

Effect of aqueous root extract of *Aristolochia indica* (Linn) on diabetes induced rats

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ABSTRACT

Aristolochia indica (Linn) commonly called Iswarmul is a rare endangered medicinal plant of India. It is reported to be stimulant, used for diarrhea and intermittent fever this plant is a remedy for, drops, loss of appetite and good for snake bite. The purpose of the present research was to evaluate the anti hyperglycemic effect of *A.indica* on blood glucose and also to evaluate its toxicity on liver function, kidney function, and diabetic related hormones like insulin and testosterone levels in allaxon induced male rats. From our findings it is confirmed that allaxon has a fair chance of leading to liver damage and the root extract of *A.indica* may have the protective action against liver damage. However kidney function seems to be normal, may be because of short time exposure to diabetes. The root extract was found to be hypoglycemic and anti diabetic in function. By this study we can conclusively state that *A.indica* may act as antidiabetic herbal drug. But more careful investigations are needed.

Keywords: *Aristolochia indica*, root extract, antidiabetic, medicinal plant, allaxon

INTRODUCTION

Diabetes mellitus is a disease characterized by chronic hyperglycaemia and glucosuria produced by an absolute or relative insufficiency of insulin. The ailment may result into the development of further metabolic and anatomic disturbances among which is Lipemia, hypercholesterolaemia, loss of weight, ketosis, arteriosclerosis, gangrene, pathologic changes in the eye, neuropathy, renal disease and coma [1,2]. Hyperglycemia and glucose intolerance are common manifestations of several types of hormonal disturbances or imbalances, of which the most important is diabetes mellitus [3]. This disease is the seventh leading cause of death in the world. Diabetes mellitus is one of the oldest diseases known to mankind and yet with the tremendous scientific advances witnessed in this century, medical science cannot claim that it knows all that needs to be known about this disease, including its management. This is the main reason for the persistent interest all over the world to explore alternative remedies. A number of reviews have been published in the last three decades on plants screened for hypoglycemic activity in India [4-20] and elsewhere [16-18]. Very recently, two exhaustive reviews have been published based on global literature survey on 150 plants and 343 plants [20] from different parts of the world. Ancient Indian physicians termed diabetes mellitus as "Madumeha" (honey urine), and it has been treated orally with several medicinal plants or their extracts based on folk medicine [19]. The pathogenesis of diabetes mellitus and the possibility of its management by the oral administration of hypoglycemic agents have stimulated greater interest in recent years [20]. Today, more than 200 traditional medicinal plants have been used for the treatment of diabetes mellitus and widely practiced in South India. Plant drugs are frequently considered to be less toxic and freer from side-effects than synthetic ones [21]. Synthetic oral hypoglycemic agents can produce a series of side-effects including hematological, gastrointestinal reactions, hypoglycemic coma, and disturbances in liver and kidney metabolisms. In addition, these preparations are not ideal for use during pregnancy [22]. Many medicinal plants are also in trouble from over harvesting and destruction of habitat. Population growth, urbanization and the unrestricted collection of medicinal plants from the wild is resulting in an overexploitation of natural resources [41]. A series of novel pyrimidine derivatives were synthesized from chalcones and evaluated for their pharmacological activities. Chalcones were

prepared by treatment of Furan-2 Carbaldehyde with different acetophenones by Claisen-Schmidt Condensation. Various Pyrimidine derivatives were prepared by reaction of Chalcone with Urea, Thiourea and Guandine HCl in ethanolic sodium hydroxide [42].

Aristolochia indica

Aristolochia indica Linn., a native of India and is commonly named as Iswar mul . It is a rare endangered medicinal plant. It is a twining herb, semiwoody, leaves are cordate or ovate, exstipulate; flowers are irregular, often offensively smelling, perianth is globose with a purple dilated and trumpet-shaped mouth with a strap-shaped brown purple appendage or lip behind; fruit is a subglobose capsule. Its roots are widely used in inflammations, biliousness, and dry cough. It is good for snake bite also. The leaf of the plant or the roots of the plant is said to be a specific antidote for cobra poisoning. It is also reported to be a stimulant, and used for diarrhea and intermittent fever. This plant is also a remedy for dropsy and loss of appetite. The present investigation attempts to evaluate the antihyperglycemic effect of *A.indica* . And also to evaluate its toxicity on liver function, kidney functions.

MATERIALS AND METHODS

Adult Male albino rats of Wister strain weighing 150-180 gms were used. Rats were divided into four groups. Namely, Control (C), Allaxon induced (DI), Allaxon induced treated with insulin (I), Allaxon induced treated with *A.indica* root extract (AI) .

Rats were injected intraperitoneally with freshly prepared solution of alloxan monohydrate in normal saline at a dose of 150mg/kg of body weight except controls. After two weeks rats with moderate diabetes that exhibited glycosuria and hyperglycemia were taken for the experiment. Previously authenticated medicinal plants were collected from Eastern Ghats of Southern India, the plant root materials were dried under shade and grinded to a coarse powder. Powdered plant materials (each 25g) were individually extracted with water (200ml) and then filtered. The root extract was given to alloxan induced rats (AI) in aqueous solution daily using an intra gastric tube for two weeks. Two weeks later the animals were sacrificed and the blood was collected from all 4 groups in tubes containing potassium oxalate. Serum was separated for the estimation of glucose, cholesterol, SGOT, SGPT, ALP, triglycerides, Urea, uric acid, insulin and testosterone. Estimations were done using standard modern methods.

RESULTS AND DISCUSSION

Diabetes mellitus is a complex disorder that characterized by hyperglycemia resulting from malfunction in insulin secretion and/or insulin action both causing by impaired metabolism of glucose, lipids and protein [23]. The chronic hyperglycemia of diabetes is associated with long term damage, dysfunction and failure of various organs [24]. In diabetic rats, the utilization of impaired carbohydrate leads to accelerate lipolysis, resulted in hyperlipidemia [25,26]. Despite the presence of known antidiabetic medicine in the pharmaceutical market, diabetes and the related complications continued to be a major medical problem. Recently, some medicinal plants have been reported to be useful in diabetes worldwide and have been used empirically as antidiabetic and antihyperlipidemic remedies [27-32]. Antihyperglycemic effects of these plants are attributed to their ability to restore the function of pancreatic tissues by causing an increase in insulin output or inhibit the intestinal absorption of glucose or to the facilitation of metabolites in insulin dependent processes.

Allaxon is a substance that induces “chemical diabetes” in a wide variety of animal species by damaging the insulin secreting pancreatic β -cell, resulting in a decrease in endogenous insulin release [33, 34]. Numerous studies demonstrated that a variety of plant extracts effectively lowered the glucose level in alloxan-induced diabetic

Animals In the present study Diabetes induced group showed significantly elevated levels of glucose and cholesterol as allaxon is capable of destroying pancreatic beta cells and result in non availability of insulin to the cells. When such groups are treated with insulin, blood glucose, restored to normal as expected. Allaxon induced rats showed significant increase ($p < 0.05$) in the levels of glucose, triglycerides and SGOT (mean of 151.5 mg/dl, 202 mg/dl, 159.75 U/L) (Table-1). It was also noted that *A.indica* capable of restoring the blood glucose, cholesterol, triglycerides to normal and showing strong hypoglycemic activity. The exact mechanism in reducing blood glucose level is not well understood. But the probable cause of reduction of blood glucose might be due to increased uptake of glucose peripherally and increased sensitivity of insulin receptor. In accordance to the present finding some author also reported reduction of blood glucose following administration of insulin.

A.indica could play a role in repairing the damage of pancreatic beta cells and promoting insulin synthesis thereby lowering the level of plasma glucose. *A.indica* might have increased the glucose utilization in diabetic rats by promoting insulin secretion in pancreas. The activities of SGOT and SGPT are cytosolic marker enzymes reflecting

hepatocellular necrosis as they are released into the blood after cell membrane damage. Therefore, we used the activities of GOT, GPT in the circulation as indicators of hepatic damage. In the present study, all treatment groups with experimental plant extracts effectively reduced plasma GOT, GPT activities in diabetic rats, suggesting that the aqueous extracts of experimental plants may prevent hepatic injury associated with diabetes.

As per the result, elevated level is an indication of cellular leakage and loss of functional activity of cell membrane in liver by alloxan. Lower level of enzyme content in serum was observed in *A.indica* treated group. This is a definite indication of hepatoprotective action of root extract. The increases in plasma lipid, TC and TG levels occur in diabetes, which is related with significant changes in lipid metabolism and structure [35]. Although abnormalities in cellular cholesterol metabolism could be partly responsible for the changes in the plasma cholesterol levels in diabetes, the precise mechanisms underlying these enzymatic changes have yet to be elucidated [36, 37]. Several plant constituents are known to reduce TG [38] which is usually increased in the serum of diabetes [39]. Such a significant increase in TG may be due to the lack of insulin under diabetic condition, while insulin activates the enzyme lipoprotein lipase and hydrolysis TG under normal condition. In the present study, the administration of aqueous extracts from experimental plants does not effectively reduced TG in alloxan-induced diabetic rats. This may be due to short exposure period. Diabetes Mellitus also causes renal damage due to abnormal glucose regulation, including elevated glucose and glycosylated protein tissue level, haemodynamic changes within the kidney and oxidative stress. Urea and uric acid are organic waste products produced during the breakdown of aminoacids. Creatinine is generated in the skeletal muscle tissue by the breakdown of creatinine phosphate. Their increased level in serum is an indication kidney disorder. It was found that urea, creatinine and uric acid levels were normal in all the experimental groups. Many oral hypoglycemic agents are normally metabolized or cleared by the kidneys and so accumulate in uraemic patients thus increasing the risk of hypoglycemia and toxicity [40]. Our results on the creatinine, urea and uric acid are very close to normal range and are not significant. Alloxan induced rats showed significantly reduced levels of insulin (mean of 4.57 U/L) and testosterone (mean of 60.75mg/dl). The oral administration of root extract caused an increase in the insulin and testosterone levels though not statistically significant.

The result shows the normalizing effects of *A.indica* on hepato cellular damage and suppression of gluconeogenesis. Hypoglycemic action may be through potentiation of pancreatic secretion of insulin from beta cells or due to enhanced transport of blood glucose to the peripheral tissues. This was clearly evidenced by the increased level of insulin in diabetic rats treated with AI. Testosterone has been reported to play a major role in the regulation of fluid dynamics of the testis. Male female reproductive alteration has been widely reported with diabetes including testosterone production. *A.indica* has been used as remedy for sterility. It is proved from the result, that it can restore the testosterone level to normal there by increasing the potency. Since small number of animals was used in the present study, some more experimental and clinical trials should be conducted to evaluate the efficacy of this drug on diabetic complications. From our findings our study confirmed that alloxan has a fair chance of leading to liver damage and the root extract of *A.indica* may have the hepatoprotective action and can act as potent anti diabetic herbal drug. But more careful investigations are needed to testify its safety.

Table- 1 Effect of aqueous root extract of *A. indica* on glucose, cholesterol, triglycerides, SGOT, SGPT, ALP, Urea creatinine, Insulin and Testosterone of control and experimental animals

Parameters	Control	Induced (DI)	Insulin (I)	<i>A.indica</i> (AI)
Blood glucose Mg/dl	104±5.55	181±2.49*	96.25±1.08	105±4.04
Cholesterol Mg/dl	140±5.51	127.25±3.64	113.5±2.51	106±2.13
Triglycerides Mg/dl	122.75±11.8	202±1.81*	131±3.91	135.75±2.88
SGOT U/L	49.5±4.24	159±5.64*	147±4.45*	64.2±3.0
SGPT U/L	43.5±8.58	109.2±3.11	56.5±3.91	62.75±6.6
ALP U/L	8.05±0.7	19.42±3.23	16.4±1.16	10.47±2.57
Urea Mg/dl	40.25±1.74	38.±0.61	39.75±1.78	47.25±2.48
Creatinine Mg/dl	0.6±0.79	0.55±0.19	0.45±0.11	0.5±0.35
Uric acid Mg/dl	5.9±1.08	6.8±0.45	4.1±1.06	3.97±0.10
Insulin µ/ml	11.5 ±0.96	4.57± 0.24*	17.7 ± 5.36	9.8 ± 0.46
Testosterone Mg/dl	162± 6.04	60.95± 9.19	159.±5.36	192.5± 6.86

Values are mean ±SE for five animals in each group Values differ significantly at P<0.05, student 't' test

REFERENCES

- [1]. Andrew I.R., Scott, Belinda E., Clarke, Helen Healy, Michael D., Emden and Scott C., Bell, **2000**. *J. of the Pancreas*, **14**: 208-210.
- [2]. Swanston-Flatt, S.K., Day, C., Bailey C.J. and Flatt, P.R., **1990**. *Diabetologia*, **33**: 462-4.
- [3]. Forster, D., **1987**. Harrison's Principles of Internal Medicine, 11th ed, edited by Braunwal's *et al.*, Mc Graw-Hill Co, New York, pp: 1778.
- [4]. Mukherjee, S. K. and Mukherjee, S., **1966**. *J Res Indian Med*, 1-9.
- [5]. Mehta K.C., 1982. *Current Med Pract* 26 (10): 305.
- [6]. Aiman, R., **1970**. *Indian J Physiol & Pharmacol* 14 (2): 65. 5.
- [7]. Chaudhury, R.R. and Vohora, S. B., **1970**. Banaras Hindu University, Varanasi (India), ,p. 57.
- [8]. Karnick, C. R., **1972**. *Acta Phytother Amst* 19 :141.
- [9]. Satyavati, G. V., Raina, M K. and Sharma, M. **1976**. Indian Council of Medical Research, Vol. 1.
- [10]. Mukherjee, S.K., **1981**. *J Diabetic Asso India* 21 (Suppl) : 97.
- [11]. Nagarajan, S., Jain, H.C. and Aulakh, G.S., 1982. Regional Research Laboratory, Jammu (India), p. 584.
- [12]. Satyavati, G.V., **1984**. Indian National Science Academy, New Delhi, p. 119.
- [13]. Patnaik, G.K. and Dhawan, B.N., **1986**. Indian National Science Academy, New Delhi, p. 45.
- [14]. Das, P.K., Dasgupta, G. and Mishra, A.K. **1986**. Dhawan, B.N. (Ed), INSA, New Delhi, p. 72.
- [15]. Satyavati, G.V., Gupta, A.K., Tandon, N., **1987**. Medicinal Plants of India Vol. 2, Indian Council of Medical Research, New Delhi.
- [16]. Sever, B.O. **1980**. Oral hypoglycemic plants in West Africa. *J. Ethnopharmacol* 2 : 109.
- [17]. Handa, S.S., Chawla, A.S. **1989**. Hypoglycemic plants—A review. *Fitoterapia* 60 (3): 195.
- [18]. Atta-ur-Rahman and Khurshid Zaman. **1989**. *J. Ethnopharmacol* 26: (2):1.
- [19]. Singh, K.N., Chandra, V. and Barthwal, K.C. **1975**. *Indian J Physiol Pharmacol* 19 (3): 167.
- [20]. Singhal, P.C. and Joshi, L.D. **1984**. *Curr Sci* 53 :91.
- [21]. Nadkarni AK. **1992**. *Indian Materia Medica.*, Vol. I. 2nd ed. Bombay:
- [22]. David, E.M., 2001. *Nature*. 44:821-6.
- [23]. Momin A., **1985**. Role of indigenous medicine in primary health care. In: *Proceeding of First International Semina on Unani Medicine*. New Delhi, India.
- [24]. Altan, N. and Kilic, N., **1997**. *Gen Pharmacol*, 28:795-6.
- [25]. Scheen, J.A., **1997**. *Drug*, 54:355-368.
- [26]. Lyra, R., Oliveira, M., Lins D., and Cavalcanti, N., **2006**. *Endocrinol. Metabo*, 50: 239-249.
- [27]. Morel, D.W. and Chisolm, G.M. **1989**. *J. Lipid Res.*, 30:1827-1834.
- [28]. Granner, D.K., **1996**. Harper's Biochemistry, 24th Edn., Appletonand Lange, Connecticut, USA, pp: 586-587.
- [29]. Mitra, S.K., Gopumadhavan, S., Muralidhar, T.S., Anturlikar S.D., and Sujatha, M.B., **1996**. *J. Ethnopharmacol.*, 54:41-46.
- [30]. Shukla, R., Sharma, S.B. Puri, D. Pabhu K.M. and Murthy, P.S., **2000**. *Indian J. Clinical. Biochem.*(Suppl.), 15: 169-177.
- [31]. Bhattaram, V.A., Ceraefe, M., Kohlest, C., Vest M. and Deundorf, H., **2002**. *Phytomed.*, 9: 1-36.
- [32]. Mahomed, I.M. and Ojewole, J.A., **2003**. *Clin. Pharmacol.*, 25: 617-623.
- [33]. Hou, Z., Zhang and Wu, Z., **2005**. *Diabetes Res. Clin. Pract.*, 68: 3-11.
- [34]. Huang, T.H., Kota, B.P., Razmovski V., and .Roufogalis, B.D., **2005**. *Basic Clin. Pharmacol.Toxicol.*, 96: 3-14.
- [35]. Borch-Johnsen, K., Andersen P.K., Deckert. T., **1985**. 28-590-6.
- [36]. Grenfell, A., Watkins, P.J., **1986**. *Clin Endocrinol Metab* 15:783-805.
- [37]. Chang, W.C., Yu, Y.M., Wu, C.H., Tseng Y.H., and Wu, K.Y., **2005**. *J. Physiol. Pharmacol.*, 83: 423-430.
- [38]. Sochar, M., Baquer N.Z., and Mclean, P., **1985**. *Mol.Physiol.*, 7: 51-68.
- [39]. Retnam, V.J., Nerurkar, S.V., Gupta M.H., and Bhandarkar, S.D., **1983**. *J. Postgr. Med.*, 29: 193-200.
- [40]. Bopanna, K.N., Kannan, J., Sushma, G., Balaraman R. and Rathod, S.P., **1997**. *J.Pharmacol.*, 29: 162-167.
- [41]. Ahmad Najar.Z. and Agnihotri,S.,**2012**. *Asian Journal of Plant Science and Research*, 2 (3):220-223.
- [42]. Vishal D. Joshi, Mahendra D. Kshirsagar and Sarita Singhal. *Der Pharmacia Sinica*, **2012**, 3 (3):343-348.