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African medicinal plant derived products as therapeutic arsenals against multidrug resistant microorganisms

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Infectious diseases due to resistant pathogenic strains are rampant and the burden is worsened by the emergence and spread of microorganisms resistant to cheap and effective first-choice drugs. Medicinal plants could be an alternative solution to this and the aim of the present review is to summarize available evidence and knowledge concerning African medicinal plants used to treat multidrug resistant (MDR) bacteria, fungi and protozoa infectious agents. A literature search using the keywords: Africa, medicinal plants and multi-resistant microorganisms on google scholar, African Index Medicus, PubMed, Medline and EMBASE was conducted. We also scanned reference lists for important citations. Key pharmaceutical journals, workshop and conference proceedings were reviewed. Common medicinal plants found are *Brucea javanica*, *Prunus Africana*, *Mangifera indica, Picralima nitida, Aloe arborescence*, *Aloe striata, Vernonia adoensis, Markhamia tomentosa, Garcinia lucida, Garcinia kola, Phyllanthus muellerianus, Gladiolus gregasius, Sida alba, Trichila heudelotti, Piptadeniastrum africana* and *Dorstenia picta*. Most researches on the use of medicinal plants to treat multidrug resistant agents were conducted in South Africa, Nigeria, Cameroon, Congo, Kenya, Zimbabwe, Burkina Faso and Uganda. African medicinal plants possess important therapeutic agents that can be used as new phyto-medicines against MDR microorganisms.

Key words: Africa, medicinal plants, therapeutic products and multidrug resistant microorganisms.

INTRODUCTION

The spread of microorganisms which are resistant to cheap and effective first-choice drugs, although a natural phenomenon, is becoming a public health concern. Favorable factors accounting for this include auto-medication, treatment outside of recognized treatment centers and consumption of drugs without medical supervision and during insufficient length of time. Other confounding factors include frequent movements of population, overcrowding which provides opportunities for the rapid spread of microorganisms including multidrug

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resistant strains (Njunda et al., 2012). Multidrug resistance to as many as seven antibiotics has been observed in many epidemiological studies in Africa (Iruka and Sosa, 2008; Njunda et al., 2012). Antibiotics that usually face resistance are ampicillin, amoxicillin, co-trimoxazole, gentamicin, ceftriaxone and augmentin (amoxicillin + clavulinic acid) because of their wide indiscriminate use. Microorganisms that usually cause antibiotherapy failure include those that affect the urogenital tract such as beta-lactamase producers *Neisseria gonorrhoeae, Escherichia coli*, *Pseudomonas aeruginosa*, *Proteus mirabilis*, methicilin resistant *Staphyloccocus aureus* (MRSA) and mycoplasmas (Njunda et al., 2011). Those responsible for pulmonary infections include *Mycobacterium tuberculosis*, *Klebsiella pneumonia and Streptococcus pneumonia*. Agents responsible for gastrointestinal infections include *Escherichia coli*, *Entamoeba histolica*, *Salmonella typhi and Shigella dysenteriae* (Njunda et al., 2011).

Various mechanisms to acquire or develop intrinsic resistance to antibiotics which are developed by pathogens include active efflux of drugs, alteration of target sites, enzymatic degradations and propagation of resistance genes (Sibanda and Okoh, 2007). Bacterial resistance to penicillin is expanding to cephalosporins leading to the development of plasmid-mediated extended spectrum β-lactamases (ESBLs) strains. As new antimicrobial compounds are discovered, there is a need to assess their potentials in combination therapies with old antibiotics that have been rendered ineffective by the development of resistant strains (Sibanda and Okoh, 2007).

Management of infectious diseases caused by beta-lactam-resistant bacteria strains in developing countries where efficient antibiotics are not affordable for the majority of the population is becoming urgent and alternative agents can be obtained from medicinal plants. In Africa, medicinal plants are used in the fight against many infectious ailments; they still play a great role as therapeutic agents in many African countries (Kuete et al., 2011). They may form a good source of antimicrobial medications or resistance modifying agents to be discovered. Treatment of endemic infections using available natural resources would provide more efficient drugs to patients. Many medicinal plants and their derived products now form part of the therapeutic arsenals of Africa, faced with ever increasing infectious diseases, emerging and re-emerging infectious diseases due to multidrug resistant microorganisms and immune deficient diseases such as HIV/AIDS. It is estimated that more than 5,000 active principles have been identified in fruits, vegetables and grains, but a large percentage still remain unknown and need to be studied to increase our understanding of their health benefits (Kuete and Efferth, 2010).

Studies on the antimicrobial properties of medicinal extracts on resistant strains of microorganisms are scanty and only few antimicrobial agents as isolated compounds have been proven to possess inhibitory properties on multidrug resistant microorganisms. However, phytomedicines as antimicrobial agents have been evaluated scientifically in various countries in Africa. They present a low risk of resistance development to their action, because they are complex mixtures, making microbial adaptability very difficult (Daferera et al., 2003). This review summarizes the currently available knowledge on medicinal plants used to treat multidrug resistant infections and the efficacy of plant-derived extracts and compounds across Africa.

METHODOLOGY

A literature search using the keywords: Africa, medicinal plants and multi-resistant microorganisms on Google scholar, African Index Medicus, PubMed, Medline and EMBASE was conducted. We also scanned reference lists for important citations. Key pharmaceutical journals, workshop and conference proceedings were reviewed. African researchers of medicinal plants were contacted.

RESULTS

Plant compounds with activity against multi-resistant bacteria pathogens in Africa

Some isolated pure compounds of plant origin have been reported to have resistance modifying activities *in vitro*. This has prompted the search for such compounds from a variety of medicinal plants. Some of the compounds which have been observed to have direct antimicrobial activity were also able to potentiate the activity of antibiotics when used at low minimum inhibitory concentration (MIC) levels. For instance the antimicrobial property of tea (*Camellia sinensis*) is due to polyphenols (Kim et al., 2000). Bioassay directed fractionation of its extracts revealed its content in bioactive components such as epicatechin gallate (ECG), epigallocatechin gallate (EGCG), epicatechin (EC) and caffeine (CN). Used in combination *in vitro,* ECG and CG reduced MIC values for oxacillin from 256 and 512 to 1 and 4 mg/L against methicilin resistant *Staphyloccocus aureus* (MRSA) (Kim et al., 2000). Ethyl gallate is a congener of alkyl gallates, purified from a dried pod of tara (*Caesalpinia spinosa*) native to South America, intensified beta-lactam susceptibility in MRSA and MSSA strains (Kim et al., 2000).

Twenty six species of medicinal plants belonging to 19 families were described in previous studies were shown to possess antimicrobial properties on multidrug resistant bacteria species in six different countries across Africa (Table 1). These plants are used in traditional folk medicine against all types of infectious ailments including gastrointestinal, pulmonary, genito-urinary tracts and skin and skin infections. Seeds, stem barks, leaves, bulbs, twigs and roots are the plants' parts extracted using mostly methanol, water and acetone as major solvents. Although these studies indicated inhibitory activities on

Table 1. Plants used in Africa against multi-resistant bacteria species with evidence of their antimicrobial properties.

Family	Species	Country	Traditional treatment	Plant parts used	Solvent used/screened activity	Bioactive compounds	Microbial strains	Antibiogram resistance profile	References
Anacardiaceae	*Mangifera indica*	Zimbabwe	cough and diarrhea	twigs and leaves	Ethanolic extract, efflux inhibitory activity of extract comparable to reserpine	tannins, phenols, alkaloids, glycosides	*K. pneumonia* ; S. aureus ; *P. aeroginosa* ; *Bacillus cereus*	-	Chitemerere and Mukanganyama 2011
Apocynaceae	*Picralima nitida* (Stapf.) T. & H.Durand	Cameroon	Hypertension, fever, malaria, anti-inflammatory, antimicrobial	Leaves, seeds	Methanolic:1.25<MIC≥10 mg/ml	-	*E. coli* 25922 , *E. aerogenes* *E. cloacae, K. pneumoniae K. oxytoca, S. marcescens, P. aeruginosa, A. baumannii* *S. aureus U127 Enterococcus sp. P054*	AMX, Pip, CE, AMX, Pip, CE, AMX, Pip, CE, ESBL, ESBL, ESBL, cephalosporinase producer, AMX, Pip, CE, AMX, Pip, CE, penicillin	Gangoué-Piéboji et al., 2009
Ashodelaceae	*Aloe arborescence*	South Africa	Treatment of diarrhoea and stomach ailments	Leaves	Acetone. C=0.078mg/ml	TLC fingerprint revealed the presence of flavonoids and triterpenoids	*S. typhimurium*	ESBL positive Amx, Amp, aztreonam, Pip/tazobactam, COT Oxazole and Tet with reduced susceptibility to CI	Bisi-Johnson et al., 2012
	Aloe striata;	South Africa	Treatment of diarrhoea and stomach ailments	Leaves	Acetone. C=0.078 mg/ml	TLC fingerprint revealed the presence of flavonoids and triterpenoids	*S. typhimurium*	ESBL positive Amx, Amp, aztreonam, Pip/tazobactam, COT Oxazole and Tet with reduced susceptibility to CI	Bisi-Johnson et al., 2012
Asteraceae	*V. adoensis*	Zimbabwe	boiled decoction active against TB	Leaves	Ethanolic extract. Efflux inhibitory activity of extract with reserpine as reference	-	*K. pneumonia*, S. aureus, *P. aeroginosa*, *B. cereus*	-	Chitemerere and Mukanganyama 2011
Bignoniaceae	*Markhamia tomentosa* (Benth) K. Schum	Nigeria	Anti snake venom/bite, sore eyes, heart pain, scrotal elephantiasis	Leaves	methanolic extract	-	*S. aureus;* NCTC6571 *B. subtilis ;* NCIB 3610 *P. aeruginosa*. ATCC 10145	PV CE EM ; Aug Tet PV CE EM ; Nal PV CE EM	Aladesanmi et al., 2007
Clusiaseae	*Garcinia lucida*	Cameroon	Gastric ulcer, fermentation of palm wine, gynecological infections, anti-poison, gastro-intestinal infections, snake bites	Seeds, stem bark	Methanolic: 1.25 <MIC ≥ 10 mg/ ml	-	*E. coli* 25922 ,*E. aerogenes E. cloacae, K. pneumoniae, K. oxytoca, S. marcescens, P. aeruginosa ,A. baumannii*	AMX, Pip, CE ; AMX, Pip, CE, AMX, Pip, CE, ESBL ESBL, ESBL, AMX, Pip, CE, AMX, Pip, CE	Gangoué-Piéboji et al., 2009

Table 1. Contd.

	Garcinia kola	Cameroon	Gastric ulcer, fermentation of palm wine, gynecological infections, anti-poison, gastro-intestinal infections, snake bites	Leaves	Methanolic:1.25 <MIC ≥ 10 mg/ ml	-	*E. coli* 25922 ,*E. aerogenes E. cloacae, K. pneumoniae, K. oxytoca, S. marcescens P. aeruginosa, A. baumannii*	AMX, Pip, CE, AMX, Pip, CE, AMX, Pip, CE, ESBL ESBL, ESBL, AMX, Pip, CE, AMX, Pip, CE	Gangoué-Piéboji et al., 2009
Euphorbiaceae	*Phyllanthus muellerianus*	Cameroon	Use for infectious ailments	Stem barks	Methanolic	Ant, Fla, Pol	*E. coli, K. pneumonia, P. aeruginosa,P. mirabilis, S. flexneri, S. typhi*	All resistant against, Amp Augmentin	Assob et al., 2011
	Bridelia micantha (Hochst.) Baill.	Cameroon	Cough, antimicrobial,diarrhoea, gastric ulcer, intestinal worms, eye diseases	Stem barks	Methanolic:1.25 <MIC ≥ 10 mg/ml	-	*E. coli* 25922 ,*E. aerogenes, E. cloacae, K. pneumoniae, K. oxytoca, S. marcescens P. aeruginosa, A. baumannii*	AMX, Pip, CE, AMX, Pip, CE, AMX, Pip, CE, ESBL ESBL, ESBL, cephalosporinase producer	Gangoué-Piéboji et al., 2009
Moraceae	*Dorstenia picta*	Cameroon	Diarrhoea, infected wounds, anti-inflammatory, antimicrobial, eye diseases, snake bites	leaves	Methanolic: 1.25 <MIC ≥ 10 mg/ ml	-	*E. coli* 25922 , *E. aerogenes E. cloacae, K. pneumonia,. K. oxytoca, S. marcescens P. aeruginosa, A. baumannii*	AMX, Pip, CE, AMX, Pip, CE, AMX, Pip, CE, ESBL ESBL, ESBL, AMX, Pip, CE, AMX, Pip, CE	Gangoué-Piéboji et al., 2009
	Dorstenia Bateri	Cameroon		Twigs	CH2Cl2/MeOH (1:1) or in MeOH, 5<MIC>36 µg/ml	Flavoids : isobachalcone (IBC), kanzanol C (KAN), 4-hydroxylonchocarpin (4-LCP), stipulin (SPL), amentoflavone (AMF)	*N. gonorrhoea*	NGCS5 (_L+)	Kuete et al., 2010
Myrtaceae	*Psidium guajava*	South Africa	Use in the treatment of diarrhoea and stomach ailments	Leaves	Acetone: C=0.312-0.625 mg/ml	TLC fingerprint revealed the presence of flavonoids and triterpenoids.	*S. Typhimurium*	ESBL positive Amx, Amp, aztreonam, Pip/tazobactam, COT Oxazole and Tet with reduced susceptibility to CI	Bisi-Johnson et al., 2012
	Calistermon citrinus Skeels	Zimbabwe	Antibacterial, hemorrhoid treatment	Leaves	Ethanolic extract, efflux inhibitory activity of extract comparable to reserpine	-	*K. pneumonia,* S. aureus, *P. aeroginosa Bacillus cereus*	-	Chitemerere and Mukanganyama 2011

Table 1. Contd.

Iridaceae	*Gladiolus gregasius* Baker	Cameroon	Use for infectious ailments	Bulbs	Methanolic	Sap Tan Gly CG RS	E. coli, K. pneumonia, *P. aeruginosa, P. mirabilis, S. flexneri, S. typhi*	All resistant against Amp Augmentin	Assob et al., 2011
Malvaceae	*Sida alba* L.	Burkina Faso	Use in treating infectious diseases in children, malaria, fever, pain, variola, antibacterial, anti-inflammatory, analgesic activities and hepatoprotective	Leaf stems	Aqueous/acetone (80%, v/v). Synergistic effect when polyphenol rich fractions are combined to COT	Polyphenols	*Shigella dysenteriae Shigella boydii Enterococcus faecalis Proteus mirabilis*	All resistant to COT	Kiessoun et al., 2012
Meliaceae	*Trichila heudelotti*	Nigeria	Sores, heart troubles, pile	Leaves	Methanolic extract ID obtained at 250 mg/ml	-	*E. coli* NCTC 10418 ,*S. aureus* , NCTC6571 *B. subtilis* , NCIB 3610 *P. aeruginosa*. ATCC 10145	Nal Aug Tet Amx CL PV CE EM , PV CE EM , Aug Tet PV CE EM , Nal PV CE EM	Kuete et al., 2010
Mimosaceae	*Piptadeniastrum africana*	Cameroon	Use for infectious ailments	Leaves	Methanolic	Fla Pol Cou Gly CG RS	*E. coli, K. pneumonia, P. aeruginosa,P. mirabilis, S. flexneri, S. typhi*	All resistant against Amp Augmentin	Assob et al., 2011
Nyctaginaceae	*Boerhavia diffusa*	Nigeria	Diabetes, anti inflammatory, Abscess, boils	Leaves	methanolic	-	*B. subtilis* NCIB 3610	Aug Tet PV CE EM	Kuete et al., 2010
Ochnaceae	*Campylobacter densiflorum* (De Wild. & T.Durand) Farron	Cameroon	Chest and gastric pains	Leaves, roots	Methanolic: 1.25 <MIC ≥ 10 mg/ ml	-	*E. coli* 25922 , *E. aerogenes E. cloacae, K. pneumoniae, K. oxytoca, S. marcescens P. aeruginosa, A. baumannii*	AMX, Pip, CE, AMX, Pip, CE, AMX, Pip, CE, ESBL ESBL, ESBL, AMX, Pip, CE, AMX, Pip, CE	Gangoué-Piéboji et al., 2009
	Campylobacter zenkeri (Engl. ex Tiegh.) Farron	Cameroon	Chest and gastric pains	Roots	Methanolic: 1.25 <MIC ≥ 10 mg/ ml	-	*E. coli* 25922 , *E. aerogenes E. cloacae, K. pneumoniae, K. oxytoca, S. marcescens P. aeruginosa, A. baumannii*	AMX, Pip, CE, AMX, Pip, CE, AMX, Pip, CE, ESBL ESBL, ESBL, AMX, Pip, CE	Gangoué-Piéboji et al., 2009

Table 1. Contd.

Passifloraceae	*Barteria fistulosa Mast.*	Cameroon	Infected wounds, fever, rheumatism	stem bark	Methanolic, 1.25 <MIC ≥ 10 mg/ ml	-	*E. coli* 25922 , *E. aerogenes E. cloacae, K. pneumoniae K. oxytoca, S. marcescens P. aeruginosa, A. baumannii*	AMX, Pip, CE, AMX, Pip, CE, AMX, Pip, CE, ESBL ESBL, ESBL, AMX, Pip, CE	Gangoué-Piéboji et al., 2009
Phytolacaceae	*Hileria latifolia* (Lam.) H.Walt	Cameroon	Use for infectious ailments	leaves	Methanolic	Tri St Cou Gly CG RS	*E. coli, K. pneumonia, P. aeruginosa,P. mirabilis,S. flexneri, S. typhi*	All resistant against Amp Aug	Assob et al., 2011

Antibiotics: Nal: Nalidixic acid; Ofl: Ofloxacin; Aug: Augmentin; Amp: Ampicillin; Tet: Tetracycline; Amx: Amoxycillin; Cot: Cotrimoxazole (Trimethoprim/sulpha methoxazole); Nit: Nitrofurantoin; Gen: Gentamycin; CL: Chloramphenicol; CI: Ciprofloxacin; PV: Penicillin V; CE: Cephalothin; EM: Erythromycin. Pip: piperacillin ; ESBL: Extended spectrum beta lactamases; L+: betalactactamase producer; Alk: Alkaloids; Tri: Triterpens; St: Sterols; Ant: Anthraquinons; Fla: Flavonoids; Pol: Polyphenols; Sap: Saponins; Tan: Tannins; Cou: Coumarins; Gly: Glycosides; CG: Cardiac glycosides; RS: Reducing sugars; TLC: Thin Layer Chromatography.

activities on many gram+ and gram- multidrug resistant bacteria strains, only few presented the phytochemical composition of these plants. Alkaloids, flavonoids, phenols and triterpens appear to be the main compounds identified. Microbial strains that dominated in the studies were *Escherichia coli, K. pneumonia, S. dysenteriae, E. faecalis, Salmonella typhi, P. aeruginosa, S. aureus methicillin resistant and Bacillus subtilus, Neisseria gonorrhea betalactamase*+. They were found to be resistant to a wide range of antibiotics including amoxicillin, ampicillin, augmentin, cephalotin, ciprofloxacin, ofloxacin, cotrimoxazol, methicillin. Particularly of interest, the study done in Burkina Faso on the aqueous acetone (80%) of *Sida alba* L., a synergistic effect was observed when polyphenol rich fractions of this plant were combined to cotrimoxazole against *Shigella dysenteriae, Enterococcus faecalis* and *Proteus mirabilis* (Konaté et al., 2012). This is an indication that polyphenols could act in combination to cotrimoxazole for potentialization in order to increase its efficacy.

In Cameroon, the studies focused on beta-lactam-resistant bacteria (*K. pneumoniae, K. oxytoca, Enterobacter cloacae, Serratia marcescens, Acinetobacter baumannii, S. aureus* and *Enterococcus sp.*) and reference strains of bacteria (*E. coli* ATCC 35218, *Enterobacter aerogenes* ATCC 29751, *E. aerogenes* ATCC 13048, *P. aeruginosa* ATCC 27853 and *Enterococcus hirae* ATCC 9790) by using disc-diffusion and agar-dilution assays (Gangoué-Piéboji et al., 2009). The minimal inhibitory con-centration (MIC) values of different plant extracts against the tested bacteria were found to range from ≤ 0.3 to ≥ 10 mg/ml. This study revealed that the most active plant extracts were *Dorstenia picta* and *Bridelia micrantha* on beta-lactam-resistant gram-negative bacilli and the extracts from *Bridelia. micrantha*, *Mallotus oppositifolius*, *Garcinia lucida*, *Garcinia kola*, *Campylospermum densiflorum* (leaves) and *Campylospermum zenkeri* (root) on beta-lactam-resistant gram-positive cocci (Gangoué-Piéboji et al., 2009). Another innovative approach in searching for new arsenals against multi-resistant bacteria was seen in the study carried out in Zimbabwe by Chitemerere and Mukanganyama (2011), who found that the ethanolic leaves extract of *Calistermon citrinus* Skeels rich in tannins, phenols, alkaloids and glycosides showed an efflux inhibitory activity against *S. aureus, K. pneumonia, P. aeruginosa* and *B. subtilus* comparable to that of reserpine. Reserpine is an alkaloid and is a reference efflux inhibitor with a useful counteracting mechanism against microorganisms' resistance. Antimicrobial activity of *Temnocalyx obovatus* (Rubiaceae) root extracts used in folk medicine in Zimbabwe deployed significant activity against bacterial (*S. aureus, E. coli, Clostridium perfringens*) and fungal (*Aspergillus niger* and *Candida albicans)* species with MIC values ranging from 10 to 60 µg/ml(Muna and Fauzia, 2012).

Other efflux inhibitory mechanisms were observed by Aiyegoro et al. (2009) who showed that the activity of presumed plant antimicrobials against gram+ and gram- organisms was significantly

enhanced by synthetic multidrug-resistance (MDR) inhibitors of MDR efflux proteins. Combinations of antibiotics are progressively being used in the treatment of drug resistant infections; this is advantageous because they deploy various mechanisms of action. The production of intrinsic antimicrobial compounds by plants can have a MDR inhibitory property that improves the inhibitory effect of antibiotics (Aiyegoro et al., 2009). The use of *Catha edulis* extracts for instance at sub-inhibitory levels was reported to reduce the MIC values of tetracycline and penicillin G against resistant oral pathogens, *Streptococcus oralis*, *Streptococcus sanguis* and *Fusobacterium nucleate.* Polyphenols (epicatechin gallate and catechin gallate) were also found to be able to reverse beta-lactam resis-tance in methicillin resistant *S. aureus* (MRSA). Whereas diterpenes, triterpenes, alkyl gallates, flavones and pyri-dines showed resistance modulating abilities on various antibiotics against resistant strains of *S. aureus (*Aiyegoro et al., 2009*)*. The methanolic and ethylacetate extracts of *Phyllanthus muellerianus* and *Piptadeniastum africanus* were found to be highly active against gram+ and gram- infectious resistant microorganisms with MIC varying from 2.5 to 0.31 mg/L. The *in vivo* acute toxicity study carried out on the methanolic extracts of these two plants indicated that they were not toxic (Assob et al., 2011). This is important because selective inhibition is crucial to conclude on the efficacy of antimicrobial compounds.

Other studies from Cameroon on plant extracts showed interesting results due to their exceptional inhibitory power on both bacteria and fungi. Among these are *Bersama engleriana*, *Dorstenia angusticornis*, *Dorstenia barteri, Diospyros canaliculata, Diospyros crassiflora, Newbouldia laevis,* and *Ficus cordata* (Kuete et al., 2010). Compounds like isobavachalcone, kanzanol C and 4-hydroxylonchocarpin isolated from *Dorstenia* spp., plumbagin, crassiflorone and diospyrone isolated from *Diospyros* spp., and also new boudiaquinone and lapachol isolated from *Newbouldia laevis* (16) displayed important inhibitory activity against resistance microorganisms. *Thecacoris annobonae* Pax & K. Hoffm (Euphorbiaceae) has a significant antimicrobial (MIC < 10 µg/ml) activity against *Mycobacterium tuberculosis* H37Rv, *B. cereus* and *P. aeruginosa* (Kuete et al., 2011). The effect of combinations of the methanolic extract of *Helycrisum pendunculatum* leaves and selected antibiotics evaluated using the time-kill assay method showed a synergy rate of 59.1% (Extract + Tetracycline; Extract + Amoxycillin), 54.6% (Extract + Penicillin G; Extract + Chloramphenicol), 63.6% (Extract + Ciprofloxacin; Extract + Oxytetracycline), 68.2% (Extract+ Erythromycin) and 27.3% (Extract + Ampicillin) on all isolates at both ½ MIC and MIC values. Overall, synergistic response could attain 60% of all combinations of extract and antibiotics against all tested organisms (Aiyegoro et al., 2009).

In Libya, antituberculosis activity was obtained with dichloromethane extract of *Tulbaghia violacea* Harv. against *M. aurum; Marrubium vulgare L., Pistacia lentiscus L, Quercus coccifera L, Thymus capitatus (L.)* Hoffm. & Link are active against *M. tuberculosis* (Aiyegoro et al., 2009; Korir et al., 2012).

Plant compounds with efficacy against multi-resistant fungi pathogens in Africa

A good number of studies have been done on the efficacy of medicinal plants against fungi. In Nigeria, *Sphenoceutrum jollyanum* Pierre (Menispermaceae) used in traditional medicine as chewing sticks and for stomach pains was shown to possess significant antifungal activity against *Candida albicans*, *Candida pseudotropicalis* and *Trichophyton rubrum.* In South Africa (Aladesanmi et al., 2007), extract of the rhizomes *Gunnera perpensa* was proven effective against *Penicillium notatum, Aspergillus flavus* and *A. niger* (LC_{50} values ranging from 0.07 to 3.81). This is important as these fungi have been implicated in cases of immune-compromised patients that frequently develop opportunistic and superficial mycosis (Nkomo and Kambizi, 2009).

An important antifungal activity was obtained with the acetone bark extract of *Erythrina caffra* Thunb. The bark of *E. caffra* is used in South Africa to treat sores, tuberculosis, respiratory infections, wounds, abscesses, arthritis and toothache. Dose dependent inhibitory activity was observed against a wide range of fungi strains (*Candida krusei, C. albicans*, *Candida neoformans*, *Candida rugosa*, *P. notatum*, *A. niger*, *Aspergillus terreus*, *Aspergillus flavus*, *Absidia corymbifera*, *Candida glabrata*, *Trichophyton mucoides*, *Trichophyton tonsurans* and *Fusarium Sporotrichioides)* (Nkomo and Kambizi, 2009) with MIC and minimum fungicidal concentrations (MFC) values ranging between 0.625 and 20 mg/ml and indicating fungicidal activity (Olajuyigbe and Afolayan, 2012). In Cameroon, another study presented the efficacy of *Ficus polita* (Moraceae) against *C. albicans* (Kuete et al., 2011). The bark and roots infusions are used in the treatment of infectious diseases, abdominal pains and diarrhea. Phytochemical analysis of the plant indicated the presence of compounds with enough evidence of their antimicrobial microbial activities such as lupeol, betulinic acid, ursolic acid, b-sitosterol, sitosterol-3-O-b-D-glucopyranoside (Kuete et al., 2011).

Cryptolepis sanguinolenta Lindl. Schltr. (Periplocaceae) is a shrub that grows in the rainforest and the deciduous belt forest, found in the west coast of Africa. *In vitro* study showed inhibitory activity against bacteria species (specifically, enteric pathogens, most notably *E. coli* and vibrio) as well as against *Candida* spp. (Iwu et al., 1999). *Aframomum melegueta* (Zingiberaceae) is a perennial herb used as an aphrodisiac and against measles and leprosy, taken for excessive lactation and post partum

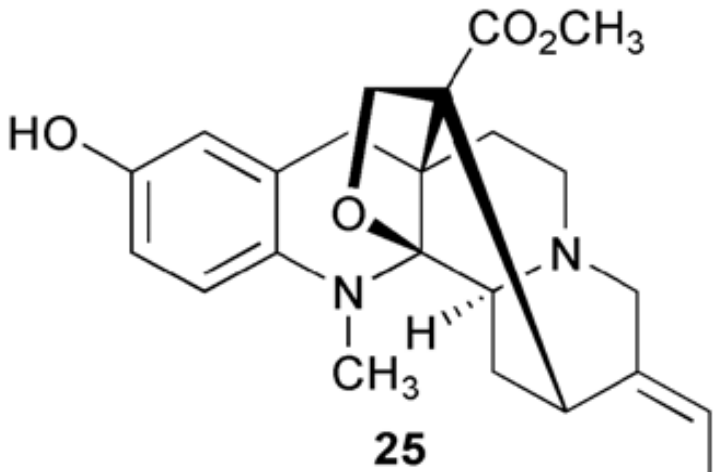

Figure 1. Akuamine.
Source: Titanji et al. (2008).

hemorrhage, purgative, galactogogue and anthelmintic and hemostatic agent contains gingerol, shagaol, paradol in its essential oil; its antifungal antishistosomal activities have also been demonstrated (Iwu et al., 1999; Kuete et al., 2011). Xylopic acid, one of the constituents of *Xylopia aethiopica*, Ethiopian Pepper (Abbibacceae) is active against *C. albicans* (Kuete et al., 2011; Korir et al., 2012). Some extracts from Cameroonian medicinal plants including those from *Bersama engleriana*, *Dorstenia angusticornis*, *Dorstenia barteri*, *Diospyros canaliculata*, *Diospyros crassiflora*, *Newbouldia laevis* and *Ficus cordata* exhibited a wide range of inhibitory activity on both bacteria and fungi (Kuete et al., 2011). In Kenya, hexane extracts of *Senna didymobotrya* used in folk medicine showed notably inhibitory activities on *Microsporum gypseum*, *Trichophyton mentagrophyte* and *Microsporum gypseum* (Omoregie and Sisodia, 2012).

Plants with anti-malarial and other anti-protozoa multi-resistant efficacy

Malaria is a serious health concern in Sub-Saharan Africa where it kills a child below five years every thirty seconds and more than 90% of deaths occur due to this pathology (Nsagha et al., 2011). Anti-malarial multidrug resistance is a major public health problem in the world especially in Africa where the health systems are weak resulting in many prescriptions by unqualified health personnel (Nsagha et al., 2012) and home-based treatment (Htut, 2009) which affects its control. Over the years, anti-malaria drug resistance has become one of the most important problems impeding malaria control efforts (Sendagire et al., 2005). This led to the discovery of other antimalarial agents from medicinal plants such as quinine from cinchona bark and artemisinin from *Artemisia annua* (Saxena et al., 2003). One of such plants with anti-malarial and anti-protozoa potentials on the African continent is *Brucea sumatrana* Roxb., a shrub belonging to the family Simaroubaceae (Ehata et al., 2012). An important inhibitory activity was obtained *in vitro* with the seeds' crude extracts of *B. sumatrana* against *Trypanosoma cruzi*, *T. brucei brucei, Leishamania infantum* and chloroquine and pyrimethamine-resistant K1 strain of *P. falciparum* in the Democratic Republic of Congo (Ehata et al., 2012).

Plants from Western Cameroon were screened *in vitro* for their antiplasmodial activity and cytotoxicity.

Dacryodes edulis exhibited the highest antiplasmodial activity, followed by *Vernonia amygdalina, Coula edulis* and *Eucalyptus globulus*. *Dacryodes edulis* is a multi-purpose plant in African folk medicine, as its various parts are used as a remedy for parasitic skin diseases, jigger, mouthwash, tonsillitis, sickle cell and malaria (Zofou et al., 2011). Its phytochemistry revealed the presence of phenolic compounds which have previously been shown as having antiplasmodial activity (Zofou et al., 2011). An alkaloid, akuamine (Figure 1) from the seeds of *Picralima nitida* possesses activity against Plasmodium (Titanji et al., 2008). *V. amygdalina* and *Eucalyptus globulus* extracts exhibited high activity ($1 < IC_{50} \leq 10$ µg/ml) on both chloroquine sensitive and multiresistant strains of *P. falciparum* ($10 < IC_{50} \leq 25$ µg/ml) (Titanji et al., 2008).

Antiprotozoal activities of *Albizia zygia* (Fabaceae) stem bark and methanolic seeds' extract of *Harungana madagascarensis* was obtained against *P. falciparum* K1 chloroquine-resistant strain, *Leishmania donovani*, *Trypanosoma cruzi, Trypanosoma brucei rhodesiense*, protozoa responsible for malaria, visceral leishmaniasis, Chagas disease and African trypanosomiasis by Lenta et al. (2007). In Congo, it was found that the extracts from

Enanatia chlorantha stem bark, *Napoleona vogelii* stem bark and *Quassia africana* root bark are active with IC_{50} values ranging between 1.87 and 5 µg/ml, against *Trypanosoma cruzi, Leishmania infantum* and *P. falciparum* K1 (Musum), 7α- obacunyl acetate and a cycloartane derivative which are isolated compounds from the dichloromethane - methanol (1:1) extract of the stem bark of *Entandrophragma angolense* (Meliaceae) with good activity, IC_{50} of 2 and 5.4 µg/ml, respectively test against chloroquine resistant strain W2 of *P. falciparum* malaria parasite in Cameroon (Bickii et al., 2007; Sha'a, et al., 2011). In Benin, two sesquiterpenic lactones isolated (1(15-acetoxy-8β-[(2-methylbutyryloxy)]-14-oxo-4,5-cis-acanthospermolide) and 2 (9α-acetoxy-15-hydroxy-8β-(2-methylbutyryloxy)-14-oxo-4,5-trans-acanthospermolide)) from the aerial parts of *Acanthospermum hispidum* D.C showed *in vitro* antiplasmodial activity against the chloroquine-sensitive strain (3D7) (IC_{50} of 2.9 ± 0.5 and 2.23 ± 0.09 µM, respectively), *Trypanosoma brucei brucei* (IC_{50} of 2.45 ± 0.49 and 6.36 ± 1.42 µM, respectively) and *Leishmania mexicana mexicana* (IC_{50} of 0.94 ± 0.05 and 2.54 ± 0.19 µM, respectively) (Ganfon et al., 2012).

In Nigeria, the ethanolic extract of *Jatropha tanjorensis* leaves showed moderate sensitivity against *P. falciparum.* Alkaloids, saponins, anthraquinones, tannins and flavonoids are probably responsible for this activity (Ouattara et al., 2006; Omoregie and Sisodia, 2012). Ethanol extract of *V. amygdalina* induced an important inhibitory activity against *P. falciparum* with an IC_{50} of 11.2 µg/ml (Ouattara et al., 2006; Sha'a et al., 2011). Whereas in Burkina Faso, methanolic extracts of *Swartzia madagascariensis* and *Combretum glutinosum* as well as alkaloidal extracts of *Tinospora bakis* were proven to be active against *P. falciparum* chloroquine-resistant strain W2 *in vitro* (5 µg/ml < IC_{50} < 50 µg/ml) (Ouattara et al., 2006; Dzomba and Muchanyereyi, 2012).

DISCUSSION

In Africa, attitudes towards traditional, herbal medicines vary strongly because of the confusion between herbal medicine and witchcraft (Wright et al., 1988). The use of medicinal plants is often associated with superstition and therefore rejected by some people. However, there are many Africans who prefer traditional methods of treatment (Wright et al., 1993). The Chinese plant, *Artemisia annua* is cultivated in East African countries to supply pharmaceutical manufacturers in Europe (Wright et al., 1993). The bark of *Prunus africana* is used in making treatments for prostate cancer (Wright et al., 1993). *Brucea sumatrana* have been proven to possess antiprotozoal activity against *Trypanosoma cruzi*, *T. brucei brucei*, *Leishmania infantum* and chloroquine and pyrimethamine-resistant K1 strain of *P. falciparum*. These are in consonance with findings from the Asian species that were investigated for their various biological activities such as antimalarial, antiprotozoal against amoeba (Camacho et al., 2003; Sawangjaroen and Sawangjaroen, 2005), *Toxoplama gondii* and *Giardia intestinal (*Camacho et al., 2003*)*, *Trypanosoma brucei brucei* and *Leishmania donovani* (Sawangjaroen and Sawangjaroen, 2005), *Blastocystis hominis* (Bawm et al., 2008), *Trypanosoma evansi* (Subeki et al., 2007) and *Babesia gibsoni* (Elkhateeb et al., 2008; Okokon and Nwafor, 2009). Other studies on medicinal plants have been reported from Cameroon (Lenta et al., 2007; Djeussi et al., 2013), Nigeria (Runyoro et al., 2006; Balagon et al., 2010), South Africa (Wright et al., 1993), Tanzania (Owuor and Kisangau, 2006), Uganda (Sendagire et al., 2005), Kenya (Mehjabeen et al., 2011) and Congo (Wright et al., 1988).

CONCLUSION AND FUTURE PROSPECTS

Several *in vitro* and *in vivo* antimicrobial activities have been carried out on traditional medicinal plants and found to be good sources of numerous therapeutic agents, however only few studies on the efficacy of medicinal plants and their derived compounds have been done so far on resistant strains of microorganisms. Many complementary and alternative medicines are being given more consideration because a large number of antimicrobial agents derived from traditional medicinal plants are available for treating various infectious diseases. In most of the studies, interesting antimicrobial properties of extracts against MDR strains were obtained, suggesting their potency, but only few studies have actually addressed the issue of selective toxicity.

Emphasis should be oriented towards the discovery of antibiotic resistance modifying compounds from plants sources which offer greater chances of reversing the resistance pattern of many antimicrobials which otherwise will be abandoned. Combined therapies of plants extracts and their derived products have to be assessed *in vivo* as well as to determine their clinical relevance. This will surely lead to the production of phytomedicines or medicinal plant-derived therapeutic agents. In order to attain this goal, research institutions in Africa should move further and put in place strong protocols geared towards the evaluation and comparison of the cost-effectiveness and safety-tolerance levels of the medicinal plants and their derived products against multidrug resistant microbial agents. African states should reinforce these efforts by putting in place a common policy that fosters the integration of traditional and modern medicines.

Competing interests

The authors declare that they have no competing interest

in this study.

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REFERENCES

Aiyegoro OA, Afolayan AJ, Okoh AI (2009). Synergistic interaction of *Helichrysum pedunculatum* leaf extracts with antibiotics against wound infection associated bacteria. Biol. Res. 42:327-338.

Assob JCN, Kamga HLF, Nsagha DS, Njunda AL, Nde PF, Asongalem AE Njouendou AJ, Sandjon B, Penlap VB (2011). Antimicrobial and toxicological activities of five medicinal plant species from Cameroon Traditional Medicine. BMC Compl. Alter. Med. 11:70.

Assob JCN, Kamga HLF, Nsagha DS, Njunda AL, Nde PF, Asongalem AE Njouendou AJ, Sandjon B, Penlap VB (2011). Antimicrobial and toxicological activities of five medicinal plant species from Cameroon Traditional Medicine. BMC Compl. Alter. Med. 11:70.

Aladesanmi AJ, Iwalewa EO, Adebajo AC, Akinkunmi EO, Taiwo BJ, Olorunmola FO, Lamikanra A (2007). Antimicrobial and Antioxidant Activities of Some Nigerian Medicinal Plants. Afr. J. Tradit. CAM. 4 (2): 173 – 184.

Balagon MF, Cellona RV, Abalos RM, Gelber RH, Saunderson PR (2010). The efficacy of a four-week, ofloxacin-containing regimen compared with standard WHO-MDT in PB leprosy. Lepr. Rev. 81:27–33.

Bawm BS, Matsuura H, Elkhateeb A, Nabeta K, Subeki NN, Oku Y, Katakura K (2008). "*In vitro* Antitrypanosamal activities of quassinoid compounds from the fruits of a medicinal plant, *Brucea javanica*," Vet. Parasitol. 158(4):288- 294.

Bickii J, Feuya GRT, Tchouankeu JC, Tsamo E (2007). The antiplasmodial agents of the stem bark of *Entandrophragma angolense* (Meliaceae). Afr. J. Trad. CAM. 4(2):135-139.

Bisi-Johnson MA, Chikwelu LO, Eloff J, Bolorunduro BS, Kamaldeen B, Vasaikar S, Adefisoye MA (2012). Can herbal remedies be the answer to multidrug resistance? Profile of drug resistance in *Salmonella* species in Eastern Cape, South Africa. J. Exp. Integr. Med. 2(2):147-153.

Camacho MDR, Phillipson JD, Croft SL, Solis PN, Marshall SJ, Ghazanfar SA (2003). Screening of plant extracts for antiprotozoal and cytotoxic activities. J. Ethnopharmacol. 89(2-3):185-191.

Chitemerere TA, Mukanganyama S (2011). In vitro antimicrobial activity of some selected medicinal plants from Zimbabwe. Afr. J. Plant Sci. Biotech. 5(1):1-7.

Daferera DJ, Ziogas BN, Polissiou MG (2003). The effectiveness of plant essential oils on the growth of *Botrytis cinerea, Fusarium sp*. and *Clavibacter michiganensis* subsp. *michiganensis*. Crop. Prot. 22:39-44.

Djeussi DE, Noumedem JAK, Seukep JA, Fankam AG, Voukeng IK, Tanke SK, Nkuete HAL, Kuete V (2013). Antibacterial activities of selected edible plants extracts against multidrug-resistant Gram-negative bacteria. BMC Compl. Alter. Med. 13:164.

Dzomba P, Muchanyereyi N (2012). Potential Antimicrobial Plant Extract Based Therapeutics from *Temnocalyx obavatus* Roots. Eur. J. Med. Plants 2(3):209-215.

Ehata MT, Phuati AM, Lumpu SN, Munduku CK, Phongi DB, Lutete, GT, Kabangu OK, Kanyanga RC, Matheeussen A (2012). *In vitro* antiprotozoal and cytotoxic activity of the aqueous extract, the 80% methanol extract and its fractions from the Seeds of *Brucea sumatrana* Roxb. (Simaroubaceae) growing in Democratic Republic of Congo. Chin. Med. 3:65-71.

Elkhateeb A, Yamasaki M, Maede M, Katakura K, Nabeta K, Matsuura H (2008). "Anti-Babesial Quassinoids from the Fruits of *Brucea javanica*." Nat. Prod. Commun. 3(1):1-4.

Ganfon H, Bero J, Tchinda AT, Gbaguidi F, Gbenou J, Moudachirou M, Frédérich M, Quetin-Leclercq J (2012). Antiparasitic activities of two sesquiterpenic lactones isolated from *Acanthospermum hispidum* D.C. J. Ethnopharmacol. 141(1):411-417.

Gangoué-Piéboji P, Eze N, Djintchu AN, Ngameni B, Tsabang N, Pegnyemb D E, Biyiti L, Ngassam P, Koulla-Shiro S, Moreno G (2009). The *in-vitro* antimicrobial activity of some traditionally used medicinal plants against beta-lactam-resistant bacteria. Infect. Dev. Ctries. 3(9):671-680.

Htut ZW (2009). Artemisinin resistance in *Plasmodium falciparum* malaria. N. Engl. J. Med. 361:1807-1808.

Iwu MM, Duncan AR, Okunji CO (1999). New Antimicrobials of Plant Origin. New antimicrobials of plant origin. In: J. Janick (ed.), Perspectives on new crops and new uses. ASHS Press. pp. 457–462.

Iruka NO, Sosa A (2008). Antibiotic resistance in Africa- Discerning the enemy and plotting a defense. http://www.tufts.edu/med/apua/about_issue/africahealth.pdf

Kim HS, Shibata Y, Ikemoto NK, Ishizuka N, Murakami Y, Sugimoto N, Kobayashi M, Wataya Y (2000). Potent *in vivo* antimalarial activity of 3,15-Di-O-ace- tylbruceolide against *Plasmodium berghei* Infection in Mice." Parasitol. Int. 48(3):271-274.

Konaté K, Hilou A, Mavoungou JF, Lepengué AN, Souza A, Barro N, Datté JY, M'Batchi B, Nacoulma OG (2012). Antimicrobial activity of polyphenol rich fractions from *Sida alba* L. (Malvaceae) against co-trimoxazol resistant bacteria strains. Ann. Clin. Microbiol. Antimicrob.11:5.

Korir RK, Mutai C, Kiiyukia C, Bii C (2012). Antimicrobial activity and safety of two medicinal plants traditionally used in Bomet District of Kenya. Res. J. Med. Plant 6:370-382.

Kuete V, Efferth T (2010). Cameroonian medicinal plants: pharmacology and derived natural products. Frontiers Pharmacol. 123:1-19.

Kuete V, Kamga J, Sandjo LP, Ngameni B, Poumale, HMP, Ambassa P, Ngadjui BT (2011). Antimicrobial activities of the methanol extract, fractions and compounds from *Ficus polita* Vahl. (Moraceae). BMC Complement. Alter. Med. 11:6.

Kuete V, Ngameni B, Mbaveng AT, Ngadjui B, Marion MJJ, Lall N (2010). Evaluation of flavonoids from *Dorstenia barteri* for their antimycobacterial, antigonorrheal and anti-reverse transcriptase activities. Acta Trop. 116:100–104.

Kiessoun K, Hilou A, Mavoungou JF, Lepengué AN, Souza A, Barro Datté N, M'Batchi JBY, Nacoulma GO (2012). Antimicrobial activity of polyphenol rich fractions from *Sida alba* L. (Malvaceae) against co-trimoxazol resistant bacteria strains. Ann. Clin. Microbiol. Antimicrob. 11:5.

Kuete V, Efferth T (2010). Cameroonian medicinal plants: pharmacology and derived natural products. Front. Pharmacol. 123: 1-19.

Lenta BN, Vonthron-Sénécheau C, Fongang SR, Tantangmo F, Ngouela S, Kaiser M, Tsamo E, Antone R, Weniger B (2007). *In vitro* antiprotozoal activities and cytotoxicity of some selected Cameroonian medicinal plants. J. Ethnopharmacol. 111(1):8-12.

Mehjabeen MA, Noor J, Zia-ul-haq M, Mehboob SA, Asma W, Saeedul-H (2011). Antimicrobial screening of some plants of medicinal importance. Pak. J. Bot. 43(3):1773-1775.

Muna MB, Fauzia R El-G (2012). Antibacterial activity of medicinal aqueous plant extracts against *Mycobacterium tuberculosis*. Mal. J. Microbiol. 8(3):203-206.

Njunda AL, Nsagha DS, Assob JCN, Palle JN, Kamga, HLF, Nde PF, Ntube MNC, Weledji PE (2011). Genital mycoplasmas in women attending the Yaoundé University Teaching Hospital in Cameroon. J. Pub. Health Afr. 2:e16

Njunda AL, Assob JCN, Nsagha DS, Kamga HLF, Awafong MP, Weledji EP (2012). Epidemiological, clinical features and susceptibility pattern of shigellosis in the Buea Health District, Cameroon. BMC Res. 5:54.

Nkomo M, Kambizi (2009). Antimicrobial activity of *Gunnera perpensa* and *Heteromorpha arborescens* var. abyssinica. J. Med. Plants Res. 3(12):1051-1055.

Nsagha DS, Elat, JBN, Ndong PAB, Tata PN, Tayong MN, Pokem F, Wankah CC (2012). Feasibility of home management using ACT for childhood malaria episodes in an urban setting. Drug Healthc. Patient Saf. 4:118.

Nsagha DS, Njunda AL, Kamga HLF, Assob JCN, Shey CW, Nsagha SM, Njamnshi AL (2011). Knowledge and practices relating to malaria in Ndu community of Cameroon: signs and symptoms, causes and prevention. J. Public Health Epidemiol. 3(6):294-300.

Okokon JE, Nwafor PA (2009). Antiplasmodial activity of root extract and fractions of *Croton zambesicus.* J. Ethnopharmacol. 121:74-78.

Olajuyigbe OO, Afolayan AJ (2012). *In vitro* pharmacological activity of the crude acetone extract of *Erythrina caffra* Thunb: antibacterial and antifungal assessment. J. Med. Plants Res. 6(9):1713-1720.

Omoregie ES, Sisodia BS (2012*). In vitro* antiplasmodial activity and cytotoxicity of leaf extracts of *Jatropha tanjorensis.* Bayero J. Pure Appl. Sci. 5(1):90–97.

Ouattara Y, Sanon S, Traoré Y, Mahiou V, Azas N, Sawadogo L (2006). Antimalarial activity of *Swartzia madagascariensis* Desv. (Leguminosae), *Combretum glutinosum* Guill. & Perr. (Combretaceae) and *Tinospora bakis* miers. (Menispermaceae), Burkina Faso medicinal plants. Afr. J. Trad. CAM. 3 (1):75-81.

Owuor B, Kisangau DP (2006). Kenyan medicinal plants used as antivenin: a comparison of plant usage. J. Ethnobiol. Ethnomed 2:7.

Runyoro DKB, Ngassapa OD, Matee MIN, Joseph CC, Moshi MJ (2006). Medicinal plants used by Tanzanian traditional healers in the management of *Candida* infections. J. Ethnopharmacol. 106(2):158-165.

Sawangjaroen N, Sawangjaroen K (2005). "The effect of extracts from anti-diarrheic Thai medicinal plants on the *in vitro* growth of the intestinal protozoa parasite *Blastocytis hominis*." J. Ethnopharmacol. 98(1-2):67-72.

Saxena S, Pant N, Jain DC, Bhakuni RS (2003). Antimalarial agents from plant sources. Curr. Sci. 85:1314-1329.

Sendagire H, Kyabayinze D, Swedberg G, Kironde F (2005). *Plasmodium falciparum*: Higher incidence of molecular resistance markers for sulfadoxine than for pyrimethamine in Kasangati, Uganda. Trop. Med. Int. Health 10:537-543.

Sha'a KK, Oguche S, Watila IM, Ikpa TF (2011). *In vitro* antimalarial activity of the extracts of *Vernonia amygdalina* commonly used in traditional medicine in Nigeria Sci. World J. 6(2): 5-9.

Sibanda T, Okoh O (2007). The challenges of overcoming antibiotic resistance: Plant extracts as potential sources of antimicrobial and resistance modifying agents. Afr. J. Biotechnol. 6(25):2886-96.

Subeki HM, Tabahashi K, Nabeta K, Ya-masaki M, Maede Y, Katakura K (2007). Screening of Indonesian medicinal plant extracts for antibabesial activity and isolation of new quassinoids from *Brucea javanica*. J. Nat. Prod. 70(10):1654-1657.

Titanji VPK, Zofou D, Ngemenya MN (2008). The Antimalarial Potential Of Medicinal Plants Used For The Treatment Of Malaria In Cameroonian Folk Medicine. Afr. J. Trad. CAM 5(3):302-321.

Wright CW, Anderson MM, Allen D, Phillipson JD, Kirby GC, Warhurst DC, Chang HR (1993). Quassinoid exhibit greater selecwtivity against *Plasmodium falciparum* than against *Entamoeba histolytica, Giardia intestinalis* or *Toxoplasma gondii in vitro*." J. Eukaryot. Microbiol. 40(3):244- 246.

Wright CW, O'Neill MJ, Phillipson JD, Warhurst DC (1988). Use of microdilution to assess *in vitro* antiamoebic activities of *Brucea javanica* Fruits, *Simaruba amara*, Stem, and a number of quassinoids. Antimicrob. Agents Chemother. 32(11):1725-1729.

Zofou D, Tene M, Ngemenya MN, Tane P, Titanji VPK (2011). *In vitro* Antiplasmodial Activity and Cytotoxicity of Extracts of Selected Medicinal Plants Used by Traditional Healers of Western Cameroon. Malar. Res. Treat. 42:1-6.