Effects of *Murraya koenigii* leaf extract on impaired gastrointestinal motility in streptozotocin-induced diabetic rats

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**Objective:** The present study was to investigate the effects of *Murraya koenigii* leaf (MKL), an Indian herb, on glucose homeostasis, intestinal transit time, response to exogenous acetylcholine of smooth muscles of distal colon, and intestinal thiobarbituric acid reactive substance (TBARS) level in streptozotocin (STZ)-induced diabetic rats.

**Methods:** Male adult Wistar rats were used in this study. Diabetes was induced in the rats by STZ (70 mg/kg, intravenously). The treatments of MKL extract (300 and 500 mg/kg) and glibenclamide were started after stabilization of blood glucose level (13 d after single dose of STZ), while the standard drug cisapride or vitamin E was given from the last week (8th week) of experimentation. At the end of the study, the rats were sacrificed and evaluated for gastrointestinal motility, the contractile response of distal colons and the TBARS content. The gastrointestinal motility was evaluated by measuring the intestinal transit rate of charcoal meal. The contractile response of distal colon was measured in terms of evaluating the dose-response curve with increasing doses of acetylcholine, and the TBARS content was measured by calculating the level of polynsaturated fatty acid in homogenates of intestines of the diabetic rats.

**Results:** MKL significantly decreased the blood glucose level at the 30th (*P*<0.05) and 60th (*P*<0.01) day of MKL administration (300 and 500 mg/kg). The gastrointestinal motility significantly (*P*<0.05) reduced after 9 weeks in diabetic rats and it was correlated to the decrease of the percent response of acetylcholine on distal colons (*P*<0.01) and the increase of TBARS (as an index of oxidative stress) in intestines (*P*<0.05), while prior treatment with MKL (300 and 500 mg/kg) up to 9 weeks increased the gastrointestinal motility demonstrated by the increase in the activation of cholinergic response to acetylcholine on distal colons (*P*<0.05). The TBARS also decreased after 9-week treatment with MKL (*P*<0.05).

**Conclusion:** The present study suggested that MKL had protective effect against gastrointestinal disturbances in diabetes by controlling glucose level as well as defending against peripheral damage of cholinergic neurons by providing antioxidant shelter, so it may be helpful in diabetic patients with impaired gastrointestinal motility.

**Keywords:** *Murraya*; diabetes mellitus, experimental; gastrointestinal motility; cholinergic agents; thiobarbituric acid reactive substances; plant extracts; rats
Long-standing diabetes may be associated with gastrointestinal complications such as nausea and vomiting secondary to gastroparesis, diarrhea, constipation, and abdominal pain\(^1\). Although most often associated with type 1 or insulin-dependent diabetes, gastrointestinal complications may also appear in long-standing poorly controlled type 2 diabetes\(^5\).

The cause of gastrointestinal dysfunction in diabetes mellitus appears to be multifactorial. Potential causes include vagal nerve dysfunction\(^4\), sympathetic nerve damage\(^7\), damage to enteric nervous system\(^6\), and hyperglycemia\(^10\). Gastrointestinal dysmotility not only affects patients by causing symptoms and posing a heavy burden of illness but also causes decreased quality of life with decreased work productivity. Gastrointestinal dysmotility also impacts the quality of life of patients with other disorders such as in diabetes\(^11\).

Oxidative stress has a well-established role in the pathogenesis of chronic complications of diabetes mellitus and is a measure of steady state level of reactive oxygen species (ROS) in the biological system\(^13\). The conditions that lead to the over production of the precursors to the ROS and/or reduce the efficiency of inhibitory and scavenging system are shown to be responsible for the development of oxidative stress. Under diabetic condition, ROS are produced through the glycation reaction in various tissues and are reported to play a role in the development of chronic complications including gastrointestinal dysmotility in diabetes mellitus\(^13\, 14\). On the basis of these observations, it is concluded that patients with diabetes mellitus may show gastrointestinal disturbance due to the damage of gastrointestinal neurons by results of oxidative stress\(^10\). Previously we found the beneficial effect of *Murraya koenigii* leaf (MKL) extract on gastrointestinal motility through cholinergic pathway and calcium pathway in mice\(^12\). The reported literature on *M. koenigii* also indicated that it contains antioxidant phytochemical constituent alkaloids\(^7\, 18\). So by considering our previous results on gastrointestinal motility and presence of antioxidant alkaloids, the present study was designed to evaluate the effects of ethanolic extract of MKL on gastrointestinal dysmotility in streptozotocin (STZ)-induced diabetic rats. The study was also undertaken to evaluate the mechanism involved in gastrointestinal dysmotility.

1 Materials and methods

1.1 Authentication of plant The fresh leaves of *M. koenigii* were collected from its natural habitat at Sakoli village in Nagpur region, Maharashtra, India. The plant was authenticated by Dr. N. M. Dongarwar of Botany Department, RTM Nagpur University, Nagpur, India. A voucher specimen (No: 9439) was deposited at the Herbarium, Department of Botany, RTM Nagpur University, Nagpur, India.

1.2 Extraction of MKL The collected leaves of *M. koenigii* were dried under shade, underwent crushing in electric blender to form powder and were subjected to extraction by Soxlets apparatus (J-Seal Glassware Pvt. Ltd. Mumbai, India) by using ethanol as a solvent. The extract was concentrated by evaporation at room temperature and was used for pharmacological studies. The product yield was found to be 5.3%. Suspension of ethanolic extract was prepared in 0.5% carboxymethyl cellulose using Tween-20 (0.2% volume ratio) as a suspending agent.

1.3 Drugs and reagents STZ, a gift sample from Nicholas Piramal, Mumbai (Sigma Aldrich, USA), was prepared in cold citrate buffer (pH 4.5, 0.1 mol/L) and injected intravenously in a single dose. Cisapride (Davis Pharma, Hyderabad, India) was prepared similarly as plant extract and given orally. Vitamin E (20%) was dissolved in soya oil and given orally (Loba Chemie, Mumbai, India). All the reagents and chemicals used in present study were of analytical grade. All the drugs were injected after stabilization of blood glucose level from the 13th day of STZ injection in a constant volume of 1 mL/kg of body weight.

1.4 Experimental animals All the experiments were carried out on male Wistar albino rats, weighing 180–200 g, purchased from the laboratory animal house, Departments of Animal husbandry, Chhattisgarh University, Raipur, India. The animals were fed standard laboratory rat chow and water ad libitum. The animals were acclimatized for 1 week before starting the experiment and were maintained in standard conditions of temperature and humidity with 12-h light/12-h dark cycle. All the experiments were carried out in accordance with the standards laid down by the Committees for the Control and Supervision of Experiments on Animals (CPCSEA), Ministry of Environment and Forests, Government of India, New Delhi.

### Related Articles


were carried out in male Wistar rats (body weight 180 to 220 g). The rats had free access to food and water, and they were housed in a natural light/dark cycle. The rats were acclimatized to the laboratory conditions for at least one week before experiment. Experiments were carried out between 9 AM and 6 PM. The Institutional Animal Ethics Committee approved the experimental protocol and the care of laboratory animals was taken according to the guidelines of Committee for the Purpose of Control and Supervision on Experiments on Animals, Ministry of Forests and Environment, Government of India (registration number 729/02/a/ CPCSEA).

1.5 Experimental design

1.5.1 Phytochemical evaluation of MKL MKL was screened for the presence of phytoconstituents by chemical as well as by a thin layer chromatography (TLC) system[19, 20].

1.5.2 Induction and assessment of diabetes in rats STZ was injected intravenously in a single dose of 70 mg/kg to male Wister rats. The age-matched control rats received an equivalent volume of citrate buffer and were used along with diabetic rats as normal control considered as group 1. The STZ-treated rats were given 5% glucose water for 24 h to prevent mortality due to the initial drug-induced hypoglycemia. After 13 d, the mortality of rats (because of cytotoxic action of STZ and unstable blood glucose level) was reduced to zero. All the survival diabetic rats showing stable with more than 2 500 mg/L glucose level were randomly divided into 6 groups (groups 2 to 7) each consisting of 5 rats. Group 1 as a normal vehicle control received 0.5% sodium carboxy methyl cellulose with Tween-20 (0.2% volume ratio). Group 2 as a diabetic control also received vehicle. Groups 3 and 4 diabetic rats received MKL 300 and 500 mg/kg, per oral (p.o.), respectively. Group 5 diabetic rats received standard drug glibenclamide (10 mg/kg, p.o.). Groups 6 and 7 received vitamin E (20%) in soya oil or cisapride (20 mg/kg) orally, one week before the end of study as a standard drug for determination of antioxidant activity and gastrointestinal motility, respectively. All the groups of rats received the treatments for 9 weeks for evaluation of the preventive effect of MKL on the progression of gastrointestinal complication in diabetes. The standard drugs cisapride or vitamin E were given from the end of the 8th week of induction of diabetes because the diabetic complications were generally observed after 6 to 8 weeks of induction of diabetes according to the previous reported literature[21-24]. The blood glucose levels were determined at the 30th and the 60th day from respective treatment groups except groups 6 and 7.

1.5.3 Gastrointestinal motility (transit time) determination At the end of study, all the groups of rats were administered with 4% activated charcoal meal and 20 min later killed by cervical dislocation for determination of intestinal transit. The small intestines were removed from the pyloric sphincters to the ileocecal junction and the distance travelled by the charcoal meal was recorded and expressed as percentage of intestinal transit using the following formula. The intestinal transit of charcoal meal was determined by the modified Janse’s method[24, 25]. The formula is as follows:

\[ \text{Transit} \% = \frac{\text{Distance travelled by charcoal meal}}{\text{Total length of small intestine}} \times 100\% \]

1.5.4 Percent response of acetylcholine on distal colons Immediately after cleaning and measuring the length of large intestines, distal colons were cut and used for in vitro study. The distal colons were dissected out and mounted under a resting tension of 0.5 g in an organ bath containing continuously aerated Tyrode’s solution. Dose-response curve was obtained with increasing doses of acetylcholine. Percent response of acetylcholine was calculated by considering the 100% response of higher dose of acetylcholine on distal colons of normal rats (n=3).

1.5.5 Determination of thiobarbituric acid reactive substance After sacrificing the rats during evaluation of gastrointestinal motility, 2 g pieces of small intestines were isolated from respective groups of rats and homogenized in potassium chloride solution (0.15 mol/L) respectively. Homogenates were centrifuged and supernatant was used as a source of polynsaturated fatty acid for determination of extent of thiobarbituric acid reactive substances (TBARS). The content of TBARS as a index of lipid peroxidation or oxidative stress[26] was measured as per our previous work[27].

1.6 Statistical analysis Results were expressed as the mean±standard deviation (SD). For statistical analysis of the data groups, means were compared by one-way analysis of variance followed by Dunnett-t test for multiple comparisons (P<0.05, P<0.01) using Graph Pad Prism version 5.0.

2 Results

2.1 The yield of extract The yield for ethanolic extract of MKL was calculated to be 7.4% (w/w, weight ratio).

2.2 Phytochemical evaluation of MKL Preliminary phytochemical data revealed the presence of carbohydrates, gums, mucilage, proteins, triterpenoids, cardiac glycosides, alkaloids, flavonoids and phenolic compounds. The TLC system gave several spots, one of which gave the specific R\text{f} value nearly 0.60 and gave the dragendorff test positive representing the spot of alkaloids.
2.3 Assessment of diabetes  Treatments with MKL extract (300 and 500 mg/kg, p. o.) and glibenclamide (10 mg/kg, p. o.) decreased the blood glucose level at the 30th and 60th day significantly. The more relevant values were observed at the 60th day of treatment ($P<0.01$) (Table 1).

<table>
<thead>
<tr>
<th>Group</th>
<th>$n$</th>
<th>Blood glucose level (Mean±standard deviation, mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vehicle control</td>
<td>5</td>
<td>853.0±39.1</td>
</tr>
<tr>
<td>Diabetic control</td>
<td>5</td>
<td>3 675.1±172.3*</td>
</tr>
<tr>
<td>MKL extract (300 mg/kg)</td>
<td>5</td>
<td>3 675.1±172.3*</td>
</tr>
<tr>
<td>MKL extract (500 mg/kg)</td>
<td>5</td>
<td>3 675.1±172.3*</td>
</tr>
<tr>
<td>Glibenclamide (10 mg/kg)</td>
<td>5</td>
<td>3 675.1±172.3*</td>
</tr>
</tbody>
</table>

* $P<0.01$, vs vehicle control (0 d); ** $P<0.01$, vs diabetic control (30 d); $$$ P<0.01$, vs diabetic control (60 d). MKL: *Murraya koenigii* leaf.

2.4 Gastrointestinal motility determination  The gastrointestinal dysmotility decreased in percent transit after 9 weeks in diabetic rats compared with the vehicle control ($P<0.05$). Treatment with MKL (300 and 500 mg/kg) significantly ($P<0.05$) protected from the effect of diabetes-induced gastrointestinal dysmotility (Table 2). The effect of MKL was comparable to the standard drugs vitamin E and cisapride.

2.5 Determination of percent response to acetylcholine  Percent response to acetylcholine decreased ($P<0.01$) on distal colonic smooth muscle of diabetic rats (Table 3). The treatment with MKL (300 and 500 mg/kg) increased the percent response ($P<0.05$) of distal colons compared with diabetic rats.

2.6 Determination of TBARS  The results indicated a significant ($P<0.05$) increase in intestinal TBARS content in diabetic rats compared with vehicle control. While the treatment with MKL showed a significant ($P<0.05$) reduction in the level of TBARS dose-dependently (Table 4).

### Table 1  Effects of MKL extract on blood glucose level in diabetic rats (Mean±standard deviation, mg/L)

<table>
<thead>
<tr>
<th>Group</th>
<th>$n$</th>
<th>0 d</th>
<th>30 d</th>
<th>60 d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vehicle control</td>
<td>5</td>
<td>853.0±39.1</td>
<td>3 675.1±172.3</td>
<td>3 675.1±172.3</td>
</tr>
<tr>
<td>Diabetic control</td>
<td>5</td>
<td>3 675.1±172.3</td>
<td>1 784.6±155.3</td>
<td>1 784.6±155.3</td>
</tr>
<tr>
<td>MKL extract (300 mg/kg)</td>
<td>5</td>
<td>3 675.1±172.3</td>
<td>1 784.6±155.3</td>
<td>1 784.6±155.3</td>
</tr>
<tr>
<td>MKL extract (500 mg/kg)</td>
<td>5</td>
<td>3 675.1±172.3</td>
<td>1 784.6±155.3</td>
<td>1 784.6±155.3</td>
</tr>
<tr>
<td>Glibenclamide (10 mg/kg)</td>
<td>5</td>
<td>3 675.1±172.3</td>
<td>1 784.6±155.3</td>
<td>1 784.6±155.3</td>
</tr>
</tbody>
</table>

* $P<0.01$, vs vehicle control (0 d); ** $P<0.01$, vs diabetic control (30 d); $$$ P<0.01$, vs diabetic control (60 d). MKL: *Murraya koenigii* leaf.

### Table 2  Effects of MKL extract on gastrointestinal motility in diabetic rats (Mean±standard deviation, %)

<table>
<thead>
<tr>
<th>Group</th>
<th>$n$</th>
<th>Percent transit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vehicle control</td>
<td>5</td>
<td>62.79±6.27</td>
</tr>
<tr>
<td>Diabetic control</td>
<td>5</td>
<td>46.02±8.58</td>
</tr>
<tr>
<td>MKL extract (300 mg/kg)</td>
<td>5</td>
<td>68.89±6.89</td>
</tr>
<tr>
<td>MKL extract (500 mg/kg)</td>
<td>5</td>
<td>73.81±4.78</td>
</tr>
<tr>
<td>Vitamin E (20%)</td>
<td>5</td>
<td>58.14±7.09</td>
</tr>
<tr>
<td>Cisapride (20 mg/kg)</td>
<td>5</td>
<td>61.85±9.96</td>
</tr>
</tbody>
</table>

* $P<0.05$, vs vehicle control; ** $P<0.05$, vs diabetic control. MKL: *Murraya koenigii* leaf.

### Table 3  Percent response to exogenous acetylcholine of distal colons in diabetic rats (Mean±standard deviation, %)

<table>
<thead>
<tr>
<th>Group</th>
<th>$n$</th>
<th>0.1</th>
<th>0.2</th>
<th>0.4</th>
<th>0.6</th>
<th>0.8</th>
<th>1.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vehicle control</td>
<td>5</td>
<td>52.21±6.34</td>
<td>57.65±5.42</td>
<td>63.23±7.33</td>
<td>69.70±6.37</td>
<td>69.70±6.37</td>
<td>100</td>
</tr>
<tr>
<td>Diabetic control</td>
<td>5</td>
<td>15.45±4.54*</td>
<td>21.32±5.42*</td>
<td>30.35±5.76**</td>
<td>39.49±6.54**</td>
<td>45.32±4.55**</td>
<td>51.62±5.67**</td>
</tr>
<tr>
<td>MKL extract (300 mg/kg)</td>
<td>5</td>
<td>32.34±6.78△</td>
<td>39.07±7.34△</td>
<td>45.76±7.78△</td>
<td>54.67±6.89△</td>
<td>60.59±4.58△</td>
<td>69.70±5.80△</td>
</tr>
<tr>
<td>MKL extract (500 mg/kg)</td>
<td>5</td>
<td>41.32±6.43△</td>
<td>48.44±4.32△</td>
<td>57.42±5.64△</td>
<td>69.65±7.44△</td>
<td>78.78±6.67△</td>
<td>87.46±4.76△</td>
</tr>
<tr>
<td>Vitamin E (20%)</td>
<td>5</td>
<td>36.78±5.58△</td>
<td>51.23±6.32△</td>
<td>60.25±6.55△</td>
<td>66.43±7.54△</td>
<td>83.87±6.77△</td>
<td>91.22±5.89△</td>
</tr>
<tr>
<td>Cisapride (20 mg/kg)</td>
<td>5</td>
<td>34.33±4.34△</td>
<td>42.45±5.45△</td>
<td>49.32±5.67△</td>
<td>58.34±7.65△</td>
<td>65.97±6.55△</td>
<td>72.56±6.22△</td>
</tr>
</tbody>
</table>

* $P<0.01$, vs vehicle control; ** $P<0.05$, vs diabetic control; △ $P<0.05$, vs vehicle control; △△ $P<0.01$, vs diabetic control. MKL: *Murraya koenigii* leaf.

### Table 4  Effects of MKL extract on intestinal TBARS in diabetic rats (Mean±standard deviation)

<table>
<thead>
<tr>
<th>Group</th>
<th>$n$</th>
<th>Absorbance of TBARS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vehicle control</td>
<td>5</td>
<td>0.220±0.025</td>
</tr>
<tr>
<td>Diabetic control</td>
<td>5</td>
<td>0.430±0.031*</td>
</tr>
<tr>
<td>MKL extract (300 mg/kg)</td>
<td>5</td>
<td>0.210±0.018△</td>
</tr>
<tr>
<td>MKL extract (500 mg/kg)</td>
<td>5</td>
<td>0.190±0.018△</td>
</tr>
<tr>
<td>Vitamin E (20%)</td>
<td>5</td>
<td>0.250±0.026△</td>
</tr>
</tbody>
</table>

* $P<0.05$, vs vehicle control; △ $P<0.05$, vs diabetic control. MKL: *Murraya koenigii* leaf; TBARS: thiobarbituric acid reactive substance.

### 3 Discussion

Chronic complications of diabetes involving gastrointestinal tract are reported to cause considerable morbidity in patients with diabetes mellitus [41]. Since glucose infusions are reported to inhibit gastric motility and efferent activity in the vagus nerve, the abnormal gastrointestinal motility among diabetic patients seems to be a clinical manifestation of diabetic autonomic neuropathy [41]. A well recognized impact of long-standing diabetes...
mellitus on gastrointestinal tract of human being is delayed gastric emptying and decreased antrum contractility\(^\text{[5]}\). These effects are attributed to diabetes-induced gastroparesis and neuropathy\(^\text{[6, 7]}\). Our previous study was to investigate the protective effect of *M. koenigii* on neuropathic pain in diabetic animals\(^\text{[22]}\). Several studies demonstrated the gastrointestinal dysmotility in diabetic animals\(^\text{[30, 31]}\). This study was then undertaken to evaluate the influence of *M. koenigii* on gastrointestinal dysmotility in diabetic rats. In the present study, the gastrointestinal complication was evaluated by determining the gastrointestinal dysmotility as a common clinical feature of diabetes mellitus that involves autonomic neuropathy or an impaired cholinergic neurotransmission and reduced smooth muscle response to neurotransmitter\(^\text{[6,30]}\).

In the present study, a single dose of STZ injection significantly increased the blood glucose level as induction of diabetes. STZ induced diabetes in rats by β cell destruction\(^\text{[10]}\), while the standard drug glibenclamide decreased the blood glucose level (Table 1), which indicated that this was a type 2 diabetic model, because glibenclamide needs some pancreatic β-islet to turn out the action\(^\text{[30, 34]}\). Treatment with MKL normalized (\(P<0.01\)) the blood glucose level dose-dependently after 9 weeks of treatment which was comparable to glibenclamide (Table 1). The results also showed that MKL could protect the rats from gastrointestinal dysmotility due to induction of chronic diabetic condition (Table 2). The effect of MKL on gastrointestinal motility was dose-dependent and it was comparable to cisapride. The effect of MKL on gastrointestinal dysmotility was also comparable to vitamin E which was similar to earlier reported finding in diabetic rats\(^\text{[25]}\). The results of present findings on gastrointestinal motility were also supported with our previous findings on acceleratory effect of MKL on gastrointestinal motility through calcium and cholinergic innervations in mice\(^\text{[15, 16]}\).

The malfunctioning in the gastrointestinal tract in diabetes may be associated with the oxidative damage of autonomic neurons and down regulation of muscarinic receptors in colonic smooth muscles, respectively\(^\text{[15, 16]}\). The results of the distal colonic smooth muscle indicated a significant (\(P<0.01\)) reduction in the contractile response of smooth muscle to exogenous acetylcholine (1 mg/mL). Same result was found on distal colon of the MKL-treated diabetic rats (Table 3).

Oxidative stress has an important role in tissue damage associated with chronic complications of diabetes mellitus\(^\text{[19]}\). It is suggested that malfunctioning in the gastrointestinal tract in diabetes is associated with the oxidative stress. The drugs which have antioxidant property may be used to protecting from development of gastrointestinal dysmotility in diabetes. Recently it is shown that antioxidant vitamin E has a beneficial role in the gastrointestinal motility in diabetic animals\(^\text{[21]}\). In the present study, oxidative stress was induced by development of chronic diabetic condition and we measured lipid peroxidation of unsaturated fatty acids which is commonly used as indexes of increased oxidative stress and subsequent cytotoxicity\(^\text{[23, 27]}\). In the present study, elevated level of lipid peroxidation in intestines of the diabetic rats may be due to the enhanced production of ROS and TBARS\(^\text{[22, 21]}\). The significant increase in intestinal TBARS content in 9-week diabetic rats compared with control rats indicated the elevated level of lipid peroxidation and tissue damage. However, prior administration of MKL extract significantly reduced the level of TBARS dose-dependently, indicating a decrease rate of lipid peroxidation and prevention from damage to intestine (Table 4).

In the present study, the phytochemical data revealed the presence of alkaloids in the extract of MKL. Previous literature also showed the presence of alkaloid as a major chemical constituents in MKL and reported the antioxidant activity\(^\text{[17, 18, 29]}\). Thus the same constituents may be responsible for the antioxidant activity of MKL in the present study.

In conclusion, the present study demonstrated that treatment with ethanolic extract of MKL could antagonize gastrointestinal disturbance in diabetes by controlling the glycemic level and defend against peripheral damage of cholinergic neurons by providing antioxidant shelter. However, more efforts are still needed for the isolation, characterization and biological evaluation of the active principles of *M. koenigii* extract.

4 Acknowledgments

The authors are thankful to Dr. Knemani, Diabetology Division of Nicholas Piramal Research Laboratory, Mumbai, India, for providing gift sample of STZ to carry out the research work.

5 Conflict of interest statement

The authors declare that there are no conflicts of interest and no agency is involved for financial support for this research work.

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可因氏越橘叶提取物对链脲佐菌素致糖尿病大鼠胃肠活动的影响

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目的：探讨印度草药可因氏越橘叶子的提取物对链脲佐菌素所致糖尿病大鼠的血糖调节、小肠通过时间、远端结肠平滑肌对外源性乙酰胆碱的应答情况及小肠内酰胺巴比妥酸反应物水平的影响。

方法：使用成年雄性Wistar大鼠，通过静脉注射链脲佐菌素（70 mg/kg）建立糖尿病大鼠实验模型。造模后13天大鼠血糖稳定后使用可因氏越橘叶子提取物及格列本脲治疗，实验最后一周（第8周）给予标准药西沙比利或维生素E。实验结束时处死大鼠，测量其胃肠活动，测量远端结肠收缩反应及酰胺巴比妥酸反应物含量。通过测量餐后小肠通过时间衡量胃肠活动；通过不断增加外源性乙酰胆碱刺激，测量剂型效应曲线衡量远端结肠收缩情况；通过测量大鼠小肠缩窄内多肽不饱和脂肪酸含量确定酰胺巴比妥酸反应物含量。

结果：可因氏越橘叶子的提取物（300及500 mg/kg）在给药后30和60 d显著降低了大鼠的血糖水平（P＜0.05, P＜0.01）。与空白对照组比较，实验9周后模型组大鼠的胃肠活动显著下降（P＜0.05），且与远端结肠对外源性乙酰胆碱刺激的反应降低（P＜0.01）及小肠缩窄内酰胺巴比妥酸反应物含量升高（P＜0.05）有关。而使用可因氏越橘叶子的提取物（300及500 mg/kg）治疗9周的大鼠胃肠活动较模型组增加，表现为远端结肠对外源性乙酰胆碱刺激的反应增加（P＜0.05），而小肠缩窄内酰胺巴比妥酸反应物含量与模型组相比亦有降低（P＜0.05）。

结论：可因氏越橘叶子的提取物对糖尿病并发症引起的胃肠活动下降有保护作用，表现为控制血糖和对外周胆碱能神经元的保护作用。所以该植物有可能用于治疗糖尿病病人的胃肠功能减退。

关键词：九里香属；糖尿病；实验性；胃肠活动；胆碱能药；巴比妥酸反应物；植物提取物；大鼠