PREPRINT

Antidiabetic, Anti-hyperlipidemic & Hepatoprotective effect of a Polyherbal Unani formulation "Qurs Tabasheer" in STZ-diabetic wistar rats

Danish Ahmed[*ψ], Manju Sharma[¥], Alok Mukerjee[¶], Raja Kamal Kant [ψ], Vikas Kumar [ψ]

Corresponding Author: [ψ] *Danish Ahmed, Department of Pharmaceutical Sciences, Faculty of Health Sciences, Sam Higginbottom Institute of Agriculture, Technology & Sciences (SHIATS)-Deemed University, Uttar Pradesh, Allahabad, INDIA,

Telephone: +919369589923,
Email- danish.ahmed@shiats.edu.in, danishjhamdard@gmail.com,

[¥] Department of Pharmacology, Faculty of Pharmacy, Jamia Hamdard, New Delhi, INDIA,
Email- manjusharma72@gmail.com

[¶] United Institute of Pharmacy, UCER, Naini, Allahabad, INDIA
Email- alokmukerjee2107@gmail.com

Abstract

The present study was undertaken to evaluate the antihyperglycemic ,antihyperlipidemic and hepatoprotective effect of a traditional unani formulation "Qurs Tabasheer" in streptozotocin (STZ) induced diabetic wistar rats. Up till now no study was undertaken to appraise the efficacy of "Qurs Tabasheer" in the diabetic rats. Qurs Tabasheer is a unani formulation restraining preparations from six various herbs namely Tukhme Khurfa *(Portulaca oleracea seed),* Gule Surkh (*Rosa damascena flower*)*,* Gile armani (*Arminium bole),* Gulnar *(Punica granatum flower),* Tabasheer *(Bambusa arundinasia dried exudate on node),* Tukhme Kahu *(Lactuca sativa Linn seed)*. Effect of Qurs Tabasheer was assessed in STZ (60 mg/kg, i.p single shot) induced diabetic wistar rats. STZ produced a marked increase in the serum glucose, Total Cholesterol, LDL cholesterol, VLDL Cholesterol, Triglycerides and trim down the HDL level. We have weighed up the effect of Qurs Tabasheer on hepatic activity through estimating levels of various liver enzymes viz. Hexokinase, Glucose-6-Phosphatase and Fructose-1-6-biphosphatase in STZ diabetic wistar rats. In STZ-induced diabetic wistar rats level of Hexokinase, and Glucose-6-Phosphatase was decreased to a significant level while the level of fructose-1-6-biphophatase was augmented. Therapy with Qurs Tabasheer for 30 days to STZ-induced diabetic rats significantly reduces the level of serum glucose, total cholesterol, triglycerides, glucose-6-phosphatase and fructose-1-6-biphosphatase, while magnitude of HDL cholesterol and hexokinase was amplified. Antihyperglycemic, antihyperlipidemic activity of Qurs Tabasheer suspension in STZ- induced wistar rats was found to be more effective than oral hypoglycemic drug Glimepiride.

Keywords: Diabetes mellitus, Hepatoprotective, Hyperlipidemia, Polyherbal, Qurs Tabasheer, Unani formulation.

Introduction:

Diabetes mellitus is rapidly reaching epidemic proportions in many areas of the world. According to WHO an estimated 80 million people in India will suffer from diabetes by the year 2030 [1]. The purported Indian Phenotype proposed to have inimitable biochemical as well as clinical idiosyncrasy in the Indians of Asia. This assemblage of abnormalities is well thought-out to be one of the foremost factors contributing to raise pervasiveness of type 2 diabetes in Indians of Asia.

Diabetes mellitus is linked with prejudice glucose metabolism that escorts to a rise in free radical production and augmentation in the lipoprotein and triglyceride levels. Experimental diabetes in animals has endowed with extensive approach into the physiologic and biochemical clutter of the diabetic state. Many of the disorder have been characterized in hyperglycemic animals. Significant changes in lipid metabolism also crop up in diabetes [2]**.** Deregulation of hepatic enzymes such as hexokinase, glucose-6-phosphatase, fructose-1-6-biphosphatase occurs in diabetic rats [3] [4].

Alternative and traditional medicines have scores of advantages over the conventional medicines. Despite many conventional therapies are present in the market to curtail the diabetes and its complications, traditional medicines such as Unani formulations has unambiguous advantage of being almost free from adverse effects. Diversity, flexibility, easy accessibility, broad continuing acceptance in developing countries and increasing popularity in developed countries, relative low cost, low levels of technological input, relative low side effects and growing economic importance are some of the positive features of traditional medicine (WHO 2002).

Polyherbal formulation more willingly than monotherapeutic herbal formulation are frequently used because of the synergistic effect. Many polyherbal formulation such as Okudiabet [5] Diashis [6] , Diasulin [7] etc. have revealed their efficacy and potency against diabetes.

Qurs Tabasheer is composed of 6 (six) medicinal plants (Table 1). Till now no research has been reported on Qurs Tabasheer's hypoglycemic, antihyperlipidemic and hepatoprotective activity on STZ- induced diabetic rats. The present exploration was undertaken to study the effect of Qurs Tabasheer, a polyherbal unani formulation on alterations in plasma glucose, glycated heamoglobin (A1c), total cholesterol, triglycerides, hexokinase, glucose-6-phosphatase, fructose-1-6-biphosphatase along with weight variation in STZ-induced diabetic wistar rats. The results obtained from Qurs Tabasheer were weighed against standard drug Glimepiride.

S.No.	**Botanical name**	**Hindi name (common name)**	**Family**	**Part used**	**Composition* (%)**
1	*Portulaca oleracea*	Tukhme Khurfa	Portulacaceae	*Seed*	10
2	*Rosa damascena*	Gule Surkh	Rosaceae	*Flower*	10
3	*Armenian bole*	Gile Armani/Silicate of magnesia			10
4	*Punica granatum*	Gulnar	Lythraceae	*Flower*	10
5	*Bambusa arundinacea*	Tabasheer	Poaceae	*Dried exudate on node)*	50
6	*Lactuca sativa Linn*	Tukhme Kahu	Asteraceae	*Seed*	10

Table 1. Qurs Tabasheer (Composition & concentration)

*Stock sample used in the experiment

Materials and Methods

Preparation of test Unani formulation:

The six medicinal plants stated above were obtained from different sources viz. Bio India Biologicals (BIB) Corporation, Hyderabad, India, Green Earth Products Pvt. Ltd. New Delhi, India, & Raj Hans Products, Mumbai, India. The plants were confirmed by experts from Department of Botany, Sam Higginbottom Institute of Agriculture, Technology & Sciences. The preferred parts of the six medicinal plants were kept and dried in an incubator for about 24 hours at 37°C. The dried parts were then trampled and minced in the ratio specified in Table 2. This polyherbal formulation was prepared according to the procedure specified by Pandy *et al*. [8]

Reagents and Chemicals

Streptozotocin solution was prepared by dissolution in 0.1 M citrate buffer (pH = 4.5).

Streptozotocin (STZ) was procured from Sisco Research Laboratory, Pvt. Ltd. Mumbai, India. Glimepiride was generous gift from Ranbaxy Laboratories, Gurgaon, India. Chemical including ethyl alcohol, trichloro acetic acid, diethyl ether, and citric acid was purchased from CDH, Mumabi, India. All other chemicals and bioassay kits were purchased from Sigma Chemical Company Inc. (St. Louis, MO, USA) and Span Diagnostics, Surat, India.

Animals

Male Wistar rats, weighing between 190-230g, were procured from Central Animal House Facility, Animal Husbandry Department, Sam Higginbottom Institute of Agriculture, Technology & Sciences Allahabad. All animals were provided with standard pellets and drinking water ad libitum. All experiments and protocols described in the current study are in accordance with guidelines of Committee for the Purpose of Control and Supervision on Experiments on

Animals (CPCSEA). Water used for the solution preparation and glassware washing was passed through an Easy Pure UF water purification unit (Thermolyne Barnstead, NH, USA).

Induction of Diabetes

Wistar rats were injected intraperitoneally with STZ dissolved in 0.1 M citrate buffer (pH=6.5) at 60 mg/kg. Animals of control group were received equal volume of vehicle. After 48 hours of STZ injection, blood glucose of the induced rats was estimated. The rats depicting FBG ≥ 230 mg/dL considered to be diabetic.

Statistical Analysis

Data was put across as the mean ± SEM. For statistical analysis of the data, group means were compared by one-way analysis of variance (ANOVA) followed by Dunnett's 't' test, which was used to identify difference between groups. P value <0.05 was considered significant.

Experimental Design

In our experiment, rats were randomized into six groups comprising of five animals each group as discussed below:

Group I: Normal control rats received citrate buffer (pH=4.5) for 28 days. (1mL/kg p.o.)

Group II: Normal control rats received Qurs Tabasheer (200 mg/kg p.o.) and continued for 28 days

Group III: STZ-diabetic rats received STZ (intraperitoneally, 60 mg/kg, single shot)

Group IV: Qurs Tabasheer treated diabetic rats received Qurs Tabasheer (50 mg/kg p.o.) and continued for 28 days.

Group V: Qurs Tabasheer treated diabetic rat received Qurs Tabasheer (100 mg/kg p.o) and continued for 28 days.

Group VI: Qurs Tabasheer treated diabetic rat received Qurs Tabasheer (200 mg/kg p.o) and continued for 28 days.

Group VII: Glimepiride treated diabetic rats received Glimepiride (1 mg/kg p.o.) and continued for 28 days.

Drug was given to the rats with the help of oral catheter every morning. At the finish of the drug treatment all the animals was faster overnight but allow free access to water. Rats were divided into the above seven groups for 28 days of study. The duration of drug treatment was set to be 28 days for the reason that 28 days were the threshold in our pilot experiments.

Results

To evaluate the effect of Qurs Tabasheer on STZ-induced diabetes mellitus rats, several biochemical estimations were carried out in all groups of experimentally induced diabetes rats for the estimation of plasma glucose, serum cholesterol, serum triglycerides, glycated heamoglobin (A1c), hexokinase, glucose-6-phosphatase and fructose-1-6-biphophatase. (TABLE). The following pharmacological effects were observed:

Effect on Glycemic control

The mean blood glucose level in rats fed on normal diet (normal control wistar rats, group I) was almost invariable throughout the experimental study. In unison, the blood glucose level of normal control rats treated with Qurs Tabasheer kept on normal diet (group II) was close to the normal control rats. On the contrary, the blood glucose level of STZ- treated wistar rats (STZ-diabetic control) was increased to a significant level ($P<0.01$). When STZ-induced diabetic rats (FBG≥230 mg/dL) was treated with Qurs Tabasheer with dose of 200 mg/kg (group VI), lowering in blood glucose was observed to maximum as compared to the dose of 50 mg/kg (group IV) and 100 mg/kg (group V) respectively (FIG 1).

Effect on the levels of Plasma Insulin

Plasma insulin levels of STZ-induced diabetic rats was significantly lower as compared to the normal control (group I) and Qurs Tabasheer treated normal control (group II) rats. Qurs Tabasheer boost the level of plasma insulin in dose dependent manner. (FIG 2)

Effect on the levels of Glycated Heamoglobin (A1c)

Glycated heamoglobin (A1c) of STZ-induced treated diabetic rats was increased to a momentous level. Level of A1c was normal in the wistar rats fed with normal diet (group I) in conjunction with the normal control rats received Qurs Tabasheer with dose of 200 mg/kg (group II). When STZ-induced diabetic rats were treated with Qurs Tabasheer with dose viz. (200 mg/kg), level of glycated heamoglobin (A1c) was significantly reduced, compared to the groups received 50 mg/kg (group IV) and 100 mg/kg (group V) of Qurs Tabasheer correspondingly. (FIG 3)

Effect on the levels of Total Cholesterol

It is perceptible from figure 3 that serum cholesterol levels of untreated diabetic rats was significantly higher than those in normal rats (group I) as well as in normal control rats receiving Qurs Tabasheer (group II). Upon administration of unani herbal formulation Qurs Tabasheer (50mg/kg), (100 mg/kg and 200 mg/kg, group IV, V & VI) in the STZ-induced diabetic rats the level of serum cholesterol lowered to a considerable level with maximum effect seen in the group administered with 200 mg/kg of Qurs Tabasheer. While the group received only glimepirde (1mg/kg) (group VII) shows no significant changes in the serum cholesterol. (FIG 4)

Effect on the levels of Serum Triglycerides

The administration of Qurs Tabasheer in normal control rats shows a slight decrease in the serum triglyceride level. On contrary, level of serum triglycerides significantly increased in STZ-induced diabetic rats (group III). Upon administration of different doses of Qurs Tabasheer (50 mg/kg, 100 mg/kg & 200 mg/kg) the level of serum triglycerides subordinate to a good extent. The maximum lowering of serum triglycerides was appeared in group received Qurs Tabasheer at a dose of 200 mg/kg. (FIG 5)

Effect on the levels of Hexokinase

To evaluate the effect of Qurs Tabasheer on distressed hepatic activity, we administered Qurs Tabasheer to normal as well as in STZ-induced diabetic rats. Hexokinase level decreased in a considerable in STZ-treated diabetic rats. Administration of Qurs Tabasheer in normal rats shows little or no significant changes in the level of hepatic hexokinase. STZ-induced diabetic rats received Qurs Tabasheer shows exponential increase in the level of hepatic hexokinase. (FIG 5). Group received Glimepiride develop slight increase in the level of hepatic hexokinase (group VII). (FIG 6)

Effect on the levels of Glucose-6-Phosphatase

It is evident from figure that upon administration of STZ to wistar rats the level of glucose-6-phosphatase was declined to a considerable level. Qurs Tabasheer when administered to normal control rats shows little or no changes in the levels of glucose-6-phosphatase. STZ-induced diabetic rats received Qurs Tabasheer with the dose of 200 mg/kg (group VI) shows remarkable increase in the level of glucose-6-phosphatase when weighed against the dose of 50 mg/kg (group IV) and 100 mg/kg (group V). STZ-induced diabetic rats' administered with Glimepiride (1 mg/kg) shows a trivial boost in the level of glucose-6-phosphatase. (FIG 7)

Effect on the levels of Fructose-1-6-biphosphatase

STZ-induced diabetic rats develop high levels of Fructose-1-6-biphosphatase. Upon administration of Qurs Tabasheer to normal control rats the level of Fructose-1-6-biphosphatase does not change much. When STZ-induced diabetic rats received Qurs Tabasheer, shows significant decrease in the level of Fructose-1-6-biphosphatase with the dose of 200 mg/kg (group VI). Effect of 50 mg/kg (group IV and group V) and 100 mg/kg of Qurs Tabasheer was subordinate as compared to 200 mg/kg. (FIG 8)

Effect on weight variation

Administration of Qurs Tabasheer demonstrates weight gain in STZ-induced diabetic rats. (FIG 9)

Discussion

The cytotoxic action of Streptozotocin (STZ) is mediated by reactive oxygen species (ROS). Streptozotocin (STZ) penetrates the β-cells via glucose transporter (GLUT2) and causes alkylation of the DNA. [9] [10]**.** The alkylating activity of STZ is related to its nitrosourea motiety. [11]. According to West *et al.* [12] Streptozotocin action in β-cells is being an adjunct to distinctive amendment in blood insulin and glucose concentrations. Two hours after STZ administration, hyperglycemia develops with concomitant plunge in insulin level. After six hours, hyperglycemia develops with high levels of insulin. Finally, severe hyperglycemia develops with decrease in insulin levels [12].

In the present research exertion, the administration of Qurs Tabasheer revealed the balanced decrease in the blood glucose, serum cholesterol, serum triglycerides, & fructose-1-6-biphosphatase while showed a significant decrease in body weight, hepatic hexokinase, & glucose-6-phosphatase. (Table 2) The plausible mechanism of action of Qurs Tabasheer could be

unswerving with the evocative effect of sulfonylureas which bolster the insulin secretion by closure of the K^+ -ATPase channels, membrane depolarization and increase in Ca^{++} ions influx.

In this perspective, various medicinal plants of Qurs Tabasheer viz. *Portulaca oleracea* [13] *Rosa damasceneI* [14], *Punica granatum* [15], *Bambusa arundinacea,* [16] *Lactuca sativa Linn* [17] (ingredients of Qurs Tabasheer) have been pragmatic to show analogous effects. Body weight of Qurs-Tabasheer administered STZ-induced diabetic rats was significantly increased (Table 2, Figure 9). This effect may be due to the competence of Qurs Tabasheer to abridged hyperglycemia. Administration of Qurs Tabasheer to STZ-induced diabetic rats decreases the plasma glucose level (Table 2, Figure 1), perhaps due to the augmented quantity of insulin in diabetic rats. Additionally, Qurs Tabasheer might improve the utilization of glucose and crafts the adipose tissues more sensitive towards the insulin by enhancing the PPAR-γ dependent mRNA expression, to reduce the case of insulin resistance. In this framework, other researchers [18] have reported that *Punica Granatum* flower extract (one of the ingredients of Qurs Tabasheer) targets the PPAR-γ for plummeting insulin resistance. Many other scientists have also reported that *Portulaca oleracea, Rosa damascene, Punica granatum, Bambusa arundinacea,* and *Lactuca sativa Linn*. have noteworthy anti-hyperglycemic and glucose tolerance effect in the experimentally induced diabetic rats. The enhanced level of glycated heamoglobin (A1c) in STZ-induced diabetic rats is primarily due to the excessive production of glucose in the blood which further reacts with blood heamoglobin to construct glycated heamoglobin.[19]. Qurs Tabasheer lowers the glycated heamoglobin (A1c) in STZ-induced diabetic rats (Table 2, Figure 3). The plausible cause of reduced glycated heamoglobin is the diminution of blood glucose level.

We have reported in our present research that Qurs Tabasheer also amends the imperative glucose metabolizing enzymes in liver (Table 2). Hepatic hexokinase is a prime enzyme that converts glucose into glucose-6-phosphate. Decreased level of hexokinase STZ-induced diabetic rats can be accountable for diminished glycolysis which results in decreased utilization of

glucose for energy production. [20] **.** The Qurs Tabasheer administered STZ-induced diabetic rats significantly amplify the level of hepatic hexokinase.(Table 2, Figure 6). Increased level of hepatic hexokinase cause increased glycolysis and consequently improves the utilization of glucose. Another vital enzyme of liver that regulates the glucose metabolizing enzyme is glucose-6-phosphatase. Other scientists, depicted the enhanced activity of gluconeogenetic enzyme in diabetic states. [21]**,** [22]. Diabetes increases the activity of glucose-6-phosphatase [23] . The increased activity of glucose-6-phosphatase was depicted in the STZ-induced diabetes mellitus rats (Table 2). Raised amount of Administration of glucose-6-phosphatase enhances the production of fats from carbohydrates. [24]**.** Qurs Tabasheer significantly reduces the level of glucose-6-phosphatase (Figure 7). Activity of Fructose-1-6-biphosphate was considerably raised in STZ-induced diabetic rats (Table 2). Qurs Tabasheer lowers the activity of this gluconeogenetic enzyme to a considerable extent (Figure 8).

Plasma insulin levels in STZ-induced diabetic rats were diminished significantly (Table 2) Plasma insulin levels were found to be increased a substantial level in Qurs Tabasheer treated diabetic rats (Figure 2). This increase may be a corollary to the decreased level of the glucose-6-phosphatase and fructose-1-6-biphosphatase.

Earlier researches have demonstrated that in STZ-induced diabetic rats, insulin paucity is coupled with hypercholesterolemia and hypertriglyceridemia. As HMG Co-A reductase enzyme is accountable for the synthesis of cholesterol and insulin has an inhibitory effect on HMG-Co-A reductase. It is obvious that deficiency of insulin will improve the generation of cholesterol and triglycerides [25]. Administration of Qurs Tabasheer to STZ-induced diabetic rats decreased the level of total cholesterol and triglycerides (Table 2, Figure 4 &5). As the levels insulin has been increased in Qurs Tabasheer treated diabetic rats, which may be the outcome of decreased cholesterol and triglycerides level.

It is worth mentioning that Qurs Tabasheer efficiently trims down the levels of blood glucose, total cholesterol, triglycerides and gluconeogenetic enzymes without producing any adverse

effect viz. hypoglycemia. The results from the present study indicate the administration of Qurs Tabasheer, has significantly protective effects against STZ-induced diabetic state. This significant protection of Qurs Tabasheer may be due to synergistic effect of the constituents of the drug. The antidiabetic effect of Qurs Tabasheer was more effectual than Glimepiride. These finding strengthen the observation that naturally occurring compounds of plant origin are much more effective in controlling diabetes than synthetic oral hypoglycemics. Further, biochemical and pharmacological investigations are in progress in our laboratory to explicate the mechanism of action of the Qurs Tabasheer.

S.No	Biochemical Parameter	Normal Control	Normal Control + Qurs Tabasheer (200 mg/kg)	STZ-diabetic control	STZ-diabetic + Qurs Tabasheer (50 mg/kg)	STZ-diabetic + Qurs Tabasheer (100 mg/kg)	STZ-diabetic + Qurs Tabasheer (200 mg/kg)	STZ-diabetic + Glimepiride
1.	Fasting plasma glucose (mg/dL)	84.64±3.634	78.64±3.091	301.1±5.345	194.2±2.873*	133.8±4.149*	88.52±3.923***	101.1±4.106
2	Fasting Plasma Insulin (µU/mL)	11.22±0.2080	11.80±0.3041	2.708±0.2008	4.866±0.3105	6.890±0.1796*	9.674±0.2214**	7.430±0.2577
3.	Glycated Heamoglobin (A1c) (%)	1.594±0.07737	1.600±0.08961	3.444±0.2352	1.718±0.09896	1.874±0.09239**	2.594±0.2068***	1.878±0.04271
4.	Total Cholesterol (mg/dl)	77.98±4.946	85.60±3.832	166.8±3.133	152.6±3.320	133.9±3.762*	118.9±5.337**	164.2±5.620
5.	Triglycerides (mg/dl)	82.52±5.211	77.54±2.119	124.3±3.229	118.9±3.214	102.0±1.360**	100.9±3.313**	129.0±3.316
6.	Hexokinase (µg/mg of tissue)	148.4±1.606	142.5±1.888	102.7±1.732	107.3±1.875	128.2±3.487**	137.6±3.432***	121.2±1.511
7.	Glucose-6-Phosphatase (unit/mg of tissue)	10.27±0.1574	10.22±0.3006	15.79±0.6483	14.45±0.5288	12.99±0.5063*	10.06±0.2851***	15.08±0.5064
8.	Fructose-1-6-biphosphatase (unit/mg of tissue)	30.30±0.7938	30.04±0.8185	51.19±1.223	48.20±1.272	38.19±1.389*	34.67±1.700**	41.02±1.236
9.	Weight Variation (g)	201.8±4.664	208.0±4.713	134.5±3.681	137.2±3.374	144.9±4.532*	150.8±2.453**	155.3±2.409

Table 2: Biochemical parameters at the end of study.

The data are expressed in mean ± SEM) (n = number of animals in each group = 5). The comparisons were made by ANOVA followed by Dunnett's test.

ns-non-significant; STZ-streptozotocin

*P < 0.05 is considered as significant.

**P < 0.01 is considered as very significant.

***P < 0.001 is considered as extremely significant.

Acknowledgement: Authors are thankful to Prof. (Dr.) Mohd. Ali for his valuable phytochemical and pharmacognostical suggestions.

Author Disclosure Statement: Authors declares no conflict of interest.

References

1. Wild S, Roglic G, Green A, Sicree R, King H.Global prevalence of diabetes: Estimates for the year 2000 and projections for 2030. Diabetes Care 2004; 27: 1047-53

2. Sochar M, Baquer NZ, Mclean P: Glucose under utilization in diabetes. Comparative studies on the changes in the activities of enzymes of glucose metabolism in rat kidney and liver. *Mol Physiol* 1985, 7:51-68.

3. Effect of acute diabetes on rat hepatic glucose-6-phosphatase activity and its messenger RNA level. Liu Z, Barrett EJ, Dalkin AC, Zwart AD, Chou JY. Biochem Biophys Res Commun. 1994 Nov 30;205(1):680-6

4. Change in the lipid profile, lipogenic and related enzymes in the livers of experimental diabetic rats: effect of insulin and vanadate, Dhananjay Gupta, Jayadev Raju, Jaya Prakash R., Najma Zaheer Baquer, Diabetes Research and Clinical Practice - October 1999 (Vol. 46, Issue 1, Pages 1-7)

5. Ogbonnia S. O, Mbaka G. O, Adekunle A, Anyika E. N, Gbolade O. E, and NwakakwaN, Agric. Biol. J. N. Am., 2010, 1(2): 139-145

6. Effect of *Diashis*, a polyherbal formulation, in streptozotocin-induced diabetic male albino rats Bera Tushar K, De Debasis, Chatterjee Kausik, Ali Kazi M, Ghosh Debidas Year : 2010 | Volume: 1 | Issue Number: 1 | Page: 18-24

7. Sarvanan R & Pari L, Antihyperlipidemic and antiperoxidative effects of diasulin, a polyherbal formulation in alloxan induced hyperglycemic rats, BMC, Compliment Altern Med, 5 (2005)

8. Pandey VN, Raiagopalan SS, Chowdharry DP. An effective Ayurvedic hypoglycemic formulation. J Res Ayur Sid, 1995; 16: 1-14

9. Schnedl WJ, Ferber S, Johnson JH, Newgard CB: STZ transport and cytotoxicity. Specific enhancement in GLUT2-expressing cells. Diabetes 43: 1326-1333, 1994.

10. Thulesen J, Orskov C, Holst JJ, Poulsen SS, Short-term insulin treatment prevents the diabetogenic action of streptozotocin in rats. Endocrinology 138: 62-68, 1997.

11. Bennett RA, Pegg AE, Alkylation of DNA in rat tissues following administration of streptozotocin. Cancer Res 41: 2786-2790, 1981.

12. West E, Simon OR, Morrison EY, Streptozotocin alters pancreatic beta-cell responsiveness to glucose within six hours of injection into rats. West Indian Med J 45: 60-62, 1996.

13. Dawei Gao, Qinwang Li, and Yusheng Fan, Hypoglycemic effects and mechanisms of Portulaca oleracea L. in alloxan-induced diabetic rats , Journal of Medicinal Plants Research Vol. 4(19), pp. 1996-2003, 4 October, 2010.

14. A. Gholamhoseinian et al. Inhibitory effect of methanol extract of Rosa damascena Mill. Flowerson a-glucosidase activity and postprandial hyperglycemia in normal and diabetic rats Phytomedicine16(2009)935–941.

15. Sarah Rachel Katz et al. Punica granatum: Heuristic Treatment for Diabetes Mellitus, Journal of Medicinal Food. June 2007, Vol. 10, No. 2: 213-217.

16. Nazreen et al. Hypoglycemic Activity of Bambusa Arudinacea Leaf Ethanolic Extract in Streptozotocin Induced Diabetic Rats, Pharmacologyonline 1: 964-972 (2011)

17. R. Roman-Ramos et al. Anti-hyperglycemic effect of some edible plants, Journal of Ethnopharmacology, Volume 48, Issue 1, 11 August 1995, Pages 25–32

18. Tom H.W. Huanga et al. Anti-diabetic action of Punica granatum flower extract: Activation of PPAR-γ and identification of an active component, Toxicology and Applied Pharmacology Volume 207, Issue 2, 1 September 2005, Pages 160–169

19. L. Pari et al. Antidiabetic effect of diasulin, a herbal drug, on blood glucose, plasma insulin and hepatic enzymes of glucose metabolism in hyperglycaemic rats, Diabetes, Obesity and Metabolism, 6, 2004, 286–292

20. Latha M, Pari L. Antihyperglycaemic effect of Cassia auriculata in experimental diabetes and its effects on key metabolic enzymes involved in carbohyrdrate metabolism. Clin Exp Pharmacol Physiol 2003; 30: 38–43.

21. Baquer NZ, Gupta D, Raju J. Regulation of metabolic pathways in liver and kidney during experimental diabetes, effects of antidiabetic compounds. Indian J Clin Biochem 1998; 13: 63–80

22. Raju J, Gupta D, Araga RR, Pramod KY, Baquer NZ. Trigonella foenum graecum (Fenugreek) seed powder improves glucose homeostasis in alloxan diabetic rat tissues by reversing the altered glycolytic, gluconeogenic and lipogenic enzymes. Mol Cell Biochem 2001; 224: 45–51

23. Z.Q. Liu et al. Effect of Acute Diabetes on Rat Hepatic Glucose-6-Phosphatase Activity and Its Messenger RNA Level, Biochemical and Biophysical Research Communications Volume 205, Issue 1, 30 November 1994, Pages 680–686

24. Bopanna KN, Kannan J, Sushma G, Balaraman R. Antidiabetic and antihyperlipidemic effects of Neem seed kernel powder on alloxan diabetic rabbits. Ind. J. Pharmcol. 1997; 29: 162-7.

25. Gold AH. The effect of diabetes and insulin on liver glycogen synthetase activation. J Biol Chem. 1970;245:903–5

***Corresponding Author**: Danish Ahmed, Department of Pharmaceutical Sciences, Faculty of Health Sciences, Sam Higginbottom Institute of Agriculture, Technology & Sciences (SHIATS)-Deemed University, Allahabad, Uttar Pradesh, INDIA

E-mail: danish.ahmed@shiats.edu.in, danishjhamdard@gmail.com