



# Cameroonian medicinal plants: pharmacology and derived natural products

Victor Kuete<sup>1,2</sup> and Thomas Efferth<sup>2\*</sup>

<sup>1</sup> Department of Biochemistry, Faculty of Science, University of Dschang, Dschang, Cameroon

<sup>2</sup> Department of Pharmaceutical Biology, Institute of Pharmacy, University of Mainz, Mainz, Germany

## Edited by:

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## \*Correspondence:

Thomas Efferth, Department of Pharmaceutical Biology, Institute of Pharmacy and Biochemistry, University of Mainz, Staudinger Weg 5, 55128 Mainz, Germany.  
e-mail: efferth@uni-mainz.de

Many developing countries including Cameroon have mortality patterns that reflect high levels of infectious diseases and the risk of death during pregnancy and childbirth, in addition to cancers, cardiovascular diseases and chronic respiratory diseases that account for most deaths in the developed world. Several medicinal plants are used traditionally for their treatment. In this review, plants used in Cameroonian traditional medicine with evidence for the activities of their crude extracts and/or derived products have been discussed. A considerable number of plant extracts and isolated compounds possess significant antimicrobial, anti-parasitic including antimalarial, anti-proliferative, anti-inflammatory, anti-diabetes, and antioxidant effects. Most of the biologically active compounds belong to terpenoids, phenolics, and alkaloids. Terpenoids from Cameroonian plants showed best activities as anti-parasitic, but rather poor antimicrobial effects. The best antimicrobial, anti-proliferative, and antioxidant compounds were phenolics. In conclusion, many medicinal plants traditionally used in Cameroon to treat various ailments displayed good activities *in vitro*. This explains the endeavor of Cameroonian research institutes in drug discovery from indigenous medicinal plants. However, much work is still to be done to standardize methodologies and to study the mechanisms of action of isolated natural products.

**Keywords: medicinal plants, ethnopharmacology, Africa**

## PUBLIC HEALTH CONCERN AND DISEASES IN CAMEROON

Health care is a basic service essential in any effort to combat poverty, and is often promoted with public funds in Africa to achieve this aim (Castro-Leal et al., 2000). Nevertheless, curative health spending is not always well targeted to the poorest, representing about 50.5% of Cameroonian (Edmondson, 2001). Many developing countries including Cameroon have mortality patterns that reflect high levels of infectious diseases and the risk of death during pregnancy and childbirth, in addition to cancers, cardiovascular diseases and chronic respiratory diseases that account for most deaths in the developed world (WHO, 2009). In Cameroon, 3 out of 20 patients are able to buy prescribed drugs in hospitals and one out of every 1000 patients are able to see a specialist. Health care activities are coordinated by the Ministry of Public Health which receives the second highest budgetary allocation per ministry each year (Speak Clear Association of Cameroon, 2004). Health facilities are either run as government services or private services managed by the various churches and other private individuals. There are also traditional doctors that play a great role as far as the provisions of health care services are concerned. The major diseases associated with high degree of risk within the population include food or waterborne diseases (bacterial and protozoal diarrhea, hepatitis A and E, and typhoid fever), vector borne diseases (malaria and yellow fever), water contact diseases (schistosomiasis), respiratory diseases (meningococcal meningitis), and animal contact diseases (rabies) (Index mundi, 2008). Very often, there is a coexistence of many infectious diseases. Ammah et al. (1999) demonstrated that high proportion of patients (33%) had malaria coexisting with typhoid (*Salmonella typhimurium*, *Salmonella paratyphi*, and *Salmonella*

*typhi* infections). In the Cameroonian population, the lifetime risk of developing active tuberculosis once infected, in absence of HIV infection, is about 10%, meanwhile this increases tenfold in HIV infected individuals (Noeske et al., 2004). Malaria remains the leading cause of morbidity in Cameroon, and among the top five causes of mortality. Malaria represents approximately 45–50% of health consultations, and 23% of admissions (Edmondson, 2001). The unsatisfactory management of all diseases throughout the continent as well as in Cameroon, which allows partially treated and relapsed patients to become sequentially resistant, may play a significant role in the development of resistance for infectious diseases (Jones et al., 2008; McGaw et al., 2008). Effective treatment of diseases is challenging for various reasons, including lack of accessibility and elevated expense of drugs and low adherence owing to toxicity of second-line drugs. It is all too likely that the emergence of resistance will be experienced in the future, exhausting the current arsenal of chemical defenses at our disposal. For this purpose, new drugs are urgently needed, and research programs into alternative therapeutics including medicinal plants investigations should be encouraged.

## BIODIVERSITY AND PROTECTED AREA IN CAMEROON

The biodiversity of Cameroon in term of protected land area, number of plant and some animals groups with threatened species are summarized in **Table 1** and **Figure 1**.

Cameroon has a rich biodiversity, with about 8,620 plants species and several animal groups (EarthTrends, 2003), encountered in both protected (about 8%), and unprotected areas. About 155 plant species are classified by the International Union for the Conservation

**Table 1 | Biodiversity and protected area in Cameroon, Sub-Saharan Africa, and the World (Source: EarthTrends, 2003).**

	Cameroon	Sub-Saharan Africa	World
<b>Total land areas</b>	47,544	2,429,241	13,328,979
<b>PROTECTED AREA (000 HA)</b>			
<b>Extent of protected areas by IUCN Category (000 ha), 2003</b>			
Total protected area (Categories I–V)	3,741	264,390	1,457,674
Marine and Littoral protected areas <sup>a</sup>	389	–	417,970
Protected areas as a percent of total land area	8.0%	10.9%	10.8%
<b>Biosphere reserves in 2002</b>			
Number of sites	3	46	408
Total area (000 ha)	876	–	439,000
<b>NUMBER AND STATUS OF SPECIES</b>			
<b>Higher plants</b>			
Total known species (number)	8,260	–	–
Number of threatened species	155	–	5,714
<b>Mammals</b>			
Total known species (number)	409	–	–
Number of threatened species	40	–	1,137
<b>Breeding birds</b>			
Total known species (number)	165	–	–
Number of threatened specie	15	–	1,192
<b>Reptiles</b>			
Number of total known species	210	–	–
Number of threatened species	1	–	293
<b>Amphibians</b>			
Number of total known species	171	–	–
Number of threatened species	1	–	157
<b>Fish</b>			
Number of total known species	138	–	–
Number of threatened species	27	–	742

IUCN, International Union for the Conservation of Nature and Natural Resources; Categories I, Nature Reserves, Wilderness, Areas; Categories II, National Parks; Category III, Natural monument; Category IV, Habitat/species management area; Category V, Protected landscape/seascape.

<sup>a</sup>Marine and littoral protected areas are not included in the “Total area protected” above; <sup>b</sup>Includes IUCN categories I–V, marine and littoral protected areas are excluded from these totals.

(–): data not available.

of Nature and Natural Resources (IUCN) as threatened species. Threatened species used as medicinal plants include *Thecacoris anno-bonae* Pax & K. Hoffm (Euphorbiaceae) (Cheek, 2004), *Pausinystalia johimbe* (K. Schum) (Rubiaceae) (Ngo Mpeck et al., 2004), *Prunus africana* (Hook. f.) Kalkm (Rosaceae) (Focho et al., 2009). *Ancistrocladus korupensis* D. W. Thomas & Gereau (Ancistrocladaceae), *Carpolobia lutea* G. Don (Polygalaceae), *Dacryodes edulis* (G. Don) H. J. Lam. (Burseraceae), *Enantia chlorantha* Oliv (Annonaceae), *Garcinia man-nii* Oliv. (Clusiaceae), *Garcinia cola* Heckel (Clusiaceae), *Gnetum afri-canum* Welw. (Gnetaceae), *Invingia gabonensis* Baill. (Irvingiaceae), *Massularia acuminata* (G. Don) Bullock (Rubiaceae), *Pentaclethra macrophylla* Benth. (Leguminosae), *Baillonella toxisperma* Pierre var. *obovata* Aubrév. & Pellegr. (Sapotaceae), *Calamus deeratus* Mann & Wendl. (Palmae), *Cola acuminata* (P. Beauv.) Schoot et Endl. (Sterculiaceae), *Eremospatha macrocarpa* (Mann & Wendl.) Wendl. (Palmae), *Raphia regalis* Becc. (Palmae), *Raphia vinifera* P. Beauv. (Palmae) and *Ricinodendron heudelotti* (Baill.) Pierre (Euphorbiaceae) (Koné, 1997). Protected zones include both land (3,741 ha) and marine areas (389 ha) (EarthTrends, 2003).

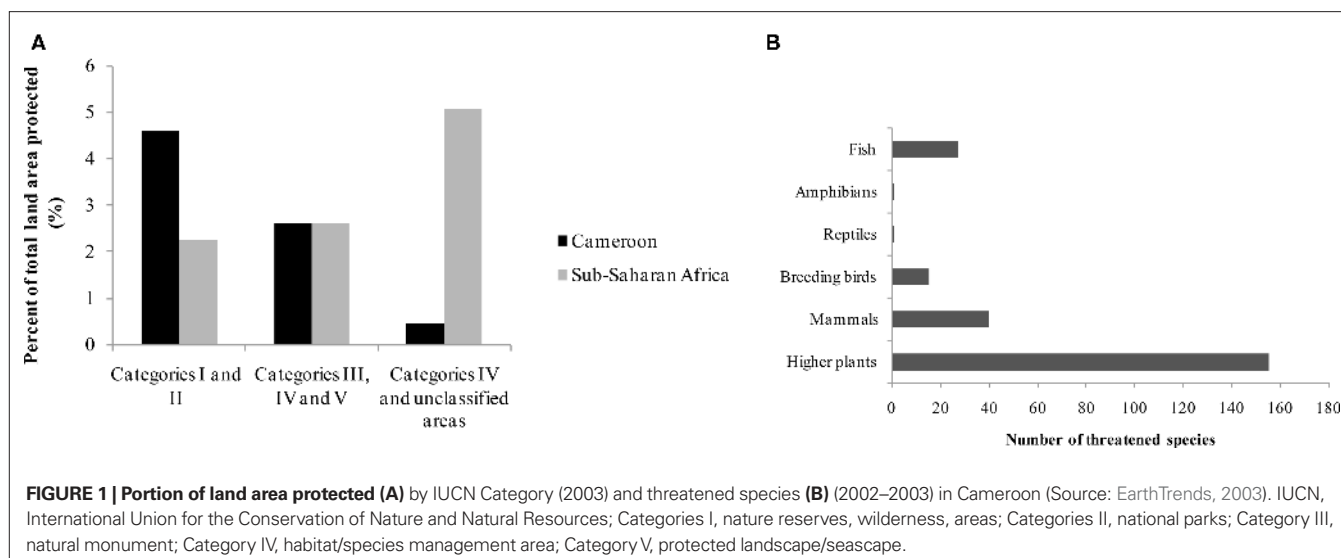
### ETHNOBOTANICAL USES OF MEDICINAL PLANTS IN CAMEROON

Traditional healing plays an integral role in black African culture as it provides primary health care needs for a large majority (about 80%) of the population (WHO, 2002). In Cameroon, there is a rich tradition in the use of herbal medicine for the treatment of several ailments. Unfortunately, the integration of traditional medicine in the health system is not yet effective, due to its disorganization (Nkongmeneck et al., 2007). However, the government strategies of health envisage the organization of traditional medicine in order to provide the main trends for the development and its integration (Anonymous, 2006). Adjanohoun et al. (1996) provided a useful review of the traditional use of medicinal plants in Cameroon, although much work remains to be done regarding the documentation of existing ethnobotanical knowledge. Jiofack et al. (2010) also documented the traditional use of 289 plants species belonging to 89 families against 220 pathologies. Sixty eight percent of the documented plants are used to treat more than twenty important diseases. They are used as decoction, infusion, maceration, powder, powder mixtures, plaster, calcinations, and squeeze in water, boiling, cooking with young cock or sheep meat or groundnut paste, direct eating, juice, fumigation, and sitz bath (Jiofack et al., 2010). The most recurrent diseases or disorders treated are typhoid, male sexual disorders, malaria, gonorrhoea, gastritis, rheumatism, fever, dysentery, diarrhea, dermatitis, boils, cough, wounds, syphilis, sterility, sexually transmitted diseases, ovarian cysts, and amoebiasis, with more than two hundred plants being used to cure these diseases or disorders (Jiofack et al., 2010).

### INVESTIGATION OF THE PHARMACOLOGICAL POTENTIAL OF MEDICINAL PLANTS OF CAMEROON

#### ANTIMICROBIAL ACTIVITY

Plants are widely used traditionally for the treatment of microbial infections. A review of the antimicrobial potential of Cameroon medicinal plants (Kuete, 2010a) reported more than 58 species *in vitro* active extracts or isolated compounds. Cut-off points for activity in term of IC<sub>50</sub>-values were set to 100 µg/ml for extract and 25 µM for compounds



(Cos et al., 2006). However, in the case of antimicrobial evaluation of extracts and compounds, determination of  $IC_{50}$  is not the optimal parameter for significance, most of the reported data being given as MIC values. Kuete (2010a) also set the bar as follows for extract: significant ( $MIC < 100 \mu\text{g/ml}$ ), moderate ( $100 < MIC \leq 625 \mu\text{g/ml}$ ) or weak ( $MIC > 625 \mu\text{g/ml}$ ). For compounds, this stringent endpoints criteria were: significant ( $MIC < 10 \mu\text{g/ml}$ ), moderate ( $10 < MIC \leq 100 \mu\text{g/ml}$ ), and low or negligible ( $MIC > 100 \mu\text{g/ml}$ ) (Kuete, 2010a). More than 50 microorganisms were found to be sensitive to such extracts and significant activity with minimally inhibiting concentrations (MIC) of less than  $100 \mu\text{g/ml}$  (Kuete, 2010a). Some of the extracts including those from *Bersama engleriana*, *Dorstenia angusticornis*, *Dorstenia barteri*, *Diospyros canaliculata*, *Diospyros crassiflora*, *Newbouldia laevis*, and *Ficus cordata* exhibited a wide range of activity on both bacteria and fungi (Kuete, 2010a).

Some of the bioactive compounds such as diospyrone (23), crassiflorone (24), newbouldiaquinone (25), newbouldiaquinone A (26), laurentixanthone A (30), laurentixanthone B (31), smeathxanthone B (32), cheffouxanthone (33), bangangxanthone A (34), globulixanthone C (35), D (36) and E (37), moracin T (43), and U (44), nkolbisine (59), norerythroaveolide (60), were isolated and characterized for the first time from Cameroonian medicinal plants (Kuete, 2010a). Other compounds such as plumbagin (27), lapachol (28) (found to be inactive *in vivo* in some cases), isobavachalcone (47), 4-hydroxylonchocarpin (48), kanzonol C (49) exhibited interesting activities and were suggested as potential candidates for new antimicrobial drug (Kuete, 2010a). Though compound 28 is known to possess good antimicrobial activity *in vitro*, it will be necessary to assess its *in vivo* efficacy. However this compounds was active *in vitro* against intracellular amastigotes of *Leishmania braziliensis* and inactive *in vivo* using hamster infected model (Lima et al., 2004). *Thecacoris cf. annobonae* Pax & K. Hoffm (Euphorbiaceae) exhibited significant antimicrobial ( $MIC < 10 \mu\text{g/ml}$ ) activities against *Mycobacterium tuberculosis* H37Rv, *Bacillus cereus* and *Pseudomonas aeruginosa* (Kuete et al., 2010b). The extract from *T. annobonae* was reported to induce *E. coli* death through the inhibition of  $H^+$ -ATPase-mediated proton pumping (Kuete et al., 2010b). Investigations the mode of resistance of the microorganisms

to bioactive compounds isolated from Cameroonian medicinal plants have shown that efflux by AcrAB-TolC pumps was one of the likely mechanisms of defense of Gram-negative bacteria to compounds 23 and 47 (Kuete et al., 2010c).

#### ANTIMALARIAL ACTIVITY

In Cameroon, several plant species are used to treat malaria. A review on traditionally used plants reported up to 217 species (Titanji et al., 2008). Some of these plants were screened *in vitro* for their activity against *P. falciparum* and more than 100 bioactive compounds were isolated (Titanji et al., 2008), most of which, however, showed only low or modest antimalarial activities. In the present review, we focus only on plant extract and compounds that exhibited considerably high activities. The proposed cut-off points for *in vitro* activity of antimalarial extracts based on their  $IC_{50}$  values can be categorized as follows:  $IC_{50} < 0.1 \mu\text{g/ml}$  (very good);  $0.1\text{--}1 \mu\text{g/ml}$  (good);  $1.1\text{--}10 \mu\text{g/ml}$  (good to moderate);  $11\text{--}25 \mu\text{g/ml}$  (weak),  $26\text{--}50$  (very weak),  $>100 \mu\text{g/ml}$  (inactive) (Willcox et al., 2004a). The following inhibition percentages were proposed for *in vivo* activity of antimalarial extracts at a fixed dose of 250 mg/kg/day: 100–90% (very good activity); 90–50% (good to moderate); 50–10% (moderate to weak); 0% (inactive) (Willcox et al., 2004a). Several plant extracts from Cameroonian medicinal plants were reported for their antimalarial activities (Table 2), the most active ( $IC_{50} < 1 \mu\text{g/ml}$ ) being that from *Enantia chlorantha* (Boyom et al., 2009).

Some isolated compounds were also reported for their antimalarial activities (Table 2). An  $IC_{50}$  of  $1.5 \mu\text{M}$  was chosen as cut-off point for several compounds (Calas et al., 1997). The threshold for *in vitro* chloroquine resistance has been defined as  $IC_{50} > 100 \text{ nM}$  (Ringwald et al., 1996). According to Mahmoudi et al. (2006), compounds with  $IC_{50} > 5 \mu\text{M}$  were considered as inactive against parasite development, compounds with  $IC_{50}$  between 0.06 and  $5 \mu\text{M}$  being active, and values of  $IC_{50} < 0.06 \mu\text{M}$  implying the drugs to be very toward *P. falciparum*. We will take into consideration up to  $IC_{50} < 20 \mu\text{g/ml}$  to report on the activity of antimalarial compounds isolated from Cameroonian medicinal plants. So far, active compounds isolated belong to three main groups of secondary metabolites, terpe-

**Table 2 | Plants used in Cameroon to treat malaria, with evidence of their activities.**

Family	Species <sup>a</sup>	Traditional treatment	Plant part used	Bioactive (or potentially active) compounds <sup>b</sup>	Screened activity
Acanthaceae	<i>Thomandersia hensii</i> De Wild and Th. Dur (LB Th 0301)	Malaria, diarrhea, colitis, furuncles, abscesses, syphilis, ulcers, urogenital disorders, intestinal parasites, debility, tiredness, edema, rheumatism, eye inflammations (Letouzey, 1985; Ngadjui et al., 1994).	Bark, leaves, pulp, sap, roots	Not identified	IC <sub>50</sub> < 30 µg/ml reported for hexane extract from the stem bark on <i>P. falciparum</i> W2 (Indochina I/CDC) chloroquine-resistant strain (Bickii et al., 2007b)
Annonaceae	<i>Uvariopsis congolana</i> (De Wild) Fries (37016/HNC)	Malaria (Boyom et al., 2009)	Bark, leaves	Not identified, but plants of this family were reported to contain acetogenins <sup>c</sup>	IC <sub>50</sub> < 5 µg/ml reported for the crude extract from the leaves and bark on <i>P. falciparum</i> strain W2 (Boyom et al., 2009)
	<i>Polyalthia oliveri</i> Engl. (19416 SRF/Cam)	Malaria (Boyom et al., 2009)	Bark		IC <sub>50</sub> < 5 µg/ml reported for the crude extract from the bark on <i>P. falciparum</i> strain W2 (Boyom et al., 2009)
	<i>Enantia chlorantha</i> Oliv. (32065/SRF/Cam)	Malaria (Boyom et al., 2009)	Bark, leaves	Not identified	IC <sub>50</sub> < 1 µg/ml reported with the crude extract from the leaves and bark on <i>P. falciparum</i> strain W2 (Boyom et al., 2009)
Apocynaceae	<i>Picralima nitida</i> Stapf (LB Pn 0301)	Malaria, diarrhoea, intestinal worms, gonorrhoea, inflammation (Letouzey, 1985; Ezeamuzie et al., 1994; Fakeye et al., 2000)	Bark, roots, seeds; fruits	Not identified	IC <sub>50</sub> < 30 µg/ml reported for the methanol and dichloromethane–methanol 1:1 extracts from the seeds and bark on <i>P. falciparum</i> W2 (Indochina I/CDC) chloroquine-resistant strain (Bickii et al., 2007b)
Euphorbiaceae	<i>Croton zambesicus</i> Muell. Arg. (8204/SRFCam)	Malaria (Boyom et al., 2009)	Bark	Not identified	IC <sub>50</sub> < 10 µg/ml reported for the crude extract from the bark on <i>P. falciparum</i> strain W2 (Boyom et al., 2009)
	<i>Neoboutonia glabrescens</i> Müll. Arg. Prain (7433/SRFCam)	Malaria (Boyom et al., 2009)	Bark, leaves	Not identified	IC <sub>50</sub> < 10 µg/ml reported for the crude extract from the leaves and bark on <i>P. falciparum</i> strain W2 (Boyom et al., 2009)
Guttiferae	<i>Symphonia globulifera</i> Linn f. (50788/HNC)	Stomach and skin aches, laxative for pregnant women, general tonic, Malaria (Aubreville, 1950; Irvine, 1961; Ngouela et al., 2006).	Bark	Gaboxanthone ( <b>38</b> ); symphonin ( <b>39</b> ); globuliferin ( <b>40</b> ); guttiferone A ( <b>50</b> ) (Ngouela et al., 2006).	IC <sub>50</sub> < 20 µM on <i>P. falciparum</i> reported for compounds <b>38–40</b> and <b>50</b> (Ngouela et al., 2006).
Lauraceae	<i>Beilschmiedia zenkeri</i> Engl.	Not reported	Bark	5-Hydroxy-7,8-dimethoxyflavone; pipyahyine; betulinic acid (Lenta et al., 2009)	IC <sub>50</sub> < 5 µM on chloroquine-resistant <i>P. falciparum</i> reported for pipyahyine (Lenta et al., 2009)
Meliaceae	<i>Entandrophragma angolense</i> Welwitsch C.D.C. (29933/HNC)	Malaria (Bickii et al., 2007a)	Bbark	22-Hydroxyhopan-3-one; 24-methylenecycloartenol ( <b>8</b> ); tricosanoic acid; methylangolensate; 7α-acetoxylidihydronomilin ( <b>9</b> ); 7α-obacunylacetate ( <b>10</b> ) (Bickii et al., 2007a)	IC <sub>50</sub> < 20 µg/ml on <i>P. falciparum</i> W2 strain reported for compounds <b>8–10</b> . The dichloromethane – methanol (1:1) extract of the stem bark of that plant exhibited IC <sub>50</sub> of 18.8 µg/ml (Bickii et al., 2007a)

(Continued)

Table 2 | Continued

Family	Species <sup>a</sup>	Traditional treatment	Plant part used	Bioactive (or potentially active) compounds <sup>b</sup>	Screened activity
	<i>Khaya grandifoliola</i> C.D.C. (PM 098/95/HNC)	Malaria (Obih et al., 1985; Bray et al., 1990; Weenen et al., 1990).	Bark and seeds	Methylangolensate ( <b>1</b> ); 6-methylhydroxyangolensate ( <b>2</b> ); gedunin ( <b>3</b> ); catechin; 7-deacetylkhivorin ( <b>4</b> ); 1-deacetylkhivorin ( <b>5</b> ); swietenolide ( <b>6</b> ); 6-acetylswietenolide ( <b>7</b> ) (Bickii et al., 2000)	IC <sub>50</sub> < 20 µg/ml on <i>P. falciparum</i> W2 strain reported for bark and seeds extracts; compounds <b>1–7</b> . Compound <b>3</b> exhibited an additive effect when combined with chloroquine (Bickii et al., 2000)
	<i>Turreanthus africanus</i>	Malaria and other fevers (Zhou et al., 1997)	Bark, seeds, leaves	16-oxolabda-8 ( <b>17</b> ), 12( <i>E</i> )-dien-15-oic acid; methyl-14, 15-epoxylabda-8 ( <b>17</b> ), 12( <i>E</i> )-diene-16-oate; turreanin A (Ngemenya et al., 2006)	None of the active compounds exhibited IC <sub>50</sub> < 20 µg/ml on <i>P. falciparum</i> F 32, chloroquine sensitive strain (Ngemenya et al., 2006)
Moraceae	<i>Artocarpus communis</i> J.R. & G. Forst (43982 HNC)	Malaria (Boyom et al., 2009)	Bark, leaves	Not identified	IC <sub>50</sub> < 10 µg/ml reported for the crude extract from the leaves and bark on <i>P. falciparum</i> strain W2 (Boyom et al., 2009)
	<i>Dorstenia convexa</i> De Wild (53450 HNC)	Malaria (Boyom et al., 2009)	Twigs	Not identified	IC <sub>50</sub> < 10 µg/ml reported with the crude extract from the twigs on <i>P. falciparum</i> strain W2 (Boyom et al., 2009)
Zingiberaceae	<i>Aframomum zambesiaticum</i> (Baker) K. Schum (37737HNY)	Malaria (Kenmogne et al., 2006)	Seeds	Aulacocarpin A ( <b>11</b> ); aulacocarpin B; 3-deoxyaulacocarpin A ( <b>12</b> ); methyl-14 <i>n</i> , 15-epoxy-3 <i>b</i> -hydroxy-8( <b>17</b> ), 12-elabdadien-16-oate; galanolactone; zambesiacolactone A ( <b>13</b> ); zambesiacolactone B ( <b>14</b> ); aframodial (Kenmogne et al., 2006)	IC <sub>50</sub> < 20 µM on <i>P. falciparum</i> reported for compounds <b>11–14</b> (Kenmogne et al., 2006)
	<i>Reneilimia cincinnata</i> (K. Schum.) Bak.	Malaria (Tchuendem et al., 1999)	Fruits	Oplodiol ( <b>17</b> ); 5 <i>E</i> ,10(14)-Germacradien-1β,4β-diol ( <b>16</b> ); 1(10) <i>E</i> ,5 <i>E</i> -germacradien-4β-ol ( <b>15</b> ) (Tchuendem et al., 1999)	IC <sub>50</sub> < 5 µM reported on <i>P. falciparum</i> D6 and W2 strains for compounds <b>15–17</b> on <i>P. falciparum</i> D6 strain (Tchuendem et al., 1999)

<sup>a</sup>HNC or SRFK: Cameroon National herbarium code; LB, Laboratory of Botany, Yaoundé.

<sup>b</sup>Compounds characterized for the first time in Cameroonian medicinal plant are underlined.

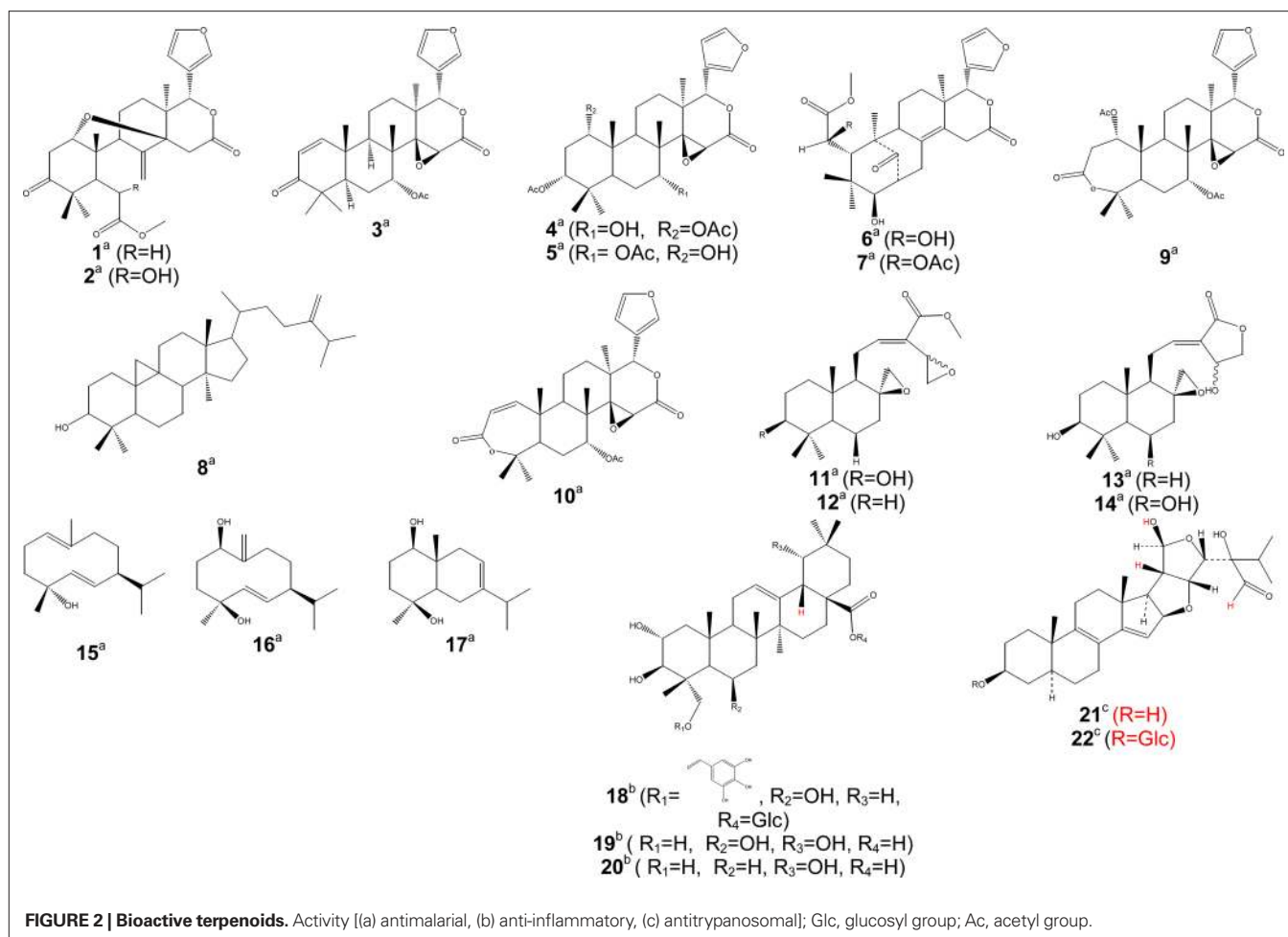
<sup>c</sup>Annonaceous acetogenins are inhibitors of complex I (NADH: ubiquinone oxidoreductase) in mitochondrial electron transport systems (Lewis et al., 1993), and NADH oxidase of plasma membranes (Morré et al., 1995), two enzymes found in *Plasmodium falciparum*.

noids (**Figure 2**), phenolics (**Figure 3**), and alkaloids (**Figure 4**). Antimalarial terpenoids including sesqui-, di-, and triterpenoids are the most frequently isolated compounds from Cameroonian plants. Several natural products were reported as being active against *Plasmodium falciparum*, with IC<sub>50</sub> values below 20 µg/ml, including methylangolensate (**1**); 6-methylhydroxyangolensate (**2**); gedunin (**3**); 7-deacetylkhivorin (**4**); 1-deacetylkhivorin (**5**); swietenolide (**6**); 6-acetylswietenolide (**7**) (Bickii et al., 2000); 24-methylenecycloartenol (**8**); 7α-acetoxidihydronomilin (**9**); 7α-obacunylacetate (**10**) (Bickii et al., 2007a); aulacocarpin A (**11**); 3-deoxyaulacocarpin A

(**12**); zambesiacolactone A (**13**), and B (**14**) (Kenmogne et al., 2006); 1(10)*E*,5*E*-germacradien-4β-ol (**15**); 5*E*,10(14)-germacradien-1β,4β-diol (**16**); oplodiol (**17**) (Tchuendem et al., 1999); IC<sub>50</sub> < 5 µg/ml were obtained for compounds **3** (1.25 µg/ml), and **10** (2 µg/ml) (Bickii et al., 2000, 2007a), while values below 5 µM were recorded for compounds **12** (4.97 µM) (Kenmogne et al., 2006), **15** (1.54 µM); **16** (1.63 µM) and **17** (4.17 µM) (Tchuendem et al., 1999).

Phenolic compounds (**Figure 3**) such as gaboxanthone (**38**); symphonin (**39**); globuliferin (**40**); guttiferone A (**50**) (Ngouela et al., 2006) also exhibited antimalarial activities when tested on





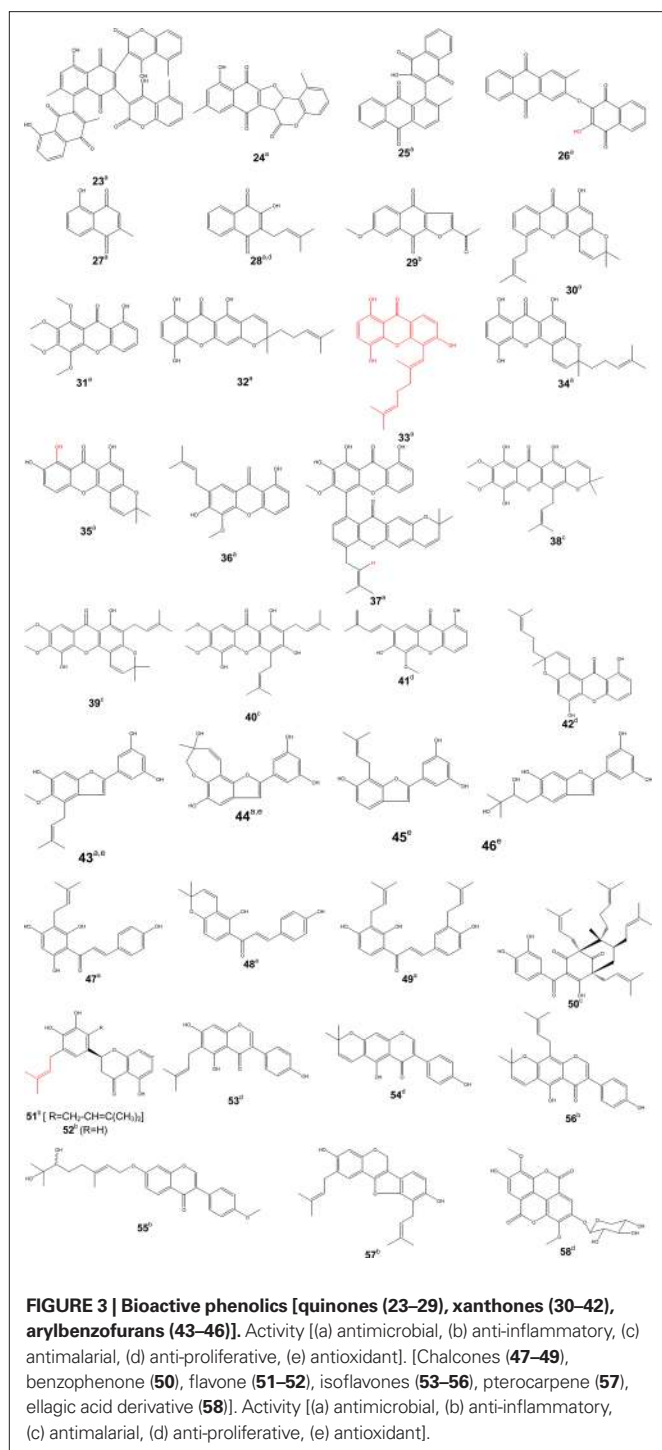
*P. falciparum*.  $IC_{50}$  values below  $5 \mu\text{g/ml}$  were reported with compounds **38** ( $3.53 \mu\text{M}$ ); **39** ( $1.29 \mu\text{M}$ ); **40** ( $3.86 \mu\text{M}$ ) and **50** ( $3.17 \mu\text{M}$ ) (Ngouela et al., 2006). Few alkaloids from Cameroonian medicinal plants (Figure 4) were characterized. For example, pipyahyine (**61**) exhibited good activity ( $IC_{50} < 5 \mu\text{M}$ ) toward chloroquine-resistant *P. falciparum* (Lenta et al., 2009).

Studies dealing with the mechanisms of action of antimalarial compounds are still limited. However, some of the extracts from Cameroonian medicinal plants such as those from *Annonaceae* species were suggested to exert their antiplasmodial activity by the inhibition of vital parasitic enzymes such as cysteine proteases (Boyom et al., 2009).

#### OTHER ANTI-PARASITIC ACTIVITIES

Parasitic trypanosomatids cause a number of important diseases, including human African trypanosomiasis, Chagas disease, and leishmaniasis. More than 60 million people living in 36 sub-Saharan Africa countries are at risk of contracting sleeping sickness, caused by *Trypanosoma brucei gambiense* and *T. b. rhodesiense* (WHO, 2007). It is estimated that currently 300,000–500,000 people were infected in 2001, with 50,000 deaths annually (Fairlamb, 2003; WHO, 2007). *Leishmania* species cause a spectrum of disease ranging from self-healing cutaneous lesions to life-threatening visceral infections, with 2 million new cases occurring annually (WHO,

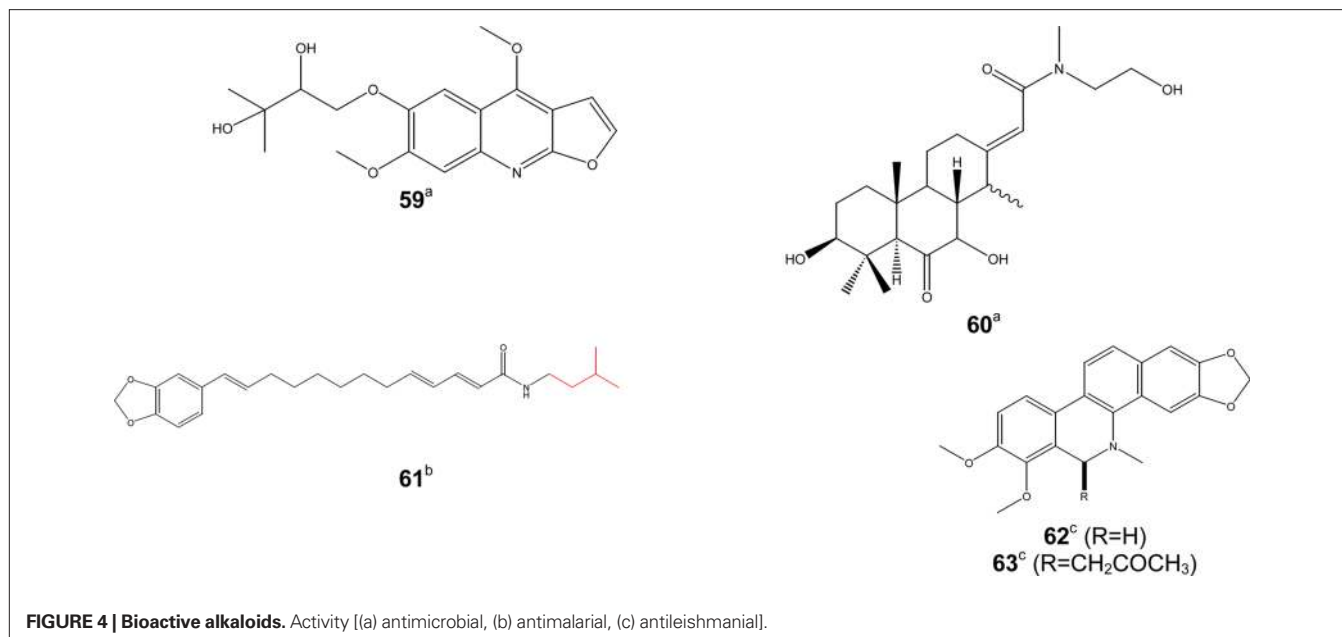
2005). It is estimated that about 200 million people worldwide are currently affected by schistosomiasis, a disease caused by flatworms belonging to the genus *Schistosoma*. The disease is usually chronic and debilitating, with severe consequences on the urinary tract where *S. haematobium* is the organism involved and major damage to the intestinal tract where *S. mansoni*, *S. intercalatum* or *S. japonicum* are involved (Jatsa et al., 2009). In humans, *Toxoplasma* infections are widespread and lead to severe diseases in individuals with immature or suppressed immune system. Consequently, toxoplasmosis became one of the major opportunistic infections of the AIDS epidemic (Luft and Remington, 1992). Toxoplasmosis also affects *T. gondii*-negative women during pregnancy and is a serious threat for embryos. Despite the huge impact of these parasitic diseases, the drugs used for their treatment are often toxic, marginally effective, administered by injection only, expensive, and/or compromised by the development of resistance (Ouellette et al., 2004; Croft et al., 2005). Only few researchers in Cameroon focused on antitrypanosomal and antileishmanial compounds from medicinal plants. Available published data on traditionally used medicinal plants are compiled in Table 3. Herein, similar cut-off points as indicated above for antimalarials have been considered for activities against trypanosomal, leishmanial and schistosomal pathogens. Compounds with good antileishmanial activities were isolated from *Garcinia lucida* (Clusiaceae), with  $IC_{50}$



values of 2.0 and 6.6  $\mu\text{g/ml}$ , respectively, for dihydrochelerythrine (62) and 6-acetyldihydrochelerythrine (63) against *L. donovani* (Fotie et al., 2007). Significant antitrypanosomal activities were also reported for stigmastane derivatives, vernoguinsterol (21) and vernoguinoside (22) (Figure 2) isolated from *Vernonia guineensis* (Asteraceae), against bloodstream trypanostigotes of *Trypanosoma brucei rhodesiense* with  $\text{IC}_{50}$  values ranging from 3 to 5  $\mu\text{g/ml}$  (Tchinda et al., 2002).

## ANTI-PROLIFERATIVE ACTIVITY

Screenings of medicinal plants used as anticancer drugs has provided modern medicine with effective cytotoxic pharmaceuticals. More than 60% of the approved anticancer drugs in United State of America (from 1983 to 1994) were from natural origin (Stévigny et al., 2005; Newman and Cragg, 2007). The diversity of the biosynthetic pathways in plants has provided a variety of lead structures that have been used in drug development. In this last decade, investigations on natural compounds have been particularly successful in the field of anticancer drug research. Early examples of anticancer agents developed from higher plants are the antileukemic alkaloids (vinblastine and vincristine), which were both obtained from the Madagascar periwinkle (*Catharanthus roseus*) (Voss et al., 2005). The development of the highly automated bioassay screening based on colorimetric methods that quantified the proliferation of cell culture (Mosmann, 1983) of a huge number of plants extracts have permitted to find that many plant families (Guittiferae, Rubiaceae, Apocynaceae, Euphorbiaceae, Solanaceae, etc.) exhibited a great potential of anti-proliferative activity (Hostettmann et al., 2000; Whelan and Ryan, 2003). A large number of plant extracts have shown the *in vitro* and *in vivo* antitumor activities (Hostettmann et al., 2000). In the US NCI plant screening program, a crude extract is generally considered to have *in vitro* cytotoxic activity if the  $\text{IC}_{50}$  value following incubation between 48 and 72 h, is less than 20  $\mu\text{g/ml}$ , while it is less than 4  $\mu\text{g/ml}$  for pure compounds (Boik, 2001). This cut-off point for good cytotoxic compound has also been defined as 10  $\mu\text{M}$  (Brahemi et al., 2010). Despite the exceptional biodiversity of Africa, few scientific studies have been carried out in the continent regarding the anti-proliferative properties of medicinal plants. However, some Cameroonian plants and derived natural products were tested for their anti-proliferative effects. Five medicinal plants widely used in cancer treatment, *Sida acuta*, *Sida cordifolia*, *Sida rhombilifolia*, *Urena lobata*, *Viscum album*, were recently screened for their cytotoxicity against Hep G2 hepatocarcinoma cells rather showed moderate anti-proliferative effects (Pieme et al., 2010). However, studies based on the inhibition of Crown Gall tumors revealed pronounced tumor reducing activity of extracts from the roots and leaves from *Bersama engleriana* (Kueete et al., 2008). An  $\text{IC}_{50}$  of 27.16  $\mu\text{g/ml}$  was reported for *Antiaris africana* in DU-145 prostate cancer cells, while even better activity ( $\text{IC}_{50}$  of 13.84  $\mu\text{g/ml}$ ) was recorded in Hep G2 hepatocarcinoma cells (Kueete et al., 2009). One of the most active compounds isolated from *A. africana*, 3,39-dimethoxy-49-O- $\beta$ -D-xylopyronosyllellagic acid (58) (Figure 3) exhibited considerable anti-proliferative activities toward HepG2 ( $\text{IC}_{50}$  of 3.84  $\mu\text{g/ml}$ ) and DU-145 ( $\text{IC}_{50}$  of 6.24  $\mu\text{g/ml}$ ) cells (Kueete et al., 2009). Compound 28, the main constituent of a Cameroonian medicinal plant, *Newbouldia leavis* (Bignoniaceae) was found to be very active against DU-145 cells with an  $\text{IC}_{50}$  of 64.59 nM (Eyong et al., 2008). Wightone (53) and alpinumisoflavone (54) isolated from *Erythrina indica* (Leguminosae) were reported to be cytotoxic (effective dose of 0.78 and 4.13  $\mu\text{g/ml}$ , respectively) when tested against KB nasopharyngeal cancer cells (Nkengfack et al., 2001). Globulixanthenes A (41) and B (42) isolated for the first time in the Cameroonian medicinal plant, *Symphonia globulifera* L. f. (Clusiaceae), showed good anti-proliferative activities against human KB cells, with  $\text{IC}_{50}$  values of 2.15 and 1.78  $\mu\text{g/ml}$ , respectively (Nkengfack et al., 2002). Compound



**FIGURE 4 | Bioactive alkaloids.** Activity [(a) antimicrobial, (b) antimalarial, (c) antileishmanial].

**47** isolated from *Dorstenia barteri* (Ngameni et al., 2007) and *D. turbinata* (Ngameni et al., 2009) was cytotoxic toward a wide spectrum of tumor cell lines, including ovarian carcinoma OVCAR-8 cells, prostate carcinoma PC3 cells, breast carcinoma MCF-7 cells, and lung carcinoma A549 cells (Jing et al., 2010). Compound **47** significantly ablated Akt phosphorylation at Ser-473 and Akt kinase activity in cells, which subsequently led to inhibition of Akt downstream substrates and evoked significant levels the mitochondrial pathway of apoptosis (Jing et al., 2010). Nishimura et al. (2007) demonstrated that compound **47** induced apoptotic cell death with caspase-3 and -9 activation and Bax upregulation in neuroblastoma cell lines. Compound **47** inhibited MMP-2 secretion from U87 glioblastoma cells (Ngameni et al., 2007). Compounds **48** and **49** also isolated from *Dorstenia turbinata* (Moraceae), inhibited the matrix metalloproteinase (MMP)-2 secretion from brain tumor-derived glioblastoma cells (Ngameni et al., 2006).

#### ANTI-INFLAMMATORY AND ANALGESIC ACTIVITIES

Pain is one common health problem with substantial socioeconomic impact because of its high incidence. It is a symptom of many diseases and it is estimated that 80–100% of the population experience back pain at least once in the life time (Jain et al., 2002). The treatment of pain requires analgesics including inflammatory products. Hence, most of the non-steroidal anti-inflammatory agents also have analgesic activity. The inhibition of prostaglandin E<sub>2</sub> (PGE<sub>2</sub>) and nitric oxide (NO) production has been proposed as a potential therapy for different inflammatory disorders (Nowakowska, 2007). Although, many analgesics and anti-inflammatory agents are present on the market, modern drug therapy is associated with some adverse effects like gastrointestinal irritation (Jain et al., 2002; Osadebe and Okoye, 2003), fluid retention, bronchospasm, and prolongation of bleeding time. Therefore, it is necessary to search for new drugs with less adverse effects. Medicinal plants have been used for the development of new drugs and continue to play an invaluable role for the progress of drug discovery (Raza et al., 2001). Plant extracts

can be an important source of safer drugs for the treatment of pain and inflammation. Several medicinal plants and derived products were screened for their anti-inflammatory and analgesic properties (Table 4). Bark extract as well as terpenoids from *Combretum molle* (Combretaceae),  $\beta$ -D-glucopyranosyl 2 $\alpha$ ,3 $\beta$ ,6 $\beta$ -trihydroxy-23-galloylolean-12-en-28-oate (**18**); combregenin (**19**); arjungenin (**20**) (Figure 2) showed good activities against carrageenan-induced paw edema in rat (Ponou et al., 2008). A naphthoquinone, 2-acetyl-7-methoxynaphthol[2,3-b]furan-4,9-quinone (**29**), isolated from the anti-inflammatory crude extract of *Milletia versicolor* inhibited 12-O-tetradecanoylphorbol 13-acetate (TPA)-induced acute ear edema and phospholipase A<sub>2</sub> (PLA<sub>2</sub>) acute mouse paw edema (Fotsing et al., 2003). Isoflavones, griffonianone D (**55**) (Figure 3) isolated from *Milletia griffoniana* (Yankep et al., 2003), warangalone (**56**) isolated from the bark of *Erythrina addisoniae* (Talla et al., 2003), and erycristagallin (**57**) isolated from the root of *Erythrina mildbraedii* (Njamen et al., 2003), showed marked effectiveness as an anti-inflammatory on PLA<sub>2</sub>-induced paw edema and on TPA-induced ear edema in mice (Njamen et al., 2003; Talla et al., 2003). Flavonoids sigmoidin A (**51**) and B (**52**) (Figure 3) isolated from *Erithrina sigmoidea*, and compound **57** were also effective against TPA-induced ear edema (Njamen et al., 2003, 2004).

#### ANTI-DIABETIC ACTIVITY

Diabetes mellitus is a group of metabolic disorders with one common manifestation, hyperglycemia (WHO, 1980, 1985). Chronic hyperglycemia causes damage to eyes, kidneys, nerves, heart, and blood vessels (Mayfield, 1998). It is caused by inherited and/or acquired deficiency in insulin production of the pancreas, or by unresponsiveness toward insulin. It results either from inadequate secretion of hormone insulin, an inadequate response of target cells to insulin, or a combination of these factors (Malviya et al., 2010). Diabetes is projected to become one of the world's main disablers and killers within the next 25 years (Malviya et al., 2010). The management of diabetes is a global problem and a successful treatment



**Table 3 | Plants used in Cameroon to treat some parasitic infections with evidence of their activities.**

Family	Species <sup>a</sup>	Traditional treatment	Plant part used	Bioactive (or potentially active) compounds <sup>b</sup>	Screened activity <sup>c</sup>
Annonaceae	<i>Polyalthia suaveolens</i> Engl. & Diels (1227/SRFK)	Rheumatic pains (Surville, 1955)	Not specified	Polyveoline; 3- <i>O</i> -acetyl greenwayodendrin; POLYSIN; greenwayodendrin-3-one (Ngantchou et al., 2010)	Antitrypanosomal activity: weak activity for polyveoline (IC <sub>50</sub> : 32 μM); 3- <i>O</i> -acetyl greenwayodendrin (IC <sub>50</sub> : 54 μM); mixture of polysin and greenwayodendrin-3-one (IC <sub>50</sub> : 18 μM) against <i>T. brucei</i> (Ngantchou et al., 2010)
Asteraceae	<i>Vernonia guineensis</i> Benth. (BUD 301)	Anthelmintic, anti-poison, malaria, jaundice (Iwu, 1993)	Leaves	Vernoguinsterol ( <b>21</b> ); vernoguinolide ( <b>22</b> ) (Tchinda et al., 2002)	Antitrypanosomal activity: significant for compounds <b>22</b> and <b>23</b> against four strains of bloodstream trypomastigotes <i>T. b. rhodesiense</i> with IC <sub>50</sub> values in the range 3–5 mg/ml (Tchinda et al., 2002)
Guttiferae	<i>Garcinia lucida</i> Vesque (5768/HNC)	Gastric infections, anti-poison (Nyemba et al., 1990)	Bark	Dihydrochelerythrine ( <b>62</b> ); 6-acetyldihydrochelerythrine ( <b>63</b> ); lucidamine A (Fotie et al., 2007)	Antileishmanial activity: Significant activity for compounds <b>62</b> and <b>63</b> and moderate for lucidamine A against <i>L. donovani</i> . Also, 100% inhibition of promastigote at 100 μg/ml were reported for all the above compounds (Fotie et al., 2007)
Meliaceae	<i>Turraeanthus africanus</i> (Welw. ex C.D.C.) Pellegr (8233/HNC)	Asthma, stomachache, intestinal worms, and inflammatory diseases (Ekwalla and Tongo, 2003)	Aerial parts, roots	Turraeanthin C; sesamin (Vardamides et al., 2008)	Antitoxoplasmal activity: Moderate activity for turraeanthin C and low activity for crude bark extract and sesamin. Inhibition of parasite growth at 10 μg/ml was found to be 55% for turraeanthin C, 20% for sesamin and 40% for crude extract (Vardamides et al., 2008)
Verbenaceae	<i>Clerodendrum umbellatum</i> Poir (7405/HNC)	Epilepsy, headache, intestinal helminthiasis, irregular menstruation, infective dermatitis, asthma, metaphysical powers, whitlow, vulvovaginitis (Adjahoun et al., 1996; Jatsa et al., 2009)	Not specified	Not identified but, flavonoids, saponins, saponosides, tannins, and triterpenes were detected in the leaves aqueous extract (Jatsa et al., 2009)	Antischistosomal activity: 100 % reduction rate reported for mice infected with <i>S. mansoni</i> when treated with 160 mg/kg body weight of aqueous leaves extract (Jatsa et al., 2009)

<sup>a</sup>HNC or SRFK: Cameroon National herbarium code; BUD, Herbarium of the Botany Department of the University of Dschang, Cameroon).

<sup>b</sup>Compounds characterized for the first time in Cameroonian medicinal plant are underlined.

<sup>c</sup>Screened activity: *Leishmania donovani* (*L. donovani*); *Schistosoma mansoni* (*S. mansoni*); *Toxoplasma gondii* (*T. gondii*); *Trypanosoma brucei rhodesiense* (*T. b. rhodesiense*); *Trypanosoma brucei* (*T. brucei*).

has not yet been discovered. The total number of persons affected globally is projected to rise from 246 million in 2007 to 380 million in 2025, if prevention measures will not be scaled up (Bennett, 2007). In Africa, the number of diabetic patients in 2006 was 10.4 million, and it is expected to increase to 18.7 million in 2025.

The annual mortality linked to diabetes worldwide is estimated to be above one million. In Cameroon, the prevalence of diabetes increased from 2% in 1998 (in a study supported by the World Diabetes Foundation, WDF) to 5% in 2003 and 6.5% in 2007 (in another WDF study, Walgate, 2008). Medicinal plants have been

**Table 4 | Plants used in Cameroon as anti-inflammatory and analgesic agents, with evidence of their activities.**

Family	Species <sup>a</sup>	Traditional treatment	Plant part used	Bioactive (or potentially active) compounds <sup>b</sup>	Screened activity <sup>c</sup>
Acanthaceae	<i>Acanthus montanus</i> (Nees) T. Anderson (1652/SRF61CAM)	Cough, hypertension, skin infection, boil, witches, dysmenorrhoea, pain, epilepsy, miscarriages, heart troubles, rheumatic pain, syphilis (Burkill, 1985; Adjanohoun et al., 1996; Babu et al., 2001; Noumi and Fofi, 2003; Igoli et al., 2005; Nana et al., 2008)	Leaves	Not identified	Leave extract showed analgesic and anti-inflammatory properties and the proposed mechanism was the inhibition of the prostaglandins pathway at 200 mg/kg in rats. Also, this extract at 200 mg/kg body weight in rats reduced carrageenan-induced edema, and formalin-induced pain (Asongalem et al., 2004).
Anacardiaceae	<i>Sclerocarya birrea</i> (A. Rich.) Hochst (7770/HNC)	Boils and blood circulation problems, rheumatism, infectious diseases, inflammation (Mojeremane and Tshwenyane, 2004; Fotio et al., 2009)	Bark	Not identified	Bark extract inhibited albumin-induced paw edema (Ojewole, 2004), Formalin- or Freund's adjuvant (CFA)-carrageenan-, histamine, or serotonin-induced paw edema (Fotio et al., 2009) in rats
Caesalpinaceae	<i>Erythrophleum suaveolens</i> , Guillemin & Perrottet (HN001AD)	Anti-poison, dermatitis, infectious disease, convulsion, inflammation due to snake bite, cardiac problems, headaches, migraines edema, rheumatism, asthma (Dalziel, 1937; Bouquet, 1969; Leiderer, 1982; Neuwinger, 1998)	Bark	Not identified	Extract from the bark and fractions at 19.2 µg/ml showed inhibition of carrageenin-induced paw edema in rats; Hexane fraction inhibited the 5-lipoxygenase activity (Dongmo et al., 2001)
Combretaceae	<i>Combretum molle</i> R.Br. ex G.Don (6518/SRF/CAM)	Fever, abdominal pains, convulsion, worm infections, AIDS (Bessong et al., 2004)	Bark	β-D-glucopyranosyl 2α,3 β,6β-trihydroxy-23-galloylolean-12-en-28-oate ( <b>18</b> ); combregenin ( <b>19</b> ); arjungenin ( <b>20</b> ), arjunglucoside I, combreglucoside (Ponou et al., 2008)	Bark extract, compounds <b>18–20</b> showed good activity against carrageenan-induced paw edema in rat (Ponou et al., 2008)
Crassulaceae	<i>Kalanchoe crenata</i> Andr. (50103/YA/HNC)	Earache, smallpox, headache, inflammation, pain, asthma, palpitation, convulsion, general debility (Dimo et al., 2006)	Not specified	Not identified	n-Butanol fraction inhibited carrageenan-, histamine-, serotonin-, and formalin-induced paw edema in rats (Dimo et al., 2006)
Euphorbiaceae	<i>Bridelia scleroneura</i> (42088/HNC)	Abdominal pain, contortion, arthritis, inflammation (Watt and Breyer-Brandwijk, 1962; Théophile et al., 2006)	Bark, roots	Not identified	Crude bark extract showed peripheral and central analgesic and anti-inflammatory activity against acute inflammation processes in rats (Théophile et al., 2006)
Euphorbiaceae	<i>Uapaca guineensis</i> (41501/HNC)	Fever, inflammation, pain, skin diseases, and sexual dysfunction (Vivien and Faure, 1996)	Not specified	Not identified	Bark crude extract showed analgesic activity, and inhibited carrageenan-induced inflammation in rats (Nkeh-Chungag et al., 2009)

(Continued)

Table 4 | Continued

Family	Species <sup>a</sup>	Traditional treatment	Plant part used	Bioactive (or potentially active) compounds <sup>b</sup>	Screened activity <sup>c</sup>
Guttiferae	<i>Allanblackia monticola</i> Staner L.C. (61168/HNC)	Amoebic dysentery, diarrhea, indigestion, pulmonary infections, skin diseases, headache, inflammation, and generalized pain (Raponda-Waker and Sillans, 1961)	Bark	Betulinic acid, lupeol, and amangostin (Nguemfo et al., 2009)	Crude extract from the bark, lupeol, betulinic acid, and a-mangostin inhibited paw carrageenan-induced edema rat (Nguemfo et al., 2007, 2009)
Leguminosae	<i>Erythrina addisoniae</i> Hutchinson & Dalziel (41617/HNC)	Dysentery, asthma, venereal diseases, boils, and leprosy (Talla et al., 2003)	Bark	Warangalone ( <b>56</b> ) (Talla et al., 2003)	Bark extract and compound <b>56</b> showed an anti-inflammatory on the PLA <sub>2</sub> -induced paw edema and 12- <i>O</i> -tetradecanoylphorbol 13-acetate-induced ear edema in mice (Talla et al., 2003)
	<i>Erythrina mildbraedii</i> Harms (50452/HNC)	Dysentery, stomach pains, venereal diseases, asthma, female sterility, ulcers, boils and various types of inflammations (Oliver-Bever, 1986)	Bark, roots	Erycristagallin ( <b>57</b> ) (Njamen et al., 2003)	Root bark extract inhibited the carrageenan-induced mouse paw whilst compound <b>57</b> inhibited the PLA <sub>2</sub> -induced mouse paw edema and mouse ear edema induced by 2- <i>O</i> -tetradecanoylphorbol 13-acetate (Njamen et al., 2003)
	<i>Erythrina sigmoidea</i> Hua	Female infertility, stomach pain, and gonorrhoea (Giner-Larza et al., 2001)	Bark	Sigmoidin A ( <b>51</b> ) and B ( <b>52</b> ) (Njamen et al., 2004)	Compound <b>51</b> inhibited PLA <sub>2</sub> -induced paw edema in mice, while both compounds <b>51</b> and <b>52</b> were found to be effective 12- <i>O</i> -tetradecanoylphorbol 13-acetate-induced ear edema (Njamen et al., 2004)
	<i>Millettia versicolor</i> Welw. (32315/HNC)	Intestine parasitosis, rheumatism, pain, infertility (Adjanohoun et al., 1988; Bouquet, 1969)	Not specified	2-acetyl-7-methoxynaphthol[2,3-b]furan-4,9-quinone ( <b>29</b> ) (Fotsing et al., 2003)	CH <sub>2</sub> Cl <sub>2</sub> fraction from methanol crude bark extract inhibited carrageenan-induced paw edema and TPA-induced acute ear edema in mouse as well as compound <b>29</b> (Fotsing et al., 2003)
	<i>Millettia griffoniana</i> Baill. (32315/SRF/HNC)	Boils, insects bits, inflammatory affections like pneumonia, and asthma, infertility, amenorrhoea, menopausal disorders (Sandberg and Cronlund, 1977)	Bark, roots	griffonianone D ( <b>55</b> ) (Yankep et al., 2003)	Extract of the root bark and compound <b>55</b> showed anti-inflammatory effects via inhibition of PLA <sub>2</sub> -induced mouse paw edema and TPA-induced acute mouse ear edema (Yankep et al., 2003)
Solanaceae	<i>Solanum torvum</i> Swartz. (21103/HNC)	Fever, wounds, tooth decay, haemostatic properties, pain, anti-inflammation (Henty, 1973; Ndebia et al., 2007)	Leaves	Not identified	Crude extract from the leaves inhibits both acetic acid- and pressure-induced pain at 300 mg/kg body weight of rats, and also anti-inflammatory activity on carrageenan-induced paw edema (Ndebia et al., 2007)

<sup>a</sup>HNC or SRFK: Cameroon National herbarium code.

<sup>b</sup>Compounds characterized for the first time in Cameroonian medicinal plant are underlined.

<sup>c</sup>Screened activity: TPA (2-*O*-tetradecanoylphorbol 13-acetate); PLA<sub>2</sub> (phospholipase A<sub>2</sub>).

reported to be useful in diabetes worldwide and have empirically been used as anti-diabetic and anti-hyperlipidemic remedies. Anti-hyperglycemic effects of these plants were attributed to their ability to restore the function of pancreatic tissues by increasing insulin output, inhibiting the intestinal absorption of glucose, or enhancing metabolism of insulin-dependent processes. Several plant preparations were traditionally used in Cameroon to treat diabetes. Some of them were screened for their bioactivity, but most of the studies were not pursued until the isolation of active principles. Plants with hypoglycaemic activities include *Anacardium occidentale*, *Sclerocarya birrea*, *Ageratum conyzoides*, *Ceiba pentandra*, *Kalanchoe crenata*, *Bridelia ndellensis*, *Irvingia gabonensis*, *Bersama engleriana* and *Morinda lucida* (Table 5).

### ANTIOXIDANT ACTIVITIES

The common link between oxidants and inflammatory reactions, infections, cancer, and other disorders has been well established (Mongelli et al., 1997; Wang et al., 1999). However, this may not really be of therapeutic relevance, but more of a preventive medicine. In chronic infections and inflammation as well as in other disorders, release of leukocytes and other phagocytic cells readily defends the organism from further injury. The cells do this by releasing free oxidant radicals, and these by-products are generally reactive oxygen species (ROS) such as super oxide anion, hydroxyl radical, nitric oxide, and hydrogen peroxide that result from cellular redox processes (Ames et al., 1993; Mongelli et al., 1997). At low or moderate concentrations, ROS exert beneficial effects on cellular responses and immune function. At high levels, however, free radicals and oxidants generate oxidative stress, a deleterious process that can damage cell structures, including lipids, proteins, and DNA (Pham-Huy et al., 2008). Oxidative stress plays a major role in the development of chronic and degenerative ailments such as cancer, autoimmune disorders, rheumatoid arthritis, cataract, aging, cardiovascular, and neurodegenerative diseases (Willcox et al., 2004b; Pham-Huy et al., 2008). Antioxidants act as free radical scavengers by preventing and repairing damages caused by ROS and, therefore, can enhance the immune defense and lower the risk of cancer and degenerative diseases (Ames et al., 1993; Pham-Huy et al., 2008). In recent years, there is an increasing interest in finding antioxidant phytochemicals, because they can inhibit the propagation of free radical reactions, and thereby protect the human body from diseases (Terao and Piskula, 1997). Several medicinal plants of Cameroon were screened for their antioxidant properties and a number of bioactive compounds was isolated (Table 6). Omisore et al. (2005) considered the cut-off point for antioxidant activity as 50 µg/ml. Samples with  $IC_{50} > 50$  µg/ml were classified as being moderately active, while samples with  $IC_{50} < 50$  µg/ml were judged as having high antioxidant capacity. In the present paper, samples will be considered to have high or significant antioxidant capacity with  $IC_{50} < 50$  µg/ml (extract) or  $IC_{50} < 10$  µg/ml (compounds), moderate antioxidant capacity with  $50 < IC_{50} < 100$  µg/ml (extract) or  $10 < IC_{50} < 20$  µg/ml (compounds) and low antioxidant capacity with  $IC_{50} > 100$  µg/ml (extract) or  $IC_{50} > 20$  µg/ml (compounds). Extracts from 42 medicinal plants of Cameroon used for the treatment of anemia, diabetes, AIDS, malaria, and obesity were recently screened for antioxidant properties, with

a considerable number showing good activities (Agbor et al., 2007). Many of them exhibited high inhibition percentages on the basis of Folin, Ferric reducing antioxidant power (FRAP), and DPPH (1,1-diphenyl-2-picrylhydrazyl) assays. Plants with good activities included *Alchornea cordifolia* (Euphorbiaceae), *Dacryodes edulis* (Burseraceae), *Ocimum basilicum* (Lamiaceae), *Harungana madagascariensis* (Hypericaceae), *Cylicodiscus gabunensis* (Mimosaceae), *Coleus coprosifolius* (Lamiaceae) (Agbor et al., 2007). Arylbenzofurans isolated from the bark of *Morus mesozygia* (Moraceae), moracin T (43), moracin U (44), moracin S (45); moracin R (46) also showed strong DPPH scavenging capability with  $IC_{50}$  values of 4.12, 5.06, 6.08, and 7.17 µg/ml, respectively (Kapche et al., 2009). The activity of the crude extract of this plant was also reported as significant ( $IC_{50}$ : 5.92 µg/ml), by means of the DPPH scavenging assay (Kapche et al., 2009).

### OTHER ACTIVITIES

Other studies involving Cameroon medicinal plants include their action on human fertility and enzymatic activities. However, few studies have focused on these activities, explaining the scarcity of published data.

Some plants with positive effects on the reproductive system based on studies using experimental rats have been reported. They include *Aloe buettneri* (Liliaceae), *Justicia insularis* and *Dicliptera verticillata* (Acanthaceae) and *Hibiscus macranthus* (Malvaceae), locally used to regulate the menstrual cycle and to treat dysmenorrhea or infertility in women (Telefo et al., 1998); *Basella alba* (Basellaceae) (Moundipa et al., 2005), and *Mondia whitei* (Periplocaceae) traditionally claimed to increase libido (Watcho et al., 2001).

Some compounds from Cameroonian plants were investigated for the ability to interfere with the activity of some enzymes such as xanthine oxidase, phosphodiesterase I, or prolyl endopeptidase. Xanthine oxidase catalyzes the oxidative hydroxylation of hypoxanthine or xanthine using oxygen as a cofactor, and the resulting end products are superoxide anion ( $O_2^{\cdot-}$ ) and uric acid. The inhibitors of xanthine oxidase enzyme can prevent the generation of excess superoxide anions (Chung et al., 1997). Phosphodiesterase I successively hydrolyzes 5'-mononucleotides from 3'-hydroxyl-terminated ribo- and deoxyribo-oligonucleotides. The enzyme has been widely utilized as a tool for structural and sequential studies of nucleic acids. The 5'-nucleotide phosphodiesterase isozyme-V test is useful in detecting liver metastasis in breast, gastrointestinal, lung, and various other forms of cancers (Lei-Injo et al., 1980). Prolyl endopeptidase catalyzes the hydrolysis of peptide bonds at the L-proline carboxy terminal and, thus, plays an important role in the biological regulation of proline-containing neuropeptides and peptide hormones, which are recognized to be involved in learning and memory (Szeltner et al., 2000). The stilbene glycosides isolated from *Boswellia papyrifera* (Del.) Hochst (Burseraceae), *trans*-4',5-dihydroxy-3-methoxystilbene-5-O- $\{\alpha$ -L-rhamnopyranosyl-(1-2)- $[\alpha$ -L-rhamnopyranosyl-(1-6)]- $\beta$ -D-glucopyranoside and *trans*-4',5-dihydroxy-3-methoxystilbene-5-O- $[\alpha$ -L-rhamnopyranosyl-(1-6)]- $\beta$ -D-glucopyranoside exhibited significant inhibition of phosphodiesterase I and xanthine oxidase (Atta-ur-Rahman et al., 2005). Triterpenes such as 3- $\alpha$ -acetoxy-27-hydroxylup-20(29)-en-24-oic acid, 11-keto- $\beta$ -boswellic acid,  $\beta$ -elemenic



**Table 5 | Plants used in Cameroon to treat diabetes, with evidence of their activities.**

Family	Species <sup>a</sup>	Traditional treatment	Plant part used	Bioactive (or potentially active) compounds	Screened activity <sup>b</sup>
Anacardiaceae	<i>Anacardium occidentale</i> L. (41935/HNC)	Diabetes mellitus (Kamtchouing et al., 1998)	Leaves	Not identified	Leaves extract showed anti-diabetes activity through protective role against the diabetogenic action of STZ and hypoglycemic effects in rats (Kamtchouing et al., 1998; Sokeng et al., 2007)
Asteraceae	<i>Sclerocarya birrea</i> (A. Rich.) Hochst (7770/HNC)	Diabetes, diarrhea, dysentery, gangrenous rectitis, fevers, stomach disorders, ulcers, sore eyes (Watt and Breyer-Brandwijk, 1962; Bryant, 1966; Gelfand et al., 1985; Dieye et al., 2008)	Leaves, bark, roots	Not identified	Bark extracts have been reported to exert hypoglycemic in rats following acute and chronic treatments (Ojewole, 2003; Dimo et al., 2007; Gondwe et al., 2008), acting directly on insulin-secreting cells (Ndifossap et al., 2010)
Bombacaceae	<i>Ageratum conyzoides</i> L. (19050/SFR/Cam)	Cough, fever, skin disease, diabetes, bleeding due to external wounds, furuncle, eczema, carbuncle, headaches (Laverigne and Véra, 1989; Tsabang et al., 2001)	Whole plant	Not identified	Leaves extract showed hypoglycemic and anti-hyperglycemic activities in STZ-induced diabetic rats (Nyunai et al., 2009)
	<i>Celiba pentandra</i> (L) Gaertner (43623/HNC)	Diuretic, diabetes, hypertension, headache, dizziness, constipation, mental trouble, fever, peptic ulcer, rheumatism, leprosy (Noumi et al., 1999; Ngounou et al., 2000; Noumi and Dibakto, 2000; Noumi and Tchakonang, 2001; Ueda et al., 2002)	Bark, leaves, roots	Not identified	Roots extract reduced hyperglycemia in STZ-induced diabetic rats (Dzeufiet et al., 2006)
Crassulaceae	<i>Kalanchoe crenata</i> (WEKC) (60103/YA/HNC)	Inflammatory diseases, diabetes (Kamgang et al., 2008)	Whole plant	Not identified but terpenoids, tannins, polysaccharides, saponins, flavonoids and alkaloids were identified from the leaves (Kamgang et al., 2008)	Ethanol extract of the whole plant was found to possess significant hypoglycemic effect in normal rats by lowering blood glucose levels and anti-hyperglycemic effect by lowering and maintaining glycemia at normal levels in diabetic rats (Kamgang et al., 2008)
Euphorbiaceae	<i>Bridelia ndellensis</i> Beille (9676/HNC)	fever, rheumatism, diarrhea, and diabetes (Addae-Mensah and Achenbach, 1985; Onunkwo et al., 1996; Sokeng et al., 2005)	Not specified	Not identified	Ethyl acetate and dichloromethane extracts and fractions of the bark significantly lowered blood glucose levels in type 2 diabetic rats (Sokeng et al., 2005)
Irvingiaceae	<i>Irvingia gabonensis</i> (Aubry Lecomte ex O'Rorke) Baill. (28054/HNC)	Gonorrhea, gastrointestinal and hepatic disorders, wounds infection, diabetes, analgesis (Ngondi et al., 2005)	Bark, fruits, leaves, roots	Not identified	Seeds extract showed modulatory effect on diabetes induced dyslipidemia (Dzeufiet et al., 2009) in rats
Meliasthaceae	<i>Bersama engleriana</i> Gurke (24725/HNC)	Cancer, spasms, infectious diseases, male infertility, diabetes (Wachto et al., 2007)	Leaves, Stem bark, roots	Not identified but flavonoids, phenols, triterpenes, saponins, and anthraquinones were detected in all parts of the plant (Kuete et al., 2008)	Leaves extract showed hypoglycemic properties (Njike et al., 2005)
Rubiaceae	<i>Morinda lucida</i> Benth	Uncontrolled adult cases of diuresis not necessarily associated with diabetes but linked to general body weakness and rapid loss of weight (Kamanyi et al., 1994)	Not specified	Not identified	Root extract showed potent hypoglycemic effects in both normoglycemic and alloxan-induced diabetic mice (Kamanyi et al., 1994)

<sup>a</sup>HNC or SRFK: Cameroon National herbarium code.

<sup>b</sup>Screened activity: streptozotocin (STZ).

**Table 6 | Plants used in Cameroon with evidence of their as antioxidant activities.**

Family	Species <sup>a</sup>	Traditional treatment	Plant part used	Bioactive (or potentially active) compounds <sup>b</sup>	Screened activity <sup>c</sup>
Ebenaceae	<i>Diospyros sanza-minika</i> A. Chevalier (9649/SRFCam)	Epilepsy, paralysis, convulsions, spasm, pains (Burkill, 1985)	Leaves	11- <i>O-p</i> -hydroxybenzoylnorbergenin; 4- <i>O</i> -(30-methylgalloyl)norbergenin; 4- <i>O</i> -syringoylnorbergenin; norbergenin; 4- <i>O</i> -galloylnorbergenin; quercitol (Tangmouo et al., 2009)	DPPH scavenging activity: significant for 4- <i>O</i> -galloylnorbergenin, moderate for norbergenin, 11- <i>O-p</i> -Hydroxybenzoylnorbergenin, 4- <i>O</i> -(30-Methylgalloyl)norbergenin and 4- <i>O</i> -Syringoylnorbergenin (Tangmouo et al., 2009)
Guttiferae	<i>Garcinia polyantha</i> Oliv (1337/SRF/Cam)	Dressing for wounds (Bouquet, 1969)	Sap	Bangangxanthone A; bangangxanthone B; 2-hydroxy-1,7-dimethoxyxanthone; 1,5-dihydroxyxanthone (Lannang et al., 2005)	DPPH scavenging activity: bangangxanthone A isolated from the bark showed the best activity with an IC <sub>50</sub> = 87.0 μM while the standard value for BHA was IC <sub>50</sub> = 42.0 μM (Lannang et al., 2005)
	<i>Garcinia afzelii</i> Engl.	Bacterial infections, dental caries (Adu-Tutu et al., 1979; Waffo et al., 2006)	Leaves; flowers	Afzeliixanthenes A; afzeliixanthenes B (Waffo et al., 2006)	DPPH scavenging activity: Significant for the crude extract and moderate for Afzeliixanthenes A and B (Waffo et al., 2006)
Hypericaceae	<i>Harungana madagascariensis</i> Lam. (32358/HNC)	Diarrhea, dysentery, indigestion, poor pancreatic function (Berhaut, 1975; Prajapati et al., 2003)	Not specified	Harunmadagascarins A and Harunmadagascarins B, harunganol B and harungin anthrone (Kouam et al., 2005)	DPPH scavenging activity: IC <sub>50</sub> of 60.97; 64.76 were recorded with harunmadagascarin and harunganol B respectively (Kouam et al., 2005)
Meliaceae	<i>Carapa grandiflora</i> sprsgue	Arthritis, general fatigue, skin diseases and as febrifuge (Ayafor et al., 1994)	Seeds	Quercitrin (Omisore et al., 2005)	DPPH scavenging activity: low for quercetin (Omisore et al., 2005)
Mimosaceae	<i>Entada rheedii</i> Spreng (19966/SRI/CAM)	Jaundice (Nzowa et al., 2010)	Seeds	Rheediinoside A; rheediinoside B (Nzowa et al., 2010)	ABTS+ scavenging activity: moderate for rheediinoside B; low for rheediinoside A; DPPH scavenging activity: low activity for rheediinoside A and rheediinoside B (Nzowa et al., 2010)
Moraceae	<i>Dorstenia convexa</i> De Wild (53450 HNC)	Malaria (Boyom et al., 2009)	Twigs	Bartericins A; stigmasterol; isobavachalcone (Omisore et al., 2005)	DPPH scavenging activity: low bartericin A and isobavachalcone and stigmasterol (Omisore et al., 2005)
	<i>Dorstenia barteri</i> Bureau (44016/HNC)	Snakebite, rheumatic, infectious diseases, arthritis (Tsopmo et al., 1999)	Whole plant	Bartericins A, and B; stigmasterol; isobavachalcone; 4-hydroxyonchocarpin (Omisore et al., 2005)	DPPH scavenging activity: significant for twigs extract (Omisore et al., 2005)
	<i>Dorstenia mannii</i> Hook. f. (2135/HNC)	Rheumatism, stomach disorders (Bouquet, 1969)	Leaves	Dorsmanin F; 6,8-diprenyleriodictyol (Omisore et al., 2005)	DPPH scavenging activity: low for 6,8-diprenyleriodictyol, and dorsmanin F (Omisore et al., 2005)
	<i>Morus mesozygia</i> Stapf. (4228/SRFK)	Arthritis, rheumatism, malnutrition, debility, pain-killers, stomach disorders, wound infections, gastroenteritis, peptic ulcer, infectious diseases (Burkill, 1985; Noumi and Dibakto, 2002)	Bark	Moracin R (43); moracin S (45); moracin T (43); moracin U (44) (Kapche et al., 2009)	DPPH scavenging activity: significant for bark crude extract, compounds 43-46 (Kapche et al., 2009)

(Continued)

Table 6 | Continued

Family	Species <sup>a</sup>	Traditional treatment	Plant part used	Bioactive (or potentially active) compounds <sup>b</sup>	Screened activity <sup>c</sup>
Piperaceae	<i>Piper umbellatum</i> Linn (6516/SRF/ CAM)	Poisoning, pitting edema, fetal malpresentation, filariasis, rheumatism, hemorrhoids, dysmenorrheal, general pains (Tabopda et al., 2008)	Whole plant	Piperumbellactams A; piperumbellactams B; piperumbellactams C; <i>N-p</i> -coumaroyl tyramine (Tabopda et al., 2008)	DPPH scavenging activity; Moderate activity reported for piperumbellactams A and low activities for piperumbellactams B; C; <i>N-p</i> -coumaroyl tyramine (Tabopda et al., 2008)

<sup>a</sup>HNC or SRFK: Cameroon National herbarium code.

<sup>b</sup>Compounds characterized for the first time in Cameroonian medicinal plant are underlined.

<sup>c</sup>Screened activity: DPPH or 1,1-diphenyl-2-picryl hydrazyl radical assay (evaluates the ability of antioxidants to scavenge free radicals; Hydrogen-donating ability is an index of the primary antioxidants; these antioxidants donate hydrogen to free radicals, leading to non-toxic species and therefore to inhibition of the propagation phase of lipid oxidation [Lugasi et al., 1998]); ABTS+: 2,2-azinobis (3-ethylbenzothiazoline-6-sulfonic acid) diammonium radical cation; BHA: 3-t-butyl-4-hydroxyanisole; Significant activity ( $IC_{50} < 50 \mu\text{g/ml}$ ), moderate activity ( $50 < IC_{50} < 100 \mu\text{g/ml}$ ), low activity ( $IC_{50} > 100 \mu\text{g/ml}$ ).

acid, 3  $\alpha$ -acetoxy-11-keto- $\beta$ -boswellic acid, and  $\beta$ -boswellic acid also exhibited prolyl endopeptidase inhibitory activities (Atta-ur-Rahman et al., 2005).

## CONCLUSION

The present review presents an overview of medicinal plants research in Cameroon and is intended to serve as scientific baseline information for the documented plants as well as a starting point for future studies. The paper draws attention on some active metabolites and plant extracts, with the potential for new drugs or improved plant medicines. The review inevitably shows the richness of the Cameroon flora as medicinal resource and demonstrates the effectiveness of numerous traditionally used plants. Presently, there is an urgent necessity for standardization of plant-derived drugs, as their use is still empirical. There is also an urgent requirement

to standardize methods and cut-off points for describing their bioactivities. Other recommendations include parallel screenings by using cytotoxicity tests to preclude non-specific cytotoxicity from being interpreted as efficient following *in vitro* screening. The elucidation of the mechanisms of action of biologically active extracts and compounds should be strengthened and given priority in future investigations as already shown for natural products from other parts of the world (Kong et al., 2009; Youns et al., 2010; Konkimalla and Efferth, 2010).

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