

Antioxidant and antimicrobial activity of *Ficus sycomorus* fruit and leaf extracts

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ABSTRACT

Objective: The aim of this study was to determine the antioxidant and antimicrobial activity of *Ficus sycomorus* fruit and leaf extracts obtained from the Turkish Republic of Northern Cyprus.

Materials and Methods: Fruits and leaves of *F. sycomorus* were collected from the Kyrenia region of Northern Cyprus in July 2018. The leaf and fruit samples were extracted with the distilled water, methanol, ethanol, acetone and chloroform solvents (1:10 [w/v]). After evaporation, samples were suspended in methanol at the final concentration of 100 mg/mL. The antimicrobial activity of the leaf and fruit extracts was evaluated using the Kirby-Bauer Disk Diffusion Method. Total phenolic content (TPC) and total flavonoid content (TFC) of the extracts were determined using the methods reported by Stankovic in 2011 and Sharm and Vig in 2013. Antioxidant activity of samples was tested using free radical scavenger method.

Results: The leaf extracts of *F. sycomorus* was active. The inhibition zone diameters ranged from 1.8mm to 13.00 mm. Fruit extracts and methanol controls showed no inhibitory effect on strains. However, bacteriostatic activity against *Enterococcus faecalis* was observed in fruit-water extract. The highest antimicrobial activity was shown against *Staphylococcus aureus* (13 mm) for ethanolic extracts at 100 mg/mL concentration. Minimal inhibition concentration (MIC) for ethanolic extract was observed starting at 25 mg/mL concentration against *S. aureus*. Although, no antimicrobial activity was observed in fruit extracts, the highest 2,2-diphenyl 1-picrylhydrazyl (DPPH) activity and phytochemical content were recorded in fruit extracts.

Conclusion: These results demonstrate that leaf extracts of *F. sycomorus* can be used as a curative agent for the treatment of *S. aureus* and fungal infections and may be effective against pathogenic microorganisms that are resistant to antibiotics. Antioxidant content of fruit and leaf extracts can be effective against the negative effects of free radicals.

Keywords: Antioxidant activity, *F. sycomorus*, *S. aureus*

1. INTRODUCTION

Ficus sycomorus belongs to the Moraceae, which is a family of flowering plants, containing about forty genera and more than thousand species. This family is the best commonly found in tropical and subtropical areas and is often referred to as the mulberry family or the fig family [1]. The plant is indigenous to African countries and mostly grows well in tropical countries like Oman. It also grows in the Arabian Peninsula and in Lebanon. It is also found in Cyprus, Madagascar, Israel and Egypt. The plant grows to a height of about 10 to 20 m. The branches of the plant begin from the lower part of the body and form shapes like umbrellas. The *F. sycomorus* leaves are dark green, yellow-veined, heart-shaped and about 10 to 14 cm long. The diameter

of the fruits is about 2 to 3 cm and round. The fruits are green when they are raw, and they become yellow or red when they ripen [2]. In Northern Cyprus, the *F. sycomorus* fruit is known as 'Cümbez' 'Pharaoh fruit' among the people. The tree of cümbez is known to give fruit seven times a year. When the tree gives fruit, the fruit is scratched with a knife and the fruit is mature. Scratched fruits ripen after about 7-10 days and become ready to be consumed. The most well-known *F. sycomorus* plant in Northern Cyprus is located in the courtyard of the Lala Mustafa Paşa Mosque in Famagusta. The mosque was originally built as the Cathedral of Saint Nicholas. It is estimated that the tree was erected in 1298 when the construction of the cathedral began.

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The height of the tree is 15 meters and the estimated age is 715. The body of the tree is surrounded by smaller branches growing from the main body. The body is divided into 7 branches after 2.70 meters. Each branch around the main body is said to have coincided with a century. It is the oldest and most vivid tree in Cyprus. The fact that this tree is the oldest tree in the history of the all island and witnessed many events from the past to the present make the historical Cümbez tree in this region culturally important [3, 4].

Extracts of fruit, leaf, root and stem bark of the plant are used to treat various ailments such as cough, diarrhea, skin infections, jaundice, snake bites, chest diseases, cold, dysentery, stomach disorders, lactation disorders, liver disease, epilepsy, tuberculosis, helminthiasis, infertility, and diabetes mellitus [5, 6].

Constantly developing technology, environmental pollution, contaminated waters, radiation, heavy metals, pesticides and oxygen metabolism in living cells cause the formation of free radicals in the human body [7]. Free radicals are known to cause many diseases, particularly cancer. Antioxidants protect our body against all damages caused by free radicals that threaten human health. The importance of foods containing antioxidants should be known and consumed in order to prevent the spread of cancer disease in Cyprus and all over the World. Another important problem is the resistance of bacteria to antibiotics. Nowadays, all around the world, exploratory work is going on to find effective solution against drug resistant bacteria [8]. The discovery of new antimicrobials through plants provides new approaches and benefits for minimizing antibiotic resistance. In many studies, it has been mentioned that *Ficus* species have potential antibacterial activity [9].

The facts that this important Cypriot plant has a value to the culture it belongs to, and that it is rare and not widely known and that there is no study that has been conducted on it in North Cyprus or in Turkey make this study worthwhile and valuable.

This study aimed to screen phytochemical properties and pharmacological activities of leaf and fruit extracts of *F. sycomorus*. The leaf and fruit extracts of the plant were prepared for the analysis using acetone, ethanol, pure water and methanol solvents. The minimum inhibitory concentration (MIC) regarding the antimicrobial activity of these medicinal plants was also examined.

2. MATERIALS and METHODS

Chemicals, Culture Media and Antibiotics

Ethanol, methanol, chloroform, acetone, 2,2-diphenyl-1-picrylhydrazyl (DPPH), sodium nitrite (NaNO_2) and sodium hydroxide (NaOH) were purchased from Sigma-Aldrich, (Germany). Mueller Hinton Agar Butylated hydroxytoluene (BHT), Folin-Ciocalteu reagent, sodium bicarbonate (NaHCO_3) and gallic acid standard were purchased from Merck KgaA, (Germany). Aluminum chloride hexahydrate ($\text{AlCl}_3 \cdot 6\text{H}_2\text{O}$), Phoenix ID Broth and Nystatin (Oxoid, 100 units) were purchased from ACROS, BD Phoenix and Oxoid (United

Kingdom). Blank antimicrobial discs, tetracycline (Bioanalyse Limited, 30 μg), ciprofloxacin (Bioanalyse Limited, 5 μg) and teicoplanin were purchased from (Bioanalyse Limited, 30 μg) Bioanalyse Limited, (Turkey).

Collection and Preparation of Plant Material

Fruits and leaves of *F. sycomorus* were collected from the Kyrenia region of Northern Cyprus in July 2018. The collected fruit and leaves were washed by distilled water to remove dust and soil and then dried. The washed fruits were cut into thin slices with a knife and dried in a food dehydrator machine and the washed leaves were dried at room temperature. The dried leaves and fruits were grounded with an electric mixer and stored in a +4°C refrigerator until the day of use in the laboratory.

Preparation and Extraction of Leaf and Fruit Extracts

The leaf and fruit samples were extracted with the distilled water, methanol, ethanol, acetone and chloroform solvents (1:10 [w/v]) in the shaker for 72 hours at room temperature. Solvents, after being filtered by Wattman No. 4 paper (Camlab, UK), were evaporated and then samples were suspended in methanol at the 100 mg mL^{-1} final concentration. The extracts were kept refrigerated at +4°C for phytochemical analysis for the antioxidant, and antimicrobial activity.

Antimicrobial Test

The antimicrobial activity of the leaf and fruit extracts were evaluated by the Kirby-Bauer Disk Diffusion Method [10]. A total of 1 fungal and 7 bacteria species (*Escherichia coli*, *Enterobacter cloacae*, *Klebsiella* spp., *Bacillus subtilis*, *Enterococcus faecalis*, *Staphylococcus aureus*, *Staphylococcus epidermidis* and *Candida albicans*) were used for the antimicrobial test. The antibacterial activity was performed on Mueller Hinton Agar. 10 μL of the microbial suspension was taken with a pipette and transferred to the center of Mueller Hinton agar and then spreaded homogeneously on the surface with a wooden cotton applicator stick. The sterile antimicrobial blank discs impregnated with 20 μL of the extracts were strategically placed away from each other. Methanol solvent and standard antibiotics were used as negative and positive controls, respectively. Tetracycline for *B. subtilis*, *S. aureus* and *S. epidermidis*; Ciprofloxacin for *E. coli*, *E. cloacae* and *Klebsiella* spp.; Nystatin for *C. albicans* and Teicoplanin for *E. faecalis* were used as the positive controls. The plates were kept at room temperature for 20-30 minutes. Then, the plates were placed in the incubator for 18-24 hours at 35°C. Following the incubation, the inhibition zones around the discs were evaluated. MIC of the extracts that showed antibacterial activity against test microorganisms was determined. This analysis was performed based on fact that the lowest inhibitory concentration determines the effectiveness on the test microorganisms (*S. aureus* and *C. albicans*). In this test, the 12.5, 25, 50, 75 and 100 mg mL^{-1} concentrations of extracts were investigated for their inhibitory effects against various microorganisms.

Total Antioxidant Test

The antioxidant activity of extracts were determined by DPPH Radical Scavenging Method. This method is based on the reduction of DPPH, a dark violet color compound and the absorbance reduction was measured by Ultraviolet-Visible (UV-Vis) spectrophotometer [11]. The antioxidant activities of the extracts, which were expressed as the activity of capturing free radicals, were determined by the use of DPPH radicals according to the method of Yilmaz, and Türkmen, et al. [12, 13]. DPPH radicals (0.025 g/L) prepared in 3.9 mL methanol was added to 100 µL of the extracts. The mixture was incubated at room temperature and in the dark for 30 minutes. In this analysis based on the opening of purple color of the DPPH solution, the residual amount of DPPH was measured at 515 nm by using spectrophotometer. Inhibition of DPPH was calculated as percent by the following formula. All analyzes were repeated 3 times. For the Control value: Methanol + DPPH, For Blank: Methanol, Against Blank (methanol): Methanol + DPPH (control), Against Blank: Plant sample + DPPH were used. BHT at 200 µg mL⁻¹ concentration was used as standard antioxidant substance.

$$\text{Inhibition \%} = \left[\frac{\text{Control Absorbance} - \text{Sample Absorbance}}{\text{Control Absorbance}} \right] \times 100$$

Total Flavonoid Content (TFC)

According to the method reported by Sharma and Vig (2013), 1 mL of extracts were diluted with 5 mL of distilled water [14]. 0.3 mL NaNO₂ (5%) was added to the samples and incubated for 5 min at room temperature. Then, 0.6 mL of AlCl₃.6H₂O (10%) was added to the mixture and after incubation under the same conditions, 2 mL of 1M NaOH was added and the final volume of reaction mixture was completed to 10 mL with distilled water. The absorbance of the prepared mixtures was determined spectrophotometrically at 510 nm. Routine equivalent standard was used by solving in distilled water at 0-125 mg/mL concentrations. All analyzes were repeated 3 times and calculated according to the slope value ($y = 10,954x$). TFC was expressed as mg routine equivalents (mg RE/g) per gram.

Total Phenolic Content (TPC)

Soluble phenolic content of fruit and leaf extracts were determined using Folin-Ciocalteu reagent. 0.5 mL of extracts were incubated in a water bath at 45°C for 45 minutes with the addition of 2.5 mL of Folin-Ciocalteu reagent (10%) and 2.5 mL of NaHCO₃ (7.5%). The absorbance of the mixtures was measured spectrophotometrically at 765 nm. According to the calibration graph using gallic acid as standard, the TPC is expressed as mg gallic acid equivalents (mg GAE/g) per gram [15]. Gallic acid standard was used by solving it in distilled water at 0-150 µg/mL concentrations. All analyzes were repeated 3 times and calculated according to the slope value ($y = 8,8286x$).

Statistical Analysis

Statistical analysis was performed for antioxidant activity, TFC and TPC results. In order to determine significant differences between

the samples, the software SPSS 22.0 for Windows (SPSS Inc., Chicago, IL, USA) was used. Variance analysis (ANOVA) and Tukey multiple comparison tests were performed. Each spectrophotometric analysis was repeated at least three times. ($P < 0.05$).

3. RESULTS

The range of the percentage extraction yield of the leaf and fruit extracts was very extensive: from 4.8% to 51.65% (Table I). The highest yield was calculated as 51.65% and 32.45% in the methanolic and aqueous fruit extracts. However, the yield of the leaf extracts were lower than that of fruit samples. This value for leaf extracts ranged from 4.8% to 11.4%. For both fruit and leaf samples, the high yield was observed in methanolic extracts.

Negative control (methanol) showed no inhibitory effect on strains. All leaf extracts displayed no antibacterial activity against *B. subtilis*, *S. epidermis*, *E. coli*, *Klebsiella* spp., *E. cloacae* and *E. faecalis*. However, the prepared fruit samples showed no inhibitory effect on tested microorganisms, except on *E. faecalis*. Aqueous fruit extract had bacteriostatic activity on this bacteria (Table IV), (Figure 3). As seen from Table II, leaf acetone, methanol and ethanol extracts had only antibacterial activity against *S. aureus*. The most effective extract on *S. aureus* was ethanolic leaf sample with the 13 mm zone diameter (Table II; Figure 1). This activity was lower than inhibition diameter of tetracycline positive control (23 mm). Remarkable antifungal activity of acetone and ethanol leaf extracts was observed on *C. albicans* (Table III; Figure 2). While control of nystatin resulted in 15 mm against *C. albicans*, the effect of extracts ranged between 10mm and 12 mm. MIC analysis was performed for leaf acetone, methanol and ethanol extracts showing antimicrobial activity on *S. aureus* and *C. albicans*.

Table I. Percentage yield of leaf and fruit extracts

Name of Extract	Amount of leaf and fruit extracts after evaporation (g)	Percent yield of leaf and fruit extracts (%)
Leaf-Water	0.85	8.5
Leaf-Methanol	1.14	11.4
Leaf-Ethanol	0.53	5.3
Leaf-Chloroform	0.53	5.3
Leaf-Acetone	0.48	4.8
Fruit-Water	6.49	32.45
Fruit-Methanol	10.33	51.65
Fruit-Ethanol	5.48	27.4
Fruit-Chloroform	0.68	3.4
Fruit-Acetone	0.97	4.85

Table II. Diameter of the inhibition zone (mm) of the leaf extracts (100 mg/mL concentration, 20 µL) against *B. subtilis*, *S. aureus* and *S. epidermidis*

Microorganisms tested	Leaf-Acetone	Leaf-Chloroform	Leaf-Methanol	Leaf-Ethanol	Leaf-Water	Methanol (NC)	Tetracycline (PC)
<i>B. subtilis</i>	-	-	-	-	-	-	25
<i>S. aureus</i>	11	-	10	13	-	-	23
<i>S. epidermidis</i>	-	-	-	-	-	-	14

(-) represents a no inhibition zone against microorganism. PC: Positive control, NC: Negative control

Table III. Diameter of the inhibition zone (mm) of the leaf extracts (100 mg/mL concentration, 20 µL) against *C. albicans*

Microorganisms tested	Leaf-Acetone	Leaf - Chloroform	Leaf-Methanol	Leaf-Ethanol	Leaf-Water	Methanol (NC)	Nystatin (PC)
<i>C. albicans</i>	10	-	-	12	-	-	15

(-) represents a no inhibition zone against microorganism. PC: Positive control, NC: Negative control

Table IV. Diameter of the inhibition zone (mm) of the fruit extracts (100 mg/mL concentration, 20 µL) towards *E. faecalis*

Microorganisms tested	Fruit-Acetone	Fruit - Chloroform	Fruit-Methanol	Fruit-Ethanol	Fruit-Water	Methanol (NC)	Teicoplanin (PC)
<i>E. faecalis</i>	-	-	-	-	1.8	-	19

(-) represents a no inhibition zone against microorganism. PC: Positive control, NC: Negative control

Table V. Minimum inhibitory concentration (MIC) values of leaf-acetone, leaf-ethanol and leaf methanol extracts against the *S. aureus*

Microorganisms tested	Leaf-Acetone (12.5 mg/mL)	Leaf-Acetone (25 mg/mL)	Leaf-Acetone (50 mg/mL)	Leaf-Acetone (75 mg/mL)	Leaf-Acetone (100 mg/mL)	Methanol (NC)	Tetracycline (PC)
	<i>S. aureus</i>	-	-	-	9	11	-
Leaf-Ethanol (12.5 mg/mL)		Leaf-Ethanol (25 mg/mL)	Leaf-Ethanol (50 mg/mL)	Leaf-Ethanol (75 mg/mL)	Leaf-Ethanol (100 mg/mL)	Methanol (NC)	Tetracycline (PC)
-		9	11	13	13	-	26
Leaf-Methanol (12.5 mg/mL)		Leaf-Methanol (25 mg/mL)	Leaf-Methanol (50 mg/mL)	Leaf-Methanol (75 mg/mL)	Leaf-Methanol (100 mg/mL)	Methanol (NC)	Tetracycline (PC)
-	-	-	8	10	-	24	

(-) represents a no inhibition zone against microorganism. PC: Positive control, NC: Negative control

Table VI. Minimum inhibitory concentration (MIC) values of leaf-acetone and leaf ethanol extracts against the *C. albicans*

Microorganisms tested	Leaf-Acetone (12.5 mg/mL)	Leaf-Acetone (25 mg/mL)	Leaf-Acetone (50 mg/mL)	Leaf-Acetone (75 mg/mL)	Leaf-Acetone (100 mg/mL)	Methanol (NC)	Nystatin (PC)
	<i>C. albicans</i>	-	-	-	9	10	-
Leaf-Ethanol (12.5 mg/mL)		Leaf-Ethanol (25 mg/mL)	Leaf-Ethanol (50 mg/mL)	Leaf-Ethanol (75 mg/mL)	Leaf-Ethanol (100 mg/mL)	Methanol (NC)	Nystatin (PC)
-		-	10	11	12	-	13

(-) represents a no inhibition zone against microorganism. PC: Positive control, NC: Negative control

Table VII. Total phenolic content (TPC), Total flavonoid content (TFC) and antioxidant activity (DPPH scavenging) of different leaf extracts of *Ficus sycomorus*

Sample	TPC (mg GAE/g)	TFC (mg RE/g)	DPPH (%)
Leaf-water	*3.72±0.08 ^b	*0.19±0.015 ^c	*1±2.55 ^d
Leaf-acetone	*2.55±0.38 ^c	*1.38±0.306 ^a	*33±3.38 ^b
Leaf-chloroform	*7.09±0.23 ^a	*1.24±0.064 ^{ab}	*42±0.13 ^a
Leaf-ethanol	*2.23±0.00 ^c	*1.37±0.246 ^a	*18±0.13 ^c
Leaf-methanol	*2.38±0.09 ^c	*0.84±0.107 ^b	*47±2.17 ^a
BHT (200 µg mL ⁻¹)			*26.29±0.18 ^e

Values are mean ± Standard Deviation (SD) of three replicate analyses. 100 mg/mL concentration was used for the tests. *(The presented datas are mean of triplicate determinations (n=3), ± Standard Deviation. The difference between the values expressed by the different symbols in table (a-c, and a-e) is significant (P<0.05)). BHT: Butylated hydroxytoluene

Table VIII. Total phenolic content (TPC), Total flavonoid content (TFC) and antioxidant activity (DPPH scavenging) of the different fruit extracts of *Ficus sycomorus*

Sample	TPC (mg GAE/g)	TFC (mg RE/g)	DPPH (%)
Fruit-water	*5.62±0.05 ^c	*0.07±0.004 ^d	*76±2.23 ^b
Fruit-acetone	*11.29±0.39 ^a	*1.38±0.021 ^a	*86±0.06 ^a
Fruit-chloroform	*7.78±0.33 ^b	*1.08±0.058 ^b	*69±1.21 ^c
Fruit-ethanol	*1.93±0.27 ^d	*0.32±0.009 ^c	*86±4.78 ^a
Fruit -methanol	*1.91±0.33 ^d	*0.12±0.013 ^d	*86±0.19 ^a

Values are mean ± Standard Deviation (SD) of three replicate analysis. 100 mg/mL concentration was used for the tests. *(The presented datas are mean of triplicate determinations (n=3), ± Standard Deviation. The difference between the values expressed by the different symbols in table (a-d and a-c) is significant (P<0.05)).

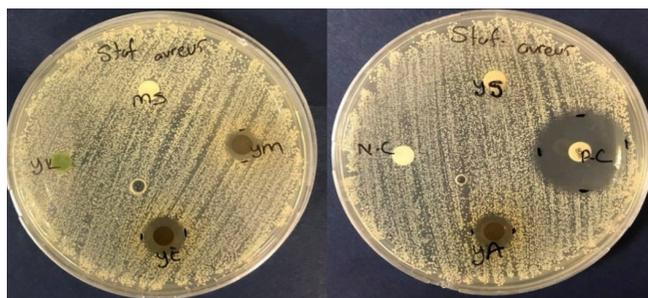


Figure 1. Inhibition zone of leaf-acetone (YA), leaf-methanol (YM) and leaf-ethanol (YE) extracts against *S. aureus*

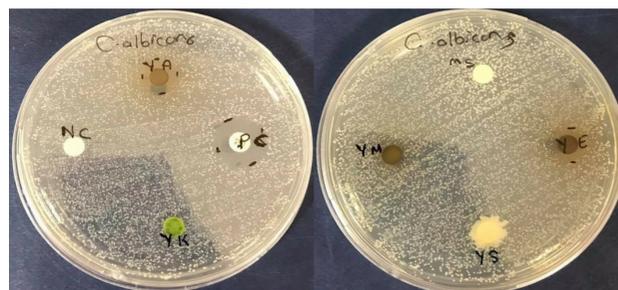


Figure 2. Inhibition zone of leaf-acetone (YA) and leaf-ethanol (YE) extracts towards *C. albicans*



Figure 3. Bacteriostatic activity of fruit-pure water (MS) extract towards *E. faecalis*, no inhibition zone of other fruit and leaf extracts

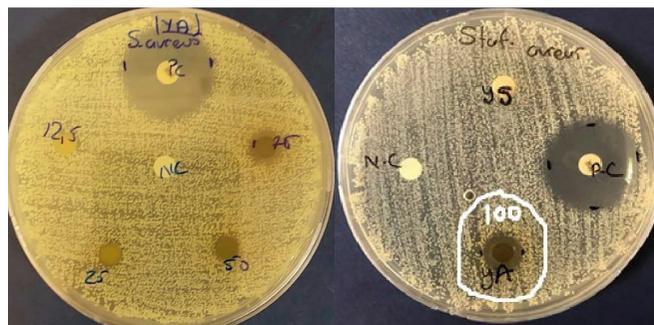


Figure 4. The inhibition zone towards *S. aureus* at different concentration of the leaf-acetone extracts (YA)

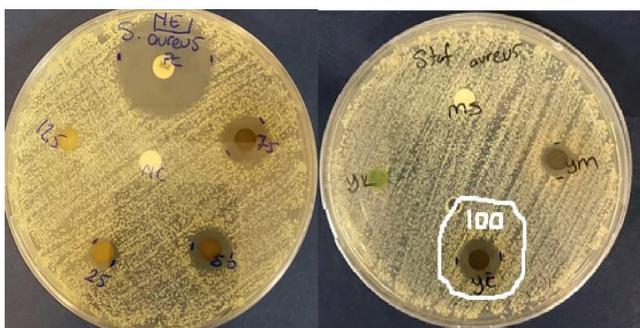


Figure 5. The inhibition zone towards *S. aureus* at different concentration of the leaf-ethanol extracts (YE)

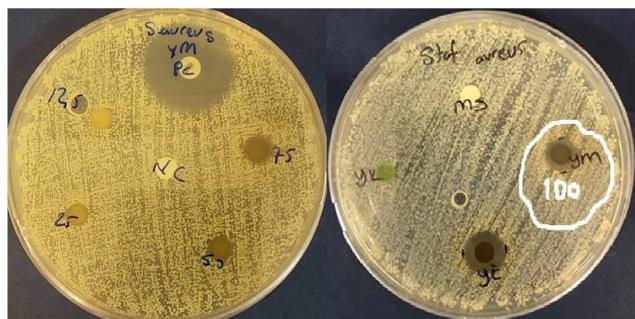


Figure 6. The inhibition zone towards *S. aureus* at different concentration of the leaf-methanol extracts (YM)

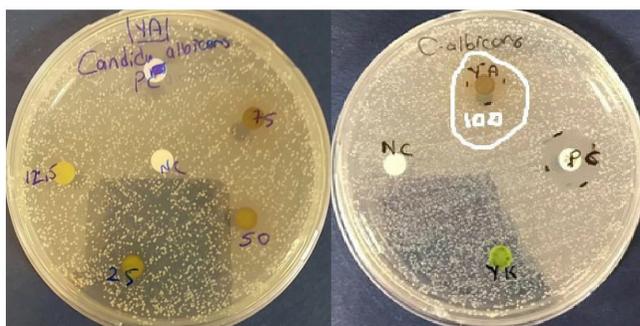


Figure 7. The inhibition zone towards *C. albicans* at different concentration of the leaf-acetone extracts (YA)

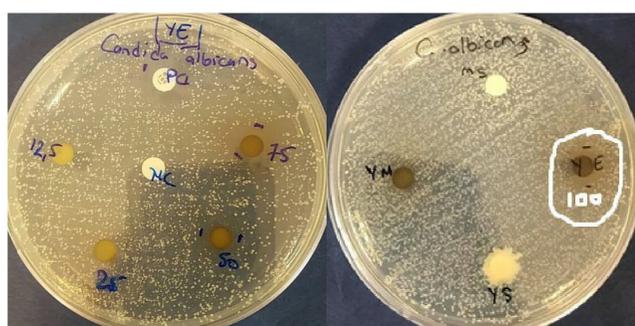


Figure 8. The inhibition zone towards *C. albicans* at different concentration of the leaf-ethanol extracts (YE)

Minimum inhibitory concentration value for leaf acetone was observed starting at 75 mg/mL concentration against *S. aureus* and *C. albicans* (Table V-VI; Figure 4, 7). MIC values of ethanolic and methanolic leaf extracts were 25 and 75 mg/mL on *S. aureus* (Table V; Figure 5, 6). MIC value (50 mg/mL) of ethanolic leaf extract observed against *C. albicans* was lower than that of acetone sample (Table VI; Figure 8).

In this present study, all quantitative examination of phytochemical analysis and DPPH were found statistically significant ($P < 0.05$). As can be seen in Table VII-VIII, TPC and TFC of the extracts ranged from 1.91 ± 0.33 to 11.29 ± 0.39 mg GAE/g; from 0.07 ± 0.004 to 1.38 ± 0.306 mg RE/g, respectively. High TPC value was calculated as 11.29 ± 0.39 mg GAE/g in the acetone fruit extract. However, the lower TPC values ranging from 1.93 ± 0.27 to 1.91 ± 0.33 mg GAE/g were obtained from ethanolic and methanolic extracts. Highest TFC was identified in acetone leaf and fruit extracts, 1.38 ± 0.306 and 1.38 ± 0.021 mg RE/g. The TFC was noted as minimum in aqueous fruit extract (0.07 ± 0.004). In leaf extracts, chloroform extract was the highest TPC value (7.09 ± 0.23). Chloroform has the least polarity index in the test solvent used but which yielded the highest phenolic substances. This may be due to the high hydrophobicity of the compounds. The results of flavonoids for all leaf samples were lower than the results of phenolic substances. This is because flavonoids are the subgroup of phenolics.

2,2-diphenyl-1-picrylhydrazyl radical scavenging activity was evaluated by comparing it with the standard antioxidant activity of BHT. The DPPH activity of *F. sycomorus* samples was not comparable with that of BHT testing at $200 \mu\text{g mL}^{-1}$ concentration. The antioxidant activity of DPPH was observed in the leaf extracts ranging from $1 \pm 2.55\%$ to $47 \pm 2.17\%$. TPC and TFC values of leaf methanolic extract showed the highest antioxidant activity ($47 \pm 2.17\%$) but still they were lower than the values of chloroform and acetone extracts that had the maximum contents. Even though the low DPPH activity ($1 \pm 2.55\%$), aqueous leaf extract had the high TPC content (3.72 ± 0.08). The free radical scavenging capacity of fruit extracts was higher than that of the leaf extracts. Based on the polarity of solvents, the highest antioxidant activity of DPPH for fruit samples was recorded as 86% in methanol, ethanol and acetone extracts. According to Table VII-VIII, inhibition % values ranged from $1 \pm 2.55\%$ to 86 ± 0.06 . According to these results, the presence of antioxidant compounds of fruit and leaf extracts could be effective against the negative effects of free radicals. Our results also indicated the effect of extraction solvents on antioxidant activity and phytochemical contents in bioactivity studies of plants.

4. DISCUSSION

Four Gram-positive, three Gram-negative bacterial strains and one fungal strain were tested for antimicrobial activity of the extracts. Extracts did not show any inhibitory activity against three Gram-negative bacterial strains. However, a moderate activity was observed against one of the four Gram-positive bacterial strains, *S. aureus* and one fungal strain (Table II-III). The inhibition zone to *S. aureus* and *C. albicans* at concentrations of 25, 50, 75, 100 mg/mL and 50, 75, 100 mg/mL of leaf extract was in the range of 8-13 mm and 9-12 mm, respectively (Table V-VI). The antimicrobial activity of fruits and leaves of *F. sycomorus* extracts differentiated according to the species of microorganisms tested, the solvents used and extraction process.

Ghareeb et al., reported leaf-methanol extract of *F. sycomorus* which showed antimicrobial activity against *E. coli* (14 mm), *S. aureus* (27 mm) and *C. albicans* (16 mm) but no antifungal activity to *A. niger* [16]. In addition, the methanolic and ethanolic leaf extracts showed inhibitory effect on test microorganism, *S. aureus*. [17]. Similar results were reported by Saleh and Al-Mariri (2017), who recorded that the acetone leaf extract of *F. sycomorus* showed good antibacterial activity against *Listeria monocytogenes*, *S. aureus*, *Bacillus cereus*, *Escherichia coli* O:157, *Salmonella typhimurium*, *Brucella melitensis*, *Proteus mirabilis*, *Yersinia enterocolitica* O:9, *Pseudomonas aeruginosa* and *Klebsiella pneumonia* [18]. This antibacterial activity on *S. aureus* (9 mm) was lower than the inhibition diameter of our leaf acetone extract (11 mm). However, in Braide et al's study no inhibition zone against *E. coli*, *Klebsiella spp.*, *S. aureus* and *P. aeruginosa* was observed in the leaf-methanolic extract [8].

In this study, inhibition against *C. albicans* and *S. aureus* at 100 mg/mL was observed. *S. aureus* causes superficial skin lesions (boils, shallots), localized abscesses, deep-seated infections, severe skin infections (furunculosis), infection of hospital-acquired surgical wounds and food poisoning. *C. albicans* causes fungal urinary tract infections (UTI), genital fungal infections, fungal skin infections and oral thrush. The susceptibility of *C. albicans* and *S. aureus* to leaf extracts of *F. sycomorus* was shown to be effective against diseases caused by these organisms and can be used as a healing agent.

In the study of Saleh et al., the MIC was evaluated by microdilution broth method to establish the susceptibility of pathogens to the acetone-leaf extract [9]. These values were found 7.3 mg/mL for resistant *S. aureus* and 6.6 mg/mL for sensitive *S. aureus*. In another study of Saleh and Al-Mariri, the MIC value of leaf-acetone extract against *S. aureus* was 130.2 mg/mL [18]. This value was rather higher than that of our acetone extract value (75 mg/mL.). Similar to our results, Jouda et al., showed that the MIC value was 25 mg/mL for leaf-ethanol extract against *S. aureus* [17]. Also, MIC value of leaf-methanolic extract against *S. aureus* was determined as 6.25-3.125 and 8.7-9.2 mg/mL in Saleh et al., and Jouda et al., studies which was lower than that of ours [9, 17].

The antioxidant activity and phytochemical properties of the *F. sycomorus* extracts were solvent dependent. In our study the total

content of phenolic and flavonoid compounds varied in different fractions based on polarities of solvents ranging from 1.91 ± 0.33 to 11.29 ± 0.39 mg GAE/g; 0.07 ± 0.004 to 1.38 ± 0.021 mg RE/g (Table VII-VIII). The fruit extracts exhibited the highest DPPH removal activity followed by chloroform ($69 \pm 1.21\%$), water ($76 \pm 2.23\%$), acetone, ethanol and methanol (86 ± 0.06 - 4.78%) (Table VII-VIII). This indicated that antioxidant activity was solvent – independent but was strongly dependent on the fruit samples taken from the *F. sycomorus*. The fruit extracts of *F. sycomorus* showed stronger antioxidant capacity as compared to leaf extracts.

Similarly, Al-matani et al., reported that the extractive yields of the *F. sycomorus* fruit varied depending on the polarity of solvents used [1]. The highest amount of total extractable compound was in the hexane extract (18.8%). This value was rather lower than that of our methanol extract (51.65%). Whereas, 11.09% and 4.06% the total extractable content value of methanolic and aqueous *F. sycomorus* leaf extracts reported by El Sayed et al., was higher than the values of this study [20].

Al-matani et al., predicated that TPC values of *F. sycomorus* fruit extracts were in the range of 3.43 ± 2.16 and 81.56 ± 0.43 mg GAE/100 g [1]. These were quite lower than the TPC values of *F. sycomorus* fruit extract calculated per g. El Sayed et al., noted as 124.00 ± 4.96 and 26.31 ± 3.76 mg GAE/g of the TPC of leaf methanol and water extract, which was dramatically higher than our results [20]. Moreover, we found out that in El-Beltagi et al's study, TFC values of *F. sycomorus* extracts (2.48 ± 0.16 and 12.58 ± 0.01 mg QE/ g) were much higher than our results [19].

This study supported previous reports by Samuel et al., and El Sayed et al. on the DPPH radical scavenging activity of *F. sycomorus* fruit and leaf extract prepared by different solvents [20, 21]. In our study, the ethanolic extract of *F. sycomorus* fruit gave the high antioxidant activity ($86 \pm 4.78\%$) as compared with the values reported (72.471%) by El-Beltagi et al. [19]. Antioxidant results of our study were in accordance with the results of Abdel-Aty et al., who found the highest value of DPPH radical scavenging activity (above 75%) in *F. sycomorus* latex extract [22].

In conclusion, *F. sycomorus* may be used as an alternative to antibiotics that are resistant to pathogenic microorganisms. In this study, leaf extracts were found to be more effective than fruit extracts against gram-positive *S. aureus* bacteria. It can also be used as medicine or food against infections caused by various bacteria or fungi. Fruits and leaves of *F. sycomorus* can be consumed as antioxidants against free radicals formed in the human body.

In the light of our findings, we think that *in-vivo* and *in-vitro* antioxidant mutagenic toxicity tests can guide the future studies on the effect of eukaryotic cells.

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Compliance with Ethical Standards

Authors' Contributions: Concept – M.S.O., F.T.; Design – M.S.O., F.T., H.A.M.T.; Supervision – M.S.O.; Resource – M.S.O., K.S., E.G., H.A.M.T.; Materials – M.S.O., K.S., E.G., H.A.M.T.; Data collection and/or Processing – M.S.O., F.T., E.G.; Analysis and/or interpretation – M.S.O., F.T., K.S., H.A.M.T.; Literature search – M.S.O., F.T.; Writing – M.S.O., F.T., H.A.M.T.; Critical Reviews – M.S.O., K.S., H.A.M.T.

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