Journal of Ethnopharmacology 231 (2019) 73–79

Contents lists available at ScienceDirect

Journal of Ethnopharmacology

journal homepage: www.elsevier.com/locate/jethpharm

Prevalence, management and ethnobotanical investigation of hypertension in two Guinean urban districts

M.S.T. Diallo[a,b,c], M.S. Traore[a,b], M.A. Balde[a,b], A.K. Camara[a], E.S. Baldé[a,b], S. Traore[b], K. Oulare[b], T.S. Diallo[b], S. Laurent[c], R.N. Muller[c], E. Tuenter[d], L. Pieters[d], A.M. Balde[a,b,*]

[a] Department of Pharmacy, University Gamal Abdel Nasser of Conakry, BP 1017, Guinea
[b] Research and Valorization Center on Medicinal Plants Dubreka, BP 6411 Conakry, Guinea
[c] Service de Chimie Générale, Organique et Biomédicale; Laboratoire de RMN et d'Imagerie Moléculaire, Université de Mons, Belgium
[d] Natural Products & Food Research and Analysis (NatuRA), Department of Pharmaceutical Sciences, University of Antwerp, Belgium

ARTICLE INFO

Keywords:
Hypertension
Ethnobotanical investigation
Hymenocardia acida leaves
Uapaca togoensis stem bark

ABSTRACT

Ethnopharmacological relevance: Hypertension is an important public health challenge in low- and middle-income countries, and in many African countries including Guinea medicinal plants are still widely used for its treatment.

Materials and Methods: The objective of this study was to determine the prevalence of hypertension in two Guinean urban districts (Pounthioun and Dowsare), to describe its management and to collect information on traditional herbal remedies. A total of 316 participants entered the study, 28.2% (89/316) men and 71.8% (227/316) women. Of these, 181 were from Dowsare (50 men and 131 women) and 135 from Pounthioun (39 men and 96 women). The mean age of subjects was 40.8 ± 14.0 years (range18 − 88years), while the majority of subjects (63.3% or 200/316) were 45–74 years old.

Results: The overall prevalence of hypertension was 44.9% (142/316): 46.4% (84/181) from Dowsare and 43.0% (58/135) from Pounthioun. Ethnobotanical investigations among hypertensive patients led to the collection of 15 plant species, among which *Hymenocardia acida* leaves and *Uapaca togoensis* stem bark were the most cited. Phytochemical investigation of these two plant species led to the isolation and identification of isovitexin and isoorientin from *H. acida*, and betulinic acid and lupeol from *U. togoensis*.

Conclusion: The presence of these constituents in *Hymenocardia acida* leaves and *Uapaca togoensis* stem bark may at least in part support their traditional use against hypertension in Guinea.

1. Introduction

Hypertension is an important public health challenge worldwide because of its high prevalence and concomitant increase in risk of disease (Kearney et al., 2004). Its prevalence is increasing rapidly due to rising longevity and the increasing prevalence of contributing factors such as unhealthy diet, obesity and physical inactivity (Cappuccio and Miller, 2016). In the African and American regions, a prevalence of 46% and 35% was reported, respectively (WHO, 2013). In low- and middle-income countries many people do not seek treatment for hypertension because it is prohibitively expensive (Cappuccio and Miller, 2016); Onyango et al. (2017)). Presently, there are various antihypertensive drugs with different mechanisms of action. Although these drugs are effective, most of them can have very annoying side effects, and in some cases they are unavailable to many rural dwellers due to precarious drug distribution and the manpower required (Ayinde et al., 2010). That is why medicinal plants are frequently used for management of hypertension in numerous African countries (Baldé et al., 2006a, b; Tra et al., 2008; Tahraoui et al., 2007; Nuwaha and Musinguzi, 2013; Olisa and Oyelola, 2009; Osamor and Owumi, 2010). In Guinea, hypertension is a major public health problem. A recent study indicated a prevalence of 29.9% within the adult population aged 25 years and older (Camara et al., 2016). In Lower Guinea, a high prevalence is reported in the urban zone (32%) and the rural area (27–69%) (Baldé et al., 2006a; N'Gouin-Claih et al., 2003). The objective of this study is to determine the prevalence of hypertension in two Guinean urban districts (Pounthioun and Dowsare), to describe its management and to collect information on herbal remedies traditionally used for its treatment.

* Corresponding author at: Department of Pharmacy, University Gamal Abdel Nasser of Conakry, BP 1017, Guinea.
E-mail address: bmaliou2002@yahoo.fr (A.M. Balde).

https://doi.org/10.1016/j.jep.2018.07.028
Received 15 May 2018; Received in revised form 4 July 2018; Accepted 25 July 2018
Available online 26 July 2018
0378-8741/

2. Material and methods

2.1. Study of prevalence

This study was carried out from May to July 2009 in Pounthioun and Dowsare, two urban districts of the prefecture of Labe, Republic of Guinea. A total of 316 volunteers aged 18 and over were selected. The questionnaire and oral interviews were based on the standardised model designed by the Research and Valorization Center on Medicinal Plants (CRVPM)-Dubréka. The information concerned socio-demographic data (age, sex); life habits such as smoking, consumption of alcohol, kola nuts (rich in caffeine), "Maggi Cube" (flavor enhancer) and "Soumbara" (obtained by fermentation of the seeds of *Parkia biglobosa* and traditionally considered as a flavor enhancer and as an antihypertensive ingredient); family medical history (hypertension); anthropometric parameters (weight, height); and blood pressure. Anthropometric measurements were done in standing position, height without shoes. Weight was determined using a digital scale (Krups, Germany; maximum weight 130 kg). The Body Mass Index (BMI) was calculated as weight (kg) divided by height (m^2). Overweight was defined as $25 \leq BMI < 30$, obesity corresponded to a BMI of ≥ 30 and underweight to a BMI of < 18.5.

2.1.1. Measurement of blood pressure

Blood Pressure (BP) was measured by a trained health worker by means of a single calibrated and validated digital sphygmomanometer (TOPCOM® BPM Arm 1480, The Netherlands) after the subject had been sitting for at least 15 min and with the arm resting at heart level. Abstinence from food, kola nuts, nutritional supplements, caffeinated beverages and cigarettes for a minimum of 2 h was requested for all patients before the appointment. BP was recorded as three serial measurements at intervals of 5 min. Each measurement was performed with the participant in a seated position and on the left upper arm. The mean of the last two blood pressure measurements was used in the analysis. Hypertension was defined as a mean systolic BP ≥ 140 mmHg and/or a mean diastolic BP ≥ 90 mmHg, or being on drug therapy for hypertension. The BP category was defined according to the 2013 European Society of Hypertension / European Society of Cardiology Guidelines for the management of arterial hypertension (Mancia et al., 2013).

2.2. Ethnobotanical investigation

The ethnobotanical data were collected from the hypertensive patients using herbal remedies. The interviews mainly focused on the herbals' local name, plant part used, method of preparation, plant procurement and concomitant use with conventional antihypertensive drugs.

2.3. Statistical analysis

All statistical analyses were performed using SPSS 19.0 for Windows (SPSS). Bivariate comparisons were performed using x^2 test for categorical variables. Results are presented as mean ± standard deviation (SD). A p value < 0.05 was considered statistically significant.

2.4. Ethical considerations

Approval of the internal Ethic Committee of CRVPM-Dubreka was obtained before the initiation of the study. The information sheet and/or oral consent form (available in both French and Foulani (the local language) were read and explained to each participant who, if agreeing to take part, gave consent either by signing his or her name or applying a left thumbprint.

2.5. Phytochemical analysis

2.5.1. Plant material

Plant materials consisted of *Hymenocardia acida* Tul. (Phyllanthaceae) leaves and *Uapaca togoensis* Pax (Phyllanthaceae) stem barks which were harvested in Labe (November 2010). Their botanical identification was done by the botanists from the "CRVPM-Dubreka". Voucher specimens were deposited at the Herbarium of the CRVPM: No. D61HK1 and D172HK1 for *H. acida* and *U. togoensis,* respectively. Each plant part was dried at room temperature and reduced to powder.

2.5.2. Chemical screening

Based on standard qualitative methods (Harborne, 1973; Wagner and Bladt, 1996) the plant extracts were screened for the presence of chemical constituents such as cardiac glycosides, alkaloids, tannins, flavonoids, saponins, terpenoid, anthraquinones and carbohydrates. The methanol, chloroform and aqueous extracts were submitted to Thin Layer Chromatography TLC on silica gel Merck 60 F_{254} plates (layer thickness 0.2 mm) with a mobile phase of ethyl acetate / acetic acid / formic acid / water (74:1:1:24; upper phase) for flavonoids; hexane / ethyl acetate (1:1) for terpenes and sterols; chloroform / acetone / ammonia solution 25% (8:2:0.5) for alkaloids.

2.5.3. Fractionation and isolation

2.5.3.1. Uapaca togoensis. An aliquot of 4910 mg of the chloroformic extract of stem bark (Ut1) was subjected to column chromatography on silica gel 60 (Merck, 0.063–0.200 mm) eluted with a gradient of increasing polarity of mixtures of chloroform and methanol. Based on their TLC profile (silica gel 60F_{254} plates, 0.25 mm layer thickness, Merk) with chloroform / ethyl acetate (80:20) as the mobile phase, similar fractions were combined to give 18 major subfractions (Ut1-1 to Ut1–18). Fraction Ut1-1 (670.3 mg) was purified by mean of repetitive column chromatography on silica gel with a chloroform/ ethyl acetate gradient to yield Ut1-1-1 to Ut1-1-6. Subfraction Ut1-1-1 (117 mg) was subjected to preparative TLC on silica gel 60 F_{254} plates, 1 mm layer thickness (Merck) with chloroform / ethyl acetate (60:40) as mobile phase to give compound **1** (18 mg).

Fraction Ut1–3 (163.6 mg) was purified by repetitive column chromatography with a chloroform / ethyl acetate gradient to yield four subfractions Ut1–3-1 to Ut1–3-4. Subfraction Ut1–3-2 (110 mg) was subjected to preparative TLC with chloroform / acetone (9.5:0.5) as mobile phase to give compound **2** (8 mg).

2.5.3.2. Hymenocardia acida (polar extract). An aliquot of 2500 mg of the ethanolic extract of *H. acida* was submitted to column chromatography using Sephadex LH_{20} as stationary phase and ethanol as eluent. Based on their TLC profile, 10 similar fractions were collected and combined (Ha1-Ha10). Fraction Haf 1–3 (346 mg) was rechromatographed using Sephadex LH-20, and further purification led to the isolation of **3** (95 mg).

2.6. Spectroscopic methods

NMR spectra (^{1}H- and ^{13}C NMR, DEPT-135 and −90) were recorded at 30 °C on a Bruker DRX-400 instrument (Rheinstetten, Germany) operating at 400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR, using standard software packages. Chemical shifts (δ) are reported in ppm units downfield from tetramethylsilane (TMS), using TMS or the solvent signal as the internal standard. Fast Atom Bombardment (FAB) mass spectra using NBA (*m*-nitrobenzyl alcohol) as the liquid matrix were recorded on a VG 70 SEQ instrument (Micromass, Manchester, UK). The FABMS was obtained using direct injection.

Table 1
Characteristics of the study population.

	Dowsaré (n = 181)		Pounthioun (n = 135)		Total Men n = 89 (%)	Total Women n = 227 (%)	Total n = 316
	Men n = 50 (%)	Women n = 131(%)	Men n = 39 (%)	Women n = 96(%)			
Averageages (years)					56.1 ± 16.1	51.6 ± 14.4	52.8 ± 15
18–24	2 (4)	3 (2.29)	–	1 (1.04)	2 (2.24)	4 (1.76)	6 (1.90)
25–34	7 (14)	19 (14.50)	2 (5.12)	10 (10.41)	9 (10.11)	29 (12.77)	38 (12.02)
35–44	8 (16)	24 (18.32)	4 (10.25)	12 (12.5)	12 (13.48)	36 (15.85)	48 (15.19)
45–54	13 (26)	25 (19.08)	3(7.69)	24 (25)	16 (17.97)	49 (21.58)	65(20.57)
55–64	5 (10)	36 (27.48)	9 (23.07)	30 (31.25)	14 (15.73)	66 (29.07)	80 (25.32)
≥ 65	15 (30)	24(18.32)	21(54)	19(20)	36(40.44)	43 (19)	79 (25)
life habits							
Alcohol	–	1 (0.76)	–	–	–	1(0.44))	1(0.32)
Tabac	7 (14)	1 (0.76)	1(0.74)	1 (1.04)	8 (8.98)	2 (0.88)	10 (3.16)
Kola	15 (30)	51 (38.93)	14 (10.37)	38 (39.58)	29 (32.58)	89(39.20)	118 (37.34)
''Soumbara''	34 (68)	84 (64.12)	38 (28.14)	85 (88.54)	72 (80.89)	169 (74.44)	241(76.26)
''CubMaggi''	30 (60)	92 (70.22)	18 (46.15)	71 (73.95)	48(53.93)	163(71.80)	211 (66.77)
Educational background							
Illiterate	20 (40)	115 (87.78)	16 (41.02)	85 (88.54)	36(69.66)	200 (76.65)	236 (74.68)
Primarylevel	14 (28)	8 (6.10)	13 (33.33)	4 (4.16)	27(30.33)	12 (5.28)	39(12.34)
Secondarylevel	9 (18)	3 (2.30)	6 (15.38)	5 (5.20)	15 (16.85)	8(3.52)	23(7.28)
Higheducationlevel	7 (14)	5 (3.81)	4 (10.25)	2 (2.08)	11(12.35)	7(3.08)	18(5.70)
Familyhistory of illness							
Hypertension	4 (8)	2 (1.52)	–	–	4 (4.49)	2 (0.88)	6 (1.90)
Diabetes	–	7 (5.34)	1 (2.56)	4 (4.16)	1(1.12)	11(4.84)	12 (3.80)
Hypertension level							
Optimal BP	17 (34)	30 (23.66)	13 (33.33)	31 (32.29)	30 (33.70)	61 (26.87)	91(28.79)
Normal BP	4 (8)	21 (16.03)	5 (12.82)	12 (12.5)	9 (10.11)	33 (14.53)	42 (13.29)
Normal high BP	5 (10)	20 (15.26)	8 (20.51)	8 (8.33)	13 (14.60)	28 (12.33)	41(12.97)
– Grade 1SD hypertension	6 (12)	8 (6.10)	–	6 (6.25)	6 (6.74)	14 (6.16)	20 (6.33)
– Grade 1hypertension isolated systolic	3 (6)	7 (5.34)	3 (7.69)	15 (15.62)	6 (6.74)	22 (9.69)	28 (8.86)
– Grade 1isolated diastolic hypertension	3 (6)	5 (10)	3 (7.69)	5 (5.20)	6 (6.74)	10(4.40)	16 (5.06)
– Grade 2SD hypertension	1 (2)	16 (12.21)	3 (7.69)	11 (11.45)	4 (4.49)	27(11.89)	31 (9.81)
– Grade 2isolated systolic hypertension	2 (4)	1 (0.76)	2 (5.12)	3 (3.12)	4 (4.49)	4 (1.76)	8 (2.53)
– Grade 2 isolated diastolic	–	1(0.76)	–	1 (1.04)	–	2 (0.88)	2 (0.63)
– Grade 3,SD hypertension	9 (18)	22 (16.79)	2 (5.12)	3 (3.12)	11 (12.35)	25 (10.01)	36 (11.39)
– Grade 3,Systolic isolated hypertension	–	–	–	1 (1.04)	–	1 (0.44)	1 (0.32)
Body Mass Index							
Underweight BMC (kg/m^2) < 18.5	5 (10)	2 (1.52)	2 (5.12)	5 (5.21)	7 (7.86)	7 (3.08)	**14** (4.43)
Normal weight BMC (kg/m^2) 18.5–24.9	36 (72)	63 (48.09)	28 (71.79)	42 (43.75)	64 (78.65)	105 (46.26)	168 (53.16)
Overweight BMC(kg/m^2) 25.0–29.9	8 (16)	36 (27.48)	9 (23.07)	34 (35.42)	17 (19.10)	70(30.84)	88 (27.85)
Obesity type 1 BMC (kg/m^2) 30.0–34.9	1 (2)	18 (13.74)	–	11 (11.46)	1(1.12)	29 (12.78)	30 (9.49)
Obesity type 2 IMC (kg/m^2) 35.0–39.9	–	11(8.40)	–	3(3.13)		14(6.17)	14 (4.43)
Obesity type 3: IMC ≥ 40	–	1 (0.76)	–	1 (1.04)		2 (0.88)	2 (0.63)

Legend: BP = Blood pressure; S = Systolic; D = Diastolic; SD = Systolic and diastolic; BMC = Body Mass Index.
Optimal BP (S/D: < 120/ < 80); Normal BP (S: 120–129 and/or D: 80–84); Normal high BP (S: 130–139 and/or D: 85–89); Grade 1 (S: 140–159 and/or D: 90–99); Grade 2 (S: 160–179 and/or D: 100–109); Grade 3 (S: ≥ 180 and/or D: ≥ 110) [Recommandations 2007 ESH/ESC; www.sfhta.eu/wp-content/uploads/2012/10/EHS-2007].

3. Results

3.1. Epidemiological investigation

3.1.1. Characteristics of the study population

As shown in Table 1, a total of 316 participants (89/316 men or 28.2% and 227/316 women or 71.8%) entered in the study. Of these, 181 were from Dowsare (50 men and 131 women) and 135 from Pounthioun (39 men and 96 women). The ratio women / men was 2.55 (227/89), i.e. 2.62 (131/50) for Dowsare and 2.46 (96/39) for Pounthioun. The mean age of the subjects was 40.8 ± 14.0 years (range18–88 years), while the majority of subjects (200/316 or 63.3%) were between 45 and 74 years. An above-normal BMI was observed for 42.4% (134/316) of the cohort (18/89 men and 116/227 women). From these, 46/134 (45 women and 1 man) were obese (BMI ≥ 30 kg/m^2). Concerning the level of education, 74.7% (236/316) were illiterate (62 men and 174 women). Among the educated people, 12.3% (39/316) and 7.3% (23/316) had some primary and secondary schooling, respectively, while 5.7% (18/316; 11 men and 7 female) had attended a higher education institution.

3.1.2. Prevalence of hypertension

There were 142 hypertensive subjects (84 from Dowsare and 58 from Pounthioun) giving an overall prevalence of hypertension of 44.9% (142/316). The prevalence among men (37/89 or 41.6%) and women (105/227 or 46.3%) was not significantly different (p = 0.45). The average age of hypertensive subjects was 56.9 ± 11.6 years, ranging between 25 and 88 years. According to the age bracket the prevalence of hypertension was 10.5% (4/38) among participants aged 25–34 years., 18.7% (9/48) for participants aged 35–44, 58.5% (38/65) for participants aged 45–54, 56.2% (45/80) for participants aged 55–64% and 58.2% (46/79) for subjects of more than 64 years old. All patients in the 18–24 age group were normotensive. Among the hypertensive patients (Table 1), 45.1% (64/142) were on grade 1, 28.9% (41/142) on grade 2% and 26.1% (37/142) on grade 3. Grade 1 was recorded for 20.2% (18/89) in the male group (12/50 in Dowsare; 6/39 in Pounthioun) and 20% (46/227) in the female group (20/131 in Dowsare; 26/96 in Pounthioun). In the hypertensive patients, a total of 9.0% (8/89) in the male group (3/50 in Dowsare; 5/39 in Pounthioun) and 14.5% (33/227) in the female group (18/131 in Dowsare; 15/39 in Pounthioun) were classified in grade 2. In addition, 12.3% (11/89) patients in the male group (9/50 in Dowsare; 2/39 in Pounthioun) and 11.5% in the female group (22/131 in Dowsare; 4/96 in Pounthioun) were ranked as grade 3.

Considering the consumption of "Maggi Cube", 61.3% (87/142) of the hypertensive patients and 71.3% (124/174) of the normotensive patients were concerned. The consumption of "Soumbara" was reported by 80.3% (114/142) of the hypertensive patients and 83.9% (146/174) of the normotensive ones. Among the 106/316 consumers of kola nuts, 52.8% (56/106) were hypertensive. Among the hypertensive patients, 31.0% (44/142; 10 men and 34 women) were overweight, and 21.1% (30/142; 1 man and 29 women) were obese. The prevalence of hypertension (51.4%) was significantly higher ($p = 0.022$) in hypertensive patients (73/142 or 51.4%) than in normotensive patients (60/174 or 34.5%). None of the subjects admitted to drink alcohol, and only 10 (8 men and 2 women) admitted being smokers, from which only two patients were hypertensive. Concerning a family history of hypertension, only 4.2% (6/142) of the patients were concerned.

3.1.3. Detection

Overall 45.8% (65/142) were aware of being hypertensive. Only 6.2% of them (4/65) were receiving drug therapy, but none of them had his blood pressure adequately controlled (i.e. ≤ 140/90 mmHg). The detection rate was almostidentical for men 54.3% (20/37) and women 54.1% (57/105).

3.1.4. Management

All the known hypertensive patients (65/142 or 45.8%; 48 female and 17 male) used medicinal plants to deal with their hypertension. Of these, 93.8% (61/65) used exclusively medicinal plant species intermittently, while only 4 patients (6.2%, 4/65) used a combination of medicinal plants and conventional medicine.

3.1.5. Control

None of the patients on any treatment was adequately under control (SBP/DBP < 140/90 mmHg). Among the hypertensive patients who used the medicinal plants, 35.4% (23/65) had grade 1 hypertension; 41.5% (27/65) had grade 2 hypertension and 23.1% (15/65) had grade 3 hypertension.

3.2. Ethnobotanical investigation

An ethnobotanical survey resulted in the collection of 15 recipes among which 13 were composed of one plant and 2 recipes of two plants (Table 2). Of these, 15 plants species belonging to 11 botanical families were identified. The most cited recipes were *Hymenocardia acida* leaves (25), *Uapaca togoensis* stem bark (22), *H. acida* leaves mixed with *U. togoensis* stem bark (10), *Combretum micranthum* leaves (9), *Xylopia aethiopica* fruit and leaves, *Uvaria chamae* leaves (5) and *Piliostigma thoninguii* stem bark (5).

The most frequently used plant parts were leaves (11 citations), followed by the stem bark (4 citations), root and fruits (1 citation for each). The remedies were prepared with water either as decoction (73.3%, 11/15) or infusion (26.6%, 4/15), which were given orally. On the procurement of recipes, 54.8% (35/65) of the interviewed patients purchased them on the market, while 45.1% (30/65) of patients

Table 2
Plant species recorded as antihypertensive by the patients.

No.	Plant species	Voucher specimen number	Vernacular name (Local name)	Family	Plant part (preparation form)	citations	posology
1.	*Hymenocardia acida* Tul.	D61HK1 Ex 62HK530	Pellitoro (F)	Hymenocardiaceae	Le (Dc)	15	1 cup twice 2 times per daily
2.	*Uapaca togoensis* Pax.	D172HK1 Ex 107HK635	Yalague Peté(F)	Phyllantaceae	Sb (Dc)	12	1cup twice 2 times per daily
3.	*Hymenocardia acida* Tul.		Pellitoro (F)	Hymenocardiaceae	Le (Dc)	10	1cup twice 1–3 times per day
	Uapaca togoensis Pax.		Yalague Peté(F)	Phyllantaceae	Sb (Dc)		
4.	*Combretum micranthum* G.Don	D36H1Ex 38HK450	Kankaliba (F)	Combretaceae	Le (Dc)	9	1 cup twice 2 times per daily
5.	*Hibiscus sabdariffa* L.	D77HK3	Bissabe (calyx)	Malvaceae	C(Dc)	1	1 cup twice 3 times per daily
6.	*Uvaria chamae* P.Beauv	D5HK4 ex 6HK24	Boyle (F)	Annonaceae	Le (Dc)	5	1 cup twice 2 times per daily
7.	*Piliostigma thoninguii* Schumach	D25HK Ex 27HK412	Barké (F)	Caesalpiniaceae	Sb (Dc)	5	1 cup twice 2 times per daily
8.	*Xylopia aethiopica* A.Rich.	D5HK3	Guilé (F)	Annonaceae	Le (Dc)	1	1 teaspoon per day
					Fr (If)	1	1 teaspoon per daily
9.	*Citrus medica* L.	D118HK2	Katthiou (F)	Rutaceae	Le (If)	1	1 teaspoon 2 times per daily
10.	*Lantana camara* L.	D135HK1	Ponpontiaani (F)	Verbenaceae	Le (If)	1	1 cup 2 times per daily
11.	*Dialium guineense* Willd	D25HK3 Ex 27HK407	Meeko (F)	Caesalpiniaceae	Le (Dc)	1	1 teaspoon 3 times per daily
	Cassia sieberiana	D25HK2 Ex 27HK308	Sindja (F)	Caesalpiniaceae	Le (Dc		
12.	*Tamarindus indica* L.	D25HK Ex 27HK419	Dyabbhe (F)	Caesalpiniaceae	Sb (Dc)	1	1 teaspoon 2 times per daily
13.	*Mangifera indica* L.	D3HK2 ex 3HK31	Mango Seny (F)	Anacardiaceae	Le (Dc)	1	1 cup 2 times per daily
14.	*Harungana madagascariensis* Hook	D62HK2 Ex 63HK554	Soungala (F)	Hypericaceae	Rb(If)	1	1 cup 2 times per daily
15.	*Persea americana* Mill.	D67HK1 Ex 68HK563	Piya (F)	Lauraceae	Le(Dc)	1	One glass cup taken daily

Legend: Le = leaves, Sb = stem bark, R = root, F = Fulani, TH = traditional healer, Mc = maceration, Dc = decoction. If = infusion.

harvested the plant recipes themselves. As for side effects, a diuretic potency was reported by most of the patients using herbal medicines, in particular recipes based on *H. acida, C. micranthum, U. togoensis* and *H. sabdariffa*.

3.3. Phytochemical analysis

Aiming to isolate some constituents from the two most cited plant species *viz. H. acida* and *U. togoensis*, a phytochemical investigation was realized on the apolar (chloroform) and polar (methanol and aqueous) extracts. The presence of flavonoids, terpenoids, saponins, carbohydrates, tannins and sterols was observed in both plant species. Two compounds were isolated from each plant species, *viz.* compounds **1–2** from *U. togoensis* and compounds **3a** and **3b** from *H.acida.*

The ^{1}H NMR spectrum of compound **1** exhibited six tertiary methyl singlets at δ 0.73, 0.80, 0.92, 0.94, 0.95 and 1.23, an allylic methyl group at δ 1.67 (3 H, s, Me-30), a secondary hydroxyl group at δ 3.15 (dd, $J = 11.2$ and 6.2 Hz) and an exomethylene group at δ 4.58 (1 H, br s, H-29a) and δ 4.71 (1 H, br s, H-29b). The ^{13}C NMR spectrum confirmed the presence of a vinyl group at δ 150.38 and 109.69 ppm, and a secondary alcohol at δ 79.02. As shown in Table S1, the ^{13}C NMR spectral data of **1** supported the ^{1}H NMR assignments, and were quite superimposable to those of lupeol, a pentacyclic triterpenoid (Mahato and Kundu, 1994; Burns et al., 2000; Fotie et al., 2006). Thus, compound **1** was identified as lupeol.

The ^{1}H NMR spectrum of compound **2** revealed the presence of terminal methylene hydogens at δ 4.67 (br s, H-29a) and δ 4.54 (br s, H-29b) and an allylic methyl group at δ 1.63 (3 H, s, Me-30). It also showed five methyl singlets at δ 0.63, 0.75, 0.85, 0.91, 0.91 and one singlet of a secondary hydroxyl group at δ 3.31. The ^{13}C NMR spectrum confirmed the presence of a vinyl group at δ 150.3 and 109.55, a carboxylic acid at δ 177.15 and secondary alcohol at δ 76.71. Based on the ^{1}H NMR spectrum and due to the ^{13}C NMR similarity of **2** with previously reported data (Table S1), compound **2** was identified as betulinic acid (Mahato and Kundu, 1994; Chatterjee et al., 1999).

Compound **3** was isolated as a mixture (95 mg) in a relative ratio of 1:2, according the MS and NMR spectra. The MS data indicated two molecular ions at *m/z* 431 [M-H]$^-$ for **3a** and *m/z* 447 [M-H]$^-$ for **3b**, respectively. Based on the accordance of their ^{1}H- and ^{13}C NMR spectra (Table S2 and S3) with those of previously reported flavones, compounds **3a** and **3b** were identified as the known C-glucosylflavones isovitexin and isoorientin, respectively (Hosoya et al., 2005; Peng et al., 2005; Kumazawa et al., 2000).

4. Discussion

Hypertension is highly prevalent in both investigated districts of Labé : 46.4% (84/181) in Dowsare and 43.0% (58/135) in Pounthioun. Such high prevalences, which could be related to lifestyle, environmental factors like psychosocial stress, and overweight, are more or less similar to those found in most West African countries such as Gambia and Sierra Leone (44.8%) (Awad et al., 2014), Nigeria (47%) (Ekanem et al., 2013), Burkina Faso (40.2%) (Niakara et al., 2007) and Togo (36.7%) (Yayehd et al., 2013). In these two districts, the prevalence rate increased with age in both men and women: from 10.5% (4/38) in the age group of 25–34 years to 57.2% (91/159) for the subjects of more than 50 years old. This was in accordance with a previous study in Lower Guinea indicating a very high rate of hypertension in adult patients over 54 years of age (46%) as compared with the youngest patients (16%) (Baldé et al., 2006a). This is also in agreement with previous studies indicating the lowest prevalence of hypertension among the younger population ($\leq$35 years) and highest prevalence around 70% in people aged of 70 years and more (Awad et al., 2014; Dewhurst et al., 2013; Kayima et al., 2013). Our prevalence estimates are similar to those of 43.6% reported in urban areas of middle Guinea (Balde *et al.*, 2006b) but higher than those found in Lower Guinea (29.9%) (Balde *et al.*, 2006a). The analysis of the food habits of the population studied indicates a wide consumption of the bouillon “Maggi Cubes” as flavor enhancer, “Sumbara”, which is also a flavor enhancer, obtained by fermentation of the seeds of *Parkia biglobosa* and traditionally considered as an antihypertensive ingredient, and the kola nut, which is rich in caffeine. The consumption of “Maggi Cubes”, “Sumbara” or kola nuts was not clearly related to the prevalence of hypertension in these two districts when comparing the hypertensive and normotensive patients who consume them. However, “Sumbara” is widely considered in Guinea as a good substitute to “Maggi Cubes” along with an antihypertensive potential. On the other hand, most national and international guidelines and position statements for cardiovascular disease prevention and control, universally recommend dietary salt reduction as an important strategy to prevent hypertension and associated cardiovascular disease in both hypertensive and normotensive individuals (Poulter et al., 2015). The fact that few or no patients admitted being smokers or alcohol drinkers could be linked to an embarrassment of recognizing a social transgression.

Various risk factors including obesity, age, alcohol use, diabetes mellitus and smoking are associated with hypertension in developing countries (Awuah et al., 2014). In this study, age and BMI had a significant association with hypertension. This result is similar to that found in a previous study realized in three regions of Guinea (Baldé et al., 2006a). With regard to family history of hypertension, only few patients (4.2%, 6/142) were concerned. In fact, most hypertensive patients are unaware of the status of their parents in urban as well as in rural Guinean areas.

In the present study, 45.8% (65/142) hypertensive subjects knew about their status of health and all used traditional medicine for their treatment. Only 2.8% (4/142) of hypertensive subjects also used a modern treatment for the management of their hypertension. This could be due to financial, geographical and/or cultural considerations since most Guinean people especially in rural areas have no access to the high cost modern therapies for the management of their hypertension. Control and management of hypertension remains a major problem in sub-Sahara Africa. In numerous countries like Ghana, Cameroon and Kenya a low rate of awareness, treatment and control of hypertension was reported (Awuah et al., 2014; Dzudie et al., 2012). From this study, the low rate awareness of people could be related to their educational level. Based on these results, the implementation of a national program for the control of cardiovascular diseases, particularly for hypertension, must be brought into practice.

The ethnobotanical survey conducted among hypertensive patients led to the collection of 15 plant species. Among the cited plant species in Labé, *C. micranthum*, *M. indica*, *X. aethiopica*, *H. acida*, *P. americana*, *P. thoninguii* and *H. sabdariffa* were also used for management of hypertension in other African countries like Nigeria and Togo (Mensah et al., 2009; Atowadi et al., 2014; Karou et al., 2011). Previous investigations provide evidence to support the antihypertensive activity of some plant species such as *C. micranthum, X. aethiopica* and *H. sabdariffa* (Seck et al., 2016; Somova et al., 2001; Herrera-Arellano et al., 2004, 2007). The two most cited plant species by patients were *H. acida* and *U. togoensis.* Phytochemical screening of *H. acida* and *U. togoensis* showed the presence of flavonoids, terpenoids, saponins, tannins and sterols. The presence of flavonoids, proanthocyanidins and sterols in *H. acida* has been described (Mojiminiyi et al., 2007; Sofidiya et al., 2009). Moreover, the antihypertensive properties of the proanthocyanidins and flavonoids are widely described in the literature (Ibrahim et al., 2007; Medina-Remón et al., 2013); their mechanisms of action are related to a vasodilatory effect or inhibition of the angiotensine-converting-enzyme (ACE) (Upadhyay and Dixit, 2015; Draijer et al., 2015; Nwanna et al., 2014; Guerrero et al., 2012; Ottaviani et al., 2006). Previous laboratory investigations provide evidence to support the antihypertensive activity of *H. acida*: the methanolic extracts from *H. acida* leaf, trunk and root bark showed a concentration-dependent vasorelaxant effect on isolated rat aortic rings with functional endothelium, while the root bark extract exerted a significant *in vivo* effect in spontaneously hypertensive rats (Nsuadi Manga et al., 2013). Our previous investigations on root bark of *H. acida* have led to the isolation and identification of the cyclopeptide alkaloids hymenocardine and its *N*-oxide, hymenocardinol and hymenocardine-H (Tuenter et al., 2016). However, cyclopeptide alkaloids have not been associated with anti-hypertensive activity (Tuenter et al., 2017). However, the antihypertensive activity of isovitexin and isoorientin (potential Angiotensin Converting Enzyme-inhibitors) and lupeol has been already reported (Lacaille-Dubois et al., 2001; Saleem et al., 2003; Andrikopoulos et al., 2003). Particularly, isovitexin and isoorientin are considered as potential Angiotensin Converting Enzyme-inhibitors; lupeol has been described to improve hypertension and dyslipidemia in strokeprone spontaneously hypertensive rats (SHRSP) (Ardiansyah et al., 2012). betulinic acid has been reported to ameliorate metabolic disorders such as hypertension in mice (Yoon et al., 2017) and showed a significant relaxant effect on endothelium-intact vessels in a concentration-dependent manner ($p < 0.05$) in rats (Rios et al., 2012; Fu et al., 2011).

5. Conclusion

This study not only indicated the high prevalence of hypertension in the urban area of the prefecture of Labé , but also highlights the alarming lack of blood pressure control in hypertensive patients. All the hypertensive patients used medicinal plants intermittently, and *H. acida* along with *U. togoensis* were the most cited plant species. Phytochemical studies of these species are in progress, but the antihypertensive activity may be related to the presence of isovitexin and isoorientin in *H. acida*, lupeol and betulinic acid in *U. togoensis.* The national implementation in Guinea of a preventive program on cardiovascular diseases appears to be urgent.

Conflict of interest

The authors declare no financial or commercial conflict of interest.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jep.2018.07.028.

References

Andrikopoulos, N.K., Kaliora, A.C., Assimopoulou, A.N., Papapeorgiou, V.P., 2003. Biological activity of some naturally occurring resins, gums, and pigments against *in vitro* LDL oxidation. Phytother. Res. 17, 501–507.

Ardiansyah, A., Yamaguchi, E., Shirakawa, H., Hata, K., Hiwatashi, K., Ohinata, K., Goto, T., Komai, M., 2012. Lupeol supplementation improves blood pressure and lipid metabolism parameters in stroke-prone spontaneously hypertensive rats. Biosci. Biotechnol. Biochem. 76, 183–185.

Atowadi, S.E., Olowoniyi, O.D., Daikwo, M.A., 2014. Ethnobotanical survey of some plants used for the management of hypertension in the Igala speaking area of Kogi State, Nigeria. Annu. Res. Rev. Biol. 4, 4535–4543.

Awad, M., Ruzza, A., Mirocha, J., Setareh-Shenas, S., Pixton, R., et al., 2014. Prevalence of hypertension in the Gambia and Sierra Leone, western Africa: a cross-sectional study. Cardiovasc. J. Afr. 25, 269–278.

Awuah, R.B., Anarfi, J.K., Agyemang, C., Ogedegbe, G., Aikins, A., 2014. Prevalence, awareness,treatment and control of hypertension in urban poor communities in Accra, Ghana. J. Hypertens. 32, 1203–1210.

Ayinde, B.A., Omogbai, E.K.I., Onwukaeme, D.N., 2010. Hypotensive effects of 3,4-dihydroxybenzyaldehyde isolated from the stem bark of *Musanga cecropioides*. J. Pharmacogn. Phytother. 1, 4–9.

Baldé, A.M., Traore, M.S., Toure, M., Diallo, D., Keita, A., et al., 2006a. Hypertension artérielle en Guinée: epidémiologie et place de la phytothérapie dans la prise en charge dans les zones urbaines et rurales de Fria, Boké, Forecariah (Basse Guinée). Pharm. Méd. Trad. Afr. 12, 19–43.

Baldé, M., Baldé, N., Kaba, M., Diallo, I., Diallo, M., et al., 2006b. Hypertension: epidemiology and metabolic abnormalities in Foutah-Djallon in Guinea. Mali. Méd. 21, 19–22.

Burns, D., Reynolds, W.F., F.,W., Buchanan, G., Reese, P.B., et al., 2000. Assignment of ^{1}H and ^{13}C spectra and investigation of hindered side-chain rotation in lupeol derivatives. Magn. Reson. Chem. 38, 488–493.

Camara, A., Baldé, N.M., Diakité, M., Sylla, D., Baldé, E.H., et al., 2016. High prevalence, low awareness, treatment and control rates of hypertension in Guinea: results from a population-based STEPS survey. J. Hum. Hypertens. 30, 237–244.

Cappuccio, F.P., Miller, M.A., 2016. Cardiovascular disease and hypertension in sub-Saharan Africa: burden, risk and interventions. Intern. Emerg. Med. 11, 299–305.

Chatterjee, P., Pezzuto, J.M., Kouzi, S.A., 1999. Glucosidation of betulinic acid by *Cunninghamella* species. J. Nat. Prod. 62, 761–763.

Dewhurst, M.J., Dewhurst, F., Gray, W.K., Chaote, P., Orega, G.P., et al., 2013. The high prevalence of hypertension in rural-dwelling Tanzanian older adults and the disparity between detection, treatment and control: a rule of sixths? J. Hum. Hypertens. 27, 374–380.

Draijer, R., de Graaf, Y., Slettenaar, M., de Groot, E., Wright, C.I., 2015. Consumption of a polyphenol-rich grape-wine extract lowers ambulatory blood pressure in mildly hypertensive subjects. Nutrients 30, 3138–3153.

Dzudie, A., Kengne, A.P., Muna, W.F., Ba, H., Menanga, A., et al., 2012. Prevalence, awareness, treatment and control of hypertension in aself-selected sub-Saharan African urban population: a cross-sectional study. BMJ Open 2, 1217.

Ekanem, U.S., Opara, D.C., Akwaowo, C.D., 2013. High blood pressure in a semi urban community in south-south Nigeria: a community-based study. Afr. Health Sci. 13, 56–61.

Fotie, J., Bohle, D.S., Leimanis, M.L., Georges, E., Rukunga, G., et al., 2006. Lupeol long-chain fatty acid esters with antimalarial activity from Holarrhena floribunda. J. Nat. Prod. 69, 62–67.

Fu, J.-Y., Qian, L.-B., Zhu, L.-G., Liang, H.-T., Tan, N.-Y., Lu, H.-T., Lu, J.-F., Wang, H.-P., Xia, G., 2011. Betulinic acid ameliorates endothelium-dependant relaxation in L-NAME-induced hypertensive rats by reducing oxidative stress. Eur. J. Pharm. Sci. 44, 385–391.

Guerrero, L., Castillo, L., Quinones, M., Garcia-Valve, S., Arola, L., et al., 2012. Inhibition of angiotensin-converting enzyme activity by flavonoids: a structure-activity relationship studies. PLoS One 7 (11), e49493. https://doi.org/10.1371/journal.pone.0049493.

Harborne, J.B., 1973. Phytochemical Methods: a Guide to Modern Techniques of Plant Analysis. Chapman and Hall, London-New York (278p).

Herrera-Arellano, A., Flores-Romero, S., Chavez-Soto, M.A., Tortoriello, J., 2004. Effectiveness and tolerability of a standardized extract from Hibiscussabdariffa in patients with mild to moderate hypertension: a controlledand randomized clinical trial. Phytomed 11, 375–382.

Herrera-Arellano, A., Miranda-Sanchez, J., Avila-Castro, P., Herrera-Alvarez, S., Jimenez-Ferrer, J.E., et al., 2007. Clinical effects produced by a standardized herbal medicinal product of *Hibiscus sabdariffa* on patients with hypertension. A randomized, double-blind, lisinopril controlled clinical trial. Planta Med. 73, 6–12.

Hosoya, T., Yun, Y.S., Kunugi, A., 2005. Five novel flavonoids from *Wasabia japonica*. Tetrahedron 61, 7037–7044.

Ibrahim, H., Sani, F.S., Danladi, B.H., 2007. Phytochemical and antisickling studies of the leaves of *Hymenocardia acida* Tul. (Euphorbiaceae). Pak. J. Biol. Sci. 10, 788–791.

Karou, S.D., Tchacondo, T., Tchibozo, M.A.D., Abdoul-Rahaman, S., Anani, K., et al., 2011. Ethnobotanical study of medicinal plants used in the management of diabetes mellitus and hypertension in the Central Region of Togo. Pharm. Biol. 49, 1286–1297.

Kayima, J., Wanyenze, R.K., Katamba, A., Leontsini, E., Nuwaha, F., 2013. Hypertension awareness, treatment and control in Africa: a systematic review. BMC Cardiovasc. Disord. 13, 1–11.

Kearney, P.M., Whelton, M., Reynolds, K., Whelton, P.,K., He, J., 2004. Worldwide prevalence of hypertension: a systematic review. J. Hypertens. 22, 11–19.

Kumazawa, T., Minatogawa, T., Matsuba, S., Sato, S., Onodera, J., 2000. An effective synthesis of isoorientin: the regioselective synthesis of a 6-C-glucosylflavone. Carbohydr. Res. 17, 507–513.

Lacaille-Dubois, M.A., Franck, U., Wagner, H., 2001. Search for potential angiotensin converting enzyme (ACE)-inhibitors from plants. Phytomed 8, 47–52.

Mahato, S.B., Kundu, A.P., 1994. ^{13}C NMR spectra of pentacyclic triterpenoids-a compilation and some salient features. Phytochemistry 37, 1517–1575.

Mancia, G., Fagard, R., Narkiewicz, K., Redon, J., Zanchetti, A., Bohm, M., et al., 2013. ESH/ESC Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Societyof Cardiology (ESC). J. Hypertens. 31, 1281–1357.

Medina-Remón, A., Estruch, R., Tresserra-Rimbau, A., Vallverdú-Queralt, A., Lamuela-Raventos, R.M., 2013. The effect of polyphenol consumption on blood pressure. Mini Rev. Med. Chem. 8, 1137–1149.

Mensah, J.K., Okoli, R.I., A. A. Turay, A.A., Ogie-Odia, E.A., 2009. Phytochemical analysis of medicinal plants used for the management of hypertension by Esan people of Edo state. Niger.; Ethnobot. Leafl. 13, 1273–1287.

Mojiminiyi, F.B., Dikko, M., Muhammad, B.Y., Ojobor, P.D., Ajagbonna, O.P., et al., 2007. Antihypertensive effect of an aqueous extract of the calyx of *Hibiscus sabdariffa*. Fitoterapia 78, 292–297.

N'Gouin-Claih, A.P., Donzo, M., Barry, A.B., Diallo, A., Kabine, O., et al., 2003. Prévalence de l'hypertension artérielle en milieu rural guinéen. Arch. Mal. Coeur Et. Vaiss. 96, 763–767.

Niakara, A., Fournet, F., Gary, J., Harang, M., Nebie, L.V.A., et al., 2007. Hypertension, urbanization, social and spatial disparities: a cross-sectional population-based survey in a West African urban environment (Ouagadougou, Burkina Faso). Trans. R. Soc. Trop. Med. Hyg. 101, 1136–1142.

Nsuadi Manga, F., El Khattabi, C., Fontaine, J., Berkenboom, G., Duez, P., et al., 2013. Vasorelaxant and antihypertensive effects of methanolic extracts from *Hymenocardia acida* Tul. J. Ethnopharmacol. 2, 623–631.

Nuwaha, F., Musinguzi, G., 2013. Use of alternative medicine for hypertension in Buikwe and Mukono districts of Uganda: a cross sectional study. BMC Complement. Altern. Med. 13, 301.

Nwanna, E.E., Ibukun, E.O., Oboh, G., Ademosun, A.O., Boligon, A.A., et al., 2014. HPLC-DAD Analysis and *In-Vitro* Property of Polyphenols Extracts from (*Solanum Aethiopium*) Fruits on α -Amylase, α -Glucosidase and Angiotensin - 1- Converting Enzyme Activities. Int. J. Biomed. Sci. 4, 272–281.

Olisa, N.S., Oyelola, F.T., 2009. Evaluation of use of herbal medicines among ambulatory hypertensive patients attending a secondary health care facility in Nigeria. Int. J. Pharm. Pract. 17, 101–110.

Onyango, M.J., Kombe, I., Nyamongo, D.S., Mwangi, M., 2017. A study to determine the prevalence and factors associated with hypertension among employees working at a call centre Nairobi Kenya. Pan-Afr. Med. J. 27, 178.

Osamor, P.E., Owumi, B.E., 2010. Complementary and alternative medicine in the management of hypertension in an urban Nigerian community. BMC Compl Altern. Med. 10, 36.

Ottaviani, J.I., Actis-Goretta, L., Villordo, J.J., Fraga, C.G., 2006. Procyanidin structure defines the extent and specificity of angiotensin I converting enzyme inhibition. Biochimie 88, 359–366.

Peng, J., Fan, G., Hong, Z., Chai, Y., Wu, Y., 2005. Preparative separation of isovitexin and isoorientin from Patrinia villosa Juss by high-speed counter-current chromatography. J. Chromatogr. A 1074, 111–115.

Poulter, N.R., Prabhakaran, D., Caulfield, M., 2015. Hypertension. Lancet 386, 801–812.

Rios, M.Y., Lopez-Martinez, S., Lopez-Vallejo, F., Madina-Franco, J.L., Villalobos-Molina, R., Ibarra-Barajas, M., Navarrete-Vasquez, G., Hidalgo-Figueroa, Hernandez-Abreu, O., Estrado-Soto, S., 2012. Vasorelaxant activity of some structurally related triterpenic acids from *Phoradendron reichenbachianum* (Viscaceae) mainly by NO production: *Ex vivo* and *in silico* studies. Fitoterapia 83, 1023–1029.

Saleem, R., Ahmad, S.I., Ahmed, M., Faizi, Z., Zikr-ur-Rehman, S., et al., 2003. Hypotensive activity and toxicology of constituents from Ceiba stem bark. Biol. Pharm. Bull. 26, 41–46.

Seck, I.M., Diop, A.E., Ka, F.E., Doupa, D., Diouf, B., et al., 2016. Antihypertensive efficacy of *Combretum micranthum* and *Hibiscus sabdariffa*: a randomized controlled trial versus ramipril. Nephrol. Dial. Transplant. 31 (Suppl. 1), 120.

Sofidiya, M.O., Odukoya, O.A., Afolayan, A.J., Familoni, O.B., 2009. Phenolic contents, antioxidant andantibacterial activities of *Hymenocardia acida*. Nat. Prod. Res. 23, 168–177.

Somova, L.I., Shode, F.O., Moodley, K., Govender, Y., 2001. Cardiovascular and diuretic activity of kaurene derivatives of *Xylopia aethiopica* and *Alepidea amatymbica*. J. Ethnopharmacol. 77, 165–174.

Tahraoui, A., El-Hilaly, J., Israili, Z.H., Lyoussi, B., 2007. Ethnopharmacological survey of plants used in the traditional treatment of hypertension and diabetes in south-eastern Morocco (Errachidia province). J. Ethnopharmacol. 110, 105–117.

Tra, Bi, F.H., Irié, G.M., N'Gaman, K.C.C., Mohou, C.H.B., 2008. Études de quelques plantes thérapeutiques utilisées dans le traitement de l'hypertension artérielle et du diabète: deux maladies émergentes en Côte d'Ivoire. Sci. Nat. 5, 39–48.

Tuenter, E., Exarchou, V., Baldé, A., Cos, P., Maes, L., Sandra Apers, S., Pieters, L., 2016. Antiplasmodial cyclopeptide alkaloids from root bark of *Hymenocardia acida*. J. Nat. Prod. 79, 1746–1751.

Tuenter, E., Exarchou, V., Apers, S., Pieters, L., 2017. Cyclopeptide Alkaloids. Phytochem. Rev. 16, 623–637.

Upadhyay, S., Dixit, M., 2015. Role of Polyphenols and Other Phytochemicals on Molecular Signaling (Article ID 50425). Oxid. Med. Cell. Longev. 15. https://doi.org/10.1155/2015/504253.

Wagner, H., Bladt, S., 1996. Plant Drug Analysis, 2nd ed. Springer Verlag, Berlin, Heidelberg, New York, pp. 3–6.

World Health Organization (WHO), 2013. A global brief on Hypertension: silent killer, global public health crisis (39 pages).

Yayehd, K., Damorou, F., Akakpo, R., Tcherou, T., N'Da, N.W., et al., 2013. Prevalence and determinants of hypertension in Lome (Togo): results of a screening in May 2011. Ann. Cardiol. Angiol. 62, 43–50.

Yoon, J.J., Lee, Y.J., Han, B.H., Choi, E.S., Kho, M.C., Park, J.H., Ahn, Y.M., Kim, H.Y., Kang, D.G., Lee, H.S., 2017. Protective effect of betulinic acid on early atherosclerosis in diabetic apolipoprotein-E gene knockout mice. Eur. J. Pharmacol. 796, 224–232.