

Prevention of Aloe Vera extract on Glucose, serum lipids in fructose-fed adult male rats.

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Abstract

Background: Aloe Vera has been introduced as a traditional anti-diabetic agent. The aim of this survey was to evaluate the effect of aqueous extract of Aloe Vera on blood glucose, serum insulin and lipids profiles in fructose-fed male rats.

Methods: The experiment was performed on 45 Wistar-Albino adult male rats that randomly divided into control (A) and four test groups (B, C, D, and E). Control group was fed with water, but test groups took fructose-enriched water (10%, w/v) and received 0, 100, 150 and 200mg/Kg of Aloe Vera aqueous extract, respectively for 4 weeks. At the end of study, animals were anesthetized, sacrificed and blood samples were collected. Serum glucose, insulin and lipid levels were measured. Obtained data were analyzed by SPSS software, via ANOVA, Tukey and Chi-square statistical tests. Results were expressed as mean±SE. Statistical difference were recognized significant by P<0.05.

Results: Results revealed that serum glucose and insulin levels were significantly decreased in group E but HDL value in groups D and E were significantly increased, compared with those of the group B. In addition, water consumption in groups D and E were significantly decreased but food intake was significantly increased just in group E in comparison with those of group B.

Conclusion: The results obtained from this survey showed that Aloe Vera aqueous extract affects serum blood sugar, insulin and lipids profile in fructose-fed male rats. Further studies are warranted to elucidate precise involved mechanisms.

Key words: Aloe Vera, Glucose, Fructose, Insulin resistance, rat

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Introduction

Diabetes mellitus is one of the most prevalent endocrine diseases and is a growing health problem in most countries [1]. It conveys a large number of problems in socioeconomic status of patients throughout the world and is an important cause of prolonged ill health and early death [1-3]. Diabetes mellitus is clinically recognized by chronic rising in the serum glucose levels and often accompanies symptoms of the polydipsia, polyuria and weight loss [3, 4]. The prevalence and incidence of diabetes is increasing in most populations, being more prominent in developing countries. The number of diabetic patients in Iran is approximately estimated 1.5 million now (5). According to the WHO reports, prevalence of diabetes mellitus in years 1995, 2000, 2025 in Iran will be 5.5, 5.7, and 6.8%, respectively [6]. Insulin resistance is a major metabolic disorder that plays an important role in developing type II diabetes mellitus [7]. Studied showed that herbal medicines have recently been focus of research works because of their popularity and few side effects [8]. On the other hand, WHO recommends thorough evaluation of efficacy and safety, and standardization of medicinal plants for the treatment of diabetes [9]. Aloe Vera has along history of use as a topical and oral therapeutic agent [10]. Aloe Vera belongs the Liliaceae family, of which there are about 360 species [11], and use as traditional treatment for their laxative, anti-inflammatory, immunostimulant, antiseptic, wound and burn healing, and anti-tumoral effects [11-13]. In the past 20 years, there have also been reports on the antidiabetic and antioxidant activity of Aloe Vera extract [14-20]. Oral administration of Aloe Vera gel extract in streptozotocine-induced diabetic rats can cause a significant reduction in fasting blood glucose and plasma levels of high-density lipoprotein (HDL); although, it can cause increased in plasma levels of low-density lipoprotein

(LDL) and very low-density lipoprotein (VLDL) [9]. Rajasekaran *et al.* showed that Aloe Vera affects lipid profile in diabetic rats [20]. Beppu *et al.* showed that Aloe Vera has Hemostatic effects on blood glucose in mice [21]. Previous reports have shown that fructose-enriched diet developed insulin resistance and dyslipidemia in human and animal models [22-25]. This diet caused metabolic effects similar to those observed in metabolic syndrome, in which insulin resistance and dyslipidemia are observed among patient with insulin resistance [26]. Increased delivery of triglycerides or non-esterified fatty acids to the muscles interferes with the utilization of glucose, through the principles of randle cycle [26-28]. According to our knowledge, the effect of Aloe Vera aqueous extract on fructose-fed has not been previously investigated. The present study was carried out to evaluate the effects of Aloe Vera aqueous extract on high-fructose diet induced insulin resistance in fructose-fed male rats.

Methods

The study was performed on 45 mature normoglycemic male Wistar-Albino rats, weighing 110 ± 20 gr which were separately housed in cages (one rat per cage). Animals had free access to water and food. Rats were maintained in room temperature at 23 ± 2 °C on a light/dark cycle. Insulin resistance was induced in normoglycemic male Wistar-albino rats by fructose solution 10% (w/v) in tap water that was prepared every day. Animals were divided in five groups (n=9) [9] as follow and all groups received standard diet: A group took tap water, B group, tap water supplemented with 10% (w/v) fructose [27], C group, tap water supplemented with 10% (w/v) fructose and 100 mg/kg Aloe Vera extract per day by gavages, D group, tap water supplemented with 10% (w/v) fructose and 150 mg/kg Aloe Vera extract per day by gavages, E group, tap water supplemented

with 10% (w/v) fructose and 200 mg/kg Aloe Vera extract per day by gavages. Food and water intake of all groups were daily measured. Animal were weighted two times, before and after the period of the experiment. The experiment was carried out for 4 weeks. At the end of experiment, rats were fasted for 14-16 hours [16], then all sacrificed by cervical decapitation, under high dose of ether anesthesia. Blood samples were collected and blood glucose, insulin, HDL, LDL, Total Cholesterol (TC) and Triglyceride (TG) levels were measured. Serum glucose, TG, and TC levels were measured by standard methods adapted for a RA 1000 analyzer (Technicon, USA). Serum HDL was measured by precipitation of non-HDL lipoproteins with dextran/MgSO₄ followed by enzymatic cholesterol assay. LDL calculated by Friedwald formula. Serum insulin levels were determined by ultra sensitive rat insulin kit (DRG, France), using double-antibody enzyme-linked immunosorbent assay (ELISA). Insulin resistance were calculated by HOMA index; HOMA-IR: $\text{FPI(Fasting Plasma Insulin)} \times \text{FPG(Fasting Plasma Glucose)} / 22.5$ [29, 30].

Data were analyzed by SPSS (version 11) software. Variance analysis was used for

comparison of the groups. Tukey test as a post hoc multiple comparison tests was used to compare healthy control and diabetic groups. Data on Insulin were analyzed by Chi-square statistical test. P-values less than 0.05 were considered as significant.

Results

Obtained data showed that blood glucose and serum insulin in E group were significantly decreased compared with those of B group (Table 1). In addition, HDL in E group was significantly decreased in the D and E groups compared with those of B group (Table 1). On the other hand, water intake in the E and D groups significantly increased compared with those of B group (Table 1), but food intake significantly increased only in E group compared with those of B group (Table 2). Final weight in E group significantly decreased compared with those of B group (Table 2). Based on the HOMA index, animals which took fructose-enriched water showed insulin resistance. Insulin resistance values in A, B, C, D and E groups were 2.22, 8.33, 7.1, 6.33 and 3.67, respectively.

Table 1. Effects of Aloe Vera aqueous extract on serum glucose, insulin and HDL, and water intake in test groups (n=9)

Groups	Glucose(mg/dl)	Insulin(iu/l)	HDL(mg/dl)	LDL(mg/dl)	TC(mg/dl)	(TG)(mg/dl)
A	98.25±3.04	0.51±0.18	22.12 ±1.24	24.12±4.3	53.75±7.46	75.25±4.87
B	122.55±9.61	1.53±0.3	19.55 ±1.42	23.22±1.79	55±4.4	77.88±10.6
C	114.33±4.56	1.38±0.27	19.33 ±2.6	22.55±2.18	49.88±3.46	78.55±8.83
D	116±4.63	1.23±0.24	28.88 ±2.07 ^c	23.22±1.91	54.11±4.46	66.44±9.29
E	106±4.3.63a	0.78±0.17 ^b	27.44±2.21 ^d	22.22±2.55	49.55±6.53	57.44±9.29

A group: received standard rodent diet and tap water. B group: received standard rodent diet and tap water supplemented with 10% (w/v) fructose. C group received standard rodent diet and tap water supplemented with 10% (w/v) fructose and 100mg/kg Aloe Vera extract per day by gavages. D group received standard rodent diet and tap water supplemented with 10% (w/v) fructose and 150mg/kg Aloe Vera. E group received standard rodent diet and tap water supplemented with 10% (w/v) fructose and 200mg/kg Aloe Vera extract. Data are mean ± SE values for groups of 9 animals in each.

Values are statistically significant: a, P=0.05 as compared with B group. b, P=0.04 as compared with B group. c, P= 0.01 as compared with B group. d, P= 0.01 as compared with B group.

Table 2. Food intake, First and final weight in test groups

Groups	first weight (gr)	Final weight (gr)	Food intake (gr) mean±SE	Water intake (ml)
A	112.75±6.42	181.87±5.29	40.68±4.17	95.25±2.03
B	115.44±6.69	200.44±5.05	48.6±4.45	106.06±2.13
C	114.44±7.06	197.33±7.15	46.41±4.3	106.02±1.71
D	110.88±3.19	183.88±7.55	45.68±4.56	96.24±2.41 ^c
E	110.75±9.38	179.6±5.05 ^a	63.3±4.5 ^b	69.09±1.9 ^d

A group: received standard rodent diet and tap water. B group: received standard rodent diet and tap water supplemented with 10% (w/v) fructose. C group received standard rodent diet and tap water supplemented with 10% (w/v) fructose and 100mg/kg Aloe Vera extract per day by gavages. D group received standard rodent diet and tap water supplemented with 10% (w/v) fructose and 150mg/kg Aloe Vera. E group received standard rodent diet and tap water supplemented with 10% (w/v) fructose and 200mg/kg Aloe Vera extract. Data are mean ± SE values for groups of 9 animals in each.

Values are statistically significant: a, P=0.04 as compared with A group. b, P=0.03 as compared with A group. c, P=0.006 compared with B group, d, P=0.002 compared with B group.

Discussion

The results obtained from this survey showed that the administration of Aloe Vera extract significantly reduced blood glucose and serum insulin in E group and that it had no deleterious effects on the other groups. HDL value in D and E groups significantly increased compared with those of B group. Water intake in D and E groups reduced but food intake significantly increased compared with those of B group. Our results are in concordance with that of Rajasekaran *et al.* who showed decreasing effects of 200 mg/kg and 300 mg/kg doses of Aloe Vera on blood glucose in normal fasted rats, oral glucose-load rats and diabetic rats which induced by streptozotocine [19]. In both of the studies, Aloe Vera extract decreased blood glucose, although in present study animals showed insulin resistance while in Rajasekaran *et al.* study animals were diabetic induced by STZ. Blood glucose and serum insulin which decreased in the present study may be due that Aloe Vera extract affects insulin receptors in membrane of skeletal muscles and fat cells or activates them to increase glucose uptake from blood stream terminates to decrease the blood glucose. When blood glucose decreases, its stimulating effects removes from β cells in pancreas and insulin secretion decreases. The former results did not confirm by Alper *et al.* and this may be due to the differences

of plant extract or to the differences in the experimental diabetic animals [13]. In addition, the results obtained from the present study showed that HDL value in D and E groups decreased which is in accordance with results of Rajasekaran *et al.* study [15, 16]. In aforementioned study, all lipoproteins showed changes, although in the present study only HDL increased. This difference may be attributed to varied methods or different doses of Aloe Vera extract dosage which used in these experiments. Increased HDL value in E group may be due to improvement in insulin secretion, and glucose metabolism in skeletal muscles and fat cells. Water intake decreased in D and E groups, this may be due to decrease in blood glucose and blood osmolarity, which decreases stimulating effects on hypothalamus and decrease polydipsia which induced by insulin resistance. Food intake increased in E group compared with those of B group which may be due to improved insulin secretion, insulin resistance and glucose metabolism. On the other hand, in E group, final weight decreased compared with those of B group which may attribute to animal age and ATP utilization in this group.

The results of this study indicate that Aloe Vera aqueous extract can improve insulin secretion, blood glucose and lipid profile in fructose-fed male rats. Further studies are

warranted to elucidate precise involved mechanisms.

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