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ACUTE HYPOGLYCAEMIC STUDIES OF CRUDE DRUG OF CASSIA ALATA LEAVES

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Abstract: In recent years, the phyto-therapy is gathering remarkable appreciation in treatment of chronic disorders. The herbal formulations with hepatoprotective, anticancer, antidiabetic, immunomodulatory and lipid lowering effects have widespread acceptability. At present, 'Diabetes mellitus' is one of the serious chronic disorders and has become a global health problem. The present investigation intended to confirm antidiabetic claim of *Cassia alata* Linn. (Family – Leguminosae). The hypoglycaemic activity had been assessed on normal and streptozotocin (STZ) induced diabetic Wistar albino rats using oral test drug. Drug was given in form of dried powder of leaf at the dose of 0.5 g/kg b.w. Prior to the study; the safe dose of drug was selected on the basis of acute oral toxicity testing. In case of normal rats, the test drug showed insignificant hypoglycaemic action but it reduced blood glucose concentration significantly (by 9.2%) in STZ induced diabetic rats. The drug effect was compared with that of standard hypoglycaemic drug i.e. glibenclamide (0.01 g/kg b.w.) which exhibited 20.73% decrease in blood glucose concentration. Thus preclinically, the crude drug of *C. alata* was proved to be effective hypoglycaemic agent.

Key Words: *Cassia alata*, acute toxicity, antidiabetic, streptozotocin.

INTRODUCTION

Today, the world is facing increasing risk of a serious chronic disorder called 'Diabetes mellitus'. Currently 10% of global population is suffering from it (Sammaiah and Shrivastava, 2008). Diabetes mellitus is a group of disorders caused by an inability to produce or use insulin. It shows disordered utilization and storage of proximate nutrients such as carbohydrates, proteins and lipids. Among many forms of Diabetes mellitus, Type II occurs predominantly and affects major population i.e. 90% of diabetic patients (Pullaiah and Naidu, 2003). There are various causal factors that lead to development of Diabetes mellitus, some of them are genetic constitution, hormonal imbalance, ageing, obesity, faulty food habits, physical-mental stress etc.

Till the date, insulin and synthetic oral hypoglycemic agents like sulphonylureas and biguanides are the major players in management of this disease. In spite of the availability of synthetic drugs, there is an ever-increasing demand of antidiabetic herbal options. This is because oral administration of insulin is not possible and repeated insulin injections lead to many adverse side effects. Synthetic oral hypoglycemic drugs are also proved to be equally harmful if taken for prolong period. Hence the pharmacological screening and development of new herbal antidiabetic drugs is immediate need of drug science (Harvey and Champse, 2009, Guyton and Hall, 2008, Satoskar et.al. 2007, Xia and Wang, 2006, Brunton et. al, 2006, Mukhtar et.al. 2004). Therefore through the present work, an attempt has been made to confirm antidiabetic claim of *Cassia alata* Linn.

Cassia alata Linn. is a large erect shrub that produces prominent terminal and axillary inflorescences of pretty golden yellow flowers. The plant is cosmopolitan in distribution. It grows wild and also cultivated as an ornamental plant throughout many states of India. Various parts of *C. alata* are used for diverse healing actions. According to Ayurvedic literature leaves cure vata, cough and skin diseases. They act as diuretic, cathartic, purgative, laxative, emmenagogue, abortifacient, anti-inflammatory, etc. (Kirtikar and Basu, 2001, Nadkarni, 1976, Ross, 1999, Anonymous, 1992). It is reported that leaves of *Cassia alata* are used for antidiabetic property in North East India and Jamaica (Kumar, 2002). Pharmacologically petroleum ether extract of leaves had been proved to be anti-hyperglycaemic in streptozotocin induced hyperglycaemic rats (Palanichamy and Nagarajan, 1990, Palanichamy et. al. 1988). As the tribal people have been utilizing whole drug of leaf, it felt relevant to assess hypoglycaemic action using acute treatments of crude drug of powdered leaf material.

MATERIALS AND METHODS

Plant Material

The samples of leaves of *Cassia alata* were procured from various regions of Mumbai. The mature leaves were obtained during their flowering season of May to July. The botanical identity was confirmed using the standard herbaria at Blatter Herbarium of St. Xavier's College, Mumbai (Accession No. Blat. 15515). Leaf samples were subjected to artificial drying at 40°C and ground to form powder. The powdered drug samples were moderately coarse as they were seivable through mesh no. 710 with 0.710 mm size of aperture (Evans, 2001, Anonymous, 2007). It was stored in closed, airtight containers with silica bags.

Animals

Laboratory bred male Wistar albino adult rats weighing 200–250 g were used for the studies. All the animals were procured from Haffkine Bio-Pharmaceutical Corporation, Mumbai. The animals were housed in standard environmental conditions of temperature (21±2°C), humidity (55±10%) and a 12-hour light-dark cycle. They were supplied with commercial pellet diet and water *ad libitum*. The experimental protocol was approved by the Institutional Animal Ethic Committee of R.J. College, Mumbai (Registration No. 525/02/a/CPCSEA, Approval No.- 8/5-8-2010).

Chemicals

The different chemicals used during the study were streptozotocin (Sisco Pharmaceutical Limited, Mumbai) and glibenclamide (Aventis Pharma Limited, Verna, Goa). Glucometer with Blood gluco-strips (SugarScan Thyrocare Technology Limited, Navi Mumbai), all reagents and chemicals were of analytical grade.

Acute Toxicity Study

The acute toxicity study was carried out as per the procedure given in OECD Guideline No. 420 (OECD, 2004). The male Wistar albino rats (200-250 g) were used in the study. After the sighting study, the drug of *C. alata* at the dose of 2 g/ kg body weight was given to five animals. The animals were continuously observed for 14 days for mortality and general behaviour. No change in behaviour and death were observed till the end of the study. The drug was considered safe up to the dose of 2 g/kg body weight. From the results, test drug dose of 0.5 g/kg body weight was chosen for the efficacy studies.

Induction of Diabetes by Streptozotocin

Rats were fasted for 16 hours and then a single intraperitoneal injection of 0.05 g/kg body weight Streptozotocin (STZ) in a 0.1 M Citrate buffer (pH 4.5) was given to them. The fasting blood glucose levels were checked after 3 days. The rats with stable fasting blood glucose level above 250 mg/ dl were used for the acute and sub-acute efficacy studies. After induction of diabetes all the animals were kept in laboratory on normal diet (Santhakumari et. al. 2003, Chattopadhyay et al. 1997).

Acute Study on Normal Rats

To determine the hypoglycaemic activity of the drug, normoglycaemic rats were fasted for 18 hours. They were divided into two groups of six rats each. Group I served as normal control and received orally 2% gum acacia (vehicle). Group II animals were fed with test drug of *C. alata* at oral dose of 0.5 g/kg body weight in vehicle. The samples of blood were obtained zero, second, third, and fourth hour of the treatment. The blood glucose levels were determined using a glucometer (Bhopale et. al. 2007, Neeli et. al. 2007).

Acute Study on Streptozotocin induced Diabetic Rats

For testing drug activity on diabetic rats, 18 hour fasted animals were distributed into three groups, each containing six rats. Group III served as diabetic control and was given 2% gum acacia vehicle. Group IV was fed test drug of *C. alata* at the dose of 0.5 g/kg body weight in vehicle. Dosing of 0.01 g/kg body weight of the standard oral hypoglycaemic agent glibenclamide was done for group V. The blood was withdrawn by tail vein puncturing. The samples of blood were obtained at zero, second, third, and fourth hours of the treatment. The blood glucose levels were determined using a glucometer (Bhopale et. al. 2007, Neeli et. al. 2007).

Statistical analysis

The values of all parameters are expressed as Mean ± SE in tables. The data was statistically analysed by student t test and one-way ANOVA test. P values <0.05 and <0.01 were considered to be significant (Ghosh, 2005).

RESULTS AND DISCUSSION

In acute oral toxicity study, at dose of 2 g/ kg body weight of *Cassia alata* mortality was not observed. The animal behaviour was found to be unchanged. Therefore 0.5 g/kg body weight dose of drug was considered safe and used for further investigation.

In acute treatment the effect of single dose (0.5 g/kg body weight) of test drug was checked till 4th hour of drug administration. Statistical analysis of data showed that test drug produced insignificant reduction in blood glucose levels of normal rats (Group II) as shown in Table 1.

Table No. 1 Acute study on normal rats

Gr. No.	Groups	Mean Blood Glucose Levels in mg/dl ± Standard Error			
		0 Hr	2 Hrs	3 Hrs	4 Hrs
I	Normal Control	91.83 ± 4.9	79.33 ± 5.8 (13.61)	74.17 ± 7.4 (19.24)	72.83 ± 8.9 (20.69)
II	*C. alata* 0.5 g/kg b.w.	82.33±7.8	69.67±8.0 (15.39)	62.50±10.4 (24.09)	54.67±6.7 (33.61)
t values		*1.04*	*0.97*	*0.91*	*1.63*
P values		*0.166*	*0.178*	*0.192*	*0.067*
n = 6 in each group, df = 10, Table $t_{[0.05]}$ = 2.228					
Values in parentheses indicate % reduction in glucose level as compared to 0 Hr					

In case of diabetic rats (Group IV) test drug produced significant decrease in blood glucose level at 3rd hour (5.68%) while the standard drug started action at 4th hour after drug administration. At 4th hour, diabetic rats (Group IV) and standard drug rats (Group V) exhibited quite significant (P<0.05) results with 9.2% and 20.73% reduction in comparison with diabetic control respectively. (Table 2)

Table No. 2 Acute study on diabetic rats

Gr. No.	Groups	Mean Blood Glucose Levels in mg/dl ± Standard Error			
		0 Hr	**2 Hrs**	**3 Hrs**	**4 Hrs**
III	**Diabetic Control**	481.33 ± 27	481.67 ± 11.6 (- 0.07)	486.17 ± 28.7 (- 1.00)	484.17 ± 26.1 (- 0.59)
IV	***C. alata*** 0.5 g/kg b.w.	417.00 ± 18.2	408.00 ± 17.9 (2.16)	393.33 ± 17.9 **(5.68)***	378.67 ± 18.3 **(9.20)****
V	**Standard** 0.01 g/kg b.w.	482.33 ± 5.5	460.17 ± 14.9 (4.59)	413.5 ± 13.9 (14.27)	382.33 ± 11.8 **(20.73)****
F values		*3.35*	*3.20*	*5.35*	***9.30***
$CD_{[0.05]}$				*77.68*	*72.28*
$CD_{[0.01]}$				*102.23*	*95.12*
P values		*0.063*	*0.070*	*0.018*	*0.003*
n = 6 in each group, df_1 = 2 and df_2 = 15, Table $F_{[0.05]}$ = 3.68					
Values in parentheses indicate % reduction in glucose level as compared to 0 Hr					
***** and ** indicate significant results at P<0.05 and P<0.01 in comparison with Diabetic Control Group**					

CONCLUSION

Streptozotocin produces diabetic condition in rats by selectively damaging insulin producing pancreatic β-cells. Consequently it leads to abnormally raised levels of blood glucose, triglycerides and cholesterol while protein level is considerably lowered. These conditions are analogous to human diabetes. In diabetes treatment, the utmost important factor is to maintain abnormally elevated blood glucose concentration within normal range. The present work involved preclinical study of hypoglycaemic potential of leaves of *Cassia alata* in diabetic rats. The drug was ineffective on normal rats. But in diabetic rats, the hypoglycaemic activity might be the result of the synergistic action of antidiabetic active principles of leaves. The drug showed remarkable activity in acute treatment. It can be said that, in comparison with standard oral hypoglycaemic drug, *Cassia alata* showed moderate action. It can be used in polyherbal formulations in combination with other herbal options. In conclusion *Cassia alata* leaves are effective oral hypoglycaemic agent. Further studies involving sub acute treatment and elucidation of action of active phytochemicals are in progress.

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