Evaluating the effect of *Acacia modesta* leaves extract on blood glucose, serum Lipids, liver and kidney functions in diabetic and non-diabetic rats

Nisar Khan, Mushtaq Ahmed, Rahmet Ali Khan, Shahtamas Khan, Sana Gul

Department of Biotechnology, University of Science and Technology Bannu, 28100, KPK, Pakistan
Rahmatgul_81@yahoo.com, Ahmed213@yahoo.com

Abstract: Objective: In the present study a traditional medicinal plant, *Acacia modesta* leaves extract was assessed in alloxan induced diabetic rats to reveal the anti-diabetic activity and serum lipids, hepatic and renal functions, total bilirubin and total proteins. *Acacia modesta* leaves extract was administered orally (200 and 400 mg/kg body weight) to six groups of albino rats for three weeks. The effects of Acacia modesta on blood glucose were studied and the levels of serum lipids, liver enzymes and kidney parameters were estimated and compared with standard drug glibenclamide. **Results:** Treatment with *Acacia modesta* leaves extract and glibenclamide resulted in significantly reduced blood glucose in 200 mg/kg body weight (75.674%) and 200 mg/kg body weight (73.565%) in comparison with controls. There was a significant decrease in serum lipids, liver enzymes and kidney parameters in both low and high doses when compared to diabetic controls. The results suggest that the methanol extract of *Acacia modesta* leaves possess anti-diabetic activity by decreasing the plasma blood glucose level, with subsequent increase in body weight. The serum profiles of lipids (triglycerides, cholesterol, LDL and serum HDL levels), liver (ALT, ALP and total bilirubin), kidney (Urea and Creatinin) and total protein also significantly ($p<0.05$) recovered to normal level with extract. The results indicate the possibility that this could be effective plant extract to retard or prevent diabetes and the development of complications of diabetes.

[Nisar Khan, Mushtaq Ahmed, Rahmet Ali Khan, Shahtamas Khan, Sana Gul. **Evaluating the effect of *Acacia modesta* leaves extract on blood glucose, serum Lipids, liver and kidney functions in diabetic and non-diabetic rats.** *Biomedicine and Nursing* 2016;2(1): 39-45]. ISSN 2379-8211 (print); ISSN 2379-8203 (online). http://www.nbmedicine.org. 7. doi:10.7537/marsbnj02011607

Key words; Allaxon, *Acacia modesta*, anti-diabetic, serum lipids, kidney profile, liver enzymes, total bilirubin

1. Introduction

Diabetes Mellitus (DM) is a complex metabolic disorder that involves abnormalities in both insulin secretion and its action in peripheral tissue. DM has become a global epidemic and a major health concern in both developing and developed countries. As a disease, it kills more individuals on a per annum basis than AIDS and breast cancer combined (1). Diabetes mellitus is recognised by chronic hyperglycaemia and is associated with long term damage, dysfunction and failure of various body organs by involvement of micro and macro-vasculature (2). The micro-vascular involvement mostly effects retina, renal glomeruli and peripheral nerves, while macro-vascular involvement results in dyslipidemia, formation of reactive oxygen species (ROS) (3). A large number of anti-diabetic medicines are available in the pharmaceutical market for diabetes and its related complications; however, currently no effective therapy is available to cure the disease. WHO Expert Committee on Diabetes has recommended investigating traditional herbal medicines (4) and in this regard more than 400 medicinal plant species have been compiled. These herbal products are gaining popularity in developing and developed countries due to their lesser side effects and low cost (5). *Acacia modesta* is a species of Acacia and its common name is Khaor, Palosa, a member of Fabaceae family (subfamily-Mimosaceae), is a perennial tree commonly found in Pakistan. It is used as miswak (tooth brush) for teeth cleaning in various parts of India and Pakistan due to its antimicrobial properties. The main active ingredients are alkaloids, flavonoid, saponins, tannin, and phenolic compounds (6). The extracts of *Acacia modesta* root have bacteriostatic effect against some gram negative and gram positive bacteria, its seeds, leaves and bark are used to cure asthma, cough, chronic bronchitis, fever, as well as in abdominal pain, dysentery, gonorrhea and rheumatism (7). One study conducted in India has shown the hypoglycemic activity of seeds of Acacia modesta as a part of compound recipe in normal albino rats but its hypoglycemic effect in diabetes remains to be investigated (8). Recently, it has been demonstrated that the protective effect of *Acacia modesta* is most likely because it's free- radical scavenging activity (6). Owing to the diverse medicinal applications and reported hypoglycemic effects of some members of genus Acacia. The current study however attempts to explore the biochemical effect of *Acacia modesta* on blood sugar, serum lipids and liver and kidney functions. So, the present study is performed to study the proposed mechanism beyond anti-hyperglycemic

influences of *Acacia modesta* on alloxan induced diabetic rats.

2. Material And Methods

This study was conducted from November 2012 to November 2013 at the Deptt. of Biotechnology, university of Science and Technology Bannu. *Acacia modesta* leaves were collected from the vicinity of district Bannu and its species was confirmed in the Department of Botany, Bannu University. *Acacia modesta* extract was prepared in 70% aqueous methanol after crushing and macerating *Acacia modesta* leaves.

Animals

Healthy albino rats of either sex were selected for the study. The study was carried in accordance with the rules and regulation laid by the Institutional Animal Ethics Committee. The study was conducted on 36 healthy both male and female albino rats weighing 170–175 gram. The rats were housed in steel cages with 12 hours dark-light cycle, at a temperature of 25–30 °C. The animals were on free water access and standard pellet diet throughout the experiment.

Induction of diabetes

The animals were fasted overnight (14–16 hours) before induction of diabetes by alloxan. The animals were injected 150 mg/Kg body weight (b. wt.) fresh alloxan intraperitonealy, prepared by dissolving in normal saline solution. On 3rd post-treatment day, diabetes was confirmed by measuring fasting blood glucose levels. The rats who did not show fasting blood glucose levels >200 mg/dl, or showed any other symptomatic illness were excluded from the study. Blood glucose levels of the rats were estimated by collecting the blood samples from the tail vain by using Accu-check Glucometer.

Experimental design

In this experimental study, a total of 36 rats were divided into 6 equal groups 1, 2, 3, 4, 5, and 6. Group-1 consisted of normal rats, group-2 diabetic control rats, group-3 diabetic rats treated with glibenclamide, group-4 and group-5 diabetic rats treated with *Acacia modesta* extract and group-6 non-diabetic rats treated with extract. The rats of group-3 were given single morning dose of 10 mg/Kg b. wt., glibenclamide, group-4 and group-5 were given single dose of 200 mg/Kg b. wt. and 400 mg/Kg b. wt., *Acacia modesta* extract respectively and Group 6: non-diabetic rats received extract of *Acacia modesta* at dose of 200 mg/kg b. wt. by intragastric tube for 3 weeks. Blood sample were collected from the vein of the tail tip at 0 day, 7th day, 14th day and 21st day for blood glucose levels. On day 21 of treatment, after 8 hours of fast, all animals were scarified by decapitation. Blood were withdrawn for serum lipids (total cholesterol, triglyceride, LDL and HDL), renal function tests (urea and creatinine), liver enzymes (ALT and ALP), total bilirubin and total protein. These tests were measured after mixing serum with respective auto reagents and absorbance was taken by homogeneous Enzymatic Calorimetric methods using Auto Analyzer.

Statistical analysis

Results were analyzed statistically on the Graph Pad instat version 5 software using Student's t test for paired data and one way ANOVA using Dennett's Multiple Comparison Test. A difference in the mean values of $P<0.05$ were considered significant. (9).

3. Results

Effect on body weight and blood glucose

The body weight and glucose concentrations of rats treated with AM leaves extract and alloxan are presented in (Table-1) and (Table-2). There was an increase in the body weight in the normal control rats (4.96%) and rats treated with 200 mg/kg extract (9.125%) and 400 mg/kg (4.637%), while there was a decrease in the body weights of rats treated with alloxan (–12.151%). A statistically significant reduction in weight ($p<0.05$) was noticed in alloxan induced diabetic rats as compared to normal controls. The rats treated with AM extract or glibenclamide showed a significant increase in their body weight as compared to diabetic control rats. However, gain in weight between rats treated with plant extract was found to be more significant. There was more significant ($p<0.05$) increase (11.764%) in the body weight of non-diabetic rats treated with 200 mg/kg extract as compared to normal control rats. Glucose concentrations remained unchanged in the normal group at the end of the experiment. In rats treated with alloxan, there was a significant increase in blood glucose level compared to normal. AM leaves extract at the doses of 200 mg, and 400 mg/kg, significantly attenuated the alloxan-induced elevated blood glucose concentration by 75.674% and 73.969%, respectively.

Effect on serum lipids

Table-4 shows comparison of lipid profile (total cholesterol, triglyceride, high density lipoprotein (HDL) and low density lipoprotein (LDL) between the normal and experimental rats. Compared with normal rats, diabetic rats showed significantly raised levels of serum total cholesterol, triglyceride and LDL levels but found decreased levels of HDL. Treatment of diabetic rats with AM leaves extract (200, and 400 mg/kg b. wt.) resulted significant ($p<0.05$) reduced levels of triglyceride, total cholesterol and LDL as compared to the diabetic controls, while the levels of

HDL were increased significantly. Only the levels of triglyceride and LDL in diabetic rats treated with glibenclamide showed a significant difference (p<0.05) from that of the diabetic controlled rats. Within the two treatment (200, and 400 mg/kg b. wt.) groups, the difference in the levels of total cholesterol, TG, LDL and HDL were found to be non significant. (Table-1) shows comparison of body weight between control and experimental rats.

Effect on kidney biochemical marker level

The results of the effect of AM extract 200, and 400 mg/kg b. wt. on the serum biochemical marker level of kidney including urea, creatinine and serum total protein levels in non-diabetic and diabetic rats are shown in (Table-5), respectively. The results showed that the serum total protein levels obtained for diabetic rats were significantly (p<0.05) lower, compared to the levels obtained for non-diabetic rats. It was also recorded that treatment of rats with these doses of the extract produced a dose-dependent increase in serum total protein concentration among and within the non-diabetic and diabetic animals, compared with the corresponding non-treated animals. The results also showed that a highly significant (p<0.05) decreases in urea, creatinine and increases in serum total protein levels associated with activities of kidney in diabetic rats when compared to non-diabetic rats. Administration of *Acacia modesta* leaves extract significantly (p<0.05) erased the toxicity caused by diabetes at serum biochemical marker level of kidney. This gives a clear sign that diabetic condition may cause damages or some disorders to the functional state of the kidney. Treatment with AM showed a significant (p<0.05) dose-dependent decrease in the urea, creatinine and increase in serum total protein levels and recovered the activities of kidney in both diabetic and non-diabetic rats when compared to the control. However, the dose-dependent effects of AM on the serum biochemical marker level of kidney of diabetic and non-diabetic rats were significantly different when compared to the control. Treatment of non-diabetic rats with extract (200 mg/kg body weight) also showed significant (p<0.05) effect on serum level of urea and total protein as compared to the control group. The results obtained from this study showed that AM extract may be used to protect the kidney against diabetes-induced damages or disorders.

Effect on liver enzymes

The changes in the activities of hepatic enzymes: Alkaline phosphatase (ALP), alanine aminotransferase (ALT) and total bilirubin of study groups are presented in Table 4. An obvious increase in the total bilirubin, ALP and ALT level was noticed in diabetic animals. Both doses of extract lead to significant reversed changes in the activities of liver enzymes ALP, ALT and total bilirubin. The results showed that extract at dose 400 mg/kg to diabetic rats to have stronger effect on liver enzymes compared with dose 200mg/kg. The results obtained from this study showed that AM extract may be used to protect the liver tissues against diabetes-induced damages or disorders.

4. Discussion

In DM, insulin insufficiency or tissue resistance impairs carbohydrate, protein, lipid metabolism resulting in hyperglycemia. The same has been elucidated by numerous biochemical and molecular studies conducted in the last century (10). Elevated blood glucose level causes damage of blood vessels with an eventual coronary artery disease, stroke, nephropathy, neuropathy, etc. In the present studies, albino rats developed diabetes after receiving a single dose of alloxan, a known β-cytotoxin that damages insulin secreting β-cells of islets (11). The Alloxan induced diabetic rats receiving *Acacia modesta* leaves extract showed a significant reduction of their fasting blood glucose levels in comparison to diabetic control rats. Administration of extract at dose 200 mg/kg and dose 400 mg/kg led to a major reduction in fasting serum glucose about 75.678% and 73.969% respectively, at the end of experiment (Table-2). Our results are consistent with the study conducted by Singh KN *et al* (12) who reported that seeds of *Acacia modesta* decrease the elevated blood glucose levels in normal albino rats. Recent Phytochemical studies have shown that the hypoglycemic effect of these plants is due to presence of tannins and polyphenols having anti-oxidant property (13). Polyphenols inhibit α-glucosidase enzyme from the intestine and initiate release of insulin from the β-cells of pancreas (14, 15). Based on decreased glucose levels in rats treated with *Acacia modesta* extract, it can be suggested that the possible mechanism of action of aqueous methanol extract from *Acacia modesta* could be related to anti-oxidant activity that aids to recovery from impaired glucose metabolism through release of insulin from the pancreas. Many closely related plants of this genus have also showed hypoglycemic effects. Ray et al (16) conducted a study in albino rats to see the effect of *Acacia catechu* and concluded that extract has hypoglycemic effect in both normal and diabetic rats. This study is in favor of our study; Ahmad et al. (17) conducted a study showing the anti-diabetic effects of a closely related plant, *Acacia nilotica* in diabetic rabbits. Its hypoglycemic effect is mediated through action of flavonoid.

Alloxan is associated with a significant loss of body weight as compared to normal controls. The muscle wasting with loss and degradation of the

structural proteins is probably due to hyperglycemia (18). When these diabetic rats were treated with *Acacia modesta* extract (200 mg/kg and 400 mg/kg body weight), a significant gain in body weight was noticed as compared to diabetic control rats (Table-1). The increase in body weight is probably due to protein anabolic effect and reversal of gluconeogenesis and glycogenolysis by the improvement of insulin secretion as a result of insulinotropic effect of *Acacia modesta* extract (19). Another possible reason of increase in body weight may be the presence of tannins and polyphenols in the *Acacia modesta* leaves (20).

The level of serum lipids usually increases in diabetes, and such elevation represents a risk factor for coronary heart disease. Hypertriglyceredemia is a common abnormality in DM in addition to hyperglycemia. In diabetics, the concentration of LDL cholesterol is significantly different from that seen in non-diabetics as in our study. Diabetic patients typically have smaller, dense oxidized LDL particles, which may increase atherogenicity, even if the absolute concentration of LDL cholesterol is not elevated (21). A significant increase in triglyceride (TG) levels and an increasing trend towards levels of total cholesterol in diabetic rats as compared to normal controls was shown in the present study. The administration of aqueous methanolic extract (200 mg/kg and 400 mg/kg body weight) from *Acacia modesta* effectively reduced TG, total cholesterol and LDL levels in Alloxan induced diabetic rats (Table-4). The results are consistent with Sochar *et al* (22) and Arkkila *et al* (23) who showed significant changes in lipid metabolism in the serum of diabetics. The increase in TG and total cholesterol levels in Alloxan induced diabetic rats may be due to lack of insulin under diabetic conditions. The decrease in TG level may be due to increased insulin release from the β-cells of pancreas that activates lipoprotein-lipase enzyme that hydrolysis TG (24). Our study showed an increase in HDL and a decrease in LDL levels, protecting the diabetics from atherosclerotic disease probably due to control of diabetes by the *Acacia modesta* extract as seen in a study done by Maciejewski *et al* (25).

Drugs, viral infections, alcohol and other chemical agents may damage the liver. The injury to liver is characterized by hepatic necrosis and lipid per-oxidation resulting in elevated levels of liver enzymes and bilirubin (26). An increase in the ALT, ALP and bilirubin activities was recorded in diabetic rats in comparison with normal rats, indicating an altered liver function in diabetic condition. *Acacia modesta* extracts significantly ($p<0.05$) controlled ALT, ALP and total bilirubin in the diabetic rats. In diabetic animals a change in the serum enzymes is directly related to changes in the metabolism in which these enzymes are involved. The increased levels of transaminases which are active in the absence of insulin because of increased availability of amino acids in diabetes (27, 28) are responsible for the increased gluconeogenesis and ketogenesis observed in diabetes. In the present study, the *Acacia modesta* leaves extracts significantly ($p<0.05$) decreased total bilirubin, ALT and ALP enzyme activities (Table-3). Hence, the improvements noticed in the levels of these enzymes are as a consequence of an improvement in the carbohydrate, fat and protein metabolism. The restoration of total bilirubin, ALT and ALP levels after treatment also indicates a revival of insulin secretion. Treatment of non-diabetic group with extract (200 mg/kg body weight) also showed significant effect on serum level of ALT and total bilirubin as compared to control group. Results of non-diabetic treated group indicated that the extract can be used to control the increased level of ALT in non-diabetic condition (Table-3).

The status of kidney function may be provided by analysis of blood (29). During normal condition the serum level of urea and creatinine remains at normal unless there is pathogenesis. The high levels of urea and creatinine indicate the kidney injuries induced through diabetes and chemical treatment (30, 31, 32). Our results of diabetic group showed increased in blood urea, creatinine and decreased level of total protein indicating renal injuries. The level of serum creatinine does not rise until at least half of the nephron of kidney is destroyed or damaged (33). The data of this study showed that plant extract of *Acacia modesta* leaves significantly ($p<0.05$) restored urea and creatinine and increased the level of serum total proteins in blood as shown in (Table-5). Treatment of non-diabetic group with extract (200 mg/kg body weight) also showed significant ($p<0.05$) effect on serum level of urea and total protein as compared to the control group. Results of non-diabetic treated group indicated that the extract can be used to control the increased level of urea in non-diabetic condition (Table-5). The present study suggests that *Acacia modesta* leaves extract possess significant hypolipidemic and hypoglycemic activity. Oral administration of *Acacia modesta* was found to be safe because no apparent toxicity was observed under the experimental conditions it did not cause organ toxicity (liver, heart and kidney). Although to confirm the adverse effect of *Acacia modesta* leaves extract biochemical studies were carried out showed that *Acacia* did not affect other blood chemistry parameters.

Table 1: Effect of extracts of *Acacia modesta* leaves (AML) on body weight of diabetic rats

Groups					
	0th day	**7th day**	**14th day**	**21st day**	**% Variation**
Normal	170±2.35	174.16±0.27	176±0.65	178.66±1.98	4.96%
Diabetic Control	171.83±4.69	167.16±2.35	159.83±1.31	151±5.72	12.151%
10mg/kg Glibenclamide	175.83±0.48	174.5±0.185	175.83±0.48	173.33±0.77	1.432%*
200mg/kg AML + alloxan	170.33±4.0	176±1.165	181.33±1.3	185.66±3.66**	9.125%**
400mg/kg AML + alloxan	168.5±9.475	170±0.8	174.81±3.68	176.5±4.52*	4.637%*
200mg/kg AML alone	170±7.875	178±3.875	185±0.375	190±2.125*	11.764%**

Data represented as mean ± S.D values of 6 animals each. *p<0.001, indicate significance at **p<0.05 (Dunnett t-test); diabetic control was compared with the normal, extract and standard treated groups were Compared with the diabetic control.

Table 2: Effect of *Acacia modesta* leaves (AML) extract on blood glucose levels

Groups					
	0th day	**7th day**	**14th day**	**21st day**	**% Variation**
Normal	70.66± 0.227	70.16±0.02	70±0.1	70±0.1	0.938%
Diabetic Control	222.5±9.85	240±1.1	246.16±1.98	260.16±8.98	15.605%
10mg/kg Glibenclamide	249.8±41.43	189.16±11.11	140.3±13.32	88.5±39.32**	95.359%**
200mg/kg AML + alloxan	242.8±27.79	227.3±20.24	169.3±75.54	109.5±38.86**	75.674%**
400mg/kg AML + alloxan	212.6±30.32	170.5±9.187	127.6±12.262	97.8±27.162*	73.969%**
200mg/kg AML alone	97±1.125	96±0.625	94±0.375	92±1.375*	5.291%*

Data represented as mean ± S.D values of 6 animals each. Indicate significance at *p<0.001, **p<0.05 (Dunnett t-test); diabetic control was compared with the normal, extract and standard treated groups were compared with the diabetic control.

Table-3 Effect of *Acacia modesta* leaves (AML) extract on liver function tests;

Treatment	**ALT (u/l)**	**Bilirubin (mg/dl)**	**ALP (u/l)**
Control	32±0.88	0.69±0.071	198.5±10.638
Diabetic Control	56±8.91	2.11±0.50	251.8±45.41
10mg/kg Glibenclamide	36±0.75	0.59±0.112*	121.8±13.37**
200 mg/kg AML + alloxane	27±2.92*	0.6±0.108*	81±1.86
400 mg/kg AML + alloxane	28±2.51*	0.6±0.108*	104±8.80*
200 mg/kg AML alone	26±3.33**	0.6±0.108*	128±10.84**

Data represented of 6 animals each as mean ± S.D values. *, ** indicate significance at *p<0.001, **p<0.05 (Dunnett t-test); the normal was compared with the diabetic control, the diabetic control were compared with the standard and extract treated groups.

Table-4 Effect of *Acacia modesta* leaves (AML) extract on Serum lipids:

Treatment	**Total Cholesterol (mg/dl)**	**Triglycerides (mg/dl)**	**High density Lipoprotein (mg/dl)**	**Low density Lipoprotein (mg/dl)**
Control	91±10.98	131±0.5	56±9.8	86.6±19.97
Diabetic Control	171.5±25	261.3±58.77	437.8±1.34	113.8±7.89
10mg/kg Glibenclamide	125±4.21*	102±12.46*	41.5±3.13**	41.8±40.09*
200mg/kg AML+alloxane	96±8.75*	56±33.04**	39±2.23*	56±33.38**
400mg/kg AML+alloxane	107±3.83*	124±2.62*	50±7.15*	36±42.33*
200 mg/kg AML alone	103±5.62*	105±11.12**	32±0.89*	52±35.19**

Data represented of 6 animals each as mean ± S.D values. *, ** indicate significance at *p<0.001, **p<0.05 (Dunnett t-test); the normal was compared with the diabetic control, the diabetic control were compared with the standard and extract treated groups.

Table -5 Effect of *Acacia modesta* leaves extract (AML) on serum urea, creatinine and total protein of rat:

Treatment	Serum Urea (mg/dl)	Serum Creatinine (mg/dl)	Serum total protein (mg/dl)
Control	49.1±0.22	0.66±0.102	7.3±0.383
Diabetic Control	126.3±34.3	2.18±0.51	5.2±0.47
10mg/kg Glibenclamide	30±8.76*	0.57±0.138*	6.2±0.065*
200mg/kg AML+alloxane	40±4.29*	0.9±0.004*	6.7±0.138*
400mg/kg AML+alloxane	30±8.76*	0.5±0.167*	6.5±0.057*
200 mg/kg AML alone	19±13.68**	0.7±0.085*	6.3±0.024*

Data represented of 6 animals each as mean ± S.D values. *, ** indicate significance at *p<0.001, **p<0.05 (Dunnett t-test); the normal was compared with the diabetic control, the diabetic control were compared with the standard and extract treated groups.

Conclusion

This investigation supports that *Acacia modesta* leaves extract have anti-diabetic activities and effective in decreasing concentrations of blood glucose serum lipids, liver enzymes and kidney biochemical marker levels both in diabetic and non diabetic rats. Results demonstrate positive effect on liver and kidney function. Administration of extract likely represents a safe and effective means to reduce the risk factors for the development of diabetic complications. More research on *Acacia modesta* leaves extract should be undertaken because it has new potential management of diabetes, kidney and liver disorders.

Acknowledgement

Author is thankful to Chairman Department of Biotechnology, Bannu University for his marvelous guidance, constant encouragement and for providing necessary facilities to carry out this research work. Author is also thankful to Dr Rahmat Ali Khan for providing the research assistance. The authors' work reported herein is not supported by any agency.

References

1. Ernst K. From the President. Diabetes Educator 1995; 21: 398.
2. Hink U, Li H, Mollnau H, Oelze M, Matheis E, Hartmann M, et al. Mechanisms underlying endothelial dysfunction in diabetes mellitus. Circ Res 2001; 88:14–22.
3. Cosentino F, Eto M, Paolis PD, Loo B, Bachschmid M, Ullrich V, et al. High glucose causes upregulation of cyclooxygenase 2 and alters prostanoid profile in human endothelial cells, Role of protein kinase C and reactive oxygen species. Circulation 2003; 107: 1017–23.
4. WHO Expert Committee on Diabetes Mellitus Second Report Series 646, Geneva; 1981; p. 61.
5. Roman-Ramos R, Flores-Saenz JL, Alarcon-Aguilar FJ. Antihyperglycemic effect of some edible plants. J Ethnopharmacol. 1995; 48: 25–32.
6. Khan, N., Ahmad, M., Khan, R.A., Khan, S.T., Muhammad, N. 2014. World Applied Sci J 30(3): 286-293.
7. Hongxiang, H., George T., and Vay, L.W. (2009). Hypoglycemic herbs and their action mechanisms. Chinese Medicine. 4, 11-16.
8. Nukatsuka M, Yoshimura Y, Nishida M, Kawada J. Importance of the concentration of ATP in rat pancreatic beta cells in the mechanism of streptozotocin-induced cytotoxicity. J Endocrinol 1990; 127: 161–5.
9. Snedechor GW, Cochran WG. Statistical methods Ames, I ìA. Iowa State Univeristy Press, 1994.
10. Davis EA, Soong SA, Byrne GC, Jones TW. Acute hyperglycaemia impairs cognitive fnction in children with IDDM. J Pediatr Endocrinol Metab 1996; 9: 455-461.
11. Szkudelski T. The mechanism of alloxan and streptozotocin action in B cells of rat pancreas. Physiol Res 2001; 50: 536-546.
12. Sing KN, Chandra V, Barthwal KC. Hypoglyceamic activity of Acacia arabica, Acacia benthami and Acacia modesta leguminous seed in normal albino rats. Ind J Physiol Pharmacol. 1975, 19; 167-8.
13. Kumar R. Chemical and biochemical nature of fodder tree tannins. J Agriculture Food Chem 1983; 31:1346–66.
14. Liu X, Kim JK, Li Y, Li J, Liu F, Chen X. Tannic acid stimulates glucose transport and inhibits adipocyte differentiation in 3T3-L1 cells. Am J Clin Nutr 2005;135:165–71.

15. Tiwari AK, Madhusudana RJ. Diabetes mellitus and multiple therapeutic approaches of Phyto-chemicals: present status and future prospects. Curr Sci 2002; 83: 30–8.
16. Ray DK, Sharatchandra KH.Thokchom IS. Antipyretic, antidirrhoeal, hypoglyceamic and hepatoprotective activities of ethyl acetate extract of Acacia catechu Wild, in albino rats. Indian J Pharmacol 2996; 36, 408-13.
17. Ahmed M, Zaman F, Sharif T, Zabta M. Antidiabetic and hypolidemic effects of aqueous methanolic rxtract of Acacia nilotica pods in alloxan tnduced diabetic rabbits. Scand J Lab Amin Sc, 2008; 36, 29-34.
18. Rajkumar L, Govidarajulu P. Increased degradation of dermal collagen in diabetic rats. Ind J Exp Biol 1991; 29: 1081–3.
19. Kim JS, Jung BJ, Choi CW, Kim SC. Hypoglycemic and antihyperlipidemic effect of four Korean Medicinal plants in alloxen induced diabetic rats. Am J Biochem Biotech 2006; 2:154–60.
20. Pande MB, Talpada PM, Patel ZN, Purohit LP, Shukla PC. Note on processed babul feeding to mature Kankrej bullocks. Indian J Animal Sci 1980; 52: 798–9.
21. Lamarche B, Tchernof A, Moorjni S, Cantin B, Dagenais GR, Lupien PJ, et al. Small, dense, low density lipoprotein particles as a predictor of the risk ischemic heart disease in men; Prospective results from the Quebec Cardiovascular study. Circular 1997; 95: 69-75.
22. Socher M, Baquer NZ, Mclean P. Glucose under utilization in diabetes: comparative studies on the changes in the activities of enzymes of glucose metabolism in the rat kidney and liver. Mol Physiol 1985; 7: 51–68.
23. Arkkila PE, Koskinen PJ, Kantola IM, Ronnemma T, Seppanen E, Vikari JS. Diabetic complications are associated with liver enzyme activities in people with type 1 diabetes mellitus. Diabetes Res Clin Pract 2001; 52:113–8.
24. Lee KT, Shon IC, Kim DH, Choi JW, Kwon SH, Park HJ. Hypoglycemic and hypolipidemic effect of tectorigenin and kaikasaponin III in streptozotocin induced diabetic rats and their antioxidant activity in-vitro. Arch Pharm Res 2000;23: 461–6.
25. Maciejewski R, Rusinski P, Burski K, Figura T. Changes in glucose, cholesterol and serum lipid function levels in experimental diabetes. Ann Univ Mariae Curie Sklodowska 2001; 56: 363–8.
26. Ramachandra SS, Quereshi AA, Viswanath SA, Patil T, Prakash T, Prabhu K, Veeran GA. Hepatoprotective activity of *Calotropis procera* flowers against paracetamol-induced hepatic injury in rats. Fitoterapia 2007; 78: 451-54.
27. Bondy, P.K., James, D.F., Farrar, B.W. 1949. Studies on the role of the liver in the liver in human carbohydrate metabolism by the venous catheter technique patient with diabetes ketosis, before and after the administration of insulin. J Clin Invest (28): 1126–1133.
28. Felig, P., Marliss, E., Ohman, J.L., Cahill, C.lF. 1970. Plasma amino acid levels in diabetic ketoacidosis. Diabetes Jr (19): 727–729.
29. Khan, M.R., Rizvi, W., Khan, G.N., Shaheen, S. 2009. CCl4-induced nephrotoxicity in rats: Protective role of Digeramuricata (L.) Mart. J Ethnopharmacol (122): 91–99.
30. Abraham, P., Wilfred, G., Cathrine, S.P. 1999. Oxidative damage to lipids and proteins of the lungs, testis and kidney of rats during CCl4 intoxication. Clinical ChimicaActa (289): 177–179.
31. Srinivasan, M., Rukkumani, R., Sudheer, A.R., Menon, V.P. 2005. Ferulic acid, a natural protector against carbon tetrachloride induced toxicity. Fundament and Clinic pharmacol (19); 491–496.
32. Dalle, Donne, I., Rossi, R., Colombo, R., Giustarini, D., Milzani, A. 2006. Biomarkers of oxidative damage in human diseases. Clinic Chem (52): 601–623.
33. Doi, K., Kurabe, S., Shimazo, N. 1991. Systematic histopathology of rats with carbon tetrachloride induced hepatic cirrhosis. Laboratory Animals (25): 21–25.

3/16/2016