

## Antidiabetic effects of methanolic extract of *Centella asiatica* (Linn.) on induced hyperglycemic rats

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### ABSTRACT

Experiments were conducted to study the effect of *Centella asiatica* (Linn) on induced hyperglycemic rats. The results of the present study indicates that methanolic extract of *Centella asiatica* significantly reduce the blood glucose and plasma levels in Streptozotocin induced hyperglycemic rats both in acute and chronic cases.

**Key words:** Antidiabetic, *Centella asiatica* Linn. hyperglycemic rats.

### INTRODUCTION

Diabetes is one of the major health problem affecting significant portion of the population world wide. It is recognized that 90% patients are of type II diabetes and the remainder are of type I. Although these two types of diabetes differ vastly in their pathogenesis, a most common feature is prescribed long term hypoglycemia (Anosa *et al.*, 2002) leading to macro-vascular and micro-vascular complications. Both epidemiological studies (Linu *et al.*, 1993, Klein *et al.*, 1994, and Stolk *et al.*, 1995) and clinical trials (Abraira *et al.*, 1995 and Onkubo *et al.*, 1995) have established that hyperglycemia is the principal cause of complications. The disorder is frequently associated with long term damage. Which lead to failure of organism like eyes, kidneys, heart and blood vessels.(ICMR, 2005).

In recent years, India has witnessed a rapidly exploiting epidemic of diabetes. Indeed, India today leads the world with its largest number of diabetic people in any given country. Who estimates that there are 32 million people with diabetes in India in 2005, Which projected to rise to 80 million by the year 2030. Increase in prevalence in rapid in urban areas from 2% in 1970s to 15% in 2005 and rural

areas also it is now beginning to increase (ICMR, 2005).

*Centella asiatica* (L.) (Family: Umbellierase) is a prostrate, faintly aromatic, stoloniferous, perennial herb, up to 2 m long, found plentifully as a weed in crop fields. In Ayurveda this plant is used for various medicinal purposes. It is traditionally used as a remedy for leprosy and other skin diseases, helps to improve memory, strengths the nervous system and used as a blood purifier. Looking into its medicinal importance in the present work attempts have been made to investigate the effect of methanolic extract of *Centella asiatica* (L.) on induced hyperglycemic rats.

### MATERIAL AND METHODS

#### Collection of plant and preparation of extraction

Identified and authenticated *Centella asiatica* (L.) plants were collected from Krishna river bank, Krishna District, A.P. The collected plant material was subjected to shade drying and coarsely powdered. The extraction was prepared with the methanol solvent using Soxhlet apparatus. The methanolic extract thus obtained was stored and used in the present study.

Experimental Animals: Male Sprague- Dawley rats weighing 150-200gms, bred in animal house, Andhra Lyola College, Vijayawada were used. The animals were housed in an air-conditioned animal room at 23± 2° c temperature with 12 hrs light/12 hrs dark photoperiod and maintained with free access to water and specified feeding . Glycemic conditions with regard to the animal house and cages were taken care.

#### Induction of hyperglycemia

Diabetes was induced by single i.v injection of streptozotocin (50mg/kg/bw) dissolved in citrate buffer (.01M, Ph 4.5). Induction of diabetic condition was confirmed by blood glucose estimation over a period of 3 weeks.

Biochemical investigation: Blood glucose and plasma insulin levels were determined at different time intervals. The animals were sacrificed under mild anesthesia and blood samples were collected.

Statistical Analysis: All the results are expressed mean ± SEM, and the degree of significance was determined by using students't test.

## RESULTS AND DISCUSSION

### Effect of methanolic extract on normal rats (Acute studies)

The effect of methanol extract of *Centella asiatica* 250 mg/kg/bw on fasting blood sugar was assessed in normal rats in various time intervals (2 h, 4 h, 8 h) (Table-1). It is recorded that the blood glucose levels in normal rats could not be lowered by the methanolic extract (P<0.01) as compared to the treated groups and to the pretreatment levels. While the oral administration of TBD did not cause any reduction of blood glucose levels within 4 h of treatment. The results are presented in Table-2, shows that normal rats treated with *Centella asiatica* extract did not show any reduction of blood glucose levels until the 21<sup>st</sup> day (P<0.05). The TBD (250 mg/kg/bw) also did not produce hypoglycemic activity as observed through blood glucose levels till 21<sup>st</sup> day.

### Effect of methanolic extract in streptozotocin induced diabetic rats (Chronic Studies)

The effect of *Centella asiatica* methanol extract on the fasting blood sugar levels of diabetic rats is shown in Table 3. In streptozotocin injected rats, the administration of *C. asiatica* reduced blood

**Table 1: Blood glucose levels after single administration of methanolic extract of *Centella asiatica* (500 mg/kg/bw) within 8 h in normal rats**

Treatment group	Base linevalues	2h	4h	8h
Control	79.88 ± 2.34	78.97± 2.64	79.86 ± 2.63	80.12 ± 3.22
<i>Centellaasiatica</i> (500mg/kg /bw)	83.67 ± 3.19	86.18 ± 3.14*	79.96 ± 3.28**	81.70 ± 2.9**
Tolbutamide (250mg/kg/bw)	86.24 ± 3.85	81.34 ± 3.32	79.83 ± 2.86	78.18 ± 3.57

\*P<0.05 \*\* P<0.01

**Table 2: Blood glucose levels after administration of methanolic extract of *Centella asiatica* (250 mg/kg/bw) within 21 days in normal rats**

Treatment group	Base line values	3 <sup>rd</sup> day	9 <sup>th</sup> day	21 <sup>st</sup> day
Control	83.34 ± 3.4	81.68 ± 3.23	79.96 ± 3.4	81.88 ± 3.6
<i>Centella asiatica</i> (500mg/kg/bw)	79.94 ± 4.12	80.78 ± 3.22	79.84 ±4.6)	80.65 ± 3.89*
Tolbutamide (250mg/kg/bw)	81.42 ± 3.8	79.8 ± 3.16	80.8 ± 3.3*	79.34± 2.7*

\*P<0.05

glucose levels as compared to the base line values. A significant reduction in the blood glucose levels was reported at 4<sup>th</sup> hour ( $P < 0.001$ ).

The percentage protection of blood glucose level was observed after administration of methanolic extract in diabetic rats in acute study at 2 h, 4 h, and 8 h intervals fall in to 13.7 and 23.4% for 2h and 4h, respectively. It was found to be slightly effective than TBD (22.5% at 4<sup>th</sup> hour Vs base line), which also gradually and significantly decreased hyperglycemia without reaching the same normal value obtained with *C. asiatica*.

### Chronic studies

In diabetic rats, the repeated oral administration (Long term) of *Centella asiatica* elicited a highly significant decrease of blood glucose levels, which attained normalization at the 15<sup>th</sup> day ( $P < 0.001$ ) and continued to fall until the peak effect at the 21<sup>st</sup> day. The hypoglycemic potency of TBD (250 mg/kg/bw) appeared in this study, less effective than the *Centella asiatica* at the dose of 250 mg/kg/bw. The TBD also reduced hyperglycemia at 21<sup>st</sup> day ( $P < 0.001$ ) and it reached its maximum reduction at the end of the study.

Values are Expressed in Mean  $\pm$  SEM for groups of six animals each. Values in parenthesis indicate the percentage lowering of blood sugar in comparison to the basal reading. All groups were compared with their basal values.

Values are Expressed in Mean  $\pm$  SEM for groups of six animals each. Values in parenthesis indicate the percentage lowering of blood sugar in comparison to the basal reading. All groups were compared with their basal values.

The results of present study indicates that the streptozotocin can act as an effective diabetogenic agent (Dulin and Wyse, 1969). It is a beta cell cytotoxic agent and can be used to induce diabetes in rodents (Rerup, 1970). When animals are injected with streptozotocin (65 or 75 mg/kg), it produces a significant hyperglycemic condition (Hoftiezer and Carpenter, 1973).

In the present study it has been reported that treatment with *Centella asiatica* whole plant

methanolic extract reduces the lowering of blood sugar level and it may be due to the stimulating effect on insulin release from regenerated beta cells of the pancreas or may be due to increased cellularity of the islet tissues and regeneration of the beta cells. Similar were studies made by earlier workers (Pushpa *et al.*, 1981).

It has been observed to promote insulin induced glucose uptake by the tissues restricting glucose load or by promoting unrestricted endogenous insulin action. The data presented give evidence for increased insulin secretion and beta cell number after the administration of methanol extracts of *Centella asiatica* suggesting possible regeneration or repair of the islets of langerhans in streptozotocin treated rats.

The experiments of Loubatieres (1944,1946), who established that the probable mode of action of sulphonylureas was by the release of pancreatic insulin, which was confirmed by Houssay and Penhos (1956). Unlike the sulphonylureas, GS does not enhance insulin release in normal rats under normoglycaemic (120 mg/dl) conditions, but enhances the hormone release in diabetic islets.

In the present study the *Centella asiatica* methanol extract assume significance, because of their ability to regenerate partially the damaged endocrine tissue, such that the insulin content/islet number increases by therapy. It was reported that the destruction of beta cells in juvenile, maturity-onset and experimentally induced diabetes was irreversible and this report is the first giving evidence of a reversal of the damage to the insulin producing cells by a drug. The mitotic studies are needed to confirm the appearance of new cells.

Hooper (1889) isolated a crude alcohol-soluble extract having this antisaccharogenic property and named it as gymnemic acid. The Gymnemic acid (a glycoside) was purified and characterised by Stocklin (1967) as a D-glucuronide of a hexa-hydroxy. However, this purified did not show any antidiabetic activity.

Mhasker and Caius (1930) analysed the leaves and reported the presence of 0.95%

hentriacontane, in addition to chlorophylls, phytin, resins and anthraquinone derivatives, which give a purgative effect to the leaves. None of the isolates

were found to have antidiabetic activity, although the whole leaf powder was able to bring down blood glucose levels not only in experimental diabetes.

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