Hypoglycemic and hypolipidemic effects of *Oligomeris linifolia* in Alloxan-induced diabetic mice

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Abstract

The current study was focused to evaluate the hypoglycemic and hypolipidemic effect of methanolic extracts of *Oligomeris linifolia* in Alloxan-induced diabetic mice. Albino mice were orally treated for 15 days with methanolic extract of *Oligomeris linifolia* at dose of 200 mg/kg body-weight. The antidiabetic effect was analyzed by measuring blood glucose (BG) at 0, 3, 6, 9, 12, and 15 days. Total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), Serum Bilirubin (SBR), Alkaline Phosphatase (ALP), Alanine Aminotransferase (ALT), Urea, Creatinine, and triglycerides (TG) levels at sacrifice (day 16) were measured. Glibenclamide (10 mg/kg) was used as standard. Alloxan-induced diabetic mice showed adequate to significant increase in the level of BG, TC, TG, LDL-C, SBR, ALT, ALP, Urea, Creatinine, while HDL-C and body-weight were decreased as compared to control group (non-diabetic mice). Administration of plant methanolic extract to Alloxan-induced dabetic mice at a dose of 200 mg/kg body-weight resulted in a notable decrease in BG, TC, TG, LDL-C, SBR, ALT, ALP, Urea and Creatinine whereas HDL-C level and body-weight were increased markedly after 15 days as compared to diabetic control group. The methanolic extract at the dose of 200 mg/kg, produced similar results compared to group treated with Glibenclamide.

Keywords: *Oligomeris linifolia,* White Albino mice, Antidiabetic activity, Lipid profile

Introduction

Natural source is one of the major hub for medicinal analogue [1]. Diabetes Mellitus is the most common metabolic and chronic disorder indicated by rise in blood glucose level due to relative or complete insulin deficiency [2]. In the long term the disease is associated with various complications including renal, eyes, neurological and cardiovascular disorders [3]. Diabetes Mellitus has symptoms such as excess urination, fatigue, glycosuria (increased urine glucose level), blurry vision, and delayed wound healing [4]. One of the impairments of the immune system is destruction of the β-cells of pancreas within Islets of Langerhans and therefore development of insulin-dependent diabetes. Immune system is affected by several environmental and genetic factors which lead to the attack of lymphocytes, causing pancreatitis. This inflammatory reaction leads to insulitis and diabetes [5, 6] and without proper treatment, vascular, cardiac, neurological, renal damage and neuropathy can occur. Diabetes Mellitus is mostly controlled with Treatment of diabetes in-

cludes healthy diet, regular exercise, and medication [7]. The primary major treatment is the use of anti-diabetogenic drugs, but side effects of these drugs limits their use [8]. Due to lesser side effects, there is a long history of medicinal plants usage and nowadays, they are being widely used to treat various diseases [9].

Plant *Oligomeris linifolia* Vahl belongs to family Resedaceae which contains 107 species with 8 to 12 genera [10]. Physically *O. linifolia* is like chubby having low height around 50 centimeters with many rigged stems. The leaves size is about 45 mm in length and with 0.52 mm width [11]. It is mostly present in Southeast Asia, Middle East, North America, North Africa and south of Europe [12]. The literature data has revealed that this plant has exhibited various pharmacological activities including antioxidant, antifungal and antibacterial activities [13]. The current study was undertaken to investigate the hypoglycemic effect of methanolic extract of *O. linifolia* in a non-obese diabetes model.

Experimental design Collection and Identification

The plant was collected in flowering season from various regions of Bannu District, Khyber Pakhtunkhwa, Pakistan. Plant specimen was identified by Dr. Faizan Ullah, Asociate Professor, Department of Botany, Univeity of Science and Technology, Bannu.

Extraction

Plant was initially rinsed through tap water and then with distilled water. The plant was then dried under shade. The shade dried plant material (1.5 kg) was chopped and soaked in 80% aqu. methanol for one week and was filtered by using filter paper. After filtration, rotary evaporator was utilized for evaporation of methanol to obtain crude plant extract [14].

Animals

In current research, White Albino mice (age 3-4 weeks, weighed 20-22 g with a mean of 21 g) were used. The mice were purchased from National Institute of Health Sciences, Islamabad, Pakistan. The “White albino mice” were placed in controlled conditions i.e., temperature 25C°-27 C° with 12hr darkness photoperiod with rodent-pellets as feed along with water. The Internationally accepted standard ethical guidelines for laboratory animal use and care were adopted in the experiment [14].

Induction of Hyperglycemia

In current study, the investigational mice were abstained from eating for 8-12 hrs, however, there was no restriction on water to drink.

“Hyperglycemia” was induced experimentally by a single intraperitoneal dose of 150 mg/kg body weight of freshly prepared alloxan10% monohydrate obtained from Department of Biotechnology, University of Science and Technology, Bannu.

After 48 hrs, blood glucose level of the animals was checked by using glucometer. Mice with blood glucose level of 200mg/dl and above were used for further investigation.

Experimental Design

The experimental models were divided randomly into four groups, each group with five mice (both sex). Group 1 consisted of normal mice orally directed with 0.1 ml “normal saline”; Group 2 consisted of alloxan induced diabetic mice orally managed with 0.1 ml normal “saline; Group 3 consisted of alloxan treated mice orally managed with 10 mg/kg “Glibenclamide”. Group 4 comprised of “alloxan-induced diabetic-mice” (150 mg/kg) orally administered with plant extract of 200 mg/kg body-weight. The investigation was carried out for 15 days. Glycaemia and body weights were measured at an interval of 3 days for 15 days. After one day of last treatment (day 16), all the groups of mice were sacrificed by cervical dislocation. Blood was collected for measuring total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), Serum bilirubin

(SBR), Alkaline Phosphatase (ALP), Alanine Aminotransferase (ALT), Urea, Creatinine, and triglycerides (TG) levels by using commercial kits (INMESCO (Germany).

Statistical analysis

The reported data statistically analyzed by ANOVA. The lipid profile parameters were analyzed using one-way ANOVA wile for blood glucose determination two ways ANOVA was used.

Results and Discussion

Effects of oligomeris linifolia on Body Weight and lipid profile

In current investigation it was observed that alloxan substantially reduced body-weight of mice-as compared to control group, measured at an interval of 3 days for 15 days. Administration of doses of plant *Oligomeris linifolia* extract rescue remarkably in the body-weight. The plant species *O.linifolia* reduces adverse effects on body weight when supplemented at 200 mg/kg body weight as compared to Glibenclamide.The diabetic condition in mice (untreated diabetics) raised TC, LDL-C and TG concentrations while, the HDL-C level were lower as compared to control mice (nondiabetic mice). As shown in table 1, the elevated level of TC, LDL-C and TG recovered significantly. However, the decrease in HDL level was also restored by effective doses of *O. linifolia* extract.

Effects of oligomeris linifolia on blood glucose

Table 2 shows the effects of methanolic extract of *O. linifolia* on blood glucose levels of White Albino mice after 15 days of continuous treatment. Significant and continuous reduction of blood glucose level was observed in alloxan-treated mice groups after 15 days of the treatment. Groups of mice treated with *O. linifolia* and glibenclamide exhibited significant decrease in blood glucose level as compared to diabetic control, measured at 0th day to 15th day of the experiment.

Table 1: Effects of Oligomeris linifolia on body weight, lipid profile on Alloxan-induced diabetic mice

Groups	Body weight(g)			Lipid profile(mg/dl)								
	Initial	Final	% Variation	TC	LDL-C	HDL-C	TG	ALT	SBR	ALP	Urea	Creatinine
Normal Control	21±0.2a	25±0.4a	0.0016	100±0.6	80±031a	32±015a	200 ±0.447	23±0.02a	0.55±0.08a	223±0.04	40±0.004a	0.40±0.002a
Diabetic Control (Untreated Diabetic)	20±0.19b	16±0.31b	-0.0025	163±0.63b	110±0.24b	20±031b	235±0.31b	98±031b	0.67±0.002b	283±0.06b	44±0.07b	0.56±0.003b
Diabetic + Glibenclamide (10 mg/kg)	19±0.2c	21±0.44c	0.0009	118±0.24c	73±020c	46±0.21c	153±0.002c	59±0.06c	0.80±0.04c	371±0.08c	43±0.020c	0.47±0.004c
Diabetic + Methanolic Extract (200 mg/kg)	19±0.15c	21±0.32c	0.0009	116±0.63d	75±0.22c	45±0.20c	144±0.002d	26±0.04d	0.53±0.002c	259±0.05c	38±0.019c	0.40±0.005c

Table 2: Effects of *Oligomeris linifolia* on blood glucose in Alloxan-induced diabetic mice

Groups	Fasting blood glucose level (mg/dl)						
	Initial	Day of treatment					
		Day 0	Day 3	Day 6	Day 9	Day 12	Day 15
Normal Control	135 ±3.11	138±1.91	140±3.6	147±2.11	145±2.14	140±3.23	130±2.56
Diabetic Control (Untreated Diabetic)	129 ±2.78	210±2.89	243±3.12	250±2.13	275±3.75	280±3.65	290±4.13
Diabetic+ Glibenclamide (10 mg/kg)	128 ±1.89	210±2. 89	197±2.12	180±1.96	150±2.89	140±3.14	129±2.87
Diabetic+ Methanolic Extract (200 mg/kg)	130 ±2.02	210 ±2. 89	190±2.9	175±4.12	140±3.11	12±0.91	115±4.21

±standard error.

Alloxan is a toxic glucose analogue that preferentially accumulates in pancreatic beta cells via the GLUT2 glucose transporter. Alloxan selectively inhibits glucose-induced insulin secretion through specific inhibition of glucokinase, and causes a state of insulin-dependent diabetes through its ability to induce ROS formation, resulting in the selective necrosis of beta cells. [15]. Alloxan produces oxygen radicals in the body, which cause pancreatic injury and could be responsible for increased blood sugar as well as lipid peroxidation. In diabetic mice treated with *O. linifolia* extract, a significant decrease in blood glucose level was observed as compared to respective baseline values (day 0). It could be believed that this plant with this anti-diabetic potential may contains certain antioxidant constituents which are useful in treatment of diabetes [16-18]. The *in vitro* antioxidant property of *O. linifolia* previously reported [13] further supported our result that the constituents with antioxidant property may have their anti-diabetic potential [19–21].

Conclusion

Results of the current investigation showed that methanolic extract of *Oligomeris linifolia* possess antidiabetic effect and favorable effects on diabetic hyperlipidemia. Alloxan-induced diabetic mice showed adequate to significant increase in the level of BG, TC, TG, LDL-C, SBR, ALT, ALP, Urea, Creatinine, while HDL-C and body-weight were decreased as compared to control group (non-diabetic mice). Administration of the methanolic plant extract to Alloxan-Induced Diabetic mice at a dose of 200 mg/kg body-weight resulted in a notable decrease in BG, TC, TG, LDL-C, SBR, ALT, ALP, Urea and Creatinine; HDL-C level and body-weight were increased markedly after 15 days as compared to diabetic control group. All these effects could be the result of bioactive compounds present in *Oligomeris linifolia* extracts.

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