Antioxidant, antidiabetic and antifungal activities of leaf and bark ethanol extracts of *Mangifera indica* and their antagonistic biochemical effects

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Abstract. Mango (*Mangifera indica* L.), a member of the Anacardiaceae family, is one of the most economically significant tropical fruit crops worldwide. Both mango leaves and bark have been traditionally used for their medicinal properties. Locally, individuals tend to combine different parts of medicinal plants in an attempt to increase their therapeutic potency; however, the adverse effects of such combinations are mostly unreported. The present study investigated the biochemical activities and phyto-constituents of ethanol extracts from the leaves and bark of *Mangifera indica* individually and in combination. The antioxidant properties of these extracts were evaluated using various assays, including 2,2-diphenyl-l-picrylhydrazyl, 2,2'-azinobis(3-ethylbenzothiazoline-6-sulphonic acid radical scavenging assays, ferric reducing antioxidant power assay and total antioxidant activity assay along with the analysis of total phenolic and flavonoid contents. The anti-diabetic activity was evaluated through *in vitro* assays of α-glucosidase and α-amylase inhibition and antifungal properties were assessed against the fungal pathogen, *Fusarium solani*. Gas chromatography-mass spectrometry analysis revealed numerous bioactive compounds, such as phenols, sesquiterpenes, terpenoids, fatty acids and esters. The results demonstrated marked antioxidant, anti-diabetic and antifungal activities which were highest in the bark extract. However, combining the bark with leaf extract of *Mangifera indica* was antagonistic as the biochemical activities were significantly reduced.

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Introduction

In low-income countries around the globe, the reliance on medicinal plants for the prevention and treatment of several ailments is very high. Several reports have shown the potential of some medicinal plants in the treatment of illness linked to oxidative stress and inflammation. An imbalance between oxidants and antioxidants, which results in stress, arises due to the increasing formation of highly reactive radicals, which outpaces the antioxidant protective mechanism, causing the harmful consequences of highly reactive ions (1). Antioxidants are substances that balance off the production of reactive oxygen species (ROS), reducing the levels of oxidative stress (2). Superoxide (O_2), peroxyl (ROO), hydroxyl (OH), hydrogen peroxide (H_2O_2) and other small molecules formed from oxygen are examples of ROS, which are energetic and reactive small molecules (3). Globally, the occurrence of diabetes mellitus (DM) is increasing due to exponential growth (4). Oxidative stress is a key mechanism in the development of diabetic issues (5). Any plant, including those with edible fruits, that has chemicals in one or more of its organs that have medicinal value or that serve as building blocks for the creation of effective medications is considered medicinal. One such plant with edible fruits is *Mangifera indica L.* (*M. indica*) popularly known as mango, which belongs to the Anacardiaceae family. It is one of the most economically significant tropical fruit crops worldwide and a crucial traditional crop (6). Various parts of the mango tree, including the leaves and bark, are traditionally used in folk medicine to treat a variety of ailments. Mango leaves (MLs) have been reported to contain the following minerals: Calcium, magnesium, iron, sodium, potassium, phosphorus, nitrogen and some vitamins. Protein is a significant biomolecule also found in mango leaves. Traditionally, ML extracts have been used in the treatment of a variety of illnesses, including diabetes, syphilis, renal disease, bronchitis, diarrhea, asthma, scabies, respiratory issues and urinary disorders (7,8).

The phytochemicals found in ML extracts have the potential to exhibit a wide range of biological and pharmacological properties that inhibit inflammatory, tumor, allergy, oxidizing agents and, diabetes, among others (9). MLs have been widely touted as an effective ethnomedicine against

DM. Inhibiting the enzymes α-amylase and α-glucosidase, which control postprandial glucose absorption, is one of the most efficient methods for treating DM (10). According to previous research, phenolics and flavonoids included in MLs provide them with the ability to function as antioxidants (11). MLs contain phenolic compounds, such as flavonoids and polyphenols. These compounds function as potent antioxidants by scavenging free radicals, which are highly reactive molecules that can cause cellular damage. The phenolic content in MLs contributes significantly to their antioxidant capacity. Specific flavonoids, such as quercetin, and carotenoids such as β-carotene found in MLs contribute to their antioxidant properties. These compounds have been found to be associated with various health benefits, including antioxidant and anti-inflammatory effects. MLs may contain enzymatic antioxidants, such as superoxide dismutase and catalase. These enzymes play a role in the detoxification of ROS, contributing to the overall antioxidant defense system. The reducing power of MLs is indicative of their ability to donate electrons and reduce oxidized molecules. ML extracts may have antibacterial qualities against a range of microorganisms, such as fungi and bacteria, according to several studies. *M. indica* leaves contain phenolic compounds including terpenes and terpenoids, as well as antinutrients, such as saponins and glycosides as the main phytochemicals that have an antibacterial effect (12).

Traditionally, mango bark (MB) extract has been used in the treatment of a variety of illnesses, including anemia, scabies, skin infections, diabetes, menorrhagia, diarrhea and syphilis (13). MB extract has been shown to exhibit antioxidant activity (14,15). It is considered to have therapeutic qualities, such as antibacterial and anti-inflammatory actions (16). MB extracts have been used traditionally in medicine to treat infections, reduce inflammation and speed up the healing of wounds. Of note, in the bid to increase the therapeutic potency of the mango plant, the leaves and bark are often combined locally to achieve potent health effects. To the best of our knowledge, the present study is one of the first of its kind to report a decline in biochemical activity as a result of the antagonistic nature of combining the bark and leave extracts from *M. indica*.

Materials and methods

Chemicals. The reagents used in the present study were of laboratory grade for analyses. Ethanol, 2,2-diphenyl-l-picrylhydrazyl (DPPH), quercetin, gallic acid (GA), aluminum chloride, sulphuric acid, ammonium molybdate, sodium phosphate, 2,4,6-tris(2-pyridyl)-s-triazine, 2,2'-azinobis(3-ethylbenzothiazoline-6-sulphonic acid (ABTS), NaOH, 3,5-dinitrosalicyclic acid reagent and others, were purchased from MilliporeSigma.

Sample collection. *M. indica* (mango leaves and bark) were collected from Moniya in Akinyele Local Government Area, Ibadan, Oyo State, South-west Nigeria. Plant samples were identified at the herbarium at the University of Ibadan, and a voucher number of 23335 was allocated. The collected samples were rinsed thoroughly with pre-distilled water. The leaves and barks were air-dried at room temperature for 21 days. The dried leaves and barks were then ground using an electric blender and they were stored in foil paper and sealed with a paper tape after weighing.

Test organism. For the present study, *Fusarium solani* was used. The fungi were isolated from a soil sample and obtained from the National Institute for Horticultural Research (NIHORT), Ibadan, Oyo State, Nigeria.

Preparation of M. indica leaf and bark extracts. Extraction was performed following the method described in the study by Karigidi *et al* (17), with slight modifications. The mango leaves and bark were pulverized using a blender and a total of 183 g mango leaf powder and 176.7 g mango bark powder were macerated each in 1.8 liters of ethanol in various containers for 72 h with stirring at intervals. The mixture was then filtered using a muslin cloth to separate the ethanol extract from the solid plant material. The filtered ethanol extract was transferred into a clean container and the extract was concentrated by evaporating the ethanol using a rotary evaporator (RE-52A), supplied by Scitek Global Co., Ltd. at a reduced temperature of 40˚C to obtain the ML and MB (MB) extracts. Equal quantities of leaf and bark extracts were mixed to obtain the combined extract (MBML).

Preparation of stock solution. The stock solutions of ML and MB extracts were prepared separately by dissolving 15 mg of each extract in 15 ml ethanol (equivalent to 1 mg/ml).

Phytochemical and antioxidant analysis

Total phenolic content (TPC). The TPC of the ethanol extracts of *M. indica* leaf and bark, independently and in combination, was obtained spectrophotometrically (18) using a UV Visible Spectrophotometer supplied by Scitek Global Co., Ltd., British standard (752N). Each extract (1 ml) was added to 1 ml of 10% Folin-Ciocalteu phenol reagent supplied by MilliporeSigma, followed by 10 ml of 7% Na_2CO_3 solution supplied by MilliporeSigma, after 3 min. Subsequently, 5 ml pre-distilled water were added and thoroughly mixed. The product was kept in a dark cupboard for 1 h and 30 min. The absorbance reading was taken using UV Visible Spectrophotometer by Scitek Global Co., Ltd. (752N) at 750 nm. TPC was evaluated using a standard GA plot and expressed in μg of GA equivalent.

Total flavonoid content (TFC). The TFC was obtained spectrophotometrically following the procedure described in the study by Zhisten *et al* (19) and using the modification described in the study by Talukdar (20). A total of 1 ml of 2% ethanolic $AlCl_3$ solution was mixed with 1 ml of each extract. After leaving the mixture for 45 min on a laboratory bench, the absorbance reading was taken using a UV Visible Spectrophotometer by Scitek Global Co., Ltd. (752N) at 420 nm. The standard used was quercetin and the TFC was evaluated from the standard plot and expressed as the quercetin equivalent in μg/mg.

Total antioxidant capacity (TAC). The TAC of each extract was obtained using phosphomolybdate (21) supplied by MilliporeSigma. A total of 0.5 ml of each extract was added to 4 ml reagent (0.6 M sulphuric acid, 28 Mm sodium phosphate and 4 mM ammonium molybdate). The product formed was shaken together and heated (95˚C) for 90 min. The mixtures formed with each extract were allowed to cool and absorbance

reading was taken using UV Visible Spectrophotometer by Scitek Global Co., Ltd. (752N) at 765 nm. The TAC value was obtained from the ascorbic acid standard plot and expressed as its equivalent.

DPPH radical scavenging activity. This assay was estimated following the procedure described in the study by Gyamfi *et al* (22). A total of 1 ml of the extracts (0.1-0.5 mg/ml) was added to 4.0 ml DPPH (30 mg/l prepared in methanol). All samples were thoroughly mixed and left for 35 min; the absorbance was then measured using UV Visible Spectrophotometer by Scitek Global Co., Ltd. (752N) at 520 nm. Ascorbic acid (15 mg/15 ml) was the standard solution, while the DPPH alone without extract was the control.

Ferric reducing antioxidant power (FRAP) assay. FRAP assay was performed using a previously modified method (23). Acetate buffer (300 mmol/l), TPTZ (10 mmol/l) and $FeCl_3 \cdot 6H_2O$ (20 mmol/l) were mixed at a ratio of 10:1:1 (v/v/v) to prepare the FRAP reagent. After pre-heating at 37˚C, each of the extracts and FRAP reagent was added to a 96-well plate and incubated in the dark at 37˚C for 10 min. The absorbance was recorded at 593 nm using an Epoch2 microplate reader supplied by Thermo Fisher Scientific, Inc.

ABTS free radical scavenging activity. The ABTS mopping activity was carried out following the procedure described in the study by Re *et al* (24). The stock solution was formed from a mixture of ABTS aqueous solution (7 mM) with a 2.45 mM aqueous solution of potassium persulfate in equal amounts; the product obtained was made to stand in an unlit cupboard for twelve to sixteen hours. Subsequently, ABTS product formed was added to 1 ml of each extract at various concentrations (0.5 to 5 mg/ml). The following step was to incubate at room temperature in a dark space for ~10 min. For the control, 2 ml ABTS product were added to 1 ml pre-distilled water. The absorbance reading was taken using UV Visible Spectrophotometer by Scitek Global Co., Ltd. (752N) at 743 nm. Trolox was the standard used. The procedure was repeated to obtain triplicate values. The percentage ABTS scavenged was calculated as percentage inhibition: I%=[(Ao-As)/Ao] x100, where Ao represents the absorbance value of the control and As represents the absorbance value of the extract.

Antidiabetic activity

α-amylase inhibition experiment. The inhibition experiment against α-amylase was carried out using the dinitrosalicylic acid (DNS) method (25). Briefly, 1 ml of the extract (50, 100, or 200 μg/ml) and acarbose (100 μg/ml) was first incubated with 1 ml α-amylase for 30 min prior to the addition of 1% w/v of 1 ml of starch solution. The product formed was then incubated at 37˚C for 10 min. The reaction was terminated by the addition of 1 ml DNS reagent, supplied by MilliporeSigma (12.0 g of sodium potassium tartrate tetrahydrate in 8 ml of 2 M NaOH and 96 mM 3,5-dinitrosalicylic acid solution). This was followed by heating in a boiling water bath for 5 min. The control was prepared without the extract, and the blank was without α-amylase. The absorbance was measured using UV Visible Spectrophotometer by Scitek Global Co., Ltd. (752N) at 540 nm. Acarbose was used as a reference. The inhibition was calculated as follows: Inhibition (%) formula=ODC-OBC/ODC x100, where ODC represents the absorbance of enzyme-substrate reaction with 30% DMSO serving as the control, while ODB represents the absorbance of enzyme-substrate with plant sample.

α-glucosidase inhibition experiment. The α-glucosidase enzyme inhibitory activity was determined following the method described in the study by Fouotsa *et al* (26). The α-glucosidase was first mixed with 500 μg/ml extract in 100 mM phosphate-buffered saline (pH 6.8). Subsequently, 0.7 mM 4-nitrophenyl-α-D-glucopyranoside (pNPG) supplied by MilliporeSigma in phosphate-buffered saline was added as a substrate. This reaction mixture was incubated in a 96-well microplate at 37˚C for 15 min. The α-glucosidase activity was determined by measuring the p-nitrophenol release from the hydrolysis of pNPG at 405 nm in a microplate with Gen5 software supplied by BioTek Instruments. Acarbose was used as the standard compound for this assay. The percentage of α-glucosidase inhibitory activity was calculated as follows: % inhibition=Ao-At÷Ao x100, where Ao is the absorbance of enzyme-substrate reaction with 30% DMSO and At is the absorbance of enzyme substrate with plant extract.

Antifungal assay. Antifungal assay of the extracts was performed using Mueller Hinton agar (MHA) plates supplied by MilliporeSigma, by agar well diffusion (27). *Fusarium solani* was inoculated in Muller Hinton broth (MHB) supplied by MilliporeSigma and incubated at 37˚C to adjust the turbidity to 0.5 McFarland standards giving a final inoculum of $1.5x10^8$ CFU/ml. The MHA plates were cultured with the above maintained microbial inoculum. Extracts of 50 mg/ml concentration were prepared in 50% DMSO. A total of five wells of 6 mm were bored in the cultured lawn media in a sterile cork borer (6 mm). The wells contained 50 μl plant extract each with the positive control (tioconzole, 50 mg/ml) and negative control (50% DMSO). Diffusion occurred for ~15 min at room temperature and incubation for 18-24 h at 37˚C. Plates were observed to form a clear zone of inhibition (ZoI) around the well and measurements were taken in mm afterwards.

Determination of MIC and MBC. For the determination of MIC and MBC, the broth microdilution technique was used (28). For this purpose, 2-fold serial dilutions of tbe extracts were prepared directly in sterile 96-well microdilution plates with flat bottom wells containing MHB to obtain various concentrations. The bacterial inoculum was added at a final concentration of 10^6 CFU/ml by diluting 1:100 the 0.5 McFarland turbidity culture in MHB. Finally, 5 μl bacteria were added to the wells apart from those of the negative control. Tioconazole was used as a positive control. The plate was covered with a sterile lid and incubated for 24 h at 37˚C. Resazurin (0.003%) was added to each well of the microtiter plate and was incubated at 37˚C for 3-4 h. The wells showing bacterial growth exhibited a pink color; however, the wells without bacterial growth remained blue. The lowest concentration of the extract that completely inhibited bacterial growth was taken as the MIC. The MBC was also determined with incubation for 18 h at 37˚C after streaking well content on nutrient agar plates.

Gas chromatography mass spectroscopy (GC-MS). GC-MS was carried out as previously described by Sermakkani and Thangapandian (29). Identification of the extracts was

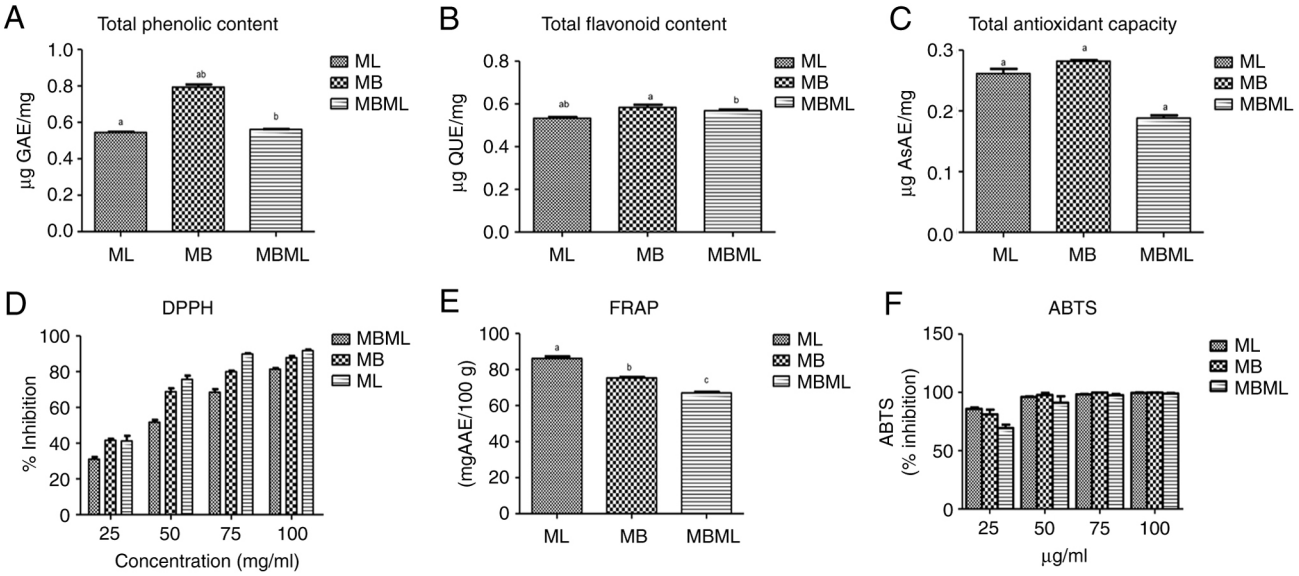

Figure 1. Phytochemicals and antioxidant activities of ethanol extracts of *Mangifera indica* leaf, bark and the combined leaf and bark extracts. (A) Total phenolic content, (B) total flavonoid content, (C) total antioxidant capacity, (D) DPPH scavenging activity, (E) FRAP, and (F) ABTS. Values are presented as the mean ± standard deviation of triplicate readings, n=3. Bars with the same superscript letter indicate significant differences (P<0.05). ML, *Mangifera indica* leaf; MB, *Mangifera indica* bark; MBML, *Mangifera indica* leaf and bark combination; DPPH, 2,2-diphenyl-l-picrylhydrazyl; FRAP, ferric reducing antioxidant power; ABTS, 2,2'-azinobis(3-ethylbenzothiazoline-6-sulphonic acid.

determined by their molecular structure and the value of their weight. The spectral peaks obtained were compared with mass spectra database of National Institute of Standards and Technology.

Statistical analyses. Data analyses were performed using one-way analysis of variance (ANOVA) with the least significant difference using Tukey's post hoc test. Values are presented as the mean ± SD (triplicate readings). A value of P<0.05 was considered to indicate a statistically significant difference.

Results

Yield of ethanol extracts. The dry weight of *M. indica* leaves prior to extraction was 183.04 g and the final weight after extraction was 84.4 g. The percentage yield of *M. indica* leaves was 46.15%. The dry weight of *M. indica* bark was 176.71 g and the final weight after extraction was 19.22 g. The percentage yield of *M. indica* bark was 10.88%.

Antioxidant activities

TPC. The TPC present in the ethanol extracts of *M. indica* leaves (ML) and bark (MB) and a mixture of *Mangifera indica* leaves and bark (MBML) is illustrate din Fig. 1A. The bark extract exhibited the highest phenolic content (0.79±0.015) followed by the leaf extract (0.54±0.004) and the extract combination (0.56±0.002). The result of the bark extract was significantly (P<0.05) higher than the other extracts.

TFC. The TFC of the ethanol extracts ML, MB, and MBML is presented in Fig. 1B. The MB extract exhibited the highest flavonoid presence (0.58±0.013), followed by MBML (0.57±0.006) and ML (0.53±0.006). The TFC of ML was significantly lower (P<0.05) than that of MB and MBML; the difference between MB and MBML was not significant.

TAC. As demonstrated in Fig. 1C, the ML and MB extracts had a high antioxidant potential. The TAC of the ethanol extract of *M. indica* bark (0.28±0.002) was higher than that of the ethanol extracts of the mixture of *M. indica* leaf and bark extract (0.19±0.005) and *M. indica* leaf extract (0.26±0.008). The TAC of MB and ML was significantly higher (P<0.05) than that of MBML, while that of MB was significantly higher (P<0.05) than that of ML

DPPH radical scavenging activity. As demonstrated in Fig. 1D, among the three extracts studied, ML had the highest percentage scavenging activity at almost all concentrations (25-100 mg/ml) of the ethanol extract, followed by MB and MBML. This assay indicated that the ML extract exhibited the highest radical scavenging activity, followed by the MB extract and the mixture (MBML). However, the differences were not statistically significant (P>0.05).

FRAP. As presented in Fig. 1E, the ethanol extract of ML had the highest reducing power, which was significantly (P<0.05) higher than the reducing power of the other extracts. However, the FRAP of the MB extract was higher than that of the mixture (MBML), although the difference was not statistically different (P>0.05).

ABTS radical scavenging ability. As illustrated in Fig. 1F, when compared with 25 mg/ml ascorbic acid, ML had the highest antioxidant activity, followed by MB and MBML. At 50 mg/ml, MB had the highest scavenging ability, followed by ML, and then MBML. In addition, at 75 mg/ml, the highest scavenging ability of MB was slightly higher than that of ML, with MBML being the lowest. At 100 mg/ml, the three extracts were only slightly different from one another: ML > MB > MBML. These results suggest that at 25 mg/ml, ML had the highest ability to scavenge the ABTS radical. At 50 mg/ml, MB had the highest ability to scavenge the ABTS radical than ML; this was also observed at 75 mg/ml. At 100 mg/ml, the three extracts had similar

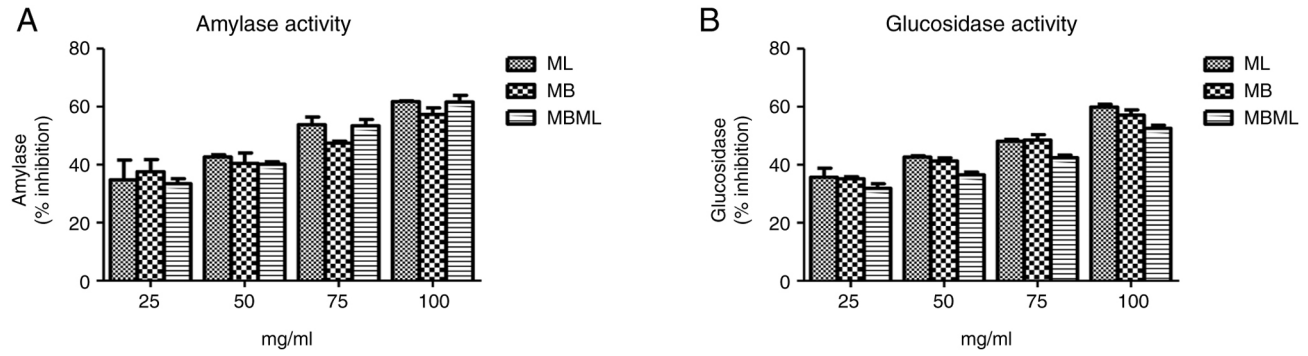

Figure 2. Antidiabetic activity of ethanol extracts of *Mangifera indica* leaf, bark and the combined leaf and bark extracts. (A) α-amylase inhibitory activity, (B) α-glucosidase inhibitory activity. ML, *Mangifera indica* leaf; MB, *Mangifera indica* bark; MBML, *Mangifera indica* leaf and bark combination.

antioxidant activities. However, the differences observed were not statistically different (P>0.05).

Antidiabetic activities

α-amylase inhibitory activity. Based on the results of α-amylase assays presented in Fig. 2A, the ethanol extracts of MB effectively inhibited the enzyme activity compared to the other extracts at 25 mg/ml. At 50 mg/ml, the ML extract was more effective at inhibiting the α-amylase than the MB extract, which was also similar to the result observed at 75 mg/ml. At 100 mg/ml, ML was still effective at inhibiting α-amylase followed by MBML; however, the MB extract had lost some of its inhibitory activity. Therefore, the inhibitory activities of these extracts, ML, MB and MBML against α-amylase vary depending on the concentration. More so, the differences in activity observed were not statistically significant (P>0.05).

α-glucosidase inhibition activity. The result of the assay for the α-glucosidase inhibitory activity of the extracts is illustrated in Fig. 2B. Among the ethanol extracts, the ML extract exhibited the most potent activity, followed by the MB and MBML extracts, against the α-glucosidase enzyme as compared to acarbose at 25, 50 and 100 mg/ml. At 75 mg/ml, the MB extract exhibited the most potent activity, followed by the ML and MBML extracts. However, these differences were not statistically significant (P>0.05).

Antifungal activities. Clear zones of inhibition were observed on plates with a higher concentration of the *M. indica* leaf extract compared to culture plates with lower concentrations. The zone of inhibition was measured in mm, as presented in Table I. The results indicated a concentration-dependent inhibition, where higher concentrations of the extracts led to larger inhibition zones. The concentrations of the *M. indica* leaf extract were 0.25, 12.5, 25, 50 and 100 mg/ml, in which the inhibition ranges were 15, 18, 20, 24 and 28 mm, respectively.

MIC. The MIC values for *Mangifera indica* leaf extract are presented in Table II. The *M. indica* leaf extract inhibited the growth of *Fusarium solani* with MIC of 0.25 mg/l. This result demonstrated that at a concentration as low as 0.25 mg/l, no growth was observed.

MBC. As shown by the results presented in Table III, the *M. indica* leaf extract killed *Fusarium solani* at a concentration as low as 12.5 mg/ml. Growth was only observed at 0.25 mg/ml. The phytocompounds present in the extract may have been responsible for the impressive bactericidal activity of the extract.

GC-MS analysis. The GC-MS analysis of the ethanol extract of *M. indica* leaf, bark, and mixture of leaf and bark revealed the presence of 16, five and six phytocompounds, respectively as presented in Tables IV-VI, while the mass spectra images of the extracts are illustrated in Fig. 3.

Discussion

Plant-based diets contain phenolic chemicals, which have been reported to be potent antioxidants. The antioxidant capacity and antidiabetic effects of *M. indica*, as well as its potential to ward off chronic illnesses, such as diabetes and other neurological conditions, have been shown to be greatly enhanced by phytochemicals, such as phenolic compounds (9,30), which makes the delicious fruit-bearing plant not only nutritious, but capable of providing medicinal functions. In the present study, the TPC of the ethanol extract of *M. indica* bark (0.79±0.015) was higher than that of the ethanol extracts of *M. indica* leaves (0.54 and the mixture of *M. indica* leaves and bark (0.56±0.002). However, the total phenolic content of the ethanol extracts of the mixture of *M. indica* leaves and bark was higher than that of *M. indica* leaves.

Phenolic components can also be grouped into several categories, including flavonoids, which have potent antioxidant activities and are known to be effective scavengers of most oxidizing molecules and free radicals (31). As shown by the results of the present study, flavonoids were present in the extracts based on the amount of total flavonoid present in each. The flavonoid content of the ethanol extract of *M. indica* bark extract (MB) (0.58±0.013) was higher than that of the ethanol extracts of the mixture of *M. indica* leaves and bark (MBML) (0.57±0.006) and *M. indica* leaves (ML) (0.53±0.006). However, the flavonoid content of the ethanol extracts of mixture of *M. indica* leaves and bark was higher than that of *M. indica* leaves. The TAC refers to the overall ability of the extracts to neutralize free radicals and prevent oxidative damage. The TACy of MB (0.28±0.002) was higher than that of ML (0.26±0.008); however, the MBML extract had the lowest activity (0.19±0.005). This result is supported by the findings of previous studies, suggesting that phenolic

Table I. Inhibition zone of *Mangifera indica* leaf extract indicating the inhibition of the growth of *Fusarium solani*.

Concentration (mg/ml)	*Fusarium solani* (mm)
100	28
50	24
25	20
12.5	18
0.25	15
DMSO	-
Tioconazole (70%)	36

The '-' symbol indicates no zone of inhibition. Tioconazole was used as the positive control and DMSO was used as the negative control.

Table II. Minimum inhibitory concentration (MIC) of *Mangifera indica* leaf extract.

Concentration (mg/ml)	*Fusarium solani*
100	-
50	-
25	-
12.5	-
0.25	-

The '-' symbol indicates no zone of inhibition.

Table III. Minimum bactericidal concentration of *Mangifera indica* leaf extract,

Concentration (mg/ml)	*Fusarium solani*
100	-
50	-
25	-
12.5	-
0.25	+

The '-' symbol indicates no zone of inhibition, while the '+' symbol indicates growth observed.

compounds significantly contribute to the antioxidant capacity of mango bark extracts (32,33).

DPPH is used for the evaluation of the antioxidant activity (34). DPPH, is a free radical donor that accepts an electron or hydrogen to become a stable diamagnetic molecule (22). As demonstrated in the present study, all three extracts were able to scavenge DPPH; however, the ML extract had the highest activity, which was followed by the MB and then MBML extracts, although the difference was not statistically significant. This further demonstrates the reduction in the therapeutic potential of *M. indica* when the bark and the leaf extracts are combined.

FRAP assay quantifies the ability of an antioxidant to reduce the Fe^{3+}/tripyridyl-striazine complex. The reducing capacity serves as a potent indicator of its antioxidant activity. The reducing power of antioxidants is a key indicator of potential antioxidant activity. The reductones can exert antioxidant activity by donating a hydrogen atom and breaking the free radical chains (35). Herein, the reducing powers of the extracts were assessed based on their ability to reduce Fe^{3+} to Fe^{2+} and the results in ascorbic acid equivalent. This result indicated that the ethanol extracts of *M. indica* leaf possessed the highest antioxidant activity. However, combining ML and MB caused a decline in their ferric reducing power.

The ABTS assay uses ABTS radicals formed by oxidation of ABTS with potassium persulphate. ABTS radical is soluble in water and organic solvents, which enables the determination of the antioxidant capacity of both hydrophilic and lipophilic compounds (36). Based on the results of the present study, as the concentration increased, the ability of MBML to scavenge ABTS radicals improved, enabling it to reach similar values to those of the ML and MB extracts. To the best of our knowledge, no published study to date has previously compared the antioxidant activities of a mixture of leaves and bark extract of *M. indica* with the individual parts.

Compounds such as ferulic acid, resveratrol, catechin, anthocyanins and quercetin, which are plant-based flavonoids and phenolics, are involved in regulating glycemia through increased glucose uptake, insulin secretion, lipid peroxidation inhibition, and the inhibition of enzymes such as α-amylase and α-glucosidase (37). The similar inhibitory activity across all extracts (MB, ML and MBML) suggests that the active compounds in ML and MB which have comparable efficacy in inhibiting α-amylase, may be able to reduce post-prandial blood glucose amounts and therefore be potent candidates in the prevention or treatment of diabetes mellitus.

The increasing inhibition with concentration for α-glucosidase inhibitory activity suggests a concentration-dependent effect for all extracts. Research has shown that various parts of the mango plant exhibit antidiabetic properties due to bioactive compounds, such as mangiferin, flavonoids and phenolic acids. The study by Aderibigbe *et al* (38) indicated that MLs exerted significant hypoglycemic activity in diabetic rats.

Previous studies have also shown that MLs possess significant antimicrobial properties due to the presence of bioactive compounds, such as mangiferin, quercetin and other phenolic compounds. The findings from the present study corroborate the findings obtained in the study by Prakash *et al* (39), which demonstrated that ML extract exhibited antimicrobial activity against various bacterial and fungal strains, including *Fusarium species*, with inhibition zones ranging from 10 to 25 mm, depending on the concentration and the microbial strain. *Fusarium solani* is a common plant pathogen; herein, the leaf extract exhibited significant inhibition of *Fusarium solani*. The microorganism, *Fusarium solani,* was susceptible to tioconzole, which was used as a positive control, while the microorganism showed resistance to DMSO, which was the negative control. The study by Meera *et al* (40) also reported similar inhibition zones for MLs against various pathogens, including *Fusarium solani*. These findings support

Table IV. GC-MS analysis of the phytoconstituents of ethanol extracts of *Mangifera indica* leaf.

Serial no.	Retention time (min)	Compound name	Molecular formula	Molecular weight	Peak area (%)
1	4.300	Phenol	C_6H_5OH	94.1	9.39
2	6.669	3-Phenoxypropionic acid	$C_9H_{10}O$	166	1.69
3	6.795	Benzene, ethoxy-	$C_8H_{10}O$	122.16	3.00
4	7.362	Pyrimidine, 5-methyl-	$C_5H_6N_2$	94.1	1.12
5	7.488	3-Methylpyridazine	$C_6H_7N_2$	108.13	1.32
6	8.100	1H-Cycloprop[e]azulene, 1a,2,3,4, 4a,5,6,7b-octahydro-1,1,4,7-tetramethyl-, [1aR-(1a.alpha., 4.alpha.,4a.beta.,7b.alpha.)]-	$C_{15}H_{24}$	204.35	15.13
7	8.226	Bicyclo[7.2.0]undec-4-ene, 4,11,11-trimethyl-8-methylene-, [1R-(1R*, 4 Z,9S*)]-	$C_{15}H_{24}$	204.35	4.99
8	8.603	Humulene	$C_{15}H_{24}$	204.35	1.62
9	8.678	1-Octen-3-yne	C_8H_{12}	108.2	1.24
10	9.050	Naphthalene, 1,2,3,4,4a,5,6,8a-octahydro-4a,8-dimethyl-2-(1-methylet henyl)-, [2R-(2.alpha., 4a.alpha.,8 a.beta.)]-	$C_{18}H_{28}$	236.41	3.23
11	10.932	Benzoic acid, 3-hydrazino-4-methyl	$C_8H_{11}ClN_2O_2$	202.64	1.22
12	10.967	1-Propyne, 1,1'-thiobis-	C_6H_6S	114.18	1.39
13	11.945	5-Ethyl-2-methyl-pyridin-4-amine	$C_8H_{12}N_2$	136.19	1.16
14	11.979	Phenol, 2-methylthioacetyl-	C_7H_8OS	140.2	1.28
15	13.347	Benzene, 4-methyl-1,2-dinitro-	$C_7H_6N_2O_4$	182.13	2.24
16	13.747	1H-Pyrrole-2-carboxylic acid, 4-formyl-3,5-dimethyl-	$C_8H_9NO_3$	167.16	1.49

GC-MS, gas chromatography-mass spectrometry.

the concentration-dependent antifungal activity observed in the present study.

Phytoconstituents are basically responsible for the antioxidant, antidiabetic and antifungal properties of ML and MB extracts. The GC-MS analysis of the ethanol extract of *M. indica* leaves revealed several bioactive compounds, including phenol, 3-phenoxypropionic acid, benzene, ethoxy-, pyrimidine, 5-methyl-, and 3-methylpyridazine, among others. Previous research has consistently identified phenolic compounds in *M. indica* leaf extracts. Adeyinka *et al* (41) highlighted the presence of phenolic compounds, which contribute significantly to the plant's antioxidant properties. Similarly, Amaechi *et al* (42) reported the identification of phenolic compounds in their GC-MS analysis, emphasizing their role in the bioactivity of the plant. Both studies identified various sesquiterpenes and hydrocarbons. Adeyinka *et al* (41) found compounds, such as 1H-cyclopropa[e]azulene and caryophyllene, which is associated with the sesquiterpenes identified in the present study. The GC-MS analysis of the ethanol extract of MB also revealed several key compounds, including phenol, 3-methylpyridazine, naphthalene, borolo[1,2-a]borne, and 4H-furo[3,2-b]pyrrole-5-carboxylic acid. In line with previous work by Sharma *et al* (43) and Singh *et al* (44), the presence of phenol was significant in the bark extract. They reported the range of phenolics contributing to the antioxidant activity and the anti-inflammatory properties, respectively. Phenolic compounds, known for their antioxidant properties, were consistently found in high concentrations across different parts of the plant. The detection of 3-methylpyridazine in the bark extract is consistent with earlier findings in the leaf extracts, where nitrogen-containing heterocycles such as pyrimidine were identified. These compounds are associated with various biological activities, including antimicrobial and anti-cancer properties, underscoring their importance in medicinal applications. The identification of 4H-furo[3,2-b]pyrrole-5-carboxylic acid aligns with findings from previous studies, suggesting common biosynthetic pathways for these metabolites within the plant. The GC-MS analysis of a mixture of *M. indica* bark and leaves revealed a diverse range of phytochemicals, including phenolic compounds, nitrogen-containing compounds, terpenoids, hydrocarbons, esters, and carboxylic acid derivatives. The presence of phenol, a major constituent in both plant parts, is notable, suggesting its significance in the plant's metabolic processes. The detection of nitrogen-containing compounds and terpenoids/hydrocarbons across all analyses highlights

Table V. GC-MS analysis of the Phytoconstituents of ethanol extracts of *Mangifera indica* bark.

Serial no.	Retention time (min)	Compound name	Molecular formula	Molecular weight	Peak area (%)
1	5.639	Phenol	C_6H_5OH	94.1	35.91
2	8.105	3-Methylpyridazine	$C_6H_7N_2$	108.13	4.49
3	9.295	Naphthalene, 1,2,3,4,4a,5,6,8a-octahydro-4a,8-dimethyl-2-(1-methylethenyl)-, [2R-(2.alpha.,4a.alpha.,8 a.beta.)]-	$C_{18}H_{28}$	236.41	16.34
4	10.783	Borolo[1,2-a]borine, octahydro-	$C_8H_{15}B$	122.02	2.79
5	14.972	4H-Furo[3,2-b]pyrrole-5-carboxylic acid, 4-(2-oxopropyl)-	$C_7H_5NO_3$	151.12	3.88

GC-MS, gas chromatography-mass spectrometry.

Table VI. GC-MS analysis of the phytoconstituents of ethanol extracts of *Mangifera indica* leaf and bark mixture.

Serial no.	Retention time (min)	Compound name	Molecular formula	Molecular weight	Peak area (%)
1	5.679	Phenol	C_6H_5OH	94.1	17.66
2	7.739	Cyclobutane carbonitrile, 3-methyl-3-phenoxy-	$C_{12}H_{13}NO$	187.26	3.39
3	8.109	Aromandendrene	$C_{15}H_{24}$	204.35	15.55
4	8.157	1H-Pyrrolo[3,4-d]pyrimidine-2,5-dione, 4,6-bis (4-hydroxyphenyl)-1-me thyl-3,4,6,7-tetrahydro-	$C_{19}H_{17}N_3O_4$	351.12	2.67
5	8.609	3-Phenoxypropionic acid	$C_9H_{10}O$	166	2.98
6	9.742	1-Octen-3-yne	C_8H_{12}	108.2	2.72

GC-MS, gas chromatography-mass spectrometry.

the plant's metabolic diversity. However, there was a noticeable reduction in the number of compounds detected in the MBML mixture compared to the single extracts of ML and MB. This reduction in the mixture could be responsible for the antagonistic attributes observed in the antioxidant activities and anti-diabetic activity, especially the α-glucosidase inhibition activity. Antagonistic interactions often results in a reduced sum of effects of the individual compounds (45). Such a reduction in activity could only be possible if some of the compounds present in the single extracts are no longer available in the mixture. This deletion of compounds may result from the complex interaction of plant components that can be elucidated by more detailed metabolomic techniques.

The possible mechanisms underlying the effect of *M. indica* extracts as reported in the present study includes the inhibition of α-amylase and α-glucosidase, whose increased activities can result in the elevation of blood glucose (hyperglycemia). It has previously been reported that some phytochemicals, particularly phenols and flavonoids can limit the release of glucose and speed up its uptake, thereby helping to ameliorate high blood sugar in type 2 diabetes (46). More so, the antioxidant activities observed showed that the plant extracts are capable of neutralizing free radicals, thereby protecting against oxidative stress. Clearly, plants compounds such as carotenoids, flavonoids and other phenolic components present in *M. indica* could have been responsible for the antioxidant, antidiabetic and antifungal activities of the extracts.

The findings of the present study can influence future plant-based drug development and clinical practices, as the findings demonstrate that different parts of a plant could solely possess favorable health-promoting potentials, but may not necessarily be as potent when combined. Therefore, further research is essential for combination therapy when developing drug candidates traditionally from medicinal plants.

In conclusion, the present study investigated the biochemical activities and phytoconstituents of the ethanol extracts from the leaves and bark of *M. indica*, both individually and in combination. The phytochemical analysis using GC-MS revealed numerous bioactive compounds, such as phenols, sesquiterpenes, terpenoids, fatty acids and esters. The results demonstrated that the ethanol extract of *M. indica* bark (MB) exhibited the highest total phenolic and flavonoid contents, indicating its superior antioxidant potential, which was closely followed by the leaf extract (ML). The mixture of leaves and bark (MBML) had the least antioxidant activity. The antidiabetic assays suggested a strong potential for MB and ML in regulating enzymes linked to diabetes and revealed that both the leaf and the bark have strong inhibitory effect on α-amylase and α-glucosidase enzymes which are crucial in managing diabetes while the antimicrobial tests

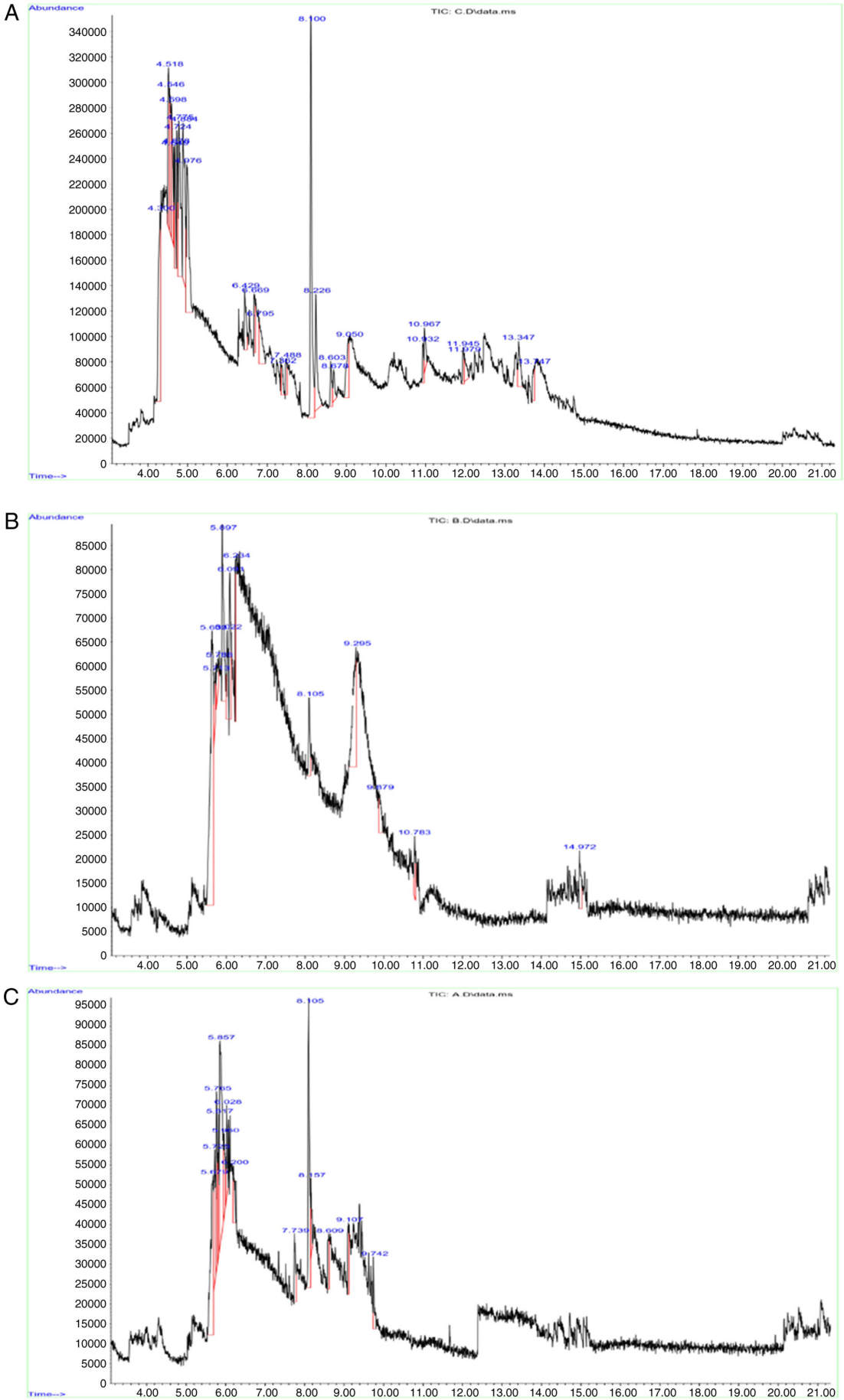

Figure 3. Mass spectra of phytocompounds identified by gas chromatography-mass spectrometry. (A) *Mangifera indica* leaf extract, (B) *Mangifera indica* bark extract, (C) mixture of leaf and bark extracts.

highlighted the efficacy of the leaf extract (ML) in inhibiting *Fusarium solani*. The ethanol extracts of *M. indica* leaf and bark exhibit considerable antioxidant, antidiabetics and antifungal activities, supporting their traditional medicinal uses individually. These findings pave the way for further pharmacological research and development of natural therapeutics from mango leaves or its bark.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

MEK designed, supervised the study and reviewed the manuscript. OEF carried out the laboratory experiments and assays, while KOK analyzed the results and reviewed the manuscript. All authors have read and approved the final manuscript. MEK, KOK and OEF confirm the authenticity of all the raw data.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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