CHAPTER 15

IN VIVO ANTI-DIABETIC ACTIVITY OF P. FRATERNUS PLANT EXTRACT AGAINST STREPTOZOTOCIN INDUCED DIABETES IN RATS
CHAPTER 15: IN VIVO ANTI-DIABETIC ACTIVITY OF PHYLANTHUS FRATERNUS PLANT EXTRACT AGAINST STREPTOZOTOCIN INDUCED DIABETES IN RATS

Streptozotocin (STZ) is an antibiotic produced by Streptomyces achromogenes (Alimohammadi et al., 2013). STZ is frequently used to induce diabetes in experimental animals through its toxic effects on pancreatic β –cell and as a potential inducer of oxidative stress. STZ induced diabetic rats are a type of animal models of type 1 diabetes mellitus and is the commonly used model for the screening of anti-hyperglycemic activities. It is well known for its selective pancreatic islet beta cell cytotoxicity and has been extensively used to induce type 1 diabetes in experimental rat model (Gandhi and Sasikumar, 2012). The mechanism by which STZ destroys β-cells of the pancreas and induces hyperglycemia is still not clear. Various actions attributed to the diabetogenic action STZ include damage to pancreatic β-cell membranes and depletion of intracellular nicotinamide adenine dinucleotide (NAD) in islet cells, induction of DNA strand breaks, an increase in the intracellular methylation reaction in pancreatic islet cells and the production of nitric oxide (NO) and free radicals (Alimohammadi et al., 2013).

15.1 Aim of the study: The present study has been undertaken with the aim to evaluate the antidiabetic activity of P. fraternus plant extract.

15.2 Materials and Methods:

a) Reagents and kits
Streptozotocin procured from Spectrchem Private Limited, Mumbai, India
Glibenclamide procured from Sigma Aldrich, Bangalore, India
Citrate buffer, pH 4.5 Sodium carboxy methyl cellulose
Accu-Chek active kits
Diagnostics kits

b) Test substance
P. fraternus plant extract was studied.

c) Animals

<table>
<thead>
<tr>
<th>Breed</th>
<th>Albino Wistar Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source</td>
<td>In-house breed animals</td>
</tr>
<tr>
<td>Number of animals</td>
<td>24 diabetic surviving rats + 6 normal rats</td>
</tr>
<tr>
<td>Total number of animals</td>
<td>30 females rats</td>
</tr>
<tr>
<td>Age when treated</td>
<td>6 to 8 weeks</td>
</tr>
<tr>
<td>Body weight when treated</td>
<td>150–200 g</td>
</tr>
<tr>
<td>---------------------------</td>
<td>-----------</td>
</tr>
<tr>
<td>Identification</td>
<td>By unique cage number and individual animal numbers marked with indelible marker pen on the tail. The animals were marked (towards the tip of tail) with the temporary animal numbers at start of acclimatization. The animals were marked with permanent animal numbers (towards the base of tail) with different color indelible marker pen before the start of test item administration.</td>
</tr>
<tr>
<td>Conditions</td>
<td>Standard Laboratory Conditions. The animal room (Room no.01) was air-conditioned with adequate air changes per hour. The animals were provided with a light cycle of 12 hours light and 12 hours dark.</td>
</tr>
<tr>
<td>Accommodation</td>
<td>Housed in groups of three in Polycarbonate cages (approximate internal dimensions of 365 mm x 202 mm x 180 mm height) with paddy husk bedding.</td>
</tr>
<tr>
<td>Diet</td>
<td>Rodent feed was provided <em>ad libitum</em>.</td>
</tr>
<tr>
<td>Water</td>
<td>Genpure RO water was provided <em>ad libitum</em>.</td>
</tr>
</tbody>
</table>

d) **Test Facility**  
Radiant Research Services Pvt. Ltd  
99/A, 8th main, 3rd phase, Peenya Industrial Area  
Bangalore – 560 058

The experiments were performed in compliance with Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) New Delhi, India (Registration No: 1803/PO/RcBi/S/2015/CPCSEA) and the project approval number is RR/IAEC/04/1-2015.

e) **Dose selection**  
The acute oral toxicity study showed that the plant extract of *P. fraternus* was devoid of any toxicity even at the dose of 2000 mg/kg, hence 200mg/kg and 400 mg/kg body weight doses were selected for the study.

f) **Preparation of citrate buffer solution**  
Citrate buffer: Dissolve 1.47 gm of sodium citrate in 50 ml distilled water. Prepare the fresh buffer solution for every group of injection.

g) **Preparation of streptozotocin solutions**  
Weigh required quantity of streptozotocin. A fresh solution of streptozotocin (50 mg/kg) was prepared in citrate buffer. Adjust the pH with monohydrate sodium citrate solution to obtain a pH of 4.5.
h) **Preparation of test solutions**
Suspension *P. fraternus* plant extract in sodium carboxy methyl cellulose to give a dose of 200 mg/ml and 400 mg/ml
Standard solution 10mg/ml

i) **Induction of experimental diabetes**
A freshly prepared solution of streptozotocin solution was injected intraperitoneally to the rats. After 48 hours of streptozotocin administration, rats with moderate diabetes (i.e. with blood glucose more than 250 mg/dL) were selected for the experiment.

Diabetes was induced in the overnight fasted rats by a single intra-peritoneal injection of 60 mg/kg body weight streptozotocin dissolved in sodium citrate buffer, pH 4.5. After the injection they had free access to food and water. The animals were allowed to drink 5% glucose solution overnight to overcome hypoglycaemic shock. The development of diabetes was confirmed after 48 hours of streptozotocin injection. The animals having blood glucose level more than 200 mg/dl were considered as diabetic and were used for the experimentation.

j) **Experimental procedure**
In the experiment a total of 30 rats (24 diabetic surviving rats, 6 normal rats) were used. The rats were divided into five groups of 6 rats each:

**Group I** - Normal control rats
**Group II** - Diabetic control rats
**Group III** - Diabetic rats treated with plant extract of *P. fraternus* (200 mg/kg body weight in sodium carboxy methyl cellulose suspension administered with an intragastric tube)
**Group IV** - Diabetic rats treated with plant extract of *P. fraternus* (400 mg/kg body weight in sodium carboxy methyl cellulose suspension administered with an intragastric tube)
**Group V** - Diabetic rats given Glibenclamide (10mg/kg body weight in sodium carboxy methyl cellulose suspension administered with an intragastric tube).

Glibenclamide is often used as a standard antidiabetic drug in STZ induced diabetes to compare the efficacy of variety of hypoglycemic drugs.

All drug treatment was given for 21 days. During treatment period daily food & water intake of rats in each group was checked. After the last treatment (21st day of drug treatment) rats were fasted overnight and sacrificed by cervical decapitation. Blood was collected and serum was used for the estimation of biochemical parameters. Liver and pancreas tissues were excised immediately and stored in ice-cold containers. The tissues
were homogenized with appropriate buffer, centrifuged and the supernatant was collected. Tissue antioxidant estimations were carried out in the homogenates.

The **biochemical parameters** analysed included fasted blood glucose levels were estimated by glucose strips (Accu-Chek active). The biochemical parameters evaluated were serum lipid profiles, liver biomarkers such as, SGPT, SGOT and ALP using diagnostics kits.

The **tissue antioxidant enzymes assays** analysed included the activities of antioxidant enzymes such as Superoxide dismutase (SOD), Catalase (CAT), Glutathione (GSH) and thiobarbituric acid reactive in liver (TBARS) were assayed by standard methods.

For **histopathological studies**, rats from control and experimental groups were perfused with 10 per cent neutral formalin solution. Pancreas was removed immediately from the rat. A portion of pancreatic tissue was dissected out and fixed out at 10% buffered neutral formal saline. After fixation, tissues were embedded in paraffin. Fixed tissues were cut at 5 µm and stained with hematoxylin and eosin (H&E). These were examined under light microscope and photomicrographs taken (Onkaramurthy et al., 2013, Ahmed and Urooj, 2008, Das et al., 2015 Patel and Sachdeva, 2014 and Emmanuel et al., 2010).

### 15.3 Statistical analysis

Statistical differences between groups were assessed by analysis of variance (ANOVA) followed by Dunnett test. \( P < 0.05 \) was considered statistically significant. All the results were expressed as mean ± SEM.

### 15.4 Results and discussion

The results obtained from the in vivo antidiabetic activity evaluation of *P. fraternus* plant extract against Streptozotocin induced diabetes in rats is discussed and presented below:

**a) Effect on body weight**

The study results of the effects on body weight are presented in **Table -15.1** and **Figure -15.1**.

<table>
<thead>
<tr>
<th>Groups</th>
<th>0th Day</th>
<th>7th Day</th>
<th>14th Day</th>
<th>21st Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>163.3±3.93</td>
<td>181.2±3.65</td>
<td>199.7±4.14</td>
<td>213.8±3.51</td>
</tr>
<tr>
<td>Group II</td>
<td>156.2±3.22</td>
<td>147±3.651</td>
<td>132±2.76</td>
<td>115.3±2.40</td>
</tr>
<tr>
<td>Group III</td>
<td>152.5±3.07</td>
<td>158.3±3.073</td>
<td>165.2±3.19</td>
<td>171.7±3.41</td>
</tr>
<tr>
<td>Group IV</td>
<td>155±2.23</td>
<td>158±2.033</td>
<td>165.2±2.05</td>
<td>167.7±2.06</td>
</tr>
<tr>
<td>Group V</td>
<td>155.3±2.70</td>
<td>165.8±3.341</td>
<td>176±3.04</td>
<td>187.2±3.04</td>
</tr>
</tbody>
</table>

Values are expressed as Mean ± SEM (n=6)

Figure -15.1: Effect of P. fraternus plant extract on body weight in STZ induced diabetic rats.

As is evident from the results presented in Table 1, the mean body weight of diabetic control animals on day 0 was 156.2 ± 3.22 g which reduced to 115.3 ± 2.40 g (- 26%) on day 21 of induction of diabetes. This decrease in body weight in diabetic animals was statistically significantly as compared to normal control animals.

Administration of P. fraternus plant extract in both doses (200mg/kg & 400mg/kg) showed significant improvement in body weight compared to diabetic groups. Mean body weight of animals in test group-1 and test group-2 increased from 152.5 ± 3.07 g & 155 ± 2.23gm on 0 day to 171.7 ± 3.41 g (+ 12.5 %) and 167.7 ± 2.06 g (+ 8 %) on day 21 of induction of diabetes respectively.

Similar results of significant improvement in body weight as compared to diabetic control group of animals were obtained with administration of standard antidiabetic drug Glibenclamide (10 mg/kg), which increased body weight from 155.3 ± 2.70 g to 187.2 ± 3.04 g (+ 20%) at the end of the study.

From the results obtained, decrease in body weight gain was observed in STZ-induced diabetic rats when compared to controls. Decreased body weight observed in diabetic control rats in comparison to normal rats indicates that loss of body weight is a result of excessive breakdown of tissue proteins. However, P. fraternus plant extract treated diabetic rats showed improved body weight to a certain extent when compared with STZ
treated rats, indicating that control over muscle wasting resulted from glycemic control. This suggests the hypoglycemic effect of *P. fraternus* plant extract in diabetic rats.

**b) Effect on blood glucose level (BGL)**

The study results of the effects on blood glucose level are presented in **Table -15.2** and **Figure -15.2**.

**Table -15.2 – Effect of *P. fraternus* plant extract on blood glucose level of STZ induced diabetic rats**

<table>
<thead>
<tr>
<th>Groups</th>
<th>Blood glucose (mg/dl)</th>
<th>0th Day</th>
<th>7th Day</th>
<th>14th Day</th>
<th>21st Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>98 ± 3.71</td>
<td>95 ± 2.20</td>
<td>110 ± 3.59</td>
<td>92 ± 1.61</td>
<td></td>
</tr>
<tr>
<td>Group II</td>
<td>304 ± 22.55</td>
<td>297 ± 20.57</td>
<td>305 ± 18.97</td>
<td>301 ± 20.49</td>
<td></td>
</tr>
<tr>
<td>Group III</td>
<td>296 ± 12.23</td>
<td>290 ± 12.65</td>
<td>261 ± 12.27</td>
<td>226.7 ± 6.40</td>
<td></td>
</tr>
<tr>
<td>Group IV</td>
<td>308 ± 16.12</td>
<td>251 ± 10.76*</td>
<td>232 ± 7.09*</td>
<td>189 ± 4.17**</td>
<td></td>
</tr>
<tr>
<td>Group V</td>
<td>338 ± 10.98</td>
<td>233 ± 5.06*</td>
<td>185 ± 2.87**</td>
<td>131 ± 4.04***</td>
<td></td>
</tr>
</tbody>
</table>

Values are expressed as Mean ± SEM.( n=6)
Values are expressed as Mean ± SEM.( n=6); * p<0.05, ** p<0.01, *** p<0.001.

**Figure -15.2: Effect of *P. fraternus* plant extract on blood glucose level in STZ induced diabetic rats**

**Table -15.2** shows variation in BGL from day 1 to day 21 in each group. Mean BGL in non-diabetic control animals ranged from 98 ± 3.71 mg/dl on 0 day to 92 ± 1.61 mg/dl on day 21 of the study.

In STZ-induced diabetic animals the BGL changes from 304 ± 22.55 mg/dl on 0 day to 301 ± 20.49 mg/dl (-0.98%) on day 21 of the study. With standard drug Glibenclamide (10mg/kg) the BGL reduced from 338 ± 10.98 mg/dl on 0 day to 131 ± 4.04 mg/dl (-
61%) on day 21. This difference was found to be highly significant when compared with diabetic control group.

*P. fraternus* plant extract in the dose of 200 mg/kg reduced BGL from 296 ± 12.23 mg/dl on day 0 to 226.7 ± 6.40 mg/dl (-23.4%) on day 21. 400mg/kg dose of test drug also significantly reduced BGL from 308±16.12 on 0 day to 189 ± 4.17 mg/dl (-38.4%) on day 21.

The blood glucose level (BGL) was higher in STZ-diabetic rats as compared to normal rats. *P. fraternus* plant extract treated groups and the Glibenclamide treated group shows significant decrease in the fasting blood glucose levels when compared with diabetic control, which was determined on the day 7 and day 14 and day 21 of the experiment. Treatment of STZ-diabetic rats with *P. fraternus* plant extract reduced the hyperglycemia when compared with STZ alone treated rats. This effect was more significant in higher dose of plant extract.

**(c) Effect on antioxidant enzymes**

It is well known that diabetes mellitus is associated with an increased production of reactive oxygen species and a reduction in anti-oxidative defenses. This defense includes the enzymes SOD, CAT and GSH. The diabetogenic action of STZ can be prevented by the superoxide dismutase and catalase; hence there is evidence to suggest that the incidence of diabetes involves superoxide anion and hydroxyl radicals. The enzyme SOD scavenges superoxide radicals (O2·−) by catalysing the conversion of two of these radicals into hydrogen peroxide and molecular oxygen (Emmanuel S, Rani MS and Sreekanth M R, 2010).

The study results of the effects on antioxidant enzymes are presented in Table -15.3 and Figure -15.3, Figure -15.4, Figure -15.5 and Figure -15.6.

**Table -15.3 – Effect of Test substance on tissues antioxidant enzymes and lipid peroxidation levels in STZ induced diabetic rats**

<table>
<thead>
<tr>
<th>Groups</th>
<th>LPO (TBARS) (µM/mg protein)</th>
<th>GSH (µM/mg protein)</th>
<th>CAT (µM of H2O2 utilized/min/mg protein)</th>
<th>SOD (U/mg protein)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>0.12±0.002</td>
<td>7.07±0.06</td>
<td>0.35±0.01</td>
<td>0.38±0.028</td>
</tr>
<tr>
<td>Group II</td>
<td>0.39±0.02</td>
<td>2.90±0.07</td>
<td>0.21±0.01</td>
<td>0.14±0.032</td>
</tr>
<tr>
<td>Group III</td>
<td>0.34±0.03</td>
<td>3.30±0.05</td>
<td>0.24±0.004</td>
<td>0.17±0.007</td>
</tr>
<tr>
<td>Group IV</td>
<td>0.27±0.03**</td>
<td>3.48±0.24*</td>
<td>0.26±0.005**</td>
<td>0.28±0.066*</td>
</tr>
<tr>
<td>Group V</td>
<td>0.19±0.01***</td>
<td>5.56±0.13***</td>
<td>0.30±0.006***</td>
<td>0.36±0.026***</td>
</tr>
</tbody>
</table>
Values are expressed as Mean ± SEM (n=6); * p<0.05, ** p<0.01, *** p<0.001.
LPO - lipid peroxidation; GSH-reduced glutathione; MDA-malondialdehyde; SOD-Super Oxide Dismutase
CAT-Catalase

Figure -15.3: Effect of test substance on SOD level in STZ induced diabetic rats

Figure -15.4: Effect of test substance on Catalase level in STZ induced diabetic rats
Oxidative stress is considered as a major pathogenesis in diabetes-related complications. The antioxidant enzymes SOD, CAT and non-enzymatic GSH levels were determined in all the groups. In the normal, Glibenclamide (standard) and *P. fraternus* plant extract (400mg/kg) treated groups, highest antioxidant levels were found in the liver compared to the antioxidant levels were found in the liver of *P. fraternus* plant extract (200mg/kg) treated group and diabetic control rat group.

STZ induced diabetic rats were found to have decreased SOD, GSH and CAT enzyme level in liver as compared to control. Administration of *P. fraternus* plant extract (400mg/kg) to the diabetic rats resulted in significant increase in the activities of SOD
(p<0.05) , GSH (p<0.05) and CAT (p<0.01). Glibenclamide (standard) group was able to reverse the altered peroxidative damage to near normal values.

STZ diabetic rats were found to exhibit significant increase in LPO (TBARS) level in liver as compared to control rats. Treatment with *P. fraternus* plant extract (400mg/kg) produced significant decrease (p<0.01) in LPO (TBARS).

**(d) Effect on liver enzymes**

Liver plays an important role in the maintenance of blood glucose level by regulating its metabolism. Hepatotoxicity is another risk associated with long term use of anti-diabetic agents.

The study results of the effects on liver enzymes (SGOT, SGPT and ALP) are presented in Table -15.4 and Figure -15.7, Figure -15.8 and Figure -15.9.

| Table -15.4 – Effect of test substance on serum biochemical parameters on streptozotocin induced diabetic rats |
| --- | --- | --- |
| Groups | SGPT (IU/ml) | SGOT (IU/ml) | ALP (IU/ml) |
| Group I | 46.7±1.03 | 66.39±3.33 | 164.5±2.83 |
| Group II | 75.96±3.77 | 270.6±22.18 | 254.2±4.64 |
| Group III | 71.46±8.60 | 222.8±23.37 | 253.4±5.08 |
| Group IV | 58.52±1.88* | 183.4±24.85* | 231.4±5.16* |
| Group V | 53.45±2.02*** | 139±7.36*** | 190.1±6.5*** |

Values are expressed as Mean ± SEM,( n=6); * p<0.05, ** p<0.01, *** p<0.001.

SGOT-Serum Glutamate Oxalo Transferase; SGPT -Serum Glutamic Pyruvic Transaminase; ALP-Alkaline phosphatase

![Figure -15.7: Effect of test substance on SGOT level in STZ induced diabetic rats](image-url)
The effect is more pronounced in Glibenclamide (standard) group (10mg/kg) group, followed by *P. fraternus* plant extract (400mg/kg, 200mg/kg) group. *P. fraternus* plant extract (400mg/kg) group shown significantly lower levels of SGOT, SGPT and ALP than *P. fraternus* plant extract (200mg/kg) in comparison to the diabetic control group.

(c) Effect on pancreas by histopathology

The study results of the effects on pancreas were studied from histopathological studies. The observations found in each group are discussed below:
Group I:

The histological observation of normal control group (non-diabetic) is presented Figure -15.11 and -15.12. These figures showed normal islets of Langerhans and β cells in pancreas.

**Figure -15.11:** Histological observations of pancreas (H&E; 10 X) in Normal control group (presence of normal pancreatic islet cells); Beta cells – 60 %, Alpha cells 40 %

![Image of histological observation of pancreas](image1)

**Figure -15.12:** Histological observations of pancreas (H&E; 40 X) in Normal control group (presence of normal pancreatic islet cells); Beta cells – 60 %, Alpha cells 40 %

10X: 10 times magnification  
40X: 40 times magnification  

Section studied shows pancreatic lobules with acini separated by fibrovascular septa. The pancreatic lobules consist of intact acinar cells with their intralobular ducts. Adequate numbers of islets are seen. The center of islet cells consists of Beta-cells (60%, Fig. Short-Arrow), while the periphery comprises of Alpha-cells (40%, Fig. Long-Arrow).
Group II:

The histological observation of positive control group (diabetic) is presented Figure - 15.13. This figure showed that the number of pancreatic islets as well as β-cells is reduced as compared to control group with most of β-cells being destroyed.

![Histological observations of pancreas](image)

**Figure -15.13: Histological observations of pancreas (H&E; 40 X) in Diabetic control group (expansion and dilated islet cells); Beta cells – 30 %, Alpha cells 65 %**

Section studied shows pancreatic lobules with acini separated by fibrovascular septa. The pancreatic lobules consist of intact acinar cells with their intralobular ducts. The numbers of islets are drastically reduced. Islet size is reduced. The beta cells which are placed in the center of the islet are reduced in number (30%). Alpha cells constitute 65% of the cells. Aggregates of inflammatory cells like lymphocytes are seen in the periphery of the pancreatic lobules.

Group III:

The histological observation of *P. fraternus* plant extract group (200mg/kg) group (diabetic + extract 200mg/kg) is presented Figure -15.14 and Figure -15.15. These figure showed that the number of pancreatic islets as well as β-cells is reduced as compared to control group with most of β-cells being destroyed.
Figure -15.14: Histological observations of pancreas (H&E; 10 X) in *P. fraternus* plant extract group (200mg/kg) (expansion and dilated islet cells); Beta cells – 35 %, Alpha cells 60 %

Figure -15.15: Histological observations of pancreas (H&E; 40 X) in *P. fraternus* plant extract group (200mg/kg) (expansion and dilated islet cells); Beta cells – 35 %, Alpha cells 60 %

Section studied shows pancreatic lobules with acini separated by fibrovascular septa. The pancreatic lobules consist of intact acinar cells with their intralobular ducts. The numbers of islets are drastically reduced. Islet size is reduced. The beta cells which are placed in the center of the islet are reduced in number (35%). Alpha cells constitute 60% of the cells. Hemorrhage and congestion is seen in some parts of the exocrine pancreas. Aggregates of inflammatory cells like lymphocytes are seen in the periphery of the pancreatic lobules.
Group IV:

The histological observation of *P. fraternus* plant extract group (400mg/kg) group (diabetic + extract 400mg/kg) is presented Figure -15.16 and Figure -15.17. These figure showed increase in pancreatic islets & number of β-cells in the pancreas.

![Image](image1.png)

**Figure -15.16:** Histological observations of pancreas (H&E; 10 X) in *P. fraternus* plant extract group (400mg/kg) (absence of dilation and prominent hyperplastic of islets); Beta cells – 50 %, Alpha cells 40 %

![Image](image2.png)

**Figure -15.17:** Histological observations of pancreas (H&E; 40 X) in *P. fraternus* plant extract group (400mg/kg) (absence of dilation and prominent hyperplastic of islets); Beta cells – 50 %, Alpha cells 40 %

Section studied shows pancreatic lobules with acini separated by fibrovascular septa. The pancreatic lobules consist of intact acinar cells with their intralobular ducts. Adequate numbers of islets are seen. The center of islet cells consists of Beta-cells (50%), while the periphery comprises of Alpha-cells (40%).
Treatment with *P. fraternus* plant extract group resulted in normalizing the pancreatic histoarchitecture quite appreciably. The damaged β-cell seen after induction of diabetes was no longer observed after treatment with extract. This indicates that the test drug causes regeneration of β-cell of islets of Langerhans of pancreas and restores normal cellular appearance and size of islet with hyperplasia. The increase in secretory granules in the cells indicates that the cells were stimulated for insulin synthesis.

**Group V:**

The histological observation of Glibenclamide group (10mg/kg) group (diabetic + Glibenclamide) is presented Figure -15.18. This figure showed increase in pancreatic islets & number of β-cells in the pancreas.

![Histological observations of pancreas (H&E; 40 X) in Glibenclamide group (10mg/kg) (absence of dilation and prominent hyperplastic of islets); Beta cells – 55 %, Alpha cells 45 %](image)

Section studied shows pancreatic lobules with acini separated by fibrovascular septa. The pancreatic lobules consist of intact acinar cells with their intralobular ducts. The numbers of islets are decreased. The center of islet cells consists of Beta-cells (55 %), while the periphery comprises of Alpha-cells (45 %).

The damaged β-cell seen after induction of diabetes was no longer observed after treatment with Glibenclamide. β-cell of islets of Langerhans of pancreas were regenerated and normal cellular appearance and size of islet with hyperplasia was restored.
15.5 Conclusion

The findings of the present study indicates that the *Phyllanthus fraternus* plant extract (400mg/kg) possesses strong antidiabetic activity against STZ induced diabetes in Wistar rats. The results suggests that the *P. fraternus* plant extract has beneficial effect on blood glucose level and ameliorative effect on regeneration of pancreatic islets and may be used as a therapeutic agent in the management of diabetes mellitus after detail in-vivo investigation. Further preclinical research into the utility of *P. fraternus* treatment may indicate its usefulness as a potential treatment in diabetic patients.