Future Natural Products
doi: 10.34172/fnp.2023.01 2023;9(1):3-9 http://futurenatprod.skums.ac.ir

Original Article

Characteristics constituents with antidiabetic significance from Indian mangrove apples

Avijit Saha[1], Tapan Seal[2], Shuvam Saha[3], Alok K. Hazra[4], Sandip Ghosh[1], Tapas Kumar Sur[1*]

[1]Multidisciplinary Research Unit, R.G. Kar Medical College and Hospital, Kolkata, India
[2]Plant Chemistry Laboratory, Botanical Survey of India, Howrah, India
[3]Department of Life Sciences, CHRIST University, Bangalore, India
[4]Analytical Research Division, Chromogen, Howrah, India

*Corresponding Author:
Tapas Kumar Sur,
Email: drtapaskumarsur@gmail.com

Received: September 25, 2022
Accepted: December 25, 2022
ePublished: June 3, 2023

Abstract

Background and aims: There is limited information on the chemical nature of the edible fruits of the mangrove *Sonneratia apetala*, which is utilized in traditional medicine in coastal areas. The goal of the current research was to identify the biologically active substances behind their therapeutic effects, particularly blood sugar regulation.

Methods: To determine the chemical fingerprint of *S. apetala* fruit extract, reversed phase high performance liquid chromatography (RP-HPLC) and gas chromatography–mass spectrometry (GC-MS) profiling were used. The antioxidant properties were thoroughly examined. α-Amylase and α-glucosidase enzymes were also used to evaluate the impact of *S. apetala* fruit extract on the regulatory mechanism for the metabolism of carbohydrates.

Results: *S. apetala* fruit extract showed high concentrations of phenolics, flavonoids, and water-soluble vitamins (C, B2, B5, and B6). Quercetin, catechin, rutin, myricetin, p-coumaric acid, ferulic acid, gallic acid, sinapic acid, and ascorbic acid were among the recognized therapeutically active substances found in RP-HPLC. The presence of β-amyrin and lupeol in *S. apetala* fruit extract was determined by the GC-MS profile. The carbohydrate-slitting enzymes α-amylase and α-glucosidase were also strongly inhibited by *S. apetala* fruit extract.

Conclusion: The fruit of *S. apetala* contains therapeutically useful polyphenolics, triterpenoids, phytosterols, and vitamins. It can lower blood sugar absorption by blocking enzymes that break down carbohydrates and has potent antioxidant qualities.

Keywords: Mangrove, *Sonneratia apetala*, RP-HPLC, GC-MS, Antioxidant, α-Glucosidase

Introduction

The mangrove apple tree or *Sonneratia apetala* Buch-Ham (Sonneratiaceae) is widely dispersed over the tropical coastal areas of the Indian Sundarbans (21°32′ and 22°40′ N and between 88°05′ and 80°00′ E), the biggest mangrove forest in the world, as well as Bangladesh (1). However, other varieties include as *S. alba*, *S. caseolaris*, *S. griffithii*, and *S. ovata* are widely grown in China and other south Asian nations such as Myanmar, Thailand, Malaysia, Indonesia, and Sri Lanka (2). In South Asian nations, including India, the bark, root, leaves, and fruits of *Sonneratia* spp. have been utilized in folk medicine to cure diabetes, ulcers, swelling, inflammation, wounds, hepatic disorders, piles, and diarrhea (3-6). Local inhabitants utilize fruits as vegetables or pickles or sour sauce. We recently reported on the antioxidant and gastroprotective properties of *S. apetala* leaves (2). Unfortunately, there are very few scientific reports regarding the chemical constituents and therapeutic benefits of the Indian mangrove apple. Analgesic, cytotoxic, bactericidal, and antioxidant properties of fruit extract of other species have been reported. The fruits of *S. caseolaris* and *S. ovate* in China were found to contain cytotoxic 6H-benzo [b, d] pyran-6-one derivatives (7). From the aerial parts of *S. caseolaris*, luteolin, and luteolin 7-O-b-glucoside, two bioactive flavonoids were found (8,9). However, despite their nutritional value, *S. apetala* fruits have not attracted much scientific research for their chemically recognized therapeutically active components. Mangroves and their metabolites are rich in steroids, triterpenes, saponins, flavonoids, alkaloids, and tannins, which are used as traditional medicines, particularly for diabetes (8,10-12). The traditional use of mangrove apples in diabetes has been reported, but their exact role in blood sugar regulation is scanty. Although mangrove apples have a history of being used to treat diabetes, little is known about how they actually work to control blood sugar levels. In this regard, the current research strategy was created to look for biologically active components in Indian mangrove apples.

Materials and Methods

Pant material

Mangrove apples (*S. apetala*) were collected in West Bengal's Indian Sunderban. After the monsoon (September–October), the fieldwork was carried out with the necessary

permission from Forest Department. The Botanical Survey of India, West Bengal, recognized the fruits.

Extract process

The mangrove fruits were thoroughly washed and dried in the shade and crushed to powder by an electric grinder. The powdered fruits (100 g) were extracted twice with hydro-ethanol (20-80%) for 6 hours at 60°C. The hydro-ethanolic extract was next concentrated in a rotary evaporator at a lower pressure (2). The dried extract (*S. apetala* fruit extract) was stored at -20°C in a vacuum desiccator. The yield was 19.3%.

Quantity bioactive substances

Total phenolics

The total phenolic content of *S. apetala* fruit extract was estimated using the Folin-Ciocalteu method as described earlier. In brief, 100 mL of *S. apetala* fruit extract (1 mg/mL methanol, 80%) was taken in test tubes. Thereafter, 1.0 mL of Folin-Ciocalteu reagent was mixed and stand for 5 minutes in dark. Thereafter, 0.8 mL of 7.5% sodium carbonate was added, mixed, and left to stand for another 30 minutes. The absorbance was measured after mixing 3 mL of deionized water at 765 nm using a UV-Vis spectrophotometer (Shimadzu UV 1800). Gallic acid equivalent (GAE) was used to express the total phenolic content in µg/mg of extract (13).

Total flavonoids

As previously mentioned, the flavonoids were estimated using the aluminum chloride method. In a nutshell, test tubes containing 100 mL of *S. apetala* fruit extract (1 mg/mL methanol, 80%) were filled with 0.8 mL of methanol, 0.1 mL of 10% aluminum chloride, 0.1 mL of 1 M potassium acetate, and 2.8 mL of deionized water. The test tubes were then left at room temperature for 30 min. The absorbance was measured at 415 nm (Shimadzu UV 1800). The total flavonoids were expressed as rutin equivalent (RE) in µg/mg of extract (14).

Reducing power

The ability of *S. apetala* fruit extract to reduce the iron (III) ions was assessed spectrophotometrically. In brief, 2.5 mL of 0.2 M phosphate buffer (pH 6.6) and 1% of 2.5 mL potassium ferricyanide were combined with 100 µL of *S. apetala* fruit extract at various concentrations, including 100, 200, 500, 800, and 1000 mg/mL. After 20 minutes of incubation at 50°C, 2.5 mL of 10% TCA was added to the tubes. After centrifugation, the upper layer of the 2.5 mL solution was combined with 0.5 mL of freshly made 0.1% ferric chloride and 2.5 mL of deionized water, and absorbance was measured at 700 nm. Reducing power was expressed as ascorbic acid equivalent (AAE) in µg/mg of *S. apetala* fruit extract extract (15).

High-performance liquid chromatography profiling

Bioactive and therapeutically potential phenolics and flavonoids in *S. apetala* fruit extract were profiled by high-performance liquid chromatography (HPLC) using a reversed-phase Acclaim C18 column (5µ, 4.6 mm × 250 mm), Dionex Ultimate 3000 liquid chromatograph (Germany) with a diode array detector, and Chromeleon 6.8 System Manager as the data processor. The standard phenolic acids (gallic acid, protocatechuic acid, gentisic acid, chlorogenic acid, p-hydroxybenzoic acid, vanillic acid, caffeic acid, syringic acid, p-coumaric acid, ferulic acid, sinapic acid, salicylic acid, and ellagic acid), as well as the flavonoids catechin, rutin, myricetin, quercetin, naringin, apigenin, and kaempferol) was used in this HPLC profile. The column was thermostatically regulated at 25°C and the mobile phase includes methanol (Solvent A) and 0.5% aq. acetic acid solution (Solvent B). By changing the ratio of solvent A to solvent B, gradient elution was accomplished. The run time was fixed at 105 min. A photodiode array UV detector was used to detect the HPLC chromatogram at 272 nm. The integrated peak area was used to measure the phenolic acids and flavonoids in *S. apetala* fruit extract, and the contents were determined using the calibration curve by plotting the peak area against the concentration of the corresponding standard sample (16,17). The method was validated according to the USP and ICH guidelines (18).

Water-soluble vitamins

Water-soluble vitamins in *S. apetala* fruit extract were assessed by HPLC using a reversed-phase Acclaim C18 column (5µ, 4.6 mm × 250 mm), Dionex Ultimate 3000 liquid chromatograph with a diode array detector, and Chromeleon 6.8 System Manager as the data processor. In brief, 1 g of *S. apetala* fruit extract was dissolved in 10 mL of deionized water. The mixture was then combined with 10 mL of 1M phosphate buffer (pH 5.5) and 1 mL of 0.1M NaOH and kept in the dark for 24 hours. The following day, the solution was filtered, and the filtrate was then transferred to a volumetric flask and diluted with deionized water to a volume of 25 mL. As previously mentioned, the standard of water-soluble vitamins C, B1, B2, B3, B5, B6, and B9 was prepared. The column was kept at 22°C and the mobile phase was made up of acetonitrile (Solvent A) and 0.01% of aqueous trifluoroacetic acid (Solvent B). The gradient elution was performed with 1% solvent A and 99% solvent B at a flow rate of 0.5 mL/min for 5 min, 1% to 25% solvent A at a flow rate of 0.5 mL/min for 16 minutes, 25% to 45% solvent A at a flow rate of 0.5 mL/min for 8 minutes, and 45% to 1% solvent A at a flow rate of 0.5 mL/min for 5 min. The total analysis time was 40 minutes. The HPLC chromatogram of the water-soluble vitamins was detected at 275 nm using a photodiode array UV detector. The water-soluble vitamins in *S. apetala* fruit extract were measured using the integrated peak area, and their contents were calculated using a calibration curve by plotting the peak area against the concentration of the relevant standard sample (19,20). The technique was approved in accordance with ICH and USP standards (18).

Gas chromatography–mass spectrometry profiling

By using gas chromatography–mass spectrometry (GG-

MS), the biologically active components in *S. apetala* fruit extract were identified (Agilent 7890B GC with 5977A MSD, Agilent, USA). A capillary column (HP 5ms, 5% diphenyl-95% dimethyl polysiloxane) with a 30 m length, 0.25 mm ID, and 0.25 m film thickness is used to effectively separate the samples. The optimal oven temperature was programmed to start at 80°C for 2 minutes, then rise to 220°C at a rate of 4°C/min, and lastly to 280°C at 5°C while maintaining the ultimate temperature for 5 minutes. The flow rate of the carrier gas, helium, was kept constant at 1 mL/min. The temperature of the MS transfer line was set at 280°C while the injector was set at 220°C. The organic component of *S. apetala* fruit extract was eluted in n-hexane and ethyl acetate solvent at a ratio of 70:30 (v/v), dried, and re-suspended with 1 mL n-hexane before analysis (21). By matching the mass spectra to those found in the NIST 14.1 collection, all components were identified. The instrument software MassHunter expressed the *S. apetala* fruit extract's GC-MS profile as a relative percentage of the total peak area .

Biological activities

Antioxidant properties

DPPH radical scavenging

Using the stable radical DPPH, the free radical scavenging activity of *S. apetala* fruit extract was assessed (1, 1-diphenyl-2-picrylhydrazyl). Butylated hydroxyl toluene (BHT) was the positive control. Test tubes were filled with 100 mL of *S. apetala* fruit extract (100, 200, 500, 800, and 1000 mg/mL), and then 3.9 mL of freshly made 0.135 mM DPPH solution in methanol was added to each test tube. After 30 min, absorbance was measured at 517 nm (Shimadzu UV 1800). The sample concentration required to scavenge 50% of DPPH (IC_{50}) was determined (2).

ABTS radical scavenging

The ability of *S. apetala* fruit extract to scavenge the radical cation 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) was evaluated. In 12 hours, cationic ABTS + is formed by reacting 7 mM ABTS with 2.45 mM potassium persulfate. The final working ABTS + solution was obtained after appropriate dilution (OD 0.7 at 734 nm). After mixing 100 µL of *S. apetala* fruit extract containing five different concentrations with 2.5 mL of diluted $ABTS^{+}$, the absorbance at 734 nm was measured 6 minutes later to assess the scavenging activity (11). The percent inhibition was calculated and expressed as IC_{50}.

Nitric oxide radical scavenging

In brief, *S. apetala* fruit extract was mixed with 0.5 mL of 1 M phosphate buffer saline and 2 mL of 10 mM sodium nitroprusside and then kept at room temperature for 150 minutes. As a positive control, a potassium nitrite solution was employed. Following incubation, 1 mL of 0.33% sulphanilic acid reagent was added to 0.5 mL of the reaction mixture containing nitrite, and the combination was then allowed to stand for 5 minutes to complete the diazotization process. After adding 1 mL of 1% naphthyl ethylene diamine dihydrochloride, the sample was read at 540 nm after 30 minutes (15). The percent inhibition was calculated and expressed as IC_{50}.

Blood sugar regulating action

α-Amylase inhibitory action

After pre-incubation, 0.5 mL of 1% (v/v) starch solution in buffer was added to each tube and incubated at 37°C for 15 minutes. The reaction was terminated with 1 mL 96 mM DNSA (3, 5-dinitrosalicylic acid) reagent, placed in a boiling water bath for 5 minutes, and cooled to room temperature. The absorbance was read at 540 nm after dilution with 2 mL deionized water (22). The percent inhibition was calculated and expressed as IC_{50}.

α-Glucosidase inhibitory action

Para-nitrophenyl-D-glucopyranoside (PNPG) was used as a substrate and α-glucosidase as an enzyme source. In brief, 0.05 mL of 10 mM PNPG was added to various concentrations of *S. apetala* fruit extract (10-1000 µg/mL) in 0.5 mL of 0.1 M phosphate buffer (pH 6.8) before being incubated at 25°C for 10 minutes. After incubation, 0.02 mL of α-glucosidase (0.5 unit/mL) was added. Incubation continued for an additional 5 minutes at 25°C. Finally, 0.3 mL of 50 mM sodium hydroxide solution was added to the tubes, and the absorbance at 410 nm was measured. Finally, 0.3 mL of 50 mM sodium hydroxide was added to the mixture and the absorbance was measured at 410 nm (22,23). The outcome was reported as a percentage of inhibition, and *S. apetala* fruit extract's IC50 values were established.

Statistical analysis

Statistical analysis was carried out using SPSS version (Chicago, IL, USA). Results were presented in a descriptive way and as a mean with standard deviation. *P* values of 0.05 or lower were used to determine statistical significance.

Results

Bioactive compounds

Compared to air-dried fruit, *S. apetala* fruit extract had a yield rate of 19.3%. According to the findings, *S. apetala* fruit extract had a total phenolic content equivalent to 42.84 µg of Gallic acid, and a total flavonoid equivalent to 31.66 µg of Rutin (Table 1). The phenolic acids and flavonoids present as secondary metabolites in *S. apetala* fruit extract were identified and quantified by RP-HPLC (Figure 1). According to the RP-HPLC fingerprint, 13 bioactive and well-known phenolic acids and flavonoids of therapeutic value were present in significant amounts in the *S. apetala* fruit extract (Table 2). The following variations in these

Table 1. Phenolic and flavonoids present in *Sonneratia apetala* fruit extract

	Total phenolic acid (µg GAE/100 µg SA)	Total flavonoids (µg RE/100 µg SA)	Reducing power (µg AAE/100 µg SA)
S. apetala fruit extract	42.84 ± 0.31	31.66 ± 0.08	11.10 ± 2.08

Data are expressed as mean ± standard deviation.

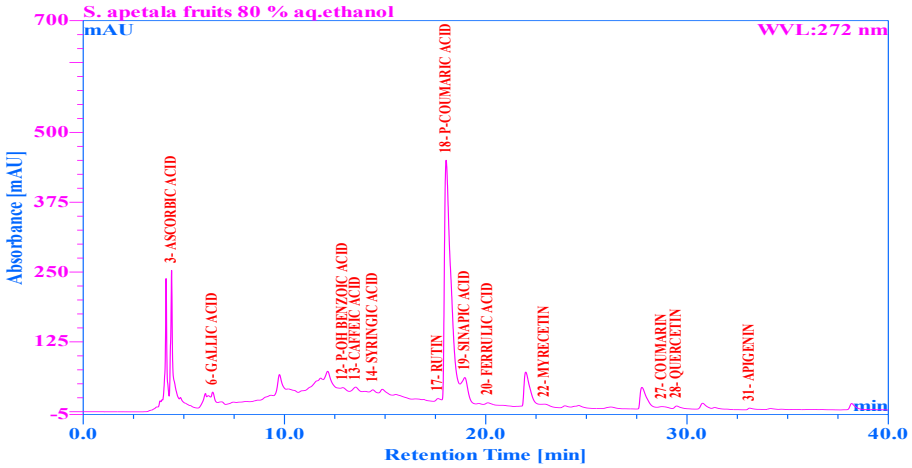

Figure 1. RP-HPLC fingerprint of *Sonneratia apetala* fruits

Table 2. HPLC profiling of *Sonneratia apetala* fruit extract

	µg/mg SA
Ascorbic acid	172.08 ± 0.015
Gallic acid	40.41 ± 0.007
Catechin	20.35 ± 0.012
Caffeic acid	0.64 ± 0.002
Syringic acid	1.82 ± 0.003
Rutin	13.05 ± 0.005
p-Coumaric acid	204.13 ± 0.006
Sinapic acid	5.28 ± 0.005
Ferulic acid	2.18 ± 0.016
Myricetin	12.27 ± 0.008
Coumarin	3.15 ± 0.009
Quercetin	4.32 ± 0.015
Apigenin	0.44 ± 0.001

Data are expressed as mean ± standard deviation.

chemicals were seen by RP-HPLV in *S. apetala* fruit extract p-coumaric acid (204.13 µg/mg) is followed by ascorbic acid (172.08 µg/mg), gallic acid (40.41 µg/mg), catechin (20.35 µg/mg), rutin (13.05 µg/mg), myricetin (12.27 µg/mg), sinapic acid (5.28 µg/mg), quercetin (4.32 µg/mg), coumarin (3.15 µg/mg), ferulic acid (2.18 µg/mg) and syringic acid (1.82 µg/mg). Four water-soluble vitamins were found in substantial amounts in the RP-HPLC of *S. apetala* fruit extract (Figure 2 and Table 3), including vitamin C (173.74 µg/mg), vitamin B2 (222.25 µg/mg), vitamin B5 (7.44 µg/mg), and vitamin B6 (1.15 µg/mg). Mangrove apple was found to contain non-polar bioactive chemicals such benzenepropanoic acid, β-amyrin, and lupeol, according to GC-MS profiling of *S. apetala* fruit extract (Figure 3 and Table 4).

Biological activities

In vitro antioxidant properties of *S. apetala* fruit extract are shown in Table 5. The fruit extract reduced the amount of DPPH radicals (IC_{50}: 672.08 µg/mL), ABTS cation inhibitory action (IC_{50}: 422.36 µg/mL), and nitric oxide radical formation (IC_{50}: 718.15 µg/mL *S. apetala* fruit extract) significantly and dose-dependently. Table 6 depict *S. apetala* fruit extract's ability to block two carbohydrate-splitting enzymes using *in vitro* method: α-amylase and α-glucosidase. The IC_{50} of α-amylase was 12.07 µg/mL, while α-glucosidase was 7.92 µg/mL.

Discussion

The fruits of *S. apetala*, often known as apple mangrove, are mostly consumed as food. According to Hossain et al, *S. apetala* fruits have a 30% carbohydrate content, 10% protein, 3% fat content, 25% fiber, and significant sources of iron and zinc (24). The current study was the first to pinpoint the presence of water-soluble vitamins namely pyridoxine, ascorbic acid, pantothenic acid, and riboflavin in its fruits. The chemical properties of *Sonneratia caseolaris* fruit revealed nutritional components in a recent study (25).

It has been documented that the fruits of *S. alba, S. caseolaris*, and *S. apetala* exhibit antioxidant, antibacterial, anti-diarrheal, and cytotoxic properties. In a recent investigation, it was reported that *S. caseolaris* fruits contain anti-diabetic characteristics (9). The majority of investigations covered *S. caseolaris, S. alba, and S. ovata species* in their various parts. Although S. apetala is the main species found in the Indian Sunderban, the world's biggest mangrove belt, there is relatively little knowledge of this species. In the current study, a thorough examination was conducted to determine the bioactive components of *S. apetala* fruit and its blood sugar-regulating characteristics.

The antioxidant system in mangroves detoxifies and regulates ROS generation, protecting them from the harmful effects of oxidative stress (26). Superoxide dismutase, peroxidase, catalase, peroxidase, and glutathione reductase are the main antioxidant enzymes, while, glutathione, ascorbic acid, tocopherols, thiols, and carotenoids are among the non-enzymatic elements found in mangroves (11). *S. apetala* fruit extract demonstrated strong antioxidant activities in this investigation by

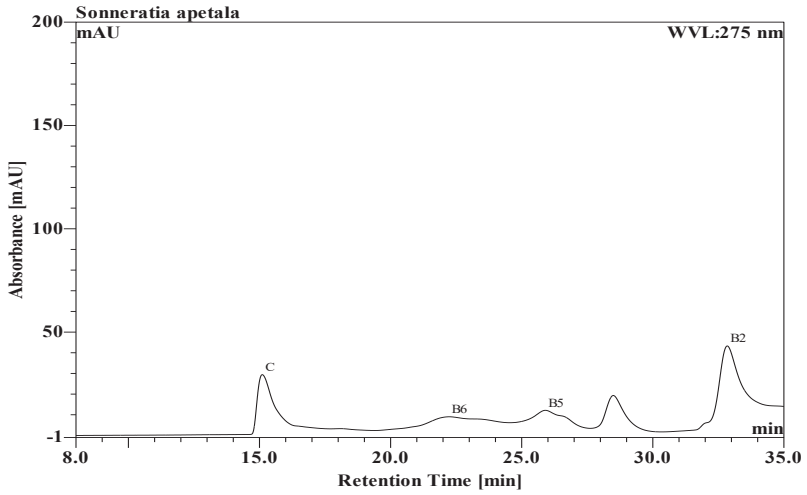

Figure 2. RP-HPLC chromatogram of water-soluble vitamins in of *Sonneratia apetala* fruit extract

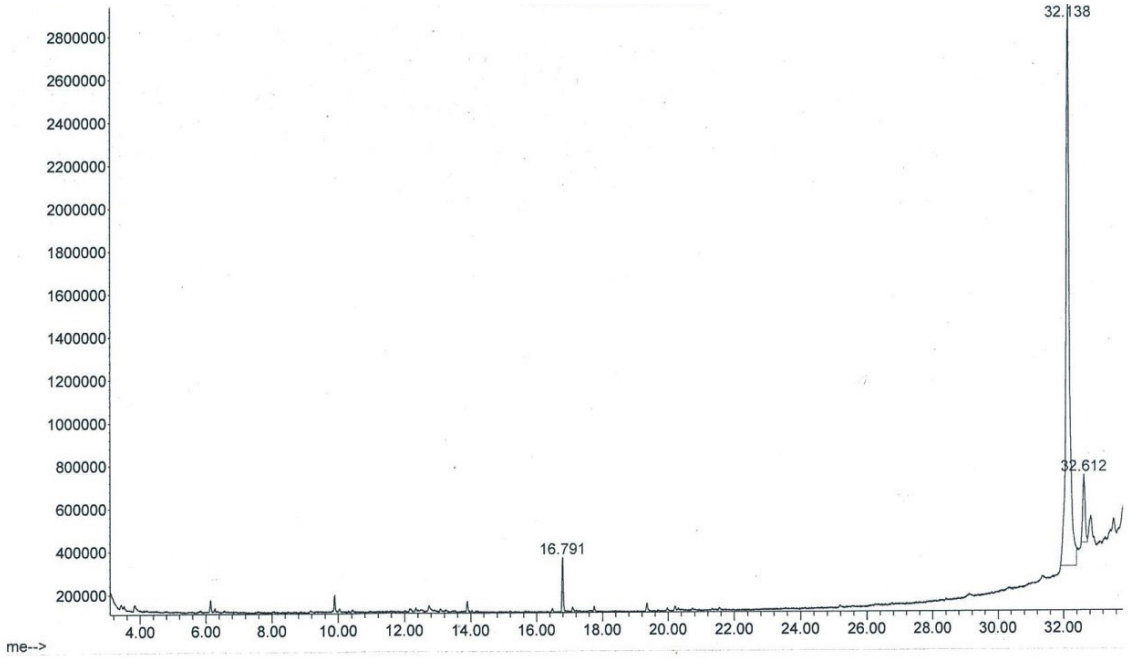

Figure 3. GC-MS chromatogram of *Sonneratia apetala* fruit extract

Table 3. Water-soluble vitamins in *Sonneratia apetala* fruit extract

Vitamins	µg/mg SA
Vitamin C	173.74 ± 0.080
Vitamin B2	222.25 ± 0.058
Vitamin B5	7.44 ± 0.023
Vitamin B6	1.15 ± 0.018

Data are expressed as mean ± standard deviation.

Table 4. GC-MS Profiling of *Sonneratia apetala* fruit extract

Peak	RT (min)	Peak height	Area (%)	Compound
1	16.791	253222	3.045	Benzenepropanoic acid
2	32.138	2622831	89.772	β-amyrin
3	32.612	317982	7.183	Lupeol

scavenging DPPH, ABTS, and nitric oxide radicals. Candidate genes for antioxidant defense capacities have been found in *S. caseolaris* in a prior investigation (27). Serious non-communicable diseases, such as diabetes, are potentially treatable with antioxidants.

According to reports, the chemistry of mangrove plants is the source of many previously known physiologically active chemicals in unique forms (8). The current spectroscopic and chromatographic studies on Indian varieties of *S. apetala* fruit extract found characteristic polyphenolic substances like quercetin, catechin, myricetin, p-coumaric acid, rutin, ferulic acid, sinapic acid, etc. as well as pentacyclic triterpenoids like β-amyrin and lupeol in significant amount (Figure 4). The majority of these components are often utilized in mainstream therapy and are known in most of the countries as dietary antioxidant supplements for health benefits. It is widely known that quercetin plays a role in up-

Table 5. *In vitro* antioxidant activities of *Sonneratia apetala* fruit extract

	IC_{50} (µg/mL SA)
DPPH	672.08 ± 0.166
ABTS	422.36 ± 0.245
Nitric oxide	718.15 ± 0.603

Data are expressed as mean ± standard deviation.

Table 6. *In vitro* anti-diabetic activities of *Sonneratia apetala* fruit extract

	α-Amylase inhibitory activity IC_{50} (µg/mL)	α-Glucosidase inhibitory activity IC_{50} (µg/mL)
S. apetala fruit extract	12.07 ± 0.86	7.92 ± 0.46

Data are expressed as mean ± standard deviation.

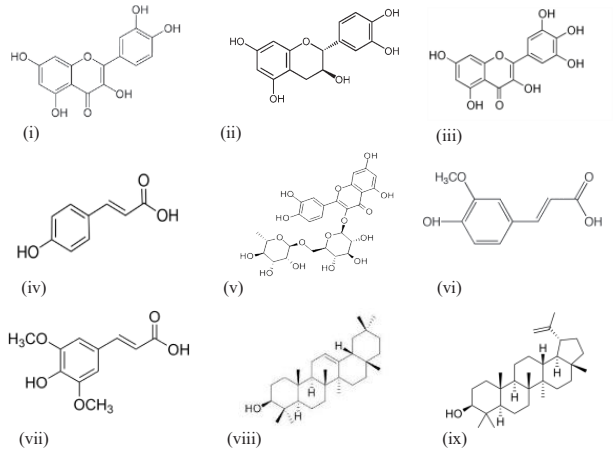

Figure 4. Bioactive compounds in of *Sonneratia apetala* fruit extract. (i) quercetin, (ii) catechin, (iii) myricetin, (iv) p-coumaric acid, (v) rutin, (vi) ferulic acid, (vii) sinapic acid, (viii) β-amyrin, and (ix) lupeol

regulating glucose transport and down-regulating fatty acid metabolism to prevent cellular oxidative stress in diabetes and other pathophysiological conditions (28,29). Additionally, it has been documented that rutin, catechin, and myricetin offer therapeutic benefits, especially for diabetes (30-32). Natural triterpenes like lupeol and β-amyrin are well known. Previous research has described their pharmacological potentials, which include anti-inflammatory, anti-diabetic, cardioprotective, hepatoprotective, and nephroprotective properties (4,33-36). In diabetes, lupeol directly inhibits the three key enzymes protein tyrosine phosphatase 1B, α-amylase, and α-glucosidase (37,38). Currently, *S. apetala* fruit extract showed a substantial potential inhibitory effect on the enzymes α-glucosidase and α-amylase, confirming its blood sugar-lowering effects in diabetes.

Conclusion

Therefore, *S. apetala* fruits not only resist oxidative stress and proinflammatory mediators in diabetes but also may lower blood sugar levels by inhibiting enzymes that split polysaccharides to glucose. Additionally, extensive pharmacokinetic studies could be used to fine-tune the effective dose of *S. apetala* fruits to increase their pharmacological action.

Authors' Contribution

Conceptualization: Avijit Saha, Tapan Seal, Sandip Ghosh, Tapas Kumar Sur.
Data curation: Avijit Saha, Tapan Seal, Tapas Kumar Sur.
Formal analysis: Tapan Seal, Shuvam Saha, Alok K. Hazra, Tapas Kumar Sur.
Funding: Tapan Seal, Shuvam Saha, Sandip Ghosh.
Investigation: Tapan Seal, Shuvam Saha, Alok K. Hazra, Tapas Kumar Sur.
Methodology: Tapan Seal, Alok K. Hazra, Tapas Kumar Sur.
Project administration: Avijit Saha, Tapan Seal, Tapas Kumar Sur.
Resources: Avijit Saha, Tapan Seal, Tapas Kumar Sur.
Supervision: Avijit Saha, Tapan Seal, Tapas Kumar Sur.
Visualization: Avijit Saha, Tapan Seal, Tapas Kumar Sur.
Writing–original draft: Tapan Seal, Tapas Kumar Sur.
Writing–review & editing: Avijit Saha, Shuvam Saha, Alok K. Hazra, Sandip Ghosh, Tapas Kumar Sur.

Competing Interests

The authors declare that there is no conflict of interests.

Ethical Approval

Not Applicable.

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Cite this article as: Saha A, Seal T, Saha S, Hazra AK, Ghosh S, Sur TK. Characteristics constituents with antidiabetic significance from Indian mangrove apples. . Future Nat Prod. 2023;9(1):3-9. doi: 10.34172/fnp.2023.01.