Investigational
Medicinal Chemistry & Pharmacology

Research Article Open Access

Anti-Klebsiella and antibiotic-potentiation activities of the methanol extracts of seven Cameroonian dietary plants against multidrug-resistant phenotypes over-expressing AcrAB-TolC efflux pumps

Valaire Y. Matieta, Victor Kuete, Armelle T. Mbaveng*

Abstract

Background: Bacterial infections continue to wreak havoc around the world with high death rates. African medicinal plants and the phytoconstituents showed high efficiency in impeding the growth of the resistance phenotypes of bacteria The present work was designed to determine the antibacterial activity of seven Cameroonian dietary plants against clinical multidrug-resistant (MDR) isolates of *Klebsiella sp.* These plants included *Persea americana* Miller (Lauraceae), *Psidium guajava* Linn. (Myrtaceae), *Mangifera indica* Linn. (Anacardiaceae), *Citrus sinensis* Linn. (Rutaceae), *Passiflora edulis* Sims (Passifloraceae), *Garcinia kola* Heckel (Guttiferae), and *Artocarpus heterophylus* Lam. (Moraceae).

Methods: Minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) determinations on the used bacterial strains alone, in the presence of an efflux pump inhibitor, phenylalanine arginine beta naphthylamide (PAβN), and in combination with antibiotics, were performed by the microbroth dilution method using a rapid colorimetric para-Iodonitrotetrazolium chloride (INT) assay.

Results: The tested botanicals had different extend of antibacterial activities, with MIC ranges of between 256 µg/mL and 2048 µg/mL. Botanicals from *Persea americana*, *Psidium guajava*, *Mangifera indica*, *Artocarpus heterophyllus*, and *Garcinia kola* bark had detected MIC values on all 15 tested *Klebsiella* strains. PAβN potentiated the activity of the botanicals on all tested bacteria, with the increase of activity ranging from 4 to more than 128-fold. The most significant increase of 4 to more than 128-fold was observed with botanicals from leaves and bark of *Psidium guajava* and *Mangifera indica*. The botanicals from the leaves of *Mangifera indica* potentiated the activity of eight out of ten tested antibiotics (Ceftriaxone, Chloramphenicol, Levofloxacin, Ampicillin, Tetracycline, Imipenem, Doxycycline, and Levofloxacin) against 100% of the tested bacteria.

Conclusion: In the present study, it was demonstrated that botanicals from *Persea Americana*, *Psidium guajava*, *Mangifera indica*, *Artocarpus heterophyllus*, and *Garcinia kola* had the highest spectrum of activity, and can be used to combat the resistance of Klebsiella species

Keywords: Antibacterial activity; botanicals; Cameroon; dietary plants; Klebsiella; multidrug resistance.

**Correspondence: Tel.: +237 676542386; E-mail address: armbatsa@yahoo.fr; ORCID: https://orcid.org/0000-0003-4178-4967 (Armelle T. Mbaveng)*

[1]Department of Biochemistry, Faculty of Science, University of Dschang, Dschang, Cameroon.

Other authors:
E-mail: yvmatieta@yahoo.com (Valaire Y. Matieta); E-mail: kuetevictor@yahoo.fr; ORCID: http://orcid.org/0000-0002-1070-1236 (Victor Kuete)

Citation on this article: Matieta VY, Kuete V, Mbaveng AT. Anti-Klebsiella and antibiotic-potentiation activities of the methanol extracts of seven Cameroonian dietary plants against multidrug-resistant phenotypes over-expressing AcrAB-TolC efflux pumps.Invest Med Chem Pharmacol. (2023) 6(1):73; Doi: https://dx.doi.org/10.31183/imcp.2023.00073

Background

Bacterial infections continue to wreak havoc around the world with high death rates. This is emphasized by the emergence of multidrug-resistant (MDR) phenotypes, including *Klebsiella pneumoniae* and *Klebsiella oxytoca*. They have developed resistance mechanisms vis-à-vis the usual antibiotics leading to the loss of their effectiveness [1, 2]. This development of antibiotic resistance is also due to the misuse of antibiotics in human and animal therapy. To face this threat, it is becoming urgent to discover novel bioactive agents. Medicinal plants constitute a promising source for novel drugs to combat both sensitive and resistant phenotypes [3-12]. In recent years, African medicinal plants and the phytoconstituents showed high efficiency in impeding the growth of the resistance phenotypes of cancer, plasmodium falciparum, or bacteria [13] [14] [15-20]. Some of the plants with prominent antibacterial activities against MDR bacteria including the AcrAB-TolC pumps expressing strains of *Klebsiella pneumoniae* include *Pentaclethra macrophylla* [21], *Dioscorea bulbifera* [22], *Canarium schweinfurthii* [23], *Theobroma cacao* [24], *Curcuma longa* [25], *Cocos nucifera, Glycine max* and *Musa sapientum* [26], and *Coffea arabica* [27]. In our continuous search for new natural products to fight against bacterial drug resistance, the present work was designed to determine the antibacterial activity of seven Cameroonian dietary plants against clinical MDR isolated of *Klebsiella sp.* These plants included *Persea americana* Miller (Lauraceae), *Psidium guajava* Linn. (Myrtaceae), *Mangifera indica* Linn. (Anacardiaceae), *Citrus sinensis* Linn. (Rutaceae), *Passiflora edulis* Sims (Passifloraceae), *Garcinia kola* Heckel (Guttiferae), and *Artocarpus heterophylus* Lam. (Moraceae).

P. americana is traditionally used to treat worms, microbial infections, malaria, diabetes, high blood pressure, stimulates uterine contractions and relief painful menstruations, urinary infections, bronchitis, rheumatism, anemia, exhaustion, hypercholesterolemia, hypertension, gastritis, and gastroduodenal ulcer, cancer, food, analgesic, as anti-inflammatory, hypoglycemic, anticonvulsant, and vasorelaxant [28-30]. Phytochemical investigations of the plant led to the isolation of kaempferol, quercetin 3-*O*-*α*-$_D$-arabinopyranosides, afzelin, quercitrin, quercetin 3-*O*-*α*-glucopyranoside, quercetin, quercetin 3-*O*-*β*-galactopyranoside, afzelin [28], persin [31], 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, and epicatechin [32]. Various parts of the plant displayed anti-inflammatory, antibacterial, antiproliferative, analgesic, anti-diabetic, cardiovascular, antihypertensive, antiviral, and wound-healing activities [21, 28, 29, 33-38]. *P. guajava* is used in the traditional medicinal system to treat wounds, ulcers, diarrhea, cholera, hypertension, obesity, diabetes mellitus, inflammation, cough, diabetes, kidney problems, diarrhea, worms, conjunctivitis, and as and antispasmodic [39-41]. Its potential bioactive secondary metabolites include tannins, myricetin, quercetin, luteolin, kaempferol, essential oils oleanic, ursolic, catecolic, guayavolic, maslinic, and ellagic acids, and *β*-sitosterol [42], The various part of the plant have shown anti-inflammatory, antiproliferative, antibacterial and antifungal, anti-diabetic, analgesic, antinociceptive, antimalarial, antitussive, hepatoprotective, anti-allergic, hypotensive, cardioprotective, and wound healing activities [41, 43, 44] [33, 39, 40, 43, 45, 46] [47-52]. *M. indica* is used traditionally to treat syphilis, inflammation, cough, hiccup, hyperdipsia, burning sensation, hemorrhages, hemoptysis, hemorrhoids, wounds, ulcers, diarrhea, dysentery, pharyngoplasty, scorpion string, wounds, ulcers, anorexia, dyspepsia, gastric disorders, asthma, mouth sores, liver diseases, urinary tract infections, diabetes, rheumatism, leucorrhea, lung hemorrhage, nerve disorders, and jaundice [41, 53, 54]. The plant contains quercetin, kaempferol, gallic acid, caffeic acid, catechins, tannins and mangiferin [55], careen, ocimene, terpinolene, myrcene, limonene, lupeol, lupeollinoleate, luteoxanthin, violaxanthin, neoxanthin, zeaxanthin, cryptoxanthin, chloromangiferamide, and bromomangiferic acid [54]. Its reported biological activities include the anti-inflammatory [56], antibacterial and antifungal [41], antiproliferative [57-60], antinociceptive [61], analgesic [62], neuroprotective [63], anti-diabetic [64], hepatoprotective [65], antimalarial [66], immunomodulatory [67], anthelmintic [68], anti-hyperlipidemia [69], and gastroprotective activities [70]. *C. sinensis* is an edible fruit with medicinal properties recognized in cases of constipation, cramps, colic, diarrhea, bronchitis, tuberculosis, cough, cold, obesity, menstrual disorder, angina, hypertension, anxiety, depression, stress, sore throats, indigestion, relieve intestinal gas and bloating, resolve phlegm, and additive for flavoring [71]. Some potential active compounds of the plant are caffeic, *p*-coumaric, ferulic, and sinapinic acids, hesperidine, narirutin, naringin, eriocitrin [72], D-limonene, *β*-myrcene, α-pinene, *β*-pinene, *γ*-terpinene, *α*-ter- pinolene, *α*-Caryophyllene, copaene, *β*-phellandrene [73], 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, hesperidin [74]. The plant has antibacterial, antifungal, antiproliferative, anxiolytic, antimalarial, anti-Trypanosoma, anti-obesity, antiosteoporosis, and insecticidal activities [41, 75-83]. *P. edulis* is used traditionally for the treatment of anxiety, insomnia, nervousness, antifungal, anti-inflammatory, antihypertensive [84], gastric trouble [85], cancer [86], tonic, digestive, sedative, diuretic, antidiarrheal, insecticide, cough, dry throat, constipation, insomnia, dysmenorrhea, colic infants, joint pain, and dysentery [87]. Its potential bioactive constituents include 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 [86], luteolin, apigenin, quercetin and its derivatives, rutin, 4-hydroxybenzoic, chlorogenic, ferulic, vanillic, caffeic, trans-cinammic, *p*-coumaric acids, vanillic acid [87], harmidine, harmine, harmane, harmol, *N*-trans-feruloyltyramine, and *cis*-*N*-feruloyltyramine [87, 88]. The pharmacological investigations of *P. edulis* revealed its Anti-inflammatory, antibacterial, antiproliferative, anti-diabetic, analgesic, anxiolytic, anti-depressant, anti-hypertensive, hepatoprotective, and anti-hyperlipidemia activities [89-95]; [84, 96-101]. *A. heterophylus* is used for health conditions such as fractures, diabetes, laxative, increases breast milk in nursing mothers, promotes anemia, diarrhea, and cough [102]. Its antibacterial activities have been demonstrated [103]. *G. kola* is used traditionally in cases of nervous alertness and induction of insomnia, wound healing, cancer, stomachache, gastritis, malaria, venereal diseases, laryngitis, and poison antidote [104]. It contains the biflavanones GB1 and GB2, the kolaflavanone GB-1a, biflavonoid complex kolaviron [105, 106], 9,19-Cyclolanost-24-en-3-ol; 9,19-cyclolanostan-3-ol,24-methylene [106]; *δ,δ*-bigarcinoic acid, *δ,δ*-bi-*O*-garcinoic acid; *γ,δ*-bi-*O*-garcinoic acid, (8*E*)-4-geranyl-3,5-dihydroxybenzophenone [107], 18-metoxycytochalasin J; cytochalasins H and J, and alternariol [108]. *G. kola* has been reported for its anti-inflammatory, diabetic, analgesic, antibacterial, antiproliferative, antimalarial, antimalarial,

anti-diabetic, hepatoprotective, nephroprotective, antinociceptive, neuroprotective, gastroprotective, and antiparasitic activities [104, 106, 109-121].

Methods

Plant material and extraction

The plant material used in the present work included seven food plants from Cameroon. They were collected in Dschang (West Region) and Loum (Littoral Region) in Cameroon and identified in the Cameroon national herbarium (HNC). They were *Persea americana* leaves and bark (57756/HNC), *Psidium guajava* leaves and bark (2884/SRFCam), *Mangifera indica* leaves and bark (1846/HNC), *Citrus sinensis* leaves and fruits (25859/HNC), *Passiflora edulis* whole plant (65104/HNC), *Garcinia kola* bark and fruits (27839/SRF-CAM), and *Artocarpus heterophylus* leaves and bark (43993/HNC). They 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 botanicals were kept at 4°C until further use.

Chemicals

The chemicals used include the bacterial growth indicator, para-Iodonitrotetrazolium chloride ≥97% (INT), antibiotics, Cefixime, Ceftriaxone, Chloramphenicol, Levofloxacin, Ampicillin, Tetracycline, Augmentin, Imipenem, Doxycycline, and Levofloxacin, and the efflux pump inhibitor, phenylalanine arginine beta naphthylamide (PAβN). They were all obtained from Sigma-Aldrich (St. Quentin Fallavier). Dimethylsulfoxide (DMSO, Sigma-Aldrich) was used to dissolve the tested samples.

Bacterial strains

The tested bacteria belong to two Klebsiella genera, *Klebsiella pneumoniae* and *Klebsiella oxytoca*. The strains of *K. pneumoniae* included the reference strain from American Type Culture Collection (ATCC) ATCC11296, and the clinical isolate available in Laboratory of Microbiology and Antimicrobial Substances of the University of Dschang, KP63, KP55, KP22, KP126, KP96, KP26, KP80, KP31, and KP44. The strains of *K. oxytoca* were also the clinical laboratory isolates, KO107, KO109, KO43, KO53, KO122, and KO58. Their bacterial features are shown in Table 1. They were sub-cultured in Mueller Hinton Agar (MHA) for their activation 24 hours prior to any use while the antibacterial testing was done in the Mueller Hinton Broth [122, 123].

Antibacterial testing

Minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) determinations on the used bacterial strains were performed using a rapid colorimetric INT test [124-126]. 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 [126]. Botanicals were also tested in the presence of PAβN at the concentration of 30 µg/mL to evaluate the role of efflux pumps on the resistance of the bacteria to the samples [127, 128]. 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 KP55 (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 [41, 129]. Activity ameliorating factor (AAF) was calculated as the ratio of the MIC of the antibiotic alone versus MIC in the combination with the botanical ($MIC_{\text{of the antibiotic alone}}/MIC_{\text{of the antibiotic with botanical}}$) [130].

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. For in-depth analyses, the established cutoff point for the antibacterial activity of botanicals towards Enterobacteria was used as follows: outstanding activity is observed when MIC ≤ 8 µg/mL, excellent activity when 8 < MIC ≤ 64 µg/mL, very good activity when 64 < MIC ≤ 128 µg/mL, good activity when 128 < MIC ≤ 256 µg/mL, average activity when 256 < MIC ≤ 512 µg/mL, weak activity when 512 < MIC ≤ 1024 µg/mL, and not active MIC > 1024 µg/mL [131]. The bactericidal or bacteriostatic effect of botanicals was determined using the ratio MBC/MIC.

Results

MICs and MBCs of botanicals

The MICs and MBCs were determined against 10 isolates or strains of *K. pneumoniae* and 5 strains of *K. oxytoca*, and the results are depicted in Table 2. The tested botanicals had different extend of antibacterial activities, with MIC ranges of between 256 µg/mL and 2048 µg/mL. Botanicals from *Persea americana*, *Psidium guajava*, *Mangifera indica*, *Artocarpus heterophyllus*, and *Garcinia kola* bark had detected MIC values on all 15 tested *Klebsiella* strains. Botanicals from *Passiflora edulis* leaf inhibited the growth of 75% of the tested bacteria while those from *Garcinia kola* and *Citrus sinensis* leaves inhibited respectively 44% and 50%. Each botanical, as well as the reference antibiotic, displayed a bactericidal effect on at least two bacterial strains.

Effect of botanicals on Klebsiella sp. in the presence of PAβN

The MIC values of botanicals in the presence of an efflux pump inhibitor (PAβN) were determined in 8 bacterial isolates to assess the role of the efflux pumps in the resistance to the tested samples (Table 3). PAβN potentiated the activity of the botanicals on all tested bacteria, with the increase of activity ranging from 4 to more than 128-fold. The most significant increase (4 to more than 128-fold) was observed with botanicals from leaves and bark of *Psidium guajava* and *Mangifera indica*.

Effect of the combinations between antibiotics and botanicals

To determine the concentration of plant extracts to be used in the associations with antibiotics, a preliminary assay was performed toward KP55. Eight of the fourteen botanicals best potentiated the activity of antibiotics at the subinhibitory concentrations of MIC/2 and MIC/4 (Data not shown). These included the botanicals from the leaves of *Persea americana*, leaves and bark of *Psidium guajava*, *Mangifera indica* leaves, *Artocarpus heterophyllus* leaves, *Citrus Sinensis* leaves, and *Passiflora edulis* leaves. These eight botanicals were further tested on eight other bacterial strains at sub-inhibitory concentrations of CMI/2 and CMI/4. The results obtained are presented in Table 4. Botanicals improved the activities of several antibiotics at MIC/2 and MIC/4 with an AAF between 2 and 128. The extracts of the leaves of *Mangifera indica* potentiated the activity of eight out of ten tested antibiotics (Ceftriaxone, Chloramphenicol, Levofloxacin, Ampicillin, Tetracycline, Imipenem, Doxycycline, and Levofloxacin) against 100% of the tested bacteria. *Psidium guajava* leaf extract improved the antibacterial activities of seven out of ten antibiotics tested (Ceftriaxone, chloramphenicol, Ampicillin, Tetracycline, Cefixime, Doxycycline, and Levofloxacin) against 100% of the tested bacteria. The bark extract of *Psidium guajava* improved the antibacterial activities of 60% of antibiotics (Penicillin, Ceftriaxone, Doxycycline, Tetracycline, Levofloxacin, and Chloramphenicol) against 100% of the tested bacteria. *Persea americana* leaf extracts potentiated the antibacterial activities of 60% of antibiotics (Ceftriaxone, Cefixime, Imipenem, Doxycycline, Levofloxacin, and Chloramphenicol) against 87.5%, 87.5%, 87.5%, 87.5%, 100%, and 100% of the tested bacteria respectively. *Citrus sinensis* leaf extracts and *Passiflora edulis* leaf extracts weakly potentiated the antibacterial activities of antibiotics against 50% to 75% of the studied bacteria.

Discussion

The antibacterial activity of plant extracts was determined by the micro broth dilution method. According to the established classification scales, no botanical had significant or outstanding antibacterial activity against the studied bacteria [131, 132]. The extract from the bark of *Psidium guajava* had a spectrum of activity of 100% against the tested bacteria, with 93.75% displaying good activities with MIC values below 256 µ/mL, followed by the extracts from the bark of *Persea americana*, *Artocarpus heterophyllus* bark, *Persea americana* leaf, *Psidium guajava* leaf, and *Mangifera indica* leaf vis-a-vis 81.25%, 62.5%, 56.25%, 56.25%, and 56.25% of the studied bacteria, respectively [131]. The other botanicals had average and weak activities [131]. The antibacterial activity of the extracts of the leaves and the bark of *Psidium guajava* obtained herein corroborates with that of [41], which highlighted the antibacterial properties of these extracts with MICs varying from 256 to 1024 µg/mL against *Klebsiela pneumoniae*. Similarly, Hackman et al. showed that the leaf extracts of this plant possess activity against carbapenem-resistant *Klebsiella pneumoniae* [133]. This activity can be due to the presence of flavonoids and other metabolites present in the extract [134]. The results obtained with botanicals from the bark and leaves of *Mangifiera indica* corroborate those of Gbala and Anibijuwon. [135], In effect, they have demonstrated that the leaves and bark of this plant have antibacterial activities against carbapeneme-resistant Enterobacteriaceae, including *Klebsiella pneumoniae*. Similarly, Dzotam and kuete (2017) also demonstrated the antibacterial activity of *Mangifera indica* extracts against *Kebsiella pneumoniae* with MICs ranging from 512 to 1024 µg/mL. The antibacterial activities of extracts from the bark and leaves *of Artocarpus heterophyllus* reported herein corroborates with the work of Dzotam and Kuete ([136]. The tested botanicals generally displayed MBC/MIC values above 4, clearly indicating that they rather have bactericidal effects [137].

Gram-negative bacteria can resist to the inhibitory effects of antibiotics through the overexpression of efflux pumps. Kuete et al. demonstrated that efflux pumps decrease the intracellular concentration of natural products and therefore their activity [127, 128]. To highlight this resistance of the studied bacteria, the PAβN, which is an efflux pump inhibitor, was used. The result showed that the activity of all the botanicals increased against all tested bacteria. This result corroborates with those of the work of Touani et al. [4]. This increase in the activity of the extracts in the presence of PAβN may be because this inhibitor blocks the bacterial efflux pumps, thereby restoring the activity of the extracts [138].

Antibiotics increasingly lose their antibacterial activity against bacteria that have become multi-drug resistant. However, it has been shown that plant extracts can modulate the activity of these antibiotics [4]. In the present study, the extracts of the leaves of *Mangifera indica*, *Psidium guajava* leaves and bark, and *Mangifera indica* leaf extracts modulated the antibacterial activity of at least six different antibiotics from different classes against 87.5% and 100 % (8/8) of bacterial isolates tested. Botanical from the seeds of Mangifera indica in combination with ampicillin previously had synergistic effects against *Klebsiella pneumoniae* Kumar et al. [139].

Finally, the extracts of the leaves of *Mangifera indica*, leaves, and bark extracts of *Psidium guajava* had synergistic effects with antibiotics and can be inhibitors of the bacterial efflux pumps. In effect, Braga et al. [140] have stated that products capable of potentiating the activity of antibiotics on more than 70% of bacteria are considered efflux pump inhibitors. The mechanisms of resistance to these antibiotics have also been highlighted in the context of our work with PAβN.

Table 1. Bacterial features of the strains of the studied *Klebsiella* species.

Souches et isolats	Features	Reference
Klebsiella pneumoniae		
ATCC 11296	Souche de reference	[127, 128]
KP63	Clinical strain : Tet^r, Chl^r, Amp^r, Atm^r	[16]
KP55	Clinical isolate MDR, Tet^r,Amp^r ,Atm^r,Cef^r	[9]
KP22	Clinical isolate MDR, Lev, Atm^r, Do^r, Imp^r, f^r	Laboratory Collection
KP126	Clinical isolate MDR, Amc^r	Laboratory Collection
KP96	Clinical isolate MDR, Atm^r, Mi^r, Amc^r,Cn^r,Ak^r	Laboratory Collection
KP26	Clinical isolate MDR, Amc^r	Laboratory Collection
KP80	Clinical isolate MDR, Prl^r, Amc^r	Laboratory Collection
KP31	Clinical isolate MDR, Ofx^r, Mi^r, Do^r, Mi^r	Laboratory Collection
KP44	Clinical isolate MDR, Atm^r Do^r, Mi^r	Laboratory Collection
Klebsiella oxytoca		Laboratory Collection
KO107	Clinical isolate MDR, Atm^r Do^r, Mi^r, Cip^r	Laboratory Collection
KO109	Clinical isolate MDR, Atm^r Do^r, Mi^r, Imp^r	Laboratory Collection
KO43	Clinical isolate MDR, Atm^r Do^r, Mi^r, Imp^r	Laboratory Collection
KO122	Clinical isolate MDR, Lev^r, F^r, Atm^r Do^r, Mi^r, Imp^r	Laboratory Collection
KO58	Clinical isolate MDR, Mi^r, Amc^r	Laboratory Collection

Table 2. MICs and MBCs (in µg/mL) of the tested botanicals against the tested strains of *Klebsiella pneumoniae* and *Klebsiella oxytoca*.

Bacterial strains	***Persea americana***						***Psidium guajava***					
	(Leaves)			**(Bark)**			**(Leaves)**			**(Bark)**		
	MIC	**MBC**	**R**	**MIC**	**MBC**	**R**	**MIC**	**MBC**	**R**	**MIC**	**MBC**	**R**
KP126	1024	2048	2	512	2048	4	512	2048	4	512	-	nd
KO43	512	1024	2	512	2048	4	512	2048	4	512	1024	2
KP31	512	2048	4	256	-	nd	512	-	nd	256	2048	8
KP44	512	2048	4	512	-	nd	512	-	nd	512	1024	2
KP46	1024	-	Nd	512	-	nd	1024	-	nd	512	-	nd
KP96	512	2048	4	512	-	nd	1024	2048	2	512	1024	2
KP80	512	1024	2	512	-	nd	1024	-	nd	512	2048	4
KO58	512	-	nd	256	-	nd	1024	2048	2	512	-	nd
KP22	1024	-	nd	1024	-	nd	512	-	nd	512	-	nd
KO122	1024	-	nd	1024	1024	1	2048	2048	1	512	-	nd
KO107	1024	-	nd	512	-	nd	512	2048	4	256	-	nd
KO109	2048	-	nd	1024	-	nd	1024	-	nd	512	1024	2
KP26	512	-	nd	256	-	nd	256	1024	8	256	-	nd
ATCC11296	512	2048	4	512	2048	4	512	2048	4	256	512	2
KP55	1024	-	Nd	512	2048	4	2048	-	nd	1024	2048	2
KP63	256	2048	8	256	2048	8	512	2048	4	512	-	nd

MIC: minimal inhibitory concentration (in µg/mL); MBC: minimal bactericidal concentration (in µg/mL); R: MBC/MIC ratio; nd: not determined.

Table 2. *Continued…*

Bacterial strains	***Citrus Sinensis***			***Passiflora edulis***			***Mangifera indica***					
	(Leaves)			**(Leaves)**			**(Leaves)**			**(Bark)**		
	MIC	**MBC**	**R**	**MIC**	**MBC**	**R**	**MIC**	**MBC**	**R**	**MIC**	**MBC**	**R**
KP126	1024	2048	2	512	2048	4	1024	2048	2	1024	2048	2
KO43	1024	1024	1	1024	2048	2	512	2048	4	256	2048	8
KP31	2048	2048	1	512	1024	2	512	2048	4	2048	2048	1
KP44	1024	1024	1	512	1024	2	256	1024	4	1024	2048	2
KP46	512	1024	2	1024	1024	1	2048	-	nd	1024	2048	2
KP96	-	-	nd	-	-	nd	2048	2048	1	1024	2048	2
KP80	2048	-	nd	2048	-	nd	1024	2048	2	1024	-	nd
KO58	2048	-	nd	2048	-	nd	512	-	nd	1024	-	nd
KP22	2048	-	nd	2048	-	nd	512	-	nd	512	2048	4
KO122	-	-	nd	-	-	nd	1024	2048	2	1024	-	nd
KO107	-	-	nd	2048	-	nd	512	-	nd	512	2048	4
KO109	-	-	nd	1024	1024	1	1024	-	nd	1024	-	nd
KP26	-	-	nd	2048	-	nd	256	1024	4	256	2048	8
ATCC11296	-	-	nd	-	-	nd	512	2048	4	512	2048	4
KP55	-	-	nd	-	-	nd	1024	2048	2	1024	2048	2
KP63	-	-	nd	2048	-	nd	256	512	2	512	1024	2

Table 2. *Continued and end.*

Bacterial strains	*Artorocarpus heterophyllus*						*Garcinia kola*						*Chloramphenicol*		
	(Leaves)			(Bark)			(Leaves)			(Bark)					
	MIC	MBC	R	MIC	MBC	R	MIC	MBC	R	MIC	MBC	R	**MIC**	**MBC**	**R**
KP126	512	2048	4	256	1024	4	1024	2048	2	512	2048	4	128	128	1
KO43	1024	2048	2	512	1024	2	1024	2048	2	1024	2048	2	128	>256	nd
KP31	1024	-	nd	512	2048	4	1024	-	nd	1024	-	nd	>256	>256	nd
KP44	1024	2048	2	256	2048	8	2048	2048	1	1024	2048	2	>256	>256	nd
KP46	1024	1024	1	512	1024	2	2048	-	nd	1024	1024	1	128	128	1
KP96	2048	2048	1	1024	1024	1	1024	2048	2	2048	2048	1	>256	>256	nd
KP80	1024	2048	2	256	2048	8	-	-	nd	1024	2048	2	>256	>256	nd
KO58	1024	-	nd	256	-	nd	-	-	nd	1024	-	nd	>256	>256	nd
KP22	1024	2048	2	1024	-	nd	-	-	nd	1024	2048	2	>256	>256	nd
KO122	2048	-	nd	1024	2048	2	-	-	nd	2048	-	nd	>256	>256	nd
KO107	1024	-	nd	1024	-	nd	-	-	nd	1024	-	nd	>256	>256	nd
KO109	2048	-	nd	2048	-	nd	-	-	nd	2048	-	nd	>256	>256	nd
KP26	512	1024	2	256	2048	8	-	-	nd	512	1024	2	>256	>256	nd
ATCC11296	512	2048	4	2048	-	nd	-	-	nd	512	2048	4	>256	>256	nd
KP55	2048	-	nd	512	-	nd	-	-	nd	2048	-	Nd	>256	>256	nd
KP63	512	2048	4	512	2048	4	1024	-	nd	512	2048	4	>256	>256	nd

Table 3. Anti-Klebsiella activity (MIC in µg/mL) of the botanicals in the presence of PAβN.

Bacterial strains	*Persia americana*						*Psidium guajava*						*Syzygium jambos*					
	Leaves			*Bark*			*Leaves*			*Bark*			*Leaves*			*Bark*		
	Alone	**+PAβN**	**R**	**Alone**	**+PAβN**	**R**	**Alone**	**+PAβN**	**R**	**Alone**	**+PAβN**	**R**	**Alone**	**+PAβN**	**R**	**Alone**	**+PAβN**	**R**
KP22	1024	64	16	1024	256	**4**	512	32	**16**	512	64	**8**	512	64	**8**	512	128	**4**
KP46	1024	64	16	512	64	**8**	1024	32	**32**	512	32	**16**	256	16	**16**	1024	32	**32**
KP55	1024	32	32	512	32	**16**	-	16	**≤64**	1024	32	**32**	1024	32	**32**	1024	64	**16**
KP63	256	≤8	≥32	256	8	**32**	512	≤8	**≥64**	512	8	**64**	256	≤8	**≥32**	256	≤8	**≥32**
KP96	512	16	32	512	8	**64**	1024	≤8	**≥128**	512	16	**32**	512	16	**32**	512	<8	**≥64**
KO107	1024	16	64	512	16	**32**	512	32	**16**	256	16	**16**	512	≤8	**≥64**	256	8	**32**
KO109	-	16	≤64	1024	16	**64**	1024	8	**128**	512	16	**32**	1024	32	**32**	1024	32	**32**
KO122	1024	64	16	1024	128	**8**	-	64	**≤16**	-	64	**≤16**	1024	32	**32**	-	64	**≤16**

- : > 1024 µg /ml; R : Activity Ameliorating Factor (AAF): MIC alone /MIC with PAβN; In bold : Significant increased; PAβN : Phenylalanine arginine beta naphtylamide; MIC: minimal inhibitory concentration;

Table 3. *Continued and end.*

Bacterial strains	*Mangifera indica*						*Chloramphenicol*		
	Leaves			*Bark*					
	Alone	**+PAβN**	**R**	**Alone**	**+PAβN**	**R**	**Alone**	**+PAβN**	**R**
KP22	512	128	**4**	512	128	**4**	512	128	**16**
KP46	-	128	**≤4**	1024	64	**16**	512	64	**8**
KP55	1024	64	**16**	1024	128	**8**	256	128	**2**
KP63	256	≤8	**≥32**	512	8	**64**	128	8	**128**
KP96	-	≤8	**≤128**	1024	8	**128**	256	64	**4**
KO107	512	32	**16**	512	16	**32**	512	32	**32**
KO109	1024	32	**32**	1024	64	**16**	512	128	**4**
KO122	1024	8	**128**	1024	≤8	**≤128**	512	16	**128**

Table 4. Anti-Klebsiella activity of antibiotics (MIC in µg/mL) in the association with botanicals and activity increasing factors (AAF)

Bacterial strains and antibiotics	ATB	Botanicals, MICs, and Activity Ameliorating Factor (AAF, in bracket)					
		Persea americana		*Psidium guajava*			
		(Leaves)		(Leaves)		(Bark)	
		MIC/2	MIC/4	MIC/2	MIC/4	MIC/2	MIC/4
Ampicillin							
KP22	32	4(**8**)	4(**8**)	4(**8**)	8(**4**)	4(**8**)	8(**4**)
KP46	512	512(1)	512(1)	32(**16**)	256(**2**)	32(**16**)	512(1)
KP63	32	8(**4**)	8(**4**)	2(**16**)	2(**16**)	2(**16**)	2(**16**)
KP96	512	512(1)	512(1)	64(**8**)	128(**4**)	512(1)	1024(0.5)
KP26	512	512(1)	512(1)	256(**2**)	512(1)	256(**2**)	512(1)
KO107	128	32(**4**)	64(**2**)	16(**8**)	64(**2**)	64(**2**)	64(**2**)
KO109	256	256(1)	512(0.5)	64(**4**)	256(1)	256(1)	256(1)
KO122	512	256(**2**)	512(1)	4(**128**)	4(**128**)	128(**4**)	128(**4**)
% Potentiation		**50%**	**37.5%**	**100%**	**75%**	**75%**	**50%**
Penicillin							
KP22	32	4(**8**)	16(**2**)	4(**8**)	8(**4**)	8(**4**)	8(**4**)
KP46	128	64(**2**)	64(**2**)	4(**32**)	4(**32**)	4(**32**)	64(**2**)
KP63	32	4(**8**)	4(**8**)	4(**8**)	4(**8**)	4(**8**)	4(**8**)
KP96	256	256(1)	512(0.5)	4(**64**)	128(**2**)	128(**2**)	256(1)
KP26	64	64(1)	64(1)	16(**4**)	64(1)	32(**2**)	32(**2**)
KO107	256	128(**2**)	512(0.5)	256(1)	256(1)	128(**2**)	128(**2**)
KO109	256	4(**64**)	8(**32**)	4(**64**)	8(**32**)	4(**64**)	8(**32**)
KO122	64	2(**32**)	8(**8**)	2(**32**)	2(**32**)	2(**32**)	2(**32**)
% Potentiation		**75%**	**62.5%**	**87.5%**	**75%**	**100%**	**87.5%**
Augmentin							
KP22	16	2(**8**)	2(**8**)	2(**8**)	2(**8**)	2(**8**)	2(**8**)
KP46	64	8(**8**)	8(**8**)	2(**32**)	2(**32**)	2(**32**)	2(**32**)
KP63	16	2(**8**)	2(**8**)	2(**8**)	2(**8**)	2(**8**)	2(**8**)
KP96	256	128(**2**)	128(**2**)	4(**64**)	16(**16**)	32(**8**)	128(**2**)
KP26	256	256(1)	256(1)	256(1)	256(1)	256(1)	256(1)
KO107	64	4(**16**)	4(**16**)	2(**32**)	2(**32**)	4(**16**)	4(**16**)
KO109	64	64(1)	64(1)	4(**16**)	16(**4**)	4(**16**)	4(**16**)
KO122	128	2(**64**)	16(**8**)	2(**64**)	2(**64**)	2(**64**)	2(**64**)
% Potentiation		**75%**	**75%**	**87.5%**	**87.5%**	**87.5%**	**87.5%**
Ceftriaxone							
KP22	32	2(**16**)	8(**4**)	4(**8**)	16(**2**)	8(**4**)	8(**4**)
KP46	64	8(**8**)	32(**2**)	2(**32**)	16(**4**)	8(**8**)	16(**4**)
KP63	64	32(**2**)	64(1)	16(**4**)	16(**4**)	2(**32**)	8(**8**)
KP96	256	256(1)	256(1)	8(**32**)	32(**8**)	64(**4**)	64(**4**)
KP26	128	32(**4**)	64(**2**)	64(**2**)	64(**2**)	64(**2**)	64(**2**)
KO107	128	32(**4**)	64(**2**)	32(**4**)	64(**2**)	32(**4**)	64(**2**)
KO109	128	32(**4**)	32(**4**)	32(**4**)	32(**4**)	32(**4**)	32(**4**)
KO122	64	2(**32**)	32(**2**)	2(**32**)	2(**32**)	2(**32**)	2(**32**)
% Potentiation		**87.5%**	**75%**	**100%**	**100%**	**100%**	**100%**
Cefixime							
KP22	128	32(**4**)	128(1)	8(**16**)	32(**4**)	128(1)	128(1)
KP46	256	32(**8**)	128(**2**)	8(**32**)	32(**8**)	32(**8**)	128(**2**)
KP63	64	64(1)	64(1)	2(**32**)	32(**2**)	2(**32**)	32(**2**)
KP96	128	64(**2**)	64(**2**)	2(**64**)	8(**16**)	32(**4**)	32(**4**)
KP26	256	64(**4**)	64(**4**)	32(**8**)	64(**4**)	32(**8**)	64(**4**)
KO107	32	8(**4**)	16(**2**)	16(**2**)	16(**2**)	8(**4**)	16(**2**)
KO109	128	32(**4**)	64(**2**)	4(**32**)	32(**4**)	16(**8**)	32(**4**)
KO122	128	4(**32**)	4(**32**)	4(**32**)	4(**32**)	4(**32**)	4(**32**)
% Potentiation		**87.5%**	**75%**	**100%**	**100%**	**87.5%**	**87.5%**
Doxycycline							
KP22	2	0.25(**8**)	0.5(**4**)	0.5(**4**)	1(**2**)	0.5(**4**)	1(**2**)
KP46	32	32(1)	64(0.5)	4(**8**)	16(**2**)	16(**2**)	16(**2**)
KP63	2	1(**2**)	1(**2**)	0.5(**4**)	0.5(**4**)	0.25(**8**)	1(**2**)
KP96	32	16(**2**)	16(**2**)	1(**32**)	8(**4**)	16(**2**)	16(**2**)
KP26	16	8(**2**)	8(**2**)	8(**2**)	8(**2**)	8(**2**)	8(**2**)
KO107	8	2(**4**)	4(**2**)	2(**4**)	2(**4**)	1(**8**)	8(1)
KO109	16	8(**2**)	16(1)	0.5(**32**)	4(**4**)	2(**8**)	4(**4**)
KO122	8	0.25(**32**)	0.25(**32**)	0.25(**32**)	0.25(**32**)	0.25(**32**)	0.25(**32**)
% Potentiation		**87.5%**	**75%**	**100%**	**100%**	**100%**	**87.5%**
Tetracycline							
KP22	8	0.5(**16**)	0.5(**16**)	0.5(**16**)	4(**2**)	2(**4**)	8(1)
KP46	8	2(**4**)	4(**2**)	2(**4**)	4(**2**)	1(**8**)	1(**8**)
KP63	8	8(1)	8(1)	1(**8**)	4(**2**)	0.25(**32**)	1(**8**)
KP96	16	16(1)	16(1)	0.25(**64**)	0.25(**64**)	8(**2**)	8(**2**)
KP26	32	8(**4**)	16(**2**)	8(**4**)	16(**2**)	16(**2**)	32(0.5)
KO107	4	0.5(**8**)	2(**2**)	0.5(**8**)	1(**4**)	1(**4**)	1(**4**)
KO109	16	4(**4**)	4(**4**)	4(**4**)	4(**4**)	4(**4**)	4(**4**)
KO122	8	0.25(**32**)	0.25(**32**)	0.25(**32**)	0.25(**32**)	0.25(**32**)	0.25(**32**)
% Potentiation		**75%**	**75%**	**100%**	**100%**	**100%**	**62.5**
Levofloxacin							
KP22	8	0.5(**16**)	2(**4**)	1(**8**)	1(**8**)	1(**8**)	2(**4**)
KP46	8	1(**8**)	4(**2**)	1(**8**)	2(**4**)	1(**8**)	1(**8**)
KP63	8	2(**4**)	4(**2**)	0.50(**16**)	1(**8**)	0.50(**16**)	1(**8**)
KP96	64	8(**8**)	8(**8**)	4(**16**)	4(**16**)	2(**32**)	4(**16**)
KP26	16	4(**4**)	8(**2**)	2(**8**)	4(**4**)	2(**8**)	4(**4**)
KO107	16	1(**16**)	2(**8**)	2(**8**)	2(**8**)	1(**16**)	4(**4**)
KO109	32	4(**8**)	8(**4**)	8(**4**)	8(**4**)	4(**8**)	8(**4**)
KO122	16	0.5(**32**)	0.5(**32**)	0.5(**32**)	0.5(**32**)	0.5(**32**)	1(**16**)
% Potentiation		**100%**	**100%**	**100%**	**100%**	**100%**	**100%**

MIC: minimal inhibitory concentration; AAF: Activity ameliorating factor, ATB: antibiotic.

Table 4. *Continued…*

Bacterial strains and antibiotics	ATB	Botanicals, MICs, and Activity Ameliorating Factor (AAF, in bracket)					
		Persea americana		***Psidium guajava***			
		(Leaves)		**(Leaves)**		**(Bark)**	
		MIC/2	**MIC/4**	**MIC/2**	**MIC/4**	**MIC/2**	**MIC/4**
Imipenem							
KP22	32	8(**4**)	8(**4**)	8(**4**)	16(**2**)	8(**4**)	8(**4**)
KP46	256	64(**4**)	128(**2**)	64(**4**)	128(**2**)	128(**2**)	128(**2**)
KP63	64	32(**2**)	64(1)	8(**8**)	32(**2**)	2(**32**)	4(**16**)
KP96	128	128(1)	512(0.25)	128(1)	128(1)	128(1)	128(1)
KP26	128	32(**4**)	64(**2**)	16(**8**)	32(**4**)	2(**64**)	16(**8**)
KO107	32	4(**8**)	8(**4**)	4(**8**)	4(**8**)	4(**8**)	8(**4**)
KO109	64	8(**8**)	64(1)	8(**8**)	16(**4**)	8(**8**)	32(**2**)
KO122	32	2(**16**)	4(**8**)	2(**16**)	2(**16**)	2(**16**)	4(**8**)
% Potentiation		**87.5%**	**62.5%**	**87.5%**	**87.5%**	**87.5%**	**87.5%**
Chloramphenicol							
KP22	512	128(**4**)	256(**2**)	64(**8**)	256(**2**)	128(**4**)	512(1)
KP46	512	256(**2**)	512(1)	128(**4**)	256(**2**)	256(**2**)	256(**2**)
KP63	128	64(**2**)	128(1)	8(**16**)	64(**2**)	8(**16**)	64(**2**)
KP96	512	256(**2**)	256(**2**)	128(**4**)	128(**4**)	256(**2**)	256(**2**)
KP26	512	128(**4**)	512(1)	128(**4**)	128(**4**)	128(**4**)	128(**4**)
KO107	256	64(**4**)	128(**2**)	128(**2**)	128(**2**)	128(**2**)	128(**2**)
KO109	512	256(**2**)	256(**2**)	256(**2**)	256(**2**)	256(**2**)	256(**2**)
KO122	512	64(**8**)	128(**4**)	16(**32**)	128(**4**)	16(**32**)	128(**4**)
% Potentiation		**100%**	**62.5%**	**100%**	**100%**	**100%**	**87 .5%**

MIC: minimal inhibitory concentration; AAF: Activity ameliorating factor, ATB: antibiotic.

Table 4. *Continued…*

Bacterial strains and antibiotics	ATB	Botanicals, MICs, and Activity Ameliorating Factor (AAF, in bracket)							
		Mangifera indica		***Artocarpus heterophyllus***		***Citrus sinensis***		***Passiflora edulis***	
		(Leaves)		**(Leaves)**		**(Leaves)**		**(Leaves)**	
		MIC/2	**MIC/4**	**MIC/2**	**MIC/4**	**MIC/2**	**MIC/4**	**MIC/2**	**MIC/4**
Ampicillin									
KP22	32	4(**8**)	4(**8**)	4(**8**)	4(**8**)	8(**4**)	8(**4**)	4(**8**)	4(**8**)
KP46	512	16(**32**)	256(**2**)	1024(0.5)	1024(0.5)	256(**2**)	256(**2**)	256(**2**)	256(**2**)
KP63	32	2(**16**)	4(**8**)	4(**8**)	4(**8**)	8(**4**)	8(**4**)	4(**8**)	8(**4**)
KP96	512	8(**64**)	32(**16**)	512(1)	512(1)	128(**4**)	128(**4**)	128(**4**)	128(**4**)
KP26	512	256(**2**)	512(1)	512(1)	512(1)	512(1)	512(1)	1024(0.5)	1024(0.5)
KO107	128	32(**16**)	32(**16**)	16(**32**)	16(**32**)	32(**16**)	64(**2**)	32(**16**)	32(**16**)
KO109	256	64(**4**)	64(**4**)	256(1)	512(0.5)	256(1)	256(1)	512(0.5)	512(0.5)
KO122	512	64(**8**)	256(**2**)	256(**2**)	512(1)	512(1)	512(1)	512(1)	512(1)
% Potentiation		**100%**	**87.5%**	**50%**	**37.5%**	**62.5%**	**62.5%**	**62.5%**	**62.5%**
Penicillin									
KP22	32	8(**4**)	16(**2**)	16(**2**)	16(**2**)	32(1)	32(1)	32(1)	32(1)
KP46	128	4(**32**)	4(**32**)	128(1)	128(1)	64(**2**)	64(**2**)	32(**4**)	32(**4**)
KP63	32	4(**8**)	4(**8**)	4(**8**)	4(**8**)	8(**4**)	8(**4**)	8(**4**)	8(**4**)
KP96	256	4(**64**)	32(**8**)	256(1)	256(1)	256(1)	256(1)	128(**2**)	128(**2**)
KP26	64	32(**2**)	64(1)	64(1)	64(1)	64(1)	64(1)	64(1)	64(1)
KO107	256	2(**128**)	4(**64**)	4(**64**)	16(**16**)	32(**8**)	32(**8**)	16(**6**)	16(**6**)
KO109	256	4(**64**)	128(**2**)	4(**64**)	4(**64**)	128(**2**)	128(**2**)	128(**2**)	128(**2**)
KO122	64	32(**2**)	32(**2**)	32(**2**)	32(**2**)	32(**2**)	64(1)	16(**4**)	32(**2**)
% Potentiation		**100%**	**87.5%**	**50%**	**62.5%**	**62.5%**	**50%**	**62.5%**	**62.5%**
Augmentin									
KP22	16	2(**8**)	2(**8**)	2(**8**)	2(**8**)	2(**8**)	4(**4**)	2(**8**)	2(**8**)
KP46	64	2(**32**)	2(**32**)	32(**2**)	32(**2**)	16(**4**)	16(**4**)	64(1)	128(0.5)
KP63	16	2(**8**)	2(**8**)	2(**8**)	2(**8**)	2(**8**)	2(**8**)	2(**8**)	2(**8**)
KP96	256	4(**64**)	8(**32**)	128(**2**)	128(**2**)	256(1)	256(1)	256(1)	256(1)
KP26	256	256(1)	256(1)	256(1)	256(1)	256(1)	256(1)	256(1)	256(1)
KO107	64	1(**64**)	1(**64**)	2(**32**)	2(**32**)	32(**2**)	32(**2**)	16(**4**)	32(**2**)
KO109	64	32(**2**)	32(**2**)	4(**16**)	8(**8**)	32(**2**)	32(**2**)	32(**2**)	64(1)
KO122	128	2(**64**)	2(**64**)	8(**16**)	8(**16**)	128(1)	128(1)	64(**2**)	64(**2**)
% Potentiation		**87.5%**	**87.5%**	**87.5%**	**87.5%**	**62.5%**	**62.5%**	**62.5%**	**50%**
Ceftriaxone									
KP22	32	16(**2**)	32(1)	8(**4**)	16(**2**)	16(**2**)	16(**2**)	8(**4**)	64(0 .5)
KP46	64	2(**32**)	2(**32**)	64(1)	64(1)	16(**4**)	16(**4**)	16(**4**)	32(**2**)
KP63	64	16(**4**)	32(**2**)	16(**4**)	32(**2**)	128(0.5)	64(1)	64(1)	128(0.5)
KP96	256	2(**128**)	4(**64**)	32(**8**)	128(**2**)	64(**4**)	64(**4**)	64(**4**)	64(**4**)
KP26	128	64(**2**)	64(**2**)	128(1)	128(1)	128(1)	128(1)	128(1)	128(1)
KO107	128	16(**8**)	32(**4**)	32(**4**)	32(**4**)	8(**16**)	8(**16**)	16(**8**)	32(**4**)
KO109	128	4(**32**)	8(**16**)	4(**32**)	8(**16**)	128(1)	256(0.5)	128(1)	256(0.5)
KO122	64	2(**32**)	8(**8**)	2(**32**)	8(**8**)	8(**8**)	16(0.5)	16(0.5)	16(0.5)
% Potentiation		**100%**	**87.5%**	**62.5%**	**75%**	**62 .5%**	**50%**	**50%**	**37.5%**

Table 4. *Continued and end.*

Bacterial strains and antibiotics	ATB	Botanicals, MICs, and Activity Ameliorating Factor (AAF, in bracket)							
		Mangifera indica (Leaves)		*Artocarpus heterophyllus* (Leaves)		*Citrus sinensis* (Leaves)		*Passiflora edulis* (Leaves)	
		MIC/2	MIC/4	MIC/2	MIC/4	MIC/2	MIC/4	MIC/2	MIC/4
Cefixime									
KP22	128	64(**2**)	128(1)	32(**4**)	32(**4**)	128(1)	128(1)	128(1)	128(1)
KP46	256	2(**128**)	16(**16**)	128(**2**)	256(1)	32(**8**)	256(1)	64(**4**)	64(**4**)
KP63	64	8(**8**)	16(**4**)	64(1)	64(1)	16(**4**)	32(**2**)	8(**8**)	32(**2**)
KP96	128	2(**64**)	2(**64**)	64(**2**)	64(**2**)	64(**2**)	64(**2**)	64(**2**)	64(**2**)
KP26	256	16(**16**)	32(**8**)	32(**8**)	32(**8**)	128(**2**)	128(**2**)	128(**2**)	128(**2**)
KO107	32	8(**4**)	8(**4**)	16(**2**)	16(**2**)	4(**8**)	4(**8**)	8(**4**)	8(**4**)
KO109	128	128(1)	128(1)	64(**2**)	64(**2**)	128(1)	256(0.5)	256(0.5)	128(1)
KO122	128	2(**64**)	2(**64**)	2(**64**)	2(**64**)	16(**8**)	64(**2**)	64(**2**)	64(**2**)
% Potentiation		**87.5%**	**75%**	**82.5%**	**75%**	**75%**	**62.5%**	**75%**	**75%**
Doxycycline									
KP22	2	1(**2**)	2(1)	1(**2**)	2(1)	1(**2**)	1(**2**)	0.25(**8**)	1(**2**)
KP46	32	0.25(**128**)	4(**8**)	32(1)	32(1)	32(1)	32(1)	32(1)	32(1)
KP63	2	0.5(**4**)	1(**2**)	2(1)	2(1)	2(1)	2(1)	1(**2**)	1(**2**)
KP96	32	0.5(**64**)	8(**4**)	32(1)	32(1)	16(**2**)	16(**2**)	16(**2**)	16(**2**)
KP26	16	8(**2**)	4(**2**)	8(**2**)	16(1)	16(1)	16(1)	16(1)	16(1)
KO107	8	1(**8**)	4(**2**)	4(**2**)	8(1)	4(**2**)	4(**2**)	4(**2**)	4(**2**)
KO109	16	8(**2**)	16(1)	1(**16**)	8(**2**)	16(1)	16(1)	16(1)	16(1)
KO122	8	0.25(**32**)	0.25(**32**)	0.25(**32**)	0.25(**32**)	2(**4**)	8(1)	4(**2**)	8(1)
% Potentiation		**100%**	**75%**	**62.5%**	**25%**	**50%**	**37.5%**	**62.5%**	**50%**
Tetracycline									
KP22	8	1(**8**)	4(**2**)	8(1)	16(0.5)	4(**2**)	8(1)	4(**2**)	4(**2**)
KP46	8	0.5(**16**)	0.5(**16**)	4(**2**)	4(**2**)	4(**2**)	8(1)	4(**2**)	8(1)
KP63	8	1(**8**)	2(**4**)	4(**2**)	4(**2**)	4(**2**)	8(1)	4(**2**)	8(1)
KP96	16	0.5(**32**)	2(**8**)	8(**2**)	8(**2**)	4(**4**)	8(**2**)	8(**2**)	16(1)
KP26	32	16(**2**)	32(1)	16(**2**)	16(**2**)	32(1)	32(1)	32(1)	32(1)
KO107	4	0.5(**8**)	1(**4**)	1(**4**)	1(**4**)	1(**4**)	1(**4**)	1(**4**)	4(1)
KO109	16	4(**4**)	4(**4**)	16(1)	16(1)	16(1)	16(1)	16(1)	16(1)
KO122	8	0.25(**32**)	0.25(**32**)	0.25(**32**)	0.25(**32**)	2(**4**)	8(1)	4(**2**)	8(1)
% Potentiation		**100%**	**87.5%**	**75%**	**75%**	**75%**	**25%**	**75%**	**12.5%**
Levofloxacine									
KP22	8	4(**2**)	4(**2**)	2(**4**)	2(**4**)	1(**8**)	4(**2**)	1(**8**)	2(**4**)
KP46	8	0.5(**16**)	4(**2**)	4(**2**)	4(**2**)	4(**2**)	4(**2**)	4(**2**)	4(**2**)
KP63	8	4(**2**)	4(**2**)	4(**2**)	8(1)	4(**2**)	4(**2**)	4(**2**)	4(**2**)
KP96	64	0.5(**128**)	4(**16**)	8(**8**)	8(**8**)	64(1)	64(1)	16(**4**)	32(**2**)
KP26	16	4(**5**)	4(**4**)	8(**2**)	8(**2**)	16(1)	16(1)	16(1)	16(1)
KO107	16	2(**8**)	2(**8**)	2(**8**)	4(**4**)	1(**16**)	1(**16**)	1(**16**)	1(**16**)
KO109	32	4(**8**)	4(**8**)	4(**8**)	4(**8**)	8(**4**)	32(1)	16(**2**)	32(1)
KO122	16	0.5(**32**)	1(**16**)	0.5(**32**)	1(**16**)	4(**4**)	8(**2**)	1(**16**)	8(**2**)
% Potentiation		**100%**	**100%**	**100%**	**87.5%**	**75%**	**62.5%**	**75%**	**75%**
Imipenem									
KP22	32	4(**8**)	16(**2**)	8(**4**)	16(**2**)	16(**2**)	16(**2**)	8(**4**)	8(**4**)
KP46	256	64(**4**)	64(**4**)	256(1)	256(1)	256(1)	256(1)	256(1)	256(1)
KP63	64	4(**16**)	16(**4**)	4(**16**)	16(**4**)	8(**8**)	32(**2**)	8(**8**)	16(**4**)
KP96	128	64(**2**)	64(**2**)	64(**2**)	64(**2**)	64(**2**)	64(**2**)	64(**2**)	64(**2**)
KP26	128	16(**8**)	64(**2**)	64(**2**)	64(**2**)	32(**4**)	64(**2**)	32(**4**)	64(**2**)
KO107	32	2(**16**)	4(**8**)	4(**8**)	16(**2**)	32(1)	32(1)	16(**2**)	16(**2**)
KO109	64	16(**4**)	32(**2**)	16(**4**)	32(**2**)	32(**2**)	64(1)	64(1)	64(1)
KO122	32	2(**16**)	2(**16**)	2(**16**)	2(**16**)	16(**2**)	16(**2**)	16(**2**)	16(**2**)
% Potentiation		**100%**	**100%**	**87.5%**	**87.5%**	**75%**	**62.5%**	**75%**	**75%**
Chloramphenicol									
KP22	512	128(**4**)	256(**2**)	128(**4**)	128(**4**)	256(**2**)	256(**2**)	256(**2**)	256(**2**)
KP46	512	32(**16**)	128(**4**)	512(1)	1024(0.5)	512(1)	512(1)	256(**2**)	512(1)
KP63	128	32(**4**)	64(**2**)	64(**2**)	128(1)	128(1)	128(1)	128(1)	128(1)
KP96	512	64(**8**)	256(**2**)	512(1)	512(1)	1024(0.5)	1024(0.5)	512(1)	512(1)
KP26	512	128(**4**)	128(**4**)	128(**4**)	128(**4**)	128(**4**)	128(**4**)	128(**4**)	128(**4**)
KO107	256	64(**4**)	128(**2**)	64(**4**)	64(**4**)	64(**4**)	128(**2**)	64(**4**)	128(**2**)
KO109	512	128(**4**)	128(**4**)	128(**4**)	128(**4**)	256(**2**)	1024(0.5)	512(1)	1024(0.5)
KO122	512	16(**32**)	256(**2**)	16(**32**)	256(**2**)	128(**4**)	512(1)	256(**2**)	512(1)
% Potentiation		**100%**	**100%**	**75%**	**62.5%**	**62.5%**	**37.5%**	**62.5%**	**37.5%**

Conclusion

In the present study, it was demonstrated that botanicals from *Persea Americana*, *Psidium guajava*, *Mangifera indica*, *Artocarpus heterophyllus*, and *Garcinia kola* had the highest spectrum of activity, and can be used to combat the resistance of Klebsiella species. PAβN also potentiated their inhibitory effects, highlighting the ability of the bacteria to expel the botanical out of the bacterial cells *via* the efflux pumps. The extracts of the leaves of *Mangifera indica*, the leaves, and the bark of *Psidium guajava*, with their antibacterial and antibiotic-potentiating activity, could be effective in the treatment of infections caused by bacteria of the genus *Klebsiella*.

Abbreviations

AAF, Activity ameliorating factor; ATCC, American Type Culture Collection; DMSO, Dimethylsulfoxide; HNC, Cameroon national herbarium; INT, para-Iodonitrotetrazolium chloride, KP, *Klebsiella pneumoniae*; KO, *Klebsiella oxytoca*; MBC, minimum bactericidal concentration; MDR, multidrug-resistant; MIC, Minimum inhibitory concentration.

Authors' Contribution

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

Acknowledgments

Authors are thankful to the Cameroon National Herbarium for the identification of the plants.

Conflict of interest

The authors declare no conflict of interest.

Article history:

Received: 03 December 2022.
Received in revised form: 02 February 2023
Accepted: 05 February 2023
Available online: 06 February 2023

References

1. Chevalier J, Pages JM, Eyraud A, Mallea M. 2000. **Membrane permeability modifications are involved in antibiotic resistance in *Klebsiella pneumoniae***. *Biochem Biophys Res Commun*. **274**(2):496-499.
2. Ghisalberti D, Masi M, Pages JM, Chevalier J. 2005. **Chloramphenicol and expression of multidrug efflux pump in *Enterobacter aerogenes***. *Biochem Biophys Res Commun*. **328**(4):1113-1118.
3. 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.
4. Touani FK, Seukep AJ, Djeussi DE, Fankam AG, Noumedem JA, Kuete V. 2014. **Antibiotic-potentiation activities of four Cameroonian dietary plants against multidrug-resistant Gram-negative bacteria expressing efflux pumps**. *BMC Complement Altern Med.* **14**:258.
5. Efferth T, Kadioglu O, Saeed MEM, Seo EJ, Mbaveng AT, Kuete V. 2021. **Medicinal plants and phytochemicals against multidrug-resistant tumor cells expressing ABCB1, ABCG2, or ABCB5: a synopsis of 2 decades**. *Phytochem Rev*. **20**(1):7-53.
6. 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**. *Pharmaceutical Biol.* **47**(11):1042-1049.
7. Efferth T, Saeed MEM, Kadioglu O, Seo EJ, Shirooie S, Mbaveng AT, Nabavi SM, Kuete V: **Collateral sensitivity of natural products in drug-resistant cancer cells**. *Biotechnology advances* 2020, **38**:107342.
8. Kuete V, Wiench B, Alsaid MS, Alyahya MA, Fankam AG, Shahat AA, Efferth T. 2013. **Cytotoxicity, mode of action and antibacterial activities of selected Saudi Arabian medicinal plants**. *BMC Complement Altern Med.* **13**:354.
9. 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.
10. Kuete V, Efferth T. 2010. **Cameroonian medicinal plants: pharmacology and derived natural products**. *Front Pharmacol.***1**:123.
11. Mbaveng AT, Kuete V, Efferth T. 2017. **Potential of Central, Eastern and Western Africa medicinal plants for cancer therapy: spotlight on resistant cells and molecular targets**. *Front Pharmacol.* **8**:343.
12. Kuete V, Ngameni B, Wiench B, Krusche B, Horwedel C, Ngadjui BT, Efferth T. 2011. **Cytotoxicity and mode of action of four naturally occuring flavonoids from the genus *Dorstenia*: gancaonin Q, 4-hydroxylonchocarpin, 6-prenylapigenin, and 6,8-diprenyleriodictyol**. *Planta Med.* **77**(18):1984-1989.
13. Zofou D, Tene M, Ngemenya MN, Tane P, Titanji VP. 2011. ***In vitro* antiplasmodial activity and cytotoxicity of extracts of selected medicinal plants used by traditional healers of Western cameroon**. *Malar Res Treat.* **2011**:561342.
14. 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.
15. 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.
16. 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.
17. 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.
18. 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.
19. 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.
20. 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.
21. 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.
22. Kuete V, Betrandteponno R, Mbaveng AT, Tapondjou LA, Meyer JJ, Barboni L, Lall N. 2012. **Antibacterial activities of the extracts, fractions and compounds from *Dioscorea bulbifera***. *BMC Complement Altern Med.* **12**:228.
23. Dzotam JK, Touani FK, Kuete V. 2016. **Antibacterial activities of the methanol extracts of *Canarium schweinfurthii* and four other Cameroonian dietary plants against multi-drug resistant Gram-negative bacteria**. *Saudi J Biol Sci.* **23**:565-570.
24. 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.
25. Manekeng HT, Mbaveng AT, Nguenang GS, Seukep JA, Wamba BEN, Nayim P, Yinkfu NR, Fankam AG, Kuete V. 2018. **Anti-staphylococcal and antibiotic-potentiating activities of seven Cameroonian edible plants against resistant phenotypes**. *Invest Med Chem Pharmacol.* **1**:7.
26. Ngaffo CMN, Tankeo SB, Guefack MGF, Nayim P, Wamba BEN, Kuete V, Mbaveng AT. 2021. **Phytochemical analysis and antibiotic-modulating activity of *Cocos nucifera, Glycine max* and *Musa sapientum* methanol extracts against multidrug resistant Gram-negative bacteria.** *Invest Med Chem Pharmacol.* **4**(2):53.
27. Moungoue Ngwaneu LS, Mbaveng AT, Nayim P, Wamba BEN, Youmbi LM, Bonsou IN, Ashu F, Kuete V. 2022. **Antibacterial and antibiotic potentiation activity of *Coffea arabica* and six other Cameroonian edible plants against multidrug-resistant phenotypes**. *Invest Med Chem Pharmacol*. **5**(2):68.
28. 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.
29. 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.
30. 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.
31. 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.
32. Yasir M, Das S, Kharya MD. 2010. **The phytochemical and pharmacological profile of *Persea americana* Mill**. *Pharmacogn Rev.* **4**(7):77-84.
33. 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.
34. 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.
35. 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.
36. Antia B, Okokon J, Okon P. 2005. **Hypoglycemic activity of aqueous leaf extract of *Persea americana* Mill**. *Indian J Pharmacol.* **37**(5):325.
37. 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.
38. 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.
39. 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.
40. 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.
41. 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.
42. 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.
43. 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.
44. Dutta BK, Rahman I, Das TK. 2000. ***In vitro* study on antifungal property of common fruit plants**. *Biomedicine.* **20**(3):187-189.

45. 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.
46. 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.
47. 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.
48. Roy CK, Kamath JV, Asad M. 2006. **Hepatoprotective activity of *Psidium guajava* Linn. leaf extract**. *Indian J Exp Biol.* **44**(4):305-311.
49. 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.
50. 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.
51. 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.
52. 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.
53. Parvez GMM. 2016. **Pharmacological activities of mango (*Mangifera indica*): a review**. *J Pharmacogn Phytochem.* **5**(3):1.
54. Ediriweera MK, Tennekoon KH, Samarakoon SR. 2017. **A review on ethnopharmacological applications, pharmacological activities, and bioactive compounds of *Mangifera indica* (Mango)**. *Evid Based Complement Alternat Med.* **2017**:6949835.
55. Andreu GL, Delgado R, Velho JA, Curti C, Vercesi AE. 2005. **Mangiferin, a natural occurring glucosyl xanthone, increases susceptibility of rat liver mitochondria to calcium-induced permeability transition**. *Arch Biochem Biophys.* **439**(2):184-193.
56. Beg AA, Baldwin AS, Jr. 1993. **The I kappa B proteins: multifunctional regulators of Rel/NF-kappa B transcription factors**. *Genes Dev.* **7**(11):2064-2070.
57. Corrales-Bernal A, Amparo Urango L, Rojano B, Maldonado ME. 2014. **[*In vitro* and *in vivo* effects of mango pulp (*Mangifera indica* cv. Azucar) in colon carcinogenesis]**. *Arch Latinoam Nutr.* **64**(1):16-23.
58. Noratto GD, Bertoldi MC, Krenek K, Talcott ST, Stringheta PC, Mertens-Talcott SU: **Anticarcinogenic effects of polyphenolics from mango (*Mangifera indica*) varieties**. *J Agric Food Chem* 2010, **58**(7):4104-4112.
59. Nguyen HX, Do TN, Le TH, Nguyen MT, Nguyen NT, Esumi H, Awale S. 2016. **Chemical constituents of *Mangifera indica* and Their antiausterity activity against the PANC-1 Human pancreatic cancer cell line**. *J Nat Prod.* **79**(8):2053-2059.
60. Ediriweera MK, Tennekoon KH, Samarakoon SR, Thabrew I, De Silva ED. 2016. **Cytotoxic and apoptotic effects of the bark of two common mango (*Mangifera indica*) varieties from Sri Lanka on breast and ovarian cancer cells**. *J Pharmaceut Res Int.* **10**(2):1-7.
61. Garrido G, González D, Delporte C, Backhouse N, Quintero G, Núñez-Sellés AJ, Morales MA. 2001. **Analgesic and anti-inflammatory effects of *Mangifera indica* L. extract (Vimang)**. *Phytother Res.* **15**(1):18-21.
62. Ojewole JA. 2005. **Antiinflammatory, analgesic and hypoglycemic effects of *Mangifera indica* Linn. (Anacardiaceae) stem-bark aqueous extract**. *Methods Find Exp Clin Pharmacol.* **27**(8):547-554.
63. Siswanto S, Arozal W, Juniantito V, Grace A, Agustini FD. 2016. **The effect of mangiferin against brain damage caused by oxidative stress and inflammation induced by doxorubicin**. *HAYATI Jf Biosci.* **23**(2):51-55.
64. Gondi M, Prasada Rao UJ. 2015. **Ethanol extract of mango (*Mangifera indica* L.) peel inhibits α-amylase and α-glucosidase activities, and ameliorates diabetes related biochemical parameters in streptozotocin (STZ)-induced diabetic rats**. *J Food Sci Technol.* **52**(12):7883-7893.
65. Ebeid HM, Gibriel AA, Al-Sayed HM, Elbehairy SA, Motawe EH. 2015. **Hepatoprotective and antioxidant effects of wheat, carrot, and mango as nutraceutical agents against CCl4-induced hepatocellular toxicity**. *J Am Coll Nutr.* **34**(3):228-231.
66. Awe SO, Olajide OA, Oladiran OO, Makinde JM. 1998. **Antiplasmodial and antipyretic screening of *Mangifera indica* extract**. *Phytother Res.* **12**(6):437-438.
67. Garrido G, Blanco-Molina M, Sancho R, Macho A, Delgado R, Muñoz E. 2005. **An aqueous stem bark extract of *Mangifera indica* (Vimang) inhibits T cell proliferation and TNF-induced activation of nuclear transcription factor NF-kappaB**. *Phytother Res.* **19**(3):211-215.
68. Latha KP, Latha MS, Vagdevi HM. 2012. **Comparative studies on anthelmintic activity of *Mangifera indica* L. Var. Thotapuri and *Mangifera indica* L. Var. Neelam root crude extracts**. *Int J Phytopharm.* **2**(1):21-24.
69. Venkatalakshmi P, Kemasari P, Sangeetha S. 2011. **Antihyperlipidemic and antioxidant activities of *Mangifera Indica* Linn., in alloxan induced rats**. *Int J PharmaceutSci Rev Res.* **11**(2):129-132.
70. Lima ZP, Severi JA, Pellizzon CH, Brito AR, Solis PN, Cáceres A, Girón LM, Vilegas W, Hiruma-Lima CA. 2006. **Can the aqueous decoction of mango flowers be used as an antiulcer agent?** *J Ethnopharmacol.* **106**(1):29-37.
71. Kuete V. 2022 **Potential of African medicinal plants against Enterobacteria: Classification of plants antibacterial agents**. In: *Advances in Botanical Research*. https://doi.org/10.1016/bs.abr.2022.1008.1006.
72. 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.
73. Kirbaşlar FG, Tavman A, Dülger B, Türker G. 2009. **Antimicrobial activity of Turkish citrus peel oils**. *Pak. J. Bot.* **41**(6):3207-3212.
74. 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.
75. Traboulsi A. 2016. 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.
76. 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.
77. 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.
78. 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.
79. 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.
80. 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.
81. 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.
82. 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.
83. 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.
84. 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.
85. 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.
86. Kannan S, Parimala B, Jayakar B. 2011. **Antibacterial evaluation of the methanolic extract of *Passiflora edulis***. *HygeiaJDMed.* **3**(1):46-49.
87. 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.
88. 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.
89. 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.
90. Dzotam JK, Touani FK, Kuete V. 2016. **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.* **16**(1):9.
91. 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.
92. 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.
93. 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.
94. 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.
95. 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.
96. 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.
97. 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.
98. 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.
99. 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.
100. 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.
101. 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.
102. Jagtap UB, Bapat VA. 2010. **Artocarpus: a review of its traditional uses, phytochemistry and pharmacology**. *J Ethnopharmacol.* **129**(2):142-166.
103. Cavalcante GM, Neto JFL, de Omena Bomfim E, Flória-Santos MJ. 2013. **Atividade antimicrobiana de *Artocarpus heterophyllus* Lam.(Moraceae) sobre o desenvolvimento de *Streptococcus pneumoniae* e *Escherichia coli***. *Scientia Plena.* **9**(2):1-7.
104. 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.
105. 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.
106. 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.
107. 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.
108. 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.
109. 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.
110. 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.
111. 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.
112. 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.
113. 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.
114. 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.
115. 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.
116. 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.
117. Onasanwo SA, Rotu RA. 2016. **Antinociceptive and anti-inflammatory potentials of kolaviron: mechanisms of action**. *J Basic Clin Physiol Pharmacol.* **27**(4):363-370.
118. 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.
119. 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.
120. 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.
121. 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.
122. 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.
123. Kuete V, Dongfack MD, Mbaveng AT, Lallemand MC, Van-Dufat HT, Wansi JD, Seguin E, Tillequin F, Wandji J. 2010. **Antimicrobial activity of the methanolic extract and compounds from the stem bark of Drypetes tessmanniana**. *Chin J Integr Med.* **16**(4):337-343.
124. 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.
125. 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.
126. 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.
127. 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.
128. 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.
129. 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.
130. 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.
131. Kuete V. 2022. **Potential of African medicinal plants against Enterobacteria: Classification of plants antibacterial agents**. In: *Advances in Botanical Research. https://doi.org/10.1016/bs.abr.2022.08.006*.
132. Kuete V. 2010. **Potential of Cameroonian plants and derived products against microbial infections: a review**. *Planta Med.* **76**(14):1479-1491.
133. Hackman HK, Arhin RE, Azumah BK, Boateng D, Nwosu B, Apenteng M. 2020. ***In vitro* antibacterial activity of *Psidium guajava* (Guava) leaves extract on carbapenem-resistant *Klebsiella pneumoniae* causing multi-drug resistant systemic infections**. *J Med Plant Res.* **14**(9):475-479.
134. Arima H, Danno G. 2002. **Isolation of antimicrobial compounds from guava (*Psidium guajava* L.) and their structural elucidation**. *Biosci Biotechnol Biochem.* **66**(8):1727–1730.
135. Gbala ID, Anibijuwon II. 2018. **Antibacterial activity of *Terminalia glaucescens*, *Mangifera indica* and *Mitracarpus villosus* on Carbapenem-resistant Enterobacteriaceae**. *Afr J Clin Exp Microbiol.* **19**(4):251-259.
136. Dzotam J, Kuete V. 2017. **Antibacterial activity of methanol extracts from six Cameroonian edible plants *Camellia sinensis, Mangifera indica, Moringa oleifera, Ananas comosus, Triumphetta pentandra* and *Artocarpus heterophyllus* against MDR Gram-Negative phenotypes**. *Afr J Integr Health*. **7**(2):49-56.
137. Cowan MM. 1999. **Plant products as antimicrobial agents**. *Clin Microbiol Rev.* **12**(4):564-582.
138. Pages JM, Amaral L. 2009. **Mechanisms of drug efflux and strategies to combat them: challenging the efflux pump of Gram-negative bacteria**. *Biochim Biophys Acta.* **1794**(5):826-833.
139. Das MK, Mandal S. 2016. ***Syzigium cumini* and *Mangifera indica* seed extracts: *In vitro* assessment for antibacterial activity alone and in combination with antibiotics against clinical bacteria.** . *J Infect Dis Preve Med.* **4**:1.
140. 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.