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PHYTOCHEMICALS PROFILE AND IN-VITRO ANTIDIABETIC POTENTIALS OF FRACTIONATED EXTRACTS OF *ENTADA AFRICANA* AND *LEPTADENIA HASTATA*

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Aim: To confirm their use in the management of diabetes and to determine the numerous phytochemicals present that may be connected to the active performance of the plants, the fractionated extracts of *Leptadenia hastata* and *Entada africana* were subjected to an in vitro experiment.

Material and methods: The plant leaves were dried, pulverized with a Sumeet CM/L 2128945 grinder, the particle size was 45.85 μm and extracted with methanol. The crude extracts were fractionated using a 30 \times 8 cm diameter column and 60 g of silica gel 60 F254 grade, using methanol as eluent and fractions were concentrated using a rotary evaporator; the fractionated extracts were run on thin layer Chromatographic plate (TLC) and their retardation factors (RF) were determined. Fractions of similar RF were pulled together and spotted again using TLC plate and the final (RF) were calculated. The crude extracts were quantified for the content of phytochemicals and the phytochemicals present in the fractionated extracts (LH_1 and EA_2) were identified using HPLC-UV detector. The extracts (LH_1 and EA_2) were tested for antidiabetic potentials using α -glucosidase and α -amylase enzymes in an in-vitro antidiabetic assay.

Results: The yields of the fractionated extracts were 10.0 mg (*Leptadenia hastata*) and 11.5.0 mg (*Entada Africana*) and designated as LH_1 and EA_2 , the RF for LH_1 and EA_2 were 0.75 ± 0.01 and 0.77 ± 0.03 respectively. The maximum amount of alkaloid was found in *E. Africana* (14.50 ± 0.25 mg/g), while tannin was not found in *L. Hastata*. In the portion of *L. Hastata* (LH_1), thirteen phytochemicals were discovered and out of these three were alkaloids. Thirteen phytochemicals were found in the *E. Africana* fraction (EA_2), with eight of them being alkaloids and flavonoids. When compared to the usual acarbose, the plants' anti-diabetic properties were superior. EA_2 had EC_{50} of 0.950.17 g/ml (α -amylase) and 0.970.41 g/ml (α -glucosidase), while LH_1 had EC_{50} of 1.00 ± 0.11 g/ml (α -amylase) and 0.90 ± 0.35 g/ml (α -glucosidase). The presence of the detected phytochemicals may be linked to the active qualities of the plants' leaves.

Conclusion: The phytochemical profile of fractionated extracts classified as flavonoids and alkaloids are stated to be antidiabetic agents, and this has proved that the researched plants have antidiabetic potential

Keywords: HPLC-UV detector, phytochemicals, α -glucosidase, α -amylase, acarbose, diabetes

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1. Introduction

The use of traditional plants for the management and treatment of various diseases is as old as ages. The use of local herbs in the management of diabetic Mellitus is a common practice in Ilorin, Kwara State, Nigeria. Nature has offered a plethora of natural sources of traditional remedies that have been utilized as cures for a variety of maladies and disorders for many years. As organic chemistry progressed, synthetic compounds became more popular for pharmacological treatment [1]. Diabetes mellitus is a group of illnesses that are characterized by bouts of hyperglycemia and glucose intolerance caused by a shortage of insulin, faulty insulin action, or both. The etiology and clinical presentation of diabetes mellitus are used to classify the disease. Type 1 diabetes, type 2 diabetes, gestational diabetes, and other kinds of diabetes mellitus are the four categories or classifications of diabetes mellitus [2]. Diabetes mellitus has been identified as the most common endocrine illness, affecting

200 million individuals worldwide (3) and expected to increase to over 366 million by 2030 [3]. [4] had reported that Diabetes mellitus could be categorized into three basic kinds based on the clinical presentation of the disorder: Type I diabetes, Type II diabetes, and gestational diabetes mellitus [5]. Thousands of plants have been claimed to have medicinal properties in Nigeria and are used to treat a variety of ailments [6]. Many of these native medicinal plants are used as spices, food plants, and medicine [7]. According to a World Health Organization (WHO) research, 80 percent of the world's population relies only on medicinal plants for primary health care [8].

E. africana belongs to the Fabaceae family, popularly known as Legumes, which is the world's third-largest seed plant order, with over 600 genera and 12000 species [9]. It is a little tree that grows in the savannah regions of most Sub-Saharan African countries. In most traditional pharmacopeia, this plant is noted

for its vulnerary activity. A decoction of the root or stem bark is used to cleanse wounds, and a powder of the same parts is used topically as a wound healer. [10] also uses fresh root or bark juice to stop bleeding. The application of roots also includes fortifying, diuretic, anti-gonococci, and anti-syphilitic properties [11]. An infusion of leaves or bark is consumed as a tonic in northern Nigeria and Ghana [11]. Other applications include anti-inflammatory [9], analgesic [12], antiproliferative [13], antiviral [14] and hepato-protective [14] and hepato-protective [14, 15].

Due to its nutritional and medicinal characteristics, *Leptadenia hastata* is an edible wild plant that is used as a vegetable and medicine in many parts of Africa. It is a member of the Apocynaceae family and the genus *Leptadenia*. It is a climber with a delicate, gloved stem that's pale white. With creeping latex stems, glabrescent leaves, glomerulus and racemus flowers, and follicular fruits, it is a voluble herb. Local healers in Nigeria boil the leaves of *L. hastata* and drink the resulting liquor to treat gonorrhoea [10]. The plant is also used to treat hypertension, catarrh, and skin problems [10, 16]. This beverage is given to youngsters by the Hausa tribe in Northern Nigeria to relieve stomach aches. In Senegal, the sap or a decoction of the root is used to treat ophthalmia. It is used in Senegal for suckling new-borns with green diarrhoea in combination with other plants. Senegalese healers also use the *L. hastata* for prostate and rheumatism symptoms [17]. Several studies have supported the use of *L. hastata* in

traditional medicine, including the discovery of phytochemical substances with antimicrobial activity [18], anti-diabetic activity [19], wound healing, and anti-inflammatory activity [20].

Aim of research was to confirm their use in the management of diabetes and to determine the numerous phytochemicals present that may be connected to the active performance of the plants, the fractionated extracts of *Leptadenia hastata* and *Entada africana* were subjected to an in vitro experiment.

2. Planning (methodology) of research

The traditional use of these selected plants for the management of diabetes in Ilorin, Kwara State, Nigeria necessitated the selection. In diabetes patients, α -amylase and α -glucosidase break down carbohydrates and raise postprandial glucose levels. Controlling postprandial hyperglycemia and lowering the risk of diabetes can be accomplished by inhibiting the activity of these two enzymes using medicinal plants. Secondary metabolites have been discovered to be responsible for active plants' ability to alleviate diseases. To achieve the goals, a standard procedure for the evaluation of phytochemicals from medicinal plants would be followed (Fig. 1).

Fractionation, antidiabetic assay, qualitative and quantitative phytochemical studies, and HPLC-UV detector for phytochemical identification will be performed on each of the selected plants. The findings of active phytochemicals and inhibitory potentials of fractionated extracts will be used to make conclusions.

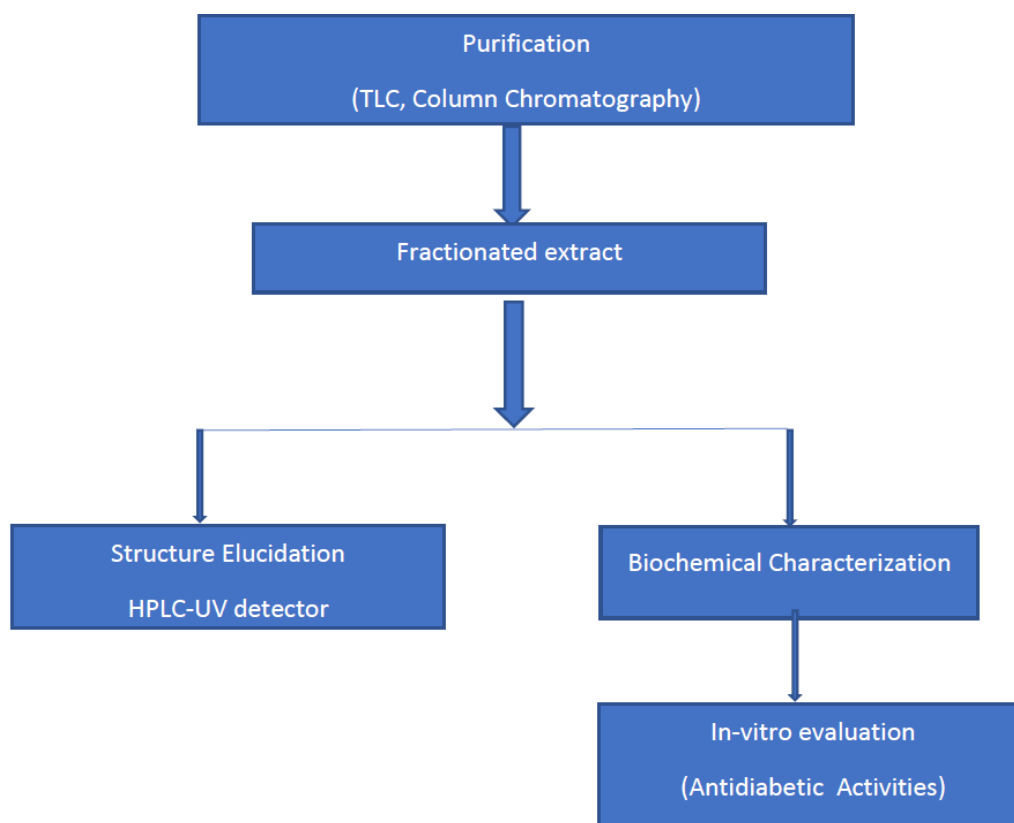


Fig. 1. A summary of the general approaches in extraction, fractionation and characterization of bioactive compounds from plant extract

3. Materials and methods

Sample collection: The plants were collected from Jalala area, university of Ilorin main campus Ilorin, Kwara State, Nigeria on the 10th of March, 2021 and identified and authenticated with voucher herbarium number UILH/001/1068/2021 for *E. africana* and UILH/002/1294/2021 for *L. hastata* in the Department of Plant Biology, University of Ilorin, Nigeria where a voucher specimen was deposited on the 15th March, 2021. The leaves were collected in a polyethylene bag and followed by air drying at room temperature.

Sample preparation: The plant leaves were dried, pulverized with a Sumeet CM/L 2128945 grinder, the particle size was 45.85µm. Powdered sample (200 gram) of *L. hastata* and *E. africana* (200 g) were soaked for five days at room temperature in methanol (600 mL) and filtered using Wattman paper. Methanol was removed from the extract using a rotary evaporator at 45 °C under reduced pressure. The bulked filtrate was concentrated at 40 °C using a water bath and kept in a desiccator for complete dehydration. The crude extracts were later stored at -4 °C until when needed.

Fractionation process: The fractionation exercise using column chromatography was carried out according to the procedure described by [21] with column size (30×8 cm column) and 60g of silica gel 60 F₂₅₄ (Scharlau, 0.06–0.20 mm thickness) without modification.

Thin Layer Chromatography: (TLC silica gel 60 F254 grade of 20×20cm) sigma grade was used. Separations of bands were recorded by calculating their retardation factors and fractions of similar R_f were pulled together as the same.

Phytochemical screening: A small portion of the crude extracts each was subjected to the phytochemical test to identify the active constituents such as alkaloids, flavonoids, phenols, saponins, and tannins according to recommended procedures [22–24].

Phytochemical quantification of crude extracts of *Leptadenia hastata* and *Entada Africana*

Determination of phenols: 500 µL of the extract was transferred to a test tube. 500 µL of the Folin-Ciocalteu solution was added, and 1 mL of sodium carbonate solution and 8 ml of distilled water were also added. The samples remained at room temperature for 30 minutes. Absorbance was measured at 760 nm spectrophotometrically. The assay was performed in triplicate and the total phenolic content was expressed as milligrams of tannic acid equivalents per gram of sample (mg TAE/g) [22].

Estimation of tannins: 500 mg of casein was weighed and transferred into a 25 ml Erlenmeyer flask, 5 ml of the extract and 5 ml of distilled water were added. After two hours the extract was filtered into a 10ml volumetric flask, and its volume was adjusted with distilled water. 500 µL of the extract was transferred to a test tube, 500 µL of the Folin-Ciocalteu solution, 1 mL of sodium carbonate solution, and 8 ml of distilled water were also added. The samples remained at room temperature for 30 minutes. Absorbance was measured at 760 nm spectrophotometrically. The assays were performed in triplicate and total tannins content was expressed as

milligrams of tannic acid equivalents per gram of sample (mg TAE/g) [22].

Quantification of flavonoids: 500 µL of the extracts were transferred to a test tube separately. 500 µL of the acetic acid solution, 2 mL of the pyridine solution, 1 ml of the reagent aluminum chloride solution, and 6 ml of 80 % methanol were added to each tube. The samples remained at room temperature for 30 minutes. Absorbance was measured at 420 nm spectrophotometrically. The test was carried out in triplicate and the flavonoid content was expressed as milligrams of quercetin equivalents per gram of sample (mgQE/g) on a dry weight basis [23].

Estimation of alkaloids: 2.5g each of the sample extract was weighed into a 250 ml beaker and 25 ml of 10 % acetic acid in ethanol was added and covered and allowed to stand for 4hrs separately. This was then filtered, and the extract was concentrated in a water bath to one-quarter of the original volume. Concentrated ammonium hydroxide was added dropwise to the extract until the precipitation is complete. The whole solution was allowed to settle, and the precipitate was collected and washed with dilute ammonium hydroxide and filtered. The residue is the alkaloids that were dried and weighed [22].

Quantification of saponins: The saponin content was analyzed using the existing procedure according to [25] without modification.

Identification of phytochemicals using HPLC-UV detector: The fractionated extracts (LH₁ and EA₂) separately were dissolved in 2.5 ml of HPLC methanol and filtered through a 0.5 micro syringe filter. Then the following chromatographic conditions were employed; Agilent Technologies HPLC 1200, the column used: zorbax eclipses, dimensions: 123, dimension of the column to be used is 125 mm × 4.6 mm.

Antidiabetic Assay

α-Amylase inhibition assay

The α-amylase inhibitory activity was determined according to the method of [26] using hog pancreatic α-amylase (EC 3.2.1.1) prepared with 0.02 M sodium phosphate buffer (pH 6.9 with 0.006 M NaCl) and 1 % starch solution as a substrate. After incubation at 25 °C for 10 min with the sample, the colour was developed by adding 1.0 mL of DNSA and further boiled for 5 min. The absorbance was measured at 540 nm, and the α-amylase activity was subsequently calculated.

$$\% \text{ Inhibition} = \frac{\text{Abs ref} - \text{Abs sample}}{\text{Abs ref}} \times 100,$$

where Abs ref – Absorbance of Reference; Abs sample – Absorbance of Sample.

α-Glucosidase inhibition assay

100 µL of the sample was incubated with 100 µL 1.0 unit/ml α-glucosidase solution in 0.1M phosphate buffer (Ph 6.8) at 37°C for 15 minutes. Thereafter, nitrophenyl-α-D-glucopyranoside solution (50 µL, 5 mM) in 0.1 M phosphate buffer (Ph 6.8) was added and the solution was incubated at 37 °C for 20 minutes. The absorbance of the released p-nitrophenol was measured at 405 nm and the inhibitory activity was calculated.

α -Glucosidase inhibitory assay followed the method of [26] using 100 μ L of α -glucosidase solution and 50 μ L of 5 mM p-nitrophenyl- α -D-glucopyranoside solution in 0.1 M phosphate buffer (pH 6.9) as substrate. The absorbance of the resulted mixture was taken at 405 nm. The α -glucosidase inhibitory activity was calculated.

$$\% \text{ Inhibition} = \frac{\text{Absorbance of reference} - \text{Absorbance of sample}}{\text{Absorbance of reference}} \times 100.$$

Data analysis

The EC₅₀ (extract concentration causing 50 % enzyme inhibition/antioxidant activity) was performed using nonlinear regression analysis on Microsoft Excel 2013 version.

4. Results and discussion

Retardation Factor

Table 1 shows the results of the fractionation exercise using column chromatography, five fractions were collected for each fractionation process, spotting was done using a paper TLC plate, the mobile phase was methanol and the stationary phase was TLC plate. Results of the retardation factor were calculated and values that were the same were pulled together, re-spotted on the TLC plate and the final RF were determined as presented in the Table 1.

Table 1

Results of retardation factors of fractionated extracts of *L. hastata* and *E. Africana*

Sample	Retardation factor (Rf)
<i>L. hastata</i> (LH ₁) and	0.75±0.01
<i>E. Africana</i> (EA ₂)	0.77±0.03

Phytochemicals

Table 2 illustrates the presence of several phytochemicals in fractionated extracts at various concentrations. Alkaloid concentrations are highest in *E. Africana* and found in higher concentrations in *L. Hastata*. Table 3 shows that *E. Africana* had the highest alkaloid content (14.50±0.2 mg/g) and flavonoid content (7.06±0.13 mg/g).

The alkaloid content of *L. Hastata* was 4.11±0.855 mg/g, whereas the flavonoid content was 3.53±0.24 mg/g. The existence of several phytochemicals such as alkaloid, flavonoid, saponin, tannins, and phenol has been connected to the therapeutic potential of plants. Alkaloid has been shown to have anti-diabetic properties and to have a variety of medicinal properties [27–31]. Flavonoids are plentiful in plants, and various studies have shown that they have anti-diabetic qualities, including not only the well-known anti-diabetic and hypoglycaemic properties, but also activity in the treatment of diabetic issues, according to [32]. In addition, when the fraction of *L. Hastata* (LH₁) was subjected to spectroscopic analysis using high-performance liquid chromatography (Fig. 2, 3), sixteen phytochemicals were identified, and the results of phytochemical quantification were used to identify the alkaloid with a concentration of (3.53±0.24 mg/g), and three alkaloids were found out of the sixteen phytochemicals present in the extract, as shown in Tables 4, 5. In addition, thirteen phytochemicals were identified from the chromatogram of *Entada Africana* (EA₂) (Fig. 4, 5), as shown in Table 6, and eight alkaloids and flavonoids were discovered from this group, as shown in Table 7.

Table 2

Results of phytochemical screening of fractionated *Leptadenia Hastata* and *Entada Africana* extracts

Sample	Alkaloid	Flavonoid	Saponin	Tannins
<i>Leptadenia Hastata</i>	++	+	+	-
<i>Entada Africana</i>	+++	++	++	+

Table 3

Showing the results of phytochemical quantification

Sample	Alkaloid (mg/g)	Flavonoid (mg/g)	Saponin (mg/g)	Tannins (mg/g)
<i>Leptadenia Hastata</i>	4.11±0.85	3.53±0.24	1.31±0.08	ND
<i>Entada Africana</i>	14.50±0.25	7.06±0.13	1.77±0.14	0.14±0.01

Note: – ND=Not detected

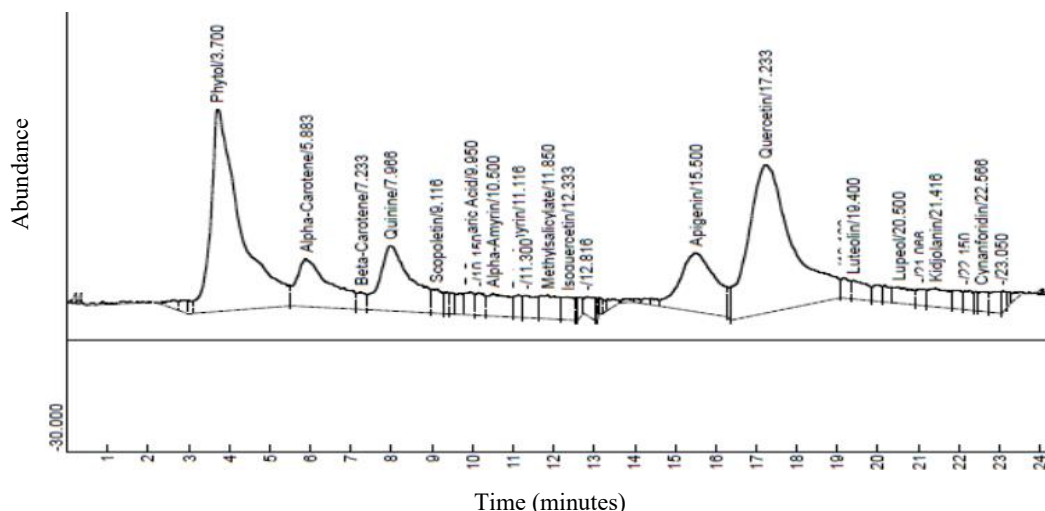


Fig. 2. Chromatogram of phytochemicals in a fractionated extract of *Leptadenia Hastata*

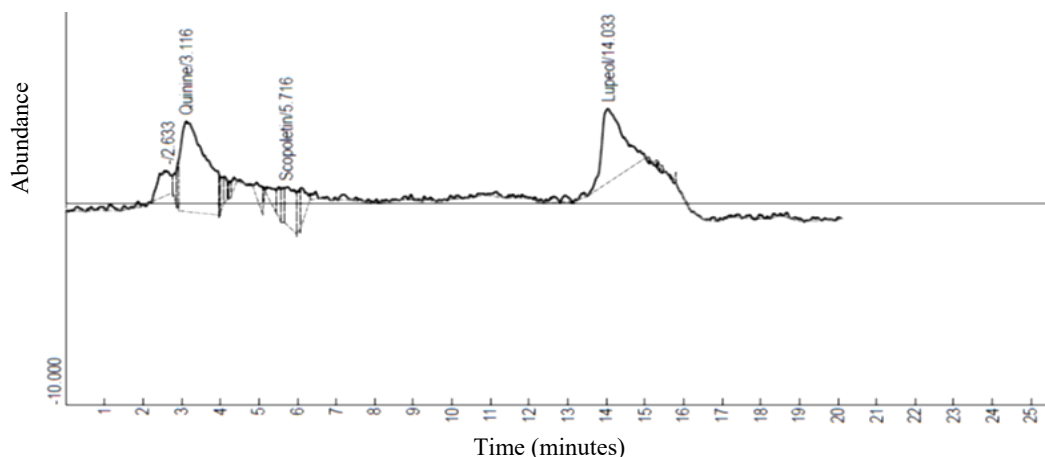


Fig. 3. A chromatogram of Alkaloids in fractionated *Leptadenia Hastata* extract

Table 4

Identified phytochemicals present in fractionated *Leptadenia Hastata* extract

Compound	Retention time (minutes)
Phytol	3.700
Alpha-Carotene	5.883
Beta-Carotene	7.233
Quinine	7.966
Scopoletin	9.116
P-Coumaric Acid	9.950
Alpha-Amyrin	10.500
Beta-Amyrin	11.116
Methylsalicylate	11.850
Isoquercetin	12.333
Apigenin	15.500
Quercetin	17.233
Luteolin	19.400
Lupeol	20.500
Kidjolanin	21.416
Cyanforidin	22.566

Table 5

Identified Alkaloids in the chromatogram of *Leptadenia Hastata*

Compound	Retention time (minutes)
Quinine	3.116
Scopoletin	5.716
Lupeol	14.033

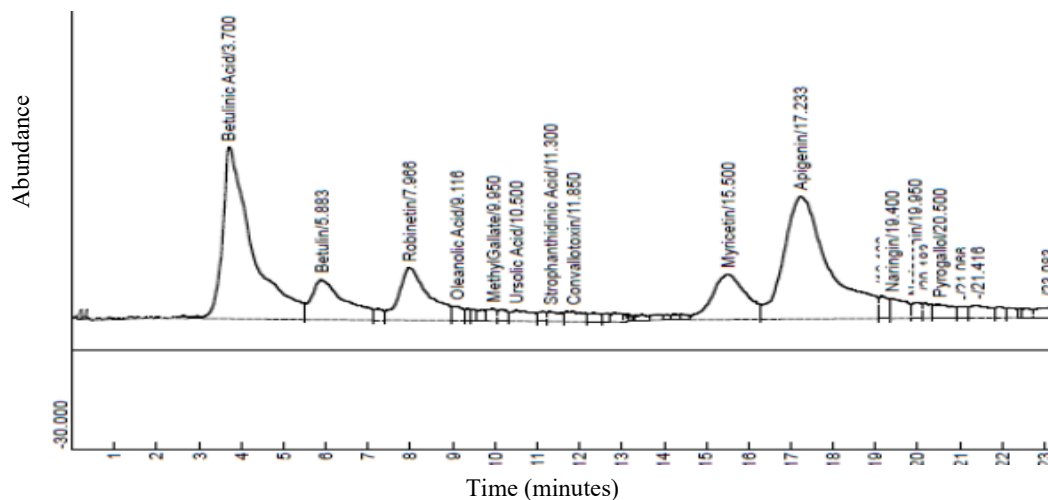


Fig. 4. Chromatogram of phytochemicals in fractionated extract *Entada Africana*

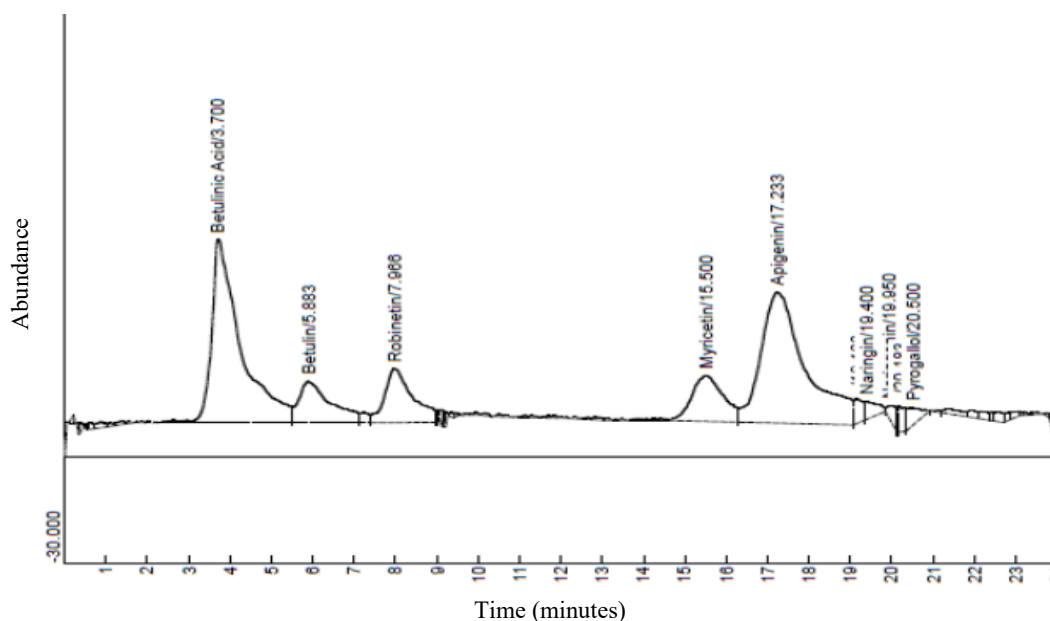


Fig. 5. Chromatogram of alkaloids and flavonoids in fractionated extract *Entada Africana*

Table 6
Identified phytochemicals in the chromatogram of fractionated extract *Entada Africana*

Compound	Retention time (minutes)
Betulinic Acid	3.700
Betulin	5.883
Robinetin	7.966
Oleanolic Acid	9.116
Methyl Gallate	9.950
Ursolic Acid	10.500
Strophanthidinic Acid	11.300
Convallotoxin	11.850
Myricetin	15.500
Apigenin	17.233
Naringin	19.400
Naringenin	19.950
Pyrogallol	20.500

Table 7
Identified alkaloids and flavonoids in fractionated extract *Entada Africana*

Compound	Retention time (minutes)
Betulinic Acid	3.700
Betulin	5.883
Robinetin	7.966
Myricetin	15.500
Apigenin	17.233
Naringin	19.400
Naringenin	19.950
Pyrogallol	20.500

Antidiabetic potentials

The importance and interest placed on medicinal plants in the drive to display their antidiabetic properties have been reported by [33]. Plants have also been revealed to be a source of bioactive chemicals that have been linked to anti-diabetic characteristics. Rural communities in poor nations like Nigeria have been highlighted as having a high reliance on traditional sources of medicine [34]. Some medicinal plants have lately been found to be helpful in the treatment of diabetes in various parts of the world, and they have been used in antidiabetic and antihyperlipidemic treatments. Plants' ability to restore pancreatic tissue function by enhancing insulin secretion, limiting glucose absorption in the intestine, or enabling metabolites in insulin-dependent individuals is central to their antihyperglycemic properties (34). From the result of Table 8, the antidiabetic potential of *E. Africana* ($EC_{50}=0.95\pm0.17 \mu\text{g/ml}$) was better than that of *L. Hastata* ($EC_{50}=1.00\pm0.11 \mu\text{g/ml}$) and these results were performed better than the standard acarbose ($1.10\pm0.15 \mu\text{g/ml}$) when tested against α -amylase. Further, the results of the two extracts were better than that of a standard drug (Acarbose $1.07\pm0.23 \mu\text{g/ml}$) when screened against the α -glucosidase enzyme.

Table 8
The EC_{50} of α -glucosidase and α -amylase

Sample	EC_{50} ($\mu\text{g/ml}$)	
	α -amylase	α -glucosidase
<i>Leptadenia Hastata</i>	1.00 ± 0.11	0.90 ± 0.35
<i>Entada Africana</i>	0.95 ± 0.17	0.97 ± 0.41
Acarbose	1.10 ± 0.15	1.07 ± 0.23

4. Discussion

According to [35], approximately 80-85 percent of the population in both developed and developing

countries rely on traditional medicine for their primary health care needs, with most of these people engaging in traditional therapy of plant extracts or active principles. According to [36], a variety of traditional plants are used to cure diabetes all around the world. Furthermore, the relevance and enormous benefits of using medicinal herbs existed long before insulin was discovered [37]. The anti-diabetic properties of the fractionated extracts from *L. Hastata* and *E. Africana* could be linked to the presence of phytochemicals such as alkaloids and flavonoids, which have already been found in the extracts. To back up this claim, [38] had identified Betulinic acid (BA) in the extract of *Entada Africana* as an antidiabetic agent. [38] also identified BA as a prospective therapeutic agent for diabetes by activating AMPK, like metformin. BA also improved mouse endurance capacity, implying that it has effects on metabolic control in addition to its anti-diabetic properties [38]. Apigenin, a flavonoid discovered in extracts of *L. Hastata* and *E. Africana*, has also been identified as an α -amylase suppressor based on its action on carbohydrate-binding areas. Inhibition of the α -amylase may occur via direct blockage of the active center at several sub-sites of the enzyme and also prevent hyperglycemia, according to [39]. [40] had reported that other chemicals shown to have anti-diabetic properties, such as Luteolin, which was discovered in the fractionated extract of *L. Hastata* and is useful in the treatment of type 2 diabetes mellitus. Luteolin's anti-diabetic properties are mediated via stabilizing blood glucose levels and enhancing insulin sensitivity in body cells [40].

Research limitations. The isolation of the identified phytochemicals could have been done if there is availability of preparative HPLC and characterization of the isolated compound could have been achieved with the use of NMR and mass spectrophotometer if available.

Prospects for further research. Further fractionation could be done to isolate the phytochemicals with anti-diabetic properties.

6. Conclusion

The phytochemical profile of fractionated extracts classified as flavonoids and alkaloids are stated to be antidiabetic agents, and this has proved that the researched plants have antidiabetic potential.

The α -glucosidase and α -amylase inhibitory potentials of the examined plants have given scientific validity to the traditional usage of the plants for the management of T2D in Kwara state, Nigeria, according to the findings. Scholars have also discovered that bioactive chemicals classed as alkaloids and flavonoids, such as luteolin, betulinic acid, and lupeol, are anti-diabetic drugs. It may be stated that the plants studied are worthy of being used in the therapy of diabetes mellitus since they contain a diverse range of phytochemicals.

Conflict of interest

The authors declare that they have no conflicts of interest.

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