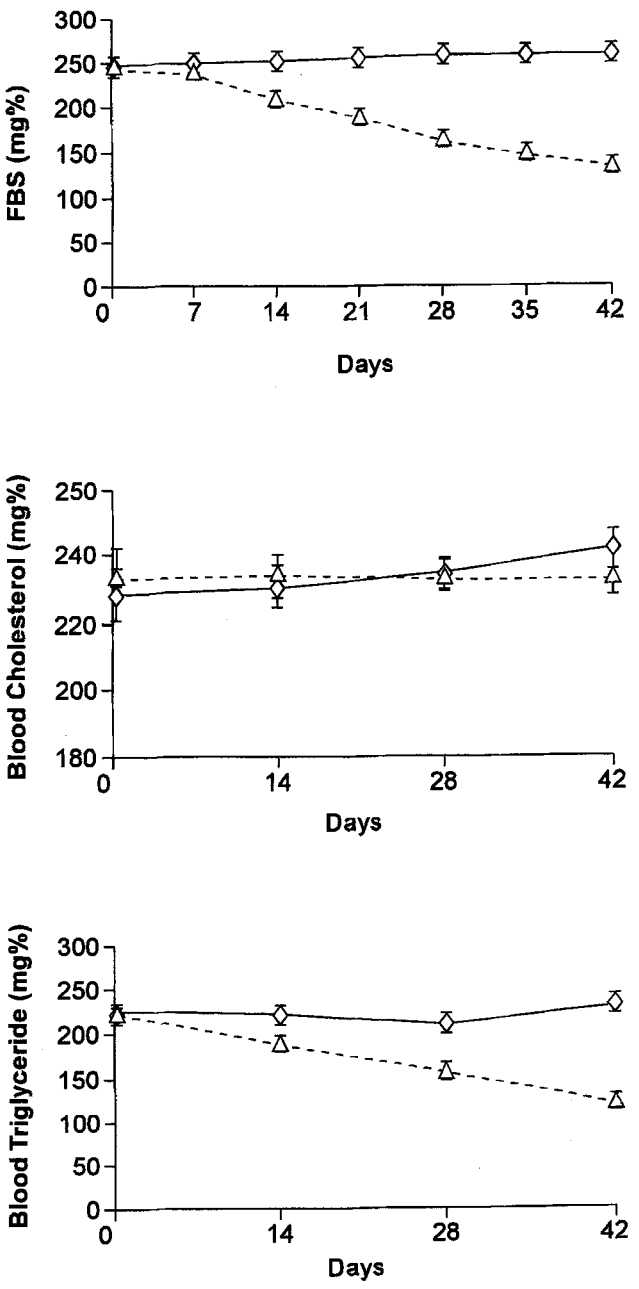

Fig. 1. The effect of aloe gel with glibenclamide on fasting blood glucose (FBS), cholesterol and triglyceride levels in diabetic patients.- ◊ - treated with glibenclamide (control); - △ - treated with aloe gel twice daily and glibenclamide (2x5 mg).

those for whom treatment with glibenclamide had failed to reduce blood sugar levels. This effect was confirmed by our results: glibenclamide alone had no effect on blood sugar or triglyceride levels. However *Aloe vera* gel, in combination with glibenclamide, exhibited antihyperglycemic activity and also decreased triglyceride levels, which are usually high in diabetic patients. The effect of aloe juice in combination with glibenclamide was not greater than the effect of aloe juice given alone (Ref to paper I).

It should be noted that even after treatment for 42 days, the blood sugar levels had not fallen to normal values; this is probably because the dose is not high enough. Further studies on the dose-activity relationship are needed.

The study also showed that aloe gel had no adverse effect on kidney and liver functions, as shown by the absence of changes in the levels of BUN, SGOT, SGPT, alkaline phosphatase, creatinine or uric acid.

Only 36 out of 40 patients were enrolled throughout the study because one patient died from car accident and another quited work. The participants with whom they had been paired were then dropped from the study. This shows that the drop outs were not due to an unfavorable response to the aloe preparation. The low drop out rate was also due to good follow up by physicians who visited the Soft Drink Center Infirmary weekly.

Aloe gel acts as a thromboxane (TxA_2) inhibitor; it promotes vasodilation and maintains homeostasis within the vascular endothelium as well as within the surrounding tissue (Heggers et al., 1993). Therefore, we believe that treatment with aloe juice might relieve peripheral blood vessel complications in diabetic patients. (This should be tested in future studies.)

All these findings lead to the conclusion that *Aloe vera*, a traditional medicinal plant, is potentially valuable for the treatment of diabetes.

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