ABSTRACT
The present study was carried out to evaluate the antidiabetic activity of Catharanthus roseus and Catharanthus alba methanolic flower extracts in alloxan induced diabetic rats for 14 days and to compare the results of two varieties in reducing blood glucose levels. At the beginning of this study preliminary phytochemical investigation was carried out on methanolic extracts of flowers of both varieties of Catharanthus. Alloxan (150mg/kg) was administered to male wistar albino rats to induce diabetes. These diabetic rats were grouped and treated with the methanolic flower extracts of catharanthus roseus and Catharanthus alba and glibenclamide separately for 14 days. Fasting blood glucose estimations and body weight measurements were carried out on 0th, 1st, 7th and 14th day of the experiment. On 14th day the serum was separated and analysed for biochemical parameter variations. The whole pancreas of rat were removed and subjected to histological examination. The methanolic flower extracts at high dose (400 mg/kg) exhibited significant (p<0.01) anti-hyperglycemic activity than methanolic flower extracts at low dose (200 mg/kg) in diabetic rats. The methanolic flower extracts also showed improvement in parameters like body weight and lipid profile as well as regeneration of β-cells of pancreas in diabetic rats. Histopathological studies reinforce the healing of pancreas, by methanolic flower extracts of both varieties, as a possible mechanism of their antidiabetic activity.

KEYWORDS: Catharanthus roseus, Catharanthus alba, methanolic extract, alloxan, blood glucose.
INTRODUCTION

DIABETES MELLITUS (DM)

It is a metabolic disorder characterized by hyperglycemia, glycosuria, hyperlipaemia, negative nitrogen balance and sometimes ketonaemia.\(^1\)

Diabetes was first documented by the Egyptians and is characterized by weight loss and polyuria. However, it was the Greek physician Aertaeus who coined the term Diabetes mellitus (DM). In Greek diabetes means “to pass through” and mellitus is the Latin word for honey (referring to sweetness). Diabetes is an important cause of prolonged ill health and premature mortality and claims more lives per year than HIV-AIDS with nearly one death every ten seconds.\(^2\)

Diabetes mellitus, or simply diabetes, is a group of metabolic diseases in which a person has high blood sugar, either because the pancreas does not produce enough insulin, or because cells do not respond to the insulin that is produced.

This high blood sugar produces the classical symptoms of polyuria (frequent urination), polydipsia (increased thirst) and polyphagia (increased hunger).

MATERIALS AND METHODS

Collection and Identification

The whole plants of Catharanthus roseus and Catharanthus alba were obtained from Mount Opera garden near Ramoji film city, Nalgonda district, Andhra Pradesh. The plant was identified by the department of horticulture, Acharya N.G.Ranga Agriculture University, Rajendranagar.

PREPARATION OF EXTRACT

Soxhlet Apparatus

The flowers were collected and shadow dried. The shade-dried flowers were subjected to pulverization to get coarse powder. The coarsely powdered flowers were used for extraction with methanol in soxlate apparatus. The extract was evaporated to dryness under vacuum and dried in vacuum desiccator (15.5% w/w). This extraction procedures were followed separately for Catharanthus roseus and Catharanthus alba.
PHYTOCHEMICAL SCREENING\textsuperscript{[28]}

Different qualitative chemical tests are performed for establishing profile of methanolic extract for its chemical composition. The following tests were performed on extracts to detect various phytoconstituents present in them.

MATERIALS

The whole plants of Catharanthus roseus and Catharanthus alba were obtained from Mount Opera garden near Ramoji film city, Nalgonda district, Andhra Pradesh. The plant was identified by the department of horticulture, Acharya N.G.Ranga Agriculture University, Rajendranagar.

Glibenclamide: Trade Name: Daonil 5mg tablet.

Glucose and triglyceride estimation assay kits: provided by Cogent, clinical chemistry division of span diagnostics Ltd.

Animals

Male Wistar albino rats (8–10 weeks) were obtained from the animal house of Nizam Institute of Pharmacy, Deshmukhi, Ramoji Film City, Hyderabad. Before and during the experiment, rats were fed with standard pellet rodent diet. Animals were housed in polypropylene cages and paddy husk was used as bedding material. After randomization into various groups and before initiation of experiment, the rats were acclimatized for a period of 7 days under standard environmental conditions of temperature, relative humidity, and dark/light cycle. Animals described as fasting were deprived of food and water for 16 hours ad libitum. Institution Animal Ethics Committee has approved the experimental protocol.

Oral Glucose Tolerance Test\textsuperscript{[18]}

Rats were divided into six groups containing six animals in each group. All animals fasted before treatment. Group I was kept as vehicle control which received 5% Tween 80 p.o., group II received glucose only, group III received methanolic extract 200 mg/kg, group IV received methanolic extract 400 mg/kg and group V and VI received only extracts (200 mg/kg and 400 mg/kg) only in a vehicle, respectively. The rats of group III and IV were loaded with glucose (3 g/kg, p.o.) 30 minutes after drug administration. Blood samples were collected from puncturing the retro orbital sinus just prior to drug administration, and 30, 90, 150 minutes after loading glucose. Serum glucose level was measured immediately by using glucose estimation kit.
Acute Oral Toxicity Studies\(^{[18]}\)

An attempt was made to determine LD\(_{50}\) of methanolic extract of Catharanthus Linn. (roseus and alba separately) at a dose of 2000 mg/kg p.o, in rats. The extracts were found devoid of mortality of the animals. Hence 5000 mg/kg was considered as cut off value. Therefore, the screening doses (methanolic extract 200 mg/kg and 400 mg/kg), selected for the evaluation of antidiabetic activity as per OECD guidelines No. 423.

TREATMENT PROTOCOL

The treatment protocol was followed for Catharanthus roseus and Catharanthus alba separately in the following way

**Group I:** Normal control (saline).

Received sterile water for injection 1ml/kg once a day

**Group II:** Alloxan treated control (150 mg/kg, ip)

Received alloxan 150mg/kg i.p once a day in saline

**Group III:** Alloxan + plant extract (low dose), (200 mg/kg, p.o).

Received alloxan 150mg/kg, i.p once a day and Catharanthus(roseus/alba)methanolic extract of 200mg/kg, p.o. once a day.

**Group IV:** Alloxan + plant extract (high dose), (400mg/kg, p.o).

Received alloxan 150mg/kg, i.p once a day and Catharanthus(roseus/alba)methanolic extract of 400mg/kg, p.o. once a day.

**Group V:** Alloxan (150 mg/kg, ip) + Standard drug Glibenclamide (5 mg/kg, p.o)

Received alloxan 150/kg, i.p once a day and glibenclamide 5mg/kg, p.o. once a day.

Whole plant extracts and standard drug glibenclamide (5 mg/kg) and saline were administered with the help of feeding cannula. Group I serve as normal control, which received saline for 14 days. Group II to Group V are diabetic control rats. Group III to Group IV (which previously received alloxan) are given a fixed dose whole plants extract (200 mg/kg, p.o), (400 mg/kg, p.o) for 14 consecutive days.

Induction of Diabetes in Experimental Animals

Rats were made diabetic by a single intraperitoneal injection of alloxan monohydrate (150 mg/kg).\(^{[29]}\) Alloxan was first weighed individually for each animal according to the body weight and then solubilized with 0.2 ml saline (154 mM NaCl) just prior to injection. Two days after alloxan injection, rats with plasma glucose levels 140 mg/dl were included in the study. Treatment with plant extracts was started 48 h after alloxan injection.
Collection of Blood Sample and Blood Glucose Determination

Blood samples were drawn from tail tip of rat at weekly intervals till the end of study (i.e., 2 weeks). Fasting blood glucose estimation and body weight measurement were done on day 1, 7, and 14 of the study. Blood glucose estimation can be done by one touch electronic glucometer using glucose test strips.

On day 14, blood was collected from retro-orbital plexus under mild ether anesthesia from overnight fasted rats and fasting blood sugar was estimated.\textsuperscript{30}

Biochemical determinations

Blood samples are collected in centrifuged tubes and kept aside for clotting, after clotting the sample was centrifuged at 5000rpm for 10 mins, serum was separated and used for biochemical estimations. Serum was separated and analyzed for serum cholesterol\textsuperscript{31}, serum triglycerides by enzymatic DHBS colorimetric method\textsuperscript{33}, serum HDL\textsuperscript{34}, serum LDL\textsuperscript{35}, serum creatinine, serum urea\textsuperscript{36} and serum alkaline phosphatase hydrolyzed phenol amino antipyrine method\textsuperscript{37} was estimated.

Histology

Preperation of buffered neutral formalin solution\textsuperscript{38}

Buffered neutral formalin 10% solution is the best overall fixative, therefore, strongly recommended for routine use, its contents are as follows:

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>37-40% formalin</td>
<td>100ml</td>
</tr>
<tr>
<td>Distilled water</td>
<td>900ml</td>
</tr>
<tr>
<td>Sodium phosphate</td>
<td>4.0gms</td>
</tr>
<tr>
<td>Sodium phosphate</td>
<td>6.5gms</td>
</tr>
</tbody>
</table>

Histology of pancreas was observed and compared only between diabetic control and Catharanthus varieties treated animals. At the end of the study the rats of these two groups were sacrificed. Pancreas were isolated and fixed in buffered neutral formalin neutral formalin solution, dehydrated with ethyl alcohol and then included in paraffin. Sections of 5\(\mu\)m were obtained by a microtome. Haematoxylin and eosin stain was applied to observe the histological pattern of the pancreatic langerhans. Medical pathologist gave comment on histologic observation.
Statistical Analysis
All the values of body weight, fasting blood sugar, and biochemical estimations were expressed as mean±standard error of mean (S.E.M.) and analyzed for ANOVA and t-test. Differences between groups were considered significant at P<0.01 and P<0.05 levels.

RESULTS
Phytochemical Screening
The preliminary phytochemical analysis of Catharanthus roseus and Catharanthus alba flower extracts revealed the presence of the following phytochemicals.

Table 1: phytochemical screening results.

<table>
<thead>
<tr>
<th>Phytochemical</th>
<th>Catharanthus roseus flower extract</th>
<th>Catharanthus alba flower extract</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkaloids</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Carbohydrates</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Glycosides</td>
<td>_</td>
<td>_</td>
</tr>
<tr>
<td>Saponins</td>
<td>_</td>
<td>_</td>
</tr>
<tr>
<td>Proteins and amino acids</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Phytosterols</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Fixed oils and fats</td>
<td>_</td>
<td>_</td>
</tr>
<tr>
<td>Phenolic compounds &amp; tannins</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Gum &amp; mucilage</td>
<td>_</td>
<td>_</td>
</tr>
<tr>
<td>Flavonoids</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Coumarin glycosides</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Tannins</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Phlobatanins</td>
<td>_</td>
<td>_</td>
</tr>
<tr>
<td>Terpenoids</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

Alloxan induced diabetes in rats
a) Glucose tolerance: Both Extracts showed significant hypoglycemic effect after 90 minutes of treatment.

b) Acute oral toxicity test: Body weight change is an important factor to monitor the animal health. Any loss in body weight is frequently the first indicator of onset of an adverse effect. A dose, which causes 10% or more reduction in the body weight, is considered a toxic dose. All the animals treated showed normal body weight at the end of 14th day as compared to day zero observations. There was no mortality recorded at the end of the study, even at the highest dose of 2000 mg/kg body weight of both Catharanthus roseus and Catharanthus alba extracts respectively.
Table 2: Acute toxicity study of methanolic extract in rats (OECD Guideline 423)

<table>
<thead>
<tr>
<th>Dose</th>
<th>Drug treatment</th>
<th>Average body wt of the animal in grams</th>
<th>Before treatment (1st day)</th>
<th>After treatment (14th day)</th>
<th>Signs of toxicity</th>
<th>Effect observed</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 mg/kg</td>
<td>Meth. Extract</td>
<td>160</td>
<td>171</td>
<td>No signs of toxicity</td>
<td>No effect</td>
<td>Nil</td>
<td></td>
</tr>
<tr>
<td>50 mg/kg</td>
<td>Meth. Extract</td>
<td>160</td>
<td>169</td>
<td>No signs of toxicity</td>
<td>No effect</td>
<td>Nil</td>
<td></td>
</tr>
<tr>
<td>300 mg/kg</td>
<td>Meth. Extract</td>
<td>168</td>
<td>176</td>
<td>No signs of toxicity</td>
<td>No effect</td>
<td>Nil</td>
<td></td>
</tr>
<tr>
<td>2000 mg/kg</td>
<td>Meth. Extract</td>
<td>173</td>
<td>179</td>
<td>No signs of toxicity</td>
<td>No effect</td>
<td>Nil</td>
<td></td>
</tr>
</tbody>
</table>

c) Blood glucose levels

In diabetic control there was a significant increase in blood glucose levels when compared to normal control (p<0.01). Diabetic rats treated with Catharanthus (roseus/alba) flower extract (400mg/kg body weight, twice a day) showed significant decrease in blood glucose levels when compared to diabetic control (p<0.01). Diabetic rats treated with glibenclamide showed significant decrease (p<0.01) in blood glucose levels.

Table 3: blood glucose levels of different groups of animals on different days treated with Catharanthus alba extract

<table>
<thead>
<tr>
<th>S. No</th>
<th>0th day</th>
<th>1st day</th>
<th>7th day</th>
<th>14th day</th>
</tr>
</thead>
<tbody>
<tr>
<td>GROUP I</td>
<td>71.33±1.20</td>
<td>74±5.00</td>
<td>75.35±3.74</td>
<td>79.00±5.19</td>
</tr>
<tr>
<td>GROUP II</td>
<td>83.35±7.42</td>
<td>200.15±18.5</td>
<td>185.00±6.05</td>
<td>115.00±5.05</td>
</tr>
<tr>
<td>GROUP III</td>
<td>88.53±12.75</td>
<td>198.50±19.59</td>
<td>155.75±19.68</td>
<td>98.33±1.86</td>
</tr>
<tr>
<td>GROUP IV</td>
<td>82.33±12.75</td>
<td>194.33±20.48</td>
<td>145.00±15.68*</td>
<td>85.67±1.56*</td>
</tr>
<tr>
<td>GROUP V</td>
<td>77.33±1.20</td>
<td>183.35±7.56</td>
<td>130.00±1.65**</td>
<td>80.19±3.33**</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SEM; n = 6 animals in each group.

**= P ≤ 0.05 (significant) Experimental groups were compared with standard

*= P ≤ 0.01 (significant) Experimental groups were compared with control
Graph 1: blood glucose levels of different groups of animals on different days treated with Catharanthus alba extract.

Table 4: blood glucose levels of different groups of animals on different days treated with Catharanthus roseus extract

<table>
<thead>
<tr>
<th>S. No</th>
<th>0th day</th>
<th>1st day</th>
<th>7th day</th>
<th>14th day</th>
</tr>
</thead>
<tbody>
<tr>
<td>GROUP I</td>
<td>71.33±1.20</td>
<td>74±5.00</td>
<td>75.35±3.74</td>
<td>79.00±5.19</td>
</tr>
<tr>
<td>GROUP II</td>
<td>83.35±7.42</td>
<td>200.15±18.5</td>
<td>185.00±6.05</td>
<td>145.00±5.05</td>
</tr>
<tr>
<td>GROUP III</td>
<td>68.53±12.75</td>
<td>150.50±19.59</td>
<td>135.75±19.68</td>
<td>114.33±1.86</td>
</tr>
<tr>
<td>GROUP IV</td>
<td>75.33±12.75</td>
<td>190.33±20.48</td>
<td>165.00±15.68*</td>
<td>135.67±1.56*</td>
</tr>
<tr>
<td>GROUP V</td>
<td>77.33±1.20</td>
<td>183.35±7.56</td>
<td>130.00±1.65**</td>
<td>80.19±3.33**</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SEM; n = 6 animals in each group.

**= P ≤ 0.05 (significant) Experimental groups were compared with standard

*= P ≤ 0.01 (significant) Experimental groups were compared with control

Graph 2: blood glucose levels of different groups of animals on different days treated with Catharanthus roseus extract.
d) **Body Weight Measurements:** Body weight decreased on administration of alloxan in group II when compared to normal control (p<0.01) and administration of plant extracts showed an increase in body weights when compared to diabetic control rats (p<0.01)

**Table 5:** body weight measurements for different groups of animals on different days treated with Catharanthus alba plant extract.

<table>
<thead>
<tr>
<th>S. No</th>
<th>0th day</th>
<th>1st day</th>
<th>7th day</th>
<th>14th day</th>
</tr>
</thead>
<tbody>
<tr>
<td>GROUP I</td>
<td>180.33±7.08</td>
<td>190.33±4.49</td>
<td>189.30±5.23</td>
<td>193.00±7.64</td>
</tr>
<tr>
<td>GROUP II</td>
<td>204.57±1.57</td>
<td>182.00±2.31</td>
<td>174.00±3.03</td>
<td>149.00±15.44</td>
</tr>
<tr>
<td>GROUP III</td>
<td>180.00±5.77</td>
<td>179.00±2.33</td>
<td>189.59±6.23</td>
<td>195.00±6.79</td>
</tr>
<tr>
<td>GROUP IV</td>
<td>192.57±7.37</td>
<td>181.35±11.30</td>
<td>186.00±12.53*</td>
<td>200.67±6.36*</td>
</tr>
<tr>
<td>GROUP V</td>
<td>201.00±5.67</td>
<td>173.67±6.33</td>
<td>178.30±6.51**</td>
<td>195.00±1.20**</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SEM; n = 6 animals in each group.

**= P ≤ 0.05 (significant) Experimental groups were compared with standard

*= P ≤ 0.01 (significant) Experimental groups were compared with control

**Graph 3:** body weight measurements of different groups of animals on different days treated with Catharanthus alba extract.

**Table 6:** body weight measurements for different groups of animals on different days treated with Catharanthus roseus plant extract.

<table>
<thead>
<tr>
<th>S. No</th>
<th>0th day</th>
<th>1st day</th>
<th>7th day</th>
<th>14th day</th>
</tr>
</thead>
<tbody>
<tr>
<td>GROUP I</td>
<td>180.33±7.08</td>
<td>190.33±4.49</td>
<td>189.30±5.23</td>
<td>193.00±7.64</td>
</tr>
<tr>
<td>GROUP II</td>
<td>209.57±1.57</td>
<td>182.00±2.31</td>
<td>174.00±3.03</td>
<td>149.00±15.44</td>
</tr>
<tr>
<td>GROUP III</td>
<td>185.00±5.77</td>
<td>180.00±2.35</td>
<td>182.00±6.23</td>
<td>195.00±6.79</td>
</tr>
<tr>
<td>GROUP IV</td>
<td>190.57±6.37</td>
<td>157.35±6.25</td>
<td>175.53±11.52*</td>
<td>185.57±5.33*</td>
</tr>
<tr>
<td>GROUP V</td>
<td>205.00±5.67</td>
<td>170.67±6.33</td>
<td>175.30±6.51**</td>
<td>195.00±1.20**</td>
</tr>
</tbody>
</table>
Values are expressed as mean ± SEM; n = 6 animals in each group.

** = *P* ≤ 0.05 (significant) Experimental groups were compared with standard

*= P ≤ 0.01 (significant) Experimental groups were compared with control

Graph 4: body weight measurements of different groups of animals on different days treated with Catharanthus roseus extract.

e) **Biochemical estimations:** It is observed that all biochemical parameters except HDL increase in group II, but Catharanthus varieties flower extracts and glibenclamide (5 mg/kg) reversed the above alloxan induce changes in group III, IV, V.

Table 7: biochemical parameters measured for all groups from the blood serum using diagnostic kits

<table>
<thead>
<tr>
<th>Groups</th>
<th>Cholesterol (mg/dl)</th>
<th>H.D.L (mg/dl)</th>
<th>L.D.L (mg/dl)</th>
<th>Creatinine (mg/dl)</th>
<th>Urea (mg/dl)</th>
<th>Alkaline phosphatase (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>140.36±2.3</td>
<td>35.73±2.5</td>
<td>90.32±1.2</td>
<td>0.53±0.3</td>
<td>30.50±2.2</td>
<td>119±3.5</td>
</tr>
<tr>
<td>II</td>
<td>270.16±9.5</td>
<td>30.00±0.9</td>
<td>185±11.4</td>
<td>2.4±0.3</td>
<td>61.6±1.6</td>
<td>270.00±2.6</td>
</tr>
<tr>
<td>III</td>
<td>186.32±2.5</td>
<td>36.22±3.3</td>
<td>120.25±1.5</td>
<td>0.88±0.4</td>
<td>43.3±4.8</td>
<td>146.35±4.9</td>
</tr>
<tr>
<td>IV</td>
<td>155.46±5.6*</td>
<td>35.53±2.1*</td>
<td>95.65±2.6*</td>
<td>0.65±0.2*</td>
<td>33.35±2.0*</td>
<td>135.49±5.5*</td>
</tr>
<tr>
<td>V</td>
<td>142.53±5.3*</td>
<td>36.73±1.5*</td>
<td>92.35±3.1*</td>
<td>0.58±0.1*</td>
<td>32.44±1.5*</td>
<td>130.75±2.5*</td>
</tr>
</tbody>
</table>

Values are given as mean ± SEM for groups of six animals each *P < 0.05. Diabetic control was compared with the vehicle control and extract treated groups were compared with the diabetic control.
f) Comparison of two extracts

TABLE 8: Comparison of antidiabetic activity of high doses (400mg/kg) of flower extracts of Catharanthus alba and Catharanthus roseus on different days

<table>
<thead>
<tr>
<th>Varieties of flowers</th>
<th>1st day</th>
<th>7th day</th>
<th>14th day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cath. roseus</td>
<td>190.33±20.48</td>
<td>165.00±15.68</td>
<td>135.67±1.56</td>
</tr>
<tr>
<td>Cath. Alba</td>
<td>194.33±20.48</td>
<td>145.00±15.68</td>
<td>85.67±1.56</td>
</tr>
</tbody>
</table>

Values are given as Mean±SEM

Graph 6: comparison between catharanthus roseus and catharanthus alba flower extracts in reduction of blood glucose levels

Histology of Pancreas

Histological examination revealed Extensive damage to the islets of Langerhans and reduced dimensions of islets in animals treated with alloxan only whereas partial restoration of normal
cellular population and enlarged size of β-cells with hyperplasia was observed by methanolic extracts. Restoration of normal cellular population size of islets with hyperplasia by glibenclamide was also observed.

**DISCUSSION**

The preliminary phytochemical investigations of flower extracts of Catharanthus roseus and Catharanthus alba reveals the presence of alkaloids, carbohydrates, tannins, flavinoids, proteins and amino acids and phytosterols, coumarin glycosides and terpenoids. Alkaloids like vindoline, vindolidine, vindolicine, vindolinine are reported to be responsible for antidiabetic activity.[27]

Alloxan has been used to induce experimental diabetes due to the selective destruction of the insulin-producing pancreatic beta-islets. Alloxan induces a multiphasic blood glucose response when injected into an experimental animal, which is accompanied by corresponding inverse changes in the plasma insulin concentration followed by sequential ultra structural beta cell changes ultimately leading to necrotic cell death.

The Present study indicates that methanolic flower extracts of both Catharanthus roseus and Catharanthus alba have good antidiabetic activity. The Alcoholic extracts exhibited significant (p<0.01) anti-hyperglycemic activities in alloxan-induced hyperglycemic rats and improved the condition of Diabetic mellitus as indicated by parameters like body weight & lipid profile along with serum creatinine, serum urea and serum alkaline phosphatase.

In diabetic control there was a significant increase in blood glucose levels when compared to normal control (p<0.01). Diabetic rats treated with Catharanthus (roseus/alba) flower extract (400mg/kg body weight, twice a day) showed significant decrease in blood glucose levels when compared to diabetic control (p<0.01). Diabetic rats treated with glibenclamide showed significant decrease (p<0.05) in blood glucose levels.

Body weight decreased on administration of alloxan in group II when compared to normal control (p<0.01) and administration of plant extracts showed an increase in body weights when compared to diabetic control rats (p<0.01).

It is observed that all biochemical parameters except HDL increase in group II, but Catharanthus varieties flower extracts and glibenclamide (5 mg/kg) reversed the above alloxan induce changes in group III, IV, V.
In this study, the damage of pancreas in alloxan-treated diabetic control rats and regeneration of β cells by glibenclamide was observed. It is found that methanolic flower extract at high dose (400 mg/kg) is more effective than the extract at low dose (200 mg/kg) after 14 days of treatment. Hence the above discussion reveals that methanolic flower extract at high dose (400 mg/kg) is more effective and shows nearly similar curative effect as standard that is, glibenclamide (5 mg/kg). Histopathological studies reinforce the healing of pancreas, by catharanthus (roseus and alba) extracts, as a possible mechanism of their antidiabetic activity.

On comparison the extracts of Catharanthus roseus and Catharanthus alba were found to be almost similarly effective in reducing blood glucose levels in alloxan induced diabetic rats, with only slightly greater antidiabetic activity with higher dose (400mg/kg) of Catharanthus alba (from 145.00±15.68:7th day to 85.67±1.56:14th day) flower extract than Catharanthus roseus (from 165.00±15.68:7th day to 135.67±1.56:14th day) flower extract.

CONCLUSION
The present study suggests that the flower extracts did not show a consistent effect on normal blood sugar levels but it effectively reversed the alloxan-induced changes in the blood sugar level and the beta-cell population in the pancreas. It also showed a protective effect when it was given prior to alloxan administration. The action of flower extracts on the pancreatic beta-cells and absence of acute toxicity may offer a new hope to the diabetics in future.

From this study can be concluded that alcoholic flower extracts of Catharanthus roseus and Catharanthus alba at high dose (400 mg/kg) exhibited significant(p<0.01) antihyperglycemic activity than flower extracts at low dose (200 mg/kg) in alloxan-induced diabetic rats on 14th day of the experiment. These extracts also showed improvement in parameters like body weight and lipid profile as well as regeneration of β-cells of pancreas and so might be of value in diabetes treatment.

On comparison the flower extract of alba showed slightly more antidiabetic activity at high dose when compared to roseus(high dose) Further investigations are required to determine the exact phytoconstituents responsible for antidiabetic effect and to conclude which variety among Catharanthus roseus and Catharanthus alba is better in treatment of diabetes mellitus.
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