Diabetes mellitus is a metabolic disorder characterized by either insufficiency of insulin or inability of cells to respond to insulin [1]. Diabetes is the most serious and common metabolic disease all over the world and it is caused mainly due to pancreatic β-cell dysfunction and insulin resistance. The chronic complications of diabetes are microvascular damage, nephropathy, neuropathy and retinopathy which is mainly caused due to significantly increased level of blood glucose level [2]. The World Health Organization (WHO) estimates that more than 220 million people worldwide have diabetes and this number is likely to more than double by 2030 [3]. The highest prevalence, as well as the long-term complications associated with diabetes, stimulates the search for the new antidiabetic agent.

In 1980 the WHO also suggested to study and find out the plants which are having potential hypoglycemic activity as the modern drugs have the less safety [4]. The present hypoglycemic drugs and insulin used for the treatment of diabetes is excessively costlier and having its own side effects which limits its use. Although many allopathic approaches are available for treatment of diabetes but none of these is ideal for treatment of diabetic patients. Insulin is associated with its stability when taken orally another hypoglycemic like sulphonyl urea and α glucosidase is associated with its own side effects [5]. Recently there is increasing trend for using plant preparations and its derivatives to treat diabetes and its complications [6].

Traditionally in ayurveda medicines consist of plant or plant product as a single plant or a combination of plants, which are considered less toxic and free from side effects when compared to synthetic drugs. P. dulce (Leguminosae) is native to tropical Asia, America and cultivated throughout the India. It is evergreen; medium-sized tree grows up to 18 m in height [7]. It is commonly known as ‘manila tamarind’ and Indian jalebi as it resembles the sour taste of tamarind and Indian sweet jalebi. The leaves of P. dulceContains cyclitol, dulcitol, octacosanol, a-spinasterol, kaempferol-3-rhamnoside, queretin and afzelin [8]. The literature survey suggests that the leaves of the plant used traditionally for leprosy, intestinal disorders, peptic ulcer, toothache, ear ache, emollient, abortifacient and larvicidal in folk medicines [9]. The leaves of the plant have reported to contain the insulin-like content which may be useful for the treatment of diabetes [10]. The leaves also reported to show antifungal and antibacterial activity [11]. Estrogenic activity was observed by isolated isoflavonoids from the root of the plant [12]. The leaves of the plant reported to have free radical scavenging properties and antymycobacterial activity [8, 9]. The Neuropharmacological activities of this plant were also demonstrated [13].

Taking into consideration the traditional claims and reported activities, P. dulce has been studied for its anti diabetic activity in diabetic animals. Hence the present study was planned to investigate the effect of P. dulce leaves on dexamethasone-induced insulin resistance in the rat.

The fresh leaves of P. dulce were collected from Jaisingpur, Sangli District, Maharashtra, India. The plant material was taxonomically authenticated by acknowledged Botanist, Dr. Mrs. U. S. Yadav at Willingdon College, Sangli, Maharashtra, India (Voucher specimen No.: WILL/Bot/2009/03). The standard drug pioglitazone was obtained from Aarti Drugs Ltd, Mumbai. The inducer dexamethasone was obtained from Cipla Pharma R and D, Vikroli. All the diagnostic kits used are of Span Diagnostics, Surat.

The fresh leaves were separated and air dried under shade for seven days. The dried plant leaves were subjected to size reduction to a coarse by the dry grinder and passed through a sieve. The powder was subjected to aqueous and ethanolic extraction. The powder material was packed into soxhlet apparatus and extracted using ethyl alcohol as a solvent. This extract was oven dried at 40 °C giving a dried extract [14]. The aqueous extract was prepared with chloroform-water by maceration for six h at room temperature. During maceration, it was subjected to occasional shaking on an
The experiment was designed for 11 d to evaluate antidiabetic activity of D. dulce leaves in dexamethasone-induced insulin resistance in albino rats. In the experiment total 35 overnight fasted rats were used. The 30 rats were rendered diabetic by the solution of 10 mg/kg of body weight by subcutaneous route for 10 d and at the same time the test samples were administered orally. The animals were randomly divided into seven groups, five animals in each group. The animals were divided into seven groups as following. Group-I: Normal control 2 ml/kg normal saline (vehicle) Group-II: Dexamethasone 10 mg/kg (s. c) + vehicle Group-III: Dexamethasone 10 mg/kg (s. c)+ vehicle + Aqueous extract 200 mg/kg Group-IV: Dexamethasone 10 mg/kg (s. c) + Aqueous extract 400 mg/kg Group-V: Dexamethasone 10 mg/kg (s. c) + Aqueous extract 200 mg/kg + Pioglitazone 20 mg/kg Group-VI: Dexamethasone 10 mg/kg (s. c) + Aqueous extract 400 mg/kg + Pioglitazone 20 mg/kg Group-VII: Dexamethasone 10 mg/kg (s. c) + Ethanol extract 200 mg/kg + Pioglitazone 20 mg/kg

The acute toxicity of aqueous and ethanolic extracts of D. dulce was determined by using wistar albino rats (150-300 g) which were maintained under the standard conditions. The animals (n=5) were fasted 12 h prior to the experiment; OECD guideline 425 procedures were adopted for toxicity studies. A single dose of extract of D. dulce at 2000 mg/kg were administered to animals. The animals were observed for seven days as animals had not shown any sign of toxicity, behavioral changes and mortality the dose increased up to 5000 mg/kg. Then animals were observed up to 7 d for toxicity, behavioral changes, and mortality [17].

The effect of both aqueous and ethanolic extract on serum glucose, triglyceride and total cholesterol level is presented in table 1. The blood glucose level was found to be increased in dexamethasone-induced diabetic rats. The blood glucose level which was increased by dexamethasone significantly (p < 0.05) reduction by aqueous extract and ethanolic extract when compared with diabetic control group. The serum triglyceride level was found to be significantly (p < 0.05) by both aqueous and ethanolic extract when compared with diabetic control group. The effect on total cholesterol level shows the significant (p < 0.05) reduction by both aqueous extract and ethanolic extract when compared with diabetic control group.

Table 1: Effect of aqueous and ethanolic extracts of D. dulce on blood glucose, triglyceride and total cholesterol levels in dexamethasone-induced diabetic rats

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<tbody>
<tr>
<td>Glucose</td>
<td>103.1 ±2</td>
<td>176.3 ±5</td>
<td>112.5 ±2</td>
<td>137.0 ±5</td>
<td>119.7 ±5</td>
<td>139.0 ±5</td>
<td>131.6 ±2</td>
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<tr>
<td>Triglyceride</td>
<td>2.34 ±2</td>
<td>5.5 ±2</td>
<td>4.23 ±5</td>
<td>2.34 ±5</td>
<td>3.12 ±5</td>
<td>3.12 ±5</td>
<td>5.23 ±5</td>
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<tr>
<td>Total Cholesterol</td>
<td>12.5 ±4</td>
<td>184.7 ±3</td>
<td>145.8 ±4</td>
<td>155.7 ±5</td>
<td>144.9 ±4</td>
<td>158.3 ±5</td>
<td>148.6 ±3</td>
</tr>
<tr>
<td>Glucose</td>
<td>103.1 ±2</td>
<td>176.3 ±5</td>
<td>112.5 ±2</td>
<td>137.0 ±5</td>
<td>119.7 ±5</td>
<td>139.0 ±5</td>
<td>131.6 ±2</td>
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</tbody>
</table>

Values are expressed as mean ±SEM (n=5). **p < 0.01, *p < 0.05 when compared with control group

The effect of both aqueous and ethanolic extract on serum glucose, triglyceride and total cholesterol level is presented in table 2. The effect on liver glycogen level shows that there was a reduction in liver glycogen level. This reduced liver glycogen level was increased significantly (p < 0.05) by both aqueous extract and ethanolic extracts. The muscle glycogen level was reduced in dexamethasone-induced diabetic rats. The aqueous and ethanolic extracts show a significant increase in muscle glycogen level when treated for eleven days. The effect on kidney glycogen level was found to increase glycogen level in dexamethasone-induced diabetic rats. The standard drug, extract and ethanolic extracts reduce significantly increased glycogen level in kidney.

Table 2: Effect of aqueous and ethanolic extracts of D. dulce on liver, muscle and kidney glycogen levels in dexamethasone-induced diabetic rats

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<tbody>
<tr>
<td>Liver</td>
<td>19.08 ±5</td>
<td>7.3 ±2</td>
<td>16.6 ±5</td>
<td>18.6 ±5</td>
<td>17.9 ±5</td>
<td>18.6 ±5</td>
<td>17.6 ±5</td>
</tr>
<tr>
<td>Muscle</td>
<td>2.9 ±1</td>
<td>7.3 ±2</td>
<td>1.8 ±2</td>
<td>2.0 ±2</td>
<td>2.8 ±2</td>
<td>2.7 ±2</td>
<td>1.95 ±1</td>
</tr>
<tr>
<td>Kidney</td>
<td>3.0 ±0.2</td>
<td>0.7 ±0.2</td>
<td>2.55 ±0.2</td>
<td>1.9 ±0.2</td>
<td>2.42 ±0.4</td>
<td>3.06 ±0.27</td>
<td>2.32 ±0.4</td>
</tr>
</tbody>
</table>

Values are expressed as mean ±SEM (n=5). **p < 0.01, *p < 0.05 when compared with control group
Effects of aqueous and ethanolic extracts of *P. dulce* leaves were tested for glucose, triglyceride, total cholesterol and glycogen level in dexamethasone-induced diabetic rats. The outcome of the present research demonstrates that *P. dulce* leaves produce significant pharmacological effects in the diabetic rats.

Gluocorticoid is extensively used as medicine for short-term acute steroid therapy can be seen in exacerbation of the chronic obstructive pulmonary disease, acute gout, chemotherapy protocols and bacterial meningitis. The chronic use of glucocorticoids suppresses the immune system and helps in organ transplantation [18]. During its use, it acts on the liver and shows increase in the level of blood glucose due to increasing in liver glyconen metabolism. Glucocorticoid also decreases the insulin sensitivity which act on cells and helps to increase glucose uptake through glucose transporters. The combined effect of this will result in an increase in blood glucose level and produces type-2 diabetes mellitus [29, 20]. It is observed that glucocorticoids and insulin have opposite effects on the metabolism of carbohydrate, protein, and fats. Insulin promotes synthesis of glycogen from glucose, so it is anabolic. Glucocorticoid increases metabolism of carbohydrate, protein and fat [21, 22]. The main mechanism by which the hyperglycemia and type-2 diabetes is produced by glucocorticoid is increased in glucose production and inhibition of insulin secretion [23, 24].

The present study reveals that significantly increased blood glucose, triglyceride, total cholesterol and decrease in muscle and liver glycogen level along with an increase in kidney glycogen level in diabetic rats compared to non-diabetic rats, which indicates diabetic was induced effectively. In dexamethasone-induced type-2 diabetes due to insulin deficiency or due to insulin resistance results in elevation of blood glucose level [25]. However, the treatment with both aqueous and ethanolic extracts treatment significantly reduces blood glucose level. The effect of both extracts was dose dependent with an increase in dose there was a reduction in blood glucose level was observed. Reduction of elevated blood glucose level is an indicator of the antidiabetic activity of *P. dulce* leaves [26]. Furthermore, it is well known that these antidiabetic effects are mediated through the action of insulin on insulin receptors [27]. Therefore *P. dulce* induced enhancement of blood glucose level could be attributed to the increase in insulin secretion, decrease in insulin resistance or participation of insulin receptors. This effect may be due to the presence of flavonoids, saponins and tannins which may be responsible for the antidiabetic potential of *P. dulce* leaves [13].

Accumulation of triglyceride and total cholesterol is an indicator of abnormal lipid metabolism and is commonly associated with diabetes mellitus. In diabetes mellitus lipase enzyme required for hydrolysis of triglycerides was in the inactive state due to insulin deficiency which leads to increase in triglyceride level. The effect of both aqueous and ethanolic extract on lipid profile reveals that both extracts produced a significant decrease in triglyceride and total cholesterol level [28].

The result suggests that there is a significant improvement in liver and muscle glyconen level while kidney glyconen level was decreased significantly when compared with diabetic control group.

**CONCLUSION**

Our study shows that both aqueous and ethanolic extracts produce an antidiabetic effect in dexamethasone-induced diabetic rats. The effects on lipid profile indicate the hypolipidemic effect of both extracts in dexamethasone-induced diabetic rats. The extracts also increase liver and muscle glyconen level while kidney glyconen level was reduced significantly. Further studies are necessary to identify the active constituent present in the extract as well as to elucidate the mechanisms by which it produces its beneficial effects.

**CONFLICTS OF INTERESTS**

All authors have none to declare.

**REFERENCES**


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