Antidiabetic Effect of *Anacyclus pyrethrum* DC in Alloxan Induced Diabetic Rats

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**Abstract:** The antidiabetic effects of aqueous root extract of *Anacyclus pyrethrum* DC (Compositae) were evaluated in alloxan induced diabetic rats. The aqueous root extract of *Anacyclus pyrethrum* at a concentration of 150 and 300 mg/kg b. wt. was orally administered to Alloxan induced diabetic rats. The elevated levels of blood glucose in the diabetic rats reverted back to near normal after treatment with the aqueous root extract of *Anacyclus pyrethrum*, suggesting the antihyperglycemic effect of aqueous root extract of *Anacyclus pyrethrum*. Thus present study suggested that aqueous extract of *Anacyclus pyrethrum* have vast therapeutic application against diabetes due to its antidiabetic properties.

**Key words:** *Anacyclus pyrethrum* • Antidiabetic activity • Alloxan • Diabetes mellitus

**INTRODUCTION**

Diabetes mellitus (DM) is a chronic disease caused by inherited or acquired deficiency in insulin secretion and by decreased responsiveness of the organs to secreted insulin [1]. DM is currently one of the most costly and burdensome chronic diseases and is a condition that is increasing in epidemic proportions throughout the world [2]. Diabetes affects about 5% of the global population [3] and the management of diabetes without any side effects is still a challenge to the medical system [4,5]. Renewed attention in recent decades to alternative medicines and natural therapies has stimulated a new wave of research interest in traditional practices. The plant kingdom has become a target for the search for new drugs and biologically active “lead” compounds [6]. Ethnobotanical information indicates that more than 800 plants are used as traditional remedies for the treatment of diabetes [7, 8], but only a few have received scientific scrutiny. One of such plants is *Anacyclus pyrethrum* Merr. has a widespread occurrence in India and believed to have good antidiabetic activity.

*Anacyclus pyrethrum* (AP) is a perennial, procumbent herb, which is found throughout India. AP root contains essential oils and an alkaloid pellitorine that is intensely pungent constituent with a mixture of isobutyl amide. Traditionally, AP plant is used in traditional system of medicine and it is regarded as a tonic to the nervous system [9]. The antibacterial and anti-inflammatory activities are reported of the AP root [10,11].

*Anacyclus pyrethrum* is commonly known as ‘Akarkara’ in Ayurvedic texts, an indigenous medicinal plant widely used as medicine for promoting rejuvenation and vitality as a Vajikaran Rasayana [12]. Oral administration of the powder of this herb has been known to arouse sexual desire and improve ejaculatory time [13]. The plant *Anacyclus pyrethrum* has been reported as an effective remedy for the treatment of a variety of diseases. Apart from being designated as an aphrodisiac, *Anacyclus pyrethrum* is widely used in folk remedies for stimulating salivary glands and found useful in toothach, paralysis of the tongue and muscles of throat as well as neuralgic affections of the teeth [13]. *Anacyclus pyrethrum* root contains a colorless
crystalline acid-amide known as pellitorine (pyrethrine). It possesses an intensely pungent taste and produces a sialogogue effect [14]. The other phytoconstituents reported in the plant include N-isobutyldienedynamide and polysaccharides [15, 16].

The objective of this investigation was to ascertain the scientific basis for the use of this plant in the management of diabetes, using alloxan induced diabetic rats.

**MATERIAL AND METHODS**

**Collection of Plant Materials:** Dried roots of Anacyclus pyrethrum DC. (Akarkara) were purchased from local market of Gwalior, Madhya Pradesh, India. The plant material was identified as per the literature of Ayurveda and by local experts of herbal gardens and were authenticated.

**Preparation of Extracts:** Anacyclus pyrethrum powder about 100 gm was soaked in 5 L of ultrapure water and shaken continuously for 24 h at room temperature. The mixture was then centrifuged at 5,000 rpm for 10 min (4°C) and the supernatant was filtered (Whatman No. 1). The sample was then freeze-dried and the dried extract was stored at 4°C before use for the experiments.

**Chemicals:** Alloxan monohydrate purchased from Span Chemical Co., Mumbai and Glibenclamide purchased from Sigma Chemical Co. (Saint Louis, MO, USA). All other chemicals used in the study were of analytical grade.

**Animals:** Wistar albino rats (150–200 g) of both sex were maintained under standard environmental laboratory conditions and fed with laboratory diet and water ad libitum. All the protocols were performed in accordance with the Institutional Animal Ethical committee (IAEC) as per the directions of the CPCSEA (Committee for the Purpose of Control and Supervision of Experiments on Animals).

**Experimental Induction of Diabetes:** The rats were injected intraperitoneal with alloxan monohydrate (Span Chemical Co., Mumbai) dissolved in sterile normal saline at a dose of 120 mg/kg b.wt. Diabetes was induced by using alloxan monohydrate as diabetogenic agent. alloxan monohydrate was dissolved in sterile normal saline immediately before use. The solution was injected intraperitoneal in the dose of 120 mg/kg b. wt. in rats. The rats were kept for 15 days to stabilize the diabetic condition. Only rats with a fasting blood glucose level of at least 200 mg/dl [17].

**Experimental Design**

**Oral Glucose Tolerance Test (OGTT):** The oral glucose tolerance test (OGTT) was performed for dose of aqueous root extract of Anacyclus pyrethrum at the dose of 150 and 300 mg/kg b.wt. and blood glucose level was measured by one touch glucometer (accu-check). The glucose level was measured at the interval of 0, 30, 60, and 120 min after the administration of extracts.

The alloxan-induced diabetic Wistar rats were randomly assigned into four groups, each group contain six rats (n = 6). Group I received 0.9% NaCl; 10 ml/kg b.w. Group II received 150 mg/kg b.wt. of aqueous root extract of Anacyclus pyrethrum. Group III received 300 mg/kg b.wt. of aqueous root extract of Anacyclus pyrethrum. Group IV received Glibenclamide 10 mg/kg b.wt.

**Statistical Analysis:** All the values in the test are presented as mean±SEM. Statistical differences between the means of the various groups were evaluated by one-way analysis of variance (ANOVA) using the SPSS program followed by Student’s-t test. P values of 0.05 or less were considered to be significant.

**RESULTS**

The mean blood glucose concentration of controlled and aqueous root extract of Anacyclus pyrethrum treated animals on 0, 30, 60 and 120 min are in Table 1.

**Table 1: The Effect of aqueous root extract of Anacyclus pyrethrum on blood glucose levels in alloxan-induced diabetic rats (mg/dl)**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>0 h</th>
<th>30 h</th>
<th>60 h</th>
<th>120 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (10 ml/kg)</td>
<td>273.5±1.0</td>
<td>272.2±1.9</td>
<td>268.2±1.2</td>
<td>262.6±2.4</td>
</tr>
<tr>
<td>Aqueous root extract of Anacyclus pyrethrum (150 mg/kg b. wt.)</td>
<td>266.3±1.8</td>
<td>253.4±4.6</td>
<td>246.7±3.5</td>
<td>231.2±3.2</td>
</tr>
<tr>
<td>Aqueous root extract of Anacyclus pyrethrum (300 mg/kg b. wt.)</td>
<td>266.0±1.2</td>
<td>251.2±3.2</td>
<td>241.2±1.8</td>
<td>226.8±3.2</td>
</tr>
<tr>
<td>Glibenclamide (10 mg/kg b. wt.)</td>
<td>266.0±4.6</td>
<td>243.2±5.6</td>
<td>239.2±2.2</td>
<td>215.8±3.6</td>
</tr>
</tbody>
</table>

Values are expressed in mean±S.E.M. (n=6)
The significant reduction (p<0.01) of blood glucose was observed at 60 and 120min of the experiment. This hypoglycemic effect may be due to depression of key gluconeogenic or the increase in the levels of glucose transporters and stimulation of uptake in peripheral tissues. Another effect of these plants extract may be that it preserve the cells of islets of langerhans of β-cells functions, which results in a significant increase in insulin activity [18-21].

DISCUSSION

The study indicates that the root aqueous extract of *Anacyclus pyrethrum* possess anti-diabetic properties which suggest the presence of biologically active components. The extract might be promoting glucose uptake and metabolism or inhibiting hepatic gluconeogenesis. Result from the phytochemical analysis of *Anacyclus pyrethrum* revealed the presence of flavonoids, which has also been isolated from the other plant and found to stimulate secretion or possess an insulin-like effect [22]. In type-II diabetes, more often the cause is the lack of insulin sensitivity or resistance to insulin action at the receptor or post-receptor level, rather than lack of insulin. New drugs are required for treatment of type-II diabetes, which increase insulin sensitivity or decrease insulin resistance. Direct effect (20% increase in 30 min) in the absence of insulin indicates that the extract has either insulin-like effect on psoas muscle (skeletal muscle) or direct stimulatory effect on the enzymes involved in the metabolism of glucose. Increase of glucose uptake in the presence of insulin suggests the possibility of increased binding of insulin to receptor in the muscle or increase in the number of insulin receptors. The enhanced uptake of glucose would lead to increased utilization of glucose from the blood. Hyperglycemia results in free radical formation through various biochemical reactions. Free radicals may also be formed via the auto-oxidation of unsaturated lipids in plasma and membrane lipids. The free radical produced may react with polyunsaturated fatty acids in cell membranes leading to lipid peroxidation. Lipid peroxidation will in turn results in elevated production of free radicals [23]. Diabetes is now considered to be a vascular disease. The cost of treating the microvascular component (retinopathy, nephropathy and neuropathy) and controlling the macrovascular component is a serious drain on health resources, particularly in developing countries. It is expected that by the year 2025 India will have 57.2 million diabetics (one sixth of the world total) [24]. Besides the prevention strategies proposed [25], the use of cost-effective therapies goes a long way towards the aforementioned goal. The authors contend that patient preferences for therapies are guided by cultural heritage and by the natural environment of the region they live in.

CONCLUSION

The present study showed that aqueous root extract of *Anacyclus pyrethrum* significantly reduced elevated blood glucose level in Alloxan diabetic rats without showing any hypoglycemic effect in normal rats. Since Alloxan effectively destroys pancreatic beta cells and causes persistent hyperglycemia, the mechanism of action of *Anacyclus pyrethrum* might involve actions other than pancreatic β cells insulin release or secretion. The antidiabetic effect of the extract could be due to increased utilization of glucose by peripheral tissues, improved sensitivity of target tissues for insulin or it may be due to improved metabolic regulation of glucose. Our findings that aqueous root extract of *Anacyclus pyrethrum* significantly reduced serum triglyceride levels in alloxan diabetic rats support its long term use not only for better control of blood glucose but also for normalization of disturbances in lipid metabolism which may prevent further predisposition of the patients to cardiovascular complications. The antiatherogenic potential of the aqueous root extract of *Anacyclus pyrethrum* indicates its usefulness not only in diabetes mellitus but also in long term complications associated with diabetes mellitus. However comprehensive research is required to identify the active constituents responsible for this effect.

It could be concluded that, *Anacyclus pyrethrum* plant is safe and rich in many constituents that are pharmacologically active and can be used in various therapeutic purposes as treatment of diabetes mellitus.

REFERENCES


