Chapter 20

Voacanga africana: Chemistry, Quality and Pharmacological Activity

Adolfina R. Koroch[1], H. Rodolfo Juliani[1], Daniel Kulakowski[1], Hanson Arthur[2], Juliana Asante-Dartey[3] and James E. Simon[1]

[1] New Use Agriculture and Natural Plant Products Program, School of Biological and Natural Resources, and the New Jersey Agricultural Experiment Station (NJAES), Rutgers, The State University of New Jersey, 59 Dudley Road, New Brunswick, NJ 08901-8520
[2]ASNAPP-South Africa, Stellenbosch, South Africa
[3]ASNAPP-Ghana, Accra, Ghana

Publication Date (Web): December 20, 2009 | doi: 10.1021/bk-2009-1021.ch020

This review examines the natural products in *Voacanga africana*, a small tree, whose seeds are the most economically important plant part though in traditional medicines the bark and root are also widely used. Voacanga is used to treat or cure a wide range of diseases in Africa. This paper also discusses the botany, chemistry and pharmacological properties and presents current and potential applications of this species. The alkaloids are the principal bioactive compounds responsible for its use in traditional medicine. The major alkaloids include voacamine, voacangine, vobasine, and ibogaime. Others include voacristine, voacamidine, voacarine, voaphylline, vobtusine, voalfolidine and tabersonine. With over 1,600 tons of seeds exported annually from Ghana and Cote D'Ivoire, voacanga is an important source of additional income for harvesters and exporters in West Africa.

Introduction

Voacanga africana is a small tree or shrub, reaching up to 6 meters in height with a low widely spreading crown. The leaves are opposite, obovate and acuminate. They are dark green and glossy above greenish-green below, usually

In African Natural Plant Products: New Discoveries and Challenges in Chemistry and Quality; Juliani, H., et al.; ACS Symposium Series; American Chemical Society: Washington, DC, 2010.

stalkless. The flowers are white borne in axiliary or terminal loosely branched glabrous inflorescences. The fruits occur mainly in pairs, spherical, mettled green with seeds wrapped in yellow pulp (*1*) (Figure 1). The seeds are the most economically important part of the plant though the bark and roots are also widely used in traditional medicines. The seeds are numerous, dark brown and ellipsoid in shape and embedded in pulp. The seeds are important annual source of additional income for harvesters and exporters in West Africa. Voacanga is sometimes planted in newly established cocoa plantations to provide shade in the first three years of establishment and finds ready use as stakes for yams. Field observation revealed that a fully grown plant yields between 2,000 - 3,000 pods. About 110-120 pods yield a kilogram of the dry seeds which gives an estimated yield of 10-23 kg/tree of seeds per plant or approximately 800-1,200kg/acre.

Traditional Uses

In Cote d' Ivore voacanga is traditionally used against leprosy, diarrhea, generalized edema, convulsions in children, madness, diuretic and infant tonic (*1-3*). Bark or root bark decoctions is drunk for cardiac spams, stomac, hernia and post partum pain, kidney troubles (*3*).

A decoction of the stem bark and root is used in the treatment of mental disorders. The latex is applied to carious teeth. A decoction of the bark is considered an analgesic and is added to embrocation mixtures used as pastes during fracture repair. In southeastern Nigeria the plant is featured in many healing rituals (*1*). Also it used to induce hallucinations and trances in religious rituals.

Also, in Congolese traditional medicine macerations of root bark of *V. africana* are used as anti- amoebial. Intestinal amoebiasis is one of the current diseases in tropical regions causing diarrhea (*4*).

Figure 1. Voacanga fruits, characteristically spherical, mettled green with seeds wrapped in yellow pulp.

Habitat and Harvesting

Voacanga africana is distributed mainly in West Africa though reaching as far as the Congo and east to Tanzania. The plant is widely distributed over secondary forests and transitional zones. It grows in the wild and is therefore subject to degradation by land clearance for farming, bushfires and unsustainable harvesting methods.

The maturity of the pods and harvesting periods vary with ecological zones and rainfall patterns. However, voacanga generally flowers in May and matures in July. The harvesting season extends from July to September. A fully-matured pod will show signs of cracking along the cleavage line.

Harvesting is done by climbing the trees to pluck the pods or pollarding the fruit-bearing branches. Pickers sometimes cut down the tree to harvest the fruits – a practice which depletes stocks in the wild and is unsustainable. A few people pluck the fruits with long sticks.

At present, there are no national and international standards nor are there any grades and norms in handling and processing the seeds, the product of commerce. This work aims to review the chemistry and pharmacological activity and develop quality control standards (QC) for *V. africana* seeds that can be used in the development of standards and norms and also to identify potential pharmacological uses of the seeds. The development of QC will help to determine the best harvesting conditions and post-harvest handling methods which will provide the optimum levels of the important chemical composition for the buyer as well as high yields for the supplier. Seed moisture content, density, clustering levels, and ash levels were investigated.

Materials and Methods

A total of 26 samples of dry seeds of Voacanga from six endemic regions in Ghana were included in this study. All procedures were run in quadruplicate.

For moisture content, seeds were dried in an oven at 85°C for 5 days to a constant dry. The loss of weight after drying was expressed as moisture percent. A sieve test was conducted to determine the relative amounts of seed clusters, whole seeds and broken seeds in the samples of *V. africana*. Two US standard sieves (size 4, opening 4.75 mm and size 10, opening 2 mm) were used to separate the samples in three groups; particles higher than 4.75 mm (seed clusters), particles between 4.75 and 2 mm (whole seeds, broken seeds), particles less than 2.0 mm (fine particles and other foreign matter). All seeds were inspected and foreign material separated. The densities of the seeds were calculated according to the weight and volume of each sample.

Total ashes and acid insoluble ashes were calculated according to the Food Chemicals Codex (*5*). Ground voacanga seeds (2 g) were placed in ceramic crucibles and then ignited at 600°C, the ashes were then dissolved in a hydrochloric acid solution, filtered and the crucible ignited at 650°C to obtained the acid insoluble ashes that represent the contamination with sand and earths. Total seed alkaloids concentration was measured according to Sreevidya and Mehrotra (*6*).

Results and Discussion

Most of Voacanga seeds have a brown color; the moisture content was below the 12%, the maximum percentage according to international standards for botanical products. Only 5 samples exceeded that amount (Table I), indicating that these seeds were improperly dried. High moisture content can decrease shelf life due to microbial growth and enzymatic reaction, leading to seed deterioration.

Regarding to the total ashes and insoluble ashes we observed that 38% of the samples showed high levels of acid insoluble ashes (Table I).

The amounts of seeds cluster is an important quality parameter, since seeds harvested from immature trees form tight clusters; very difficult to separate. When seeds are harvested immature, they are literally piled-up and allowed to ferment to facilitate their separation (Figure 2). This is not a recommended practice, since the fermentation may degrade the active principles. The amount of seed clusters among the samples was highly heterogeneous ranging from 3 (sample 4) to 89 % (sample 7) (Table II). Almost 46 % of the samples showed levels higher than 30% of clusters, suggesting that these seeds were collected from immature fruits. Only 6 samples exhibited the presence of high levels of broken seeds, indicating that these seeds were broken when collectors were trying to disaggregate the clusters.

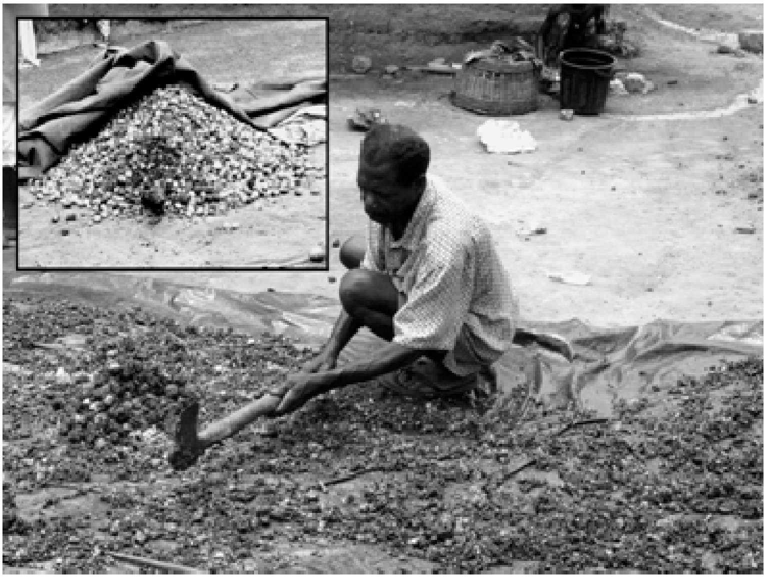

Figure 2. Immature seeds are collected, pilled up and covered to allow fermentation. After this fermentation, the seed clusters are disaggregated with the help of a tool.

Significant amount of seeds (27%) showed low densities (less than 0.4 g/ml). Our results, suggest that seed density could be a useful parameter to evaluate the quality of whole seeds since low density seeds seem to correlate with high amounts of clusters and thus immature seeds (Table II).

Table I. Color, Moisture, Total Ashes and Acid Insoluble Ashes of *Voacanga africana* from Ghana

Spl[1]	Location and Region	Color	Moisture (%)	Total ashes (%)	Acid insoluble ashes (%)
1	Tema (GAR)	dark brown-gray	10.6 ± 0.7[2]	3.6 ± 0.1	0.5 ± 0.0
2	Tema (GAR)	dark brown	13.9 ± 0.1	2.7 ± 0.0	0.5 ± 0.3
3	Tema (GAR)	light brown	9.4 ±0.1	3.2 ± 0.1	0.7 ± 0.3
4	Nsuhia (BAR)	light gray	10.6 ±0.1	3.9 ± 0.0	0.8 ± 0.1
5	Nwonmaso (CR)	dark brown	10.6 ± 0.1	3.2 ± 0.3	1.0 ± 0.4
6	Agogo (AR)	dark brown	9.9 ±0.2	5.0 ± 0.3	1.4 ± 0.0
7	Agogo (AR)	gray-brown	10.1 ±0.4	6.2 ± 1.8	1.5 ± 0.4
8	Nkrankwanta (BAR)	black	9.9 ± 0.05	9.0 ± 0.5	1.3 ± 0.2
9	Nkrankwanta (BAR)	very light gray	8.4 ± 0.1	3.2 ± 0.1	0.8 ± 0.2
10	Nkrankwanta (BAR)	brown	8.6 ± 0.4	6.8 ± 2.0	2.3 ± 0.7
11	Nkrankwanta (BAR)	light and dark gray	9.1 ± 0.03	4.9 ± 0.4	1.8 ± 0.7
12	Bepong (ER)	light gray-brown	8.4 ± 0.4	3.7 ± 0.1	0.6 ± 0.1
13	Bepong (ER)	dark brown	10.5 ± 0.2	2.5 ± 1.7	0.3 ± 0.5
14	Anyan-Denyira (CR)	dark brown	10.5 ± 1.02	3.0 ± 0.1	0.5 ± 0.1
15	Obo (ER)	dark brown	8.3 ± 0.2	2.9 ± 0.1	0.3 ± 0.0
16	Obo (ER)	light gray	8.2 ± 0.1	3.8 ± 0.4	0.9 ± 0.1
17	Obo (ER)	dark brown-black	9.1 ± 0.4	4.1 ± 0.0	0.7 ± 0.1
18	Kasapi (BAR)	gray-brown	9.7 ± 0.2	4.4 ± 0.4	1.6 ± 0.2
19	Kasapi (BAR)	very dark brown-black	10.8 ± 0.3	5.7 ± 0.2	1.7 ± 1.1
20	Ampaha (AR)	light-dark brown	19.0 ± 6.0	2.8 ± 0.0	0.6 ± 0.2
21	Ampaha (AR)	dark brown-black	11.6 ± 0.5	4.5 ± 0.1	1.7 ± 0.1
22	Sunyani (BA)	dark brown	9.3 ± 0.6	4.7 ± 0.4	1.3 ± 0.3
23	Ayiem (WR)	dark brown	15.5 ± 0.9	2.6 ± 0.0	0.6 ± 0.2
24	Hohoe (VR)	dark brown	14.0 ± 0.4	2.5 ± 0.3	0.6 ± 0.0
25	Togo	brown-black	12.4 ± 0.1	3.6 ±0.0	0.9 ± 0.1
26	Togo	light brown-gray	11.3 ± 0.3	3.8 ±0.0	1.9 ± 0.4

NOTE: [1]. Sample number. [2]. Average Value ± Standard Error. GA, Greater Accra Region, BAR, Brong Ahafo, CR, Central, AR, Ashanti, ER, Eastern, WR, Western Region, VR, Volta.

Table II – Percentage of Seed Clusters, Whole, Broken Seeds, Density and Alkaloid Content from *Voacanga africana*

Spl[1]	Average Seed Clusters %[2]	Average Whole Seeds %	Average Broken Seeds %	Average Density (g/ml)	Total alkaloids (%)
1	16 ± 1.3[3]	82.5 ± 1.3	1.2 ± 0.2	0.51 ± 0.14	0.9 ± 0.0
2	54.3 ± 0.4	44.9 ± 0.1	-	0.45 ± 0.01	0.5 ± 0.1
3	13.7 ± 4.1	85.9 ± 3.6	-	0.47 ± 0.02	0.6 ± 0.0
4	3.1 ± 2.4	96.6 ± 2.1	0.2 ± 0.06	0.47 ± 0.01	1.2 ± 0.1
5	15.1 ± 4.6	84.6 ± 4.4	0.7 ± 0.2	0.49 ± 0.01	0.4 ± 0.0
6	39.8 ± 18.1	59.2 ± 19.1	0.4 ± 0.09	0.5 ± 0.01	0.2 ± 0.0
7	89 ± 3	10.5 ± 3.1	0.5 ± 0.06	0.33 ± 0.00	1.2 ± 0.2
8	53.4 ± 3.4	46.1 ± 3.4	1.1 ± 0.6	0.41 ± 0.06	1.5 ± 0.2
9	8.3 ± 4.5	90.4 ± 4.7	1.8 ± 1.2	0.42 ± 0.01	0.8 ± 0.3
10	24.2 ± 7.1	74.9 ± 8.1	0.9 ± 0.03	0.47 ± 0.01	0.5 ± 0.2
11	28.9 ± 14.6	70.6 ± 14.4	0.4 ± 0.2	0.39 ± 0.01	0.9 ± 0.3
12	69.6 ± 4.7	29.6 ± 5.2	0.4 ± 0.2	0.41 ± 0.01	0.9 ± 0.1
13	37.7 ± 0.9	61.7 ± 1.1	0.4 ± 0.3	0.47 ± 0.01	0.5 ± 0.1
14	52.4 ± 0.6	46.8± 1.1	0.1 ± 0.04	0.39 ± 0.03	0.7 ± 0.1
15	65.1 ± 13.2	34.8 ± 13.1	0.1 ± 0.04	0.46 ± 0.01	0.3 ± 0.1
16	20.2 ± 5.8	79.5 ± 5.8	0.2 ± 0.01	0.53 ± 0.00	0.4 ± 0.2
17	38.8 ± 1.5	60.5 ± 1.8	1 ± 0.1	0.3 ± 0.01	1.0 ± 0.3
18	16.6 ± 8.2	81.5± 5.1	0.8 ± 0.4	0.37 ± 0.05	0.2 ± 0.1
19	27.6 ± 5.2	69.1 ± 3.5	2.5 ± 0.7	0.21 ± 0.08	0.3 ± 0.1
20	53.3 ± 2.2	46.5 ± 2.1	0.3 ± 0.2	0.47 ± 0.00	0.3 ± 0.0
21	10.6 ± 0.1	84 ± 3.5	2.2 ± 0.09	0.27 ± 0.01	0.9 ± 0.1
22	12.8 ± 7.3	87.1 ± 7.3	-	0.48 ± 0.02	0.3 ± 0.1
23	84.6 ± 3.4	15 ± 3	-	0.56 ± 0.04	0.2 ± 0.1
24	33.5 ± 1.2	66.2 ± 1.2	0.02 ± 0.01	0.56 ± 0.01	0.4 ± 0.1
25	15.6 ± 3.9	84 ± 4.1	0.2 ± 0.04	0.48 ± 0.00	0.6 ± 0.3
26	22.1 ± 4.1	77.5 ± 4.2	0.1 ± 0.07	0.49 ± 0.00	0.3 ± 0.1

NOTE:[1.] Sample number. [2]% is of total weight. [3]Average values ± Standard Error.

According to the number of whole seeds, samples 4 and 9 appear to be the best quality samples (Table II). The seeds were light gray in color. Sample 9 also showed high levels of broken seeds (1.8%), as well as samples 19 (2.5%) and 21 (2.2%). An acceptable value of broken seeds will be 1% or less.

Another important, classic and simple quality control parameter is the total ashes and insoluble ashes (Table I). We observed that 38% of the samples showed high levels of acid insoluble ashes indicating that they are contaminated with earth and/or sand. The results suggest that these samples were dried on the bare ground. Interventions easy to overcome the presence of sand and other soil contaminants would be to ensure all seeds are dried on materials off the ground.

Total insoluble ashes, or sand content, should be less than 1% of the ground seeds for economic reasons. Botanical products are purchased on a weight value; thus, if a large amount of sand is present in the product then the buyer is paying for a percentage of sand and not the product. As an example, one-ton sample of the seeds having a value of insoluble ashes of 3% will contain 30 kg of sand.

The total alkaloids in Voacanga seeds ranged from 0.2% to 1.5% (Table II). Highest content of alkaloids were found in samples 7 (1.2%) and 8 (1.5%).

In this initial study, there was no clear relationship between the selected quality control parameter and the alkaloid content and thus the total amount of alkaloid was not found to be correlated with the harvesting and processing of the seeds. The observed differences could be related with high genetic variation in the alkaloid content in the selected populations.

Our results suggest that the best postharvest handling method for Voacanga seeds is simply to use the seeds from mature pods, to avoid the formation of seed clusters, and subsequent fermentation that lead to seed deterioration, and which later involve additional labor. The mature seeds tend to be of higher density; being heavier than the immature seeds. Thus, the seed clusters and seed density are important parameters to assess the quality of voacanga seeds. To avoid excessive contamination with sand, the voacanga seeds need to be dried in raised platforms to avoid contact of the seeds with the bare ground. Field research has shown that by harvesting immature seeds, collectors/growers lose 40-50% of the potential yields from same population/plant

In summary, to better asses the quality of *V. africana* seeds, we propose additional standards, such as percent of clusters, density, ashes and total alkaloids (Table III). In Ghana, the seeds are purchased according to their weight. Thus, the seed clusters and seed density are important parameters to assess the quality of voacanga seeds.

Table III. Proposed Quality Control Standards for *Voacanga africana* Seeds

Characteristic	*Voacanga seeds*
Organoleptic evaluation	
Color	Dark brown or brown
Macroscopic and sieve analysis	
Extraneous/foreign matter content, % (m/m) max.	0.5
Damaged seeds, % (m/m) max.	0.5
Percent of clusters (particles > 4.75mm), % (m/m)	30
Physical-Chemical parameters	
Seed density (g/mL), min.	0.4
Moisture (%, m/m) max.	12
Total ashes, %(m/m) max.	4
Total insoluble ashes, %(m/m) max.	1
Total alkaloids, %(m/m) min.	0.5

Chemical Composition of *Voacanga* Species

Different chemical components have been isolated from different organs of *Voacanga* species. The presence of flavonoids, tannins, phenols, steroids and terpenes, alkaloids has been reported in the leaves, seeds, stem bark and roots (*4, 7, 8*).

In the past decades, many studies were conducted and reported that focused on the identification of the wide array of *V. africana* alkaloids and the main ergot alkaloids have been isolated. With the improvement of the isolation procedures many minor components have been identified (Table IV). Voacanga alkaloids have been isolated from leaves, seeds (mature and inmature), trunk and root bark (Table IV).

Analysis of root and bark extracts of *V. africana* showed the presence of the alkaloids voacamine, voacangine, and vobasine as the principal ones (*9*). Other compounds found in the plant include voacristine, voacamidine, and voacarine. Voaphylline, vobtusine, voalfolidine occur in the leaves and tabersonine is a constituent of the seeds (*1, 10*). Also the presence of ibogaine has been obtained from bark (*11*) and seed (*12*). Many papers have been published with the structural determination of minor ergot alkaloids occurring in *Voacanga* species (Table IV). Alkaloids found in Voacanga have also been found in other species of the family Apocynaceae (Table V).

Table IV. Isolated Alkaloids in *Voacanga* spp. and the Main Organ of Accumulation and Distribution

Alkaloid	*Organ distribution*	*Reference*	*Species/Sources*
amataine	Root bark	13	*V. chalotina*
-(-) tabersonine	Cell culture	14	*V. africana*
folicangine	Leaves	10,15	*V. africana*
isovoafoline		10	*V. africana*
O methyl 16 epi vincanol	seed	16	*V. africana*
subsessiline		10	
subsessiline lactone		10	
vincamol	seed	16	*V. africana*
vincamone	seed	16	*V. africana*
voacafricine	bark	17	*V. africana*
voacafrine	bark	17	*V. africana*
voacamine	Stem, bark	18, 19	*V. africana*
	Bark	11	*V. thousarsii*
		9, 20	*V. africana*
		21	*V. braceata*
voacangine	Trunk bark	22	*V. africana*
	Bark	11	*V. thousarsii*
		9, 20	*V. africana*
		21	*V. braceata*
voacangine hydroxyindolenine	Tree bark	20, 23	*V. africana*
vacorine		19	*V. africana*
		10	*V. africana*
		1	
		20	*V. africana*
		19	*V. africana*
voacristine		23-25	*V. africana*
	Bark	11	*V. thousarsii*
	Bark and bark root	1, 10, 20, 24, 26	*V. africana*
voacamidine	Bark and bark root	1, 10, 24, 26, 27,	*V. africana*
voacryptine		26	*V. africana*

In African Natural Plant Products: New Discoveries and Challenges in Chemistry and Quality; Juliani, H., et al.;
ACS Symposium Series; American Chemical Society: Washington, DC, 2010.

Table IV. Continued.

Alkaloid	*Organ distribution*	*Reference*	*Sources*
voafolidine	leaf	10	*V. africana*
voafoline	leaf	10	*V. africana*
vobasine		9, 20, 23	*V. africana*
vobtusine		10	*V. thousarsii*
	Bark	11	*V. thousarsii*
	leaves	10, 28	*V. africana*
	Bark	13	*V. chalotina*
		1, 20	*V. africana*
vobtusine-lactone	leaves	28	*V. africana*
deoxyvobtusine	leaves	28	*V. africana*
vobtusine 3-lactam Nb'-oxide		10	*V. africana*
vobtusine 3-lactam,		10	*V. africana*
ibogaine	Bark	11	*V. thousarsii*
	seeds	12	*V. africana*
iboluteine	Bark	11	*V. thousarsii*
18'-decarbonethoxyvoacamine	Bark	11	*V. thousarsii*
voaluteine	Bark	11	*V. thousarsii*
20' hydroxyl-voacamine	bark	29	*V. africana*

Table V. Voacanga Alkaloids Reported in Other Species of the Apocyanceae Family

Alkaloid	*Organ*	*Reference*	*Source specie*
amataine	roots	30	*Hedranthera barteri*
voacamine	Bark, stem	31	*Ervatamia coronaria*[1]
		32	*Peschiera laeta*[2]
		33	*P. fuchsiaefolia*
voacangine	Stem, bark	22, 34	*Tabernaemontana australis*
	Bark, stem		
		35	*T. hilariana*
	Leaves, inmature fruits	36	*T. calcarea*
		37	*P. fuchsiaefolia*
vobasine		9, 20	*Voacanga africana*
vobasine	leaves	38	*T. corymbosa*
voacristine	Stem, bark	39	*Pechiera buchtiene*
	Leaves, fruits	36	*T. calcarea*
	stem	31	*E. coronaria*
voacamidine	Stem, bark	39	*P. buchtiene*
voacorine		21	*T. braceata*
voaphylline	Stem, bark	34	*P. buchtiene*
	leaves	40	*T. divaricata*
vobatricine	Stem, bark	38	*T. corymbosa*
vobasonidine	leaves	38	*T. corymbosa*
ibogaine		22, 41	*T.iboga*
		34	*T. australis*
ibogamine		34	*T. australis*
		22	*T. iboga*
		39	*P. buchtiene*
		35	*T. hilariana*
		36	*T. calcarea*
		37	*T. fuchsiaefolia*
ibogaline		34	*T. australis*
		22	*T. iboga*

SOURCE: [1]*Ervatamia coronaria* (Jacq) Stapf (syn. *Tabernaemontana divaricata* R.Br. ex Roem. et Schult.) [2] *Peschiera* syn. *Tabernaemontana*

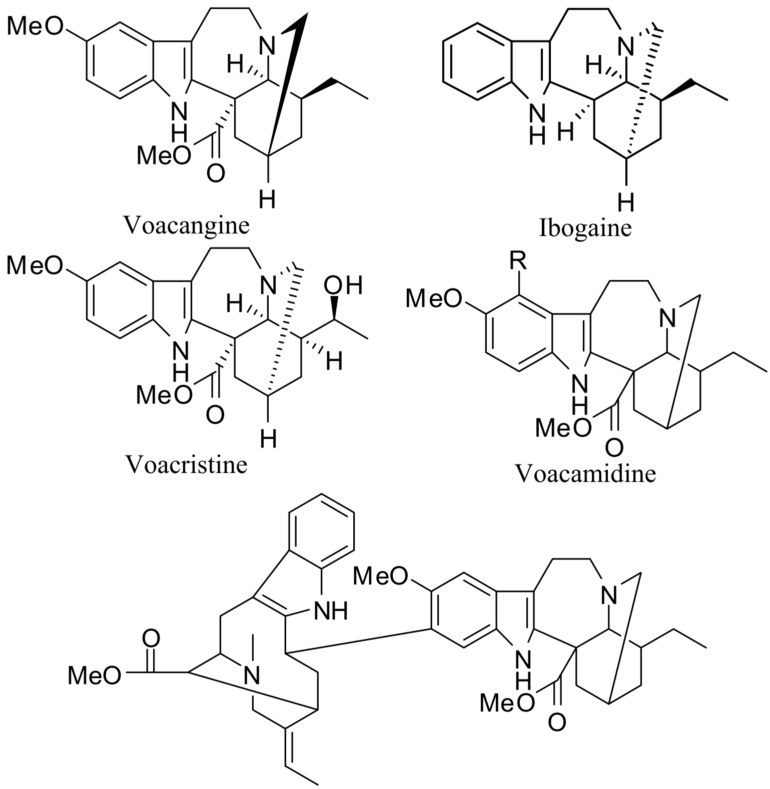

Figure 3. Chemical structures of some alkaloids isolated from Voacanga africana.

Pharmacological Activity of Voacanga Alkaloids

Traditional medicines based upon single or a mixture of plants is still commonly used across Africa, playing a significant role in the primary health care of the population. Traditional medicine is deeply rooted in a specific socio-cultural context, and thus is different among the communities yet an integral part of the family, community, village, and nation (*3, 42, 43, 70*).

The majority of plants used in traditional medicine are directly collected from the wild with few cultivated. The most common plant remedies are used as infusions, powders, decoctions (boiled for few minutes or hours), macerations (steeped in cold water for a period of time), added in foods or drinks (*3*).

Among the natural products that can be isolated from *Voacanga* species, it is the alkaloids which account for the wide range of pharmacological activies and thus medicinal uses. For instance, the bisindole alkaloid amataine isolated from Voacanga exhibited cytotoxicity effects *in vitro* and could be used in chemotherapy as cytotoxic group (*44*).

Voacamine, extracted from *Peschiera fuchsiaefolia,* has shown anticancer activity by enhancing the cytotoxic effect of DOX on Muti drug resistant cells by favouring a lethal autophagic process (*33*). Voacamine extracted from *V. africana* or *P. fuchsiaefolia* has shown imnostimulant activity, by modulating and reinforcing the immune system, thus with anti- HIV properties. The mechanism of actions was associated with an increase of TH1 cell levels relative to TH2 cells (*45*).

A mixture of alkaloids from *V. africana* and *V. obtuse* have been shown to have cardiotonic, sympatholytic and hypotensive properties (*9, 46, 47*).

In Nigeria, fruits of *V. zenkeri* have been successfully used to treat lumbago and arthritis associated with different type of cancers and inflammatory diseases (*48*). In Cameroon, *V. africana* seeds extracts are used in traditional medicine to treat orchitis, tooth decay and gonorrhea, and these uses were related to the antimicrobial and antifungal activity of the extracts (*7*). An infusion based on the bark from *V. africana* has been used for the relief stomach complaints and root decoctions for hernia pain and kidney troubles (*3*).

The antiulcerogenic effect of the bark of *V. africana* was also reported using different experimental models. Tan and collaborators (*2, 49*) showed the cytoprotection of aqueous extracts for the gastric mucosa against erosive action of corrosive agents (HCl/ EtOH). Thus, *V. africana* possess anti-ulcer properties and these properties were not related with an increase on mucus production, or reduced pepsin activity, however the cytoprotection was related to a mechanism involving the physico–chemical re-enforcement of the gastric mucous layer.

Ibogaine is a psychoactive indole alkaloid and powerful hallucinogens (*50*). Ibogaine appears to be the main alkaloid in the root of *Tabernanthe iboga*, a naturally occurring shrub from Africa. The root bark of *T. iboga* has been used for many centuries in West African ceremonies. Of interest, is that ibogaine induces several peripheral and central nervous system (CNS) effects, one of which is effective in the treatment of withdrawal symptoms and to reduce the cravings in drug addicts (*51*). Modern studies showed that ibogaine was able to interrupt addition to heroin (*52, 53*), cocaine (*54, 55*), amphetamine (*54*), nicotine (*56*), alcohol (*57*) in animals and humans (*50, 58, 59*).

V. braceata has been identified as an African botanical with hallucigenogenic potential. Stem barks of *V. braceata* contain 2.46% of alkaloids mainly voacamine/voacamine N-oxide, 20- epi voacamine and voacangine, although these alkaloids are related with ibogaine, it was concluded that there is no evidence of hallucinogenic properties reported De Smet (*21*).

Ibogaine and voacangine (one of the major alkaloid in voacanga) are closely related. Voacangine differes from iboagine in that voacangine contains an additional carboxy function (*60*). Recently, it was reported the semisynthesis of ibogaine from voacangine, obtained from bark trunk of *V. africana,* as the most promising alternative source of ibogaine (*22*). Also, it was reported the presence of the alkaloid ibogaine, in seeds and bark of voacanga (*11, 12*), supporting thus its use in ritual in tradicional medicine.

Malaria is an important parasitic disease and extensive attention has been gained in the last years (*61, 62*). Many drugs are suitable to treat malaria disese in modern therapy. Because of the rapid development of resistance toward current drugs, traditional remedies have been an important source of antimalarial drugs and provide novel and effective treatments (*61*). The bisindole alkaloid voacamine exhibit *in vitro* antiplasmodial activity against chloroquine sensitive D_6 and chloroquine resistant W_2 strains (*63, 64*). *In vivo* antiplasmodial activity of voacamine was less pronounced than that of the reference antimalarial chloroquine. This result was associated with the potential effect on nuclear division of parasite, possibly with the DNA and or protein synthesis (*65*). Moreover, voacamine, and voacamine isomers has been reported as effective to prevent or treat malaria and are non-toxic. These compounds can be combined with other effective drugs such as chloroquine, arthemisin and qinghaosu (*66*). Such studies strongly suggest additional research is warranted as the search for new antimalarial agents continues worldwide. Voacamine and its derivatives isolated from *Peschiera* or *Voacanga* may also have application and used directly as antimicrobial, antiparasitic or antiviral agents (*67*).

Extracts of the root bark of *V. africana* has demonstrated *in vitro* active antiamoebic activity (MIC =62.5 µg/ml) against *Entamoeba histolytica* supporting its' traditional use as antidiarroheic medicine (*4*). Recently, Tan and collaborators (68) reported that methanolic extracts of *V. africana* bark exhibited antimicrobial activivity against *Helibacter pylori* (human pathogen associated with gastro duodenal ulcers (*69*) and *Campylobacter jejuni*, thus providing a rationale for the wide traditional use of stem bark in traditional management of peptic ulcer disease. Moreover, these same researchers reported voacanga extracts were active against *Pseudomonas aeruginosa, Klebsiella pneumonia, Alcaligenes spp*, suggesting the possible presence of broad spectrum of antimicrobial principles.

Extracts of *V. africana* are used to treat AIDS. Phytochemical screening revealed the presence of important antioxidant bioactive molecules such as tannins, flavonoids and phenols in bark extracts (*8*). They concluded that the antioxidant activity in this medicinal plant may be a contributing factor to its therapeuctic applications. Additional medicinal applications of Voacanga have been reviewed in relation to other African medicinal plants (*3, 70*).

Conclusions

Voacanga is a well known and respected African medicinal plant used in many West African countries for a wide variety of applications. The biological activity is due largely to the presence of alkaloids found in the seeds, bark and roots. There is a quantitative and qualitative difference in alkaloid content and composition by plant tissue and species. Sustainable harvest and preservation of this key African medicinal strongly suggests that Good Agricultural and Collection Practices as recommended by the WHO should be followed (*71*). The original research presented here as well as the review of the botany, chemistry and Pharmacognosy were to assist in the development of grades and standards for the raw Voacanga seed. High quality seed well defined and characterized is just one step in the larger quality control of the final extractable alkaloids or in the standardization of the seeds and the seed extracts.

Acknowledgements

We thank the Ghanaian communities involved in these collection and commercialization studies. We also thank our ASNAPP-Ghana team who assisted in the collection and gathering of all Voacanga samples used in this study as well as some literature and field information. This work was funded by USAID, Office of Economic Growth, Agriculture and Trade (EGAT/AG) (Contract Award No. AEG-A-00-04-00012-00) in support of our Partnership for Food and Industry in Natural Products (PFID/NP) project which is part of their global economic development programs. We thank Carol Wilson, USAID Chief Technical Officer of our PFID/NP project. We also thank Jerry Brown, our original USAID project officer for his support and encouragement. This work originally began as part of the Agri-business in Sustainable African Natural Plant Products Program (ASNAPP) with funding from the USAID (Contract Award No. HFM-O-00-01-00116). We thank the Ghana Export Promotion Council, the Ghana Export Development and Investment Fund, the Ghana Forestry Commission, The Ghana Ministry of Trade and Industry, the Ghana Standards Board, the Trade Investment Program for Competitive Export Economy (TIPCEE), the Ghana Federation of Traditional Medicine, and the Practitioners and Botanical Products Association of Ghana. We also recognize the support received from the New Jersey Agricultural Experiment Station, Rutgers University and our New Use Agriculture and Natural Plant Products Program (NUANPP) for their support of this project and to the honors program at Rutgers under which Daniel Kulakowski's honors research was conducted.

References

1. Iwu, M. M. *Handbook of African Medicinal Plants*. CRC Press, Inc. Florida, 1993, p. 257.
2. Tan P.V.; Penlap, V.B.; Nyasse, B.; Nguemo, J.D.B. *J. Ethnopharmacol.* **2000,** *73*, 423-428.
3. Neuwinger, H.D. *African traditional medicine. A dictionary of plant use and applications.* Medpharm Scientific publishers: Stuttgart, Germany, **2000,** pp. 556.
4. Tona, L.; Kambu, K.; Ngimbi, N.; Cimanga, K.; Vlietinck, A.J. *J. Ethnopharmacol* **1998,** *61*, 57-65.
5. Food Chemical Codex **1996**. Committee on Food Chemical Codex. National Academy Press: Washington, DC.
6. Sreevidya, N.; Mehrotra, S. *J. AOAC Int.* **2006,** *86*, 1124-1127.
7. Gangoue-Pieboji, J.; Pegnyemb, D.E.; Niyitegeka, D.; Nsangou, A.; Eze, N.; Minyem, C.; Mbing, J.N.;' Ngassam, P.; Tih, R.G.; Sodengam, B.L.; Bodo, B. *Ann. Trop. Med. Parasit.* **2006**, *100*, 237-243.
8. Agbor, G.A.; Kuate, D.; Oben, J.E.. *Pakistan Journal of Biological Sciences* **2007,** *10*, 537-544.
9. Oliver-Bever, B. *Medicinal Plants of Tropical West Africa*. Cambridge University Press. London, 1986, p. 375.
10. Rolland, Y.; Kunesch, N.; Poisson, J.; Hagaman, E. W.; Schell, F.M.; Wenkert, E. *J. Org. Chem.* **1976,** *41*, 3270-3275.
11. Goldblatt, A.; Hootele, C.; Pecher, J. *Phytochemistry* **1970,** *9*, 1293-1298.
12. Kombian, S.B.; Saleh, T.M.; Fiagbe, N.I.Y.; Chen, X.H.; Akabutu, J.J.; Buolamwini, J.K.; Pittman, Q.J. *Brain Research Bulletin* **1997,** *44*, 603-610.
13. Bruno D.; Giordano, L.; Giovanni, P. *Heterocycles* **1980,** *14*, 201-203.
14. Stockigt, J.; Pawelka, J-H.; Rother, A.; Deus, B. *Z. Naturforsch* **1982,** *37c*, 857-860.
15. Kunesh, N.; Rolland, Y.; Poisson, J.; Majumder, P.L.; Majumder, R.; Chatterjee, A.; Agwada von, V.C.; Naranjo, J.; Hesse, M.; Schmid, H.. *Helv. Chim. Acta* **1977,** *60*, 2854-5859.
16. Pegnyemb, D.E.; Ghogomu, R.T.; Sondengam, B.L. *Phytother. Res.* **1999,** *70*,446-448.
17. Rao, K.V. *J. Org. Chem.* **1958,** 23, 1455-1456.
18. Buchi, G.; Manning, R.E.; Monti, S.A. *J. Am. Chem. Soc.* **1963,** *85*, 18993-1894.
19. Buchi G.; Manning, R.E.; Monti, S.A. *J. Am. Chem. Soc.* **1964,** *86*, 4631-4641.
20. Thomas, D.W.; Bienmann, K. *Lloydia* **1968,** *31*, 1-8.
21. De Smet, P.A.G.M. *J. Ethnopharmacol.* **1996**, *50*, 141-146
22. Jenks, C.W. *Nat Prod Lett* **2002**, *16*, 71-76.
23. Thomas, D.W.; Bienmann, K. *Tetrahedron* **1968,** 24, 4223-4231.
24. Renner U. *Experientia* **1957,** *13*, 458-469.
25. Renner U, D.A Prins. *Experientia* **1959,** *15*, 456-457.
26. Renner U, D.A Prins. *Experientia* **1961,** *17*, 106.
27. Geigy Ag JR. Patent GB865687, **1961**

28. Majumder, P.L.; Chanda, T.T.; Dinda, B.N. *Phytochemistry* **1974,** *13*, 1261-1264.
29. Geigy, A.G.J.R European patent A61K36/24; C07D519/04, **1968,**
30. Agwada von, V.C.; Naranjo, J.; Hesse, M.; Schmid, H.; Rolland, Y.; Kunesh, N.; Poisson, J.; Chatterjee, A. *Helv. Chim. Acta* **1977,** *60*, 2830-2853.
31. Henriques, A.T.; Melo, A.A.; Moreno, P.R.H.;Ene, L.L.; Henriques, J.A.P.; Schapoval, E.E.S. *J. Ethnopharmacol.* **1996,** *50*, 19-25
32. You, M.; Ma, X.; Mukherjee, R.; Farnsworth, N.R.; Cordell, G.A.; Kinghorn, A.D.; Pezzuto, J.M. *J. of Nat. Prod.*, **1994**, *57*, 1517-1522.
33. Meschini, S.; Condello, M.; Marra, M.; Formisano, G.; Federici, E.; Arancia, G. *Toxicol. In vitro* **2007**, *21*, 197-203.
34. Andrade, M.T.; Lima, J.A.; Pinto, A.C.; Rezende, C.M.; Carvalho, M.P.; Epifanio, R.A.. *Bioorg. Med. Chem.* **2005**, *13*, 4092–4095
35. Cardoso, C.A.L.; Vilegas, W.; Pozetti, G.L. *J. Chromatogr. A* **1997**, *788*, 204-206.
36. Chaturvedula, V.S.P.; Sprague, S.; Schilling, J.K.; Kingston, D.G.I. *J. Nat. Prod.* **2003**, *66*, 528-531
37. Zocoler, M.A.; de Oliveira, A.J.B.; Sarragiotto, M.H.; Grzesiuk, V.L.; Vidotti, G.J. *J. Braz. Chem. Soc.*, **2005,** *16, 6B*, 1372-1377.
38. Kam, T.S.; Sim, K.M. *Helv. Chim. Act***a** **2002,** *85*, 1027-1032.
39. Azoug, M.;, Loukaci, A.; Richard, B.; Nuzillard, J.M.; Moreti, C.; Zi~Ches-Hanrot, M.; Le Men-Olivier, L. *Phytochemistry,* **1995,** *39*, 1223 1228.
40. Kam. T.S.;, Anuradha, S.. *Phytochemistry* **1995**, *40*, 313-316
41. Kontrimaviciute, V. ; Mathieu, O. ; Balas, L. ; Escale, R. ; Blayac, J.P. ; Bressolle, F.M.M. *J. Liq. Chromatogr. R. T.* **2007,** *30*, 1077-1092.
42. Kokwaro, J.O. *Medicinal Plants of East Africa*. Kenya Literature Bureau. Nairobi, 1993, pp,401.
43. Kubukeli, P.S. *Lancet*, **1999**, Suppl. 4, *354*, pSIV24-SIV24.
44. Tizzoni, M.; Zizzi, E.; Legnazzi, P.; Gorini, G.; Marchetti, A.; Regazzetti, A. *Pharmacol. Res.* **1993,** *27*,103-104.
45. Bertelli, M.G. ; Rossi, S. ; Stauffer, E. Patent EP1491197, **2004**
46. Goutarel, R.; Gillo, L.; Mainil, J.; Janot, M. Patent GB806691, **1958**
47. Goutarel, R.; Gillo, L.; Mainil, J.; Janot, M. Patent GB806692, **1958**
48. Abubakar, M.S.; Musa, A.M.; Ahmed, A.; Hussaini, I.M. *J. Ethnopharmacol* **2007,** *11*1, 625-629.
49. Tan, P.V.; Njimi, C.K.; Ayafor, J.F. *Phytother. Res.* **1997,** *11*, 45-47.
50. Popik, P.; Layer, R.T.; Skolnick, P. *Pharmacol. Rev.* **1995,** 47, 235-253.
51. Glick, S.D.; Gallgher, C.A.; Hough, L.B.; Rossman, K.L.; Maisonneuve, I.M. *Brain Res.* **1992,** *588*, 173-176.
52. Lotsof, H.S. US Patent 4,499,096, 1985.
53. Alper, K.R.; Lotsof, H.S.; Frenken, G.M.N.; Luciano, D.J.; Bastiaans, J. *Am. J. Addiction* **1999,** 8, 234-242.
54. Lotsof, H.S. US Patent 4,587,243, 1986.
55. Alper, K.R.; Lotsof, H.S.; Frenken, C.M.N.; Luciano, D.J.; Bastiaans. J. *Ann. NY. Acad. Sci.* **2000,** *909*, 257-259.
56. Lotsof, H. S. US Patent 5,026,697, 1991.
57. Lotsof, H. S. US Patent 4,857,523, 1989

58. Lotsof, H. S. US Patent 5,152,994, 1992
59. Alper, K.R. *The alkaloids. Chemistry and Biology* **2001,** 56, 1-38
60. Gorman, M.; Neuss, N.; Cone, N.J.; Deyrup, J.A. *J. Am. Chem. Soc.* **1960**, *82*, 1142-1145.
61. Caniato, R.; Puricelli, L. *Crit. Rev. Plant Sci.* **2003**, 22, 79–105
62. Frederich, M.; Tits, M.; Angenot, L *T. Roy. Soc. Trop. Med. H.* **2008**, 102, 11-19
63. Rossi, S. ; Bertelli, M.G. Patent WO9948501, **1999**
64. Federici, E. ; Palazzino, G. ; Nicoletti, M. ; Galeffi, C. *Planta Med.*, **2000,** *66*, 93–95.
65. Ramanitrahasimbola, D. ; Rasoanaivo, P. ; Ratsimamanga-Urverg, S. ; Federici, E. ; Palazzino, G. ; Galeffi, C. ; Nicoletti, M. *Phytother. Res.* **2001,** *15*, 30-33.
66. Stella, L.; Cisse, S. Patent WO 2007014450, **2007**
67. Stella, L.; Cisse, S. Patent WO 2006029523, **2006**
68. Tan, P.V.;Boda, M.; Sonke, B.; Etoa, F-X.; Nyasse, B. *Pharmacologyonline* **2006,** *3*, 877-891.
69. Gisbert, J.P.; Pajares, J.M. *Heliobacter* **2003,** *8*, 159-167.
70. Simon, J.E; Koroch, A.R.; Acquaye, D.; Jefthas, E.; Juliani, H.R.;Govindasamy, R. The 6thNew Crops Symposium: Creating Market s for Economic Development of New Crops and New Uses. ASHS Press, Alexandria, VI. **2007**, 322-331.
71. WHO. Guidelines on Good Agricultural and Collection Practices (GACP) for Medicinal Plants. WHO, Geneva, **2003**. 72 pp.