Hypoglycaemic and Antihyperglycaemic Effect of *Syzygium cumini* Bark in Streptozotocin-Induced Diabetic Rats

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**Abstract:** The aim of the present study was to investigate the hypoglycaemic and antihyperglycaemic effect of *Syzygium cumini* (S. cumini) bark in diabetic rats. Diabetes was induced in male albino Wistar rats by a single intraperitoneal injection of streptozotocin (45 mg kg⁻¹ body weight). An aqueous extract of *S. cumini* bark (SBEt) was administered orally (75, 150 and 300 mg kg⁻¹ body weight) for 45 days and changes in blood glucose, urine sugar, food and fluid intakes and body weight were examined in diabetic rats. Glibenclamide was used as a standard reference drug. The levels of blood glucose and urine sugar were increased significantly in diabetic rats. Oral administration of SBEt to diabetic rats led to significantly decreased levels of blood glucose and urine sugar. The effect exerted by the extract at a dose of 300 mg kg⁻¹ body weight was greater than that of doses 75 and 150 mg kg⁻¹ body weight. The daily food and fluid intakes were significantly increased while the body weights were significantly reduced in diabetic rats when compared to normal rats. Treatment with SBEt significantly restored the above physiological parameters to near normal in streptozotocin diabetic rats. During oral glucose tolerance test (OGTT), long-term administration of SBEt was able to significantly decrease the blood glucose concentrations at 30, 60, 90 and 120 min when compared to the OGTT pattern of diabetic rats. The effect of SBEt at 300 mg kg⁻¹ body weight was better than glibenclamide (600 μg kg⁻¹ body weight). These results suggest that SBEt possesses a significant antidiabetic effect by attenuating the above biochemical and physiological alterations in streptozotocin diabetes. Further, our findings revealed the possible therapeutic value of *S. cumini* bark for the better control, management and prevention of diabetes mellitus progression.

**Key words:** *Syzygium cumini*, streptozotocin diabetes, antidiabetic effect, blood glucose, glucose tolerance test

**INTRODUCTION**

Diabetes mellitus is a metabolic disorder of multiple aetiology characterized by chronic hyperglycaemia with disturbance of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both. It affected about 171 million people worldwide in 2000 and the number is projected to increase to at least 366 million by 2030 (Wild et al., 2004). Epidemiological studies and clinical trials strongly support the notion that hyperglycaemia is the principal cause of complications. Effective blood glucose control is the key for preventing or reversing diabetic complications and improving quality of life in patients with diabetes. Thus sustained reduction in hyperglycaemia will decrease the risk of developing microvascular complications and most likely reduce the risk of macrovascular complications (Jerums et al., 2003).
Insulin and oral hypoglycaemic agents are the main ways to treat diabetes and are effective in controlling hyperglycaemia. However, the practical applicability of the majority of these therapeutic agents remained restricted owing to their limited action, pharmacokinetic properties, secondary failure rates and accompanying side effects (Kim et al., 2006). In addition, these therapies only partially compensate for metabolic derangements seen in diabetics and do not necessarily correct the fundamental biochemical lesion (Bhandari et al., 2005). The inability of the modern synthetic approach to provide a satisfactory answer has led to a shift in focus to alternative forms of therapy based on drugs derived from plants.

Plants have always been exemplary sources of drug and many of the currently available drugs have been directly or indirectly obtained from plants (Ozssoy-Sacan et al., 2006). Recently, the search for appropriate hypoglycaemic agents has been focused on plants used in traditional medicine partly because of leads provided by traditional medicine to natural products that may be better treatments than currently used drugs (Rates, 2001). Throughout the world many traditional plant treatments for diabetes exist (Grover et al., 2002; Oliveira et al., 2005). However, few have received scientific or medical scrutiny and the World Health Organization (WHO) has recommended that traditional plant treatments for diabetes warrant further evaluation (WHO, 1980).

In Asia and South America, the development and use of cheap and easily accessible phytomedicines from plants of the genus Syzygium in the treatment of diabetes is envisaged to circumvent these problems (Teixeira et al., 1997). Syzygium cumini (Linn.) Skeels (Synonym: Eugenia jambolana Lam.), a member of family Myrtaceae commonly known as Jamun or Jambul in Hindi and Black Plum or Black Berry in English, is a large size evergreen tree indigenous to India and is cultivated in gardens for its delicious fruit. Besides India, it is also found in South-East Asia and Eastern Africa. Out of a large number of herbal drugs stated to possess antidiabetic activity in the Ayurvedic system of medicine of India, S. cumini is being widely used by the traditional practitioners to treat diabetes over many centuries (Sagrawat et al., 2006).

Various parts of this plant have been recognized for several medicinal properties in folklore medicine. The bark of the plant is astringent, refrigerant, carminative, diuretic, digestive, anthelmintic, febrifuge, constipating, stomachic and antibacterial. The fruits and seeds are used to treat diabetes, pharyngitis, splenopathy, urethritis and ringworm infection. The leaves are antibacterial and used to strengthen the teeth and gums. The leaves have also been extensively used to treat diabetes, constipation, leucorrhea, stomachalgia, fever, gastropathy, strangury, dermopathy and to inhibit blood discharge in the faeces (Ravi et al., 2005; Sagrawat et al., 2006). The plant S. cumini is frequently used for the treatment of diabetes; it has been shown that the bark, fruit, seeds or leaves of this plant collected from diverse regions of the world and administered in different pharmaceutical preparations (e.g., tinctures and aqueous extracts) decrease blood glucose levels in diabetic animals. In addition, infusions (simple aqueous extracts prepared with hot water but without boiling) and decoctions (boiled infusions) of S. cumini have been used in traditional medicine for the treatment of diabetes mellitus (Pepato et al., 2001). Herbal drugs containing S. cumini bark (a major ingredient) under the names D-400 and Coqent db are also very popular traditional medicines for the treatment of diabetes (Mitra et al., 1995; Pan and Saravanan, 2002). This species has been extensively investigated and a number of chemical constituents from the fruits, seeds, leaves, roots, flowers and bark of the plant have often previously reported; these include acetyl oleamic acid, tannin, gallic acid, ellagic acid, quercetin, isoquercitin, kaempferol, myricetin flavonol glycoside, triterpenoids, saponins and anthocyanin (Gupta and Sharma, 1974; Jagetia and Baliga, 2002; Ravi et al., 2004; Sagrawat et al., 2006).

In addition pharmacological evaluation of this plant concerning its antidiabetic, hypolipidaemic, antioxidant, anti-HIV, antiinflammatory, antibacterial, antipyretic, radioprotective and neuropsycho-physiological activity have been shown (Ravi et al., 2004; Saravanan and Pari, 2006; Saravanan and Pari, 2007). However, despite the various bioactive phytochemical constituents and
diverse medicinal properties attributed to this plant, no detailed biochemical studies have been carried out to shed light on the role of S. cumini bark in diabetes. Hence, the present study was carried out in an attempt to investigate the possible hypoglycaemic and antihyperglycaemic effect of S. cumini bark in streptozotocin-induced diabetic rats.

MATERIALS AND METHODS

Plant Material

S. cumini bark was freshly collected (during August 2001) from plants grown in the Botanical Garden of Annamalai University, Tamil Nadu, India. The plant was taxonomically identified and authenticated at the Herbarium of the Botany Directorate, Faculty of Science, Annamalai University. A voucher specimen (No. 3314) was deposited in the Botany Department of Annamalai University. The bark was air dried at room temperature (25°C) and the dried bark was ground into fine powder with an auto-mix blender. The powdered part was kept in a deep freezer until the time of use.

Preparation of S. cumini Bark Extract

Five hundred gram of dry fine powder was suspended in 1.5 L water and then stirred magnetically overnight (12 h) at room temperature. The extract was preserved and the processes were repeated for three consecutive times with the residual powder, each time collecting the extract. The collected extract was pooled and passed through a fine cotton cloth. The filtrate was evaporated at 40°C in a low-pressure rotavapor (Rotavapor apparatus, Buchi Labortechnik AG, Switzerland) and yielded 15% of semi-solid extract. It was stored in a refrigerator at 0-4°C until used. When needed, the residual extract was suspended in distilled water and used in the study.

Drugs and Chemicals

All the chemicals and biochemicals used in this experiment were purchased from Sigma Chemical Company Inc., St Louis, Mo, USA. The chemicals were of analytical grade.

Experimental Animals

Adult male albino rats of Wistar strain weighing approximately 180-200 g were obtained from Central Animal House, Department of Experimental Medicine, Faculty of Medicine, Rajah Muthiah Medical College, Annamalai University. The animals were housed in polycarbonate cages in a room with a 12 h day-night cycle, temperature of 22±2°C and humidity of 45-64%. During the whole experimental period, animals were fed with a balanced commercial diet (carbohydrates 30%; proteins 22%; lipids 12%; vitamins 3%) (Hindustan Lever Ltd., Mumbai, India) and water ad libitum. All animal experiments were approved by the Ethical Committee, Annamalai University and were in accordance with the guidelines of the National Institute of Nutrition, Indian Council of Medical Research (ICMR), Hyderabad, India. The rats received humane care according to the criteria outlined in the Guide for the Care and Use of Laboratory Animals prepared by the National Academy of Sciences and published by the National Institutes of Health (NIH).

Induction of Experimental Diabetes

Rats were rendered diabetic by a single intraperitoneal injection of freshly prepared streptozotocin (45 mg kg⁻¹ body weight) in 0.1 M citrate buffer (pH 4.5) in a volume of 1 mL kg⁻¹ body weight (Siddique et al., 1987). Normal rats received 1 mL citrate buffer as vehicle. The animals were allowed to drink 5% glucose solution overnight to overcome the drug-induced hypoglycaemia. After 48 h of streptozotocin-administration, blood glucose levels were estimated in rats fasted overnight. Rats with a blood glucose ranging between 200-300 mg dL⁻¹ were considered diabetic and used for the experiment.
Experimental Design

In the experiment, a total of 54 rats were used. The rats were divided into 9 groups of 6 rats each as follows:

**Group 1:** Normal control rats administered gum acacia (2%) daily by gavage for 45 days.

**Group 2:** Normal rats administered SBEt (75 mg kg⁻¹ body weight) in aqueous solution daily by gavage for 45 days.

**Group 3:** Normal rats administered SBEt (150 mg kg⁻¹ body weight) in aqueous solution daily by gavage for 45 days.

**Group 4:** Normal rats administered SBEt (300 mg kg⁻¹ body weight) in aqueous solution daily by gavage for 45 days.

**Group 5:** Diabetic control rats administered gum acacia (2%) daily by gavage for 45 days.

**Group 6:** Diabetic rats administered SBEt (75 mg kg⁻¹ body weight) in aqueous solution daily by gavage for 45 days.

**Group 7:** Diabetic rats administered SBEt (150 mg kg⁻¹ body weight) in aqueous solution daily by gavage for 45 days.

**Group 8:** Diabetic rats administered SBEt (300 mg kg⁻¹ body weight) in aqueous solution daily by gavage for 45 days.

**Group 9:** Diabetic rats administered reference drug glibenclamide (600 µg kg⁻¹ body weight) in aqueous solution daily by gavage for 45 days (Pari and Saravanan, 2002).

Since diabetes is a chronic disorder requiring long-term therapy, there is a need to assess the effect of putative hypoglycaemic/antihyperglycaemic agents for a longer duration. In addition, this application would be beneficial to reveal the late onset activity profile of the agent (Sczak et al., 2005). Therefore an experiment was planned to assess the effect of SBEt for a period of 45 days in streptozotocin-induced diabetic rats. All doses were started after 48 h streptozotocin injection. No detectable irritation or restlessness was observed after each drug or vehicle administration. No noticeable adverse effect (i.e., respiratory distress, abnormal locomotion and catalepsy) was observed in any animals after the drug administration. Blood glucose levels were estimated on 15th and 30th day of the experiments to ascertain the diabetes status in different groups of rats. Throughout the experimental period, the body weight, food and fluid intake were monitored. At the end of the experimental period, the animals were deprived of food overnight and sacrificed by decapitation. Blood was collected in heparin-coated tubes and centrifuged at 1,000 g for 15 min at 4°C.

Measurement of Blood Glucose and Urine Glucose

Blood glucose was determined by the O-toluidine method (Sasaki et al., 1972). Urine glucose was assessed in fresh urine using glucose indicator sticks (Boehringer Mannheim, Germany) before and 48 h after streptozotocin administration, for the confirmation of the diabetic state of animals.
Oral Glucose Tolerance Test

The oral glucose tolerance test is the only form of glucose tolerance testing recommended for diagnosis of diabetes. The changes in blood glucose concentration, which results from an oral carbohydrate load is theoretically dependent on the rate at which carbohydrate enters the small intestine, the rate of digestion and intestinal absorption of glucose and the rate of insulin-driven metabolism. The relationship between plasma levels of glucose and insulin after an external load of glucose can be studied using OGTT (Srinivasan and Karunudev, 2005).

OGTT was performed at the end of experimental period. Prior to OGTT rats were fasted overnight (at least 12 h). Thirty minute following the various treatment schedules, each rat was given an oral glucose load, 2 g kg\(^{-1}\) body weight according to Du Vigneaud and Karr (1925) and Al-Awadi et al. (1985). Blood was withdrawn from the retro orbital sinus at -30 min (just before the administration of the extract), time 0 (prior to the glucose load), 30, 60 and 120 min after the glucose load. Blood glucose concentrations were estimated using a glucose oxidase-peroxidase reactive strips and a glucometer (Accu-check, Roche Diagnostics, USA).

Statistical Analysis

All data were expressed as mean±SD of number of experiments. The statistical significance was evaluated by one-way analysis of variance (ANOVA), using SPSS version 9.5 (SPSS, Cary, NC, USA). Individual comparisons were obtained by Duncan’s Multiple Range Test (DMRT) (Duncan, 1957). A p-value of < 0.05 was considered a significant difference between groups.

RESULTS

Prior to streptozotocin administration, basal blood glucose levels did not differ significantly between groups, whereas 2 days after streptozotocin administration they were significantly higher in diabetic rats. Normal rats were euglycaemic throughout the course of the study. The level of blood glucose was significantly increased in diabetic rats. Oral administration of SBEI and glibenclamide to diabetic rats significantly decreased the levels of blood glucose. Treatment of SBEI to normal rats also decreased the blood glucose concentrations with significant differences. In the SBEI treated groups, although a significant antihyperglycaemic effect was evident from day 15 onwards, decrease in blood glucose was maximum on completion of the 30th day in the group receiving 300 mg kg\(^{-1}\) of SBEI. The study was extended further and more significant decrease in blood glucose was observed on the 45th day. The effect exerted by the extract at a dose of 300 mg kg\(^{-1}\) was greater than that of doses 75 and 150 mg kg\(^{-1}\) body weight or of glibenclamide (600 μg kg\(^{-1}\) body weight). On the basis of these studies, dose of 300 mg kg\(^{-1}\) of SBEI was selected for further biochemical studies (Table 1).

Table 1: Effect of aqueous extract of S. cumini bark on changes in the levels of blood glucose in normal and experimental rats

<table>
<thead>
<tr>
<th>Groups</th>
<th>Fasting blood glucose (mg dL(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>15 days</td>
</tr>
<tr>
<td>1. Normal</td>
<td>73.79±4.97</td>
</tr>
<tr>
<td>2. Normal + SBEI (75 mg kg(^{-1}))</td>
<td>76.12±4.30(^{FS})</td>
</tr>
<tr>
<td>3. Normal + SBEI (150 mg kg(^{-1}))</td>
<td>75.45±4.99(^{FS})</td>
</tr>
<tr>
<td>4. Normal + SBEI (300 mg kg(^{-1}))</td>
<td>72.47±5.01(^{FS})</td>
</tr>
<tr>
<td>5. Diabetic control</td>
<td>245.25±20.35(^{**})</td>
</tr>
<tr>
<td>6. Diabetic + SBEI (75 mg kg(^{-1}))</td>
<td>235.29±19.30(^{FS})</td>
</tr>
<tr>
<td>7. Diabetic + SBEI (150 mg kg(^{-1}))</td>
<td>226.26±20.58(^{FS})</td>
</tr>
<tr>
<td>8. Diabetic + SBEI (300 mg kg(^{-1}))</td>
<td>181.29±16.21(^{**})</td>
</tr>
<tr>
<td>9. Diabetic + Glibenclamide (600 μg kg(^{-1}))</td>
<td>190.56±17.85(^{*})</td>
</tr>
</tbody>
</table>

Values are given as mean±SD from six rats in each group. Group 2, 3, 4 and 5 were compared with Group 1. Group 6, 7, 8 and 9 were compared with Group 5. * p<0.01, ** p<0.001 when compared with Group 1. * p<0.01, ** p<0.001 when compared with Group 5. NS: Not Significant.
Table 2: Effect of aqueous extract of S. cumini bark on oral glucose tolerance test in normal and experimental rats

<table>
<thead>
<tr>
<th>Groups</th>
<th>Blood glucose levels (mg dl⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 min</td>
</tr>
<tr>
<td>1. Normal</td>
<td>77.61±2.59¹</td>
</tr>
<tr>
<td>2. Normal + SBEt (300 mg kg⁻¹)</td>
<td>73.90±2.68¹</td>
</tr>
<tr>
<td>3. Diabetic control</td>
<td>265.81±14.06¹</td>
</tr>
<tr>
<td>4. Diabetic + Glibenclamide (600 μg kg⁻¹)</td>
<td>85.90±2.47¹</td>
</tr>
<tr>
<td>5. Diabetic + Glibenclamide</td>
<td>95.93±3.29¹</td>
</tr>
</tbody>
</table>

Values are given as mean±SD from six rats in each group. Values not sharing a common superscript letter(s) differ significantly at p<0.05 (DMRT).

Table 3: Effect of aqueous extract of S. cumini bark on changes in body weight, food and fluid intakes and urine sugar of normal and experimental rats

<table>
<thead>
<tr>
<th>Groups</th>
<th>Changes in body weight (g)</th>
<th>Food intake (g rat⁻¹ day⁻¹)</th>
<th>Fluid intake (ml rat⁻¹ day⁻¹)</th>
<th>Urine sugar</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Initial</td>
<td>Final</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Normal</td>
<td>179.50±6.98</td>
<td>195.65±6.25²</td>
<td>14.10±1.30³</td>
<td>65.01±6.80⁴</td>
</tr>
<tr>
<td>2. Normal + SBEt (300 mg kg⁻¹)</td>
<td>182.65±7.12</td>
<td>192.70±5.60³</td>
<td>13.85±1.26⁴</td>
<td>60.52±6.50⁵</td>
</tr>
<tr>
<td>3. Diabetic control</td>
<td>184.62±7.17</td>
<td>152.32±5.49⁴</td>
<td>34.50±3.50⁵</td>
<td>155.02±15.2⁶</td>
</tr>
<tr>
<td>4. Diabetic + Glibenclamide (600 μg kg⁻¹)</td>
<td>180.40±6.01</td>
<td>195.42±5.65⁴</td>
<td>20.06±2.03⁵</td>
<td>80.50±7.50⁶</td>
</tr>
<tr>
<td>5. Diabetic + Glibenclamide</td>
<td>181.61±4.98</td>
<td>193.10±6.14³</td>
<td>23.33±2.52⁴</td>
<td>93.01±8.63⁵</td>
</tr>
</tbody>
</table>

Values are given as mean±SD from six rats in each group. Values not sharing a common superscript letter(s) differ significantly at p<0.05 (DMRT). *: values are statistically significant at p<0.001 as compared with their initial weights NS: Not significant as compared with their initial weights. ++: indicates more than 2% sugar.

In diabetic animals, blood glucose levels reached peak at 60 min after glucose administration. Although the glucose levels started to decline, they continued to be high after 120 min. SBEt and glibenclamide treated animals showed a significant decrease at 60 and 120 min after oral glucose administration when compared with diabetic control animals. At the end of 120 min the blood glucose reached to near normal levels in diabetic rats treated with SBEt. Normal rats treated with SBEt also showed significant decrease in blood glucose at 120 min interval. The effect of SBEt was more pronounced when compared with glibenclamide (Table 2).

The mean body weight of diabetic rats was significantly decreased as compared to normal animals. Administration of SBEt to diabetic rats resulted in an increase in body weight when compared to diabetic control rats. The gain in the body weight of SBEt treated diabetic rats was significant and nearer to that of the control rats. A significant increase was observed in food and fluid intakes of diabetic rats when compared to normal rats. The intakes were decreased to near normal levels in SBEt treated diabetic rats. SBEt administration to normal rats did not alter their food and fluid intake and they were similar to that of normal animals. We also found high levels of urinary sugar in diabetic rats that was reverted back to near normal levels in diabetic rats treated with SBEt (Table 3).

**DISCUSSION**

Diabetes mellitus is a major health problem worldwide but its therapeutic management still suffers from major limitations. Global estimates suggest that three forths of the world population cannot afford the products of allopathic medicine and thus, have to rely upon the use of traditional medicines, which are largely derived from plants (Hu et al., 2003). The use of traditional medicine and medicinal plants in most developing countries, as a normative basis for the maintenance of good health, has been widely observed. Furthermore, an increasing reliance on the use of medicinal plants in society has been traced to the extraction and development of several drugs and chemotherapeutics from these plants as well as from traditionally used rural herbal remedies (Bhattaram et al., 2002; Lalita and Pari, 2003). Natural
remedies from medicinal plants are considered to be effective and safe alternative treatment for diabetes mellitus (Czsoy-Sacan et al., 2006). The present paper discussed about the antidiabetic effect of S. cumini bark in experimentally induced diabetes in rats.

Experimental diabetes in animals has provided considerable insight into the physiologic and biochemical derangement of the diabetic state. Streptozotocin, N-(methyl nicotinoyl)-D-glucosamine, is a potent DNA methylating agent and acts as a nitric oxide donor in pancreatic cells. Pancreatic β-cells are particularly sensitive to damage by nitric oxide and free radicals because of their low levels of free radical scavenging enzymes (Elsner et al., 2000; Szukudelski, 2001). It has been widely used to induce diabetes in experimental animal models allowing investigation of hypoglycaemic agents in the treatment of diabetes (Lo et al., 2004).

In this study, the intraperitoneal administration of streptozotocin to normal rats effectively induced diabetes as reflected by glycosuria, hyperglycaemia, hypoinsulinaemia, polyphagia, polydypsia and body weight loss. SBEt treatment showed a significant hypoglycaemic and antihyperglycaemic activity. The maximum reduction in glucose levels was observed in groups receiving 300 mg kg\(^{-1}\) of the extract. The capacity of SBEt to decrease the elevated blood glucose level to normal glycaemic level is an essential trigger for the liver to revert to its normal homeostasis during experimental diabetes. Significant reduction of blood glucose in diabetic rats treated with SBEt confirms previous reports demonstrating the hypoglycaemic and antihyperglycaemic effect of S. cumini bark in normal and diabetic rabbits (Rastamananga et al., 1972). Present findings also agree with the recent studies of Villasenor and Lamadrid (2006) indicating that the blood glucose lowering effect of S. cumini bark extract in oral glucose fed hyperglycaemic mice occurs within 30 min from the onset of S. cumini bark extract treatment.

The oral glucose tolerance test is a well-accepted and frequently used assay to screen hypoglycaemic activity (Zhang and Tan, 2000). SBEt might enhance glucose utilization since it significantly reduces blood glucose in normal and diabetic rats. From the data obtained with the oral glucose tolerance test, it is evident that blood glucose levels reached a peak and returned to initial normal values after 120 min in both normal and treated rats (300 mg kg\(^{-1}\) of body weight of SBEt). Elevated blood glucose levels remained high even after 2 h in diabetic control rats. SBEt treatment effectively prevented the rise in glucose in diabetic rats without causing hypoglycaemic state. This might be due to restoration of delayed insulin response or due to inhibition of intestinal absorption of glucose.

During the experimental period the normal rats showed gain in the body weight. On the other hand diabetic rats showed no significant gain in body weight over the same time period. Rasch (1980) reported that rise in body weight was far less in the poorly controlled diabetic rats as compared to well-controlled diabetic rats. Insulin is an important regulator of protein synthesis and proteolysis in skeletal muscle. Insulin resistance or deficiency results in impaired muscle protein turnover and muscle wasting (Ozsosy-Sacan et al., 2004). McNurlan and Garlick (1979) reported that the rate of protein synthesis in the liver and muscle was decreased in diabetic rats, which may account partly for the negative nitrogen balance and weight loss. Induction of diabetes with streptozotocin is associated with the characteristic loss of body weight, which is due to increased muscle wasting and due to loss of tissue proteins (Swanson-Flatt et al., 1990; Shurwark et al., 2004). Increased food consumption observed in diabetic control rats in comparison to normal rats indicates polyphagic condition due to excessive break down of tissue proteins and this may be attributed to the unavailability of glucose to the cells due to insulin deficiency. Administration of SBEt to diabetic rats showed an increase in body weight, which may be due to its protective effect in controlling muscle wasting (i.e., reversal of gluconeogenesis and glycogenolysis) and may also be due to the improvement in insulin secretion and glycemic control.
It is known that in diabetes, the sites and mechanism of pharmacological intervention in the attendant biochemical processes are diverse (Marles and Farnsworth, 1995; Njike et al., 2005). It is likely that this possibility of diversity in the hypoglycaemic mechanism of the action of drugs may also apply to the extract of S. cumini bark. The antidiabetic effect may be exerted through (both pancreatic and extra-pancreatic mechanisms) the inhibition of glucose absorption, increase sensitivity of receptors to insulin, insulase inhibiting effect, stimulation of β-cells of pancreas to secret insulin or stimulation of peripheral tissues uptake of glucose. At this juncture, Achrekar et al. (1991) reported that water extract of pulp of S. cumini stimulates release of insulin both in in vivo and in vitro studies. Bansal et al. (1981) reported that the increase in plasma insulin brought about by seeds of S. cumini may be attributed to proinsulin to insulin conversions, possibly by pancreatic cathespin B and/or its secretion. Diabetics have greater Insulinase activity than non-diabetics. The inhibition of insulinase activity from the liver and kidney (which are the main sites for insulin extraction) by extract of S. cumini, which has been reported (Achrekar et al., 1991), points to an extra-pancreatic mechanism of action also. Phytochemical examinations of this plant have indicated the presence of flavonoids and other polyphenolics such as acetyl oleanolic acid, tannin, gallic acid, ellagic acid, quercetin, isoquercetin, kaempferol, myricetin, flavonol glycoside, triterpenoids, saponins and anthocyanin in different concentrations (Gupta and Sharma, 1974; Jagtia and Baliga, 2002; Sagrawat al., 2006). Most of these compounds isolated from different plants have previously been suggested to be the active antidiabetic ingredients of various plant remedies. These natural compounds could act separately or synergistically to cause the hypoglycaemic effect (Maghram et al., 2004). The present study thus justifies the traditional use of S. cumini bark in the treatment of diabetes and has also opened avenues for further research especially with reference to the development of potent phytomedicine for diabetes mellitus from S. cumini bark. Further phytochemical and pharmacological investigations are in progress to understand the exact mechanism of action of this drug.

REFERENCES


