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## Anti Diabetic and Anti Dyslipidemia Activities of *Cleome gynandra* in Alloxan Induced Diabetic Rats

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### ABSTRACT

The study aim is to investigate the Anti diabetic an anti dyslipidemic activity of *Cleome gynandra* plant extract in alloxan-induced diabetic rats. The effects of orally administered ethanolic extract of *Cleome gynandra* on serum glucose and lipid profiles activity were examined in diabetic control and *Cleome gynandra* treated diabetic rats. While the activity of the blood glucose and lipid profiles, in the serum were assessed. The drugs were administered over a period of 7 days treatment. The *Cleome gynandra* was significantly ( $p < 0.05$ ) reduced the serum glucose, elevated dyslipidemia levels, SGOT and SGPT levels, in alloxan induced group, Metformin treated group, EECG-I group, EECG-II groups but increased the serum HDL status in all the ethanolic extract *Cleome gynandra* treated groups, compared with normal control and diabetic control. The present investigation suggested that ethanolic extract of *Cleome gynandra* was inhibits blood glucose levels and dyslipidemea in diabetes rats.

**Key words:** *Cleome gynandra*, flavonoids, blood glucose, lipid profiles, SGOT/SGPT

### INTRODUCTION

Diabetes mellitus is the most common endocrine disorder that affects more than 130 million people worldwide. It has a metabolic disorder characterized by altered metabolism of carbohydrate, lipid and protein (Das *et al.*, 1996). Uncontrolled hyperglycaemia can lead to serious damage to the various body systems (Rambhade *et al.*, 2010). The management of diabetes mellitus is considered a global problem. India will be the world's diabetes capital according to WHO Survey. It has been estimated that 2.4% of rural population and 8.4% of urban population is affected by diabetes mellitus (Sreeja *et al.*, 2003). In U.S have more than 16 million people (Chakrabarti and Rajagopalan, 2002). This disorder results deficiency of insulin and impairment of insulin action or inadequacy of insulin secretion (Kamtchouing *et al.*, 2006). The syndrome of diabetes mellitus is characterized by chronic hyperglycemia and a tendency to develop ketoacidosis (Vuksan and Sievenpiper, 2005). Alloxan is a toxic glucose analogue which selectively destroys insulin producing  $\beta$  cells in the pancreas. It is selectively toxic to insulin producing pancreatic beta cells; it accumulates in beta cells by uptake via the GLUT2 glucose transporter. Alloxan, generates free radical Reactive Oxygen Species (ROS).The beta cell toxic action of alloxan is initiated by free radicals in this redox reaction (Lenzen, 2008).

*Cleome* is the comprising 180 to 200 species of herbaceous annual or perennial plants and it has largest genus from family Cleomaceae, as a shrubs widely distributed in tropical and subtropical regions. The *Cleome* has approximately 150 species have been recorded it is restricted to tropical regions, (Raghavan, 1993). In India, fifteen species (Londhe, 2000), 12 were reported in Maharashtra (Almeida, 1998) and Kolhapur district (Yadav and Sardesai, 2002). Hooker and Thomson (1872) and Cooke (1903) put *Cleome* and other allied genera under the family Capparidaceae, however, recently all these genera are separated taxonomically and put under a separate family i.e. Cleomaceae (Hooker and Thomson, 1872; Cooke, 1903). The previous studies and until DNA studies (APG II system) found that the major Cleomaceae members are closer to Brassicaceae than Capparaceae (Stevens, 2008).

The developmental progression from C3 photosynthesis to C4 photosynthesis and this evolutionary progression are identical to Brassicaceae members (Sungwarl and Supanee, 2006; Raghavan, 1993). There is Present exploration is strictly carried out for selective species of *Cleome* viz. *Cleome chelidonii* L.f., *C. speciosa* Raf., *C. gynandra* L., *C. simplicifolia* (Camb.) Hook f. & Thoms and *C. viscosa* L. All of these species were herbs growing at same locality but in different soil types as *Cleome chelidonii* grown vigorously in moist places and also in the rocky regions, and while *C. simplicifolia* and *C. viscosa* grows luxuriantly in the black soil in rainy season. *Cleome simplicifolia* has been very short life cycle up to 3-4 months only. *C. viscosa* and *C. gynandra* grown throughout the year but more vigorously during rainy season. *C. gynandra* grows in waste water. *C. speciosa* is cultivated species growing widely in shadow places in the red soil during rainy season.

*Cleome* is called in various names such as spider flower and mountain bee plant. It has been formulated, documented, and become organized systems of medicine, such as Ayurveda, Siddha, Unani, and other systems. It has traditionally known for its different medicinal properties like paste for headache, leaf juice on earache and skin diseases. It is also used for pregnant women; Boiled leaves were used in preparation of black paint. The Species like *Cleome viscosa*, *Cleome gynandra* and *Cleome chelidonii* have been many medicinal applications, as rubifacient and counter irritant preparations and also used for rheumatism and headache (Asolkar *et al.*, 1992). *Cleome viscosa* is to be anthelmintic and also useful in fever, diarrhoea and infantile convulsion (Chatterjee and Prakash, 1991).

Although, *cleome gynadra* has been investigated for its various medicinal properties, detailed studies on its anti diabetic potential is still lacking. Keeping in view of the above, the present study was designed to determine the antidiabetic activity of *cleome gynadra* leaves in alloxan induced albino rats.

## **MATERIALS AND METHODS**

**Collection of plant materials:** Fresh leaves of *Cleome gynandra* were collected and botanically identified. The leaves were washed with distilled water, shade dried, powdered, and stored in an air tight container until future use. **Preparation of ethanolic extract-** Preparation of plant extract was done The collected fresh leaves were thoroughly cleaned with distilled water, dried well and powdered. It was soaked in absolute ethanol in cold (72 h). After three days, the extract was filtered, and then it was evaporated at 400C in cylindrical water bath for the elimination of solvent. A semisolid extract (40 g) was obtained after complete elimination of alcohol under reduced pressure. It was stored in refrigerator until used.

**Experimental animals:** White male Wister rats weighing about 150-180 g were used. They were purchased from the Mahaveer enterprises Hyderabad. They were kept under observation for about 15 days before the onset of the experiment to exclude any intercurrent infection. The chosen animals were housed in plastic well aerated cages at normal atmospheric temperature ( $25\pm 5^{\circ}\text{C}$ ) and normal 12 h light/dark cycle. Moreover, they had free access to water and were supplied daily with standard diet of known composition *ad libitum*. All animal procedures were in accordance with the recommendations of the ethical committee guidelines for Care and Use of Animals.

**Chemical agents:** Alloxan monohydrate (A) purchased from Sigma Chemical Company (St. Louis, MO USA). Cleome gynandra plant collected from chittur district of A.P, India. Metformine gift sample from Natco. Pharma. Hyderabad, India.

**Induction and treatment of diabetes:** Diabetes was induced by a single injection of alloxan ( $120\text{ mg kg}^{-1}$  i.p) after fasting for at least 16 h, in freshly prepared 1% sodium carboxy methyl cellulose, blood glucose levels were measured after 48 h alloxan administration, development of diabetes mellitus was proven by sustained hyperglycemia (diabetic rats had glycaemia  $>200\text{ mg dL}^{-1}$ ). The diabetes developed rats were selected for the study and treated with the Ethanolic extract of CG  $200\text{ mg kg}^{-1}$  per oral (p.o.), Ethanolic extract of CG  $400\text{ mg kg}^{-1}$  (p.o.) in test groups and standard group treated with Metformine  $25\text{ mg kg}^{-1}$  (p.o) for 8 consecutive days (after alloxan administration).

**Experimental design:** The rats were randomly divided into 5 groups ( $n = 6$ ) as follows:

- Group I = Control animals (sod. carboxymethyl cellulose-1%, orally)
- Group II = Diabetic animals
- Group III = Ethanolic extract of CG  $200\text{ mg kg}^{-1}$
- Group IV = Ethanolic extract of CG  $400\text{ mg kg}^{-1}$
- Group V = Metformine  $25\text{ mg kg}^{-1}$

**Biochemical evaluation:** Blood samples were collected from the retro orbital puncture of rat's on 0 and, 8th days of control, diabetic and Ethanolic extract of CG ( $200$  and  $400\text{ mg kg}^{-1}$ ) treated diabetic rats, centrifuged at 1000 rpm for 15 min. and determined the blood glucose levels (Trinder, 1969), Lipid profiles (Bucolo and David, 1973) and SGOP and SGPT (Reitman and Frankel, 1957) after 8 days treatment.

**Statistical analysis:** The data are presented as Mean $\pm$ S.D Statistical comparisons were made by one-way analysis of variance (ANOVA) and followed by Student-Neuman-Keuls test. Data were considered significant when p values were lower than 0.05.

## RESULTS

The effects of Ethanolic extract of CG  $200$  and  $400\text{ mg kg}^{-1}$  on blood glucose levels (0 and 8 days) of control, diabetic and Ethanolic extract of CG, treated diabetic rats were summarized in Table 1, respectively. Lipid profiles were represented in Table 2. The treatment with Ethanolic extract of CG  $200$  and  $400\text{ mg kg}^{-1}$  were significantly reduced the blood glucose concentration in

Table 1: Blood glucose, SGOT and SGPT levels were estimated in normal, diabetic control and treatment groups

Groups	Parameters (mg dL <sup>-1</sup> )		
	Blood glucose	SGOT	SGPT
Normal	84.3±11.2	25.0±3.0	42.6±9.0
Alloxan	357.6±62.4	56.6±8.0	86.6±8.0
Metformin (25 mg kg <sup>-1</sup> )	113.3±21.4***	32.3±3.1***	55.3±4.7***
ECG-I (100 mg kg <sup>-1</sup> )	203.6±48.6***	51.6±5.7**	76.3±3.2**
ECG-II (200 mg kg <sup>-1</sup> )	173.3±45.1***	40.6±4.2***	61.6±4.9***

Data was Mean±SD, \*\*p<0.01, \*\*\*p<0.001 vs. diabetic and control groups

Table 2: Lipid profile levels in normal, diabetic control and treatment groups

Parameters	Groups				
	Normal	Alloxan	Metformin (25 mg kg <sup>-1</sup> )	ECG-I (100 mg kg <sup>-1</sup> )	ECG-II (200 mg kg <sup>-1</sup> )
Cholesterol (mg dL <sup>-1</sup> )	84.3±1.34	304.42±6.19	120.06±3.43***	146.8±4.24**	134.48±2.39***
Triglycerides (mg dL <sup>-1</sup> )	67.76±2.3	188.19±3.33	82.66±2.47***	122.58±3.67**	115.96±3.5 ***
HDL (mg dL <sup>-1</sup> )	38.80±1.2	16.33±0.34	36.36±1.77***	28.30±2.5**	32.30±2.07 ***
LDL (mg dL <sup>-1</sup> )	124.73±1.2	218.5±05.01	119.13±4.68***	130.16±4.15**	123.98±2.87***
VLDL (mg dL <sup>-1</sup> )	14.54±0.15	36.4±01.02	12.57±0.89***	24.2±0.33**	19.29±0.70***

Data was Mean±SD, \*\*p<0.01, \*\*\*p<0.001 vs. diabetic and treatment groups

diabetics groups (p<0.001). The Ethanolic extract of CG was significantly reduced the triglycerides, LDL-Cholesterol, SGOT, SGPT and total cholesterol but increased HDL-cholesterol levels after treatment.

## DISCUSSION

Plants may act on blood glucose through different mechanisms (Chakravarthy *et al.*, 1980). Anti diabetic herbs stimulates beta cell in the pancreas and also regenerate pancreatic beta cells (Bopanna *et al.*, 1997; Chorvathova *et al.*, 1993). Fiber of plants also interferes with carbohydrate absorption, affecting blood glucose level.

Alloxan induced diabetic rats exhibited loss of body weight which is one of the threats associated with DM. Treatment with *Cleome gynandra* extract showed signs of recovery as comparable with the standard drug Metformin. Treatment with *Cleome gynandra* extract arrested elevation of glucose and lipid profiles. Administration of alloxan significantly increased the level of glucose when compared to control rats which might account for the cytotoxic effect on beta cells. Alloxan is relatively toxic to insulin producing pancreatic beta cells because it preferentially accumulates in beta cells through uptake via the GLUT2 glucose transporter. This cytotoxic action is mediated by ROS source of generation of free radical is dialuric acid, a reduction product of alloxan. The free radicals undergo dismutation to H<sub>2</sub>O<sub>2</sub>. The action of ROS increase in cytosolic calcium concentration causes rapid destruction of beta cells (Szkudelski, 2001) and decreasing the secretion of insulin which in turn increase the blood glucose level.

Treatment with *Cleome gynandra* leaf extract produced significant improvement in the levels of ALT and AST are the specific markers to assess hepatocellular damage leading to liver cell necrosis (Amacher, 1998). In present study ALT and AST activities were assessed as it is the more specific index of liver cell damage in humans (Clark *et al.*, 1973) and in experimental animals (Mitchell *et al.*, 1974). Thus lowering of these enzymes content in serum is a definite indication of

hepatoprotective action of a drug. High level of AST indicates hepato cellular damage. Activity of AST in serum was increased in alloxan intoxication *Cleome gynandra* extract afforded a significant protection against alloxan induced increase in the serum enzyme level. Ethanolic extract of *Cleome gynandra extract* may induce accelerated regeneration of liver cells by reducing the leakage of AST in to blood there by lowering its value to normal levels. ALT is more specific to the liver and a better parameter for detecting liver damage (Warnholtz *et al.*, 2001). In the present study alloxan induced ALT level was brought back to normal by the administration of *Cleome gynandra extract*. In the present study indicates that diabetic animals had prior high blood glucose level. After administration of *Cleome gynandra extract* reduced the LDL-cholesterol, total cholesterol, triglyceride levels were observed in alloxan induced rats and plant containing flavonoids and other constituents were inhibited the dyslipidemia in our study is support of further findings of Jung *et al.* (2006) reported that can inhibit lipogenesis and lower plasmatic triglycerides levels by enhancing LDL receptors expression and increasing fat bile rejection from the results of clinical studies (Knekt *et al.*, 2002). Insulin resistance was compensated by the enhanced insulin secretion, whereas persistently elevated FFAs may contribute to progressive  $\beta$ -cell failure ( $\beta$ -cell lipotoxicity) in individuals genetically predisposed to type 2 diabetes mellitus (Gu *et al.*, 1992).

*Cleome gynandra* occurs throughout the tropic and subtropic regions. It contains chemical constituents such as triterpenes, tannins, anthroquinones, flavonoids, saponins, steroids, resins, lectins, glycosides, sugars, phenolic compounds and alkaloids (Narendhirakannan *et al.*, 2005) and these are more beneficial in diabetes and its associated complications, holding hope of the new generation antihyperglycemic drug.

## CONCLUSION

Our results shown that oral administration of cleome gynandra extract has a beneficial effect on the alloxan-induces diabetes rats by reducing hyperglycaemia, dyslipidamia and improving the HDL status. This study suggests that the induction of diabetes mellitus by alloxan in rats may be prevented by flavonoids of plant constituent's administration. We hypothesized that this effect may be result of antiradical/chelatory properties of flavonoids. There is a need to continue to explore the mechanisms for anti diabetes.

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