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Research paper

Evaluation of hypolipidemic and hypoglycemic effects of *Dillenia indica L.* on alloxan-induced diabetic rats

Md Mahfuj Alam Siddiq[a], Jeasmin Akter[a], Zakia Sultana Sathi[b], Md Ruhul Kuddus[c], Mohammad A. Rashid[c*]

[a]*Department of Pharmacy, Faculty of Health and Life Sciences, Daffodil International University, Bangladesh;* [b]*Department of Neuropharmacology & Neurologic Diseases, Emory Primate Research Centre, Emory University, United States;* [c]*Phytochemical Research Laboratory, Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Dhaka, Dhaka-1000, Bangladesh*

*Corresponding author: arpharm64@du.ac.bd
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ABSTRACT

Context: *Dillenia indica* L. a tropical fruit-bearing plant native to South and Southeast Asia, has attracted scientific interest due to its rich phytochemical composition and potential therapeutic benefits in managing diabetes, lipid disorders, and oxidative stress. ***Objective***: The objective of this study was to investigate the potential antidiabetic and lipid-lowering properties of *D. indica* fruit and bark extracts in a rat model of alloxan-induced type 2 diabetes. ***Methods***: Diabetes was induced in rats using an intraperitoneal injection of alloxan (160 mg/kg) after a 12-hour fast. The chloroform fractions of *D. indica* fruit and bark (200 mg/kg) were administered intraperitoneally, with metformin (150 mg/kg) serving as the standard drug. Fasting blood glucose levels were measured at 0, 24, 40, and 50 hours. Upon completion of the experiment, blood samples were collected for the evaluation of total cholesterol (TC) and triglyceride (TG) levels. **Results:** The chloroform fraction of *D. indica* fruit significantly reduced FBG levels by 65% after 50 hours, closely matching the effect of metformin. It also decreased elevated TC and TG levels by 60% and 55%, respectively. In contrast, the bark extract initially lowered FBG but caused a 30% rebound increase at 50 hours and led to increased TC and TG levels by 28% and 54%, respectively. ***Conclusion*:** The chloroform fraction of *D. indica* fruit demonstrates potent antidiabetic and lipid-lowering activity, indicating its promise as a natural therapeutic agent for managing hyperglycemia and dyslipidemia in type 2 diabetes. The inconsistent effects of the bark extract warrant further investigation.

Keywords: alloxan, *Dillenia indica*, fasting blood glucose, intraperitoneal injection.

INTRODUCTION

Diabetes mellitus is a chronic, non-communicable (Tan et al., 2019) metabolic disease marked by high blood glucose levels triggered by insufficient insulin

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production or insulin intolerance (Dekker et al., 2006). Inadequate insulin can lead to differences in the metabolism of proteins, carbohydrates, and fats (Kharroubi et al., 2015). Chronic hyperglycemia associated with diabetes is linked to complications in the cardiovascular system, kidneys, eyes, and nervous system. Among the most common metabolic disturbances is dyslipidemia, which contributes to increased oxidative stress and impairs the body's antioxidant defense mechanisms (Diabetes Care, 2014). Approximately 2.8% of people worldwide suffer from diabetes; by 2025, that percentage is predicted to have increased to 5.4% (Patel et al., 2012), and by 2030 and 2045, that figure is projected to reach 700 million and 578 million, respectively (Saeedi et al., 2019). Bangladesh is experiencing a rise in the prevalence of diabetes.

According to estimates by the International Centre for Diarrhoeal Disease Research, Bangladesh, approximately 7.1 million individuals were living with diabetes in 2015, with an additional 3.7 million cases undiagnosed and around 129,000 deaths attributed to the disease. From 4.0% in 1995-2000 to 10.4% in 2010-2019, the prevalence of diabetes has increased 2.5 times in the last 20 years (Kharroubi et al., 2015, Patel et al., 2012, Rani et al., 2017).

Another metabolic illness known as hyperlipidemia is marked by high blood levels of triglycerides (TG) and total cholesterol (TC), which increases the risk of atherosclerosis and causes disorders of the heart and brain blood vessels (Matheus et al., 2017). Excessive fat accumulation in blood vessels narrows the cerebral and coronary arteries, increasing the risk of heart failure, coronary heart disease (CHD), stroke, myocardial infarction, and hypertension (Roth et al., 2017). Hyperlipidemia can be primary, treated with hypolipidemic drugs, or secondary, requiring treatment of the underlying condition (Asija et al., 2014). Globally, hyperlipidemia is caused by genetic factors and a high-calorie, high-fat diet (Dand et al., 2014); the main risk factors for hyperlipidemia include a sedentary lifestyle and a bad diet (Kumar et al., 2013).

The World Health Organization suggests using traditional remedies sourced from plants to treat diabetes mellitus. Many factors, including the involvement of various relevant bodies in the development and research of herbal-based medications, have contributed to the rise in the use of traditional medicines for the treatment of diabetes mellitus (García et al., 2017, Gupta et al., 2018). Furthermore, herbal medicine is encouraged for diabetes because it is less expensive and has fewer adverse effects (Ghosh et al., 2012).

Dillenia indica L. (Family: Dilleniaceae) is commonly called "Elephant tree." It is a medium-sized evergreen tree that may reach a height of 15 meters and is indigenous to Southeast Asia, which includes Bangladesh, China, India, Nepal, and Sri Lanka (Arbianti et al., 2007, Alam et al., 2012, Nayak et al., 2016). The leaves and bark exhibit astringent properties, while the fruit possesses laxative effects and is traditionally used to alleviate abdominal pain (Kritikar et al., 2003). Juices from the leaves, bark, and fruits of *D. indica* are commonly consumed to treat cancer and diarrhea (Kirtikar et al., 2001). Extracts from its fruits and leaves have demonstrated antioxidant (Sharma et al., 2001), CNS depressant (Abdille et al., 2005), and anti-inflammatory (Bhakuni et al., 1969) effects in mice. Furthermore, antibacterial qualities are demonstrated by the alcoholic leaf extract (Yeshwante et al., 2009). The plant has historically also been used to treat diabetes (Apu et al., 2010). The methanolic extract also shows a free radical scavenging effect (Sood et al., 2005). Also, in models of diabetes caused by streptozotocin and alloxan, methanolic extracts of the leaves demonstrate antidiabetic activity (Kumar et al., 2011, Kumar et at., 2011). Besides, metformin is a standard antidiabetic drug

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frequently used in experimental models due to its proven glucose-lowering effects. A dose of 150 mg/kg (i.p.) was selected based on previous studies reporting effective glycaemic control within the 150–300 mg/kg range (Gruzman et al., 2009, Patel et al., 2012). This dose remains well below the reported oral NOAEL of 200 mg/kg/day in rats, minimizing toxicity risks (Chowdhury et al., 2011), and is appropriate for evaluating comparative antidiabetic effects. This study aimed to investigate the hypoglycaemic and hypolipidemic effects of methanolic extracts from *D. indica* fruit and bark in alloxan-induced diabetic rats.

METHODS

Collection and extraction of plant material

Fruits and bark of *D. indica* were collected in November 2024 from Kantanagar village, Kaharole upazila, Dinajpur district, Bangladesh. The plant was taxonomically authenticated by experts at the Bangladesh National Herbarium, Mirpur, Dhaka (Md. Rejaul Karim, Herbarium office, Bangladesh National Herbarium, E-mail : bnh_mirpur@yahoo.com). The cleaned plant materials were cut into small pieces, air-dried, and coarsely ground. Approximately 1 kg of each sample (fruit and bark) was macerated separately in methanol for several days. The extracts were filtered using Whatman No. 1 filter paper and concentrated under reduced pressure at 40 °C using a rotary evaporator (Heidolph, UK). The residues of both fruit and bark (40.0 g) were suspended in methanol/water (200 ml, 1:9, v/v) solution and extracted with chloroform to give their extracts following the modified Kupchan method (Kumar et al. 2011). All the extracts obtained (fruit and bark) were considered for further investigation.

Drugs and chemicals used

The active drug, metformin was a generous gift sample from Opsonin Pharma Ltd., Barishal, Bangladesh. Total cholesterol (TC) and triglyceride (TG) wet reagent diagnostic kits were the products of Cromatest diagnostic kits. The manufacturer of the alloxan monohydrate used in this experiment was Sigma Ltd., USA. The glucose meter and strips were from the product of AMP Medizintechnik GmbH; Austria.

Test animals

The study was conducted with Wistar rats weighing about 125-150 gm and 4–5 weeks' old purchased from the Department of Pharmacy, Jahangirnagar University, Savar, Dhaka, Bangladesh. They were housed in colony cages (two per cage) under controlled conditions (25-27 °C, 12-hour light/dark cycle) with adequate ventilation. They were provided with standard commercial diets and water ad libitum. Animals were acclimatized to the laboratory environment for two weeks prior to experimentation. All handling and procedures followed the guidelines for animal experiments (Van et al., 1993). Before conducting any animal experiments, the ethical clearance (Ref: FHLS-REC/DIU/2024/0027) was obtained from the Ethical Review Committee of The Faculty of Health and Life Sciences, Daffodil International University, Bangladesh.

Induction of diabetes

Animals were fasted for 12 hours before receiving a freshly prepared dose of alloxan monohydrate (160 mg/kg body weight) in sterile saline via intraperitoneal injection. To prevent drug-induced hypoglycemia, food was provided after the

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injection. Starting at 96 hours post-administration, blood glucose levels were regularly monitored, and rats with glucose levels exceeding 270 mg/dL were considered diabetic and selected for further experimentation.

Preparation of active drug metformin hydrochloride and plant extracts:
Metformin hydrochloride, a microcrystalline compound, is freely soluble in saline. The dosage was prepared by dissolving metformin in saline to achieve a concentration where each 0.1 ml of solution contained 32-40 mg of the drug. Separately, fractionated extracts of *D. indica* fruit and bark were dissolved in 99% DMSO to prepare solutions delivering a dose of 200 mg/kg body weight, with each 0.1 ml containing the corresponding amount of extract.

Experimental study design
The rats were randomly assigned to five groups, each consisting of five animals. Group 1 served as the vehicle control and received only DMSO. Group 2 was designated as the diabetic control and did not receive metformin or plant extracts. Group 3 functioned as the metformin control, with metformin administered intraperitoneally at a dose of 150 mg/kg body weight following diabetes induction by alloxan. Groups 4 and 5 were treated with chloroform extracts of *D. indica* fruit and bark, respectively, administered similarly to the metformin treatment in alloxan-induced diabetic rats (Table 1). The blood glucose level was then tested by using a glucometer by pricking the blood sample from the tail vein at 0, 24, 40, and 50 hours after drug and plant extract administration by strip method (Zimmermann et al., 1983).

Table 1: Experimental design of the studies

Group-1	Normal control (given only vehicle (DMSO)
Group-2	Diabetic control (Alloxan induced)
Group-3	Diabetic + Metformin treatment (standard control-150 mg/kg b.w.)
Group-4	Diabetic + Chloroform fraction of *D. indica* Fruit - CFDIF (200 mg/kg b.w.)
Group-5	Diabetic + Chloroform fraction of *D. indica* Bark - CFDIB (200 mg/kg b.w.)

Collection of serum
At the conclusion of the treatment period, the rats were anesthetized using mild chloroform vapor, then euthanized and sacrificed. Approximately 3–5 ml of blood was collected directly from the heart using a syringe, followed by centrifugation at 4000 rpm for 10 minutes. The resulting serum was carefully preserved for subsequent biochemical analysis.

Estimation of biochemical parameters
Serum total cholesterol (TC) and triacylglycerol (TG) levels were measured using colorimetric assays with wet reagent diagnostic kits. Absorbance values were recorded, and concentrations were calculated using a Rayto semi-automated chemistry analyzer. All measurements were performed in triplicate across four samples (n = 4), following the manufacturer's instructions.

Statistical analysis
Data analysis was performed using Prism software (GraphPad Software, San Diego, CA, USA) following established protocols. Results are presented as mean ± standard error of the mean (SEM). Statistical comparisons were conducted using

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analysis of variance (ANOVA) followed by Scheffe's post-hoc test, or Student's paired or unpaired t-test as appropriate.

Euthanasia procedure

At the end of the experiment, animals were humanely euthanized under anesthesia using ketamine (80 mg/kg) and xylazine (10 mg/kg) administered intraperitoneally, followed by cervical dislocation to ensure death, in accordance with institutional animal care guidelines (Kinter et al., 2002).

RESULTS

Induction of diabetes

The effects of chloroform extracts from the fruit and bark of *D. indica* on alloxan-induced diabetic rats (AIDR) were evaluated by measuring fasting blood glucose (FGL) levels, serum triglycerides (TG), and total cholesterol (TC), with metformin serving as the standard antidiabetic reference. Alloxan develops diabetes by damaging the pancreatic beta cells that produce insulin (Kasiviswanath et al., 2005, Lenzen et al., 1988). A time-course study was conducted to assess the effects of alloxan, with the results presented in Figure 1. Blood glucose levels peaked between 50-and 80 hours post-administration, followed by a gradual decline thereafter. The blood glucose level fell to the base level at around 100 hours. Thus, to check the antidiabetic effect 50 hours of alloxan induction was used for every experiment.

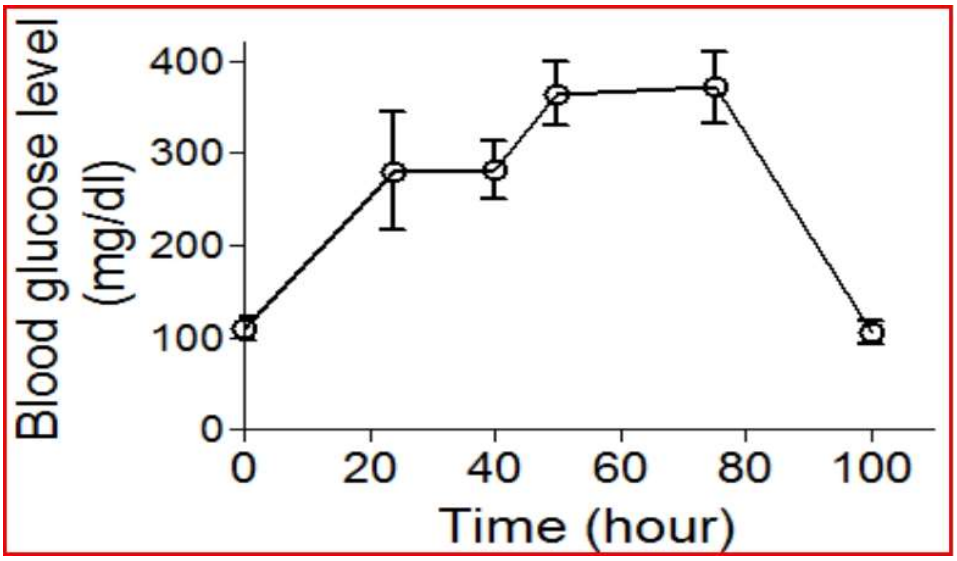

Figure 1: Time course after alloxan induction

Studies conducted *in vitro* have demonstrated that alloxan selectively damages pancreatic beta cells, causing apoptosis (Oberley 1988). This process leads to the rapid destruction of beta cells, driven by reactive oxygen species and a simultaneous significant rise in calcium levels (Jorns et al., 1997). The administration of a lower dosage of alloxan (160 mg/kg body weight) resulted in a partial loss of pancreatic beta cells, despite the animals developing persistent diabetes (Szkudelski et al., 2001). These animals therefore have beta cells that are still alive, and regeneration is possible (Stanely et al., 2000). An elevated level of

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triglycerides and plasma cholesterol are key risk factors for cardiovascular disease (Ayber et al., 2001). Furthermore, due to insulin resistance and hyperglycemia, plasma cholesterol and triglyceride levels were raised in diabetic rats (Garg 1994).

Antidiabetic activity

A single dose of alloxan monohydrate (150 mg/kg) caused a significant increase in blood glucose levels (P<0.01), as presented in Table 2 and Figure 2. Oral administration of the chloroform fruit extract of *D. indica* (CFDIF) at 200 mg/kg body weight resulted in a significant reduction (P<0.01) in blood glucose levels in diabetic rats. Additionally, the decreased insulin levels observed in diabetic rats were significantly restored following CFDIF treatment. At the conclusion of the experiment (50 hours), blood glucose levels were measured at 141.2 ± 8.2 mg/dL in the CFDIF-treated group compared to 427.7 ± 105.1 mg/dL in the group treated with chloroform bark extract (CFDIB).

In alloxan-induced diabetic rats, metformin administration resulted in a reduction of blood glucose levels by 15%, 67%, and 67% at 24, 40, and 50 hours, respectively, as shown in Table 2. In comparison, CFDIF at 200 mg/kg body weight achieved reductions of 17%, 28%, and 65% at the same time points. Notably, the maximum reduction of 65% for CFDIF at 50 hours is comparable to the effect observed with metformin (Figure 2). Additionally, treatment with CFDIB at a dose of 200 mg/kg body weight in alloxan-induced diabetic rats led to blood glucose reductions of 13% and 63% at 24 and 40 hours, respectively. Although the CFDIB initially showed hypoglycemic effects, but this reversed by 50 hours. In this study, metformin hydrochloride (150 mg/kg body weight) was used as a standard alongside CFDIF and CFDIB. The results showed that CFDIF significantly reduced blood glucose levels, likely due to the presence of bioactive hypoglycemic constituents such as alkaloids, saponins, triterpenes, and flavonoids (Goldberg, 2001).

Table 2: Effect of metformin, CFDIF, and CFDIB on fasting glucose levels in alloxan-induced diabetic rats (n= 5)

Treatments	Blood glucose level (mg/dL)			
	0 hour	24 hours	40 hours	50 hours
Normal Control	102.5 ± 5.1	104.5 ± 4.1	103.7 ± 2.5	107.5 ± 3.5
Diabetic Control	109.5 ± 13.5	411. ± 17.2*	416.0 ± 14.8*	409.2 ± 14.9*
D + Metformin	101.2 ± 17.7	347.2 ± 27.2*	136.5 ± 8.0*	135.7 ± 17.5§
D + CFDIF	85.2 ± 15.6	340.2 ± 29.7*	297.0 ± 25.4*	141.2 ± 8.2§
D + CFDIB	85.7 ± 22.2	357.2 ± 26.0*	152.0 ± 9.9§	427.7 ± 105.1*

N= Numbers of animals in each group. D= Diabetic (alloxan induced diabetic). Values are each the mean ± S.E.M. obtained from 4 experiments*P<0.01, § P<0.05# Significantly different (p<0.05) from time control after the treatment with alloxan (tested by unpaired t-test) and *Significantly different (p<0.01) from time control in the presence of drug as well as different fraction of *D. indica*. Data were analyzed by ANOVA followed by Scheffe's post-hoc tests.

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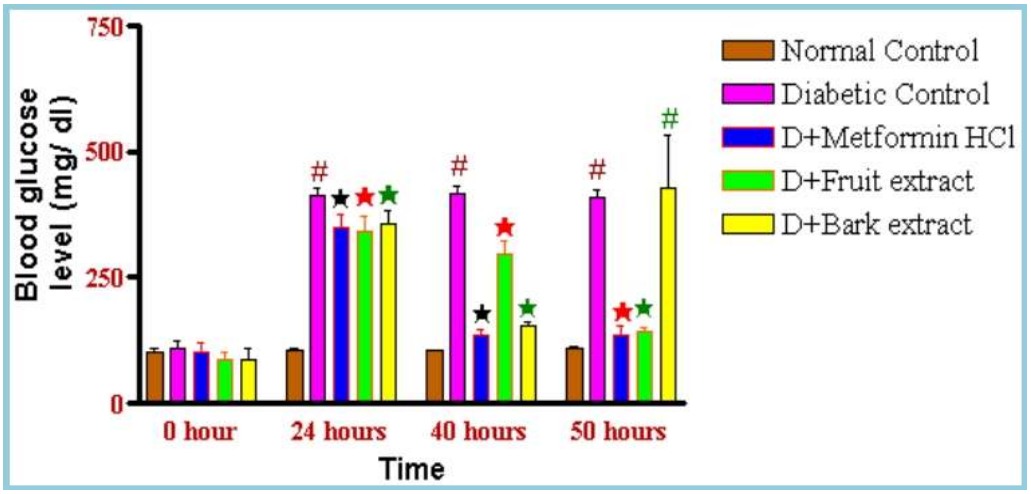

Figure 2: Evaluation of fasting blood glucose modulation by metformin, and chloroform extracts of *D. indica* fruit (CFDIF) and bark (CFDIB) in rats with alloxan-induced diabetes

Significantly different ($p<0.05$) from without alloxan treatment and ***Significantly different ($p<0.01$) from AIDR (Unpaired t-test).

Effect on serum total cholesterol levels

In diabetic rats, serum total cholesterol (TC) levels were markedly elevated relative to the normal control group. Treatment with the chloroform extract of *D. indica* (200 mg/kg body weight) resulted in a significant reduction in serum TC (103.800 ± 9.39; $P<0.05$) after 50 hours, comparable to the effect observed with the standard drug metformin, as shown in Table 3 and Figure 3.

Table 3: Effects of metformin, CFDIF, and CFDIB on serum TC level in alloxan-induced diabetic rats (n=5)

Treatment	50 hours
Normal Control	81.3 ± 6.7
Diabetic Control	166.9 ± 12.4*
D + Metformin HCl	103.800 ± 9.389511
D + CFDIF	98.3375 ± 8.236008
D + CFDIB	213.5 ± 10.7

N= Numbers of animals in each group. D= Diabetic (alloxan induced diabetic). Values are each the mean ± S.E.M. obtained from 4 experiments*$P<0.01$, §$P<0.05$

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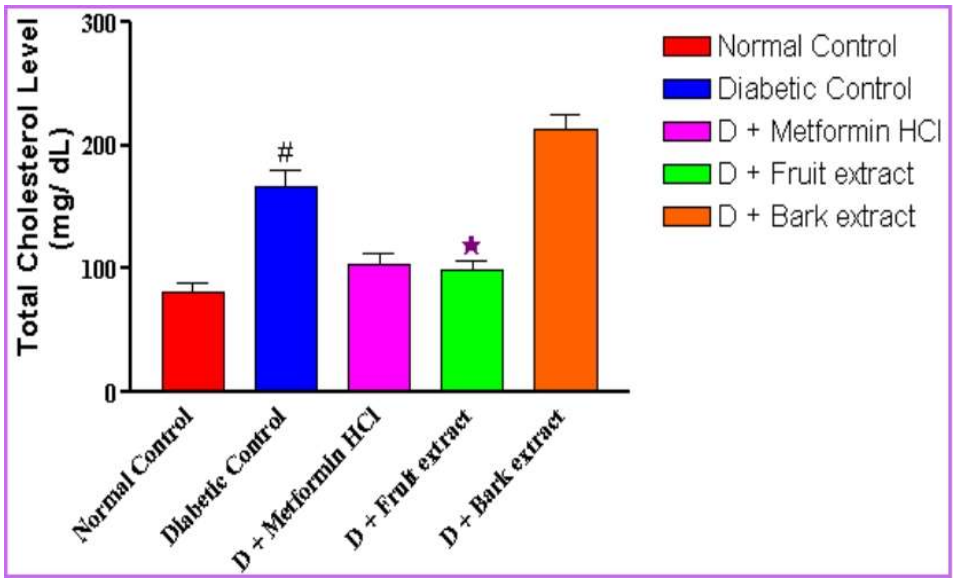

Figure 3 Serum TC Levels Following Treatment with Metformin, CFDIF, and CFDIB in alloxan-induced diabetic rats.
Significantly different ($p<0.05$) from without alloxan treatment and *****Significantly different ($p<0.01$) from AIDR (Unpaired t-test).

The effect of CFDIF and CFDIB on serum total cholesterol (TC) levels was assessed in alloxan-induced diabetic rats (Table 3). Although the CFDIF had a 60% reduction in blood TC, metformin only had a 54% reduction in TC, suggesting that CFDIF had a more significant effect (Figure 3). In contrast, the CFDIB resulted in a 28% increase in serum TC levels.

Effects on serum triglyceride levels

Administration of alloxan induced a notable increase in the level of mice's serum triglyceride (TG) compared to the control group. The CFDIF at 200 mg/kg b.w. showed (Table 4 and Figure 4) a significant decrease (58.3 ± 8.6) in the level of serum TG compared with metformin. The effects of metformin and chloroform fractions of *D. indica* fruit and bark on serum triglyceride (TG) levels were evaluated in alloxan-induced diabetic rats (Table 4). Metformin reduced serum TG levels by 22%, while the CFDIF resulted in a more significant reduction of 55%. This reduction in TG levels for the CFDIF was notably greater than that of metformin (Figure 4). Conversely, the CFDIB led to a substantial increase in serum TG levels, rising by 54.62% by the 50-hour mark of the experiment.

CONCLUSION

This study demonstrates that the chloroform fraction of *D. indica* fruit exhibits significant antidiabetic and hypolipidemic effects in alloxan-induced diabetic rats, with efficacy comparable or superior to metformin, particularly in reducing blood glucose, total cholesterol, and triglyceride levels. These findings highlight the potential of D. indica fruit as an affordable, accessible complementary treatment for diabetes, which could benefit Bangladesh's healthcare system by

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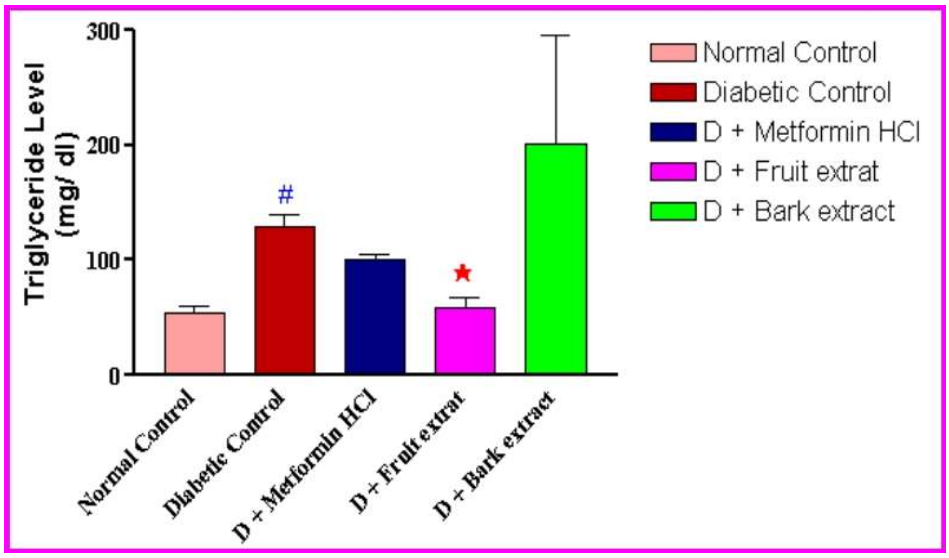
Table 4: Effects of metformin, CFDIF, and CFDIB on serum TG level in alloxan-induced diabetic rats (n=5).

Treatment	50 hours
Normal control	53.2 ± 6.9
Diabetic control	129.5 ± 10.2*
D + Metformin HCl	100.6 ± 4.4*
D + $CHCl_3$ Fruit extract	58.3 ± 8.6§
D + $CHCl_3$ Bark extract	200.2 ± 94.5

N= Numbers of animals in each group. D= Diabetic (alloxan induced diabetic). Values are each the mean ± S.E.M. obtained from 4 experiments*P<0.01, § P<0.05

Figure 4. Effects of Metformin hydrochloride, $CHCl_3$ fruit, and bark fractions of *D. indica* on serum triglyceride level in alloxan-induced diabetic rats.



Significantly different ($p<0.05$) from without alloxan treatment and *Significantly different ($p<0.01$) from AIDR (Unpaired t-test).

providing a locally sourced, cost-effective alternative to conventional drugs. Future research should focus on isolating active compounds, understanding their mechanisms, evaluating long-term safety, and conducting clinical trials to validate these effects in humans, thereby supporting the development of new plant-based therapies for diabetes management in Bangladesh.

DECLARATIONS OF INTEREST

None

DECLARATION OF HONOUR

We declare in our honor that our results are not fake and made up.

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Declaration of Conflict of Interest
No conflicts of interest are declared by the authors

References
Abdille, M. H., Singh, R. P., Jayaprakasha, G. K., & Jena, B. S. 2005. Antioxidant activity of the extracts from *Dillenia indica* fruits. *Food Chemistry*, 90(4), pp.891-896.

Apu, A. S., Muhit, M. A., Tareq, S. M., Pathan, A. H., Jamaluddin, A. T. M. & Ahmed, M. 2010. Antimicrobial activity and brine shrimp lethality bioassay of the leaves extract of *Dillenia indica* Linn. *Journal of Young Pharmacists*, 2(1), pp.50-53.

Arbianti, R., Utami, T. S., Kurmana, A. & Sinaga, A. 2007. Comparison of antioxidant activity of total phenolic content of *Dillenia indica* leaves extracts obtained using various techniques. In: *Proceedings of the 14th Regional Symposium on Chemical Engineering*, Yogyakarta, 4-5 December.

Association, A. D. 2014. Diagnosis and classification of diabetes mellitus. *Diabetes Care*, 37(1), pp.S81-90.

Asija, R., Sharma, S., Sharma, P. K., Choudhary, P. & Kumar, V. 2014. A review on antihyperlipidemic activity of various herbal plants and various experimental animal models. *Journal of Drug Discovery and Therapeutics*, 2(20), pp.71-77.

Bhakuni, D. S., Dhar, M. L., Dhar, M. M., Dhawan, B. N. & Mehrotra, B. N. 1969. Screening of Indian plants for biological activity. *Indian Journal of Experimental Biology*, 7(4), pp.250-262.

Chowdhury, M.A., et al., 2011. Subchronic toxicity study of metformin in rats. *Toxicology Mechanisms and Methods*, 21(6), pp.465–472.

Dekker, J. M. & Balkau, B. 2006. Counterpoint: impaired fasting glucose: the case against the new American Diabetes Association guidelines. *Diabetes Care*, 29(5), pp.1173-1175.

Dand, D. P. **& Patani, P. V.** 2014. Antihyperlipidemic activity of *Tephrosia purpurea* plant extracts in poloxamer 407 induced hyperlipidemic rats. *International Journal of Pharma Research*, 4(4), pp.186-193.

García-Risco, M. R., Mouhid, L., Salas-Pérez, L., López-Padilla, A., Santoyo, S. & Jaime, L. 2017. Biological activities of Asteraceae (*Achillea millefolium* and *Calendula officinalis*) and Lamiaceae (*Melissa officinalis* and *Origanum majorana*) plant extracts. *Plant Foods for Human Nutrition*, 72(1), pp.96-102.

Ghosh, S., Ahire, M., Patil, S., Jabgunde, A., Dusane, M. B. & Joshi, B. N. 2012. Antidiabetic activity of *Gnidia glauca* and *Dioscorea bulbifera*: potent amylase and glucosidase inhibitors. *Evidence-Based Complementary and Alternative Medicine*, Article ID 929051.

Goldberg, I. J. 2001. Clinical review 124: diabetic dyslipidemia: causes and consequences. *The Journal of Clinical Endocrinology & Metabolism*, 86(3), pp.965-971.

Gruzman, A., Babai, G. & Sasson, S. 2009. Adenosine monophosphate-activated protein kinase (AMPK) as a target for antidiabetic drugs. *Drug Development Research*, 70(8), pp.576–584.

Gupta, B., Sharma, I., Kohli, N., Sharma, S., Rathi, A. & Sharma, A. 2018. Preliminary clinical assessment and non-toxicity evaluation of an ayurvedic formulation BGR-34 in NIDDM. *Journal of Traditional and Complementary Medicine*, 8(4), pp.506-514.

Kasiviswanath, R., Ramsey, & Kumar, K. E. 2005. Hypoglycemic and antihyperglycemic effect of *Gmelina asiatica* Linn in normal and alloxan induced diabetic rats. *Biological & Pharmaceutical Bulletin*, 28(4), pp.729-732.

Kharroubi, A. T. **& Darwish, H. M.** 2015. Diabetes mellitus: the epidemic of the century. *World Journal of Diabetes*, 6(6), pp.850-867.

Kinter, L.B. & Roberts, D.W. 2002. A review of animal models of chemically induced pulmonary fibrosis. In: *Current Protocols in Toxicology*. John Wiley & Sons, Inc.

Kirtikar, K. R. **& Basu, B. D.** 2001. *Indian Medicinal Plants*, Vol. 1. Dehradun: Oriental Enterprises.

Kritikar, K. R. & Basu, B. D. 2003. *Indian Medicinal Plants*, Vol. 2(8). Dehradun: Oriental Enterprises, p.2604.

Kumar, S.**, Kumar, V. & Prakash, O**. 2011a. Antidiabetic and antihyperlipidemic effects of *Dillenia indica* (L.) leaves extract. *Brazilian Journal of Pharmaceutical Sciences*, 47(2), pp.373-378.

eISSN-0128-1119

DOI: http://dx.doi.org/10.71221/ajp.09308

Kumar, S.**, Kumar, V. & Prakash, O.** 2011b. Hypoglycemic, hypolipidemic and histopathological analysis of *Dillenia indica* (L.) leaves extract on alloxan-induced diabetic rats. *Asian Pacific Journal of Tropical Medicine*, 4(5), pp.347-352.

Kumar, S.**, Kumar, V. & Prakash, O.** 2011c. Free radicals scavenging effect of *Dillenia indica* leaves. *Asian Journal of Pharmaceutics and Biological Research*, 2, pp.169-173.

Matheus, D. B.**, Care, F. S., Thirssa, H. G., Pedro, H. D., Aline, A. B. & Lenita, M. S.** 2017. Hypolipidemic effect of β-caryophyllene to treat hyperlipidemic rats. *Naunyn-Schmiedeberg's Archives of Pharmacology*, 390(2), pp.1326-1335.

Nayak, P. K. **& Rayaguru, K.** 2016. Study of physical parameters of elephant apple fruit (*Dillenia indica*): an underutilized fruit of north-eastern India. *International Journal of Engineering Research and Technology*, 5(1), pp.532-535.

Oberley, L. W. 1988. Free radicals and diabetes. *Free Radical Biology and Medicine*, 5(2), pp.113–126.

Patel, D. **Prasad, S. K., Kumar, R. & Hemalatha, S.** 2012. An overview on antidiabetic medicinal plants having insulin mimetic property. *Asian Pacific Journal of Tropical Biomedicine*, 2(4), pp.320-330.

Patel, D.K., Kumar, R., Laloo, D. & Hemalatha, S. 2012. Evaluation of antidiabetic activity of extract of *Azadirachta indica* leaf in streptozotocin-induced diabetic rats. *Asian Pacific Journal of Tropical Biomedicine*, 2(2), pp.104–108.

Rani, A.**, Arora, S. & Goyal, A.** 2017. Antidiabetic plants in traditional medicines: a review. *International Research Journal of Pharmacy*, 8(6), pp.172-4.

Roth, G. A., **Johnson, C., Abajobir, A., Abd-Allah, F., Abera, S. F., Abyu, G. et al.** 2017. Global, regional, and national burden of cardiovascular diseases for 10 causes 1990 to 2015. *Journal of the American College of Cardiology*, 70(1), pp.1-25.

Sharma, H. K.**, Chhangte, L. & Dolui, A. K.** 2001. Traditional medicinal plants in Mizoram, India. *Fitoterapia*, 72(2), pp.1461-61.

Sood, S. K., **Bhardwaj, R. & Lakhanpal, T. N.** 2005. Ethnic Indian plants in cure of diabetes. [Monograph, pp.1-164].

Stanley, P., **Prince, M. & Menon, V. P.** 2000. Hypoglycaemic and other related actions of *Tinospora cordifolia* roots in alloxan-induced diabetic rats. *Journal of Ethnopharmacology*, 70(1), pp.9-15.

Szkudelski, T. 2001. The mechanism of alloxan and streptozotocin action in beta cells of the rat pancreas. *Physiological Research*, 50(6), pp.537-546.

Van-Wagenen, B. C., **Larsen, R., Cardellina, J. H., Randazzo, D., Lidert, Z. C. & Swithenbank, C.** 1993. Ulosantion, a potent insecticide from the sponge *Ulosa ruetzleri*. *Journal of Organic Chemistry*, 58, pp.335-337.

Yeshwante, S. B.**, Juvekar, A. R., Nagmoti, D. M., Wankhede, S. S., Shah, A. S. & Pimprikar, R. B.** 2009. Anti-inflammatory activity of methanolic extracts of *Dillenia indica* L. leaves. *Journal of Young Pharmacists*, 1(1), pp.63-66.

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