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Original Article

Swertia longifolia Boiss has beneficial effects on hepatic and renal functions in diabetic rats

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Abstract

Introduction: Diabetes is a multifactorial syndrome with high prevalence which may induce serious disorders in the body organs like the liver and kidney. This study aimed to compare the effects of the alcoholic extract of the aerial parts of *Swertia longifolia Boiss* on blood glucose, lipid profiles and liver and kidney function tests in streptozotocin-induced diabetes.

Methods: Thirty five male rats were put into five groups: control, diabetic control and three diabetic experimental groups which were gavaged with alcoholic extract of *Swertia longifolia Boiss* at doses of 100 and 200 mg/kg BW and glibenclamide at a dose of 10 mg/kg BW, respectively. Diabetes was induced by intraperitoneal injection of streptozotocin. At the end of day 21 blood samples were collected from all groups and the blood factors were measured and analyzed.

Results: The levels of creatinine, urea, liver enzymes, cholesterol and low density lipoprotein increased in the diabetic control group compared to the control, while the mentioned factors in the groups receiving *Swertia longifolia Boiss* alcoholic extract decreased significantly (P<0.05). In the experimental group receiving glibenclamide, the levels of creatinine, urea and lipid profiles also decreased, while the levels of liver enzymes and insulin significantly increased (P<0.05).

Conclusion: The consumption of the alcoholic extract of the aerial parts of *Swertia longifolia Boiss* by lowering lipid profiles, liver enzymes, creatinine and urea as well as increasing insulin levels had beneficial effects on the hepatic and renal functions and could alleviate the symptoms of increased glucose and hyperlipidemia in diabetic rats.

Keywords:
Diabetes;
Liver;
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Introduction

Obesity and diabetes have been identified since ancient times (Bray et al., 2009). Arthus, the Greek physician, provided the details of the illness and adopted the name of "diabetes" (meaning "a passer through, a siphon") for it, as patients never stopped drinking water and urinating. Ancient physicians recognized nausea, restlessness and thirst as other

symptoms of the disease. They also used herbal medicines to treat it. Avicenna, the famous Iranian physician, (960-1037 AD) prescribed emetics and sudorifics for the treatment of the disease and prohibited narcotics and diuretics, and recommended exercising especially horseback riding, followed by a warm bath (Bray et al., 2009; Ali et al., 2006).

Fear of diabetes and its complications still exists despite its long historical development. Currently, the prevalence of diabetes is increasing rapidly throughout the world. The World Health Organization predicts that by 2030 the number of people with diabetes will exceed 370 million (from 177 million in 2000) and the prevalence rate from 6.4% in 2010 is expected to reach 7.7% in 2030 (Rowley and Bezold, 2012; Shaw et al., 2010).

Diabetes mellitus (DM) is a chronic disorder caused by lack of insulin production by the pancreas, by hereditary factors or by ineffective secreted insulin (Prabhakar and Doble, 2011; Lin and Sun; 2010). Among the reasons for the prevalence of diabetes one can refer to age, obesity and unhealthy diets. This is a situation which needs medical care and lifestyle change (Prabhakar and Doble, 2011). The relationship between the specific effects of diabetes and tissue damage in different organs such as liver, kidneys and cardiovascular disease have been also reported (Ozougwu et al., 2013). Due to the side effects of chemical drugs, studying plants used in traditional medicine in order to achieve new compounds has become a priority. The natural products that have anti-diabetic potentials act through insulinomimetic properties, insulin secretion, inhibiting intestinal absorption of glucose or insulin-dependent metabolic processes. Among the plant compounds with hypoglycemic properties one can refer to alkaloids, peptidoglycans and terpenoids, amino acids and inorganic ions (Mokhtary et al., 2013; Asgary et al., 2010).

Different varieties of *swertia* have been used in traditional medicine to treat diabetes (HajimehdiPoor et al., 2013). These plants belong to gentianaceae family and include ingredients such as bitter secoiridoids, triterpenes, xanthones, swerchirin and alkaloids. Xanthones are reported to have significant hypoglycemic effects. *Swerchirin* remarkably stimulates insulin secretion from isolated pancreatic islets and decreases blood sugar (UPendra et al., 2010). Alkaloids also have inhibitory activity against aldose reductase enzyme. Aldose reductase, a key enzyme in the polyol pathway, reduces the conversion of glucose to sorbitol. The accumulation of sorbitol in the body causes severe disorders such as neuropathy, nephropathy and cataract (Kawanishi et al., 2003). The presence of these compounds can also contribute to the treatment of diabetes or reducing the related complications.

The aim of this study was to compare the effect of alcoholic extract of aerial parts of *Swertia longifolia Boiss* - as one of the most famous members of *swertia* family - on the levels of blood sugar, lipid profiles and liver and kidney function tests in the adult male rats with streptozotocin-induced diabetes.

Materials and methods

This experimental study was conducted on 35 male wistar rats. The ethical principles and guidelines for the use of laboratory animals issued by the Ministry of Health and Medical Education (Islamic Republic of Iran) were observed in every phase of the experiment. Animals were collected from the center for breeding laboratory animals in Arak University of Medical Sciences (Iran) and were studied in Abade Payame Noor University (Fars province of Iran). Animals were housed at 22 to 26°C for 12 hours of darkness and 12 hours of light and were randomly divided into 5 groups of 7: 1) control group, that had access to normal diet and water, 2) diabetic control group which daily received 1 ml of normal saline, 3) diabetic group treated with alcoholic extract of *Swertia longifolia Boiss* (100 mg/kg bodyweight, BW), 4) diabetic group treated with alcoholic extract of *Swertia longifolia Boiss* (200 mg/kg BW) and 5) diabetic group treated with glibenclamide (10 mg/kg BW) (Zare et al., 2012; Wen and Chen, 2007).

Induction of diabetes in rats

To Induce of diabetes, the streptozotocin drug (STZ) (Upjohn Company, USA) dissolved in saline was injected to animals intraperitoneally and at a single-dose (60 mg/kg). Twelve hours before the injection, the test animals were kept hungry with free access to water. After 48 hours, to ensure diabetes, fasting blood glucose levels were measured using EasyGluco (Combo 142, USA). Blood glucose levels higher than 220 mg/dl were considered as diabetic (Tian et al., 2010; Zarei et al., 2015a). Signs of

polydipsia and polyuria were seen in the diabetic rats. When diabetized, animals received the daily doses of the extract and glibenclamide by gavage and for three weeks (Thiruvenkatasubramaniam and Jayakar, 2010).

In the first day of the experiment (as day zero) and before the induction of diabetes, blood sugar was measured and then on a weekly basis it was measured and recorded. Test period was 21 days and during this period each day at 9 am gavage administration were performed. At the end of this period a mild anesthesia with ether was exerted and blood samples were taken from heart and after centrifugation (Minis Pin Eppendorf, Germany) at 3000 rpm the serums were separated and sent to the laboratory to measure the related factors such as: the levels of fasting blood sugar, insulin levels, liver function tests [albumin, alkaline phosphatase (ALP), the alanine aminotransferase (ALT), aspartate aminotransferase (AST) and gamma glutamyl transferase (GGT)], kidney function tests (creatinine and urea) and lipid profiles including high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglyceride (TG) and cholesterol.

Extraction method

In spring *Swertia longifolia Boiss* was collected from the mountainous areas of Darbandsar, near Chaloos (Mazandaran, Iran) at the altitudes of 2700 to 3400 meters. Its genus and species were identified by the Institute of Plant Sciences of Tehran University and preserved by the herbarium code of 492.9. For the preparation of the alcoholic extract, after supplying the aerial parts of the plant and removing the impurities, 700 grams of the plant were ground and mixed with ethanol 90% at a ratio of 1 to 5. After 24 hours the mixture was placed on a stirring device and was then filtrated. The residue was then mixed with ethanol 70% and stirred for another 24 hours on the same device. Finally, it was filtrated and added to the first extract.

Then the extract was distilled in a vacuum distiller at 60°C until the remaining volume was about one fifth of the initial one. In this case, the tank was removed and after cooling, the remaining extract was decanted for three times, each time with 50 ml of chloroform. The remainder was poured into Petri and was dried at 50°C in an oven (Finetech, Korea). Finally, using the obtained extract (about 12 g per 100 g of the ground plant) and saline in milligrams per kilogram of weight the different required concentrations were prepared (Zarei et al. 2013).

Cholesterol and triglyceride serum levels were determined using the kit supplied by Datman Kav Co (Iran) by colorimetric method. Lipoproteins were measured based on a combination of sedimentation technique and ultracentrifugation method and using the kits from Datman Kav Co. HDL was measured by sedimentation technique, too. In the first phase, sedimenting reagent was added to the serum in order to let *non*-high-density *lipoprotein* cholesterol compounds integrate. Then the compounds were sedimented by centrifugation for 10 mins.

The HDL was measured by enzymatic method. LDL was calculated according to Fried-Wald formula. The evaluation of renal and hepatic parameters was carried out using radioimmunoassay method (RIA), Pars Azmoon kit and RIA 1000 device (USA). The means obtained (Mean ± SEM) were analyzed using one way ANOVA (Tukey and Dancan tests), T-test and K related samples. Statistical analysis was done using SPSS software, version 17 ($P \leq 0.05$).

Results

In this study, two days after receiving STZ, blood glucose in the diabetic groups increased significantly compared to the control group (Table 1). Three weeks after the administration of the extract of *Swertia longifolia Boiss* at the doses of 100 and 200 mg/kg BW to the first two experimental groups and the administration of glibenclamide to the third experimental group, blood glucose levels decreased significantly compared to the diabetic control group ($P<0.05$).

The results of the statistical analysis (Table 2) showed that the levels of liver enzymes such as ALP, ALT, AST and GGT in the diabetic control group increased significantly as compared to those in the control group. The levels of ALP ($P=0.000$), ALT ($P=0.000$), AST ($P=0.001$) and GGT ($P= 0.000$) in the experimental groups receiving the extract decreased significantly in comparison to both the control group and the group receiving glibenclamide.

In the experimental group receiving glibenclamide, the levels of ALP and GGT increased but that of AST decreased significantly in comparison to the control group. However, the level of albumin in the control

Table 1: Comparison of fasting blood sugar (FBS) in different groups using different doses of ethanol extract of *Swertia longifolia Boiss* and glibenclamide.

Group / FBS	Control	Sham (diabetic control)	*Swertia longifolia Boiss* (100mg/kg)	*Swertia longifolia Boiss* (200mg/kg)	*Glibenclamide* (10mg/kg)
Pre-diabetes	70.5±15.3	70.2±12.7	64.00±9.69	69.20±18.10	69±16.7
48 hours after diabetization	70.5±13.6	302.7±71.1*	336.20±98.71	356.00±55.50	302.9±1.1
End of first week	72.7±14.6	339.3±72.8*	227.20±79.66†	288.80±75.78†	302.4±76.8†
End of second week	68.8±19.2	352±80.3*	182.00±77.35†	200.20±69.78†	132.6±89.4†
End of third week	64.7±17	353.3±123.4*	121.20±39.75†	159.80±40.10†	161.1±84.3†

* Marks a significant level compared to the control group.
† Marks a significant level compared to the sham group.

Table2: Comparison of the lipid profiles and insulin in different groups using different doses of ethanol extract of *swertia longifolia Boiss* and comparing them with glibenclamide.

Group / Parameters	Control	(diabetic control)	*Swertia longifolia Boiss* (100mg/kg)	*Swertia longifolia Boiss* (200mg/kg)	Glibenclamide (10mg/kg)
Insulin (mu/l)	0.35±0.2	0.12±0.0	.56±.13†	.48±.09†	0.682±0.1†
HDL (mg/dl)	42.25±6.0	47.50±7.9	56.20±4.91	60.40±4.46	36.50±2.0
LDL (mg/dl)	23.75±1.7	45.75±5.9*	35.00±2.07†	33.20±2.49†	39.75±3.5
Cholesterol (mg/dl)	58.50±8.4	81.00±2.0*	56.00±5.82†	52.40±3.62†	56.00±5.8†
Triglyceride (mg/dl)	52.50±7.8	43.50±2.1	31.40±2.33	46.40±3.89	44.50±6.0
Creatinine (mg/dl)	0.427±0.02	0.575±0.02*	0.478±.041†	.462±.028†	0.402±0.15†
Urea (mg/dl)	30.75±2.52	145.12±29.4*	59.60±9.42†	58.60±7.40†	84.32±0.15†
Albumin (g/dl)	3.41±0.11	3.72±0.02	3.88±.10	3.85±.23	3.32±0.18
ALP (U/l)	419±33	975±116*	341±25†	301±59†	1422±145†
AST (U/l)	140±5.1	166±4.9*	134±11.22†	129±7.42†	101±6.90†
ALT (U/l)	52.92±0.38	72.80±5.76*	48.26±4.05†	45.60±3.36†	73.17±1.08
GGT (U/l)	3.25±.47	7.00±1.58*	4.6±.67	3.80±.58†	12.00±1.08†

* marks a significant level in sham group compared to the control group. †marks a significant level in experimental groups compared to the sham group.

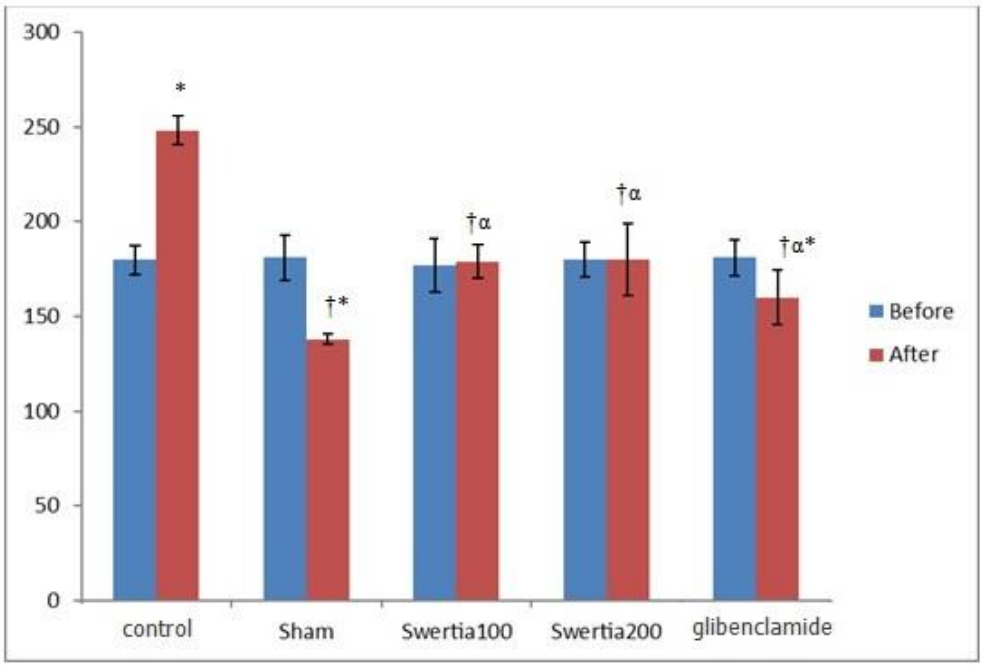

Fig.1. Effect of gavaging the alcoholic extract of *Swertia longifolia Boiss* and glibenclamide at different doses on changes in body weight (in grams)

*marks the changes in weight in both groups before and after the end of the experiment

†marks the significant changes in the sham group and the experimental group in comparison to the control group at the end of the experiment

$^{\alpha}$ marks the significant changes in the experimental group in comparison to the sham group

group compared to the diabetic control group and in all the experimental groups compared to the control group showed no significant difference (P>0.05). The levels of creatinine (P= 0.017) and urea (P= 0.017) in the control group showed a significant increase compared to those in the diabetic control group; but their levels in all experimental groups showed a significant decrease compared to the control group. The reduced level of insulin in control group was not significant in comparison to that in the diabetic control group; but the amount of insulin in all experimental groups receiving the minimum (100 mg/kg) and maximum (200 mg/kg) doses of the extract and also in the group receiving glibenclamide showed significant increases compared to the control group (P= 0.034).

The levels of cholesterol (P= 0.016) and LDL (P=0.005) in the control group compared to the diabetic control group showed a significant increase, but their level in the experimental groups receiving the extract showed significant decrease in comparison to the control group. Cholesterol levels in experimental group receiving glibenclamide were significantly lower than that in the control group. TG and HDL in the control group compared to the diabetic control group and in all experimental groups compared to the control group did not show significant changes (P>0.05).

Before and after the test period, the weight of the rats in each group (Fig. 1) were compared. The weight in the control group significantly increased which showed the natural growth during the test (P=0.000). Comparing the weights before and after the experiment in the control group (P=0.002) and in the group receiving glibenclamide (P=0.028) showed a significant decrease, but the change was not significant in the groups receiving the extract. At the end of the experiment, the weights of the rats in different groups were compared. In all diabetic groups the weights showed significant decrease when compared with the control group; however, the body weight in all experimental groups receiving the extract and glibenclamide increased significantly in comparison to the diabetic control group (P=0.000).

Discussion

In general, the research findings suggested that the creatinine, urea, liver enzymes, lipid profiles including total cholesterol and LDL levels increased in the

control group receiving STZ compared to the control group. While all these factors in the group receiving the alcoholic extract of *Swertia longifolia Boiss* decreased.

In the experimental group receiving glibenclamide, the amount of creatinine, urea and lipid profiles reduced, while the levels of liver enzymes increased which could be caused by the drug's side effects. In addition, insulin levels in all experimental groups receiving glibenclamide and the alcoholic extract showed significant increases. The findings indicated liver damage and nephropathy in the control group. In fact, STZ damages the cells by transferring a methyl group to DNA. STZ diabetogenic effects are not possibly associated with its alkylating ability, but for the reductive properties of nitric oxide (Zarei et al., 2015a; Zarei et al., 2015b) and thereby it increases the activity of guanylyl cyclase and formation of CGMP. Finally, during hypoxanthine metabolism some reactive oxygen species such as superoxide and hydroxyl radicals are produced, which may add to the effects of STZ in the process of cell deterioration (Lenzen, 2008). STZ selectively and with low-affinity and through glucose transporter 2 (GLUT2) enters pancreatic beta cells through the plasma membrane.

Besides inducing diabetes, the importance of the transfer will be known by observing kidney damage and especially liver damages like the creation of fatty liver, elevated liver enzymes as well as increased creatinine and blood urea. The main cause of these disorders is the destruction of hepatocytes and nephrons. So, the increases of recent factors in the diabetic groups in present study are consistent with the results of other studies (HajimehdiPoor et al., 2013). This is because of the fact that diabetes and insulin reduction stimulate the flow of fatty acids to the liver. Also, due to the lower synthesis of apoprotein B, lipoprotein secretion from the liver reduces, too. This action causes the accumulation of fat in hepatocytes and ultimately leads to their destruction and the increase in liver enzymes (Zarei et al., 2015a; Zarei et al., 2015b).

There are three key defects in patients with hyperglycemia (DM): increased hepatic glucose production, decreased insulin secretion and insulin functional disorders. Conventional medicines in the treatment of diabetes act through increasing insulin sensitivity, increasing insulin production or reducing hepatic glucose released into the blood (Prabhakar and Doble, 2011). Glibenclamide stimulates the release of more insulin from the pancreas. It blocks the potassium receptors in islet beta cells.

Insulin is a hormone that is secreted by the pancreas and controls blood sugar level. Glibenclamide is not commonly used in the treatment of patients with type I diabetes (insulin-dependent), because basically in these patients the pancreas is not able to produce insulin. However, its long-term use increases the sensitivity of peripheral tissues such as liver, muscle and fat tissues to insulin, but this mechanism is secondary. The main effect of glibenclamide is hypoglycemia, however, other side effects such as gastrointestinal disorders, weight gain and yellowing of the eyes or skin (Jaundice) may occur (Zarei et al., 2015b). As in this study, the drug reduced blood sugar levels and fat but had no significant effects on the liver enzymes and even in some cases it increased them.

Controlling diabetes without any side effects is still a major challenge in medicine. The ethnobotanical information about medicinal plants show that about 800 plants are used for DM control. So far the anti-diabetic effects of about 450 plants have been studied in the laboratory, but only the mechanisms of 109 ones have been identified (Kameswararao et al., 2003; Solati and Soleimani, 2010). Medical herbs have multiple beneficial activities including: changing the metabolism of carbohydrates by multiple mechanisms, activating the release of insulin and beta cell function, increasing glucose reabsorption as well as their antioxidant properties.

Besides, the medicinal plants effective in the treatment of diabetes act by inhibiting intestinal absorption of glucose and inhibiting hepatic glucose production. The main active ingredients of these plants are alkaloids, glycosides, steroids, carbohydrates, glycopeptides, terpenoids, amino acids and inorganic ions (Maiti et al., 2005). The plants in Swertia family also contain significant amounts of flavonoids, terpenoids and xanthonoides. Therefore, many positive effects including the preventing glucose increase and lipid profiles increase in the diabetic rats in our study can be attributed to these effective components (HajimehdiPoor et al., 2013).

Studies showed that the extract of *swertia chirayita* at a dose of 250 mg/kg BW, in normal rats significantly

reduced blood sugar while it increased insulin levels without affecting the liver glycogen content. In addition, when the extract was administered for 28 days, the liver glycogen content significantly increased which was related to the possible effects of the extract on insulin resistance. The administration of swercherine at a dose of 50 mg/kg in rats significantly stimulated the release of insulin from the islets and lowered blood glucose (Patel et al., 2012).

Among the basic components of the plant one can also refer to methyl swertian and bellidifolin, the oral administration of which at a dose of 200 mg/kg could reduce blood sugar within a week. The anti-diabetic mechanism of *Swertia japonica* is based on the correction of insulin resistance which plays an important role in the treatment of diabetes mellitus type 2. It is possible to find other species of Swertia effective in the treatment of diabetes.

The only species of the plant which grows in Iran is *Swertia longifolia Boiss* whose effects on diabetes were investigated in this study, however, the results of this experiment are consistent with those carried out on other species of the plant; it is possibly because of the fact that this plant also contains a significant amount of methyl swertian, bellidifolin and etc (UPendra et al., 2010; Peesa, 2013).

The presence of different compounds in this genus ensures numerous biological effects including hepatoprotective, anti-inflammatory, anti-carcinogenic, hypoglycemic, anti-oxidant ones as well as positive effects on the central nervous system. The plant contains xanthonoides (HajimehdiPoor et al., 2013) which may both inhibit acetylcholinesterase and neutralize free radicals (Rana and Rawat, 2005; Wszelaki et al., 2010).

The mechanism of insulin secretion from beta cells in response to changes in blood glucose concentration is a complicated process. Primarily, an amount of glucose which goes into beta cells by the GLUT2 is phosphorylated by glucokinase enzyme. The modified glucose is metabolized to produce ATP (Prabhakar and Doble, 2008). The increase in the ratio of ATP to ADP leads to the blockage of potassium channels dependent on ATP, cell depolarization and activation of voltage-dependent calcium channels and ultimately stimulating insulin secretion (Prabhakar and Doble, 2008). This insulin stimulation accelerates reabsorption, manipulation and storage of glucose by a cascade of messages. In diabetic patients the capacity to produce insulin is destroyed because of the apoptosis of beta cells of the pancreas or insensitivity to insulin. Cytokines, lipuloxicity and glucotoxicity are three main factors involved in beta cell apoptosis (Hui et al., 2004). In the present research fat and sugar increased in the diabetic group helped STZ in the destruction of pancreatic cells, too.

Alkaloids are among the active components of the plant. Intravenous administration of alkaloids to alloxan-induced diabetic rabbits caused rapid hypoglycaemic effects whereas it had no effect on the rabbits without pancreas. High fiber content plants have anti-diabetic properties. It is probable that these compounds reduce the secretion of glucagon and somatostatin. Alkaloids are natural amines with pharmacologic effects on humans and animals. Resveratrol, is a phytoalexin (a group of antibiotics compounds that are produced by plants as part of the immune system) (Penumathsa et al., 2008). Alkaloid berberine has the potential of lowering blood sugar and is found in some plants such as barberry (Taheri et al., 2012; Jamwal, 2012).

The pharmaceutical importance of the active phytochemical ingredients of plants as remedies to help lower blood fats, overweight and obesity has long been known. Some of these compounds are xanthonoides, saponins, flavonoids, alkaloids and coumarin terpenes which are also among the components of *Swertia longifolia Boiss* (Singh et al., 2013). Phyto molecules play a key role in the treatment of obesity. They may reduce the absorption of food fat, increase energy expenditure in the body and reduce the process of cell differentiation and proliferation by preadipocytes or may increase the breakdown of the fat stored in body. The fat in diet is one of the compounds that are responsible for obesity. So, to inhibit the digestion and absorption of fats, pancreatic lipase is a suitable target for the development of obesity drugs. Such inhibitors can be plant components, plant secondary metabolites and microbial sources (Yang et al., 2008). Some of the compounds present in swartia such as methyl swertian and bellidifolin act as blood sugar and fat reducing agents by increasing the secretion of insulin and decreasing blood glucose and liver enzymes (HajimehdiPoor et al., 2013; Yang et al., 2008). The plant's chemical phyto molecules can be extracted, purified and used for the treatment of obesity (Puri et

al., 2012).

The results of this study indicated the extract of the plant increases the secretion of insulin. Phosphorylation reaction rates of glucose and glucose metabolism in muscle cells and adipose is proportional to the speed of glucose transport into the cell. Glucose and similar sugars need insulin carrier to pass through the cell membrane and in most tissues, insulin is responsible for strengthening the carrier system. The number of carriers increases under the influence of insulin. When insulin increases and activates such key enzymes like glucokinase and pyruvate kinase in hepatic glycolysis reactions, glucose consumption in glycolytic pathway increases and indirectly prevents glucose release in blood plasma. On the other hand, insulin by decreasing the activity of glucose-6-phosphatase enzyme in the liver prevents glucose release. Because of the fact that glucose-6-phosphate cannot pass through liver cell membrane, the activity of insulin keeps glucose within the liver cells. So, the hypoglycemic activity of the plant seems to be reasonable and is consistent with the results of other studies (HajimehdiPoor et al., 2013, Haugaard and Marsh, 1952) .

One of the effects of insulin which leads to a decrease in plasma glucose concentration, is the dilatory effects resulting from inhibiting gluconeogenesis. Phosphoenol pyruvate *carboxy* kinase is the key enzyme in the liver gluconeogenesis from non-carbohydrate, which catalyzes the reaction of converting oxaloacetate to phosphoenol pyruvate. Insulin inhibits the expression of the enzyme. In the liver and adipose tissues, insulin has a strong deterrent effect on the lipolysis that in its turn, indirectly leads to anabolic effects. By activating a special phosphatase enzyme, insulin inhibits the activity of lipase, which is involved in the breakdown of fats. The inhibitory effect of insulin in response to lipolysis leads to a decrease in the concentration of free fatty acids in the bloodstream and eventually to an increase in the effects of insulin on glucose metabolism, hence a reduction in the amount of blood fat by the plant extract (HajimehdiPoor et al., 2013; Haugaard and Marsh, 1952).

Conclusion

Though glibenclamide had promising effects on insulin secretion, blood sugar and blood fat reduction, it had little effect on liver function tests and in some cases, it even increased liver enzymes which may be due to its side effects. But after *Swertia longifolia Boiss* extract was administrated to diabetic rats, the levels of liver enzymes, lipid profiles, as well as urea and creatinine reduced. The results showed that the plant extract in addition to reducing blood sugar and blood fat, had protective effects on liver and kidney. *Swertia longifolia Boiss* extract also increased insulin levels. In general, medical herbs have multiple beneficial activities including changing the metabolism of carbohydrates by multiple mechanisms, enabling the release of insulin and improving the functioning of the beta cells, increasing the reabsorption of glucose, antioxidant effects, inhibiting the absorption of intestinal glucose and hepatic glucose production. The main active components of the herbs which are effective on diabetes include: alkaloids, glycosides, steroids, polysaccharides, carbohydrates, glycopeptides, terpenoids, amino acids and inorganic ions.

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Conflict of interest

None declared.

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