EFFECTS OF JAMBOLAN SEED TREATMENT ON BLOOD SUGAR, LIPIDS AND UREA IN STREPTOZOTOCIN INDUCED DIABETES IN RABBITS

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Summary : In Newzealand rabbits a single intravenous injection of streptozotocin (STZ 65 *mg/kg*) elevated the levels of blood sugar to 340 *mg* percent, which was associated with glycolysis, ureamia, hypercholesterolemia, hypertriglyceridemia and loss of body weight. Oral administration of jambolan seed (*1 g/kg*) in casein diet significantly lowered the elevated postmeal (1½ hr after) values of blood sugar, cholesterol, FFA and triglyceride down to levels comparable to phenformin. Jambolan seed treatment failed to check ureamia. Weight loss was checked by phenformin and jambolan seed but the gain was not equivalent to that recorded in nondiabetic control. Like phenformin, jambolan seed too failed to control glycogenolysis in STZ–induced diabetes.

Key words : streptozotocin (STZ) free fatty acid (FFA) glucose tolerence test (GTT)

INTRODUCTION

Long before the use of insulin, indigenous remedies have been used for the treatment of diabetes. One of the indigenous remedies is jamoon or jamdlan or java plum *(Eugenia jambolana).* It belongs to the family Myrtaceae. It is a common subtropical fruit of India. Indian Ayurvedic Vaidyas have long been prescribing seed powder and fruit pickle to diabetic patients to keep diabetes under control and this is in practice in large population within diabetics. Its antidiabetic effect is mentioned in Ayurvedic literature but not sufficient authentic data are available. Sepaha and Bose (7) and Jagodzinski *et al.* (2) had tried to assess its hypoglycaemic activity and the parameter of the activity was only blood sugar. In the present study Jambolan's antidiabetic effect is compared with the hypoglycaemic drug phenformin, as standard therapy. In addition several other parameters were also studied.

MATERIAL AND METHODS

Twenty male healthy white Newzealand rabbits each weighing about 2.5 *kg.* were selected. Moderate diabetes was induced in 15 rabbits fasted for 24 hr by single injec-

tion (iv) of STZ 65 *mg/kg* body weight dissolved in citrate buffer at pH 4.0 (5). At the same time a group of 5 normal rabbits were injected with citrate buffer alone, which served as the non-diabetic control group. The 15 rabbits given STZ were divided into 3 separate groups with 5 rabbits in each group.

The day after STZ injection, the rabbits of all the groups were injected with glucose (ip) 1.75 *g/kg* body weight and glucose tolerance test (G.T.T.) was performed (9). From then on, the rabbits in all the groups were fed with normal casein diet. From day 3, 1½ hr after the intake of food, postmeal blood samples were collected prior to the commencement of hypoglycaemic treatments. On day 4, the groupwise treatments were commenced. Group I was designated as uncontrolled diabetic, and was fed normal casein diet every day. Group II was fed with phenformin tablet (DBI 25 *mg*/rabbit) in a small amount of casein diet. After this mixture was consumed, more casein diet was served. Group III was fed with jambolan seed powder (1 *g/kg* body weight). Group IV of the nondiabetic rabbits was fed like the Group I. These four treatments were continued for a period of three weeks. During this period the blood samples were collected from the ear veins, at three day intervals and samples were analysed by the micro method for blood sugar (9), blood urea(10), serum cholesterol (11), FFA (8), triglyceride (3) and serum creatinine (6). On day 22, again G.T.T. was repeated after overnight fasting. On day 23, the animals were sacrificed by sodium pentobarbitone (30 *mg/kg*), and samples of liver and muscles obtained from these animals were analyzed for glycogen contents (4). The weight of each animal was recorded both before beginning the treatment and before sacrifice, and weight loss or gain over the initial body weight was determined.

RESULTS AND DISCUSSION

The data on blood sugar, glycogen, and body weight are presented in Table I. The blood sugar levels were significantly elevated in STZ-treated rabbits. The cumulative mean blood sugar levels of all the seven observations during the "after-treatment" period indicate that jambolan seed lowered the blood sugar values to levels comparable with those seen with phenformin treatment and in control animals. The liver glycogen was drastically reduced in all the diabetic groups, and phenformin and jambolan seed failed to produce an increase in glycogen content equivalent to that observed with nondiabetic control. Similarly, the muscle glycogen values were also adversely affected with STZ treatment and the muscle glycogen under phenformin or jambolan seed treatments were significantly different from those observed with uncontrolled diabetics. In uncontrolled diabetics there was weight loss whereas in nondiabetic control rabbits there was increase

TABLE I : Postmeal blood sugar, glycogen and body weight in diabetic rabbits as affected by phenformin and jambolan seed.

Group	Treatments	Mean blood sugar (mg/100 ml±SD)			Mean liver glycogen (g% of wet tissue±S.D.)	Mean muscle glycogen (g% of wet tissue±S.D.)	Mean body weight (g) (lost(—) or gained(+) ±S.D.)
		Initial	After treatment				
I)	Uncontrolled diabetic	230.20±8.79	309.61±54.98	P<0.05	1.33±0.34	0.33±0.130	(—)85.08±30.10
II)	Phenformin	250.40±8.06	101.96±12.50	P<0.001	2.00±0.37	0.40±0.080	(+)47.29±43.63
III)	Jambolan–1 g	320.00±8.28	107.75±7.54	P<0.001	1.68±0.39	0.30±0.078	(+)12.01± 7.22
IV)	Nondiabetic control	95.20±10.05	101.28±11.12		5.80±0.37	0.86±0.082	(+)77.28±16.81

TABLE II : Blood urea, serum cholesterol, FFA, triglyceride and serum creatinine in streptozotocin induced diabetic as affected by phenformin and jambolan seed (mean post meal values±SD)

Gr.	Treatments	Blood urea (mg/100 ml)		Serum cholesterol (mg/100 ml	
		Initial	After treatment	Initial	After treatment
I)	Uncontrolled diabetic	40.0±3.8	**66.7±26.1	25.0±4.5	*37.9±6.5
II)	Phenformin	45.0±1.9	41.7±6.5	25.0±7.4	*12.9±3.7
III)	Jambolan 1 gm	45.5±2.8	*51.6±2.2	25.0±3.2	*12.7±4.6
IV)	Nondiabetic control	38.0±1.1	38.8±1.4	17.1±2.6	16.4±1.8

FFA (mg/100 ml)		Triglyceride (mg/100 ml)		Serum creatinine (mg/100 ml)	
Initial	After treatment	Initial	After treatment	Initial	After treatment
18.2±5.6	*29.8±4.9	140.6±7.2	**184.1±32.7	1.9±0.5	*2.7±0.1
26.0±8.0	*12.4±3.0	120.1±11.8	*86.7±10.5	1.6±0.3	1.6±0.1
32.0±7.5	**10.7±1.8	150.0±21.5	**92.1±15.1	1.7±0.4	*2.4±0.1
14.0±2.7	11.0±2.6	115.2±3.9	107.6± 7.9	1.5±0.4	1.4±0.5

't-test' significant at 0.05 P*, 0.01 P** when after treatment values are compared with initial values.

in body weight. With phenformin and jambolan seed the body weight was increased, over the initial body weight.

G.T.T. The data are shown in Fig 1. The glucose curve for the normal rabbit was a typical glucose curve. There was around 45 *mg* difference between the fasting value and the blood sugar value at 1 hr after glucose. This was the peak observed and at 1½ hr the blood sugar level dropped to that observed at half an hr. At 2 hr the blood sugar returned to nearly the fasting level. In the STZ-injected rabbits initial fasting value itself was nearly double of that in normal rabbits. The highest value was recorded after 1 hr which was nearly double the fasting value, but after 2 hr the blood sugar unlike the normal was not the same as the fasting of normal but higher than fasting. All the STZ-injected rabbits showed similarity in trend. It is interesting to note that after the treatment with phenformin, the values of blood sugar in G.T.T. declined immensely and the curve more or less resembled the normal one. In the group fed jambolan 1 *g* the peak value (320 *mg* percent) was observed at 1½ hr after glucose, this high value did not drop to normal limit within two hr. After 21days of treatment

with jambolan all the blood sugar values came down to normal limits and a small peak was observed at 1 hr and not at 1½ hr.

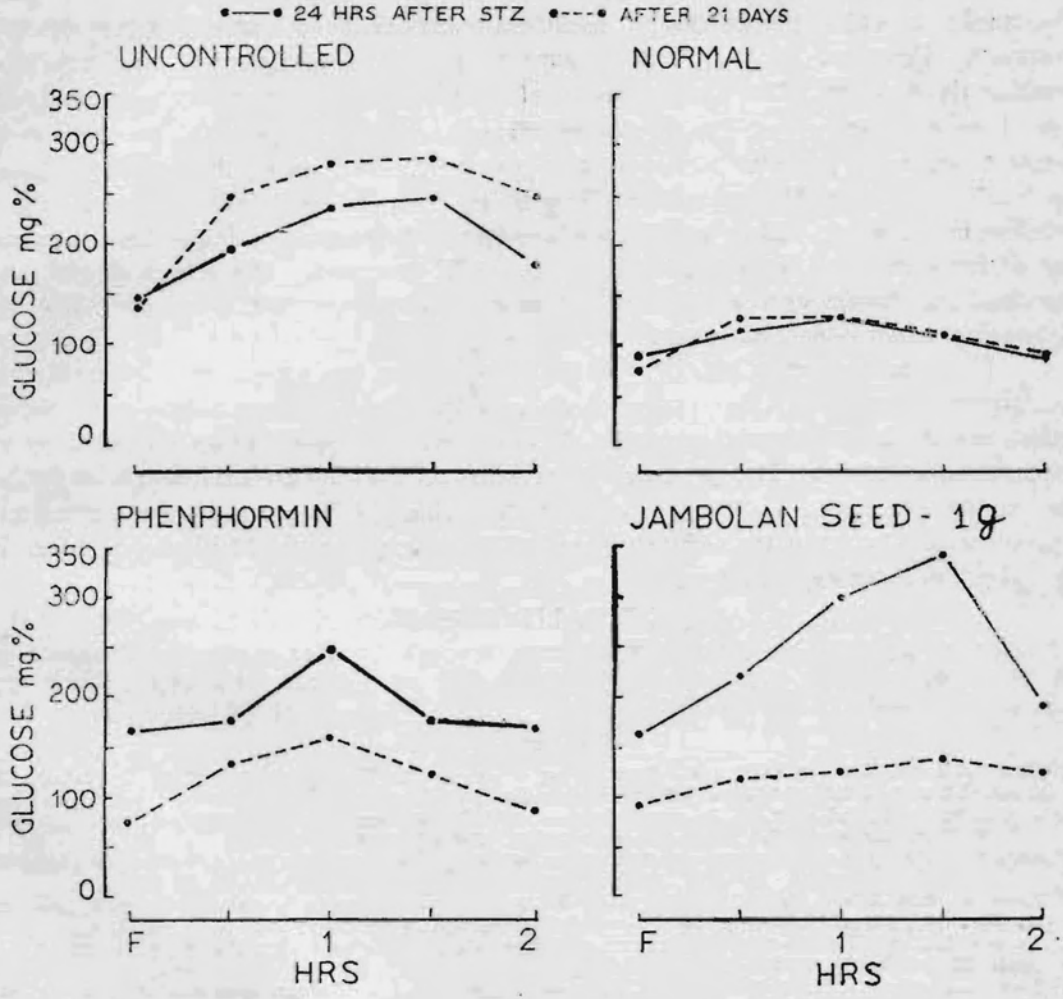

Fig. 1 : GTT in diabetic rabbits as affected by phenphormin and jambolan seed.

The data on postmeal values of blood urea, serum creatinine, serum cholesterol, FFA and triglyceride are presented in Table II. STZ treatment elevated initial blood urea (except Group I). However, initial serum creatinine levels were unaffected. Initial cholesterol in the diabetic groups did not differ significantly from non-diabeticc ontrol

but FFA values were increased significantly (except Group I). Initial triglyceride values were also significantly raised (except Group II). This suggests that serum cholesterol, FFA and triglyceride may or may not be elevated at least at the begining of diabetes. This might plausibly the be due to indifferent metabolic behaviour of rabbits to STZ treatment. However, all the "after treatment" values in uncontrolled diabetics were significantly elevated. The blood urea level after phenformin treatment was similar to that of nondiabetic control; it was also significantly reduced by jamolan seed treatment. Serum creatinine level with jambolan seed treatment remained significantly elevated at the level of uncontrolled diabetics. The serum creatnine levels were normalised with phenformin treatment. Since blood urea is linked with serum creatinine there is indication of impairment of kidney functions due to STZ-treatment. The effects of jambolan seed and phenformin were significant in respect of metabolites viz. cholesterol, FFA and triglyceride which were normalised.

The results indicate that the jambolan seeds act like phenformin in respect of hypoglycaemic activity (7,2). The lipolysis was found to be connected to glycaemic to activity which might have been caused through activation of cyclic AMP breakdown by phosphodiesterase (1). The jambolan seed failed to prevent ureamia which might be due to the reduction in plasma volume leading ultimately to production of circulatory failure by affecting the renal blood flow. Alternatively increased breakdown of protein may also be a contributory factor.

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