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Chemical constituents and antibacterial activity from the fruits of *Ficus sur* Forssk

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Abstract

Background: *Ficus sur* Forssk is used in traditional African medicine in the treatment of skin diseases, epilepsy, jaundice, pain, inflammation, anemia, sexually transmitted diseases, and diarrhea. We described here the chemical study and antibacterial properties of *F. sur* ethanol extract.
Methods: Separation and isolation of compounds were performed using common chromatographic methods. The structures of compounds were determined by spectrometric and spectroscopic analyses including MS and NMR data and comparison with reported ones in the literature. The microdilution method was used to evaluate the antibacterial activity of the isolated compounds, fractions, and crude EtOH extract against five multidrug-resistant (MDR) bacteria.
Results: Ten known compounds (**1-10**) were isolated including six pentacyclic triterpenoids (**1-6**) and four steroid derivatives (**7-10**) including 11-oxo-*β*-amyrin acetate (**1**), olean-12-en-3-one (**2**) *β*-amyrin palmitate (**3**), *β*-amyrin (**4**), *β*-amyrin acetate (**5**), lupeol acetate (**6**), ergosterol peroxide (**7**), (22*R*)-3*β*-stigmast-5-ene-3,22-diol (**8**), *β*-sitosterol (**9**) and *β*-sitosterol 3-O-*β*-D-glucopyranoside (**10**). The chemophenetic significance of the isolated compounds was discussed. The crude extract exhibited the lowest minimal inhibitory concentration (MIC) value on *Salmonella typhi* 001 (MIC = 64 µg/mL). Fractions FA and FB showed antibacterial activity against all the tested microorganisms with MIC ranging from 16 to 512 µg/mL. Fraction A showed the highest activity with the least MIC of 16 µg/mL on *Escherichia coli* 009 while the most active among isolated compounds were *β*-amyrin palmitate (**3**) against *Salmonella typhi* (MIC = 32 µg/mL) and *β*-amyrin acetate (**5**) against *Escherichia coli* 001 and *Klebsiella pneumoniae* 008 (MIC = 64 µg/mL). This work reports the antibacterial activity of the crude ethanol extract, fractions, and isolated compounds from the selected plant.
Conclusion: The research work presented here shows that *Ficus sur* Forssk fruits possess compounds that could be valued in the treatment of bacterial diseases. These results support the traditional uses of this plant for the treatment of some bacterial diseases happening in Cameroon.

Keywords: *Ficus sur* ; Moraceae; Chemical constituents; chemophenetic significance; Antibacterial activity.

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Background

The genus *Ficus* belongs to the Moraceae family with approximately 750 species distributed in tropical regions of Africa, Asia, and Australia [1]. About 100 species are represented in Africa and over 600 in Asia and Australia [1]. In Cameroon, some plants of this genus are used for the treatment of several diseases [2-4]. The plants of *Ficus* genus showed several biological properties, including antibacterial [5-9], antioxidant [10-11], anti-inflammatory [8, 12-13], cytotoxicity [5, 14-15], hepatoprotective [16], antitumoral [17], anticonvulsant [18] and antifungal activities [19-20]. *F. sur* Forssk is a large tree, with a spreading canopy of approximately 12 m in height, but reaching 25 to 30 m in some other areas. It is an indigenous medicinal plant found in KwaZulu-Natal, South Africa, it occurs from southern Cape northwards throughout eastern South Africa, to tropical Africa, Senegal, Cape Verde Islands, Ethiopia, and Yemen [21]. This plant is used in traditional African medicine in the treatment of epilepsy, pain, and inflammations [4]. Ethanol extract of this plant possessed a significant anticonvulsant effect, thereby confirming the traditional uses of this plant in the treatment of epilepsies [22]. Fresh leaves of this plant are used as a blood builder for boosting iron levels and treating diarrhea, anemia, and sexually transmitted diseases [23-25]. The root and bark decoctions are used in traditional medicine to treat a variety of ailments including pulmonary tuberculosis, influenza, and skin diseases [26].

The previous phytochemical studies on some species of the genus *Ficus* reported the isolation of terpenoids, steroids, flavonoids, coumarins, ceramides, cerebrosides, aliphatic alcohols, and alkaloids [5-6, 27-30]. The previous phytochemical investigations on fruits and leaves of selected species led to the isolation of one triterpenoid (lupeol), one steroid (*β*-sitosterol), one pheaophytin (pheaophytin a), and one flavonoid (epicatechin) [31]. To the best of our knowledge the antibacterial activity of the ethanolic extract of fruits of this plant and some of its isolated compounds has not yet been well established. In the course of our ongoing search for potent bioactive compounds from Cameroonian medicinal plants [32-33], the chemical constituents and antibacterial activity of EtOH extract from the fruits of *F. sur* were investigated.

Methods

General experimental procedure

For this study, ethanol was used for the extraction of the plant material meanwhile *n*-hexane, dichloromethane, ethyl acetate and methanol were used as pure or binary mixtures at different polarities for the purification of compounds. Column chromatography (CC) was performed using silica gel (230-400 mesh) or Sephadex LH-20. Thin-layer chromatography (TLC) was performed on Merck pre-coated silica gel (60 F_{254}) aluminium foil (Merck). Compound spots were detected by spraying the plate with diluted sulfuric acid (20%) or ceric sulfate before heating at about 100 °C or by visual inspection under UV lamp at 254 nm and 366 nm. 1D and 2D NMR spectra were recorded on Advance NEO spectrometers operating at 400 or 500 MHz for ^{1}H and 100 or 125 MHz for ^{13}C. Chemical shifts (δ) were expressed in ppm with reference to the TMS. EIMS spectra were obtained on a JEOL 600-H1 mass spectrometer, operating in the positive mode.

Plant material

The fruits of *F. sur* Forssk were collected in Bafoussam (West region of Cameroon) in March 2020. The plant was kindly identified by Mr. Tchatchouang Ngansop Eric, a Botanist at the Cameroon National Herbarium (Yaounde, Cameroon) by comparison with the voucher specimen kept under the number 21654/SFR/CAM.

Extraction and isolation

The air-dried and powdered of fruits of *F. sur* Forssk (600 g) was macerated with 5 L of ethanol three times at room temperature (about 27°C) for 48 h each. The extract was freed from solvent under vacuum at low temperature (40°C) to afford 19 g of crude extract (CE). Part of this extract (18 g) was subjected to column chromatography (CC) over silica gel (Merck, 230-400 mesh) eluting with gradient mixtures of n-hexane-EtOAc, and EtOAc-MeOH. One hundred and ten (110) fractions of 250 mL each, were collected and combined according to their TLC profiles to afford four major fractions labelled FA (4 g ; *n*-hexane/EtOAc, 100:0-90:10, *v/v*), FB (3.5 g ; *n*-hexane/EtOAc, 90:10-40:60, *v/v*), FC (3 g ; EtOAc/MeOH, 100:0-80:20, *v/v*) and FD (5 g ; EtOAc/MeOH/ 80:20-0:100, *v/v*). Compound **9** (18.2 mg; *n*-hexane/EtOAc, 9.5:0.5, *v/v*) precipitated from the fraction B. Fraction A (3.5 g) was subjected to CC over silica gel (Merck 230-400 mesh), eluting with *n*-hexane/EtOAc mixture by increasing polarities. This resulted in the isolation of **1** (10 mg; *n*-hexane/EtOAc, 9.5:0.5, *v/v*) and **3** (10 mg; *n*-hexane/EtOAc, 9.7:0.3, *v/v*). Fraction B (3.0 g) was also purified by open CC over silica gel as stationary phase and eluted with a gradient of *n*-hexane/EtOAc (100:0-50:50, *v/v*) to afford **6** (10 mg ; n-hexane/EtOAc, 9.5:0.5, *v/v*), **2** (40 mg ; *n*-hexane/EtOAc, 9:10, *v/v*), **4** (30 mg ; *n*-hexane/EtOAc, 9.5:0.5, *v/v*) and **5** (30 mg ; *n*-hexane/EtOAc, 9.5:0.5, *v/v*). Fraction C (2.5 g) was purified by open CC over silica gel as stationary phase and eluted with a gradient of *n*-hexane/EtOAc (80:20-20:80, *v/v*) followed by (EtOAc/MeOH 80:20-0:100, *v/v*) to afford 80 subfractions of 75 mL each. These subfractions were collected and combined according to their TLC profiles into three major subfractions labelled FC1, FC2 and FC3. Subfraction FC2 (30 mg) was further subjected to Sephadex LH-20 purification with CH_2Cl_2/MeOH (50:50, *v/v*) to yield **7** (15 mg; CH_2Cl_2/MeOH 50:50, *v/v*). Subfraction FC3 (80 mg) was further subjected to CC over silica gel eluted with a gradient of *n*-hexane/EtOAc (80:20-20:80, *v/v*) and (EtOAc/MeOH 80:20-0:100, *v/v*) to afford **8** (12 mg; *n*-hexane/EtOAc, 80:20, *v/v*). Compound **10** (90 mg; EtOAc/MeOH, 90:10, v/v) precipitated from fraction FD.

Bacteria strains and conservation

The microorganisms tested included two resistant strains [*Pseudomonas aeruginosa* ATCC0032 (*P. aeruginosa*) and *Staphylococcus aureus* ATCC25923 (*S. aureus*)] [34] and three resistant clinical isolates obtained from the Medical Bacteriology Laboratory of "Centre Pasteur", Yaoundé, Cameroon [*Klebsiella pneumoniae* 008 (*K. pneumoniae*), *Escherichia coli* 009 (*E. coli*) and *Salmonella typhi* 001 (*S. Typhi*)]. The microorganisms were preserved at -18°C on Mueller Hinton Agar (MHA) (OXOID, Denmark) and subcultures were freshly prepared before use. Mueller Hinton Broth (MHB) (OXOID, Denmark) was used as the basic enrichment medium for aerobic culture at 37°C with stirring at 150 rpm in the various tests.

Preparation of bacterial inocula

A fresh 18 h bacterial colony was taken from MHA and suspended in 0.9% sterile saline to reach a concentration of 1.5 × 10^8 colony-forming unit/mL (CFU/mL) corresponding to a 0.5 McFarland turbidity standard. These bacterial suspensions were then diluted with MHB to get a cell concentration of 1.5 × 10^6 CFU/mL.

Antibacterial assay

The antibacterial activity of the crude ethanol extract (CE), four fractions (FA, FB, FC, and FD), and eight pure compounds (**1-8**) was determined against two strains and three clinical isolates multidrug-resistant bacteria as reported by Mativandlela et al. [38]. Briefly, the samples were dissolved in 2% tween 20/MHB (*v/v*) and serially diluted twofold in a 96-well microplate previously loaded with 100 µL of MHB. Then, 100 µL of inoculum (1.5 × 10^6 CFU/mL) prepared in MHB was added to each well and the final concentrations of the samples ranged from 0.5 to 1024 µg/mL. The antibiotic chloramphenicol (CHL) and the vehicle (2% tween 20) were used as the positive and negative controls respectively. After mixing the bacterial cells with the samples, they were incubated at 37°C for 18 h, after which 40 µL of 0.2 mg/mL p-iodonitrotetrazolium chloride (INT) (Sigma Aldrich, Germany) was added to each well, followed by incubation at 37°C for 30 min. Viable bacteria reduced the yellow dye to pink and the lowest concentration of the sample that completely inhibited bacterial growth was considered as the minimal inhibitory concentration (MIC). To measure the minimal bactericidal concentration (MBC) values, 50 µL of the sample-treated cells, which did not show any visible colour change during MIC determination, into 150 µL of fresh MHB medium [35]. These mixtures were incubated at 37°C for 48 h. The sample concentrations to which no colour change was observed after the addition of INT were considered as bactericidal concentrations, and the lowest one was recorded as the MBC. These antibacterial tests were conducted in triplicate.

The Kuete [36] scale was used to compare MICs obtained from herbal extracts, fractions, and pure compounds. According to this scale, the antibacterial activity of a plant extract or derived fraction is low if MIC>625 µg/mL, moderate if 100<MIC≤625 µg/mL or significant if MIC≤100 µg/mL. For antibiotics and isolated compounds, sample with MIC≤10 µg/mL, 10<MIC≤100 µg/mL or MIC>100 µg/mL is considered to have significant, moderate, or low activity respectively. Gatsing and Adoga [37] rating scale was also used to determine the bactericidal and bacteriostatic potency of extracts, fractions, and pure compounds. Thus, when the MBC/MIC ratio ≤ 4, the extracts, fractions, and pure compounds are bactericidal, and when the MBC/MIC ratio > 4, the extracts, fractions, and pure compounds are bacteriostatic.

Results

The structures of the isolated compounds were determined by means of spectroscopic and spectrometric data and comparison of recorded data to those of reported compounds in the literature. They were identified as : 11-oxo-*β*-amyrin acetate (**1**) [38], olean-12-en-3-one (**2**), *β*-amyrin palmitate (**3**), *β*-amyrin (**4**) [39], *β*-amyrin acetate (**5**) [40], lupeol acetate (**6**) [31], Ergosterol peroxide (**7**) [9, 41], (22*R*)-3*β*-stigmast-5-ene-3,22-diol (**8**) [42-43], *β*-sitosterol (**9**) [5] and *β*-sitosterol 3-O-*β*-D-glucopyranoside (**10**) [44] (Figure 1).

MS and NMR data of the isolated compounds

11-oxo-β-amyrin acetate (**1**) : white powder; mp 259-260°C ; EI-MS m/z (rel. int. %): 482 $(M)^+$ (37.7), 467 $(M\text{-}CH_3)^+$ (7.2), 423 $(M\text{-}OAc)^+$ (11.6), 422 (17.0), 407 (21.0), 273 (100.0), 232 (91.3), 217 (17.4), 175 (37.7), 135 (55.8); ^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm) 5.52 (1H, s, H-12), 4.50 (1H, dd, *J* = 4.0, 12.0 Hz, H-3), 2.75 (1H, m, H-2), 2.32 (1H, s, H-18), 2.09 (3H, s, H-32), 1.27 (3H, s, H- 27), 1.17 (3H, s, H-25), 1.15 (3H, s, H-26), 0.93 (3H, s, H-29), 0.86 (3H, s, H- 24), 0.86 (3H, s, H-30), 0.79 (3H, s, H-23), 0.78 (3H, s, H-28).

Olean-12-en-3-one (**2**): white powder; mp 166-167°C ; EI-MS m/z (rel. int. %): 424 $(M)^+$ (18.3), 409 $(M\text{-}CH_3)^+$ (11.3), 218 (100.0), 205 (11.2),189 (20.1); ^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm) 5.13 (1H, t, *J* = 4.0 Hz, H-12), 2.53 (1H, m, H-2a), 2.36 (1H, m, H-2b), 1.08 (3H, s, H-23), 1.06 (6H, s, H-24 and H-25), 1.04 (6H, s, H-26 and H-28), 0.89 (3H, s, H-29 and H-30), 0.79 (3H, s, H-27).

β-Amyrin palmitate (**3**): colourless oil; EI-MS m/z (rel. int. %): 664 $(M)^+$ (3.6), 649 $(M\text{-}CH_3)^+$ (1.5), 409 (6.7), 218 (100.0), 203 (19.8), 189 (15.6) ; ^{1}H-NMR (500 MHz, $CDCl_3$): δ (ppm) 5.27 (1H, bs, H-12), 4.48 (1H, t, *J* = 9.0 Hz, H-3), 2.28(2H, *J* = 9.0 Hz, H-2'), 1.60 (2H, m, H-3'), 1.26-1.23 (24H, m, H-4'-H-15'), 1.10 (3H, s, H-27), 0.99 (3H, s, H-26), 0.95 (3H, s, H-25), 0.94 (3H, s, H-26), 0.89 (3H, s, H-16'), 0.86 (3H, s, H-30), 0.85 (6H, s, H-29 and H-28), 0.82 (3H, s, H-24), 0.70 (3H, s, H-23).

β-Amyrin (**4**): white powder; mp 187-190°C ; EI-MS m/z (rel. int. %): 426 $(M)^+$ (7.1), 411 $(M\text{-}CH_3)^+$ (4.4), 218 (100.0), 203 (58.9),189 (35.5), 175 (14.7); ^{1}H-NMR (500 MHz, $CDCl_3$): δ (ppm) 5.16 (1H, t, *J* = 3.5Hz, H-12), 3.20 (1H, m, H-3), 1.95 (1H, m, H-9), 1.89 (1H, m, H-18), 1.11 (3H, s, H-27), 0.98 (3H, s, H-24), 0.94 (3H, s, H-26), 0.92 (3H, s, H-25), 0.85 (6H, s, H-29 and H-30), 0.81 (3H, s, H-28), 0.77 (3H, s, H-23).

β-amyrin acetate (**5**) : white powder; mp 224-226^{0}C, EI-MS m/z (rel. int. %): 486 $(M)^+$ (6.9), 453 (2.9), 408 $(M\text{-}OAc)^+$ (2.2), 393 (2.1), 218 (100.0), 203 (26.6), 189 (20.6); ^{1}H-NMR (500 MHz, $CDCl_3$): δ (ppm) 5.11 (1H, m, H-12), 4.48 (1H, m, H-3), 2.03 (3H, s, H-32), 1.05 (3H, s), 0.83 (3H, s), 0.99 (3H, s), 0.96 (3H, s), 0.86 (6H, s), 0.85 (3H, s), 0.78 (3H, s).

lupeol acetate (**6**) %): white powder; EI-MS m/z (rel. int. %): 486 $(M)^+$ (12.9), 453 (5.4), 408 $(M\text{-}OAc)^+$ (4.5), 393 (6.1), 218 (100.0), 203 (72.6), 189 (20.2); ^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm) 4.66 (1H, bs, H-29b), 4.55 (1H, bd, H-29a), 4.45 (1H, m, H-3), 2.36 (1H, m, H-18), 2.02 (3H, s, H-32), 1.66 (3H, s H-30), 1.01 (3H, s, H-26), 0.92 (3H, s, H-27), 0.83 (3H, s, H-23), 0.82 (3H, s, H-24), 0.81 (3H, s, H-25), 0.78 (3H, s, H-28).

Ergosterol peroxide (**7**) : white powder ; 179-182°C ; EI-MS m/z (rel. int. %): 428 $(M)^+$ (8.7), 410 $(M\text{-}OH)^+$(11.6), 396 (14.5), 396 (14.5), 377 (14.5), 285 (21.8), 152 (36.4) ; ^{1}H-NMR (500 MHz, $CDCl_3$): δ (ppm) 6.48 (1H, d, *J* = 8.5 Hz, H-7), 6.22 (1H, d, *J* = 8.5 Hz, H-6), 5.19 (1H, dd, *J* = 7.5, 15 Hz, H-22), 5.12 (1H, dd, *J* = 8.5, 15.5 Hz, H-23), 3.94 (1H, m, H-3), 0.98 (3H, d, *J* = 7.0 Hz, H-21), 0.89 (3H, d, *J* = 7.0 Hz, H-28), 0.86 (3H, s, H-19), 0.81 (3H, s, H-18), 0.80 (3H, d, *J*=8 Hz, H-26), 0.79 (3H, d, *J* = 7.0 Hz, H-27).

(22R)-3*β*-stigmast-5-ene-3,22-diol (**8**) : white powder; EI-MS m/z (rel. int. %): 430 (M)+ (10.2), 412 $(M\text{-}OH)^+$(17.0), 302 (100), 284 (72.6), 269 (65.9), 255 (23.7), 213 (59.0), ^{1}H-NMR (500 MHz, $CDCl_3$): δ (ppm) 5.33 (1H, d, *J* = 5.0 Hz, H-6), 3.70 (1H, m, H-22), 3.50 (1H, m, H-3), 1.23 and 1.03 (2H, m, H-23), 0.99 (3H, s, H-19), 0.90 (3H, d, *J* = 7.0 Hz, H-21), 0.88 and 0.87 (6H, d, *J* = 7.0 Hz , H-27 and H-26), 0.78 (3H,d, *J* = 7.0 Hz, H-29), 0,69 (3H, s, H-18).

β-Sitosterol (**9**): white powder; EI-MS m/z (rel. int. %): 414 $(M)^+$ (100), 399 $(M\text{-}CH_3)^+$ (57.6), 396 (76.2), 381 (69.1), 329 (66.4), 303 (93.7), 273 (52.1), 255 (79.8), 231 (51.9), 213 (96.1); ^{1}H-NMR (500 MHz, $CDCl_3$): δ (ppm) 5.33 (1H, d, *J* = 5.0 Hz, H-6), 3.50 (1H, m, H-3), 0.99 (3H, s, H-19), 0.90 (3H, d, *J* = 6.6 Hz, H-21), 0.86 (3H, t, *J* = 7.2 Hz, H-29), 0.82 (3H, d, *J* = 6.6 Hz, H-27), 0.79 (3H, d, *J* = 6.6 Hz, H-26), 0.66 (3H, s, H-18).

β-Sitosterol 3-O-*β*-D-glucopyranoside (**10**): white powder; ESI-MS m/z (rel. int. %): ^{1}H-NMR (500 MHz, $CDCl_3$ + CDCL3): δ (ppm) 5.29 (1H, d, *J* = 5.0 Hz, H-6), 4,36 (1H, d, *J* = 7.9 Hz, H-1'), 3.78 and 3.70 (1H, m, H-6'), 3.50 (1H, m, H-3), 3.39 (1H, m, H-5'), 3.38 (1H, m, H-4'), 3.21 (1H, m, H-2'), 3.16 (1H, m, H-3'), 0.93 (3H, s, H-19), 0.85 (3H, d, *J* = 6.6 Hz, H-21), 0.79 (3H, t, *J* = 7.2 Hz, H-29), 0.73 (3H, d, *J* = 6.6 Hz, H-27), 0.77 (3H, d, *J* = 6.6 Hz, H-26), 0.62 (3H, s, H-18).

The minimal inhibitory concentrations and minimal bactericidal concentrations were determined on the crude ethanolic extract, fractions, and compounds isolated from *F. sur* fruits against some resistant bacteria (Table 1). The crude extract showed significant activity against *S. typhi* (MIC = 64 µg/mL) and moderate activities against other microorganisms tested. While fraction A which is the best of all fractions showed significant activities against *E. coli* (MIC = 16 µg/mL) and *S. typhi* (MIC = 64 µg/mL). The isolated compounds showed variable activities (32 ≤ MIC ≤ 512 µg/mL) on all bacteria tested. Among them, moderate activities have been observed with *β*-amyrin palmitate (**3)** against *S. typhi* (MIC = 32 µg/mL) and *β*-Amyrin acetate (**5)** against *E. coli* (MIC = 64 µg/mL) and *K. pneumoniae* (MIC = 64 µg/mL). Expected fraction FA, which is bacteriostatic against *S. aureus* (MBC/MIC = 8); *β*-amyrin palmitate (**3**), *β*-Amyrin acetate (**5**), and fraction FA are bactericidal against all germs tested (MBC/MIC ≤ 4).

Discussion

Ficus species are rich sources of bioactive secondary metabolites such as flavonoids, stilbenes, triterpenoids, xanthones, ceramides, cerebrosides, steroids, and phenolic compounds [5, 6, 29-30, 45-46]. Ten compounds (**1-10**) (Fig. 1) are herein reported from the fruits of *F. sur* belonging to both pentacyclic triterpenes including oleanane (**1-5**) and lupane (**6**) type skeletons and steroids (**7-10**). Eight of the isolates mainly compounds **1-4**, **6**-**8**, and **10** are reported hereby for the first time from this species. However, 11-oxo-*β*-amyrin acetate (**1**) has been previously detected by GC-MS in *Dorstenia arifolia* Lam. (Moraceae) [47] and isolated from the fruits of *F. pandurata* [48]. While olean-12-en-3-one (**2**), *β*-amyrin palmitate (**3**) and *β*-amyrin (**4**) were previously isolated from the figs of *F. vallis-choudae* Delile by Bankeu et al. [39]. *β*-amyrin palmitate (**3**) was also obtained from the fruits of *Ficus aurata* [49]. Likewise, *β*-amyrin acetate (**5**) has been isolated from *Ficus sur* [40], lupeol acetate (**6**) was isolated from the stem bark of *F. burtt-davyi* [50], *F. carica* [51], *F. thonningii and F. pumila* [52] and the steroid ergosterol peroxide (**7**) was evidenced in the roots of *F. nervosa* [9]. The latter has also been highlighted from the trunk bark and leaves of *Baphia leptobotrys* Harms (Fabaceae) [41], from the fruits of *Enterolobium contortisiliquum* (Vell.) Morong (Caesalpinioideae) [53] and from *Fungus Aspergillus* sp. EJC 04 (Trichocomaceae) [54]. We report hereby for the first time the occurrence of the steroid (22*R*)-3*β*-stigmast-5-ene-3,22-diol (**8**) from the *Ficus* genus. It has however been reported from *Aphanamixis grandifolia* Bl. (Meliaceae) [55] and *Thelocactus bicolor* (Cactaceae) [43]. The *β*-sitosterol (**9**) and its 3-*O*-glucoside (**10**) are considered ubiquitous in the plant kingdom and therefore have been reported in many species of *Ficus* so far [6, 39, 48, 51, 56-60].

According to Kuete [36] scale on medicinal plant, the crude ethanolic extract of F. sur fruits has significant activity against *S. typhi* and moderate activity against *K. pneumoniae, E. coli* and *S. aureus*. The wide range of antibacterial activity presented by this extract could be explained by the qualitative and/or quantitative variation of various groups of potentially active secondary metabolites it contains [61-62]. Indeed, at the molecular level, the different compounds (terpenoids and steroids) isolated from this plant could act in synergy and be partly responsible for the observed activity [63]. The crude extract was split into main fractions, and fractions FA and FB showed significant and moderate activities. The results obtained with the fractions FA and FB could reflect the high concentration of antibacterial compounds in these fractions compared to the fractions FC and FD which showed no activity. It also appears that the activity of the fraction FA was higher than that of the crude extract. This could be due to the low concentration of active metabolites in the crude extract compared to the fraction FA [64] or to the dilution of active metabolites by other inactive metabolites present in the crude extract. The antibacterial activity of plants is linked to the diversity and complexity of their secondary metabolites.

Concerning the isolated compounds, *β*-amyrin palmitate (**3**) and *β*-amyrin acetate (**5**) showed the best antibacterial activities. The differences observed in the activity of these two compounds (**3** and **5**) could be attributed to the acyl group at position 3 of *β*-amyrin (**4**). In some cases, the activity of **5** was higher than that of **1** (11-oxo- *β*-amyrin acetate), which could be due to the oxo group at position 11 of **1**. Except with *E. coli*, *β*-amyrin (**4**) and its 3-keto derivative (**2**) showed the same activity against the other microorganisms. Nevertheless, these compounds showed mostly low or moderate activity compared to the crude extract and the fractions that showed significant activity on some microorganisms. This could be due to the synergistic effect of the compounds with each other when combined in the same extract/fraction [65]. Finally, the overall activities of this plant could be due to the presence of several antimicrobial compounds with moderate activities.

Likewise, the MBC/MIC values were used to define the bactericidal and bacteriostatic potentials of compounds. Thus, according to the classification scale of Gatsing and Adoga [37], our results showed that *β*-amyrin palmitate (**3**), 3-acetoxy-*β*-amyrin (**5**), and the fraction FA exhibited a bactericidal effect on all the tested bacteria, except on *S. aureus* that fraction FA presented a bacteriostatic effect. These results agree with those reported by Ramde-Tiendrebeogo et al. [66], Kuete et al. [65], and Aref et al. [67] which showed similar effects on crude extracts of *Ficus sur* Forssk. and *Ficus sycomorus* L. and secondary metabolites of Ficus *polita* Vahl. and *Ficus carica* L. respectively.

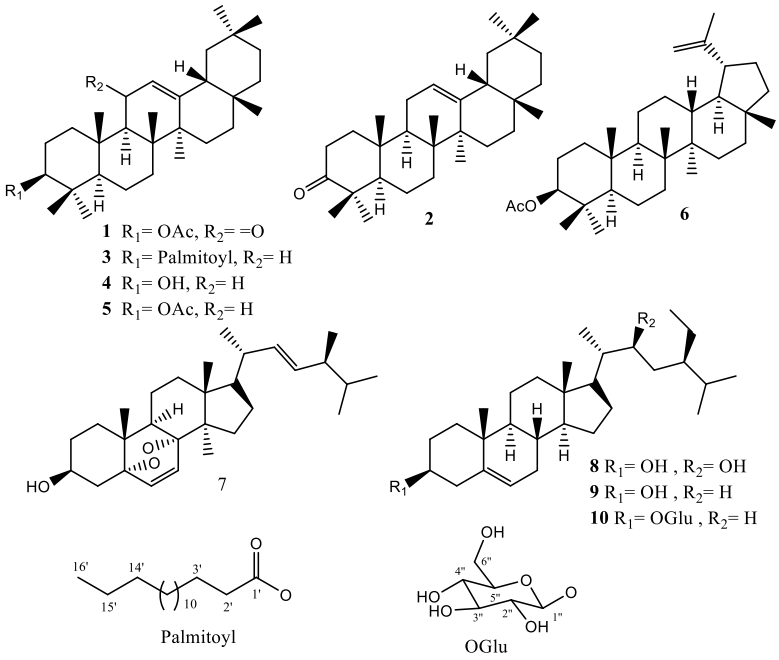

Figure 1. Chemical structures of isolated compounds (**1**-**10**) from the fruits of *Ficus sur* Forssk

Table 1. MIC and MBC (µg/mL) of crude extract, fractions, and some isolated compounds from the fruits of *F. sur* against resistant bacteria.

Bacteria	Tested samples and MIC and MBC in parenthesis (µg/mL)													
	Crude extract	Factions				Compounds								Reference Drug
	CE	FA	FB	FC	FD	1	2	3	4	5	6	7	8	CHL
Pseudomonas aeruginosa ATCC0032	512 (-)	256 (1024)	1024 (-)	-	-	256 (512)	512 (-)	256 (512)	512 (-)	256 (512)	512 (-)	512 (-)	256(-)	2 (16)
Klebsiella pneumoniae 008	256 (1024)	128 (512)	512 (1024)	-	-	128 (256)	256 (512)	128 (256)	256 (512)	64 (256)	512 (-)	128 (256)	128 (256)	1 (4)
Escherichia coli 009	256 (1024)	16 (32)	256 (512)	-	-	256 (512)	128 (512)	128 (256)	256 (512)	64 (256)	128 (512)	128 (256)	128 (256)	1 (2)
Salmonella Typhi 001	64 (128)	64 (256)	256 (512)	-	-	128 (256)	128 (512)	32 (128)	128 (256)	128 (256)	512 (-)	128 (256)	128 (256)	1(2)
Staphylococcus aureus ATCC25923	128 (256)	128 (1024)	256 (1024)	-	-	256 (1024)	256 (512)	256 (512)	256 (1024)	128 (512)	512 (-)	512 (-)	128 (512)	2 (16)

- : MIC and MBC values above 1024 µg/mL for crude extract and fraction, values above 512 µg/mL for pure compounds. CHL: Chloramphenicol MIC: Minimal Inhibitory Concentrations; MBC: Minimal Bactericidal Concentration

Conclusion

The compounds described in this study enrich the knowledge of the genus *Ficus* in particular and strengthen the natural products database. It provides further information regarding the possible chemotaxonomic markers present in the species *F. sur* Forssk, the genus *Ficus*, as well as the Moraceae family. Eight compounds **1**-**4**, **6**-**8**, and **10** were isolated for the first time from *F. sur* and one (**8**) for the first time from the *Ficus* genus. The antibacterial activity obtained supports the previous antibacterial activity observed with the plants of *Ficus* genus.

Additional file

NMR spectra of the isolated compound. Available at https://www.investchempharma.com/imcp64-supplementary-file/

Abbreviations

CC : Column Chromatography
TLC : Thin-Layer Chromatography
UV : UltraViolet
TMS : Tetra Methyl Silane
MS : Mass Spectrometry
EI : Electron Impact
ATCC : American Type Culture Collection
MIC : Minimal Inhibitory Concentration
MBC : Minimal Bactericidal Concentration
INT : p-IodoNitrotetrazolium chloride
SFR/CAM : Society of Forest Reserve of Cameroon
^{1}H-NMR : Proton Nuclear Magnetic Resonance
CHL : Chloramphenicol
MHA : Mueller Hinton Agar
MHB : Mueller Hinton Broth

Authors' Contribution

FLMD isolated the compounds. FLMD, GTMB and ARDN contributed to compounds identification. GTK carried out the antibacterial activity of samples. FLMD, GTK, ARDN, GTMB and BLN wrote the original draft. FLMD, RF, BLN and ARDN methodology. A-t-W and MT supervised the work. All authors have read and agree to the published version of the manuscript.

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Conflict of interest

The authors declare no conflict of interest

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