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The best African plant-derived antibacterial products for clinical perspectives: The state-of-the-art

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Abstract

Background: The global burden of bacterial infections remains a serious health concern. In the present review, we have summarized the best botanicals and phytochemicals from the flora of Africa that deserve clinical studies to develop novel antibacterial drugs to combat enterobacteria, *Pseudomonas aeruginosa*, Gram-positive bacteria, and mycobacteria.

Methods: Data were retrieved from scientific databases such as PubMed, Scopus, ScienceDirect, Google Scholar, and Web of Science using the keywords "African country and plant and antibacterial" and plants or phytochemicals with outstanding antibacterial activities following established cutoff point standards were selected.

Results: The identified botanicals were from Acacia polyacantha, Alchornea floribunda, Artemisia abyssinica, Beilschmiedia acuta, Eriosema glomeratum, Harungana madagascariensis, Macaranga capensis, Macaranga conglomerata, Macaranga kilimandscharica, Mangifera indica, Piper nigrum, Piptadeniastrum africanum, and Uapaca togoensis. The phytochemicals identified included 2-(4-hydroxyphenyl)-ethyltriacontanoate (1), 1,3,5,6-tetrahydroxyxanthone (2), 1,3,5,7-tetrahydroxyxanthone (3), 8,8-bis-(dihydroconiferyl) diferulate (4), 2-hydroxy-3-methoxy-9,10-dioxo-9,10-dihydroanthracene-1-carbaldehyde (5), allanxanthone D (6), angusticornin B (7), bartericin A (8), diospyrone (9), dorsmanin C (10), gancaonin Q (11), isobavachalcone (12), isoliquiritigenin (13), laburnetin (14), O¹-demethyl-3',4'-deoxy-psorospermi-3',4' diol (15), plumbagin (16), and vismiaquinone (17).

Conclusion: These plant-derived products deserve clinical investigations to develop novel antibacterial agents to combat bacterial infections.

Keywords: Africa; antibacterial; botanicals; phytochemicals

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Background

The global burden of bacterial infections remains a serious health concern. This situation is more complicated as bacteria continually develop various resistance mechanisms to existing and newly discovered antibiotics [1-4]. It was reported that up to 700,000 people worldwide die yearly due to drug resistant infections [5]. It was also projected that by 2050, the number of deaths due to microbial infections will reach 4.73 million in Asia, 4.15 million in Africa, 0.39 million in Europe, 0.392 million in Latin America, 0.317 million in North America, and 0.022 million in Oceania [6]. In-depth search of new antibacterial drugs should remain a priority for scientists to limit as much as possible the damage caused by infectious diseases, including those caused by resistant pathogens. The role of medicinal plants as a good source of drugs to tackle human ailments including the various type of diseases with resistant phenotypes has been largely documented [7-35]. Increasingly, new strategies for discovering new bioactive substances from natural sources include the use of multidrugresistant models. This has been particularly successful in the search for novel anticancer, antibacterial, and antifungal drugs, as well as new antiparasitic and antiviral drugs in the last two decades. Numerous research teams such as those of Professors Thomas Efferth of the University of Mainz in Germany and Victor Kuete of the University of Dschang in Cameroon have invested heavily in recent years in multidrug-resistant models of cancer cells and bacteria overexpressing efflux pumps [36-43]. The role of African plants and their constituents as potential sources of antibacterial agents have deeply been demonstrated [44-46]. The ability of many of the antibacterial plants from the flora of Africa and their constituents to prevent the development of multidrugresistant (MDR) bacteria has been reported [47-51]. The research for novel plant-derived antibacterial agents has been particularly fruitful in some African countries such as Egypt, South Africa, Nigeria, Tunisia, and Cameroon. In the present review, the stateof-the-art antibacterial drug discovery from the resource of Africa will be highlighted.

Methods

Data were retrieved from scientific databases such as PubMed, Scopus, ScienceDirect, Google Scholar, and Web of Science using the keywords "African country and plant and antibacterial" and plants or phytochemicals with outstanding antibacterial activities following cutoff point standards earlier established for enterobacteria, *Pseudomonas aeruginosa*, Gram-positive bacteria, and mycobacteria [52-55].

Results and discussion

History of the antimicrobial drug research in Africa

When using the combination of keywords (country + plant + antibacterial) in the PubMed database, though not accurate, an idea of the history of medicinal plant research in Africa about bacterial infections has been determined (Table 1). The first paper on the topic was published on the Egyptian plant *Nigella sativa* L Ranunculaceae) by Toppozada and co-workers in 1965 [56]. In general, in most African countries, this research began in the 70s

in Nigeria, Kenya, and Ghana, 80s in Sudan, 90s in South Africa, Cameroon, Morocco, Ethiopia, and Algeria, and even in 2000 in Tunisia. By April 2024, the number of scientific publications in the PubMed database related to the above combination of keywords showed a huge gap between African countries, with countries such as Egypt, South Africa, Nigeria, Tunisia, and Cameroon appearing in the top 5 with more than 300 published papers. Other African countries with more than 100 scientific publications included Morocco, Ethiopia, and Algeria, meanwhile less than 100 papers were found for Kenya, Ghana, and Sudan (Table 1).

The antibacterial cutoff points

In 2008, the first threshold values were suggested by Fabry et al. as minimal inhibitory concentration (MIC) values below 8 mg/mL for botanicals with noteworthy antimicrobials [57]. Since then, things have evolved and plant extracts with MIC values above 1000 µg/mL are now considered not active. Later on, Simoes et al. suggested the MIC in the range of 100 to 1000 μ g/mL for phytochemicals as antimicrobial agents [58]. Also, Jimenez-Arellanes suggested MICs between 100-200 µg/mL as interesting for crude extracts [59]. In 2010, Kuete [60] suggested ranking the antibacterial effects of plant-derived products as follows: significant (MIC < 100 µg/mL), moderate (100 < CMI≤625 µg/mL) or weak (CMI>625 µg/mL) for crude extracts and also that significant (MIC <10 μ g/mL), moderate (10 <MIC ≤ 100 μ g/mL), and low (MIC> 100 µg/mL) for natural compounds. In 2017, Tamokou et al. [61] further suggested the following cut-off points for edible parts of the plants: as highly active (MIC below 100 μ g/mL), significant (100 \leq MIC \leq 512 μ g/mL), moderate (512 < MIC ≤ 2048 μ g/mL), low (MIC > 2048 μ g/mL) and not active (MIC > 10 mg/mL) for botanicals but also the following for phytochemicals: highly active (MIC below 1 µg/mL or 2.5 μ M), significantly active (1 ≤ MIC ≤10 μ g/mL or 2.5 ≤ MIC < 25 μ M), moderately active (10 < MIC ≤ 100 μ g/mL or 25 ≤ MIC < 250 μ M), low activity (100 < MIC ≤ 1000 μ g/mL or 250 ≤ MIC < 2500 μ M), and not active (MIC > 1000 μ g/mL or > 2500 μ M).

In 2023, Kuete and his team provided a rational basis for the classification of the antibacterial activity of plant-based products, taking into account the percentage of active extract in a selected bacterial type; from such basis, the following values were proposed.

In Enterobacteriaceae: outstanding when MIC $\leq 8 \mu g/mL$; excellent when 8 < MIC $\leq 64 \mu g/mL$; very good when 64 < MIC $\leq 128 \mu g/mL$; good when 128 < MIC $\leq 256 \mu g/mL$, average when 256 < MIC $\leq 512 \mu g/mL$, weak when 512 < MIC $\leq 1024 \mu g/mL$, and not active MIC >1024 $\mu g/mL$ for botanicals, outstanding when MIC $\leq 2 \mu g/mL$, excellent when 2 < MIC $\leq 4 \mu g/mL$, very good when 4 < MIC $\leq 8 \mu g/mL$, good when 8 < MIC $\leq 32 \mu g/mL$, average when 32 < MIC $\leq 64 \mu g/mL$, weak when 64 < MIC $\leq 512 \mu g/mL$, and not active when MIC >512 $\mu g/mL$ for plant constituents [52];

In Pseudomonas aeruginosa: outstanding when MIC \leq 32 µg/mL, excellent when 32 < MIC \leq 128 µg/mL, very good when 128 < MIC \leq 256 µg/mL, good when 256 < MIC \leq 512 µg/mL, average when 512 < MIC \leq 1024 µg/mL, weak or not active when MIC values >1024 µg/mL for crude extracts, outstanding when MIC \leq 4 µg/mL, excellent when 4 < MIC \leq 32 µg/mL, very good when 32 < MIC \leq 128 µg/mL, good when 128 < MIC \leq 256 µg/mL, average when 256 < MIC \leq 512 µg/mL, weak or not active when MIC values >512 µg/mL for phytochemicals [53];

In Gram-positive bacteria: outstanding when MIC ≤ 8 µg/mL, excellent when 8 < MIC ≤ 40 µg/mL, very good when 40 < MIC ≤ 128 µg/mL, good when 128 < MIC ≤ 320 µg/mL, average when 320 < MIC ≤ 625 µg/mL, weak when 625 < MIC ≤ 1024

 μ g/mL and not active when MIC values > 1024 μ g/mL for crude extracts, outstanding when MIC \leq 2 μ g/mL, excellent when 2 < MIC \leq 4 μ g/mL, very good when 4 < MIC \leq 8 μ g/mL, good when 8 < MIC \leq 32 μ g/mL, average when 32 < MIC \leq 64 μ g/mL, weak when 64 < MIC \leq 512 μ g/mL, and not active when MIC > 512 μ g/mL for phytochemicals [54];

In mycobacteria: outstanding when MIC $\leq 6 \mu g/mL$, excellent when $6 < MIC \leq 16 \mu g/mL$, very good when $16 < MIC \leq 25 \mu g/mL$, good when $25 < MIC \leq 39 \mu g/mL$, average when $39 < MIC \leq 156 \mu g/mL$, weak when $156 < MIC \leq 2048 \mu g/mL$, and not active MIC >2048 µg/mL for crud extracts, outstanding when MIC $\leq 2.5 \mu g/mL$, excellent when $2.5 < MIC \leq 5 \mu g/mL$, very good when $5 < MIC \leq 8 \mu g/mL$, good when $8 < MIC \leq 10 \mu g/mL$, average when $10 < MIC \leq 20 \mu g/mL$, weak when $20 < MIC \leq 512 \mu g/mL$, and not active when MIC >512 µg/mL for for phytochemicals [55].

The best botanicals and phytochemicals

In the present review, the latest cut-off points proposed by Kuete and his team will be used to report the botanicals and phytochemicals with outstanding antibacterial effects identified in the flora of Africa against various bacterial species.

Against Enterobacteria

Number of African plant extracts were investigated against Enterobacteria, mainly Escherichia coli, Enetrobacter aerogenes, Enterobacter cloacae, Klebsiella pneumoniae, and Providencia stuartii. Many of them displayed outstanding (MIC ≤8 µg/mL) against at least one bacterium belonging to Enterobacteriaceae family. The crude methanol extract from the roots of Macaranga capensis Benth. (Euphorbiaceae) displayed MIC values of 4 µg/mL against E. coli ATCC8739 and the MDR AG102 and Enterobacter aerogenes EA27 strains, 8 µg/mL against Klebsiella pneumoniae ATCC11296 and the MDR KP55 and Providencia stuartii NAE16 strains [62]; The MIC values of 8 µg/mL or lower were recorded with the bark methanol extract of Harungana madagascariensis Lam. ex Poir. (Hypericaceae) against E. coli ATCC8739, ATCC10536, and W3110 [63] as well as the stem extract of Macaranga conglomerata Brenan (Euphorbiaceae) against E. coli ATCC8739, AG102, EA27 strains, KP55 strains [62]. The methanol extract from the roots of Macaranga kilimandscharica Pax. Showed MIC value of 8 µg/mL against Enterobacter aerogenes ATCC13048, K. pneumoniae ATCC11296, K. pneumoniae KP55, and P. stuartii ATCC29914 strains [62]. The bark methanol extract of Beilschmiedia acuta Kosterm (Lauraceae) had a MIC value below 8 µg/mL against K. pneumoniae ATCC11296 [64]. The methanol extract of the leaves of Acacia polyacantha Willd. (Fabaceae) and Uapaca togoensis Pax. (Euphorbiaceae) displayed a MIC value of 8 µg/mL against P. stuartii ATCC29914 [65] and PS2636 [66] strains, respectively

Several phytochemicals identified in African plants also displayed outstanding (MIC $\leq 2 \mu g/mL$) antibacterial activities against Enterobacteria. For instance, the phenylpropanoid 8,8-bis-(dihydroconiferyl) diferulate (**4**) isolated from *Hypericum roeperianum* had MIC value of 0.5 $\mu g/mL$ against *E. coli* ATCC8739, *K. pneumoniae* KP55, and *P. stuartii* ATCC29914, 1 $\mu g/mL$ against AG102, and *P. stuartii* NEA16 strains, 2 $\mu g/mL$ against *E. aerogenes* ATCC13048, CM64, and *K. pneumoniae* ATCC11296 strains [67], meanwhile, two other xanthones isolated from *H. roeperianum*, 1,3,5,7-tetrahydroxyxanthone (**3**) and 1,3,5,6-tetrahydroxyxanthone (**2**) also displayed a MIC value of 2 $\mu g/mL$ against *E. coli* ATCC8739, *E. aerogenes* ATCC13048, and *K. pneumoniae* KP55 strains [67]. The naphthoquinone plumbagin

(16) isolated *Diospyros canaliculata, Diospyros crassiflora* had a MIC value of 2 μ g/mL against AG100A [68-70]. The chemical structures are shown in Figure 1.

Against Pseudomonas aeruginosa

P. aeruginosa is frequently resistant to many commonly used antibiotics [71, 72]. This bacterium including its resistant phenotype was sensitive to various African plant extracts and their phytochemicals [14, 45, 47, 64, 73-76]. Many of the reported botanicals (MIC \leq 32 µg/mL) displayed outstanding and phytochemicals (MIC \leq 4 µg/mL) against *P. aeruginosa*. For instance, the dichloromethane-methanol 1:1 extract from roots of M. kilimandscarica [62] displayed MIC values of 16 µg/mL against P. aeruginosa PA01 and the MDR PA124 strain, meanwhile, the MIC of 32 µg/mL was recorded against PA01 with the methanol extract from the bark of H. madagascariensis Lam ex. Poir (Hypericaceae) [63] and the bark of Mangifera indica Linn. (Anacardiaceae) [77], the fruits of Piper nigrum L. (Piperaceae) [47], the root extracts of *M. capensis* and the stem of *M.* conglomerata [62]. Against PA124, the methanol extract from M. capensis had a MIC of 16 µg/mL [62], meanwhile, that of the bark of Beilschmiedia acuta Kosterm. (Lauraceae) had a MIC of 32 µg/mL [64]. Akoue and his team demonstrated that the methanol extract from the leaves of Piptadeniastrum africanum (Hook. F.) Brenan (Fabaceae) and Tristemma mauritianum J.F. Gmel (Melastomataceae) displayed MIC a value of 3.13 µg/mL against P. aeruginosa PA383 strain, those from the fruits of Alchornea floribunda Müller Arg. (Euphorbiaceae) and Eriosema glomeratum (Guill. & Perr.) Hook. F. (Fabaceae) had MIC a value of 6.25 µg/mL meanwhile that from the fruits of Medinilla mirabilis (Gilg) Jacq.-Fél. (Melastomataceae) displayed a MIC of 12.5 µg/mL [78].

Several phytochemicals from African medicinal plants displayed outstanding antibacterial (MIC \leq 4 µg/mL) effects, and consequently be considered as good candidates to develop phytodrugs. In effect. the flavonoid dorsmanin C (10) isolated from the Cameroonian medicinal plant Dorstenia mannii had a MIC of 4 µg/mL against PA01 strain [79]. Against P. aeruginosa CRPA LMP0102U strain, the flavonoid bartericin A (8) isolated from Dorstenia angusticornis had a MIC of below 0.31 µg/mL [11], the phenylpropanoid 2-(4-hydroxyphenyl)-ethyltriacontanoate (1) isolated from Newbouldia laevis had a MIC of 0.31 µg/mL [80], anthraquinones 2-hydroxy-3-methoxy-9,10-dioxo-9,10dihydroanthracene-1-carbaldehyde (5) isolated from N. laevis [80] and the xanthone allanxanthone D (6) isolated from Allanblackia gabonensis [81] had a MIC value of 0.61 µg/mL, another anthraquinone, vismiaquinone (17), isolated from Vismia laurentii displayed a MIC value of 2.44 µg/mL [82]. Against P. aeruginosa ATCC27853, Teke et al. recorded a MIC value of 0.62 µg/mL for the flavonoid isoliquiritigenin (13) isolated from Trilepisium madagascariense [83]. The chemical structures are shown in Figure 1.

Against Gram-positive bacteria

Gram-positive bacteria are responsible for several serious hospital and community infections such as nosocomial infections, sepsis, pneumonia, and toxinosis [84, 85]. This antibacterial control of Gram-positive pathogens is hampered by the development of MDR phenotypes [86]. Medicinal plants are an undeniable source of medicine to fight bacterial resistance of Gram-positive bacteria. During the three last decades, number of African medicinal plant extracts and their constituents were successfully screened against Gram-positive bacteria mostly *Staphylococcus aureus* [11, 26, 80, 82, 87-100]. Many of the tested botanicals and phytochemicals inhibited the growth of resistant strains of S. aureus [101-108]. Many of the reported botanicals (MIC $\leq 8 \mu g/mL$) displayed outstanding and phytochemicals (MIC $\leq 2 \mu g/mL$) against Grampositive bacteria. For instance, extract from *M. capensis* displayed MIC values of 4 µg/mL against S. aureus MRSA6 and MRSA3, and 8 µg/mL against ATCC25923 and MRSA3 strains [62]. Hashim and his collaborators also reported MIC values of 4 µg/mL against S. aureus ATCC25923, and 8 µg/mL against MRSA3 and MRSA6 with the crude extract from M. kilimandscharica [62]. M. conglomerata crude extract also had MIC values of 8 µg/mL against S. aureus ATCC25923 and MRSA6 [62]. The phytochemical 16 was identified as an excellent antistaphylococcal compound with a MIC value of 2 µg/mL against MRSA4 and MRSA 8 [104]. The flavonoid isobavachalcone (12) isolated from Dorstenia barteri also had MIC values of 0.3 µg/mL against Streptococcus faecalis, S. aureus, Bacillus stearothermophilus and 0.6 µg/mL against Bacillus cereus, Bacillus megaterium and Bacillus subtilis [109]. Kuete et al. the outstanding antibacterial effect effects of the flavonoids isolated from Dorstenia angusticornis, namely gancaonin Q (11) with a Mic value of 0.61 µg/mL against B. cereus and S. faecalis, 0.61 µg/mL with compound 8 against B. cereus, S. aureus, and S. faecalis, and 1.22 µg/mL against B. megaterium and B. subtilis, and 1.22 µg/mLwith angusticornin B (7) against B. cereus, B. subtilis, and S. faecalis [11].

Against mycobacteria

Tuberculosis (TB) is an infectious, endemic disease with a predominant human-to-human transmission, caused by the Mycobacterium tuberculosis Complex (MTBC) « M. tuberculosis, M. bovis, M. africanum, M. microti, M. canettii, M. caprae, M. pinnipedii, and M. mungi » [110]. It represents one of the top 10 causes of death worldwide [111] and according to the World Health Organization (WHO), an average of 10 million people develop an active form of the disease each year [112]. TB remains a public health concern in many industrialized countries, particularly when it comes to multidrug-resistant forms due to non-adherence to antituberculosis drugs, which have a long treatment duration (> 2 years) [113]. Drug-resistant strains of *M. tuberculosis* (Mtb) are of particular concern worldwide because resistance occurs soon after a new chemotherapeutic agent is introduced into the market just as with other bacterial diseases. Several secondary plant metabolites are reported to have anti-tuberculosis activity comparable to existing anti-tuberculosis drugs. Outstanding (MIC \leq 6 µg/mL) was recorded on *M. tuberculosis* H37Rv with the methanol extract from the leaves of Artemisia abyssinica Schultz Bip. (Lamiaceae) [114]. A, outstanding (MIC \leq 2.5 µg/mL) antibacterial activity was recorded with O1-demethyl-3',4'-deoxy-psorospermi-3',4' diol (15) isolated from Vismia guineensis [115] and laburnetin (14) isolated from Ficus chlamydocarpa [89] against Mycobacterium smegmatis with a MIC value of 0.61 µg/mL. Against *M. smegmatis*, diospyrone (9) isolated from *Diospyros canaliculata* (MIC of 1.22 µg/mL) [68] and isobachalcone (MIC of 2.44 µg/mL) [116] also had outstanding antimycobacterial effects. Against M. tuberculosis H37Rv strain, a MIC value of 2.44 $\mu\text{g/mL}$ was obtained with compounds 9 and 12[68, 116].



Figure 1. Chemical structures of the best antibacterial phytochemicals from the flora of Africa.

1: 2-(4-hydroxyphenyl)-ethyltriacontanoate; 2: 1,3,5,6-tetrahydroxyxanthone; 3: 1,3,5,7-tetrahydroxyxanthone; 4: 8,8-bis-(dihydroconiferyl) diferulate; 5: 2-hydroxy-3-methoxy-9,10-dioxo-9,10-dihydroanthracene-1-carbaldehyde; 6: allanxanthone D; 7: *angusticornin* B; 8: bartericin A; 9: diospyrone; 10: dorsmanin C; 11: gancaonin Q; 12: isobavachalcone; 13: isoliquiritigenin; 14: laburnetin; 15: O¹-demethyl-3',4'-deoxy-psorospermi-3',4' diol; 16: plumbagin; 17: vismiaquinone.

Table 1. History of the publications related to bacteria and plant in African countrie	es where most investigations were performed as recorded in
PubMed	

Country	Number	First paper	Publication year	Reference
Egypt	1115	The antibacterial properties of the Nigella sativa L. seeds. Active principle with some clinical	1965	[56]
South Africa	771	applications Assessment of exposure to chloramphenicol and azathioprine among workers in a South	1993	[117]
Nigeria	399	African pharmaceutical plant The antibacterial properties of the buffer extracts of chewing sticks used in Nigeria	1975	[118]
Tunisia	362	Nauplathizine, a new unusual O-heteroside	2005	[119]
Cameroon	337	Sigmoidins J and K, two new prenylated	1994	[120]
Morocco	271	Disseminating infection with Scytalidium	1993	[121]
Ethiopia	200	A novel antibacterial diterpene from <i>Premna</i>	1990	[122]
Algeria	177	HM17, a new polyene antifungal antibiotic produced by a new strain of Spirillospora	1994	[123]
Kenva	94	Antibiotic action of Solanum incanum Linnaeus	1976	[124]
Ghana	83	Antimicrobial properties of some West African medicinal plants iv. Antimicrobial activity of xylopic acid and other constituente of the fruits of Xylopia aethiopica (Apponaceae)	1977	[125]
Sudan	66	Investigation of <i>Grewia bicolor</i> Juss.	1986	[126]

*The number of plants recorded in PubMed using keywords "country + plant + antibacterial" up to April 2024.

Conclusion

In the present review, we have compiled the best botanicals and phytochemicals from the flora of Africa that deserve clinical studies to develop novel antibacterial medication to combat drug sensitive and MDR phenotypes. The infections targeted include were related to enterobacteria, Pseudomonas aeruginosa, Gram-positive bacteria, and mycobacteria. The entities include the botanicals from Acacia polyacantha, Beilschmiedia acuta, Harungana madagascariensis, Macaranga capensis, Macaranga conglomerata, Macaranga kilimandscharica, Uapaca togoensis and phytochemicals such as 8,8-bis-(dihydroconiferyl) diferulate (4), 1,3,5,7-tetrahydroxyxanthone (3), 1,3,5,6-tetrahydroxyxanthone (2), and plumbagin (16) for infections caused by enterobacteria, the crude extracts from Alchornea floribunda, B. acuta, Eriosema glomeratum, H. madagascariensis, M. conglomerata, M. kilimandscarica, Mangifera indica, Piper nigrum, Piptadeniastrum africanum and compounds such as 2-(4-hydroxyphenyl)ethyltriacontanoate (1), 2-hydroxy-3-methoxy-9,10-dioxo-9,10dihydroanthracene-1-carbaldehyde (5), allanxanthone D (6), bartericin A (8), dorsmanin C (10), isoliquiritigenin (13), and vismiaquinone (17), for infections caused by Pseudomonas aeruginosa, the crude extract from M. capensis, M. conglomerata, M. kilimandscharica and plant constituents such as compounds 8, 16, angusticornin B (7), gancaonin Q (11), and isobavachalcone (12), for infections caused Gram-positive bacteria, the crude extract from Artemisia abyssinica as well as compounds such as compound 12, diospyrone (9), laburnetin (14), and O1-demethyl-3',4'-deoxy-psorospermi-3',4' diol (15) for infections caused mycobacteria. The identified botanicals and phytochemicals deserve clinical investigations to develop novel antibacterial agents to combat bacterial infections.

Abbreviations

ATCC: American-Type Culture Collection MDR: multidrug-resistant MIC: minimal inhibitory concentration

Authors' Contribution

VK collected the data, draft the manuscript, read, and approved the final version.

Conflict of interest

The authors declare no conflict of interest.

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References

- 1. Doron S, Gorbach SL. 2008. Bacterial infections: overview. International Encyclopedia of Public Health.273–282.
- 2. Magiorakos AP, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, Giske CG, Harbarth S, Hindler JF, Kahlmeter G, Olsson-Liljequist B *et al.* 2012. Multidrugresistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. *Clin Microbiol Infect.* 18(3):268-281.
- Zhen X, Stålsby Lundborg C, Sun X, Zhu N, Gu S, Dong H. 2021. Economic burden of antibiotic resistance in China: a national level estimate for inpatients. *Antimicrob Resist Infect Control*. 10(1):5.
- Seukep AJ, Fokoua-Maxime CD, Mbuntcha HG, Chen G, Assob JCN, Tenniswood M, Sarker SD, Kuete V, Ming-Quan G. 2022. Bacterial Drug Efflux Pump Inhibitors from Plants. In: Antimicrobial Resistance: Underlying Mechanisms and Therapeutic Approaches. edu. Edited by Kumar V, Shriram V, Paul A, Thakur M. Singapore: Springer Singapore: 487-532.
- Fongang H, Mbaveng AT, Kuete V. 2023. Chapter One Global burden of bacterial infections and drug resistance. Advances in Botanical Research. 106: 1-20. https://doi.org/10.1016/bs.abr.2022.08.001.
- Dadgostar P. 2019. Antimicrobial Resistance: Implications and Costs. Infect Drug Resist. 12:3903-3910.
- Cowan MM. 1999. Plant products as antimicrobial agents. *Clin Microbiol Rev.* 12(4):564-582.
 Hortson, J. 1072. Distance and a strategies of plant.
- Harbone J. 1973. Phytochemical methods: a guide to modern techniques of plant analysis. London: Chapman & Hall.

- 9. Kuete V, Efferth T. 2011. Pharmacogenomics of Cameroonian traditional herbal medicine for cancer therapy. *J Ethnopharmacol.* 137(1):752-766. Kuete V. 2014. 21 - Health Effects of Alkaloids from African Medicinal Plants. In:
- 10. Toxicological Survey of African Medicinal Plants. edn. Edited by Kuete V: Elsevier: 611-633
- Kuete V, Simo IK, Ngameni B, Bigoga JD, Watchueng J, Kapguep RN, Etoa FX, 11. Tchaleu BN, Beng VP. 2007. Antimicrobial activity of the methanolic extract, fractions and four flavonoids from the twigs of *Dorstenia angusticornis* Engl. (Moraceae). J Ethnopharmacol. 112(2):271-277
- Kuete V, Tangmouo JG, Penlap Beng V, Ngounou FN, Lontsi D. 2006. Antimicrobial activity of the methanolic extract from the stem bark of Tridesmosternon 12
- omphalocarpoides (Sapotaceae). *J Ethnopharmacol*. 104(1-2):5-11. Kuete V, Dzotam JK, Voukeng IK, Fankam AG, Efferth T. 2016. Cytotoxicity of methanol extracts of *Annona muricata, Passiflora edulis* and nine other 13 Cameroonian medicinal plants towards multi-factorial drug-resistant cancer cell lines. Springerplus. 5(1):1666.
- 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.
- Tekwu EM, Askun T, Kuete V, Nkengfack AE, Nyasse B, Etoa FX, Beng VP. 2012. Antibacterial activity of selected Cameroonian dietary spices ethno-medically used 15. against strains of *Mycobacterium tuberculosis. J Ethnopharmacol.* 142(2):374-382. Kuete V. 2013. Medicinal Plant Research in Africa: Pharmacology and Chemistry In:
- 16
- Kuete V. 2013. Medicinal Plant Research in Africa: Pharmacology and Chemistry in: Pharmacology and Chemistry. Edited by Kuete V, 1 edn. Oxford: Elsevier. Kuete V, Mbaveng AT, Sandjo LP, Zeino M, Efferth T. 2017. Cytotoxicity and mode of action of a naturally occurring naphthoquinone, 2-acetyl-7-methoxynaphtho[2,3-b]furan-4,9-quinone towards multi-factorial drug-resistant cancer cells. 17. Phytomedicine. 33:62-68.
- Mbaveng AT, Kuete V, Mapunya BM, Beng VP, Nkengfack AE, Meyer JJ, Lall N. 18. 2011. Evaluation of four Cameroonian medicinal plants for anticancer, antigonorrheal and antireverse transcriptase activities. Environ Toxicol Pharmacol. 32(2):162-167. Nielsen TR, Kuete V, Jager AK, Meyer JJ, Lall N. 2012. Antimicrobial activity of
- 19. Selected South African medicinal plants. *BMC Complement Altern Med*. 12:74. 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 20.
- Arabian medicinal plants. BMC Complement Altern Med. 13:354.
 Omosa LK, Midiwo JO, Kuete V. 2017. Chapter 19 Curcuma longa. In: Medicinal Spices and Vegetables from Africa. edn. Edited by Kuete V: Academic Press: 425-21 435
- Kuete V, Sandjo LP, Mbaveng AT, Seukep JA, Ngadjui BT, Efferth T. 2015. 22. Cytotoxicity of selected Cameronian medicinal plants and Nauclea pobeguinii towards multi-factorial drug-resistant cancer cells. BMC Complement Altern Med. 15:309.
- Kuete V, Wansi JD, Mbaveng AT, Kana Sop MM, Tadjong AT, Beng VP, Etoa FX, Wandji J, Meyer JJM, Lall N. 2008. Antimicrobial activity of the methanolic extract and compounds from *Teclea afzelii* (Rutaceae). *S Afr J Bot.* 74(4):572-576. 23.
- Kuete V, Mbaveng AT, Zeino M, Fozing CD, Ngameni B, Kapche GD, Ngadjui BT, Efferth T. 2015. Cytotoxicity of three naturally occurring flavonoid derived 24 compounds (artocarpesin, cycloartocarpesin and isobavachalcone) towards multi-
- factorial drug-resistant cancer cells. *Phytomedicine*. 22(12):1096-1102. Sandjo LP, Kuete V, Tchangna RS, Efferth T, Ngadjui BT. 2014. Cytotoxic benzophenanthridine and furoquinoline alkaloids from Zanthoxylum buesgenii (Rutaceae), Chem Cent J. 8(1):61,
- Ngounou FN, Manfouo RN, Tapondjou LA, Lontsi D, Kuete V, Penlap V, Etoa FX, Dubois MAL, Sondengam BL. 2005. Antimicrobial diterpenoid alkaloids from Erythrophleum suaveolens (guill. & perr.) brenan. Bull Chem Soc Ethiop. 19(2):221-226.
- Dzoyem JP, Tchuenguem RT, Kuiate JR, Teke GN, Kechia FA, Kuete V. 2014. In 27 vitro and in vivo antifungal activities of selected Cameroonian dietary spices. BMC Complement Altern Med. 14:58. Mbaveng AT, Hamm R, Kuete V. 2014. 19 - Harmful and protective effects of
- 28. Instruction of the second s
- 29. Antimycobacterial, antibacterial and antifungal activities of Terminalia superba (Combretaceae). S Afr J Bot. 76(1):125-131.
- Kuete V, Sandjo L, Seukep J, Maen Z, Ngadjui B, Efferth T. 2015. Cytotoxic compounds from the fruits of *Uapaca togoensis* towards multi-factorial drug-resistant 30. cancer cells. Planta Med. 81(1):32-38.
- Maxeng AT, Chi GF, Bonsou IN, Ombito JO, Yeboah SO, Kuete V, Efferth T. 2020. Cytotoxic phytochemicals from the crude extract of *Tetrapleura tetraptera* fruits towards multi-factorial drug resistant cancer cells. *J Ethnopharmacol.* 267:113632. Nyaboke HO, Moraa M, Omosa LK, Mbaxeng AT, Vaderament-Alexe N-N, Masila V, Okemwa E, Heydenreich M, Efferth T, Kuete V. 2018. Cytotoxicity of lupeol from the 31.
- 32
- Skethinka E, neydentech M, Ellerth T, Kuele V. 2015. Cytotoxicity of tubeor hold the stem bark of Zanthoxylum gilletit against multi-factorial drug resistant cancer cell lines. Invest Med Chem Pharmacol. 1(1):10. Mbaveng AT, Damen F, Celik I, Tane P, Kuete V, Efferth T. 2019. Cytotoxicity of the crude extract and constituents of the bark of *Fagara tessmanii* towards multi-factorial drug resistant cancer cells. J Ethnopharmacol. 235:28-37. 33.
- 34. Bonsou IN, Mbaveng AT, Nguenang GS, Chi GF, Kuete V, Efferth T. 2022. Cytotoxicity, acute and sub-chronic toxicities of the fruit extract of *Tetrapleura* tetraptera (Schumm. & Thonn.) Taub. (Fabaceae). BMC Complement Med Ther. 22(1):178.
- Mbaveng AT, Omosa LK, Bitchagno GTM, Kuete JRN, Nchiozem-Ngnitedem V-A 35. Kuete V. 2023. Chapter Eleven - Potential antibacterial pharmaceuticals from the flora of Africa. Advances in Botanical Research. 107: 307-352. https://doi.org/10.1016/bs.abr.2022.08.021.
- 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.
 Kuete V, Nkuete AHL, Mbaveng AT, Wiench B, Wabo HK, Tane P, Efferth T. 2014. 36
- 37 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.

- 38. Kuete V, Efferth T. 2015. African flora has the potential to fight multidrug resistance of cancer. BioMed Res Int. 2015:914813.
- Kuete V. Fankam AG. Wiench B. Efferth T. 2013. Cytotoxicity and modes of action of 39 the methanol extracts of six Cameroonian medicinal plants against multidrugmesistant tumor cells. *Evid Based Complement Alternat Med.* 2013;285903. Kuete V, Efferth T. 2010. Cameroonian medicinal plants: pharmacology and derived
- 40. natural products. Frontiers Pharmacol. 1:123. Mbaveng AT, Kuete V, Efferth T. 2017. Potential of Central, Eastern and Western 41
- Africa medicinal plants for cancer therapy: spotlight on resistant cells and molecular targets. Front Pharmacol. 8:343. Efferth T, Kadioglu O, Saeed MEM, Seo EJ, Mbaveng AT, Kuete V. 2021. Medicinal
- 42. plants and phytochemicals against multidrug-resistant tumor cells expressing ABCB1, ABCG2, or ABCB5: a synopsis of 2 decades. *Phytochem Rev.* 20(1):7-53. Efferth T, Saeed MEM, Kadioglu O, Seo EJ, Shirooie S, Mbaveng AT, Nabavi SM,
- 43 Kuete V. 2020. Collateral sensitivity of natural products in drug-resistant cancer cells. *Biotechnol Adv.* 38:107342.
- Seukep JA, Ngadjui B, Kuete V. 2015. Antibacterial activities of Fagara macrophylla, Canarium schweinfurthii, Myrianthus arboreus, Dischistocalyx grandifolius and Tragia benthamii against multi-drug resistant Gram-negative bacteria. Springerplus. 4.567
- Tankeo SB, Lacmata ST, Noumedem JA, Dzoyem JP, Kuiate JR, Kuete V. 2014. Antibacterial and antibiotic-potentiation activities of some Cameroonian food plants 45 against multi-drug resistant Gram-negative bacteria. *Chin J Integr Med.* 20(7):546-554.
- Kuete V. 2023. Chapter Twelve Ethnopharmacology, phytochemistry and 46. Note V. 2020 of potent antibacterial medicinal plants from Africa. Advances in Botanical Research, 107:353-660. https://doi.org/10.1016/bs.abr.2022.08.022.
- 47 2013. In vitro antibacterial and antibiotic-potentiation activities of four edible plants against multidrug-resistant Gram-negative species. BMC Complement Altern Med. 13.190
- 48. 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. 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.
- Dzotam JK, Simo IK, Bitchagno G, Celik I, Sandjo LP, Tane P, Kuete V. 2018. In vitro antibacterial and antibiotic modifying activity of crude extract, fractions and 3,4,7-trihydroxyflavone from *Myristica fragrans* Houtt against MDR Gram-negative enteric
- bacteria. BMC Complement Altern Med. 18(1):15. Seukep JA, Sandjo LP, Ngadjui BT, Kuete V. 2016. Antibacterial and antibiotic-resistance modifying activity of the extracts and compounds from *Nauclea* pobeguini against Gram-negative multi-drug resistant phenotypes. *BMC Complement Altern Med.* 16:193. 51.
- Kuete V. 2023. Chapter Six Potential of African medicinal plants against Enterobacteria: Classification of plants antibacterial agents. Advances in Botanical Research. 106: 151-335. https://doi.org/10.1016/bs.abr.2022.08.006.
- Tankeo SB, Kuete V. 2023. Chapter Seven African plants acting on Pseudomonas aeruginosa: Cut-off points for the antipseudomonal agents from plants. Advances in 53
- Botanical Research. 106: 337-412. https://doi.org/10.1016/bs.abr.2022.08.007. Wamba BEN, Mbaveng AT, Kuete V. 2023. Chapter Eight Fighting Gram-positive bacteria with African medicinal plants: Cut-off values for the classification of the 54
- activity of natural products. Advances in Botanical Research. 106: 2023: 413-522. https://doi.org/10.1016/bs.abr.2022.08.008. Tchinda CF, Kuete V. 2023. Chapter Nine Potential of African flora to combat tuberculosis and drug resistance of Mycobacteria: Rationale classification of antimycobacterial agents from a natural source. Advances in Botanical Research. Toppozada HH, Mazloum HA, el-Dakhakhny M. 1965. The antibacterial properties of
- 56 the Nigella sativa I. seeds. Active principle with some clinical applications. J Egypt
- Med Assoc. 48:Suppl:187-202. Fabry W, Okemo P, Ansorg R. 1998. Antibacterial activity of East African medicinal 57.
- Jethopharmacol. 60:79-84.
 Simões M, Bennett R, Rosa E. 2009. Understanding antimicrobial activities of phytochemicals against multidrug resistant bacteria and biofilms. *Nat Prod Rep.* 58 26:746-757.
- Jimenez-Arellanes A, Meckes M, Ramirez R, Torres J, Luna-Herrera J, 2003, Activity 59. against multidrug-resistant *Mycobacterium* tuberculosis in Mexican plants used to treat respiratory diseases. *Phytother Res.* 17(8):903-908. Kuete V. 2010. Potential of Cameroonian plants and derived products against
- 60. microbial infections: a review. *Planta Med.* 76(14):1479-1491. Tamokou JDD, Mbaveng AT, Kuete V. 2017. Chapter 8 - Antimicrobial Activities of
- 61. African Medicinal Spices and Vegetables. In: *Medicinal Spices and Vegetables from Africa.* edn.: Academic Press: 207-237.
- Hashim I, Omosa LK, Nchiozem-Ngnitedem VA, Onyari JM, Maru SM, Guefack 62. MGF, Mbaveng AT, Kuete V. 2021. Antibacterial activities and phytochemical screening of crude extracts from Kenyan *Macaranga* species towards MDR phenotypes expressing efflux pumps. *Pharmacogn Commun.* 11(2):119-126. Tankeo SB, Damen F, Sandjo LP, Celik I, Tane P, Kuete V. 2016. Antibacterial activities of the methanol extracts, fractions and compounds from *Harungana*
- 63
- madagascariensis Lam. ex Poir. (Hypericaceae). J Ethnopharmacol. 190:100-105. Tankeo SB, Tane P, Kuete V. 2015. In vitro antibacterial and antibiotic-potentiation 64 activities of the methanol extracts from Beilschmiedia acuta, Clausena anisata, Newbouldia laevis and Polyscias fulva against multidrug-resistant Gram-negative bacteria. BMC Complement Altern Med. 15(1):412.
- Mambe FT, Na-Iya J, Fotso GW, Ashu F, Ngameni B, Ngadjui BT, Beng VP, Kuete V. 2019. Antibacterial and antibiotic modifying potential of crude extracts, fractions, and compounds from *Acacia polyacantha* Willd. against MDR Gram-negative bacteria.
- Evid Based Complement Alternat Med. 2019;7507549. Seukep JA, Sandjo LP, Ngadjui BT, Kuete V. 2016. Antibacterial activities of the methanol extracts and compounds from *Uapaca togoensis* against Gram-negative 66
- methanor extracts and compounds min *Daplac* and *Doplaris* against Gram-legalive multi-drug resistant phenotypes. S *Afr J Bot.* 103:1-5. Demgne OMF, Damen F, Fankam AG, Guefack MF, Wamba BEN, Nayim P, Mbaveng AT, Bitchagno GTM, Tapondjou LA, Penlap VB, Tane P, Efferth T, Kuete V. 2021. Botanicals and phytochemicals from the bark of *Hypericum roeperianum* (Hypericaceae) had strong antibacterial activity and showed synergistic effects with 67

antibiotics against multidrug-resistant bacteria expressing active efflux pumps. J Ethnopharmacol. 277:114257

- 68. Kuete V. Tanomouo JG, Marion Mever JJ, Lall N. 2009, Diospyrone, crassiflorone and plumbagin: three antimycobacterial and antigonorrhoeal naphthoquinones from
- Wo Diospyros spp. Int J Antimicrob Ag. 34(4):322-325.
 Kuete V, Omosa LK, Tala VR, Midiwo JO, Mbaveng AT, Swaleh S, Karaosmanoglu O, Sivas H. 2016. Cytotoxicity of plumbagin, rapanone and 12 other naturally 69. occurring quinones from Kenyan flora towards human carcinoma cells. BMC Pharmacol Toxicol. 17(1):60.
- 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 70 activity of some natural products against bacteria expressing a multidrug-resistant phenotype. Int Int J Antimicrob Ag. 37(2):156-161. Gale EF. 1981. Molecular basis of antibiotic action, vol. 2nd edn. Chichester,
- 71.
- 72.
- Gale EP, 1961, Molecular Joads of antibiotic action, vol. 21th edit. Critichester, Brisbane, New York and Toronto: J. Wiley.
 Alekshun MN, Levy SB. 2007. Molecular mechanisms of antibacterial multidrug resistance. *Cell.* 128(6):1037-1050.
 Fankam AG, Kuiate JR, Kuete V. 2017. Antibacterial and antibiotic resistance modulatory activities of leaves and bark extracts of *Recinodindron heudelotii*. 73. (Euphorbiaceae) against multidrug-resistant Gram-negative bacteria. *BMC Complement Altern Med.* 17(1):168. Tchinda CF, Voukeng KI, Beng VP, Kuete V. 2016. Antibacterial activities of the
- 74. 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.
- Fankam AG, Kuiate JR, Kuete V. 2014. Antibacterial activities of *Beilschmiedia* obscura and six other Cameroonian medicinal plants against multi-drug resistant 75. Gram-negative phenotypes. *BMC Complement Altern Med.* 14:241. Voukeng IK, Kuete V, Dzoyem JP, Fankam AG, Noumedem JA, Kuiate JR, Pages
- 76. 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.
- 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 77. MDR Gram-Negative phenotypes. African Journal of Integrated Health. 7(2):49-56. Akoue GN, Nguema PPM, Onanga R, Mabika AM, Ibrahim B. 2019. Nutritional
- 78. prospects, antioxidant and antibacterial activities of some food plants consumed by wild mandrill (Mandrillus sphinx) population from lékédi park (Bakoumba, Gabon). Int J Adv Res. 7(2):116-136.
- Mbaveng AT, Kuete V, Ngameni B, Beng VP, Ngadjui BT, Meyer JJ, Lall N. 2012. Antimicrobial activities of the methanol extract and compounds from the twigs of Dorstenia mannii (Moraceae). BMC Complement Altern Med. 12:83.
- Kuete V, Eyong KO, Folefoc GN, Beng VP, Hussain H, Krohn K, Nkengfack AE. 2007. Antimicrobial activity of the methanolic extract and of the chemical 80 constituents isolated from *Newbouldia laevis*. *Pharmazie*. 62(7):552-556. Azebaze AG, Ouahouo BM, Vardamides JC, Valentin A, Kuete V, Acebey L, Beng
- 81 VP, Nkengfack AE, Meyer M. 2008. Antimicrobial and antileishmanial xanthones from the stem bark of Allanblackia gabonensis (Guttiferae). Nat Prod Res. 22(4):333-341.
- Kuete V, Nguemeving JR, Beng VP, Azebaze AG, Etoa FX, Meyer M, Bodo B, Nkengfack AE. 2007. Antimicrobial activity of the methanolic extracts and compounds from *Vismia laurentii* De Wild (Guttiferae). J Ethnopharmacol. 82. 109(3):372-379.
- Teke GN, Kuiate JR, Kueté V, Teponno RB, Tapondjou LA, Tane P, Giacinti G, Vilarem G. 2011. Bio-guided isolation of potential antimicrobial and antioxidant 83. agents from the stem bark of Trilepisium madagascariense. S Afr J Bot. 77(2):319-327
- Johnson AP. 2011. Methicillin-resistant *Staphylococcus aureus*: the European landscape. *J Antimicrob Chemother*. 66 Suppl 4:iv43-iv48. 84
- Taj Y, Essa F, Aziz F, Kazmi SU. 2012. Study on biofilm-forming properties of clinical 85. isolates of Staphylococcus aureus. J Infect Dev Ctries. 6(5):403-409. Rice LB. 2006. Unmet medical needs in antibacterial therapy. Biochem Pharmacol. 86
- 71(7):991-995
- Komguem J, Meli AL, Manfouo RN, Lontsi D, Ngounou FN, Kuete V, Kamdem HW, Tane P, Ngadjui BT, Sondengam BL *et al.* 2005. Xanthones from Garcinia 87. smeathmannii (Oliver) and their antimicrobial activity. Phytochemistry. 66(14):1713-1717.
- Kuete V, Tangmouo JG, Penlap Beng V, Ngounou FN, Lontsi D. 2006. Antimicrobial activity of the methanolic extract from the stem bark of *Tridesmostemon* 88. omphalocarpoides (Sapotaceae). J Ethnopharmacol. 104(1–2):5-11.
- Kuete V, Ngameni B, Simo CC, Tankeu RK, Ngadjui BT, Meyer JJ, Lall N, Kuiate JR. 2008. Antimicrobial activity of the crude extracts and compounds from Ficus 89
- Cohamydocarpa and Ficus cordata (Moraceae). *J Ethnopharmacol*. 120(1):17-24. Kuete V, Nana F, Ngameni B, Mbaveng AT, Keumedjio F, Ngadjui BT. 2009. Antimicrobial activity of the crude extract, fractions and compounds from stem bark 90
- Antimistrobul availability of interest of the one one of the one of the one of the on 91
- Combretaceae). S Air J Bot, 76(1):125-131.
 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. 92.
- 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. 93.
- Kuete V, Metuno R, Ngameni B, Tsafack AM, Ngandeu F, Fotso GW, Bezabih M, 94 Etoa F-X, Ngadjui BT, Abegaz BM et al. 2007. Antimicrobial activity of the methanolic extracts and compounds from Treculia obovoidea (Moraceae). J
- Ethnopharmacol. 112(3):531-536. Ethnopharmacol. 112(3):531-536. Eyong KO, Folefoc GN, Kuete V, Beng VP, Krohn K, Hussain H, Nkengfack AE, Saeftel M, Sarite SR, Hoerauf A. 2006. Newbouldiaquinone A: A naphthoquinone-anthraquinone ether coupled pigment, as a potential antimicrobial and antimalarial agent from Newbouldia laevis. *Phytochemistry*. 67(6):605-609. 95.

- 96. Kuete V, Kamga J, Sandjo LP, Ngameni B, Poumale HM, Ambassa P, Ngadjui BT. 2011. Antimicrobial activities of the methanol extract, fractions and compounds from Ficus polita Vahl, (Moraceae). BMC Complement Altern Med, 11:6.
- Kuete V, Fozing DC, Kapche WF, Mbaveng AT, Kuiate JR, Ngadjui BT, Abegaz BM. 2009. Antimicrobial activity of the methanolic extract and compounds from *Morus* mesozygia stem bark. J Ethnopharmacol. 124(3):551-555.
- 98 Kuete V, Sandjo LP. 2012. Isobavachalcone: an overview. Chin J Integr Med. 18(7):543-547.
- 99. Kuete V, Mbaveng AT, Tsaffack M, Beng VP, Etoa FX, Nkengfack AE, Meyer JJM, Lall N. 2008. Antitumor, antioxidant and antimicrobial activities of Bersama engleriana (Melianthaceae). J Ethnopharmacol. 115(3):494-501.
- Kuete V, Ango PY, Fotso GW, Kapche GD, Dzoyem JP, Wouking AG, Ngadjui BT, Abegaz BM. 2011. Antimicrobial activities of the methanol extract and compounds from Artocarpus communis (Moraceae). BMC Complement Altern Med. 11:42.
- 101. 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.
- 102. 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.
- 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
- Omosa LK, Midiwo JO, Mbaveng AT, Tankeo SB, Seukep JA, Voukeng IK, Dzotam JK, Isemeki J, Derese S, Omolle RA et al. 2016. Antibacterial activity and structure-activity relationships of a panel of 48 compounds from kenyan plants against multidrug resistant phenotypes. *SpringerPlus*. 5:901.
- Ashu FA, Na-Iya J, Wamba BEN, Kamga J, Nayim P, Ngameni B, Beng VP, Ngadjui BT, Kuete V. 2020. Antistaphylococcal Activity of Extracts, Fractions, and 105 Compounds of Acacia polyacantha Wild (Fabaceae). Evid Based Complement Alternat Med. 2020:2654247.
- 106. Ekamgue B, Mbaveng AT, Kuete V. 2023. Anti-staphylococcal and antibioticpotentiating activities of botanicals from nine Cameroonian food plants towards multidrug-resistant phenotypes. *Invest Med Chem Pharmacol.* 6(1):75.
- Kuete V. 2023. Ethnopharmacology, phytochemistry and pharmacology of potent antibacterial medicinal plants from Africa. Advances in Botanical Research 107: 353-660. https://doi.org/10.1016/bs.abr.2022.08.022.
- Badawe G, Fankam AG, Mbaveng AT, Wamba BEN, Nayim P, Kuete V. 2019. Cinnamomum zeylanicum, Dichrostachys glomerata and three other plants had anti-108. staphylococcal and antibiotic modifying activity against drug-resistant phenotypes. Invest Med Chem Pharmacol. 2:25
- 109. Mbaveng AT, Ngameni B, Kuete V, Simo IK, Ambassa P, Roy R, Bezabih M, Etoa FX, Ngadjui BT, Abegaz BM et al. 2008. Antimicrobial activity of the crude extracts and five flavonoids from the twigs of *Dorstenia barteri* (Moraceae). J Ethnopharmacol. 116(3):483-489.
- van Ingen J, Rahim Z, Mulder A, Boeree MJ, Simeone R, Brosch R, van Soolingen D. 2012. Characterization of *Mycobacterium orygis* as *M. tuberculosis* complex
- Subspecies. Emerg Index Dis. 18(4):653-655. Anochie PI, Ndingkokhar B, Bueno J, Anyiam FE, Ossai-Chidi LN, Onyeneke EC, Onyeozirila AC. 2018. African medicinal plants that can control or cure tuberculosis. Int J Pharm Sci Dev Res. 4(1):001-008. WHO. 2019. Global tuberculosis
- 112, WHO, report 2019. https://www who
- int/tb/publications/global_report/en 2020. Seung KJ, Keshavjee S, Rich ML. 2015. Multidrug-Resistant Tuberculosis and Extensively Drug-Resistant Tuberculosis. Cold Spring Harb Perspect Med. 113. 5(9):a017863-a017863.
- Gemechu A, Giday M, Worku A, Ameni G. 2013. In vitro anti-mycobacterial activity 114 of selected medicinal plants against Mycobacterium tuberculosis and Mycobacterium bovis strains. BMC Complement Altern Med. 13:291. Mbaveng AT, Kuete V, Nguemeving JR, Beng VP, Nkengfack AE, Marion Meyer JJ, tuberculosis and
- Lall N, Krohn K. 2008. Antimicrobial activity of the extracts and compounds from Vismia guineensis (Guttiferae). Asian J Trad Med. 3:211-223.
- 116. Kuete V, Ngameni B, Mbaveng AT, Ngadjui B, Meyer JJ, Lall N. 2010. Evaluation of
- Nobele V, Ngarierin B, Modaverig AI, Ngagju B, Meyer JJ, Lain N. 2010. Evaluation of flavonoids from *Dorstenia* barteri for their antimycobacterial, antigonorrheal and anti-reverse transcriptase activities. *Acta Trop.* 116(1):100-104.
 Jeebhay M, Mbuli S, Uebel R. 1993. Assessment of exposure to chloramphenicol and azathioprine among workers in a South African pharmaceutical plant. *Int Arch Occup Environ Health*, 65(1 Suppl):S119-122.
- Fadulu SO. 1975. The antibacterial properties of the buffer extracts of chewing sticks used in Nigeria. *Planta Med.* 27(2):122-126. 118.
- Chaari A, Ben Jannet H, Salmona G, Mighri Z. 2005. Nauplathizine, a new unusual O-heteroside from *Nauplius aquaticus* (L). *Nat Prod Res.* 19(5):523-528.
 Nkengfack AE, Vouffo TW, Vardamides JC, Fornum ZT, Bergendorff O, Sterner O.
- 1994. Sigmoidins J and K, two new prenylated isoflavonoids from Erythrina sigmoidea. J Nat Prod. 57(8):1172-1177.
- Benne CA, Neeleman C, Bruin M, de Hoog GS, Fleer A. 1993. Disseminating infection with Scytalidium dimidiatum in a granulocytopenic child. Eur J Clin Microbiol Infect Dis. 12(2):118-121.
- Microbiol Infect Dis. 12(2):118-121.
 122. Habtemariam S, Gray AI, Halbert GW, Waterman PG. 1990. A novel antibacterial diterpene from *Premna schimperi*. *Planta Med.* 56(2):187-189.
 123. Hacène H, Kebir K, Othmane DS, Lefebvre G. 1994. HM17, a new polyene antifungal antibiotic produced by a new strain of Spirillospora. *J Appl Bacteriol.* 77(5):484-489.
- 124. Beaman-Mbaya V, Muhammed SI. 1976. Antibiotic action of Solanum incanum
- Linnaeus. Antimicrob Agents Chemother. 9(6):920-924. Boakye-Yiadom K, Fiagbe NI, Ayim JS. 1977. Antimicrobial properties of some West African medicinal plants iv. Antimicrobial activity of xylopic acid and other constituente of the fruits of *Xylopia aethiopica* (Annonaceae). *Lloydia*. 40(6):543-
- Jaspers MW, Bashir AK, Zwaving JH, Malingré TM. 1986. Investigation of Grewia 126. bicolor Juss. J Ethnopharmacol. 17(3):205-211.