Anti-diabetic activity of aqueous extract of *Ipomoea batatas* L. in alloxan induced diabetic Wistar rats and its effects on biochemical parameters in diabetic rats

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Abstract: Diabetes is a condition where the fasting blood glucose level elevated above the normal range (80-120mg/dL). This increase in blood glucose level may be due to the insulin deficiency i.e. insulin dependent diabetes mellitus (IDDM or type I) or due to insulin resistance i.e. non-insulin dependent diabetes mellitus (NIDDM or type II). Diabetes leads to severe complications in the body even life treating complications e.g. nephropathy, retinopathy, neuropathy increased vascular permeability and delayed wound healing if left untreated. Different drugs are used for the treatment of diabetes mellitus, but synthetic drugs are costly and possess severe side effects. So, more emphasis is being placed on the use of traditional medicines because these sources have fewer side effects than the synthetics drugs and are economical. So the white skinned sweet potato (*Ipomoea batatas* L.) peel-off was selected for its anti-diabetic effect as well as to see its effects on biochemical parameters. Both young (3–4 months) and old (up to 1 year) Wistar rats were selected for current study. It was found that the aqueous extract of WSSP peel-off had shown beneficial effects. In addition to the decrease in blood glucose level it also decreased protein glycation level total cholesterol, triglycerides, and LDL-cholesterol. Increase in HDL-cholesterol was also observed after treating the rats with aqueous extract of *Ipomoea batatas*. Additionally, WSSP peel-off had also shown positive results on total protein concentration, albumin, globulin, and plasma enzymes (SGOT and SGPT). Further research would be needed in order to purify the anti-diabetic components and it should be available in compact dose form for all diabetic patients.

Keywords: *Ipomoea batatas*, alloxan induced diabetes, biochemical parameters.

INTRODUCTION

Diabetes mellitus is a clinical syndrome due to relative or absolute deficiency of insulin or resistance to the action of insulin at the cellular level; as a result hyperglycemia or glucosurea occurs. Most common manifestations of diabetes are weight loss, polydipsia, polyphagia, and polyurea due to the hyperglycemia, hypoinsulinemia, and dyslipidaemia. Similarly common complications caused by the diabetes are cardiovascular diseases, neuropathy, retinopathy, and nephropathy (Kumar and Clark, 2002). Diabetes is managed by proper exercise, avoiding the carbohydrate rich diet and increasing protein diet. Oral hypoglycemic agents maintain the blood glucose concentration at a certain level (Mallick *et al*., 2007) About 10% cases of disease mellitus occur most often in the American population and 2 million populations affected by this disease are in Europe and North America (Lachmann *et al*., 2011). Diabetes is major health problem that results in reduced life quality and increase morbidity as a result of its severe dangerous and life threatening complications. Modern drugs such as Pioglitazone has better efficacy but also possess side effects like hypoglycemia, gastro-intestinal tract disturbance, obesity, water intoxication, and hyponatremia. Therefore it is important to explore such alternative source of medicine which would have better efficacy with fewer or no side effects and also cost effective. It had been reported that herbal medicines are gaining popularity to show better efficacy with no or very rare side effects proven by both *in vivo* and *in vitro* studies (Trojan-Rodrigues *et al*., 2012) Various chemical constituents or compounds obtained from medicinal plants have proven their efficacy and safety in the treatment of diabetes mellitus.

Several biochemical parameters play a momentous function in diabetes mellitus. These parameters include glucose, protein (globulin and albumin), triglycerides,

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total cholesterol, HDL cholesterol, LDL cholesterol, AST and ALT (King *et al*., 1998).

Diabetes mellitus is a persistent metabolic syndrome which is characterized by irregular increase in blood sugar level. Prolonged hyperglycemia leads to elevated risk of vascular complications and long term malfunction and damage of different organs (Ross *et al*., 2004).

Diabetes mellitus is characterized by deviation in the metabolism not only of glucose and fat but also protein. Protein intake should also be controlled in case of diabetes mellitus By obtaining optimal blood glucose level, glycosylated protein and plasma lipids it is possible to reduce complications e.g. retinopathy, nephropathy and neuropathy. Diabetes affects protein metabolism and insulin is an important controller in achieving absolute protein retention. Scarcity of insulin or action may be associated with abnormal management of dietary proteins (Beasley and Wylie-Rosett, 2013).

The development of advanced glycation end products (AGEs) is a cluster of modified proteins and lipids and potentially harms the cells leads to chronic stress conditions. Furthermore, AGEs enhance reactive oxygen species formation and impair antioxidant system. In some oxidative conditions the creation of AGEs is increased. AGEs are also involved for increased pathogenesis and diabetic complications in type 2 diabetes mellitus (Govindappa *et al*., 2015).

The abnormalities in lipid metabolism usually lead to increase in serum lipid and lipoproteins concentration in the body. The increases threat is due to low HDL-cholesterol concentration and enhanced triglyceride level. Upraise in lipid and lipoprotein levels play a considerable role in incidence of meticulous and premature atherosclerosis in diabetic patients. Postprandial hyper-triglyceridaemia results in endothelial dysfunction and atherogenesis. Chief risk factor which contributes in coronary heart disease is elevated lipid profile (Mallick *et al*., 2007). Oxidative processes e.g. oxidative alteration of LDL contributes a significant role in advancement of atherosclerosis in arterial wall. Additionally, diabetic patient indicates irregular antioxidant status protein, surplus glycosylated protein and oxidation of low density lipoprotein. Enlarged lipid per-oxidation contributes to long term tissue damage is linked with Diabetes mellitus. Increased triglycerides level, decreased HDL cholesterol, and elevated quantity of small, thick LDL particles is observed in diabetic patients. All these factors are related to characteristic lipid disorder in patient with diabetes and diabetic dyslipidaemia (Ludvik *et al*., 2004).

As diabetes is a metabolic syndrome it also affects the metabolic activities of liver. Enhanced activities of liver enzymes e.g. aspartate aminotransferase (SGOT) and alanine aminotranferase (SGPT) are indicators of Hepatocellular injury. Insulin resistance, metabolic disorder, and type 2 diabetes mellitus are linked with elevated action of these hepatic markers. Increased in liver function tests (SGOT&SGPT) was practical in type 2 diabetic patients. SGOT and SGPT enzyme concentration is powerful predictor of diabetes. Increase in liver enzymes levels in patients with diabetes mellitus outcome from effect of insulin on liver and muscle tissue. Elevated concentration of SGPT indicates fatty changes in liver and this abnormality results in development of type 2 diabetes mellitus (Hakim *et al*., 1997).

Thus, in the present study, *in-vivo* anti-diabetic activity was performed on water extract of *Ipomoea batatas*. Anti-diabetic activity of this plant was evaluated and compared with the standard anti-diabetic drug Glibenclamide on alloxan induced diabetic wistar rats.

MATERIALS AND METHODS

Preparation of plant extract

Ipomoea batatas was purchased from general market of Faisalabad (Pakistan). Plant was authenticated and sample was kept in herbarium of Pharmacology Department University of Agriculture, Faisalabad. Roots of *Ipomoea batatas* are used in present research. Roots of *Ipomoea batatas* were washed with distilled water in order to eradicate any external material or dust. Chopping of plant roots was performed using chopper and roots were powdered. Powdered root (1000 g) was done by using water (2000 ml) for the extraction purpose. Throughout the extraction process extract was shacked intermittently (3-4 times a day). Extraction was successively performed for total of 21 days (Whitty, 2015) After each extraction, extract was filtered by Whattman filter paper no 1. After filteration filtrate was evaporated to dryness using rotary evaporator under reduced pressure. The semisolid extract was dried by means of water bath. Dried extract was weighed and stored at room temperature in a closed inert container for further examination.

Experimental animals

Present study was performed on Normal male Wistar rats (Laboratory bred). Acclimatization of animals was performed for total of 14 days. Animals were kept under standard animal housing conditions i.e. in room temperature premises with dark/light cycle (12 H). During the study animals were provided with unlimited contact to standard diet and water *ad libitum*. The study was undertaken with due authorization by Institution Animal Ethical Committee. Ethical committee investigates and monitors the housing of animals and ensures that it is as per particular standards. This committee also ensures that animals used for experiment are correctly cared prior to and succeeding to experiment. Ethical committee further make definite that records are accurately maintained with

respect to experiment performed on animals. This committee observed that experiments are not performed merely for intention of achieving manual skills. This committee organize in-house training program for any animal experiment to ensure quality research and welfare of animals (Roche *et al*., 2005).

Induction of diabetes

Diabetes was induced by administration of alloxan monohydrate [150 mg/kg (S/C)], after an overnight fasting for 12 hours. Normal male wistar rats had access only to water to make them more prone to induce diabetes. Alloxan monohydrate was dissolved in (0.9% NacL sol) and injected to male wistar rats. After 3 days of alloxan monohydrate induction glucose level (GL) was monitored. Wistar rats having blood glucose level of 200 mg/dl and above after 3 days were chosen for the present study. Blood glucose level was monitored using Blood glucose test diagnostic strips (NIPRO Blood diagnostic strips). Blood glucose was determined by amputation of tail tip under mild anesthesia using NIPRO blood diagnostic strips. All rats having glucose level less than 200 mg/dl were expelled from the existing study (Surya *et al*., 2014)

Experimental group

The diet of total 36 rats was considered standard and consisted of broiler ration No. 13. The animals were kept at standard housing conditions with 12 hours light/ dark cycle. These rats were kept in animal house situated at the department of physiology and pharmacology, University of Agriculture, Faisalabad. Animals were reserved at *water ad libitum* and standard diet. The animals were divided into 6 groups. Blood glucose level (BGL) was calculated for all 6 groups and for each rat individually and recorded. Control groups are exposed only to standard diet. Control group receive neither any extract only standard diet. Diabetic groups were exposed orally to methanol extract with dose rate of 4g/Kg/day daily. Before starting the dose and at 3rd, 6rd, 9th, 12th and 15th day of the experiment blood glucose level and body weight of experimental rats were recorded.

Total number of rats was 36. The rats were divided in 6 groups. Each group contains 6 animals:
Group 1: Normal control young animals
Group 2: Normal control old animals
Group 3: Diabetic control young animals
Group 4: Diabetic control old animals
Group 5: Aqueous extract treated young diabetic rats
Group 6: Aqueous extract treated old diabetic rats
Aqueous extract (4g/kg/day) was administered orally. After completion of experiment (14 days) blood of rats was withdrawn.

Physical parameters

Body weight, feed consumption and water intake of each rats were measured daily at (9:00 AM).

Sample collection

Rats of all the groups were decapitated for set of blood samples in heparinized tubes. Plasma was separated after centrifugation and stored in small aliquots at -4°C for further investigation.

Station of analysis

In the laboratory of Department of Veterinary Physiology and Pharmacology, University of Agriculture, Faisalabad plasma biochemistry (Blood glucose level, glycation level, total proteins, cholesterol level, liver enzymes, and cardiac enzymes) were analyzed.

Plasma biochemistry

Glucose (mg/dL)

Glucose concentration (mg/dl) was determined by enzymatic colorimetric technique.

Principle

In the presence of glucose oxidase glucose was oxidized to gluconic acid and hydrogen peroxide. Hydrogen peroxide reacts with phenol and 4-aminophenazone to form a colored compound in the existence of peroxide.

Materials

a. Sample

Heparinized plasma

b. Reagent

The reagent and standard were stable upto the stated expiry date when stored at 2-8°C.

i. Buffer/Enzyme
ii. Standard 100gm/dl (5.55mmol/L)

Working reagent composition

Phosphate buffer	100mmol/L
4-aminophenzone	8.0mmol/L
Glucose oxidase	2000IU/L
Peroxidase	1000 IU/L
Chlorophenol	10mmol/L

Method

1 ml of reagent was taken in each test tubes labeled as blank, standard, and sample. Then 10 µl of sample and standard solution was added into their specific tubes. Mixed and incubated for 10 minutes at 37°C. Then standard and samples were taken into their particular cuvettes and measured the absorbance at 546 nm against reagent blank.

Calculations

$$\text{Glucose concentration} = \frac{\text{Absorbance of Test}}{\text{Absorbance of Standard}} \times \text{Standard concentration}$$

RESULTS

Body weight (g)

Mean body weight (g ±SE) of young and old rats at various days in normal and diabetic groups treated with

Table 1: Mean plasma glucose, Albumin, Globulin, Glycation, Total Cholesterol, LDL cholesterol, HDL cholesterol, Triglycerides, SGOT and SGPT (mg/dL±SE) Concentration of all treatment groups (control, diabetic, methanol and aqueous) of young and old rats at various days in normal and diabetic groups treated with water extract of sweet potato peel-off.

Biochemical Parameter	Group	Control	Diabetic	Diabetic treated	Overall mean
Glucose	Young	81.60±1.03	165.40±2.14	152.80±23.52	133.27±12.27
	Old	85.60±1.63	195.20±3.76	213.00±21.32	164.60±16.48
	Overall mean	83.60±1.13^{B}	180.30±5.37A	182.90±18.02^{A}	148.93±10.50
Albumin	Young	3.62±0.10^{c}	4.08±0.12^{ab}	4.26±0.55^{a}	3.99±0.10
	Old	3.98±0.14^{abc}	3.66±0.15^{c}	3.74±0.09^{bc}	3.79±0.08
	Overall mean	3.80±0.10	3.87±0.12	4.00±0.12	3.89±0.06
Globulin	Young	0.96±0.22^{c}	2.06±0.09	2.24±0.19	2.35±0.10^{B}
	Old	2.84±0.08	2.18±0.11	2.90±0.20	2.64±0.11^{A}
	Overall mean	0.55±0.07	0.68±0.11	0.52±0.06	0.57±0.04
Glycation	Young	0.46±0.01	2.13±0.32^{b}	0.99±0.21^{c}	0.99±0.21^{c}
	Old	1.38±0.17^{c}	3.34±0.14^{a}	2.73±0.13^{b}	2.48±0.23^{A}
	Overall mean	1.17±0.15^{C}	2.74±0.26^{A}	1.86±0.31^{B}	1.92±0.18
Total Cholesterol	Young	71.00±1.98	81.40±1.75	79.75±0.99	77.38±1.50^{B}
	Old	78.20±1.69	93.60±1.86	85.13±1.70	85.64±1.93^{A}
	Overall mean	74.60±1.71^{C}	87.50±2.36^{A}	82.44±1.29^{B}	81.51±1.42
HDL Cholesterol	Young	45.80±0.66^{a}	40.40±0.75^{c}	42.01±0.55^{bc}	42.01±0.55^{bc}
	Old	41.00±0.63^{c}	43.80±0.80^{ab}	45.16±0.88^{a}	43.32±0.62
	Overall mean	43.40±0.91	42.10±0.77	42.59±0.72	43.03±0.46
Triglycerides	Young	46.60±1.08^{c}	57.80±1.66^{b}	32.36±2.98^{d}	45.59±2.99
	Old	48.00±0.84^{c}	67.20±1.39^{a}	26.96±1.24^{e}	47.39±4.44
	Overall mean	47.30±0.68^{B}	62.50±1.87^{A}	62.50±1.87^{A}	62.50±1.87^{A}
LDL Cholesterol	Young	13.40±0.51	25.60±1.54	19.00±0.70	19.33±1.44^{B}
	Old	16.00±0.89	27.40±0.98	20.41±1.56	21.27±1.41^{A}
	Overall mean	14.70±0.65^{C}	26.50±0.91^{A}	19.70±0.84^{B}	19.70±0.84^{B}
SGOT	Young	57.20±0.58^{a}	51.20±0.97^{b}	58.60±0.51^{a}	55.67±0.94
	Old	55.67±0.94	58.80±1.02^{a}	58.80±1.02^{a}	56.13±1.24
	Overall mean	53.60±1.27^{B}	53.60±1.27^{B}	59.10±0.46^{A}	55.90±0.77
SGPT	Young	54.00±1.05	58.80±0.58	51.80±0.66	54.87±0.89^{A}
	Old	48.20±0.80	54.40±1.47	50.20±0.49	50.20±0.49
	Overall mean	50.20±0.49	56.60±1.05^{A}	51.00±0.47^{B}	52.90±0.71

water extract of sweet potato peel-off is tabulated in fig. 1. This interaction was not significant, while the interaction of overall mean of body weight with days was significantly different. The highest body weight was shown in the 7th day. Similar interaction of the overall mean with age and group was also significant. The overall of highest body was shown by the old control group rats and lowest was shown by young rats of the diabetic treated groups.

Feed Consumption (g)

Mean feed consumption (g±SE) of young and old rats at various days in normal and diabetic groups treated with water extract of sweet potato peel-off is tabulated in fig. 2. The highest feed consumption was shown by old rats of the control group in 8th day and diabetic treated rats of old groups in the 12th days. While the rats of the diabetic treated group was shown the lowest feed consumption in the 12th day. The highest interaction of the overall mean of the feed consumption with day was appeared in the 5th and 8th and lowest was shown in the 12th day respectively. The overall mean of the feed consumption with days and groups was appeared in old control rats group, while lowest was shown in the old rats of the diabetic treated group.

Water Intake (mL)

Mean water intake (mL ±SE) of young and old rats at various days in normal and diabetic groups treated with water extract of sweet potato peel-off is tabulated in fig. 3. The lowest water intake was shown by young rats of the control group in the 6th day while highest water intake was shown by the diabetic treated rats of the old age in day 11. The highest overall mean of water intake with days was appeared in the 11th day while lower was shown in the day 1st and 2nd. The overall mean of water intake with age and groups was found to be non-significant.

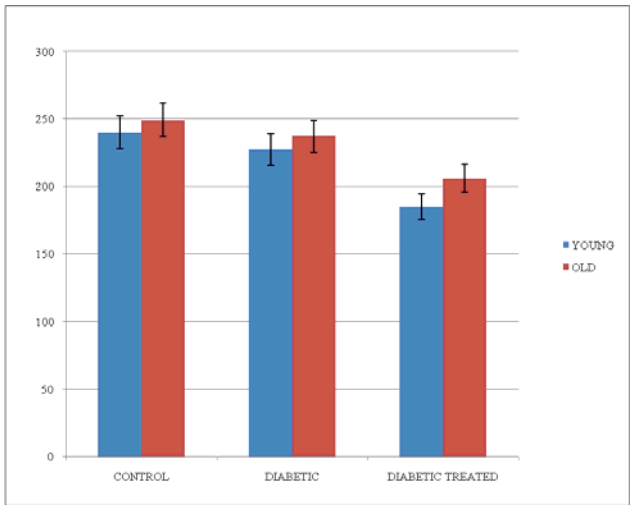

Fig. 1: Mean body weight (g ± SE) of young and old rats in normal control (C), diabetic (D) and diabetic groups treated (DT) with water extract of sweet potato peel-off.

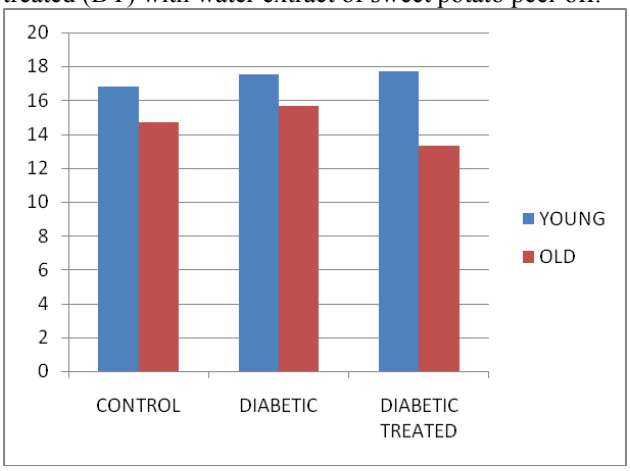

Fig. 2: Mean feed consumption (g ± SE) of young and old rats at various days in normal and diabetic groups treated with water extract of sweet potato peel-off.

Plasma biochemistry for water extract treatment

Glucose (mg/dL)

Mean glucose concentration of young and old rats of control, diabetic and diabetic treated groups are tabulated in table 1. The overall mean of glucose concentration of control group irrespective of their age was significantly lower than the diabetic and diabetic treated group rats. While the overall mean of glucose concentration of old rats irrespective of their groups was significantly higher than the young rats.

Albumin (g/dL)

Mean albumin concentration of control diabetic and diabetic treated group rats of both young and old age are tabulated in table 1. The overall mean of albumin concentration of young and old rats irrespective of their groups and the overall mean of albumin concentration of control, diabetic and diabetic treated groups irrespective of their age was found to be non-significant. While the interaction of albumin concentration with age and group was significant. The diabetic treated group rats had highest protein concentration young control group showed the lowest albumin concentration. While the old age rats, diabetic group shown the minimum concentration and control group showed the maximum concentration.

Globulin (g/dL)

Mean globulin concentration of control diabetic and diabetic treated group rats of both young and old age are tabulated in table 1. The interaction of globulin concentration with age and group was non-significant. The overall mean of globulin concentration irrespective of their age of control and diabetic treated group was no difference significantly, while overall mean of globulin concentration diabetic group rats was lower of than the control and diabetic treated group. The overall mean of globulin concentration of old rats irrespective of their group.

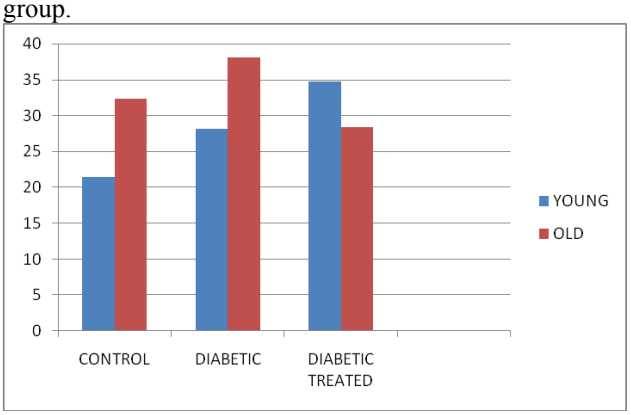

Fig. 3: Mean water intake (mL±SE) of young and old rats in normal control (C), diabetic (C) and diabetic groups treated (DT) with water extract of sweet potato peel-off

Glycation level

Mean concentration of glycation level of control, diabetic and diabetic treated groups of both young, and old age rats are tabulated in table 1. The interaction of glycation with age and groups was significant. Similarly the overall mean of glycation of groups and the overall mean of glycation of young and old rats was also significant. The overall mean of glycation of old age rats was higher than the young rats. The overall mean of glycation of diabetic treated was lower than the control group rats.

Total cholesterol (mg/dL)

Mean cholesterol concentration of control diabetic and diabetic treated group rats of both young and old age are tabulated in table 1. The interaction of cholesterol concentration with age and groups was non-significant. Overall mean of young and old rats irrespective of their groups and overall mean of control, diabetic and treated groups irrespective of their age differ significantly. The overall mean of cholesterol concentration of control was the lowest and of diabetic group was the highest irrespective of their age. Overall mean of cholesterol

concentration of old rats irrespective of their group was higher than the young rats.

HDL-cholesterol (mg/dL)

Mean concentration of HDL-cholesterol of control, diabetic and diabetic treated groups of young, and old age are tabulated in table 1. Overall mean of HDL-cholesterol concentration of all groups irrespective of their age and overall mean of young and old rats irrespective of their group was non-significant, while the interaction of HDL-cholesterol concentration with age and groups was significant. The control group rats of young age had the highest and diabetic group rats of young age had the lowest HDL-cholesterol concentration, while the control group of old age had the lowest and diabetic treated group had the highest HDL-cholesterol concentration.

Triglycerides (mg/dL)

Overall mean of triglyceride concentration of young and old age rats of all the groups are tabulated in table 1. The overall mean of triglycerides of groups irrespective of age was significant while the overall mean of triglycerides irrespective of groups was non-significant of young old rats. The interaction of triglycerides concentration with age and group was significant. The overall mean of triglyceride concentration of diabetic group rats was the highest and the of diabetic treated group rats was the lowest, irrespective of their age. Triglyceride concentration of diabetic group of young rats was higher than that of control and diabetic treated group, while diabetic treated group had the lower concentration as compared to control and diabetic group of young rats, and same sequence of increase and decrease concentration was found in old group rats.

LDL-cholesterol

Mean LDL concentration of control diabetic and diabetic treated group rats of both young and old age are tabulated in table 1. The overall mean of LDL-cholesterol concentration of all groups irrespective of age and overall mean of young and old rats irrespective of groups was significant. While the interaction LDL-cholesterol concentration with age and group was non-significant. The overall mean concentration of LDL of diabetic group rats was the highest while that of control group was the lowest irrespective of age. The overall mean of old rats was the higher as compared to young rats.

SGOT (U/mL)

Mean SGOT concentration of control diabetic and diabetic treated group rats of both young and old age are tabulated in table 1. The overall mean of SGOT concentration of group irrespective of age was significant and that of young and old rats Irrespective of groups was non-significant. The interaction of SGOT concentration with age and groups was significant. The overall mean of SGOT concentration of diabetic treated rats was higher than the control and diabetic group rats irrespective of age. The control diabetic treated group of young rats had the higher concentration as compared to diabetic rats. While in old rats of diabetic and diabetic treated group, the SGOT concentration was higher than the control group of old rats.

SGPT (U/mL)

Mean SGPT concentration of control, diabetic and diabetic treated group rats of both young and old age are tabulated in table 1. The overall mean of concentration of group irrespective of age and overall mean of concentration of young and old rats irrespective of groups was significant. While the interaction of concentration with age and group was non-significant. The concentration of overall mean of diabetic rats was higher than the control and treated group rats irrespective of age. The concentration of overall mean of young rats was higher than the old rats irrespective of their groups.

DISCUSSION

Diabetes mellitus comprise of a group of syndromes characterized by hyperglycemia, altered metabolism of carbohydrates, lipids and proteins (Deepa *et al*., 2013) Presently, the diabetes is almost become a serious public health problem, predominantly in developed countries. This shows the necessities and the importance of more efficient and alternative anti-diabetic drugs and their systemic studies to manage diabetes (Govindappa *et al*., 2015) Stimulation in insulin discharge from pancreatic *Beta cells* is one of the major mechanisms of anti-diabetic activity by natural products (Balekari and Veeresham, 2015). A range of managements including natural or plant derived medicines, dietary supplements and synthetic drugs are used to control the diabetes and associated complications (Trojan-Rodrigues *et al*., 2012) The first step towards this goal is the *in-vitro* .and *in-vivo* anti-diabetic activity assay.

Alloxan is the most widely employed agent for the induction of diabetes in experimental animal model. Alloxan evokes a sudden rise in insulin secretion in the presence or absence of glucose which appeared just after alloxan treatment. This particular alloxan-induced insulin release occurs for short duration followed by complete supression of islets response to glucose even when high concentration of glucose is present (Rohilla and Ali, 2012) Alloxan establishing a redox cycle for the generation of Reactive oxygen species (ROS) (Fröde and Medeiros, 2008). and superoxide radicals and these ROS causes the fragmantaion of DNA of pancreatic islets (Machocho *et al*., 2012) In addition alloxn causes disturbances in intracellular calcium homeostatis, which elevates cytosolic free Ca^{2+} concentration in the *Beta cells* of pancrease. The increase concentration of Ca^{2+} ion further contributs to supraphysiological insulin release that along with ROS ultimately causes damage of *Beta*

cells of pancreatic islets (Mir *et al*., 2013). Hyperglyceia was observed after 3 days of Alloxan induction (Whitty, 2015) and consistently produced the main characteristics of diabetes mellitus including polydipsia, polyphagia, polyuria, decreases insulin level, weight loss and hyperglycemia (Ghadge and Kuvalekar, 2017).

The interaction of overall mean of body weight with age and groups of diabetic treated rats was lower than the control group rats in both young and old rats after two weeks treatment with *Ipomoea batatas* potato peel-off in alloxan induced diabetic rats. In the present study, the body weight of diabetic rats after two week treatment with water extract of white skin sweet potato (WSSP) peal-off was found to be significantly lower than control group rats irrespective of their days and age. The decrease in body weight was due to the less feed intake because sweet potatoes are rich in dietary fibers and have low glycemic index with reduce digestion and delays gastric emptying time.

Decrease in body weight was also due to the improvement in glucose control after treatment with WSSP (Ludvik *et al*., 2003) Furthermore decrease in body weight may also be contributed due to increased catabolism of fats and proteins and of dehydration (Hakim *et al*., 1997). The body weight of young rats in water extract treatment was lower than the old age rats might be due to the lower age and higher growing rate. So, more energy was needed for growth in addition to metabolic needs as compared to old age rats.

The overall mean of feed intake with age and groups differ non-significantly in water extracts treatment. Diabetic rats treated with water extract of white skin sweet potato peel-off had less feed intake than the control group rats irrespective of their days and age. This may be due to high fiber contents in WSSP which decrease the appetite and control the feed intake by decreasing peristaltic movement.

The feed intake of old age rats were higher than young rats that was considered to be due to the higher body weight of old rats. Because old rats had high body weight, so they consumed high feed as compared to young rats which possess less body weight.

Water intake of diabetic rats increased after treatment with water extract irrespective of their age. This increase in water intake was due to the reason that the excretion of large volume of glucose in urine and the dehydration leads to polydipsia and thus large water intake (Mealey and Oates, 2006). Secondly the WSSP extract was rich in minerals and minerals concentration was also increased due to diabetes. Excretion of large amount of minerals in urine leads to dehydration and ultimately polydipsia. Moreover excessive thirst and frequent urination are the characteristic symptoms of type-I diabetes (Roche *et al*., 2005).

Water intake of old rats of water extract treatment showed higher water intake than young ones that might be due to that old rats have less control on diabetic symptoms compared to young rats. This difference in water intake of water treatment group might be due to possibilities that more minerals were extracted out in water extract due to inorganic nature. The overall mean of old rats was higher than the young rats in water extract treatment which indicated that young rats were more effective to the WSSP dose as compared to old rats.

Persistent hyperglycemia leads to increased risk of vascular complications, long term malfunction, and harm of different organs. Decrease in glucose level of young rats was significantly lower than the old rats of water extract treatment. The overall mean of diabetic treated group rats of water extract treatment was non-significantly different from the diabetic control group. The decrease in blood glucose level was shown by WSSP at 4 g/d dose rate by increasing insulin sensitivity (Miyazaki *et al*., 2005) and WSSP extract showed glucose lowering effect at that dose rate which was the research dose rate i.e. 4 g/day (Ludvik *et al*., 2004). This decrease in blood glucose concentration by WSSP extracts was due to the presence of high concentration of carotenoids in WSSP. It was suggested that high level of carotenoids intake decreased both blood glucose level and insulin resistance in body (Suzuki *et al*., 2002).

Alteration in the metabolism of glucose, fats, and protein are observed in diabetes mellitus. By obtaining optimal glycosylated protein level it is likely to mitigate complications e.g. retinopathy, nephropathy and neuropathy. Abnormal management of dietary proteins is due to deficiency of insulin or insulin action. The overall mean of total proteins of diabetic group rats was lower than diabetic treated rats of water extract treatment. While the overall mean of young and old rats and the interaction of total protein with age and groups was non-significant. The decrease in protein of diabetic rats was the leading symptom of diabetes (type I and type II) due to decreased uptake of amino acid in peripheral tissues. Decrease in ATP production causes decreased formation of protein and diabetes also contributed to catabolic reaction via destruction of structural protein (Rajkumar *et al*., 1991). So it is concluded that when glucose level decreased, it leads to increase in protein level by decreasing the diabetic symptoms.

The overall mean of water extract treatment group with age was non-significant. In diabetic rats the albumin concentration decreased than the normal. After 2 week treatment there was a significant increase in albumin concentration in diabetic treated rats of both young and old age. Serum albumin concentration significantly

decreased due to increased excretion of albumin in urine in diabetes mellitus (Viberti *et al*., 1994) So increase in the albumin concentration indicated the effectiveness of dose and decrease in glucose concentration. The reason for less albumin increase in old rats was the age factor as the excretion of albumin was age related (Bakala *et al*., 1995).

In diabetic water extract treated rats an increase in globulin concentration was observed as compared to diabetic rats. Level of globulin increases because of increase in total protein and albumin. The overall mean of young rats was lower than old rats. It may be due to the fact that young rats use more protein for their growth as compared to old rats while the interaction of age and group was non-significant.

Peoples suffering from diabetes are at a higher risk of developing coronary heart disease. Alteration in lipid/ lipoprotein metabolism in diabetics results in enhanced threat of atherosclerosis. The elevated atherosclerosis threat is due to overall increase in total cholesterol concentration. In overall mean of diabetic water extract treated rats there is a decreasing pattern in cholesterol level was observed. These results are similar to previous studies that decrease in cholesterol level was also due to weight loss after giving treatment of WSSP (Ludvik *et al*., 2004). Sweet potato was the most effective binder (30%) of cholesterol than 28 fiber samples of more common tropical fruits and vegetables, so its binding affinity also contributed to the decrease in cholesterol level after treatment (Lund, 1984). The overall mean of cholesterol level of young rats was lower than the old age rats. This difference in cholesterol level in young and old rats may be due to their age effect. The interaction of age and groups was non-significant in water extract treatment.

Increased triglyceride and low HDL-cholesterol concentration leads to atherosclerosis. Essential role of increased serum triglyceride concentration contribute for the risk of Coronary heart disease in type 2 diabetes. HDL posses reverse cholesterol transport so plays a defensive function against atherosclerosis. HDL by stimulating lipoprotein lipase is also associated with metabolism of triglyceride rich lipoprotein (Ludvik *et al*., 2002). The overall means of groups of young/old rats of HDL-cholesterol was non-significant in water extract treatment while the interaction of young and old rats was significant and this interaction increased after treatment in diabetic treated groups. That increase in concentration of HDL-cholesterol was proportional to the decrease in total cholesterol level after treatment with WSSP. The overall mean of LDL-cholesterol of old rats in water extract treatment was higher than the young rats. This was due to higher cholesterol level ratio in old rats. While the interaction of old and young rats with groups in water extract treatment was non-significant. The low level of HDL-cholesterol in old rats might be due to the less control of diabetes and increased glucose level leads to decrease in HDL-cholesterol (Tan, 1986). The overall mean of LDL-cholesterol was significantly decreased after two week treatment with water extract treatment. Similar decease in LDL-cholesterol was studied in previous study after WSSP treatment of diabetic patients (Ludvik *et al*., 2002). Overall mean of TG concentration of diabetic rats decreased after water extract treatment. Oral administration for six week treatment of WSSP decreased the triglycerides (TG) concentration (Kusano *et al*., 2000) The overall mean of triglycerides of young and old rats was non-significant while the interaction of TG with age and groups decreased after treatment of diabetic rats in water extract. The overall mean of TG of young rats was lower than old age while the interaction of young and old rats with group was non-significant. TG of young was higher as compared to old because diabetes was commonly associated with lipid abnormality and increased in TG concentration.

Oxidative alteration of LDL contributes a considerable role in development of atherosclerosis in arterial wall. Moreover, diabetic patients demonstrate irregular antioxidant status protein and oxidation of low density lipoprotein. Diabetes mellitus is associated with distended lipid per-oxidation which contributes to long term tissue injury. Characteristic lipid disorder in patient with diabetes is characterized by reduced level of HDL cholesterol and superior quantity of small, thick LDL particles (Kusano *et al*., 2001). The overall mean of SGPT concentration decrease in diabetic rats after treatment with water extract of WSSP peel off. Due to decrease in diabetic symptoms, the level of SGPT also decreased after treatment with water extract. The overall mean of young rats was higher than old rats. The interaction of SGPT with age and groups was not significant.

Diabetes affects the metabolic actions of liver as it is a metabolic disorder Amplified actins of liver enzymes e.g. aspartate aminotransferase (AST) and alanine aminotranferase (ALT) are markers of hepatic injury. Insulin resistance, metabolic disorder and type 2 diabetes mellitus are linked with elevated action of these markers. Increased in liver function tests (ALT&AST) was practical in type 2 diabetic patients. ALT and AST enzymes concentrations are powerful interpreter of diabetes. Increased level of ALT shows fatty changes in liver. Fatty changes results in development of type 2 diabetes mellitus. The overall mean of SGOT concentration decrease in diabetics after treatment with water extract of WSSP peel off. This high value may be due to other parallel effect of diabetes b/c sweet potato has no toxicity (Ludvik *et al*., 2002) The overall mean of SGOT of young and old rats was not significant. Interaction of SGOT of old rats with group was also non-significant and the interaction of young rats with groups increases significantly after treatment.

The formation of modified proteins and lipids are called as advanced glycation end products (AGE's). These advanced glycation end products (AGE's) have potential to damage cells. Furthermore, AGEs increase reactive oxygen species production and damage antioxidant system. Under some oxidative situation the formation of AGEs is enlarged (Jaleel *et al*., 2005) The results of glycation level of water extracts treatment of WSSP peel-off shows similar pattern. The interaction of glycation level with age and groups was significantly increased in diabetic rats after treatment with water extract of WSSP peel-off. Similarly the overall mean of glycation level of diabetic treated rats was lower than the diabetic control group rats in water extract treatment. *In vitro* experiments indicated that the sweet potato vinegar inhibited the formation of advanced glycation end product (Ye *et al*., 2004) In diabetes the non-enzymatic glycation of proteins was increased (Jaleel, Halvatsiotis *et al*., 2005, Szabo, 2009) After treatment of sweet potato peel-off water extract decrease in glycation level of diabetic rats was observed. This difference may be due to their age differences. In current study, WSSP peel-off showed beneficial effect in young (3-4 month) and old (upto 1 year) wistar rats. In addition to mitigate blood glucose level it also reduced LDL cholesterol, triglycerides, total cholesterol, and protein glycation level. Increase in HDL-cholesterol after treatment was also shown. WSSP peel-off had also shown positive results on plasma enzymes (SGPT and SGOT), globulin, albumin, and total protein concentration. Further research would be needed in order to purify the anti-diabetic components and it should be available in compact dose form for all diabetic patients.

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