Drug Promising Effect for Diabetic Mice of CARICA PAPAYA Leaves


ABSTRACT

Diabetes Mellitus is a major problem for city people worldwide. The goal of this experiment is finding the anti-diabetic and lipid metabolism enhancing by using Carica papaya leaves. This leaves are not generally eaten but these leaves were eaten during dengue fever. The leaves extract is used for the treatment of diabetes and cancer. This leaves were collected from different place of Bangladesh and made methanolic extract then this extract was feed four groups of mice. The findings indicate that the methanolic extract of C. papaya at doses of 100 mg/kg, 200 mg/kg and glibenclamide (used as reference) at a dose of 5mg/kg weight enhanced sugar metabolism. In experimental model of diabetic mellitus the same dose of C. papaya leaves extract significantly regulated the level of blood lipid profile. The oral administration of c. papaya leaves methanol extract also caused the level of serum SGPT, SGOT and CRP level return to normal state. In conclusion this research finding indicates that C. papaya leaves methanol extract contains bioactive substances with hypoglycemic potency.

Keywords: DM, HDL, LDL, ME, TC, TG.

I. INTRODUCTION

Diabetic is a main problem for modern world. Presently capital city peoples body weight is increasing and diabetics is rising. The Diabetic people are using insulin so that they cannot properly produce insulin by naturally. Lot of complication happens for accumulation of blood sugar [1]. Diabetics found in many developing and newly industrialized citizen and already many reason was drawn by researchers. Most of test related with diabetics and people are now diagnosing this disease. But there are many cheap tests available for diabetic’s detection [2]. Bangladesh is thought one of the highest risk area for diabetics and cancer risk area [3]. Diabetes is one of the global concern and statistics says that about 415 million people victims for diabetes and 5 million deaths in 2015, average 1/6 seconds die from diabetes and 46% people under treatment [4]. Bangladesh adults are main target for this disease and data analysis says that 4% in 1995 to 2000 and 5% in 2001 to 2005 to 9% in 2006 to 2010 and the amount will be 13% by 2030 [5]. Scientists had been demonstrated that coronary occlusions and blocks found between diabetic people specially those people living with High level of LDL and Low level of HDL. Many side effects found for those people using it as longtime treatment and more drugs for diabetic treatment [6]. In spite of many drug, manufacturing pharmacologist trying to find more efficient and less chemically hazardous for diabetic patient immune system and already lot of plants have been experimented and found antidiabetic activity [7]. Caricaeae family species are

Published Online: December 4, 2022
ISSN: 2795-8035
DOI: 10.24018/ejpharma.2022.2.3.47

M. R. H. Bhuiyan*
Department of Biochemistry and Molecular Biology, University of Rajshahi-6205, Bangladesh.
(e-mail: mdrkibulhasanbhuiyan3@gmail.com)

M. Maniruzzaman
Department of Pharmacy, University of Rajshahi-6005, Bangladesh.
(e-mail: manir5337pharmacy@gmail.com)

S. Akter
Department of Biochemistry and Molecular Biology, University of Rajshahi-6205, Bangladesh.
(e-mail: sabin9509@gmail.com)

S. Mehjabin
Department of Pharmacy, Varendra University, Rajshahi-6204, Bangladesh.
(e-mail: sanzia297@gmail.com)

M. R. R. Rana
Department of Public Health, Varendra University, Rajshahi, Bangladesh.
Faculty of Science & Engineering, Varendra University, Rajshahi 6204, Bangladesh.
(e-mail: rakibrana.vu@gmail.com)

M. S. Jaman
Department of Biochemistry and Molecular Biology, University of Rajshahi-6205, Bangladesh.
(e-mail: sadik09bio.ru19@gmail.com)

*Corresponding Author
good for fruits and vegetable and *carica papaya* is one of them. Recently this leaves are eaten by dengue fever people for increasing platelet level control [8], [9]. Many diseases is treated by using this tree different parts especially fruit, leaf, root and many evidence we got that treatment is taken for anemia, piles, jaundice, hemorrhage, diabetes, ulcers, convulsion, hepatitis and dysentery [10], [11]. In Bangladesh we did not find any research for its pharmacological properties. This is the main reason that we aim to finds its anti-diabetic and antihyperlipidemic as well as its medicinal properties by consuming leaves.

II. MATERIALS AND METHODS

A. Leave Collection and Confirmation

The immature leaves specially *cariceae* family species were collected from Narsindri, Dhaka and corroborated by Dr. A.H.M Mahbubur Rahman, Professor Department of Botany University of Rajshahi, Bangladesh.

B. Protocol for Leaves Extraction Making

To get rid of combustible dirt, the leaves were first washed with water and dried leaves were shed. The dry leaf was powdered using a (FFC-15, china) once it had finished drying completely and it was then placed in an airtight container for later usage. About 80 gm of the powdered substance was placed in a separate clean round bottomed glass with 400 ml of each solvent. The container and its contents were sealed with a cotton stopper and aluminum foil and maintained for 15 days with sporadic shaking and stirring. Whitman No. 1 filter paper was used to remove the residue from the extracted materials. Following that, the solvents were heated to 390 °C in a rotary evaporator under reduced pressure. Finally, until they were used the remnants were stored in tiny sterile vials.

C. Chemicals

Chemical streptozotocin is utilized and is bought from the trades worth company. Others reagent, which were purchased from chemical suppliers and its quality were measured in analytical grade.

D. Animal Care

Swiss albino mice were used as the experimental animals for this investigation at the International Cholera and Dysentry Disease Research in Dhaka, Bangladesh. Mice were raised in a polypropylene cage under ideal conditions (24.44 °C, 58.8% humidity, and a 12-hour light/dark cycle). Dry pellet food and water were given to the mice.

E. Diabetic Induction

For the objective of inducing diabetes, mice were injected with streptozotocin (60 mg/kg weight) in a 0.1 M sodium citrate buffer (pH 4.5). Control mice were given same amount of citrate buffer. Diabetic induced mice were closely monitored and given food and water. The onset of diabetic symptoms was guaranteed by fasting blood sugar measurements made from the tail vein using a mobile glucose meter (acu-check, Roche, Germany). These findings included weight loss and the fasting blood Sugar level of diabetic mice was higher than 11.50 mmol/L.

F. Experimental Groups

After a week of acclimation, mice were divided into five groups of five each. The mice were grouped as follows:  
I) Mice raised on a conventional pellet diet and water make up Group 1 (Normal control)  
II) Diabetic mice were cultured in Group 2 (the diabetic control) without any medication. 
III) Group 3 (positive control): Glibenclamide at a dose of 5 mg/kg weight was administered to diabetic mice.  
IV) Group 4 (Treated 1): Diabetic mice who received 100 mg/kg of *C.papaya* leaf extract in methanol daily for 21 days.  
V) Group 5 (treated 2): diabetic mice were administered a 200 mg/kg weight methanol extract of *C.papaya* leaves daily for 21 days.

G. Blood Sample Collection

On days 1, 5, 10, 15 and 21 in a fasted state, blood was collected from the tail vein of each group of mice using a 26 G needle and syringe. After an overnight fast, mice were sacrificed at the end of the experiments 21-day run. Mice were given a chloroform anesthesia and blood was drawn from the heart. Serum after blood clot was collected and centrifuged at 4000 rpm for 15 minutes before using stored at -75 °C until the studies were conducted.

H. Biochemical Data Determination

Enzymatic analysis was used to measure blood sugar levels. The Siemens Dimension Expand plus chemical analyzer (The Siemens Healthcare Diagnostics) was used to measure triglycerides, total cholesterol, HDL-cholesterol, LDL cholesterol.

I. Data Analysis

All parameter was shown Mean ± Standard Deviation. Data analysis was confirmed with IBM SPSS 12.0 version.

III. RESULTS

A. Effects of A *C. Papaya* Leaf Methanol Extract on Blood Sugar Levels

Mice receiving intravenous streptozotocin have higher blood sugar levels than control groups. On the other hand, diabetic mice who received oral supplements with *C. papaya* leaf extract at doses of 10 mg/kg and 200 mg/kg weight had lower blood sugar levels than the diabetic control group (Fig. 1). Falling blood sugar levels were carefully monitored in mice employed as positive controls (where Glibenclamide at a normal dose of 5 mg/kg weight was utilized). In comparison to the diabetic control group methanol extract of *C. papaya* leaves at both doses (100 mg/kg and 200 mg/kg weight) decreased blood glucose levels by 13.28%-42.50% and 13.50%-48.20%, respectively.

B. Results Of Methanolic Extract Of C. Papaya Leaves On Lipid Profile:

Fig. 2 displayed lipid profile levels of control and streptozotocin induced diabetic mice for total cholesterol triglycerides, VLDL, HDL and hypercholesterolemia. In diabetic mice treated with a methanol extract of *C. papaya* leaves, the reduction in total cholesterol was 19.20% at doses.
of 100 mg/kg and 36.20 at doses of 200 mg/kg weight, where as positive group the reduction was 33.50% at doses of 5 mg/kg weight (here, glibenclamide was used as the standard). In comparison to the diabetic control group, the treatment group total cholesterol significantly decreased during the course of 21 days’ observation period. The treated mice had lower triglyceride levels than the diabetic control group. Fig. 2 showed the serum lipid profile levels of total cholesterol, triglycerides, LDL, HDL and streptozotocin induced diabetic mice. The reduction of total cholesterol levels was 19.20% at dose 100 mg/kg and 36.20% at dose 200 mg/kg weight observed in methanol extract of C. papaya leaved treated diabetic mice, whereas in positive control group reduction was 33.50% at dose 5 mg/kg weight (here Glibenclamide used as standard) respectively. After 21 days’ observation the treatment groups showed remarkably decrease of total cholesterol compared with the diabetic control group. Serum triglyceride level of treated mice was lower than diabetic control. At doses 100 mg/kg and 200 mg/kg weight, LDL levels in the treated mice were likewise markedly lowered. Depending on the dose, the reduction was between 44.66% and 59.82%. In contrast the HDL level rose by 26.73% and 59.82%. In comparison to the diabetic control group, the treatment groups showed remarkably decrease of total cholesterol compared with the diabetic control group. Serum triglyceride level of treated mice was lower than diabetic control. At doses 100 mg/kg and 200 mg/kg weight, LDL levels in the treated mice were likewise markedly lowered. Depending on the dose, the reduction was between 44.66% and 59.82%. In contrast the HDL level rose by 26.73% and 59.82%.

C. Effects of A Methanolic Papaya Leaf Extract on SGpt, Sgot Crp and Their Amount in Blood

Glibenclamide and a methanol extract of C. papaya leaves were administered orally to diabetic mice, their serum SGPT and SGOT levels were compared to those of the normal mice (Table I). When compared to glibenclamide, the percentage of SGPT level lowering by C. papaya leaves in diabetic control groups ranged from 18.62% to 26.21%. When compared to glibenclamide, C. papaya leaves significantly decrease in SGOT levels ranged from 19.13% to 25.51%.

CRP is considered as liver infection and cardiovascular diseases marker as well as found high ratio on diabetic condition. Consumption of glibenclamide and a methanol extract of C. Papaya leaves significantly lowered the CRP levels (Table-II). When diabetic control mice compared, injection of 100 and 200 mg/kg weight doses of methanol extract of C. papaya leaves reduced the CRP level 33.21% and 39.92% respectively.

Results were presented as Mean SD. The amount of SGPT and SGOT level in the treated mice were substantially different from those in the group of diabetic control.

<table>
<thead>
<tr>
<th>Groups of Animals</th>
<th>SGPT (U/L)</th>
<th>SGOT (U/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Group</td>
<td>78</td>
<td>112</td>
</tr>
<tr>
<td>Diabetic Control</td>
<td>122</td>
<td>174</td>
</tr>
<tr>
<td>Positive Control</td>
<td>82</td>
<td>122</td>
</tr>
<tr>
<td>Diabetic + C. papaya leaves methanol extract 100 mg/kg</td>
<td>102</td>
<td>138</td>
</tr>
<tr>
<td>Diabetic + C. papaya leaves methanol extract 200 mg/kg</td>
<td>88</td>
<td>126</td>
</tr>
</tbody>
</table>

Data was express in mean standard. Lower amount to CRP level was found in diabetic mice.

IV. DISCUSSION

The result shows that mice’s weight decrease and blood sugar significantly increase three days after receiving intravenous injection of streptozotocin. However other clinical symptom of diabetic was observed. This positive outcome was similar with previous findings that also demonstrate weight loss and increasing sugar level [12], [13]. Diabetic mice consume blood glucose levels after C. papaya leaves methanol extract administration. This similarity of hypoglycemia was reported before another plant [14], [15]. Depending on the activity, the rate of intestinal sugar absorption may decrease or peripheral sugar consumption may increase. According to some researchers, brown adipose tissue and muscle cell sugar metabolism happen due to GLUT4 translocation [16]. Brown adipose tissue found uncoupling protein-1 as upregulation and hyperinsulinemia happen hepatic gluconeogenesis or increase peripheral glucose utilization [17]. This finding represented that TG,
TChol, LDL, HDL parameters decrease with the treatment of C. papaya leaves extract. Hepatic triglyceride biosynthesis acceleration may reason of hyperlipidemia with diabetes. Insulin/glucagon ration occur or may be one of the reason for releasing of VLDL without help of lipoprotein lipase [18]. The result of current investigation makes it abundantly evident medicinal effects of C. papaya leaf methanol extract have significant effect on artificially induced diabetic mice. The amount of blood sugar level was 48.20% and the dose of C. papaya methanol extract with 200 mg/kg weight seen highest active. More lipid metabolism was found by treating C. papaya leaves at dose 200 mg/kg weight and this similarity could compare with glibenclamide treated mice at 5 mg/kg weight. This dose also decreases serum total cholesterol 19.20%, triglyceride 33.20%, and LDL 26.73%, and HDL amount found increase about 32.04%. Hyperglycemia occur liver damage and diabetic mice gives good value for SGPT and SGOT [19]. By the same way diabetic mice liver function improvement was seen by the decrease level of CRP parameter. This primary result means Carica papaya immature leaf have hypoglycemic medicinal properties moreover this research has some limitation due to sample size with five mice in every group and time shortage [20]. In this way the active medicinal group was not identified and further study necessary need with long period and chromatography method.

V. CONCLUSION

These findings proved that C. papaya leaves kept positive effect for diabetic mice. This conclusion suggests that the methanol extract of C. papaya helps improvement of diabetic. Moreover, to properly comprehend its medicinal and pharmaceutical usefulness, more thorough investigation is required.

ACKNOWLEDGMENT

This research paper originally done from University of Rajshahi, Biochemistry and Molecular Biology Department. This article was written and data collected by Md Rokibil Hasan Bhiuyan the Biochemical result was conformed in Medinova Medical Services Ltd. (Dhannomdi and malibagh Branch), Dhaka by Md. Sadikuj Jaman. This paper is edited by all of coauthors.

CONFLICT OF INTEREST

Authors declare that they do not have any conflict of interest.

REFERENCES


Md. Rokibil Hasan Bhiuyan, Born In Narsindi, Dhaka, Bangladesh and Time 12 Feb 1993 He passed S.Sc, HSc Exam and Start Hons In Department of Biochemistry and Molecular Biology in University of Rajshahi, Rajshahi 6205, Bangladesh. Then He Select as Thesis Student in M.Sc. He has done lot of institute among of them Medinova and Medical Services Ltd, Dhannomdi, Dhaka as a Biochemist.

M. Maniruzzaman, (Assistant Professor, Varendra University, Department of Pharmacy). He Born in Tangail in Dhaka 1989. He earn S.Sc, H.Sc then B. Pharm, M. Pharm (thesis) from University of Rajshahi, Department of Pharmacy.
S. Akter, She Born in Rangpur, Rajshahi, Bangladesh in 1996. She got S.Sc, H.Sc, B.Sc (Hons) and M.Sc (Thesis) From University of Rajshahi, Department of Biochemistry and Molecular Biology.

S. Mehjabin, She Born In Rajshahi, Bangladesh, She Earned B. Pharm and M. Pharm (Thesis) From University of Rajshahi. Department of Pharmacy. Now she is working as Lecturer in Varendra University Rajshahi, Bangladesh in Department of Pharmacy.

M. R. Rashed Rana, Born In Rajshahi, Bangladesh in 1998. He Passed S.Sc and H.Sc from Rajshahi and Started B Pharm Then M Pharm in department of Pharmacy, Varendra University. Now he is working as Lecturer in Varendra University, Department of Public Health and passed the train in Bangabandhu Sheikh Mujib Medical University.

S. Jaman, He Born in Thakurgaon in 1990. He earn SSc Exam from Ektipur S.S High School and H.Sc from Thakurgaon Govt College. Then He Entered Department of Biochemistry and Molecular Biology in University of Rajshahi 2008 and Earned B.Sc (Hons) and M.Sc. Presently he is working as a Biochemist in Medinova Medical services Ltd, Malibagh Branch, Outer circular Road, Hosaf Tower, Malibagh, Dhaka 1213, Bangladesh. Also, he involves many institutes as a Biochemist.