Antioxidative and Antidiabetic Potentials of the Pneumatophores of *Heritiera fomes* Buch. Ham.

Mst. Serina Sultana[1], Mimi Golder[1], Biswajit Biswas[2], Utpal Kumar Karmakar[1], Bishwajit Bokshi[1], Md. Jahir Alam[3], Masum Shahriar[3] and Samir Kumar Sadhu[1]

[1]Pharmacy Discipline, Life Science School, Khulna University, Khulna 9208, Bangladesh
[2]Department of Pharmacy, Jashore University of Science and Technology, Jashore 7408, Bangladesh
[3]Department of Pharmacy, Jahangirnagar University, Savar, Dhaka 1342, Bangladesh

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ABSTRACT This research work focuses on determining the antidiabetic and antioxidative properties of ethanolic extract of *Heriteira fomes* pneumatophores. The *in vitro* antioxidative activity was tested through several qualitative and quantitative assays which revealed the radical scavenging activity of this plant. The *in vivo* antihyperglycemic activity of plant extract was confirmed by the oral glucose tolerance test in the mice model. The antidiabetic potential was tested on streptozotocin-induced diabetic rats followed by measuring several hematological parameters and lipid profiles where the extract significantly affected those parameters. The results suggest that *H. fomes* pneumatophores might be a potential source of antioxidative and antidiabetic bioactive compounds.

Key words: *Heritiera fomes*, Sundri, Sundarbans, antioxidative, antidiabetic, hematological parameters

INTRODUCTION

Modern civilized lifestyle, particularly food habits has led us to some serious health complications like diabetes, oxidative damage, cardiovascular complications, etc.[1] Diabetes mellitus, a type of metabolic deregulation, usually manifested by disordered metabolism and inappropriate hyperglycemia, caused by reduced glucose utilization resulting from a defective or scarce insulin secretory response due to the decrease in insulin synthesis (Type-I diabetes) or insulin insensitivity (Type-II diabetes). Diabetes causes macrovascular and microvascular complications in the human body as well as hastens the generation of oxidative free radicals and destruct antioxidant defense mechanisms, leading to oxidative stress which can further aggravate diabetes and its complications.[2]

Correspondence to: Samir Kumar Sadhu
Email: sksadhu1969@yahoo.com; sksadhu1969@pharm.ku.ac.bd

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Undoubtedly, this is a major threat to the world, currently affecting nearly 285 million people (20–79 years of age) with 438 million people expecting to have diabetes by 2030.[3] This imparts an increasing interest in recent years in finding hypoglycemic agents of natural substances that are traditionally being used as folk remedies.[4]

Since time immemorial, plants– especially the secondary metabolites isolated from plants, have been a highly potential source for medicines and the mangrove forest offers a plethora of secondary metabolites because of the hostile environmental conditions they have to endure like high salinity, low oxygen and temperature. Many mangrove plants have already been reported and evidenced to have antidiabetic compounds such as glycosides, alkaloids, terpenoids, flavonoids, carotenoids, etc.[5] However, the search for newer plants is always interesting as we always quest for a safer drug with the least undesired effects.[6]

Heritiera fomes Buch. Ham. belonging to the family Malvaceae (Bangla name: Sundri) an

evergreen medium to tall size tree that occurs in the Sundarbans and is most commonly found in shoreline areas like India, Myanmar, Thailand, and Northern Malaysia.[7] It has previously been reported to be used in several ailments like diabetes, goiter, diarrhea, dysentery, constipation, indigestion, stomachache, and hepatic disorders including jaundice, hepatitis, and so on.[8] Some of these activities are also evidenced scientifically, i.e., the bark of this plant has been proved to have antihyperglycemic, antioxidant and antimicrobial activity, leaf and stem extracts possess anticancer activity.[9,10]

To understand various aspects of diabetes pathogenesis as well as to discover new therapies, experimental induction of diabetes mellitus in animal models is essential. Several models like the streptozotocin (STZ)-induced model or alloxan-induced model have previously been used to induce diabetes in laboratory animals. STZ is known to induce diabetes, oxidative stress as well as several metabolic disorders in animals.[11] Hence, we used STZ-induced diabetic rats for our study. As diabetes and oxidative damage are predisposing factors to each other, therefore, in the present study the *in vitro* antioxidative potential besides the *in vivo* antidiabetic effectiveness of *H. fomes* (HF) was evaluated.

MATERIALS AND METHODS

Chemicals and reagents. STZ, the analytical grade reagents i.e., Folin-Ciocalteu (FC) reagent, Na_2CO_3, $NaNO_2$, $AlCl_3$, NaOH, H_2O_2, Na_2HPO_4. $2H_2O$, $NaH_2PO_4.2H_2O$, 2-deoxy-2-ribose, $FeCl_3$, EDTA, trichloro acetic acid (TCA), thiobarbituric acid (TBA), phenazine methosulfate (PMS), ascorbic acid, nitro blue tetrazolium (NBT), nicotinamide adenine dinucleotide (NADH) were purchased from Sigma Chemical Co., USA. The biochemical parameters estimation was performed by commercially available kits, also obtained from Sigma.

Collection, identification and extraction of plant material. The pneumatophores of HF were collected from Sundarbans, Satkhira range in April 2016 and identified by the experts at Bangladesh National Herbarium, Mirpur, Dhaka where a voucher specimen was submitted for future reference (Accession no.: DACB 44814). After collecting the pneumatophores, they were cleaned, shade-dried and ground into fine powder. 300 g of dried plant powder was taken and extracted by cold maceration method using 96% ethanol. The yield of extraction was 8.03% w/w.

Experimental animal. Swiss albino mice of 4-5 weeks and an average weight of 20-25 g were used in the oral glucose tolerance test. Young Wistar albino rats, 6-7 weeks aged and an average weight of 100-120 g, were used for STZ-induced antidiabetic test. All of the experimental animals were purchased from Jahangirnagar University, Dhaka, Bangladesh. They were kept in standard environmental conditions in the Pharmacology Laboratory of Pharmacy Discipline, Khulna University, Khulna, Bangladesh, for one week for adaptation after purchase. The animals were fed with formulated rodent food and water. All experiments were performed according to the ethical guidelines of the Animal Ethics Committee (AEC), Khulna University Research Cell, Khulna-9208, Bangladesh [Ref: KUAEC-2020/08/10].

Phytochemical screening. A qualitative test to determine the presence of different phytochemical groups like alkaloid, flavonoid, tannins, carbohydrates, phenols, saponins, proteins, gums, etc. was done with a freshly prepared solution of plant extract.[12]

Evaluation of antioxidative activity

Qualitative antioxidant activity test. In the qualitative measurement of antioxidant activity, the plant extract was suitably diluted and spotted on a previously prepared TLC plate. The chromatographic procedures were then conducted with solvents of different polarities. *n*-Hexane:ethyl acetate (2:1) as a non-polar solvent, $CHCl_3$:CH_3OH (5:1) as a medium polar solvent and $CHCl_3$:CH_3OH:H_2O (40:10:1) as a polar solvent were used. A solution of 0.02% w/v DPPH (2,2-diphenyl-1-picrylhydrazyl) in methanol was used as a detector of antioxidative components.[13]

DPPH radical scavenging activity test. DPPH free radical scavenging activity was measured by the

modified microplate method where the absorbance was taken at 517 nm using Thermo Scientific Multiskan Ex microplate photometer. The radical scavenging activity was denoted by SC_{50} (µg/ml, concentration of sample required to scavenge 50% of DPPH free radicals formation) and measured from a log concentration (sample concentration versus percent inhibition) curve using LDP line software (by Ehab Bakr)[13] Ascorbic acid was used as a standard for DPPH radical scavenging assay.

Hydrogen peroxide radical scavenging activity test. The method described by Biswas *et al.*[14] was adopted to determine the hydrogen peroxide radical scavenging activity where different concentrations of the plant extract were dissolved in phosphate buffer, a blank containing only phosphate buffer was taken in several test tubes and the absorbance was taken at 230 nm using a spectrophotometer. Here, ascorbic acid was used as standard. The antioxidant activity was articulated in terms of SC_{50} which was calculated from log concentration versus percent inhibition curve using LDP line software.

Hydroxyl radical scavenging activity test. The hydroxyl radical scavenging activity was measured by the method described by Golder *et al.*[15] which evaluated the competition between deoxyribose and HF extract for hydroxyl radicals generated with Fe^{3+} /ascorbate/EDTA/H_2O_2 system. Here, several concentrations of a serially diluted plant extract were used and the absorbance was determined spectrophotometrically at 530 nm. Ascorbic acid was used as a standard for this test. The SC_{50} value was measured from the percentage scavenged versus concentration curve using LDP line software.

Superoxide radical scavenging activity test. Superoxide radical scavenging activity was measured by the method described by Debnath *et al.*[16] which studied the reduction of NBT by NADH and PMS. Ascorbic acid was used as standard. Here, the absorbance of several concentrations of serially diluted plant extract, standard (ascorbic acid) and blank solution (containing ethanol with all other reagents i.e., phosphate buffer, PMS, NBT and NADH) were measured at 560 nm. The radical scavenging activity was measured in terms of SC_{50} and calculated from the percentage scavenged versus concentration curve using LDP line software.

Reducing power assay. Substances with reducing potential, react with potassium ferricyanide (Fe^{3+}) to form potassium ferrocyanide (Fe^{2+}), which then reacts with ferric chloride to form a ferric ferrous complex afterward. Therefore, the measurement of formed Pearls Prussian blue at 700 nm gives the information of Fe^{2+} concentration; which has an absorption maximum at 700 nm. An increase in absorbance of the reaction mixture was interpreted as increased reducing activity of the extract and the results were compared with ascorbic acid which was used as the standard. The result was presented as RC_{50} (concentration of extract required to reduce 50% of ferric content).[16]

Evaluation of antihyperglycemic activity by Oral glucose tolerance test (OGTT). Experimental mice were randomly selected and divided into 4 groups (each group containing 5 mice) each of which received specific treatment; Group I - only distilled water, Group II - glibenclamide at 10 mg/kg body weight (b.w.) dose, Group III - HF extract at 250 mg/kg b.w. dose and Group IV - HF extract at 500 mg/kg b.w. dose. Half an hour later, all the groups received glucose orally by a feeding needle. Blood glucose level was measured using the glucometer and compatible blood glucose strips at 0, 60 and 120 minutes after glucose administration.[17]

Evaluation of antidiabetic activity on STZ-induced diabetic rats. STZ (60 mg/kg b.w.) was administered to overnight fasted rats (12 h) by single intraperitoneal injection of freshly prepared solution of STZ in 0.1 M citrate buffer of pH 4.5 to induce diabetes mellitus. Equal amounts of the vehicle were given to control groups intraperitoneally. The early phase of drug-induced hypoglycemia was prohibited by treating the animals with a 5% glucose solution orally. After 48 h, the blood glucose levels were measured by tipping the tail and using a glucometer (this was considered as day 0). Rats with a glucose level over 12 mmol/l were used in the study. The

groups of animals were then treated for 14 days with single daily doses of plant extracts to evaluate the chronic effect of the plant on hyperglycemia. The blood glucose level of selected rats was then measured on days 7 and 14. On day 14, the animals were sacrificed and the blood samples were collected for hematological investigation and lipid profiling.[18]

Hematological parameters assessment and blood lipid profiling. Prior studies reported the hematological alterations in STZ-induced rats as a result of oxidative stress induced by diabetes mellitus. At the end of the test, blood samples were collected from the rats, serum was separated by centrifugation at 1500 rpm for 5 to 10 minutes and stored at -20ºC in a refrigerator. Then, blood parameters including creatinine, uric acid, blood urea nitrogen (BUN), serum glutamic pyruvic transferase (SGPT), serum glutamic oxaloacetic transaminase (SGOT) and the lipid profiles (cholesterol, triglyceride, HDL and LDL levels) were investigated.[19]

Statistical analysis. The results were analyzed using several statistical tests. For comparison of test results with the control group, a one-way ANOVA analysis was carried out with Dunnet's *t* test for $p < 0.05$. Pairwise comparison was done following the Post-hoc Tukey test ($p < 0.05$, versus standard/extract). SPSS software of IBM Corporation, New York, USA (version 16.0) was used for analyzing the data.[20]

RESULTS AND DISCUSSION

Oxidative damage ancestries to the development and progression of so many fatal diseases including neurodegenerative and cardiovascular disorders. Almost all medicinal plant shows antioxidant activity due to the inherent capacity of plants to produce non-enzymatic antioxidants such as ascorbic acid and glutathione, as well as the presence of secondary metabolites such as phenolic compounds, flavonoids, tannins.[21] The present study includes the phytochemical characterization of this plant that revealed the presence of reducing sugar, combined reducing sugar, tannins, flavonoids, saponin, steroids, alkaloids, and glycoside but proteins and gums were absent (Table 1). Earlier studies on HF have reported the presence of a magnitude of phytochemical constituents. Leaves of this plant contain reducing sugars, saponins, alkaloids, glycosides, tannins, steroids, flavonoids and gums whereas barks and stem barks exhibited the presence of tannin, proanthocyanidins.[22]

Table 1. Results of the assay for phytochemical constituents present in the HF extract.

Phytochemical groups	HF extract
Reducing sugar	+
Combined reducing sugar	+
Tannins	+
Flavonoids	+
Saponin	+
Gums	-
Steroids	+
Alkaloids	+
Glycoside	+
Proteins	-

+ (Present); - (Absent).

Mangrove plants are well known for being rich in secondary metabolites like tannins, flavonoids and alkaloids which pose antioxidative activity to adapt to the harsh coastal environment. In our current investigation, we studied the antioxidant potential of this plant by several methods due to the multidimensional features of the antioxidants and their reactive nature. In the qualitative antioxidant activity test, strong yellow spots were found on the purple background of TLC plates which demonstrates the presence of antioxidative compounds. So, the plant extract was later tested for quantitative antioxidant activity through several radical scavenging assays. In DPPH radical scavenging assay, the SC_{50} value was found to be ~49 µg/ml for HF extract and ~12 µg/ml for ascorbic acid, while the SC_{50} value observed in hydrogen peroxide radical scavenging assay was ~87 µg/ml and ~47 µg/ml for HF extract and ascorbic acid, respectively. The HF extract scavenged hydroxyl and superoxide radical with SC_{50} values of ~ 66 µg/ml and ~ 76 µg/ml,

respectively, while for ascorbic acid standard, it was ~ 39 µg/ml and~ 58 µg/ml, respectively. Finally, in the reducing power assay, the HF extract showed an RC_{50} ~47 µg/ml whereas the RC_{50} of standard (ascorbic acid) was ~29 µg/ml (Figure 1).

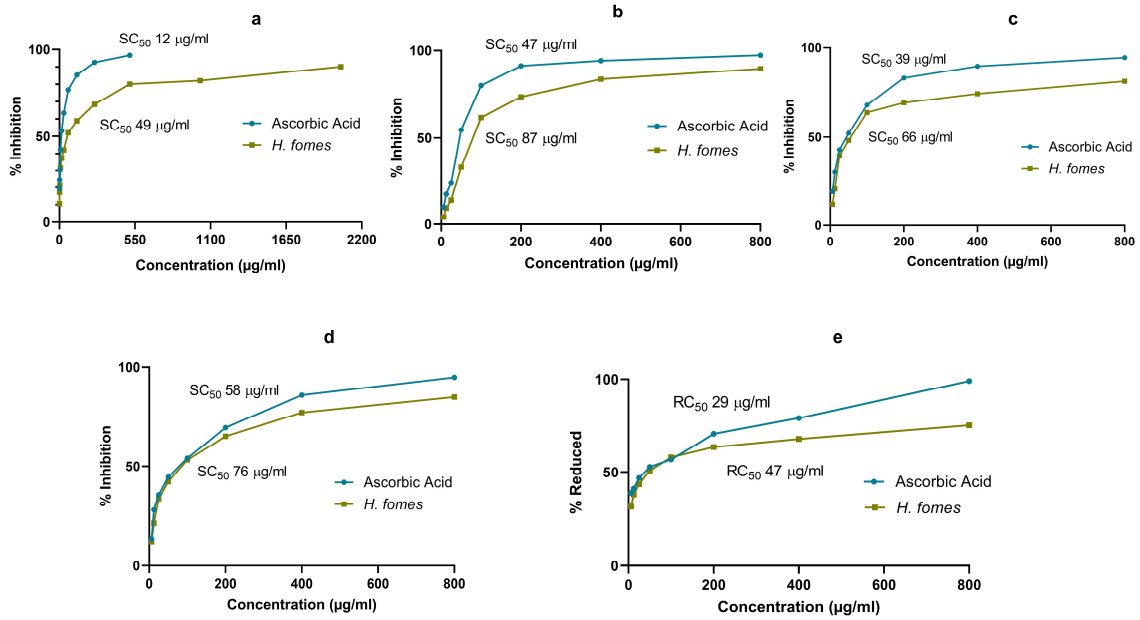

Figure 1. SC_{50} and RC_{50} values of different antioxidative assays of HF extract. Here, **a** (DPPH radical scavenging activity test), **b** (Hydrogen peroxide scavenging activity test), **c** (Hydroxyl radical scavenging activity test), **d** (Superoxide radical scavenging activity test), **e** (Reducing power assay).

So much experimental evidence is available that shows the direct relation of free radical damage to the progression and complications of diabetes. The reasons behind this may be the increase in the levels of oxidative DNA damage markers and lipid-peroxidation products as well as lowering the activity of antioxidant enzymes due to persistent hypoglycemia. All these etiological relationships direct to a theory benefit of antioxidants in the treatment or management of diabetic patients.[17] Keeping this factor in the account along with the folkloric use of this plant, we have explored the antidiabetic potential of the sample which includes a preliminary antihyperglycemic screening through OGTT followed by the STZ-induced antidiabetic activity test.

The glucose tolerance test is used to determine the struggle of the body to metabolize sugar/carbohydrate and it helps in the diagnosis of several conditions like pre-diabetes, gestational diabetes, insulin resistance and reactive hypoglycemia. The experimental sample in both doses significantly reduced the blood glucose level in mice at 60 minutes following the oral glucose administration in comparison to the control (Figure 2).

A STZ-induced antidiabetic test was carried out afterward. STZ is the commonly used chemical to induce type-II diabetes in laboratory animals which is responsible for pancreatic β-cell damage and necrosis by alkylation of pancreatic DNA and generation of free radicals like superoxide, hydrogen peroxide, nitric oxide and hydroxyl.[23] This leads to the primary factor of hyperglycemia in STZ-induced diabetes which is the apoptosis of pancreatic β-cells.[24] In the current study, the blood sugar level of all experimental animals were measured at the initial as well as at the 7th and 14th days after giving the

specified treatment in each group (Figure 3). The diabetic control group showed a significant increase in the blood glucose level as compared to the negative control. Oral administration of HF extract at 250 mg/kg and 500 mg/kg b.w. dose significantly reduced the blood glucose level of diabetic rats as compared to the standard (glibenclamide 10 mg/kg).

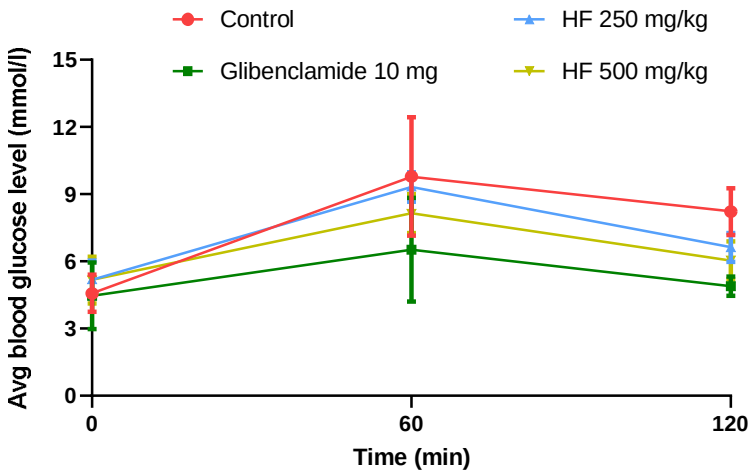

Figure 2. Effect of HF extract and standard drug on the blood glucose level of mice in the oral glucose tolerance test.

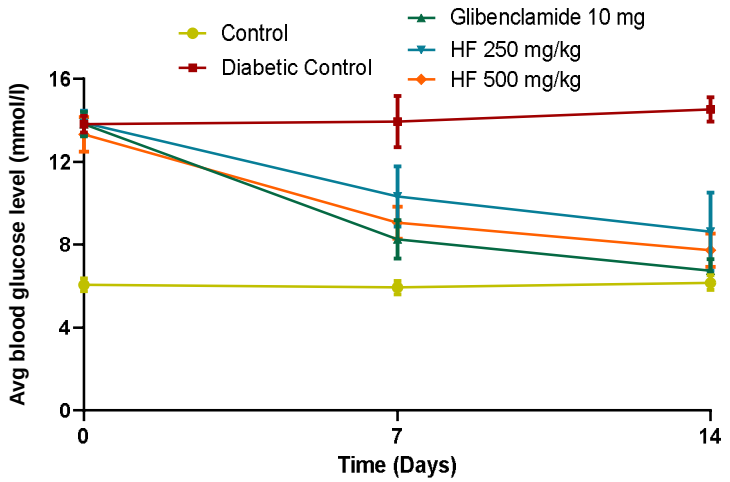

Figure 3. Effect of HF extract and standard drug on the blood glucose level of STZ-induced diabetic rats test on days 0, 7 and 14.

An increase in blood glucose level after administration of STZ is the outcome of insulin deficiency or a resistance state in the diabetic animal. Treatment with selected antidiabetic agents and plant extracts produced a varying degree of reduction in blood glucose levels. Significant elevation in blood glucose level was observed in diabetic rats compared to normal control. This represents a reversal of insulin resistance or an increase in the secretion of insulin probably by regeneration of β-cells of the pancreas.[25]

In the present study, the effects of HF extract on a series of biochemical parameters in STZ-induced diabetic rats were investigated. Here significant differences in the level of creatinine, uric acid, BUN, SGOT and SGPT were found while comparing the treated rats (standard group, HF 250 mg/kg, HF 500 mg/kg) to the diabetic control group (Table 2). Moreover, in the lipid profiling of the treatment

groups (glibenclamide, HF 250 mg/kg, HF 500 mg/kg) variations in the level of cholesterol, triglyceride, HDL and LDL were observed (Table 3).

Table 2. Effect of HF extract on blood parameters in STZ-induced diabetic rats.

Treatment	Creatinine (mg/dl)	Uric acid (mg/dl)	BUN (mg/dl)	SGOT (U/L)	SGPT (U/L)
Negative control	1.02 ± 0.13	3.81 ± 0.23	15.65 ± 0.44	4.51 ± 0.47	44.14 ± 1.27
Diabetic control	3.62 ± 0.25 $*^{\blacksquare\blacktriangle\Delta}$	5.32 ± 0.27 $*^{\blacksquare\blacktriangle\Delta}$	33.31 ± 1.36 $*^{\blacksquare\blacktriangle\Delta}$	27.56 ± 0.61 $*^{\blacksquare\blacktriangle\Delta}$	68.79 ± 1.45 $*^{\blacksquare\blacktriangle\Delta}$
Glibenclamide 10 mg/kg	1.78 ± 0.13 $*^{\theta\blacktriangle\Delta}$	3.77 ± 0.17 $^{\theta\blacktriangle}$	20.61 ± 2.65 $*^{\theta}$	15.79 ± 0.74 $*^{\theta\blacktriangle\Delta}$	49.19 ± 1.72 $*^{\theta\blacktriangle}$
HF 250 mg/kg	2.96 ± 0.13 $*^{\theta\blacksquare\Delta}$	4.43 ± 0.37$*^{\theta\blacksquare}$	23.42 ± 1.89 $*^{\theta}$	22.25 ± 0.77 $*^{\theta\blacksquare\Delta}$	59.15 ± 0.93 $*^{\theta\blacksquare\Delta}$
HF 500 mg/kg	2.42 ± 0.15 $*^{\theta\blacksquare\blacktriangle}$	4.18 ± 0.10 $^{\theta}$	21.21 ± 1.13 $*^{\theta}$	19.38 ± 1.76 $*^{\theta\blacksquare\blacktriangle}$	50.61 ± 2.20 $*^{\theta\blacktriangle}$

Data are means of five replicates ± SD (Standard deviation); * $p < 0.05$ vs. Negative Control (Dunnett's t test); $^{\theta}$ $p < 0.05$ vs. Diabetic Control; $^{\blacksquare}$ $p < 0.05$ vs Glibenclamide 10 mg/kg; $^{\blacktriangle}$ $p < 0.05$ vs HF 250 mg; $^{\Delta}$ $p < 0.05$ vs. HF 500 mg (pairwise comparison by post-hoc Tukey test).

Table 3. Effect of HF extract on lipid profile level in STZ-induced diabetic rats.

Treatment	Cholesterol (mg/dl)	Triglyceride (mg/dl)	HDL (mg/dl)	LDL (mg/dl)
Negative control	101.4 ± 9.07	123.0 ± 14.4	41.6 ± 3.21	47.2 ± 6.30
Diabetic control	98.6 ± 7.30 $^{\blacksquare\blacktriangle\Delta}$	163.8 ± 16.42 $*^{\blacksquare\blacktriangle\Delta}$	30.8 ± 4.21 $*^{\blacksquare\blacktriangle\Delta}$	59.6 ± 3.04 $*^{\blacksquare\blacktriangle\Delta}$
Glibenclamide 10 mg/kg	68.6 ± 4.16 $*^{\theta}$	92.2 ± 8.41 $*^{\theta}$	52.4 ± 5.46 $*^{\theta}$	31.2 ± 3.49 $*^{\theta}$
HF 250 mg/kg	72.8 ± 4.97 $*^{\theta}$	106 ± 4.90 $^{\theta}$	48.4 ± 3.65 $^{\theta}$	34.6 ± 4.39 $*^{\theta}$
HF 500 mg/kg	64.6 ± 4.34 $*^{\theta}$	90.4 ± 3.36 $*^{\theta}$	52 ± 5.24 $*^{\theta}$	28.2 ± 2.39 $*^{\theta}$

Data are means of five replicates ± SD (Standard deviation); * $p < 0.05$ vs. Negative Control (Dunnett's t test); $^{\theta}$ $p < 0.05$ vs. Diabetic Control; $^{\blacksquare}$ $p < 0.05$ vs Glibenclamide 10 mg/kg; $^{\blacktriangle}$ $p < 0.05$ vs HF 250 mg; $^{\Delta}$ $p < 0.05$ vs. HF 500 mg (pairwise comparison by post-hoc Tukey test).

Most significant anomalies in lipid profile were observed in the case of cholesterol and triglyceride in considering the diabetic rats. Upsurged metabolism of fatty acids from peripheral fat depots leads to the abnormally high concentration of lipid in serum.[26] Glibenclamide standard as well as plant extracts were observed to significantly lessen the serum level of cholesterol, triglyceride and LDL and significantly enhance the level of HDL in diabetic rats. The plant extract showed a moderate decrease in the level of cholesterol and triglyceride whereas, it demonstrated a greater reduction in LDL level (Table 3). In addition, increased HDL level may be beneficial in stopping complications like coronary heart diseases and atherosclerosis associated with diabetes.

Common clinical markers in diabetic nephropathy include proteinuria, albuminuria or an uplift in protein catabolism which may be responsible for the drop in protein or albumin level.[27] Furthermore, diabetes is associated with elevated BUN, uric acid and creatinine levels as a result of renal damage mediated by abnormalities in glucose regulation or elevated glucose or glycosylated protein tissue level.[28] Investigation in the current study of blood parameters reflected the aforementioned assumption as a significant increase in BUN, uric acid and creatinine levels in diabetic rats was observed compared to control rats (Table 2). Such an outcome possibly represents the uplift in insulin-mediated amino acid uptake as well as protein synthesis and inhibition of protein degradation. In addition, abnormality in liver function or metabolic changes in the liver i.e. administration of a toxin, cirrhosis of the liver due to diabetes, hepatitis and liver cancer cause an increase in SGOT and SGPT levels.[29] So, analyzing such blood parameters in diabetic rats may give an insight into the antidiabetic

effect of treatment species. Now, in considering the treatment with glibenclamide standard and HF extracts, a significant decrease in the level of creatinine, uric acid, BUN, SGOT and SGPT in diabetic rats was observed. The plant extract showed a greater decline in the level of BUN as compared to the extent of reduction of creatinine, uric acid, SGOT and SGPT.[30]

Variety of other major antidiabetic phytoconstituents was found to be present in the plant extract in their phytochemical evaluation that were proved to have antidiabetic potential i.e. alkaloids (works by inhibiting alpha-glucosidase and decreasing glucose transport through the intestinal epithelium), polysaccharides (increase serum insulin level, improve glucose tolerance), saponins (stimulates insulin release) and phenolic compounds (upsurge the sensitivity of tissues to action of the insulin).[30] From this, it may be extrapolated that the antidiabetic activity of HF extract is attributed to the enhancement of pancreatic secretion of insulin; upsurge in glucose uptake and inhibition in glucose absorption in gut mediated by the presence of antioxidative secondary metabolites like tannins, flavonoids polyphenols, alkaloids, saponins and other bioactive compounds. Further investigations are necessary for isolating the active constituents from plant sample.

CONCLUSION

In the present study, the pneumatophores of *H. fomes* have shown potential antioxidative and antidiabetic activity. Hence, the plant extract can be considered valuable in managing diabetes created by oxidative damages as well as the oxidative indemnities caused by diabetes. Further comprehensive biochemical and pharmacological investigations directed to clarify the exact mechanism of hypoglycemic action and elucidate structures of the active compounds will be fruitful.

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Conflicts of interest. The authors declare no conflict of interest.

REFERENCES

1. Rahati, S., Shahraki, M., Arjomand, G. and Shahraki, T. 2014. Food pattern, lifestyle, and diabetes mellitus. *Int. J. High Risk Behav. Addict.* **3**, e8725.
2. Soon, Y. and Tan, B. 2002. Evaluation of the hypoglycemic and antioxidant activities of *Morinda officinalis* in streptozotocin-induced diabetic rats. *Singap. Med. J.* **43**, 077-085.
3. Moree, S. S., Kavishankar, G. and Rajesha, J. 2013. Antidiabetic effect of secoisolariciresinol diglucoside in streptozotocin-induced diabetic rats. *Phytomedicine* **20**, 237-245.
4. Yang, B. K., Jung, Y. S. and Song, C. H. 2007. Hypoglycemic effects of *Ganoderma applanatum* and *Collybia confluens* exo-polymers in streptozotocin-induced diabetic rats. *Phytother. Res.* **21**, 1066-1069.
5. Dahibhate, N. L., Saddhe, A. A. and Kumar, K. 2019. Mangrove plants as a source of bioactive compounds: A review. *J. Nat. Prod.* **9**, 86-97.
6. Patel, D., Prasad, S. K., Kumar, R. and Hemalatha, S. 2012. An overview on antidiabetic medicinal plants having insulin mimetic property. *Asian Pac. J. Trop. Biomed.* **2**, 320-330.
7. Hossain, M. A., Panthi, S., Asadujjaman, M., Khan, S. A., Ferdous, F. and Sadhu, S. K. 2013. Phytochemical and pharmacological assessment of the ethanol leaves extract of *Heritiera fomes* Buch. Ham. (Family-Sterculiaceae). *J. Porphyr. Phthalocya.* **2**, 95-101.
8. Mollik, M. A. H., Hossan, M. S. and Paul, A. K., Taufiq-Ur-Rahman, M., Jahan, R. , Rahmatullah, M. 2010. A comparative analysis of medicinal plants used by folk medicinal healers in three districts of Bangladesh and inquiry as to mode of selection of medicinal plants. *Ethnobot. Res. Appl.* **8**, 195-218.
9. Wangensteen, H., Dang, H., Uddin, S. J., Alamgir, M. and Malterud, K. E. 2009. Antioxidant and antimicrobial effects of the mangrove tree *Heritiera fomes*. *Nat. Prod. Commun.* **4**, 371-376.
10. Patra, J. K. and Thatoi, H. 2013. Anticancer activity and chromatography characterization of methanol extract of *Heritiera fomes* Buch. Ham., a mangrove plant from Bhitarkanika, India. *Orient. Pharm. Exp. Med.* **13**, 133-142.

11. Raza, H. and John, A. 2012. Streptozotocin-induced cytotoxicity, oxidative stress and mitochondrial dysfunction in human hepatoma HepG2 cells. *Int. J. Mol. Sci.* **13**, 5751-5767.
12. Biswas, B., Golder, M., Abid, M. A., Mazumder, K. and Sadhu, S. K. 2021. Terpenoids enriched ethanol extracts of aerial roots of *Ceriops decandra* (Griff.) and *Ceriops tagal* (Perr.) promote diuresis in mice. *Heliyon* **7**, e07580.
13. Sadhu, S.K., Okuyama, E., Fujimoto, H. and Ishibashi, M. 2003. Seperation of *Leucas aspera*, a medicinal plant of Bangladesh, guided by prostaglandin inhibitory and antioxidant activities. *Chem. Pharm. Bull.* **51**, 595-598.
14. Biswas, B., Golder, M., Islam, T. and Sadhu, S. K. 2018. Comparative antioxidative and antihyperglycemic profiles of pneumatophores of two mangrove species *Avicennia alba* and *Sonneratia apetala*. *Dhaka Univ. J. Pharm. Sci.* **17**, 205-211.
15. Golder, M., Sadhu, S. K., Biswas, B. and Islam, T. 2019. Comparative pharmacologic profiles of leaves and hypocotyls of a mangrove plant: *Bruguiera gymnorrhiza*. *Adv. Tradit. Med.* **20**, 395-403.
16. Debnath, S., Kundu, P., Golder, M., Biswas, B. and Sadhu, S. 2020. Phytochemical characterization and evaluation of pharmacological activities of leaves of a mangrove plant species-*Aegiceras corniculatum* (L.). *Trop. J. Nat. Prod. Res.* **4**, 516-522.
17. Mazumder, K., Sumi, T. S., Golder, M., Biswas, B. and Kerr, P. G. 2021. Antidiabetic profiling, cytotoxicity and acute toxicity evaluation of aerial parts of *Phragmites karka* (Retz.). *J. Ethnopharmacol.* **270**, 113781.
18. Hebi, M., Khallouki, F., Haidani, A. and Eddouks, M. 2018. Aqueous extract of *Argania spinosa* L. fruits ameliorates diabetes in streptozotocin-induced diabetic rats. *Cardiovasc. Hematol. Agents. Med. Chem.* **16**, 56-65.
19. Nabi, S. A., Kasetti, R. B., Sirasanagandla, S., Tilak, T. K., Kumar, M. V. J. and Rao, C. A. 2013. Antidiabetic and antihyperlipidemic activity of *Piper longum* root aqueous extract in STZ induced diabetic rats. *BMC Complement. Altern. Med.* **13**, 37.
20. Mazumder, K., Biswas, B., Kerr, P. G., Blanchard, C., Nabila, A., Golder, M. and Aziz, M. G. , Farahnaky, A. 2021. Comparative assessment of nutritional, thermal, rheological and functional properties of nine Australian lupin cultivars. *Sci. Rep.* **11**, 21515.
21. Kasote, D. M., Katyare, S. S., Hegde, M. V. and Bae, H. 2015. Significance of antioxidant potential of plants and its relevance to therapeutic applications. *Int. J. Biol. Sci.* **11**, 982-991.
22. Mahmud, I., Islam, M. K., Saha, S., Barman, A. K., Rahman, M. M., Anisuzzman, M., Rahman, T., Al-Nahain, A., Jahan, R. and Rahmatullah, M. 2014. Pharmacological and ethnomedicinal overview of *Heritiera fomes*: future prospects. *Int. Sch. Res. Notices.* **2014,** 938543.
23. Szkudelski, T. 2001. The mechanism of alloxan and streptozotocin action in B cells of the rat pancreas. *Physiol. Res.* **50**, 537-546.
24. Rajkumar, L., Srinivasan, N., Balasubramanian, K. and Govindarajulu, P. 1991. Increased degradation of dermal collagen in diabetic rats. *Indian J. Exp. Biol.* **29**, 1081-1083.
25. Sezik, E., Aslan, M., Yesilada, E. and Ito, S. 2005. Hypoglycaemic activity of *Gentiana olivieri* and isolation of the active constituent through bioassay-directed fractionation techniques. *Life Sci.* **76**, 1223-1238.
26. Al-Logmani, A. S. 2009. Effects of *Nigella sativa* L. and *Cinnamomum zeylanicum* Blume oils on some physiological parameters in streptozotocin-induced diabetic rats. *Bol. Latinoam. Caribe. Plantas.* **8**, 86-96.
27. Kaleem, M., Medha, P., Ahmed, Q., Asif, M. and Bano, B. 2008. Beneficial effects of Annona squamosa extract in streptozotocin-induced diabetic rats. *Singap. Med. J.* **49**, 800.
28. Lal, S. S., Sukla, Y., Singh, A., Andriyas, E. A. and Lall, A. M. 2009. Hyperuricemia, high serum urea and hypoproteinemia are the risk factor for diabetes. *Asian J. Med. Sci.* **1**, 33-34.
29. Bursch, W. and Schulte-Hermann, R. 1986. Cytoprotective effect of the prostacyclin derivative iloprost against liver cell death induced by the hepatotoxins carbon tetrachloride and bromobenzene. *Wien. Klin. Wochenschr.* **64**, 47-50.
30. Das, S. K., Samantaray, D., Patra, J. K., Samanta, L. and Thatoi, H. 2016. Antidiabetic potential of mangrove plants: A review. *Front. Life Sci.* **9**, 75-88.