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Anti-staphylococcal and antibiotic-potentiating activities of botanicals from nine Cameroonian food plants towards multidrug-resistant phenotypes

Boris Ekamgue, Armelle T. Mbaveng, Victor Kuete*

Abstract

Background: *Staphylococcus aureus* is a commensal and pathogenic bacterium responsible for both community and nosocomial infections, superficial or deep, and benign or lethal. *Staphylococcus aureus* is a commensal and pathogenic bacterium responsible for both community and nosocomial infections, superficial or deep, and benign or lethal. Because of its infectious potential and its ability to develop resistance to many antibiotics, staphylococcal infections remain the target of reinforced clinical surveillance. To contribute to the fight against resistant staphylococcal infections, the *in vitro* assessment of the anti-staphylococcal activity of methanol extracts (or botanicals) of nine food plants from Cameroon, *Persea americana, Psidium guajava, Syzygium jambos, Vernonia amygdalina, Citrus sinensis, passiflora edulis, Carica papaya, Aframomum letestuanum,* and *Garcinia kola*), as well as the effects of the association of some of these botanicals with antibiotics against resistant and multidrug-resistant staphylococci.

Methods: The plant secondary metabolites were extracted by maceration in methanol; the microdilution method using the rapid para-Iodonitrotetrazolium chloride (INT) colorimetric method was applied to evaluate the antibacterial activities of the botanicals as well as the effects of combining these extracts with antibiotics.

Results: The botanicals had a minimum inhibitory concentration (MIC) range of 64-2048 µg/mL on the 17 staphylococcal strains and isolates tested. Extracts from *Aframomum letestuanum* seeds and *Psidium guajava* leaves and bark had the broadest activity spectra, inhibiting the growth of 95% and 85% of the studied bacteria, respectively. In the presence of an efflux pump inhibitor, reserpine, methanol extracts from *Syzygium jambos* leaves, *Psidium guajava* bark and epicarp, and *Afromomum letestuanum* epicarp showed a considerable increase in their activity. Botanicals from the leaves of *Syzygium jambos* improved the activities of tetracycline, ceftriaxone, chloramphenicol, and ampicillin against more than 80% of the tested bacteria.

Conclusion: The investigated pants, mostly *Psidium guajava, Syzygium jambos*, and *Aframomum letestuanum* could be used in the treatment of staphylococcal infections with multidrug-resistant phenotypes.

Keywords: Antibacterial activity; Cameroon; drug resistance; food plants; potentiation; *Staphylococcus aureus*.

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Background

Staphylococci are commensal Gram-positive bacteria found on the skin and mucous membranes, but also in the environment (water, air, soil) and sometimes in food or on objects. There are about forty types of staphylococci, the best known of which is *Staphylococcus aureus*; it is most frequently implicated in nosocomial and community infections. Very widespread, *Staphylococcus* causes a wide variety of diseases in humans, such as food poisoning, paronychia, septicemia, skin and soft tissue infections, endocarditis, osteomyelitis, bacteremia, and lethal pneumonia [1]. *S. aureus* is generally divided into methicillin-sensitive *Staphylococcus aureus* (MSSA) and methicillin-resistant *Staphylococcus aureus* (MRSA). The drug resistance of *S. aureus* has increased, while the infection rate of MRSA has increased globally, with effective anti-staphylococcal agents for MRSA scarcer [1]. This propels scientists to intensify the search for new antibacterial substances as an alternative to certain antibiotics that have become ineffective. Previously some African medicinal plant showed their efficiency on *S. aureus* species. They include *Tridesmostemon omphalocarpoides* [2], *Garcinia smeathmannii* [3], *Dorstenia turbinata* (Moraceae) [4], or *Pycnanthus angolensis* [5, 6]. In our continuous search of new drugs to combat the resistant staphylococcal infections, the present study was designed to evaluate the anti-staphylococcal activity of methanol extracts of nine Cameroonian food plants, as well as the effects of the association of some of these botanicals with antibiotics against resistant and multidrug-resistant staphylococci. The studied plants included *Persea americana* Miller (Lauraceae), *Psidium guajava* Linn. (Myrtaceae), *Syzygium jambos* (L.) Alst. (Myrtaceae), *Vernonia amygdalina* Del. (Asteraceae), *Citrus sinensis* Linn. (Rutaceae), *Passiflora edulis* Sims (Passifloraceae), *Carica papaya* Linn. (Caricaceae), *Aframomum letestuanum* Gagnep. (Zingiberaceae), and *Garcinia kola* Heckel (Guttiferae). Their traditional used are shown in Table 1.

Methods

Plant material and extraction

In the present study, various part of nine food plants from Cameroon were used. They were collected in Dschang (West Region) and Loum (Littoral Region) in Cameroon and identified in the Cameroon national herbarium (HNC) under a reference voucher numbers (Table 1). They are *Persea americana* leaves and bark, *Psidium guajava* leaves and bark (Myrtaceae), *Syzygium jambos* leaves and bark, *Vernonia amygdalina* leave, *Citrus sinensis* leaves and bark, *Passiflora edulis* leaves, *Carica papaya* seeds (Caricaceae), *Aframomum letestuanum* seeds and pulps (Zingiberaceae), and *Garcinia kola* leaves and bark. These plant materials were air-dried, powdered, and soaked in methanol for 48 hours. The filtrate obtained using Whatman filter paper no. 1 was evaporated over a vacuum to yield the crude extract or botanical. The extraction yield or these botanicals were determined (Table 2), and they were were kept at 4°C until further use.

Chemicals

The chemicals used include the bacterial growth indicator, para-Iodonitrotetrazolium chloride ≥97% (INT), ten antibiotics (Ceftriaxone (CRO), Tetracycline (TET), Chloramphenicol (CHL), Ciprofloxacin (CIP), Doxycycline (DOX), Imipenem (IMI), Ampicillin (AMP), Penicillin (PEN), Augmentin (AUG), and Levofloxacin (LEV)), and the efflux pump inhibitor, reserpine (RES). They were all obtained from Sigma-Aldrich (St. Quentin Fallavier). Dimethylsulfoxide (DMSO, Sigma-Aldrich) was used to dissolve the tested samples.

Culture media

Three culture media were used namely Mueller Hinton agar (MHA) for the activation of bacterial strains and isolates, Mueller Hinton broth (MHB) for microdilution tests, and Chapman (Mannitol Salt Agar) for the identification of strains/isolates of *Staphylococcus aureus*. They were purchased at Titan Biotech Ltd (Rajasthan, India). The MHB was used to determine the minimal inhibitory concentrations (MIC) and minimal bactericidal concentrations (MBC) of the studied samples.

Bacterial strains and isolates

The *Staphylococcus aureus* strains tested included the reference American Type Culture Collection (ATCC) strain, ATCC 25923, MRSA3, MRSA4, MRSA6, MRSA8, MRSA9, MRSA11, MRSA12, and nine clinical laboratory strains: ST20, ST39, ST50, ST52, ST76, ST132, ST135, ST218, and ST674. The clinical isolates are available in the Laboratory of Microbiology and Antimicrobial Substances of the University of Dschang. Their bacterial features are shown in Table 2. They were sub-cultured in the MHA for their activation 24 hours prior to any use while the antibacterial testing was done in the MHB.

Antibacterial evaluations

The MIC and MBC determinations on the used bacterial strains were performed using a rapid colorimetric INT test [7-9]. The different plant extracts and the reference drug were dissolved in DMSO-MHB. The bacterial inoculum used was 1.5×10^6 CFU/mL and the incubation conditions were 37°C for 18 h. DMSO with concentrations less than 2.5% was used as the control solvent. MIC was defined as the lowest sample concentration that prevented this change and exhibited complete inhibition of microbial growth. The MBC of the samples was further determined as previously reported [9]. Botanicals were also tested in the presence of reserpine, efflux pump inhibitor, at the concentration of 100 µg/mL to evaluate the role of efflux pumps on the resistance of the bacteria to the samples [10-12]. A preliminary assay was also performed by evaluating a combination of the plant extracts at different sub-inhibitory concentrations (MIC/2, MIC/4, MIC/8, and MIC/16) with antibiotics on ATTC25923 (Data not shown), which allowed us to select the appropriate sub-inhibitory concentration to further potentiate the effect on other bacteria. Therefore, MIC/2 and MIC/4 values were subsequently used for the combination of antibiotics in the sample on a larger number of bacteria [13, 14]. Activity ameliorating factor (AAF) was calculated as the ratio of the MIC of the antibiotic alone versus MIC in the combination with the botanical [15].

Data Analysis

Generally, botanicals were considered significantly active, moderately active, and weakly active when their MIC values were less than 100 µg/mL, between 100 and 625 µg/mL, and greater than 625 µg/mL, respectively; for antibiotics and isolated

compounds, the sample was considered to have strong activity when the MIC value≤ 10 µg/mL, moderate 10 < MIC≤ 100 µg/mL, and weak MIC> 100 µg/mL [16]. For in-depth analyses, the established cutoff point for the antibacterial activity of botanicals towards *Staphylococcus aureus* was used as follows: Outstanding activity: MIC ≤ 8 µg/mL; Excellent activity: 8 < MIC ≤40 µg/mL; Very good activity: 40 < MIC ≤128 µg/mL; Good activity: 128 < MIC ≤ 320 µg/mL; Average activity: 320 < MIC ≤ 625 µg/mL; Weak activity: 625 < MIC ≤ 1024 µg/mL; Not active: MIC values > 1024 µg/mL [17, 18]. The bactericidal or bacteriostatic effect of botanicals was determined using the ratio MBC/MIC [19].

Results

Extraction yield and physical characteristics of botanicals

The characteristics (extraction yields, aspects, and colors) of the botanicals are shown in Table 3. The extraction yields varied between 1.325% and 28.52%. *Syzygium jambos* leaf extract had the highest yield (28.52%) followed by the botanicals from *Citrus sinensis* leaf (18.56%), and *Garcinia kola* bark (17.91%). The extract of *Carica papaya* seeds presented the lowest yield (1.325%). Most of the botanicals were obtained as a paste, with a green color.

Antibacterial activities of botanicals

The evaluation of the antibacterial activity of the botanicals was carried out by determining the MIC and the MBC of each extract against 17 bacterial strains and isolates. To determine whether the various extracts had bacteriostatic or bactericidal effects, the MBC/MIC ratios were calculated, and all the results are summarized in Table 4. Botanicals tested on the different bacterial isolates and strains did not all have activities and the inhibition effects varied from 64 to 2048 µg/mL. Several botanicals had a spectrum of activity of 100%, including the extract of the leaves and the bark of *Persea americana* (17/17), the extract of the leaves and the bark of *Psidium guajava* (17/17), *Syzygium jambos* leaf and bark extract (17/17), *Afromamum letestuanum seed* and pulp extract (17/17). *Carica papaya* seed extract had no activity (0%) against the different strains and isolates tested. The other extracts showed percentage inhibitions ranging from 17.64 to 94.15%. The extracts of the seeds and pulp of *Aframomum letestuanum*, of the bark of *Psidium guajava* showed the best activities with MICs of 64 µg/mL against the ST35 isolate. Botanicals from the leaves of Psidium guajava and leaves of *Syzygium jambos* displayed MIC values of 128 µg/mL on ST35 and ST76. Fourteen (14) extracts had a bactericidal effect varying from one isolate to another. *Syzygium jambos* leaf extract showed the most bactericidal effect with a total of (13/17) followed by *Aframomum letestuanum* seeds with a total of (12/17) on the isolates and strain tested. Some extracts exhibited bacteriostatic effects among the sixteen (16) extracts; it is the *Aframomum letestuanum* pulp extract with a bacteriostatic effect against ST isolates (ST30, ST39, ST52, ST132, ST135, ST218, ST674).

Effect of reserpine on the activity of Botanicals

The evaluation of the antibacterial activity of some extracts was carried out by determining the MIC of the latter in the absence and in the presence of Reserpine, an inhibitor of efflux pumps, against 5 bacterial strains to highlight if the pumps are responsible for their resistant phenotypes (Table 5). It appears that reserpine potentiates the activity of all botanicals extracts and the antibiotic with increased AAF ranging from 2 to >128-folds. An antibacterial potential ranging from 2 to 64 µg/mL of the extracts is observed in the presence of reserpine while, in the absence of the latter, the antibacterial activity is between 256 to 2048 µg/mL. This improved activity in the presence of reserpine confirms that the tested bacterial strains and isolates use the efflux mechanism as one of the means of resistance.

Effects of the combinations of antibiotics with botanicals

A preliminary test was carried out on the strain ATCC25923 to select the plant extracts to combine with the antibiotics. It was found that among the 14 plant extracts used, eight (08) of them best potentiated the activities of the antibiotics at the sub-inhibitory concentrations of MIC/2 and MIC/4 vis-a-vis the strain ATCC25923. These are extracts of the leaves and bark of *Syzygium jambos* and *Psidium guajava*, the leaves of *Garcinia Kola*, *Passiflora edulis*, *Vernonia amygdalina*, and the pulps of *Aframomum letestuanum* (Data not shown). These eight plant extracts were used in combination with antibiotics against seven (07) other bacterial isolates; the results obtained have been recorded in Table 6.

In general, the activities of the antibiotics increased in the presence of the botanicals. Several cases of synergy were recorded with increase AAF values varying from 2 to 128-folds; However, some cases of antagonism and indifference were also observed. The pulp extracts of *Aframomum letestuanum*, leaves and bark of *Psidium guajava* and *Syzygium jambos* potentiated the activity of all antibiotics vis-a-vis 100% isolates tested. The activity of CHL on the tested bacteria increased in the presence of all the extracts with a potential ranging from 57.14% to 100%. The activity of CRO in the presence of the leaves of *Garcinia kola*, *Passiflora edulis*, *Vernonia amygdalina* and *Syzygium jambos* increased on 42.85% of the tested bacteria, and on 100% in the presence of seeds of *Afromamum letestuanum*, as well as the leaves and bark of *psidium guajava* and *Syzygium jambos*.

Discussion

The importance of African medicinal plants as a source of bioactive agents to tackle the resistant phenotypes of bacteria, cancer cells, or plasmodia has been well-documented in the recent years [8, 20-33]. In the present study, a panel of ten plant extracts has been explored for its antibacterial properties against *Staphylococcus aureus*. In regard to the available standards for the classification of the antibacterial substances from plants [16-18], it appears that three of the extracts had significant or very good antibacterial activity. These include the botanicals from the epicarp of *Afromomum letestuanum* (64 µg/mL) on ST39, ST135, that of the leaves of *Psidium guajava* and seeds of *Afromomum letestuanum* (64 µg/mL) on ST135. There are also very good activities (128 µg/mL) of the extracts of the seeds of *Afromomum letestuanum*, and the leaves and bark of *Syzygium jambos*. The antibacterial activity of the aqueous and organic extracts of guava leaves against antibiotic-resistant clinical isolates of Staphylococcus aureus strains has been previously reported (Milyani et al., 2012). The data reported corroborates with that of the present study, therefore, confirming the antibacterial activity of *Psidium guajava* leaf extract. This activity could be due to the presence of phytochemicals such as tannins, myricetin, quercetin, luteolin, kaempferol, oleanolic, ursolic, catecolic, guayavolic, maslinic, and ellagic acids, and *β*-sitosterol [34]. The extract of the leaves of *S.*

jambos showed good to average antimicrobial activity on 29% of the strains tested, confirming the antimicrobial activity of this plant reported by Wamba et al. [35] on Gram-positive bacteria. One of the constituents of this plant, myricetin [36] inhibited the growth of methicillin-resistant *S. aureus* [37]. This compound can be the active anti-staphylococcal principle of this plant. The seed and epicarp extracts of *A. letestuanum* were very active against the tested bacteria. It has been shown that plants of the genus *Aframomum* have antibacterial activities which have been attributed to the presence of terpenoids such as aframodial [38]. These results, therefore, can justify the activity obtained herein. Extracts of *Persea americana* leaves and bark showed moderate activities ranging from 256 to 1024 µg/mL against different bacterial strains and isolates. To confirm its multiple medicinal properties, a study conducted by Nathaniel et al. [39] showed that the methanolic extract of *P. americana* leaves had good antimicrobial activity against enteric microorganisms (Gram-negative bacteria and Gram-positive as well as yeasts). This, therefore, corroborates the anti-staphylococcal activity obtained in the present study. The other extracts showed weak activities vis-a-vis some strains and isolates, namely the extract of leaves of *Citrus sinensis, Passiflora edulis*, and *Vernonia amygdalina*, while the extract of the seeds of *Carica papaya* showed a weak activity against all isolates and strains tested. The absence or low activity of these extracts could be attributed either to the multidrug-resistant features of the bacterial strains tested. In this work, we observed in most cases that the MBCs are generally 4-fold higher than the MICs, or even more. This is an indication that the tested botanicals mostly had bacteriostatic effects [19].

The association of the extracts with the efflux pump inhibitor, reserpine, considerably improved their activity against 100% of the strains and isolates tested [40]. Reserpine also improved the activity of CIP, confirming that the tested bacteria use efflux pumps as a means of resistance. In effect, Gibbons et al. have demonstrated that reserpine reverses NorA-mediated resistance in S. aureus by increasing norfloxacin activity up to 4-fold [41]. Synergistic effects of botanicals in association with antibiotics were obtained, with the AAF ranging from 2 to 128. Botanicals from *Aframomum letestuanum* pulp, leaves, and bark of *Psidium guajava*, and *Syzygium jambos jambos* had synergistic effects with most of the antibiotics tested against 98.5% of the isolates. This suggests that botanicals probably inhibited the efflux pumps, increasing the activity of these antibiotics [42, 43] or simultaneously acting as the active principle with a different site of action, to potentiate the activity of the antibiotic.

Table 1. Information on the tested plants

Tested plants (Family)/Herbarium voucher number	Traditional uses	Active or potentially active constituents	Reported activity of crude extract
Citrus sinensis Linn. (Rutaceae)/ 25859/HNC	Constipation, cramps, colic, diarrhea, bronchitis, tuberculosis, cough, cold, obesity, menstrual disorder, angina, hypertension, anxiety, depression, and stress, sore throats, indigestion, relieve intestinal gas and bloating, resolve phlegm, and additive for flavoring [44]	Caffeic, *p*-coumaric, ferulic, and sinapinic acids, hesperidine, narirutin, naringin, eriocitrin [45]; essential oil [46]; 5-hydroxy-3,7,8,3′,4′-pentamethoxyflavone; 5-hydroxy-3,6,7,8,3′,4′-hexamethoxy-flavone; 3,5,6,7,8,3′,4′-heptamethoxyflavone; nobiletin; 3,5,6,7,3′,4′-hexamethoxyflavone; 3′-hydroxy-5,6,7,8,4′-pentamethoxyflavone; 4′-hydroxy-5,6,7,8,3′-pentamethoxyflavone, and hesperidin [47]	Antibacterial, antifungal, antiproliferative, anxiolytic, antimalarial, anti-Trypanosoma, anti-obesity, antiosteoporosis, and insecticidal activities [13, 48-56]; relaxant and sedative effect on dental patients [57], reduce the risk of adverse cardiovascular events [58], and inotropic depression on the atria of guinea pigs [59]; hypocholesterolemia activity [60]
Psidium guajava Linn. (Myrtaceae)/ 2884/SRF/Cam	Wounds, lesions, ulcers, diarrhea, cholera, hypertension, obesity and the control of diabetes mellitus, inflammation, cough, diabetes, kidney problems, diarrhea, used as tonic, laxative, anthelminthic, conjunctivitis, oral care, and antispasmodic [13, 61, 62]	Tannins, myricetin, quercetin, luteolin, kaempferol, essential oil, oleanic, ursolic, catecolic, guayavolic, maslinic, and ellagic acids, and *β*-sitosterol [34]	Anti-inflammatory, antiproliferative, antibacterial and antifungal, anti-diabetic, analgesic, antinociceptive, antimalarial, antitussive, hepatoprotective, anti-allergic, hypotensive, cardioprotective, and wound healing activities [13, 63, 64] [61-63, 65-67] [68-73]
Garcinia kola Heckel (Guttiferae)/ 278 39/SRF-CAM	Nervous alertness and induction of insomnia, purgative, wound healing, cancer, stomachache, gastritis, malaria, venereal diseases, laryngitis, and poison antidote [74]	3'',4',4''',5,5'',7,7''-heptahydroxy-3,8-biflavanone or GB-1; 3″,4′,4‴,5,5″,5‴,7,7″-octahydroxy-3,8″- biflavanone or GB-2; 3″,4′,4‴,5,5″,5‴,7,7″ octahydroxy-4‴-methoxy-3,8″-biflavanone) or kolaflavanone; GB-1a; biflavonoid complex kolaviron [75, 76]; 9,19-Cyclolanost-24-en-3-ol; 9,19-cyclolanostan-3-ol,24-methylene [76]; *δ,δ*-bigarcinoic acid; *δ,δ*-bi-*O*-garcinoic acid; *γ,δ*-bi-*O*-garcinoic acid; (8*E*)-4-geranyl-3,5-dihydroxybenzophenone [77]; cytochalasins: 18-metoxycytochalasin J; cytochalasins H and J; and alternariol [78]	Anti-inflammatory, diabetic, analgesic, antibacterial, antiproliferative, antimalarial, antiplasmodial, anti-diabetic, hepatoprotective, nephroprotective, antinociceptive, neuroprotective, gastroprotective, and antiparasitic activities [79], [74, 80-82], [76, 83-91]; protection effect of kolaviron against testicular oxidative damage induced by di-n-butylphthalate in rats [92]
Vernonia amygdalina Del. (Asteraceae)/ 31149/SRFK	Microbial infections, hiccups, kidney problems and stomach, discomfort, stomach-ache, gastrointestinal infections, malarial fever, cough remedy [93], malaria, purgative, parasitic infections, blood glucose levels control, and eczema [94]	Vernodalin, vernomygdin, vernonioside B1 and vernoniol B1 [95]; ricosane; vernolide; isorhamnetin; luteolin [96]; vernonioside V [97]; steroidal vernoniamyoside A-D; vernoamyoside D, vernonioside B_2 vernoamyoside [98, 99]; nicotinic acid; cumidine; salicylic acid; isoquinoline; 3-methyl-, and γ-octalactone [100]; vernolide, and vernodalol [101]	Anti-inflammatory, antibacterial, antiproliferative, antimalarial, neuroprotective, antinociceptive, and anti-diabetic activities [97], [94, 96, 102-104]; [100, 105-108]

HNC: Cameroon national Herbarium

Table 1. *(Continued and end)*

Tested plants (Family)/Herbarium voucher number	Traditional uses	Active or potentially active constituents	Reported activity of crude extract
Carica papaya Linn. (Caricaceae)/ 18647/SRF-CAM	Gastro-enteritis, oxidative stress, intestinal worms, hepatitis, cancer, contraceptive, used to treat malaria, hypertension, diabetes mellitus, jaundice, intestinal helminthiasis, used for colic, fever, beriberi, abortion, asthma, eczema, psoriasis, thirst quencher, or pain alleviator [74, 81]	Caffeic, cinnamic, Chloramphenicolorogenic, quinic, coumaric, vanillic, protocatechuic acids; naringenin; hesperidin; rutin; kaempferol [109]; myricetin; carpaine; carpine; pseudocarpaine; dehydrocarpaine I and II; ferulic acid; caffeic acid; Chloramphenicolorogenic acid; *β*-carotene; lycopene; anthraquinones glycoside; kaempferol rhamnosides, orientin 7-*O*-rhamnoside; 11-hydroperoxy-12,13-epoxy-9-octadecenoic acid; palmitic amide; 2-hexaprenyl-6-methoxyphenol [110]; campesterol, sitosterol; squalene; phytol [111]	Anti-inflammatory, antibacterial and antifungal, antiproliferative, immunomodulatory, insecticidal, anti-parasitic, anti-ulcerogenic, contraceptive, and wound healing activities [74, 112-122]
Passiflora edulis Sims (Passifloraceae)/ 65104/HNC	Anxiety, insomnia, nervousness, antifungal, anti-inflammatory, antihypertensive [123], gastric trouble [124], cancer [125], tonic, digestive, sedative, diuretic, antidiarrheal, insecticide, cough, dry throat, constipation, insomnia, dysmenorrhea, colic infants, joint pain, and dysentery [126]	Ionone-I, ionone-II, megastigma-5,8-dien-4-1, megastigma-5,8(*Z*)-diene-4-1, 4,4*a*-Epoxy-4, 4*a*-dihydroedulan, 3-hydroxyedulan, edulan-I, edulan-II, passifloric acid methyl ester [125]; luteolin, apigenin, quercetin and its derivatives, rutin, 4-hydroxybenzoic, Chloramphenicolorogenic, ferulic, vanillic, caffeic, trans-cinammic, *p*-coumaric acids, vanillic acid [126]; harmidine, harmine, harmane, harmol, *N*-trans-feruloyltyramine, and *cis*-*N*-feruloyltyramine [126, 127]	Anti-inflammatory, antibacterial, antiproliferative, anti-diabetic, analgesic, anxiolytic, anti-depressant, anti-hypertensive, hepatoprotective, and anti-hyperlipidemia activities [128-134]; [123, 135-140]
Persea americana Miller (Lauraceae)/ 57756 HNC	Worms, microbial infections, malaria, diabetes, high blood pressure, stimulate uterine contractions and relief painful menstruations, urinary infections, bronchitis, rheumatism, anemia, exhaustion, hyper-cholesterolemia, hypertension, gastritis, and gastroduodenal ulcer, cancer, food, analgesic, as anti-inflammatory, hypoglycemic, anticonvulsant, and vasorelaxant [141-143]	Kaempferol, quercetin 3-*O*-*α*-$_{D}$-arabinopyranosides, afzelin, quercitrin, quercetin 3-*O*-*α*-glucopyranoside, quercetin, quercetin 3-*O*-*β*-galactopyranoside, afzelin [141]; persin [144]; 1,2,4-trihydroxyheptadec-16-ene; 1,2,4-trihydroxyheptadec-16-yne; 1,2,4-trihydroxynonadecane; persenones A and B; (1S,6R)-8-hydroxy abscisic acid-D-glucoside; (1*R*,3*R*,5*R*,8*S*)-pi-dihydrophaseic acid-D-glucoside; catechin; epicatechin [145]	Anti-inflammatory, antibacterial, antiproliferative, analgesic, anti-diabetic, cardiovascular, antihypertensive, antiviral, And wound healing activities[66, 141, 142, 146-151]
Syzygium jambos (L.) Alst. (Myrtaceae)/ 30458/HNC	Digestive, stimulant and remedy for dental disorders, fever, diarrhoea, dysentery, and catarrh [35, 152]	Phloretin 4′-*O*-methyl ether, myrigalone G, and myrigalone B [153], myricetin, myricitrin, gallic acid [36]	Antibacterial, analgesic, antiproliferative, and antioxidant activities [35, 152-154]
Aframomum letestuanum Gagnep. (Zingiberaceae)/ 43134/HNC	Hemorrhage, muscular pains, nausea, and vomiting [155]	Alkaloids, polyphenols, flavonoids, tannins, triterpenes, sterols, saponins [155]	Antibacterial activity [155]

Table 2. Bacterial features of the strains and isolates of *Staphylococcus aureus.*

Bacterial strains or isolates	Features	References
MRSA3	Clinical isolate: OFX^{R}, KAN^{R}, TET^{R}, ERY^{R}	[156]
MRSA4	Clinical isolate: OFX^{R}, KAN^{R}, CYP^{R}, CHL^{R}, GEN^{R}, NIS^{R}, AMP^{R}	[156]
MRSA6	Clinical isolate: OFX^{R}, FMOX^{R}, KAN^{R}, TET^{R}, CYP^{R}, IMI/CIN^{R}, CHL^{R}, GENR, NIS^{R}, AMP^{R}	[156]
MRSA8	Clinical isolate: OFX^{R}, FMOX^{R}, KANR, ERY^{R}, CYP^{R}, IMI/CIN^{R}, CHLR, GENR, NISR, AMPR	[156]
MRSA9	Clinical isolate: OFX^{R}, FMOX^{R}, TET^{R}, ERY^{R}, CYP^{R}, IMI/CIN^{R}, CHL^{R}, GEN^{R}, NIS^{R}, AMP^{R}	[156]
MRSA11	Clinical isolate: OFX^{R}, KAN^{R}, ERYR, CYP^{R}, IMI/CIN^{R}, CHL^{R}, NIS^{R}, AMP^{R}	[156]
MRSA12	Clinical isolate: OFX^{R}, FMOX^{R}, KAN^{R}, ERY^{R}, IMI/CIN^{R}, CHL^{R}, GEN^{R}, NIS^{R}, AMP^{R}	[156]
ATCC 25923	Reference strain	
ST20	Clinical isolate: ERY^{R}, AMP^{R}, CIP^{R}, DOX^{R},	[10]
ST39	Clinical isolate: ERY^{R}, DOX^{R}, VAN^{R}	[10]
ST50	Clinical isolate: AMP^{R}, DOX^{R}, VAN^{R}	[10]
ST52	Clinical isolate: CHL^{R},	[10]
ST76	Clinical isolate: CIP^{R}, VAN^{R}, DOX^{R}, ERY^{R}	[10]
ST132	Clinical isolate: AMP^{R}, VAN^{R}	[10]
ST135	Clinical isolate: CHL^{R}, CEF^{R},	[10]
ST218	Clinical isolate: CHL^{R}, DOX^{R}, VAN^{R}	[10]
ST674	Clinical isolate: VAN^{R}, IMI^{R}, CHL^{R}	[10]

CHL^{R}, CYP^{R}, ERY^{R}, FMOX^{R}, IMI/CIN^{R}, KAN^{R}, MET^{R}, OFX^{R}, TET^{R}, VAN^{R}, AMP^{R}, DOX^{R}, AUG^{R}, GEN^{R}, NIS^{R}: resistant to chloramphenicol, Ciprofloxacin, Erythromycin, Flomoxef, Imipenem/Cilastatin sodium, Kanamycin, Methicillin, Ofloxacin, Tetracycline, Vancomycin, Ampicillin, Doxycycline, Augmentin, Gentamicin, and Nisin respectively. ST: *Staphycoccus aureus* ATCC: American Type Culture Collection MRSA: methicillin-resistant *Staphylococcus aureus*

Table 3. Plants and parts used, extraction yield and physical characteristics of botanicals.

Plants	Parts used	Extract yield (%)	Color	Aspects
Psidium guajava	Bark	14.65	Brown	Crystals
	Leaves	13.51	Green	Paste
Vernonia amygdalina	Leaves	7.85	Dark green	Paste
Passiflora edulis	Leaves	12.1	Light green	Paste
Aframomum letestuanum	Seeds	7.25	Brown	Oily
	Pulps	8.5	Dark brown	Paste
Garcinia kola	Leaves	15.5	Dark green	Paste
	Bark	17.91	Brown	Paste
Persea americana	Leaves	8.57	Green	Paste
	Bark	10.77	Brown	Paste
Citrus sinensis	Leaves	18.56	Green	Paste
Syzygium jambos	Leaves	28.52	Dark green	Paste
	Bark	15.57	Brown	Crystals
Carica papaya	Seeds	1.325	Light green	Oily

Table 4. MICs of the tested botanicals against the *Staphylococcus aureus* strains.

Bacterial strains	***Persea americana***						***Psidium guajava***						***Passiflora edulis***		
	Leaves			**Bark**			**Leaves**			**Bark**			Leaves		
	MIC	**MBC**	**R**	**MIC**	**MBC**	**R**	**MIC**	**MBC**	**R**	**MIC**	**MBC**	**R**	**MIC**	**MBC**	R
MRSA3	1024	2048	2	512	2048	4	2048	-	nd	512	1024	2	-	-	nd
MRSA4	256	2048	8	512	1024	2	1024	2048	2	256	256	1	1024	1024	1
MRSA6	1024	-	nd	1024	2048	2	1024	2048	2	512	1024	2	-	-	nd
MRSA 8	512	2048	2	512	2048	4	1024	2048	2	256	512	2	-	-	nd
MRSA 11	512	2048	2	2048	-	nd	1024	2048	2	512	1024	2	2048	2048	1
MRSA 12	1024	-	nd	512	2048	4	512	1024	2	512	1024	2	2048	2048	1
ATTCC25923	1024	-	nd	256	2048	8	1024	2048	2	512	512	1	-	-	nd
ST20	1024	-	nd	1024	-	nd	512	-	nd	256	512	2	-	-	nd
ST30	1024	-	nd	2048	2048	1	1024	2048	2	1024	2048	2	2048	-	nd
ST39	1024	2048	2	512	2048	4	512	-	nd	128	2048	8	2048	-	nd
ST52	512	1024	2	512	2048	4	512	-	nd	512	1024	2	1024	2048	2
ST76	1024	1024	1	512	-	nd	512	2048	4	256	1024	4	1024	2048	2
ST96	512	1024	2	512	2048	4	1024	-	nd	512	2048	4	-	-	nd
ST132	1024	2048	2	2048	2048	1	1024	2048	2	1024	1024	1	2048	-	nd
ST135	1024	1024	1	1024	-	nd	**128**	2048	8	**64**	512	8	1024	2048	2
ST218	512	1024	2	1024	-	nd	1024	2048	2	256	1024	4	2048	-	nd
ST674	1024	1024	1	512	-	nd	512	2048	4	128	1024	8	-	-	nd

No activity of *Carica papaya* was recorded in the tested bacteria; MIC: minimal inhibitory concentration (in µg/mL); MBC: minimal bactericidal concentration (in µg/mL); R: MBC/MIC ratio; nd: not determined; (-): > 2048 µg/mL.

Table 4. *Continued…*

Bacterial strains	*Syzygium jambos*						*Mangifera indica*						*Vernonia amygdalina*		
	Leaves			**Bark**			**Seeds**			**Bark**			**Leaves**		
	MIC	**MBC**	**R**	**MIC**	**MBC**	**R**	**MIC**	**MBC**	**R**	**MIC**	**MBC**	**R**	**MIC**	**MBC**	R
MRSA3	1024	2048	2	2048	2048	1	1024	1024	1	1024	1024	1	-	-	nd
MRSA4	**128**	512	4	**128**	512	4	256	2048	8	1024	2048	2	-	-	nd
MRSA6	512	1024	2	-	-	nd	512	2048	4	512	1024	2	-	-	nd
MRSA 8	512	1024	2	1024	2048	2	1024	2048	2	256	1024	4	2048	2048	1
MRSA 11	1024	1024	1	256	1024	4	256	2048	8	512	1024	2	-	-	nd
MRSA 12	1024	2048	2	1024	-	nd	1024	2048	2	1024	2048	2	-	-	nd
ATTCC25923	1024	2048	2	512	2048	4	512	2048	4	1024	1024	1	-	-	nd
ST20	1024	512	2	512	2048	4	512	2048	4	512	1024	2	-	-	nd
ST30	512	2048	4	2048	2048	1	1024	2048	2	1024	2048	2	-	-	nd
ST39	512	-	nd	2048	-	nd	1024	-	nd	1024	-	nd	-	-	nd
ST52	512	2048	4	512	2048	4	512	1024	2	1024	1024	1	2048	-	nd
ST76	**128**	1024	8	2048	2048	1	1024	1024	1	1024	2048	2	-	-	nd
ST96	512	2048	4	1024	2048	2	1024	-	nd	1024	1024	1	-	-	nd
ST132	1024	1024	1	2048	-	nd	2048	-	nd	2048	2048	1	-	-	nd
ST135	256	512	2	512	1024	2	512	512	1	512	512	1	-	-	nd
ST218	256	2048	8	1024	2048	2	1024	1024	1	1024	1024	1	-	-	nd
ST674	256	1024	8	1024	-	nd	512	2048	4	512	-	nd	2048	-	nd

Table 4. *Continued and end.*

Bacterial strains	*Garcinia kola*						*Aframomum letestuanum*						*Citrus sinensis*			Ciprofloxacin		
	Leaves			Bark			**Leaves**			**Leaves**			**Leaves**					
	MIC	**MBC**	**MIC**	**MIC**	**MIC**	**R**	**MIC**	**MBC**	**R**	**MIC**	**MBC**	**R**	**MIC**	**MBC**	R	**MIC**	**MBC**	**R**
MRSA3	2048	-	-	-	-	4	512	2048	4	-	-	nd	-	-	nd	32	64	2
MRSA4	512	1024	1024	1024	1024	8	512	2048	4	1024	-	nd	-	-	nd	1	32	32
MRSA6	2048	-	-	-	-	1	1024	-	nd	-	-	nd	-	-	nd	32	64	2
MRSA 8	1024	2048	1024	1024	1024	2	512	2048	4	1024	***I***	nd	2048	2048	1	32	64	2
MRSA 11	1024	1024	2048	2048	2048	2	512	2048	4	-	-	nd	-	-	nd	32	32	1
MRSA 12	2048	-	-	-	-	2	1024	2048	2	-	-	nd	-	-	nd	16	32	2
ATTCC2 5923	-	-	-	-	-	2	2048	-	nd	-	-	nd	-	-	nd	16	32	2
ST20	1024	-	2048	2048	2048	nd	512	1024	2	256	2048	8	-	-	nd	16	32	2
ST30	2048	2048	-	-	-	1	512	1024	2	256	2048	8	-	-	nd	16	32	2
ST39	-	-	-	-	-	4	**128**	2048	16	**64**	1024	16	-	-	nd	32	64	2
ST52	1024	2048	-	-	-	1	256	2048	4	**128**	2048	0	2048	-	nd	32	64	2
ST76	512	-	2048	2048	2048	4	**128**	2048	16	1024	2048	2	-	-	nd	32	64	2
ST96	1024	1024	-	-	-	2	512	2048	4	512	2048	4	-	-	nd	>1	32	>32
ST132	-	-	-	-	-	nd	256	2048	8	**128**	1024	8	-	-	nd	16	32	2
ST135	1024	2048	512	512	512	2	**64**	1024	16	**64**	1024	16	-	-	nd	16	32	2
ST218	512	2048	-	-	-	2	512	2048	4	256	2048	8	-	-	nd	16	32	2
ST674	512	2048	-	-	-	nd	512	2048	4	256	2048	8	2048	-	nd	8	32	4

Table 5. Anti-staphylococcal activity (MIC in µg/mL) of the botanicals in the presence of the efflux pump inhibitor, reserpine (RES).

Bacterial strains	***Psidium guajava***						***Syzygium jambos***			***Aframomum letestuanum***			***Ciprofloxacin***		
	Leaves			**Bark**			**Leaves**			**Pulp**					
	+ RES	**Alone**	**R**	**+ RES**	**Alone**	**R**	**+ RES**	**Alone**	**R**	**+ RES**	**Alone**	**R**	**+ RES**	**Alone**	**R**
MRSA 3	64	1024	**16**	64	512	**8**	16	1024	**64**	64	>2048	**>32**	0.25	32	**128**
MRSA8	256	512	**2**	64	512	**8**	64	1024	**16**	32	256	**8**	0.5	32	**64**
MRSA 11	64	512	**8**	8	1024	**128**	8	1024	**128**	32	>2048	**>64**	<0.25	32	**>128**
ST 218	64	1024	**16**	64	256	**4**	64	256	**4**	128	256	**2**	<0.25	32	**>128**
ATCC 25923	16	1024	**64**	16	1024	**64**	16	1024	**64**	<8	256	**>32**	<0.25	32	**>128**

(R): Ratio of MIC (+**RES**)/MIC (alone)

Table 6. Activity of antibiotics in the association with botanicals

Bacterial strains	Antibiotic alone	Botanicals and MIC values (µg/mL) and activity ameliorating factors (AAF, in bracket)							
		Psidium guajava				*Syzygium jambos*			
		Leaves		Bark		Leaves		Bark	
	MIC 0	MIC/2	MIC/4	MIC/2	MIC/4	MIC/2	MIC/4	MIC/2	MIC/4
Chloramphenicol									
MRSA 4	64	4(**16**)	4(**16**)	4(**16**)	4(**16**)	8(**8**)	8(**8**)	4(**16**)	4(**16**)
MRSA 8	64	4(**16**)	4(**16**)	≤4(≥**16**)	≤4(≥**16**)	4(**16**)	4(**16**)	≤4(≥**16**)	≤4(≥**16**)
MRSA 11	64	8(**8**)	4(**16**)	4(**16**)	4(**16**)	16(**4**)	8(**8**)	≤4(≥**16**)	4(**16**)
ST 20	128	8(**16**)	16(**8**)	8(**16**)	8(**16**)	16(**8**)	4(**32**)	≤4(≥**32**)	≤4(≥**32**)
ST 39	128	8(**16**)	16(**8**)	4(**32**)	4(**32**)	4(**32**)	4(**32**)	≤4(≥**32**)	4(**32**)
ST 135	64	8(**8**)	8(**8**)	8(**8**)	8(**8**)	8(**8**)	8(**8**)	8(**8**)	8(**8**)
ST 218	32	4(**8**)	4(**8**)	4(**8**)	4(**8**)	4(**8**)	4(**8**)	16(**2**)	16(**2**)
Doxycycline									
MRSA 4	8	0.5(**16**)	1(**8**)	0.5(**16**)	0.5(**16**)	0.5(**16**)	0.5(**16**)	0.5(**16**)	0.5(**16**)
MRSA 8	16	4(**4**)	8(**2**)	8(**2**)	8(**2**)	4(**4**)	4(**4**)	0.25(**64**)	0.25(**64**)
MRSA 11	32	1(**32**)	8(**4**)	0.25(**128**)	0.25(**128**)	1(**32**)	4(**8**)	1(**32**)	4(**8**)
ST 20	32	0.5(**64**)	0.5(**64**)	0.5(**64**)	0.25(**128**)	1(**32**)	1(**32**)	0.25(**128**)	0.25(**128**)
ST 39	16	0.5(**32**)	0.125(**2**)	0.125(**2**)	0.125(**2**)	0.5(**32**)	0.5(**32**)	0.25(**4**)	≤0.125(**2**)
ST 135	8	0.25(**32**)	0.25(**32**)	0.25(**32**)	0.25(**32**)	0.25(**32**)	0.25(**32**)	0.5(**16**)	1(**16**)
ST 218	8	0.25(**32**)	0.25(**32**)	0.25(**32**)	1(**8**)	0.25(**32**)	0.25(**32**)	0.25(**32**)	0.25(**32**)
Tetracycline									
MRSA 4	16	0.25(**4**)	0.25(**4**)	0.25(**4**)	0.25(**4**)	0.25(**4**)	0.25(**4**)	0.25(**4**)	0.25(**4**)
MRSA 8	8	0.25(**32**)	0.25(**32**)	0.25(**32**)	2(**4**)	1(**8**)	2(**4**)	0.25(**32**)	0.25(**32**)
MRSA 11	4	0.25(**16**)	0.5(**8**)	0.25(**16**)	2(**2**)	0.25(**16**)	0.5(**8**)	1(**4**)	4(1)
ST 20	8	0.5 (**16**)	1(**8**)	0.25(**32**)	0.25(**32**)	0.5 (**16**)	0.5 (**16**)	0.125(**64**)	0.125(**64**)
ST 39	8	0.125(**64**)	0.125(**64**)	0.125(**64**)	0.125(**64**)	0.125(**64**)	0.25(**32**)	0.125(**64**)	0.125(**64**)
ST 135	8	0.25(**32**)	0.25(**32**)	0.25(**32**)	0.25(**32**)	0.25(**32**)	0.25(**32**)	0.25(**32**)	0.25(**32**)
ST 218	4	0.25(**16**)	0.25(**16**)	0.25(**16**)	0.25(**16**)	0.25(**16**)	0.25(**16**)	0.25(**16**)	0.25(**16**)
Levofloxacin									
MRSA 4	16	0.5(**32**)	2(**8**)	0.5(**32**)	0.5(**32**)	0.5(**32**)	2(**8**)	0.5(**32**)	1(**16**)
MRSA 8	32	16(**2**)	8(**4**)	16(**2**)	16(**2**)	1(**32**)	2(**16**)	16(**2**)	16(**2**)
MRSA 11	32	1(**32**)	16(**2**)	0.5(**64**)	1(**32**)	0.5(**64**)	1(**32**)	2(**16**)	8(**4**)
ST 20	16	4(**4**)	4(**4**)	4(**4**)	2(**8**)	4(**4**)	4(**4**)	8(**2**)	4(**4**)
ST 39	32	4(**8**)	2(**16**)	1(**32**)	0.5(**64**)	2(**16**)	2(**16**)	4(**8**)	4(**8**)
ST 135	16	0.5(**32**)	0.5(**32**)	1(**16**)	1(**16**	0.5(**32**)	0.5(**32**)	0.5(**32**)	1(**16**)
ST 218	16	0.5(**32**)	0.5(**32**)	0.5(**32**)	0.5(**32**)	0.5(**32**)	0.5(**32**)	0.5(**32**)	0.5(**32**)
Ciprofloxacin									
MRSA 4	8	1(**8**)	2(**4**)	0.5(**16**)	2(**4**)	0.5(**16**)	0.5(**16**)	4(**2**)	4(**2**)
MRSA 8	32	2(**16**)	4(**8**)	1(**32**)	8(**4**)	2(**16**)	2(**16**)	0.5(**16**)	1(**32**)
MRSA 11	8	0.5(**16**)	4(**8**)	0.25(**32**)	0.25(**32**)	0.25(**32**)	1(**8**)	0.25(**32**)	2(**4**)
ST 20	4	0.5(**8**)	0.5(**8**)	0.5(**8**)	0.5(**8**)	0.125(**32**)	0.125(**32**)	0.125(**32**)	0.125(**32**)
ST 39	4	0.5(**8**)	1(**4**)	0.25(**16**)	0.5(**8**)	0.5(**8**)	0.5(**8**)	0.125(**32**)	0.125(**32**)
ST 135	16	0.25(**64**)	0.25(**64**)	0.25(**64**)	1(**64**)	0.5(**32**)	2(**8**)	0.25(**64**)	1(**16**)
ST 218	8	0.25(**32**)	0.25(**32**)	0.25(**32**)	0.25(**32**)	0.25(**32**)	0.25(**32**)	0.25(**32**)	0.25(**32**)
Ampicillin									
MRSA 4	64	4(**16**)	8(**8**)	8(**8**)	16(**4**)	16(**4**)	16(**4**)	4(**16**)	16(**4**)
MRSA 8	128	32(**4**)	64(**2**)	32(**4**)	64(**2**)	16(**8**)	32(**4**)	4(**32**)	8(**32**)
MRSA 11	256	8(**32**)	8(**32**)	2(**128**)	4(**64**)	4(**64**)	8(**32**)	16(**16**)	32(**8**)
ST 20	128	8(**16**)	8(**16**)	8(**16**)	8(**16**)	4(**32**)	4(**32**)	4(**32**)	4(**32**)
ST 39	128	4(**32**)	8(**16**)	4(**32**)	4(**32**)	8(**16**)	8(**16**)	4(**32**)	4(**32**)
ST 135	128	2(**64**)	2(**64**)	2(**64**)	8(**16**)	2(**64**)	2(**64**)	2(**64**)	2(**64**)
ST 218	32	2(**16**)	2(**16**)	8(**4**)	8(**4**)	2(**16**)	2(**16**)	32(1)	32(1)
Penicillin									
MRSA 4	64	4(**8**)	4(**8**)	4(**8**)	4(**8**)	4(**8**)	4(**8**)	4(**8**)	4(**8**)
MRSA 8	256	64(**4**)	128(**2**)	4(**64**)	4(**64**)	4(**64**)	4(**64**)	4(**64**)	4(**64**)
MRSA 11	256	16(**16**)	32(**8**)	32(**8**)	128(**2**)	32(**8**)	32(**8**)	128(**2**)	128(**2**)
ST 20	128	16(**8**)	16(**8**)	32(**4**)	32(**4**)	16(**8**)	32(**4**)	8(**32**)	8(**32**)
ST 39	32	16(**2**)	16(**2**)	16(**2**)	8(**4**)	8(**4**)	8(**4**)	16(**2**)	8(**4**)
ST 135	8	4(**2**)	4(**2**)	4(**2**)	4(**2**)	4(**2**)	4(**2**)	4(**2**)	4(**2**)
ST 218	32	4(**8**)	4(**8**)	4(**8**)	4(**8**)	4(**8**)	4(**8**)	4(**8**)	4(**8**)
Ceftriaxone									
MRSA 4	32	4(**8**)	4(**8**)	4(**8**)	4(**8**)	4(**8**)	4(**8**)	4(**8**)	4(**8**)
MRSA 8	128	16(**8**)	128(1)	64(**2**)	128(1)	4(**32**)	4(**32**)	4(**32**)	4(**32**)
MRSA 11	4	2(**2**)	2(**2**)	2(**2**)	4(1)	2(**2**)	4(1)	2(**2**)	4(1)
ST 20	16	8(**2**)	8(**2**)	8(**2**)	4(**4**)	4(**4**)	4(**4**)	4(**4**)	4(**4**)
ST 39	16	4(**4**)	4(**4**)	4(**4**)	4(**4**)	4(**4**)	4(**4**)	4(**4**)	4(**4**)
ST 135	16	4(**4**)	4(**4**)	4(**4**)	4(**4**)	4(**4**)	4(**4**)	4(**4**)	4(**4**)
ST 218	32	4(**8**)	4(**8**)	4(**8**)	4(**8**)	4(**8**)	4(**8**)	4(**8**)	4(**8**)

Table 6. *continued...*

Bacterial strains	Antibiotic alone	Botanicals and MIC values (µg/mL) and activity increasing factors (in bracket)							
		Garcinia cola		*Passiflora edulis*		*Vernonia amygdalina*		*Aframomum letestuanum*	
		Leaves		Leaves		Leaves		Epicarps	
	MIC 0	MIC/2	MIC/4	MIC/2	MIC/4	MIC/2	MIC/4	MIC/2	MIC/4
Chloramphenicol									
MRSA 4	32	16(**2**)	16(**2**)	32(1)	32(1)	32(1)	32(1)	4(**8**)	4(**8**)
MRSA 8	64	16(**4**)	32**(2)**	32**(2)**	32**(2)**	64(1)	128	4(**16**)	4(**16**)
MRSA 11	32	32(1)	32(1)	16(**2**)	32(1)	32(1)	32(1)	4(**8**)	4(**8**)
ST 20	64	32**(2)**	32**(2)**	16(**4**)	16(**4**)	32**(2)**	32**(2)**	4(**16**)	16(**4**)
ST 39	16	8(**2**)	8(**2**)	4(**4**)	4(**4**)	8(**2**)	4(**4**)	4(**4**)	4(**4**)
ST 135	64	32**(2)**	32**(2)**	32**(2)**	8(**8**)	32**(2)**	8(**8**)	32**(2)**	32**(2)**
ST 218	16	2(**8**)	2(**8**)	2(**8**)	2(**8**)	2(**8**)	2(**8**)	2(**8**)	2(**8**)
Doxycycline									
MRSA 4	8	2(**4**)	2(**4**)	2(**4**)	2(**4**)	2(**4**)	8(1)	0.25(**32**)	0.25(**32**)
MRSA 8	16	16(1)	16(1)	4(**4**)	4(**4**)	8(**2**)	8(**2**)	0.25(**64**)	0.25(**64**)
MRSA 11	32	128(0.25)	128(0.25)	8(**4**)	16(**2**)	128(0.25)	128(0.25)	8(**4**)	8(**4**)
ST 20	32	2(**16**)	4(**8**)	8(**4**)	8(**4**)	8(**4**)	8(**4**)	4(**8**)	4(**8**)
ST 39	16	8(**2**)	8(**2**)	8(**2**)	4(**4**)	8(**2**)	8(**2**)	4(**4**)	4(**4**)
ST 135	32	0.5(**64**)	2(**16**)	4(**8**)	4(**8**)	4(**8**)	4(**8**)	0.25(**128**)	0.25(**128**)
ST 218	8	0.25(**32**)	0.25(**32**)	2(**4**)	2(**4**)	2(**4**)	2(**4**)	0.25(**32**)	0.25(**32**)
Tetracycline									
MRSA 4	4	2(**2**)	2(**2**)	2(**2**)	2(**2**)	2(**2**)	2(**2**)	0.25(**16**)	0.25(**16**)
MRSA 8	8	4(**2**)	4(**2**)	1(**8**)	2(**4**)	4(**2**)	16(0.5)	0.25(**32**)	1(8)
MRSA 11	4	16(0.25)	16(0.25)	1(**16**)	4(1)	2(**2**)	4(1)	0.25(**16**)	0.25(**16**)
ST 20	2	16(0.25)	16(0.125)	1(**2**)	2(1)	2(1)	2(1)	0.5(**4**)	1(**2**)
ST 39	4	8(0.5)	8(0.5)	2(**2**)	4(1)	4(1)	4(1)	2(**2**)	2(**2**)
ST 135	8	0.25(**32**)	0.25(**32**)	8(1)	8(1)	8(1)	8(1)	0.25(**32**)	0.25(**32**)
ST 218	4	2(**2**)	2(**2**)	2(**2**)	2(**2**)	2(**2**)	2(**2**)	0.25(**16**)	0.25(**16**)
Levofloxacin									
MRSA 4	16	2(**8**)	2(**8**)	1(**16**)	4(**4**)	2(**8**)	8(**2**)	0.5(**32**)	2(**8**)
MRSA 8	32	64(0.5)	64(0.5)	2(**16**)	2(**16**)	4(**8**)	4(**8**)	0.5(**64**)	0.5(**64**)
MRSA 11	32	4(**8**)	8(**4**)	0.5(**64**)	0.5(**64**)	0.5(**64**)	0.5(**64**)	0.5(**64**)	0.5(**64**)
ST 20	16	2(**8**)	4(**4**)	4(**4**)	8(**2**)	2(**8**)	4(**4**)	2(**8**)	2(**8**)
ST 39	32	8(**4**)	16(**2**)	8(**4**)	8(**4**)	16(**2**)	16(**2**)	4(**8**)	4(**8**)
ST 135	8	1(**8**)	1(**8**)	1(**8**)	1(**8**)	1(**8**)	1(**8**)	0.5(**16**)	0.5(**16**)
ST 218	16	8(**2**)	8(**2**)	0.5(**32**)	0.5(**32**)	0.5(**32**)	0.5(**32**)	0.5(**32**)	0.5(**32**)
Ciprofloxacin									
MRSA 4	**8**	2(**4**)	8(1)	1(**8**)	2(**4**)	16(0.5)	16(0.5)	0.5(**16**)	4(**2**)
MRSA 8	32	16(**2**)	16(**2**)	8(**4**)	16(**2**)	8(**4**)	8(**4**)	1(**32**)	1(**32**)
MRSA 11	8	8(1)	8(1)	1(**8**)	2(**4**)	1(**8**)	4(**2**)	0.25(**32**)	0.25(**32**)
ST 20	4	1(**4**)	1(**4**)	1(**4**)	2(**2**)	0.25(**16**)	0.5(**8**)	0.25(**16**)	0.25(**16**)
ST 39	4	0.5(**8**)	0.5(**8**)	0.5(**8**)	1(**4**)	1(**4**)	2(**2**)	0.25(**16**)	0.5(**8**)
ST 135	64	2(**32**)	2(**32**)	2(**32**)	8(**8**)	2(**32**)	8(**8**)	32(**2**)	2(**32**)
ST 218	16	2(**8**)	2(**8**)	2(**8**)	2(**8**)	2(**8**)	2(**8**)	2(**8**)	2(**8**)
Ampicillin									
MRSA 4	64	32(**2**)	64(1)	32(**2**)	64(1)	64(1)	128(0.5)	16(**4**)	16(**4**)
MRSA 8	128	64(**2**)	64(**2**)	32(**4**)	64(**2**)	64(**2**)	64(**2**)	16(**8**)	16(**8**)
MRSA 11	256	8(**32**)	32(**8**)	256(1)	256(1)	128(**2**)	128(**2**)	2(**128**)	2(**128**)
ST 20	64	8(**8**)	8(**8**)	4(**16**)	8(**8**)	16(**4**)	16(**4**)	2(**32**)	2(**32**)
ST 39	128	8(**16**)	8(**16**)	8(**16**)	8(**16**)	8(**16**)	8(**16**)	2(**64**)	4(**32**)
ST 135	32	0.5(**64**)	2(**16**)	4(**8**)	4(**8**)	4(**8**)	4(**8**)	0.25(**128**)	0.25(**128**)
ST 218	32	32(1)	32(1)	16(**2**)	16(**2**)	16(**2**)	16(**2**)	2(**16**)	2(**16**)
Penicillin									
MRSA 4	64	32**(2)**	128(0.5)	4(**16**)	4(**16**)	64(1)	128(0.5)	4(**16**)	4(**16**)
MRSA 8	256	8(**32**)	16(**16**)	32(**8**)	64(**4**)	128(**2**)	128(**2**)	4(**64**)	4(**64**)
MRSA 11	256	128(**2**)	128(**2**)	8(**32**)	16(**16**)	128(**2**)	128(**2**)	8(**32**)	8(**32**)
ST 20	256	64(**4**)	64(**4**)	128(**2**)	256(1)	128(**2**)	128(**2**)	32(**8**)	32(**8**)
ST 39	128	32(**4**)	32(**4**)	128(1)	256(0.5)	64(**2**)	128(1)	32(**4**)	32(**4**)
ST 135	8	0.25(**64**)	0.25(**64**)	8(1)	8(1)	8(1)	8(1)	0.25(**64**)	0.25(**64**)
ST 218	32	4(**8**)	4(**8**)	8(**4**)	8(**4**)	8(**4**)	8(**4**)	8(**4**)	8(**4**)
Ceftriaxone									
MRSA 4	32	8(**4**)	8(**4**)	4(**8**)	8(**4**)	4(**8**)	8(**4**)	4(**8**)	4(**8**)
MRSA 8	128	512(0.25)	512(0.25)	32(**4**)	32(**4**)	64(**2**)	128(1)	8(**16**)	8(**16**)
MRSA 11	32	64(0.5)	128(0.25)	4(**8**)	8(**4**)	64(0.5)	128(0.25)	2(**64**)	2(**64**)
ST 20	32	32(1)	32(1)	16(**2**)	32(1)	8(**4**)	8(**4**)	4(**8**)	8(**4**)
ST 39	32	64(0.5)	128(0.25)	16(**2**)	32(1)	8(**4**)	8(**4**)	4(**8**)	4(**8**)
ST 135	16	4(**4**)	4(**4**)	4(**4**)	4(**4**)	8(**2**)	16(1)	4(**4**)	4(**4**)
ST 218	32	4(**8**)	4(**8**)	4(**8**)	4(**8**)	4(**8**)	4(**8**)	4(**8**)	4(**8**)

Table 6. *continued and end.*

Bacterial strains	Antibiotic alone	Botanicals and MIC values (µg/mL) and activity increasing factors (in bracket)							
		Garcinia cola		*Passiflora edulis*		*Vernonia amygdalina*		*Aframomum letestuanum*	
		Leaves		Leaves		Leaves		Epicarps	
	MIC 0	MIC/2	MIC/4	MIC/2	MIC/4	MIC/2	MIC/4	MIC/2	MIC/4
Imipenem									
MRSA 4	32	4(**8**)	16(**2**)	8(**4**)	16(**2**)	16(**2**)	16(**2**)	2(**16**)	2(**16**)
MRSA 8	64	16(**4**)	32(**2**)	16(**4**)	16(**4**)	16(**4**)	16(**4**)	2(**32**)	2(**32**)
MRSA 11	64	16(**4**)	16(**4**)	8(**8**)	32(**2**)	16(**4**)	16(**4**)	2(**32**)	2(**32**)
ST 20	32	32(1)	64(0.5)	16(**2**)	16(**2**)	64(0.5)	64(0.5)	2(**32**)	2(**32**)
ST 39	64	16(**4**)	32(**2**)	8(**8**)	8(**8**)	32(**2**)	64(1)	4(**16**)	4(**16**)
ST 135	64	2(**32**)	2(**32**)	2(**32**)	8(**8**)	2(**8**)	8(**8**)	32(**2**)	2(**8**)
ST 218	16	2(**8**)	2(**8**)	2(**8**)	2(**8**)	2(**8**)	2(**8**)	2(**8**)	2(**8**)
Augmentin									
MRSA 4	64	16(**4**)	32(**2**)	16(**4**)	32(**2**)	16(**4**)	32(**2**)	4(**16**)	8(**8**)
MRSA 8	128	128(1)	128(1)	32(**4**)	32(**4**)	64(**2**)	64(**2**)	2(**64**)	2(**64**)
MRSA 11	32	4(**8**)	4(**8**)	4(**8**)	4(**8**)	2(**32**)	4(**8**)	0.25(**128**)	0.25(**128**)
ST 20	64	16(**4**)	16(**4**)	16(**4**)	32(**2**)	32(**2**)	32(**2**)	8(**8**)	8(**8**)
ST 39	64	16(**4**)	16(**4**)	16(**4**)	16(**4**)	16(**4**)	16(**4**)	8(**8**)	8(**8**)
ST 135	32	0.5(**64**)	2(**16**)	4(**8**)	4(**8**)	4(**8**)	4(**8**)	0.25(**128**)	0.25(**128**)
ST 218	128	4(**32**)	8(**16**)	2(**64**)	2(**64**)	64(**2**)	64(**2**)	2(**64**)	2(**64**)

Conclusion

In the present study, we have demonstrated the anti-staphylococcal potential of 16 food plant extracts, the effect of the association of 5 of these extracts with an efflux pump inhibitor, and the effect of the association of 9 of them with antibiotics against the multidrug-resistant strains of *Staphylococcus aureus* expressing active efflux pumps. It was shown that the methanol extracts of *Syzygium jambos*, the bark of *Persea americana*, the leaves and bark of Psidium guajava, the leaves and bark of *Syzygium jambos*, and the seeds and pulps of *Afromaum letestuanum* had exploitable antistaphylococal activities. It was also demonstrated that the bacterial efflux pumps should be blocked to improve their inhibitory effects. Finally, we have demonstrated that three of the studied plants, *Psidium guajava, Syzygium jambos*, and *Afromomum letestuanum* could be used effectively alone or in combination with antibiotics in the treatment of Staphylococcus aureus infections.

Abbreviations

AAF, activity ameliorating factor; AMP, Ampicillin; AUG, Augmentin; CHL, Chloramphenicol; CIP, Ciprofloxacin; CRO, Ceftriaxone; DMSO, dimethylsulfoxide; DOX, Doxycycline; HNC, Cameroon national herbarium; IMI, Imipenem; INT, para-Iodonitrotetrazolium chloride; LEV, Levofloxacin; MDR, multidrug-resistant; MBC, minimal bactericidal concentrations; MHA, Mueller Hinton Agar; MHB, Mueller Hinton Broth; MIC, minimum inhibitory concentrations; PEN, Penicillin; RES: reserpine; TET, Tetracycline.

Authors' Contribution

BE carried out the study; ATM wrote the manuscript; VK and ATM supervised the study; All authors approved the final version of the manuscript.

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Conflict of interest

The authors declare no conflict of interest.

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References

1. Guo Y, Song G, Sun M, Wang J, Wang Y. 2020. Prevalence and therapies of antibiotic-resistance in *Staphylococcus aureus*. *Front Cell Infect Microbiol.* 10:107.
2. Kuete V, Tangmouo JG, Penlap Beng V, Ngounou FN, Lontsi D. 2006. Antimicrobial activity of the methanolic extract from the stem bark of *Tridesmostemon omphalocarpoides* (Sapotaceae). *J Ethnopharmacol.* 104(1–2):5-11.
3. Kuete V, Komguem J, Beng VP, Meli AL, Tangmouo JG, Etoa FX, Lontsi D. 2007. Antimicrobial components of the methanolic extract from the stem bark of *Garcinia smeathmannii* Oliver (Clusiaceae). *S Afr J Bot.* 73(3):347-354.
4. Ngameni B, Kuete V, Simo IK, Mbaveng AT, Awoussong PK, Patnam R, Roy R, Ngadjui BT. 2009. Antibacterial and antifungal activities of the crude extract and compounds from *Dorstenia turbinata* (Moraceae). *S Afr J Bot.* 75(2):256-261.
5. Nono EC, Mkounga P, Kuete V, Marat K, Hultin PG, Nkengfack AE. 2010. Pycnanthulignenes A-D, antimicrobial cyclolignene derivatives from the roots of *Pycnanthus angolensis*. *J Nat Prod.* 73(2):213-216.
6. Kuete V, Nono EC, Mkounga P, Marat K, Hultin PG, Nkengfack AE. 2011. Antimicrobial activities of the CH_2Cl_2-CH_3OH (1:1) extracts and compounds from the roots and fruits of *Pycnanthus angolensis* (Myristicaceae). *Nat Prod Res.* 25(4):432-443.
7. Eloff JN. 1998. A sensitive and quick microplate method to determine the minimal inhibitory concentration of plant extracts for bacteria. *Planta Med.* 64(8):711-713.
8. Fouotsa H, Mbaveng AT, Mbazoa CD, Nkengfack AE, Farzana S, Iqbal CM, Marion Meyer JJ, Lall N, Kuete V. 2013. Antibacterial constituents of three Cameroonian medicinal plants: *Garcinia nobilis*, *Oricia suaveolens* and *Balsamocitrus camerunensis*. *BMC Complement Altern Med.* 13(1):81.
9. Seukep JA, Fankam AG, Djeussi DE, Voukeng IK, Tankeo SB, Noumdem JA, Kuete AH, Kuete V. 2013. Antibacterial activities of the methanol extracts of seven Cameroonian dietary plants against bacteria expressing MDR phenotypes. *Springerplus.* 2:363.

10. Wamba BEN, Mbaveng AT, Nayim P, Dzotam JK, Ngalani OJT, Kuete V. 2018. Antistaphylococcal and antibiotic resistance modulatory activities of thirteen cameroonian edible plants against resistant phenotypes. *Int J Microbiol* 2018.1920198.
11. Kuete V, Alibert-Franco S, Eyong KO, Ngameni B, Folefoc GN, Nguemeving JR, Tangmouo JG, Fotso GW, Komguem J, Ouahouo BMW *et al*. 2011. Antibacterial activity of some natural products against bacteria expressing a multidrug-resistant phenotype. *Int J Antimicrob Agents.* 37(2):156-161.
12. Kuete V, Ngameni B, Tangmouo JG, Bolla JM, Alibert-Franco S, Ngadjui BT, Pages JM. 2010. Efflux pumps are involved in the defense of Gram-negative bacteria against the natural products isobavachalcone and diospyrone. *Antimicrob Agents Chemother*. 54(5):1749-1752.
13. Dzotam JK, Kuete V. 2017. Antibacterial and antibiotic-modifying activity of methanol extracts from six cameroonian food plants against multidrug-resistant enteric bacteria. *BioMed Res Int.* 2017:1583510.
14. Seukep JA, Sandjo LP, Ngadjui BT, Kuete V. 2016. Antibacterial and antibiotic-resistance modifying activity of the extracts and compounds from *Nauclea pobeguinii* against Gram-negative multi-drug resistant phenotypes. *BMC Complement Altern Med.* 16:193.
15. Fankam AG, Kuiate JR, Kuete V. 2017. Antibacterial and antibiotic resistance modulatory activities of leaves and bark extracts of *Recinodindron heudelotii* (Euphorbiaceae) against multidrug-resistant Gram-negative bacteria. *BMC Complement Altern Med.* 17(1):168.
16. Kuete V. 2010. Potential of Cameroonian plants and derived products against microbial infections: a review. *Planta Med.* 76(14):1479-1491.
17. Wamba BEN, Mbaveng AT, Kuete V. 2022. Fighting Gram-positive bacteria with African medicinal plants: Cut-off values for the classification of the activity of natural products. *Advances in Botanical Research. https://doi.org/10.1016/bs.abr.2022.08.008*.
18. Tankeo SB, Kuete V. 2022. African plants acting on Pseudomonas aeruginosa: Cut-off points for the antipseudomonal agents from plants. *Advances in Botanical Research. https://doi.org/10.1016/bs.abr.2022.08.007*.
19. Cowan MM. 1999. Plant products as antimicrobial agents. *Clin Microbiol Rev.* 12(4):564-582.
20. Fankam AG, Kuete V, Voukeng IK, Kuiate JR, Pages JM. 2011. Antibacterial activities of selected Cameroonian spices and their synergistic effects with antibiotics against multidrug-resistant phenotypes. *BMC Complement Altern Med.* 11:104.
21. Voukeng IK, Kuete V, Dzoyem JP, Fankam AG, Noumedem JA, Kuiate JR, Pages JM. 2012. Antibacterial and antibiotic-potentiation activities of the methanol extract of some Cameroonian spices against Gram-negative multi-drug resistant phenotypes. *BMC Res Notes.* 5:299.
22. Kuete V, Ango PY, Yeboah SO, Mbaveng AT, Mapitse R, Kapche GD, Ngadjui BT, Efferth T. 2014. Cytotoxicity of four *Aframomum* species (*A. arundinaceum, A. alboviolaceum, A. kayserianum and A. polyanthum*) towards multi-factorial drug resistant cancer cell lines. *BMC Complement Altern Med.* 14:340.
23. Kuete V, Voukeng IK, Tsobou R, Mbaveng AT, Wiench B, Beng VP, Efferth T. 2013. Cytotoxicity of *Elaoephorbia drupifera* and other Cameroonian medicinal plants against drug sensitive and multidrug resistant cancer cells. *BMC Complement Altern Med.* 13:250.
24. Kuete V, Azebaze AG, Mbaveng A, Nguemfo EL, Tshikalange ET, Chalard P, Nkengfack AE. 2011. Antioxidant, antitumor and antimicrobial activities of the crude extract and compounds of the root bark of *Allanblackia floribunda*. *Pharm Biol.* 49(1):57-65.
25. Kuete V, Vouffo B, Mbaveng AT, Vouffo EY, Siagat RM, Dongo E. 2009. Evaluation of *Antiaris africana* methanol extract and compounds for antioxidant and antitumor activities. *Pharmaceut Biol.* 47(11):1042-1049.
26. Mbaveng AT, Kuete V, Nguemeving JR, Beng VP, Nkengfack AE, Marion Meyer JJ, Lall N, Krohn K. 2008. Antimicrobial activity of the extracts and compounds from *Vismia guineensis* (Guttiferae). *Asian J Trad Med.* 3:211-223.
27. Kuete V, Wiench B, Hegazy ME, Mohamed TA, Fankam AG, Shahat AA, Efferth T. 2012. Antibacterial activity and cytotoxicity of selected Egyptian medicinal plants. *Planta Med.* 78(2):193-199.
28. Kuete V, Sandjo LP, Djeussi DE, Zeino M, Kwamou GM, Ngadjui B, Efferth T. 2014. Cytotoxic flavonoids and isoflavonoids from *Erythrina sigmoidea* towards multi-factorial drug resistant cancer cells. *Invest New Drugs.* 32:1053–1062.
29. Fankam AG, Kuiate JR, Kuete V. 2015. Antibacterial and antibiotic resistance modifying activity of the extracts from *allanblackia gabonensis, combretum molle* and *gladiolus quartinianus* against Gram-negative bacteria including multi-drug resistant phenotypes. *BMC Complement Altern Med.* 15:206.
30. Kuete V, Nkuete AHL, Mbaveng AT, Wiench B, Wabo HK, Tane P, Efferth T. 2014. Cytotoxicity and modes of action of 4'-hydroxy-2',6'-dimethoxychalcone and other flavonoids toward drug-sensitive and multidrug-resistant cancer cell lines. *Phytomedicine.* 21(12):1651-1657.
31. Tchinda CF, Voukeng KI, Beng VP, Kuete V. 2016. Antibacterial activities of the methanol extracts of *Albizia adianthifolia, Alchornea laxiflora, Laportea ovalifolia* and three other Cameroonian plants against multi-drug resistant Gram-negative bacteria. *Saudi J Biol Sci.* 24:950-955.
32. Nayim P, Mbaveng AT, Wamba BEN, Fankam AG, Dzotam JK, Kuete V. 2018. Antibacterial and antibiotic-potentiating activities of thirteen Cameroonian edible plants against gram-negative resistant phenotypes. *ScientificWorldJournal.* 2018:4020294.
33. Efferth T, Saeed MEM, Kadioglu O, Seo EJ, Shirooie S, Mbaveng AT, Nabavi SM, Kuete V. 2020. Collateral sensitivity of natural products in drug-resistant cancer cells. *Biotechnol Adv.* 38:107342.
34. Carvalho AAT, Sampaio MCC, Sampaio FC, Melo AFM, Sena K, Chiappeta AA, Higino JS. 2002. *[Atividade antimicrobiana in vitro de extratos hidroalcoólicos de Psidium guajava L. sobre bactérias gram-negativas]. Acta Farm Bonaerense.* 21(4):255-258.
35. Wamba BEN, Nayim P, Mbaveng AT, Voukeng IK, Dzotam JK, Ngalani OJT, Kuete V. 2018. *Syzygium jambos* Displayed Antibacterial and Antibiotic-Modulating Activities against Resistant Phenotypes. *Evid Based Complement Alternat Med.* 2018:5124735.
36. Sharma R, Kishore N, Hussein A, Lall N. 2013. Antibacterial and anti-inflammatory effects of *Syzygium jambos* L. (Alston) and isolated compounds on acne vulgaris. *BMC Complement Altern Med.* 13:292.
37. Xu HX, Lee SF. 2001. Activity of plant flavonoids against antibiotic-resistant bacteria. *Phytother Res.* 15(1):39-43.
38. Ayafor JF, Tchuendem MH, Nyasse AB, Tillequin F, Anke H. 1994. Aframodial and other bioactive diterpenoids from *Aframomum* species. *Pure Appl Chem.* 66:2327-2330.
39. Nathaniel OB, Selina AS, John KM, Mercy B, Sylvester AA, Michael BM. 2015. Phytoconstituents, antimicrobial and antioxidant properties of the leaves of *Persea americana* Mill cultivated in Ghana. *J Med Plants Res.* 9(36):933 939.
40. Kovač J, Gavarić N, Bucar F, Smole Možina S. 2014. Antimicrobial and resistance modulatory activity of Alpinia katsumadai seed phenolic extract, essential oil and post-distillation extract. *Food Technol Biotech.* 52(2):248-254.
41. Gibbons S, Oluwatuyi M, Kaatz GW. 2003. A novel inhibitor of multidrug efflux pumps in *Staphylococcus aureus*. *J Antimicrob Chemother*. 51(1):13-17.
42. Braga LC, Leite AA, Xavier KG, Takahashi JA, Bemquerer MP, Chartone-Souza E, Nascimento AM. 2005. Synergic interaction between pomegranate extract and antibiotics against *Staphylococcus aureus*. *Can J Microbiol.* 51(7):541-547.
43. Lorenzi V, Muselli A, Bernardini AF, Berti L, Pages JM, Amaral L, Bolla JM. 2009. Geraniol restores antibiotic activities against multidrug-resistant isolates from Gram-negative species. *Antimicrob Agents Chemother.* 53(5):2209-2211.
44. Kuete V. 2022. Potential of African medicinal plants against Enterobacteria: Classification of plants antibacterial agents. In: *Advances in Botanical Research.* doi: https://doi.org/10.1016/bs.abr.2022.1008.1006.
45. Ghasemi K, Ghasemi Y, Ebrahimzadeh MA. 2009. Antioxidant activity, phenol and flavonoid contents of 13 citrus species peels and tissues. *Pak J Pharm Sci.* 22(3):277-281.
46. Kirbaşlar FG, Tavman A, Dülger B, Türker G. 2009. Antimicrobial activity of Turkish citrus peel oils. *Pak J Bot.* 41(6):3207-3212.
47. Favela-Hernández JM, González-Santiago O, Ramírez-Cabrera MA, Esquivel-Ferriño PC, Camacho-Corona Mdel R. 2016. Chemistry and Pharmacology of *Citrus sinensis*. *Molecules.* 21(2):247.
48. Traboulsi AF, El-Haj S, Tueni M, Taoubi K, Nader NA, Mrad A. 2005. Repellency and toxicity of aromatic plant extracts against the mosquito *Culex pipiens* molestus (Diptera: Culicidae). *Pest Manag Sci.* 61(6):597-604.
49. Shalaby NMM, Abd-Alla HI, Ahmed HH, Basoudan N. 2011. Protective effect of *Citrus sinensis* and *Citrus aurantifolia* against osteoporosis and their phytochemical constituents. *J Med Plants Res.* 5(4):579-588.
50. Cardile V, Graziano AC, Venditti A. 2015. Clinical evaluation of Moro (*Citrus sinensis* (L.) Osbeck) orange juice supplementation for the weight management. *Nat Prod Res.* 29(23):2256-2260.
51. Habila N, Agbaji AS, Ladan Z, Bello IA, Haruna E, Dakare MA, Atolagbe TO. 2010. Evaluation of *in vitro* activity of essential oils against *Trypanosoma brucei brucei* and *Trypanosoma evansi*. *J Parasitol Res.* 2010:534601.
52. Bagavan A, Rahuman AA, Kamaraj C, Kaushik NK, Mohanakrishnan D, Sahal D. 2011. Antiplasmodial activity of botanical extracts against *Plasmodium falciparum*. *Parasitol Res.* 108(5):1099-1109.
53. Goes TC, Antunes FD, Alves PB, Teixeira-Silva F. 2012. Effect of sweet orange aroma on experimental anxiety in humans. *J Altern Complement Med.* 18(8):798-804.
54. Singh P, Shukla R, Prakash B, Kumar A, Singh S, Mishra PK, Dubey NK. 2010. Chemical profile, antifungal, antiaflatoxigenic and antioxidant activity of *Citrus maxima* Burm. and *Citrus sinensis* (L.) Osbeck essential oils and their cyclic monoterpene, DL-limonene. *Food Chem Toxicol.* 48(6):1734-1740.
55. Vitali F, Pennisi C, Tomaino A, Bonina F, De Pasquale A, Saija A, Tita B. 2006. Effect of a standardized extract of red orange juice on proliferation of human prostate cells in vitro. *Fitoterapia.* 77(3):151-155.
56. Camarda L, Di Stefano V, Del Bosco SF, Schillaci D. 2007. Antiproliferative activity of *Citrus* juices and HPLC evaluation of their flavonoid composition. *Fitoterapia.* 78(6):426-429.
57. Lehrner J, Eckersberger C, Walla P, Pötsch G, Deecke L. 2000. Ambient odor of orange in a dental office reduces anxiety and improves mood in female patients. *Physiol Behav.* 71(1-2):83-86.
58. Asgary S, Keshvari M. 2013. Effects of *Citrus sinensis* juice on blood pressure. *ARYA Atheroscler.* 9(1):98-101.
59. Oliveira ED, Leite TS, Silva BA, Conde-Garcia EA. 2005. Inotropic effect of *Citrus sinensis* (L.) Osbeck leaf extracts on the guinea pig atrium. *Braz J Med Biol Res.* 38(1):111-118.
60. Trovato A, Monforte MT, Barbera R, Rossitto A, Galati EM, Forestieri AM. 1996. Effects of fruit juices of *Citrus sinensis* L. and *Citrus limon* L. on experimental hypercholesterolemia in the rat. *Phytomedicine.* 2(3):221-227.
61. Nundkumar N, Ojewole JA. 2002. Studies on the antiplasmodial properties of some South African medicinal plants used as antimalarial remedies in Zulu folk medicine. *Methods Find Exp Clin Pharmacol.* 24(7):397-401.

62. Shen SC, Cheng FC, Wu NJ. 2008. Effect of guava (*Psidium guajava* Linn.) leaf soluble solids on glucose metabolism in type 2 diabetic rats. *Phytother Res.* 22(11):1458-1464.
63. Ojewole JAO. 2006. Antiinflammatory and analgesic effects of *Psidium guajava* Linn. (Myrtaceae) leaf aqueous extract in rats and mice. *Meth Find Exp Clin Pharmacol*. 28(7):441-446.
64. Dutta BK, Rahman I, Das TK. 2000. *In vitro* study on antifungal property of common fruit plants. *Biomedicine.* 20(3):187-189.
65. Chen KC, Hsieh CL, Peng CC, Hsieh-Li HM, Chiang HS, Huang KD, Peng RY. 2007. Brain derived metastatic prostate cancer DU-145 cells are effectively inhibited in vitro by guava (*Psidium gujava* L.) leaf extracts. *Nutr Cancer.* 58(1):93-106.
66. Mbaveng AT, Manekeng HT, Nguenang GS, Dzotam JK, Kuete V, Efferth T. 2018. Cytotoxicity of 18 Cameroonian medicinal plants against drug sensitive and multi-factorial drug resistant cancer cells. *J Ethnopharmacol.* 222:21-33.
67. Shaheen HM, Ali BH, Alqarawi AA, Bashir AK. 2000. Effect of *Psidium guajava* leaves on some aspects of the central nervous system in mice. *Phytother Res.* 14(2):107-111.
68. Jaiarj P, Khoohaswan P, Wongkrajang Y, Peungvicha P, Suriyawong P, Sumal Saraya ML, Ruangsomboon O. 1999. Anticough and antimicrobial activities of *Psidium guajava* Linn. leaf extract. *J Ethnopharmacol.* 67(2):203-212.
69. Roy CK, Kamath JV, Asad M. 2006. Hepatoprotective activity of *Psidium guajava* Linn. leaf extract. *Indian J Exp Biol*. 44(4):305-311.
70. Seo N, Ito T, Wang N, Yao X, Tokura Y, Furukawa F, Takigawa M, Kitanaka S. 2005. Anti-allergic *Psidium guajava* extracts exert an antitumor effect by inhibition of T regulatory cells and resultant augmentation of Th1 cells. *Anticancer Res.* 25(6 A):3763-3770.
71. Conde Garcia EA, Nascimento VT, Santiago Santos AB. 2003. Inotropic effects of extracts of *Psidium guajava* L.(guava) leaves on the guinea pig atrium. *Braz J Med Biol Res.* 36:661-668.
72. Yamashiro S, Noguchi K, Matsuzaki T, Miyagi K, Nakasone J, Sakanashi M, Sakanashi M, Kukita I, Aniya Y, Sakanashi M. 2003. Cardioprotective effects of extracts from *Psidium guajava* L. and *Limonium wrightii*, Okinawan Medicinal Plants, against ischemia-reperfusion injury in perfused rat hearts. *Pharmacology.* 67(3):128-135.
73. Chah KF, Eze CA, Emuelosi CE, Esimone CO. 2006. Antibacterial and wound healing properties of methanolic extracts of some Nigerian medicinal plants. *J Ethnopharmacol.* 104(1-2):164-167.
74. Lacmata ST, Kuete V, Dzoyem JP, Tankeo SB, Teke GN, Kuiate JR, Pages JM. 2012. Antibacterial activities of selected Cameroonian plants and their synergistic effects with antibiotics against bacteria expressing MDR phenotypes. *Evid Based Complement Alternat Med.* 2012:623723.
75. Wang X, Li R, Liu X, Huang S, Li B, Wang H, Chai X, Wang Y. 2020. Study on characteristics of biflavanones distribution in *Garcinia kola* seeds and identification of compounds in gum resin exuded from fresh slices. *J Pharm Biomed Anal.* 190:113512.
76. Iwu MM, Igboko OA, Onwuchekwa UA, Okunji CO. 1987. Evaluation of the antihepatotoxic activity of the biflavonoids of *Garcinia kola* seed. *J Ethnopharmacol.* 21(2):127-138.
77. Hioki Y, Onwona-Agyeman S, Kakumu Y, Hattori H, Yamauchi K, Mitsunaga T. 2020. Garcinoic acids and a benzophenone derivative from the seeds of *Garcinia kola* and their antibacterial activities against oral bacterial pathogenic organisms. *J Nat Prod.* 83(7):2087-2092.
78. Jouda JB, Tamokou JD, Mbazoa CD, Douala-Meli C, Sarkar P, Bag PK, Wandji J. 2016. Antibacterial and cytotoxic cytochalasins from the endophytic fungus Phomopsis sp. harbored in *Garcinia kola* (Heckel) nut. *BMC Complement Altern Med.* 16(1):462.
79. Idris AE, Seke Etet PF, Saeed AA, Farahna M, Satti GMH, AlShammari SZ, Hamza MA. 2020. Evaluation of metabolic, antioxidant and anti-inflammatory effects of *Garcinia kola* on diabetic rats. *Saudi J Biol Sci.* 27(12):3641-3646.
80. Adegbehingbe OO, Adesanya SA, Idowu TO, Okimi OC, Oyelami OA, Iwalewa EO. 2008. Clinical effects of *Garcinia kola* in knee osteoarthritis. *J Orthop Surg Res.* 3:34.
81. Kuete V, Krusche B, Youns M, Voukeng I, Fankam AG, Tankeo S, Lacmata S, Efferth T. 2011. Cytotoxicity of some Cameroonian spices and selected medicinal plant extracts. *J Ethnopharmacol.* 134(3):803-812.
82. Oluwatosin A, Tolulope A, Ayokulehin K, Patricia O, Aderemi K, Catherine F, Olusegun A. 2014. Antimalarial potential of kolaviron, a biflavonoid from Garcinia kola seeds, against Plasmodium berghei infection in Swiss albino mice. *Asian Pac J Trop Med.* 7(2):97-104.
83. Tona L, Cimanga RK, Mesia K, Musuamba CT, De Bruyne T, Apers S, Hernans N, Van Miert S, Pieters L, Totté J *et al.* 2004. *In vitro* antiplasmodial activity of extracts and fractions from seven medicinal plants used in the Democratic Republic of Congo. *J Ethnopharmacol.* 93(1):27-32.
84. Adaramoye OA, Adeyemi EO. 2006. Hypoglycaemic and hypolipidaemic effects of fractions from kolaviron, a biflavonoid complex from *Garcinia Kola* in streptozotocin-induced diabetes mellitus rats. *J Pharm Pharmacol.* 58(1):121-128.
85. Ayepola OR, Chegou NN, Brooks NL, Oguntibeju OO. 2013. Kolaviron, a *Garcinia* biflavonoid complex ameliorates hyperglycemia-mediated hepatic injury in rats *via* suppression of inflammatory responses. *BMC Complement Altern Med.* 13:363.
86. Alabi QK, Akomolafe RO, Adefisayo MA, Olukiran OS, Nafiu AO, Fasanya MK, Oladele AA. 2018. Kolaviron attenuates diclofenac-induced nephrotoxicity in male Wistar rats. *Appl Physiol Nutr Metab.* 43(9):956-968.
87. Onasanwo SA, Rotu RA. 2016. Antinociceptive and anti-inflammatory potentials of kolaviron: mechanisms of action. *J Basic Clin Physiol Pharmacol.* 27(4):363-370.
88. Farombi EO, Awogbindin IO, Farombi TH, Oladele JO, Izomoh ER, Aladelokun OB, Ezekiel IO, Adebambo OI, Abah VO. 2019. Neuroprotective role of kolaviron in striatal redo-inflammation associated with rotenone model of Parkinson's disease. *Neurotoxicology.* 73:132-141.
89. Odukanmi OA, Salami AT, Ashaolu OP, Adegoke AG, Olaleye SB. 2018. Kolaviron attenuates ischemia/reperfusion injury in the stomach of rats. *Appl Physiol Nutr Metab.* 43(1):30-37.
90. Omotoso GO, Ukwubile, II, Arietarhire L, Sulaimon F, Gbadamosi IT. 2018. Kolaviron protects the brain in cuprizone-induced model of experimental multiple sclerosis via enhancement of intrinsic antioxidant mechanisms: Possible therapeutic applications? *Pathophysiology.* 25(4):299-306.
91. Shetshak MA, Jatau ID, Suleiman MM, Ameh MP, Gabriel A, Akefe IO. 2021. *In vitro* anticoccidial activities of the extract and fractions of *Garcinia kola* (Heckel h.) against *Eimeria tenella* Oocyst. *Recent Pat Biotechnol.* 15(1):76-84.
92. Farombi EO, Abarikwu SO, Adedara IA, Oyeyemi MO. 2007. Curcumin and kolaviron ameliorate di-n-butylphthalate-induced testicular damage in rats. *Basic Clin Pharmacol Toxicol.* 100(1):43-48.
93. Akinpelu DA. 1999. Antimicrobial activity of *Vernonia amygdalina* leaves. *Fitoterapia.* 70(4):432-434.
94. Noumedem JA, Mihasan M, Kuiate JR, Stefan M, Cojocaru D, Dzoyem JP, Kuete V. 2013. *In vitro* antibacterial and antibiotic-potentiation activities of four edible plants against multidrug-resistant Gram-negative species. *BMC Complement Altern Med.* 13:190.
95. Kupchan SM, Hemingway RJ, Karim A, Werner D. 1969. Tumor inhibitors. XLVII. Vernodalin and vernomygdin, two new cytotoxic sesquiterpene lactones from *Vernonia amygdalina* Del. *J Org Chem.* 34(12):3908-3911.
96. Habtamu A, Melaku Y. 2018. Antibacterial and antioxidant compounds from the flower extracts of *Vernonia amygdalina*. *Adv Pharmacol Sci.* 2018:4083736.
97. Nguyen TXT, Dang DL, Ngo VQ, Trinh TC, Trinh QN, Do TD, Thanh TTT. 2020. Anti-inflammatory activity of a new compound from *Vernonia amygdalina. Nat Prod Res. doi:* 10.1080/14786419.14782020.11788556.
98. Wang J, Song H, Wu X, Zhang S, Gao X, Li F, Zhu X, Chen Q. 2018. Steroidal saponins from *Vernonia amygdalina* Del. and their biological activity. *Molecules.* 23(3): 579.
99. Anh HLT, Vinh LB, Lien LT, Cuong PV, Arai M, Ha TP, Lin HN, Dat TTH, Cuong LCV, Kim YH. 2021. *In vitro* study on α-amylase and α-glucosidase inhibitory activities of a new stigmastane-type steroid saponin from the leaves of *Vernonia amygdalina*. *Nat Prod Res.* 35(5):873-879.
100. Erukainure OL, Oyebode OA, Ibeji CU, Koorbanally NA, Islam MS. 2019. *Vernonia Amygdalina* Del. stimulated glucose uptake in brain tissues enhances antioxidative activities; and modulates functional chemistry and dysregulated metabolic pathways. *Metab Brain Dis.* 34(3):721-732.
101. Erasto P, Grierson DS, Afolayan AJ. 2006. Bioactive sesquiterpene lactones from the leaves of *Vernonia amygdalina*. *J Ethnopharmacol.* 106(1):117-120.
102. Uzoigwe CI, Agwa OK. 2011. Antimicrobial activity of *Vernonia amygdalina* on selected urinary tract pathogens. *Afr J Microbiol Res.* 5:1467-1472.
103. Iwalokun BB, Bamiro SB, Durojaiye OO. 2003. An Antimicrobial evaluation of *Vernonia amygdalina* (Compositae) against Gram-positive and Gram-negative bacteria from Lagos, Nigeria. *W Afr J Pharmacol Drug Res.* 19:9-15.
104. Hasibuan PAZ, Harahap U, Sitorus P, Satria D. 2020. The anticancer activities of *Vernonia amygdalina* Delile. Leaves on 4T1 breast cancer cells through phosphoinositide 3-kinase (PI3K) pathway. *Heliyon.* 6(7):e04449.
105. Abay SM, Lucantoni L, Dahiya N, Dori G, Dembo EG, Esposito F, Lupidi G, Ogboi S, Ouédraogo RK, Sinisi A *et al.* 2015. Plasmodium transmission blocking activities of *Vernonia amygdalina* extracts and isolated compounds. *Malar J.* 14:288.
106. Njan AA, Adzu B, Agaba AG, Byarugaba D, Díaz-Llera S, Bangsberg DR. 2008. The analgesic and antiplasmodial activities and toxicology of *Vernonia amygdalina. J Med Food.* 11(3):574-581.
107. Adedapo AA, Aremu OJ, Oyagbemi AA. 2014. Anti-oxidant, anti-inflammatory and antinociceptive properties of the acetone leaf extract of *vernonia amygdalina* in some laboratory animals. *Adv Pharm Bull. 4*(Suppl 2):591-598.
108. Okoduwa SIR, Umar IA, James DB, Inuwa HM, Habila JD, Venditti A. 2020. Bioguided fractionation of hypoglycaemic component in methanol extract of *Vernonia amygdalina*: an *in vivo* study. *Nat Prod Res.* 35(24):5943-5947.
109. Gogna N, Hamid N, Dorai K. 2015. Metabolomic profiling of the phytomedicinal constituents of *Carica papaya* L. leaves and seeds by 1H NMR spectroscopy and multivariate statistical analysis. *J Pharm Biomed Anal.* 115:74-85.
110. Soib HH, Ismail HF, Husin F, Abu Bakar MH, Yaakob H, Sarmidi MR. 2020. Bioassay-guided different extraction techniques of *Carica papaya* (Linn.) leaves on *in vitro* wound-healing activities. *Molecules.* 25(3):517.
111. Devmurari VV, Patel PP, Jadeja RA, Bhadaniya CP, Aghara PP, Patel AS, Tala SD, Savant MM, Ladva KD, Nariya PB. 2021. Steroid and fatty acid contents from the leaves of *Carica papaya*. *Folia Med (Plovdiv).* 63(3):422-428.
112. Jin BR, Ju JY, Nugroho A, Lee M, An HJ. 2021. *Carica papaya* leaf extract inhibits prostatitis-associated prostatic hyperplasia via the TRAF6/TAK1/MEK/NF-κB pathway. *Biomed Pharmacother.* 135:111197.
113. He X, Ma Y, Yi G, Wu J, Zhou L, Guo H. 2017. Chemical composition and antifungal activity of *Carica papaya* Linn. seed essential oil against *Candida* spp. *Lett Appl Microbiol.* 64(5):350-354.
114. Otsuki N, Dang NH, Kumagai E, Kondo A, Iwata S, Morimoto C. 2010. Aqueous extract of *Carica papaya* leaves exhibits anti-tumor activity and immunomodulatory effects. *J Ethnopharmacol.* 127(3):760-767.
115. Nakamura Y, Yoshimoto M, Murata Y, Shimoishi Y, Asai Y, Park EY, Sato K, Nakamura Y. 2007. Papaya seed represents a rich source of biologically active isothiocyanate. *J Agric Food Chem.* 55(11):4407-4413.

116. Nguyen TT, Shaw PN, Parat MO, Hewavitharana AK. 2013. Anticancer activity of *Carica papaya*: a review. *Mol Nutr Food Res.* 57(1):153-164.
117. Mojica-Henshaw MP, Francisco AD, De Guzman F, Tigno XT. 2003. Possible immunomodulatory actions of *Carica papaya* seed extract. *Clin Hemorheol Microcirc.* 29(3-4):219-229.
118. Pérez-Gutiérrez S, Zavala-Sánchez MA, González-Chávez MM, Cárdenas-Ortega NC, Ramos-López MA. 2011. Bioactivity of *Carica papaya* (Caricaceae) against *Spodoptera frugiperda* (Lepidoptera: Noctuidae). *Molecules.* 16(9):7502-7509.
119. Ekanem AP, Obiekezie A, Kloas W, Knopf K. 2004. Effects of crude extracts of *Mucuna pruriens* (Fabaceae) and *Carica papaya* (Caricaceae) against the protozoan fish parasite *Ichthyophthirius multifiliis*. *Parasitol Res.* 92(5):361-366.
120. Oloyede HO, Adaja MC, Ajiboye TO, Salawu MO. 2015. Anti-ulcerogenic activity of aqueous extract of *Carica papaya* seed on indomethacin-induced peptic ulcer in male albino rats. *J Integr Med.* 13(2):105-114.
121. Kusemiju TO, Osinubi AA, Noronha CC, Okanlawon AO. 2010. Effect of aqueous extract of the bark of *Carica papaya* on testicular histology in Sprague-Dawley rats. *Nig Q J Hosp Med.* 20(3):133-137.
122. Hakim RF, Fakhrurrazi, Dinni. 2019. Effect of *Carica papaya* extract toward incised wound healing process in mice (*Mus musculus*) clinically and histologically. *Evid Based Complement Alternat Med.* 2019:8306519.
123. Ichimura T, Yamanaka A, Ichiba T, Toyokawa T, Kamada Y, Tamamura T, Maruyama S. 2006. Antihypertensive effect of an extract of *Passiflora edulis* rind in spontaneously hypertensive rats. *Biosci Biotechnol Biochem.* 70(3):718-721.
124. Silva JR, Campos AC, Ferreira LM, Aranha Junior AA, Thiede A, Zago Filho LA, Bertoli LC, Ferreira M, Trubian PS, Freitas AC. 2006. [Extract of *Passiflora edulis* in the healing process of gastric sutures in rats: a morphological and tensiometric study]. *Acta Cir Bras.* 21 Suppl 2:52-60.
125. Kannan S, Parimala B, Jayakar B. 2011. Antibacterial evaluation of the methanolic extract of *Passiflora edulis*. *HygeiaJDMed.* 3(1):46-49.
126. He X, Luan F, Yang Y, Wang Z, Zhao Z, Fang J, Wang M, Zuo M, Li Y. 2020. *Passiflora edulis*: An Insight Into Current Researches on Phytochemistry and Pharmacology. *Front Pharmacol*. 11:617.
127. Lutomski J, Malek B, Rybacka L. 1975. Pharmacochemical investigations of the raw materials from passiflora genus. 2. The pharmacochemical estimation of juices from the fruits of *Passiflora edulis* and *Passiflora edulis* forma flavicarpa. *Planta Med.* 27(2):112-121.
128. Aba PE, Udechukwu IR. 2018. Comparative hypoglycemic potentials and phytochemical profiles of 12 common leafy culinary vegetables consumed in Nsukka, Southeastern Nigeria. *J Basic Clin Physiol Pharmacol.* 29(4):313-320.
129. Dzotam JK, Touani FK, Kuete V: Antibacterial and antibiotic-modifying activities of three food plants (*Xanthosoma mafaffa* Lam., *Moringa oleifera* (L.) Schott and *Passiflora edulis* Sims) against multidrug-resistant (MDR) Gram-negative bacteria. *BMC Complement Altern Med* 2016, 16(1):9.
130. Ramirez V, Arango SS, Uribe D, Maldonado ME, Aguillon J. 2017. Effect of the ethanolic extract of Passiflora edulis F. Flavicarpa leaves on viability, cytotoxicity and apoptosis of colon cancer cell lines. *J Chem Pharm Res.* 9:135-139.
131. Arango Varela SS, Ramírez V, Maldonado Celis ME, Uribe D, Aguillón Osma J. 2017. Cytotoxic and apoptotic activities of the aqueous fruit extract of *Passiflora edulis* Sims var flavicarpa in an in vitro model of human colon cancer. *J Chem Pharmaceut Res.* 9(9):258-264.
132. Mota N, Kviecinski MR, Zeferino RC, de Oliveira DA, Bretanha LC, Ferreira SRS, Micke GA, Filho DW, Pedrosa RC, Ourique F. 2018. *In vivo* antitumor activity of by-products of *Passiflora edulis* f. flavicarpa Deg. Rich in medium and long chain fatty acids evaluated through oxidative stress markers, cell cycle arrest and apoptosis induction. *Food Chem Toxicol.* 118:557-565.
133. Aguillón J, Arango S, Uribe D, Loango N. 2018. Cytotoxic and apoptotic activity of extracts from leaves and juice of *Passiflora edulis*. *J Liver Res Disord Ther*. 4:67-71.
134. Kuete V, Dzotam JK, Voukeng IK, Fankam AG, Efferth T. 2016. Cytotoxicity of methanol extracts of *Annona muricata, Passiflora edulis* and nine other Cameroonian medicinal plants towards multi-factorial drug-resistant cancer cell lines. *Springerplus.* 5(1):1666.
135. Barbalho SM, Damasceno DC, Spada AP, Lima IE, Araújo AC, Guiguer EL, Martuchi KA, Oshiiwa M, Mendes CG. 2011. Effects of *Passiflora edulis* on the metabolic profile of diabetic Wistar rat offspring. *J Med Food.* 14(12):1490-1495.
136. Nayak L, Panda SK. 2012. Phytochemical investigation and evaluation of analgesic activity of *Passiflora edulis* Linn leaves available in South Eastern Odisha. *Int J Pharm Bio Arch.* 3:897-899.
137. Barbosa PR, Valvassori SS, Bordignon CL, Jr., Kappel VD, Martins MR, Gavioli EC, Quevedo J, Reginatto FH. 2008. The aqueous extracts of *Passiflora alata* and *Passiflora edulis* reduce anxiety-related behaviors without affecting memory process in rats. *J Med Food.* 11(2):282-288.
138. Klein N, Gazola AC, de Lima TC, Schenkel E, Nieber K, Butterweck V. 2014. Assessment of sedative effects of *Passiflora edulis* f. flavicarpa and *Passiflora alata* extracts in mice, measured by telemetry. *Phytother Res.* 28(5):706-713.
139. Zibadi S, Farid R, Moriguchi S, Lu Y, Foo LY, Tehrani PM, Ulreich JB, Watson RR. 2007. Oral administration of purple passion fruit peel extract attenuates blood pressure in female spontaneously hypertensive rats and humans. *Nutr Res.* 27(7):408-416.
140. Lewis BJ, Herrlinger KA, Craig TA, E. M-FC, Defreitas Z, C. H-L. 2013. Antihypertensive effect of passion fruit peel extract and its major bioactive components following acute supplementation in spontaneously hypertensive rats. *J Nutr Biochem.* 24:1359-1366.
141. De Almeida A, Miranda M, Simoni I, Wigg M, Lagrota M, Costa S. 1998. Flavonol monoglycosides isolated from the antiviral fractions of *Persea americana* (Lauraceae) leaf infusion. *Phytother Res.* 12(8):562-567.
142. Ekom SE, Tamokou JDD, Kuete V. 2022. Methanol extract from the seeds of *Persea americana* displays antibacterial and wound healing activities in rat model. *J Ethnopharmacol.* 282:114573.
143. Lu QY, Arteaga JR, Zhang Q, Huerta S, Go VL, Heber D. 2005. Inhibition of prostate cancer cell growth by an avocado extract: role of lipid-soluble bioactive substances. *J Nutr Biochem.* 16(1):23-30.
144. Butt AJ, Roberts CG, Seawright AA, Oelrichs PB, Macleod JK, Liaw TY, Kavallaris M, Somers-Edgar TJ, Lehrbach GM, Watts CK *et al*. 2006. A novel plant toxin, persin, with *in vivo* activity in the mammary gland, induces Bim-dependent apoptosis in human breast cancer cells. *Mol Cancer Ther.* 5(9):2300-2309.
145. Yasir M, Das S, Kharya MD. 2010. The phytochemical and pharmacological profile of *Persea americana* Mill. *Pharmacogn Rev.* 4(7):77-84.
146. Tchana ME, Fankam AG, Mbaveng AT, Nkwengoua ET, Seukep JA, Tchouani FK, Nyassé B, Kuete V. 2014. Activities of selected medicinal plants against multi-drug resistant Gram-negative bacteria in Cameroon. *Afr Health Sci.* 14(1):167-172.
147. Dabas D, Elias RJ, Ziegler GR, Lambert JD. 2019. *In vitro* antioxidant and cancer inhibitory activity of a colored avocado seed extract. *Int J Food Sci.* 2019:6509421.
148. Padilla-Arellanes S, Salgado-Garciglia R, Báez-Magaña M, Ochoa-Zarzosa A, López-Meza JE. 2021. Cytotoxicity of a lipid-rich extract from native mexican avocado seed (*Persea americana* var. drymifolia) on canine osteosarcoma D-17 cells and synergistic activity with cytostatic drugs. *Molecules.* 26(14):4178.
149. Antia B, Okokon J, Okon P. 2005. Hypoglycemic activity of aqueous leaf extract of *Persea americana* Mill. *Indian J Pharmacol.* 37(5):325.
150. Carvajal-Zarrabal O, Nolasco-Hipolito C, Aguilar-Uscanga MG, Melo-Santiesteban G, Hayward-Jones PM, Barradas-Dermitz DM. 2014. Avocado oil supplementation modifies cardiovascular risk profile markers in a rat model of sucrose-induced metabolic changes. *Dis Markers.* 2014:386425.
151. Dzeufiet PDD, Mogueo A, Bilanda DC, Aboubakar B-FO, Tédong L, Dimo T, Kamtchouing P. 2014. Antihypertensive potential of the aqueous extract which combine leaf of *Persea americana* Mill. (Lauraceae), stems and leaf of *Cymbopogon citratus* (D.C) Stapf. (Poaceae), fruits of *Citrus medica* L. (Rutaceae) as well as honey in ethanol and sucrose experimental model. *BMC Complement Altern Med.* 14:507-507.
152. Ochieng MA, Ben Bakrim W, Bitchagno GTM, Mahmoud MF, Sobeh M. 2022. *Syzygium jambos* L. Alston: An insight into its phytochemistry, traditional uses, and pharmacological properties. *Front Pharmacol.* 13:786712.
153. Jayasinghe ULB, Ratnayake RMS, Medawala MMWS, Fujimoto Y. 2007. Dihydrochalcones with radical scavenging properties from the leaves of *Syzygium jambos*. *Nat Prod Res.* 21(6):551-554.
154. Avila-Peña D, Peña N, Quintero L, Suárez-Roca H. 2007. Antinociceptive activity of *Syzygium jambos* leaves extract on rats. *J Ethnopharmacol.* 112(2):380-385.
155. Nguenang GS, Mbaveng AT, Fankam AG, Manekeng HT, Nayim P, Wamba BEN, Kuete V. 2018. *Tristemma hirtum* and five other Cameroonian edible plants with weak or no antibacterial effects modulate the activities of antibiotics against gram-negative multidrug-resistant phenotypes. *ScientificWorldJournal.* 2018:7651482.
156. Paudel A, Hamamoto H, Kobayashi Y, Yokoshima S, Fukuyama T, Sekimizu K. 2012. Identification of novel deoxyribofuranosyl indole antimicrobial agents. *J Antibiot (Tokyo).* 65(2):53-57.