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Original Article

AMELIORATION OF *STREPTOZOTOCIN*-INDUCED HYPERGLYCEMIA AND DYSLIPIDEMIA THROUGH *ALOE DEBRANA*

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ABSTRACT

Objective: To study the antiglycemic and antidyslipidemic effects of an ethanolic extract of *Aloe debrana* leaf gel extract in streptozotocin-induced diabetic rats.

Methods: *A. debrana* leaves were collected from Enemore district; Gurage area Ethiopia. *A. debrana* gel was obtained from water-washed gel part of *A. debrana* leaves and homogenized. The resulting mucilaginous, thick and straw colored homogenate was lyophilized and extracted using 95% ethanol. Diabetes was induced in male Wistar rats by streptozotocin (53 mg/kg, i. p.). Diabetic rats were treated with glibenclamide (600µg/kg.) or *A. debrana* (300 mg/kg) for 28 consecutive days. The blood samples were collected at regular intervals to assess hypoglycemic effect of an ethanolic extract of *A. debrana*. At the end of the experiment, serum lipid profile were analyzed for all the experimental animals and compared with diabetic control.

Results: The ethanolic extract of *A. debrana* at 300 mg/kg has significant antiglycemic and antidislipidemic activities. The diabetic control animals exhibited a significant decrease in body weight compared with control animals. *A. debrana* inhibited streptozotocin-induced weight loss and significantly alter the lipid levels.

Conclusion: The ethanolic extract of *A. debrana* showed significant antiglycemic and antidislipidemic activities against streptozotocin-induced diabetes in rats.

Keywords: *A. debrana,* Antiglycemic, Antidyslipidemic.

INTRODUCTION

Diabetes mellitus is one of the most common endocrine disease, associated with a group of metabolic disorder characterized by chronic hyperglycemia with disturbances of carbohydrate, lipid, and protein metabolism resulting from defects in insulin secretion, insulin action, or both [1]. The dynamics of the diabetes and hyperlipidemia are changing rapidly in low- to middle-income countries. In 2030, diabetes may affect 472 million (approx.) of world populations. The number of adult with impaired glucose tolerance may rise from 344 million (2010) to 472 million by 2030[2]. Diabetes is one of the most common non-communicable diseases (NCDs), which are the fourth or fifth leading cause of death in most high-income countries and there is substantial evidence that it is epidemic in many economically developing and newly industrialized countries. The prevalence of the disease is estimated as 382 million people globally, or 8.3% of adults, are estimated to have diabetes. About 80% live in low- and middle-income countries. If these trends continue, by 2035, some 592 million people, or one adult in 10, will have diabetes. The largest increases will take place in the regions where developing economies are predominant [3]. The treatment of any diseases with allopathic drugs causes moderate to severe adverse events, which could cause death. Hence, the alternative systems of medicine are being explored to treat diseases [4]. Diabetes mellitus is a multifactorial disease characterized by hyperglycemia and lipoprotein abnormalities.

In Ethiopia, national data on prevalence and incidence of diabetes are lacking. However, patient attendance rates and medical admissions in major hospitals are rising [5, 6]. A population based study in northwestern Ethiopia (Gondar) showed an overall prevalence of diabetes and impaired glucose tolerance of 0.5%; a surprising low prevalence could be because most of the subjects were young (86%). Furthermore the prevalence of diabetes among older subjects (age > 40 years) was higher (2.4%) [7]. Moreover, Cohen *et al*., reported a high prevalence of diabetes (8.9%) among young (age < 30 years) Ethiopian Jews who have been to Israel for less than 4 years [8]. WHO estimated the number of diabetic cases in Ethiopia to be 800,000 by the year 2000, and the number is expected to increase to 1.8 million by 2030[9].

In Ethiopia, traditional medicine has played a significant role in treating health problems in both livestock and humans [10-13]. Knowledge of medicinal plants of Ethiopia and of their uses provides vital contribution to human and livestock health care needs throughout the country [14]. Eighty percent of human and 90% of livestock in Ethiopia depend on traditional medicine for primary health care services where modern public health services are limited or note available [15]. Traditional healers play an essential role in the delivery of primary health care to local people as they treat people in resource poor settings. These people have poor access to modern health services and could not afford the cost for modern health services [16].

For centuries plants have been used to treat human diseases including diabetes mellitus. According to the WHO, more than 150 species of plants are known to be used for the treatment of diabetes mellitus. Antidiabetic potential of the plant is mainly due to their ability to restore the pancreatic tissue activity, inhibit intestinal absorption of glucose or have insulinomimetic active compounds [17].

Members of the genus *Aloe* have been known for their current and potential use in medicine, commerce and horticulture. Aloe species have been used in folk medicine, e. g. for treatment of constipation, burns and dermatitis [18]. Gel exudate from leaves of *A. lateritia* has been used in some communities in Ethiopia for treatment of eye aliments [19]. The flora of Ethiopia and Eretria possess 46 species of *Aloe*, out of which 89% are reported to be endemic. Only five species: *A. laterita, A. macrocarpa, A. rivae, A. secundiflora and A. vituensis*, are wide spread extending to East and West Africa [20]. The two species: *A. debrana and A. trichosanta* have been collected for their bactericidal property in the suck manufacturing industry [21]. *A. vera* contains 75 potentially active constituents: enzymes, minerals, vitamins, sugars, lignin, saponins, salicylic acids and amino acids [22]. It has been claimed that the polysaccharides in *A. vera* gel have therapeutic properties such as immunostimulation, anti-inflammatory effects, wound healing, promotion of radiation

damage repair, anti-bacterial, anti-viral, anti-fungal, anti-diabetic and anti-neoplastic activities, stimulation of hematopoiesis and anti-oxidant effects [23-25]. The traditional healers in Ethiopia commonly used as antidiabetic agent as *Aloe vera* and related species. Numerous antiglycemic reports are available about *Aloe vera* but no report or study about antiglycemic roll of *Aloe debrana.* Hence, the present study is undertaken to investigate the antidiabetic and antihyperlipidemic potential of an ethanolic extract of *A. debrana* on streptozotocin (STZ)-induced insulin-dependent diabetes mellitus in rats.

MATERIALS AND METHODS

Plant collection

A. debrana leaves were collected from Enemore district; Gurage area, which is found in south-western parts of Ethiopia located approximately 250 Km from Addis Ababa, capital of Ethiopia. Then the plant was authenticated by; National Herbarium Center, Science faculty of Addis Ababa university.

Preparation of plant extract

A. debrana gel was obtained from water-washed gel part of *A. debrana* leaves and homogenized. The resulting mucilaginous, thick and straw colored homogenate was lyophilized and extracted using 95% ethanol. The extract was filtrated by Whatman filter paper No.1 and the filtrated was evaporated by rotary evaporator. The residue was stored in dry sterilized small containers at 4°C until further use.

Animals

Thirty adult apparently12 weeks' old healthy male albino rats of weighing about 140 –150 gms were used in the present study and housed in polypropylene cages and maintained standard laboratory conation. They were provided with standard pellet rat diet supplied by Kality Animal Nutrition Production Ltd., Addis Ababa Ethiopia, and water *ad libitum.* The research protocol was approved by the Research & Ethics Review committee (DRERC) of the department of medical biochemistry with approval number SOM/BCHM/015/2006 EC.

Induction of diabetes mellitus

Streptozotocin (STZ) (Sigma, St. Louis, Mo., USA) dissolved in 0.1 M cold sodium citrate buffer, pH 4.5, at a dose of 53 mg/kg was injected intraperitoneally (ip) to induce diabetes mellitus [26]. The control rats received the vehicle (buffer) alone to minimize stress induced cofounding in experimental groups. The animals were allowed to drink 5% glucose solution overnight to overcome the STZ induced hypoglycemia. After a week, the rats with moderate hyperglycemia (blood glucose level of above 250 mg/dl) were considered as diabetic rats.

Experimental design

All the thirty rats were randomly divided into five groups of six animals (n=6) in each as following treatment schedule.

Group I: Normal control rats, receiving citrate buffer alone.

Group II: STZ induced diabetic rats, used as diabetic control.

Group III: Normal rats received *A. debrana* leaf gel extract (300mg/kg) in aqueous solution.

Group IV: STZ induced diabetic rats received *A. debrana* leaf gel extract (300 mg/kg) in aqueous solution.

Group V: STZ induced diabetic rats given glibenclamide (600µg/kg) in aqueous solution.

A. debrana leaf extract and saline were administrated by Gavage's method for 28 consecutive days.

Body weight measurement

The body weight of the animals was measured and recorded at the beginning (day 0) of the experiment and at the end of the experimental period (at 28thday).

Fasting blood glucose test

The animals' fasting blood glucose (FBG) levels were measured every week interval starting from day zero till 28thday(five times) by glucose oxidase method using compact analytical device glucometer (*GlucoSure*) and blood glucose test strip (Touch-IN micro®, ApexBio, Taiwan) [27].

Collection and analyses of blood

After 28 days of the treatment the rats were fasted overnight (12 to 14 hours), scarified by cervical dislocation and blood sample was collected by cardiac puncture and serum was prepared. The total cholesterol (TC), triglyceride (TG), high density lipoprotein (HDL), and low density lipoprotein (LDL) were analyzed. Serum lipid profile was determined by autoanalyzer machine (Humastar300). The principles are as follows (laboratory procedure manual; John Hopkins 2003-2004).

Data analysis

The data were analyzed using One-way Analysis of Variance (ANOVA) followed by multiple comparisons by post Hoc Dunnett T3 *t*-test and 'p' value (<0.05) was considered statistically significant. The data were presented as mean ± SEM. Analysis was carried out by using SPSS (Statistical Package for Social Science Software for Windows version 15; SPSS Inc., Chicago, IL, USA).

RESULTS AND DISCUSSION

The ethanolic extract of the plant *A. debrana* at 300 mg/kg showed significant antidiabetic activity against STZ-induced diabetes mellitus in rats, and the effect was comparable with that of the standard drug glibenclamide.

Loss in body weight was observed in STZ-induced diabetes mellitus in rats (Table1) and was controlled by treatment with ethanolic extract of the *A. debrana*. STZ-induced diabetes mellitus was characterized by severe loss of body weight due to increased muscle wasting in diabetes [28]. STZ inducing diabetes, hypoinsulinemia, or hyperglycemia by damaging the pancreatic beta cells [29]. Administration of an ethanolic extract of the *A. debrana* to diabetic rats resulted in an increase in body weight compared to diabetic rats. The present study findings suggested that *A. debrana* treatment has positive effect on maintaining body weights in diabetic rats. The protective effect of plant fraction on body weight of diabetic rats may be due to its ability to reduce hyperglycemia. The result obtained in this experiment is in agreement with the finding of Noor *et al*., and Rehman *et al*., who reported that *A. vera* leaf gel extract has positive effect on weight gain in experimental diabetic rats [30, 31]. A gradual increase in body weights of glibenclamide treated groups but could not reach the normal control rats. Moreover *A. debrana* alone treated (group3) rats body weight was reduced significantly when compare with normal rats (group1).

Table 1: Mean body weight (gm)

Groups	Initial	Final
I	145.2±1.4^{a}	161.3±1.4^{b}
II	143.5±0.9^{a}	112.5±1.5^{c}
III	145.5±1.2^{a}	152.7±1.1^{b}
IV	144.8±1.9^{a}	148.2±1.9^{d}
V	144.0±1.3^{a}	154.3±1.3^{d}

All values are expressed as mean ± S. E. M (n=6). *P<0.05 as compared to diabetic control. One-way ANOVA followed by Dunnett T3 multiple comparison tests. The means labeled with different letters (superscripts) are significantly different.(a- there is no significant difference among the groups, c - $P < 0.001$ compared with normal control (group I); d $P < 0.001$ compared with diabetic control (group II))

The increased blood glucose was reverted in significant level in Aloe leaf gel treated diabetic rats showing the antihyperglycemic effect of the plant (table 2). The antihyperglycemic effect of this plant might be due to the presence of chemical compounds which may have the

capacity to activate peripheral tissues (liver, muscle and fat cells) to utilize glucose in a similar fashion with insulin or it may be due to selective regeneration of pancreatic β-cells to their secretory potential. *Aloe vera* may exert its antidiabetic effect by supporting and maintenance the death of cells or it may permit recovery of partially destroyed cells [30]. Also, the hypoglycemic action of the extract of herbal plants may be possible through the insulinomimictic action or by other mechanism such as stimulation of glucose uptake by peripheral tissue, inhibition of endogenous glucose production or activation of gluconeogenesis in liver [32]. Rajasekaran *et al*., reported that, the increased levels of plasma insulin indicate that the *A. vera* gel extract stimulates insulin secretion from the remnant -cells or from degenerated -cells [33].

Table 2: Fasting blood glucose level in a week interval (mg/dl)

Groups	0 day	7th day	14th day	21st day	28th day
I	73.1±1.6[a]	74.3±0.9[a]	75.7±1.4[a]	74.8±0.9[a]	75.6±1.1[a]
II	76.3±0.7[a]	294.5±1.9[b]	312.7±1.6[b]	325.2±1.7[b]	339.0±1.2[b]
III	75.3±0.8[a]	75.8±1.3[a]	74.8±1.6[a]	75.3±0.7[a]	75.0±1.3[a]
IV	76.7±1.2[a]	294.3±4.1[b]	195.3±2.4[c]	145.3±3.3[c]	118.7±2.5[d]
V	74.8±1.2[a]	293.7±3.6[b]	186.7±4.7[c]	120.8±2.6[d]	96.7±2.0[d]

All values are expressed as mean ± S. E. M (n=6). One way ANOVA followed by Dunnett T3 multiple comparison tests. The means labeled with different letters (superscripts) are significantly different.(a- no significant difference; b- $P < 0.001$ compared with normal control (group I); c and d $P < 0.001$ compared with diabetic control (group II)).

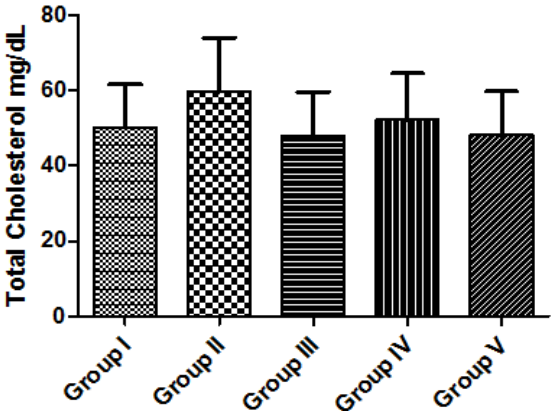

Fig. 1: Total cholesterol of different experimental groups

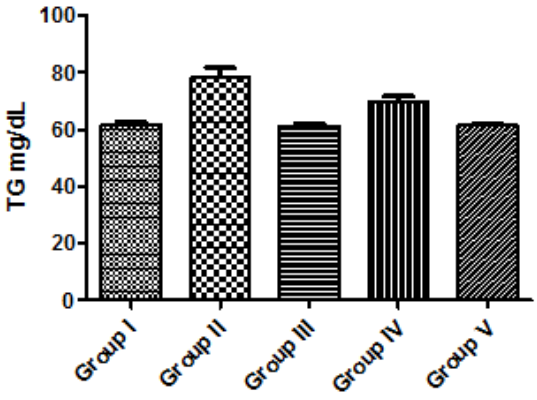

Fig. 2: Triglycerides of different experimental groups

Serum lipid profile showed that in diabetic control group there was significant increment in total cholesterol (fig.1), triglyceride (fig.2), and low density lipoprotein (fig.4) and reduction in serum high density lipoprotein (fig.3) which are all the manifestation of diabetes associated dyslipidemia. Insulin in fat metabolism whenever there is reduction and/or absence of insulin there is lipolysis and release of free fatty acids to the systemic circulation and to the liver by activating the enzyme hormone-sensitive lipase in the fat cells [34]. When the serum lipid profile of diabetic rats treated with Aloe leaf gel extract was considered there was a significant reduction in total cholesterol (fig.1), triglyceride (fig.2), and low density lipoprotein (fig.4) level, while there was a marked elevation in the serum level of 'good' high density lipoprotein (fig.3) cholesterol. The finding indicates that *A. debrana* leaf gel extract has a potential to correct diabetes induced dyslipidemia. The result obtained in this experiment is in agreement with previous works done by Lanjhiyana *et al.,* who reported the antihyperlipidemic effect of *A. vera* leaf gel extract in experimental animals which were significant when compared with diabetic groups [35].

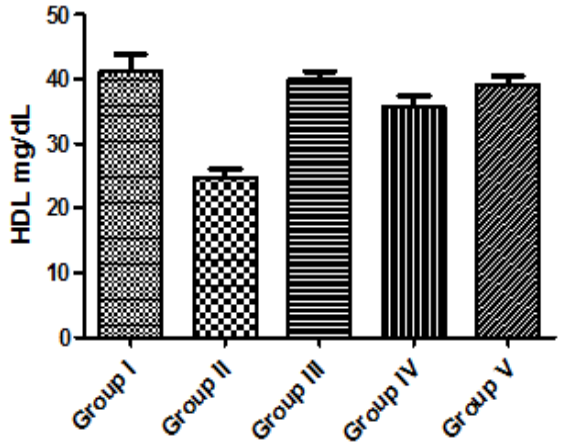

Fig. 3: HDL-cholesterol of different experimental groups

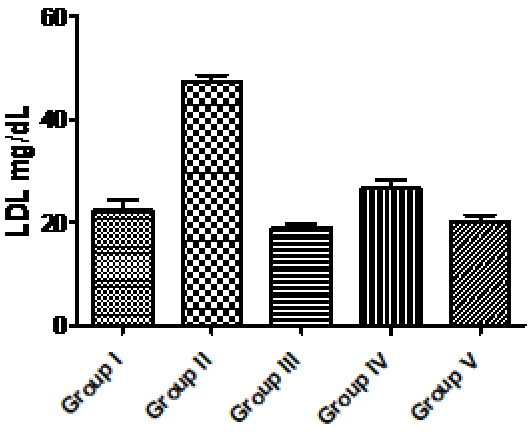

Fig. 4: LDL- cholesterol of different experimental groups

CONCLUSION

The ethanolic extract of the *Aloe debrana* leaves gel exerts an antidiabetic activity against STZ-induced diabetes mellitus in rats. It is also found to be effective in managing the complications associated with diabetes mellitus, such as hyperlipidaemia, and prevents the defects in lipid metabolism and weight loss.

CONFLICT OF INTEREST

Declared None

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