Medicinal plants from the genus *Alchornea* (Euphorbiaceae): A review of their ethnopharmacology uses and phytochemistry

[Plantas Medicinales del género *Alchornea* (Euphorbiaceae) – Review de los usos etnofarmacológicos y fitoquímicos]

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Abstract The genus *Alchornea* compromises 55 accepted and other two unresolved species (*Alchornea acerifera* Croizat and *Alchornea oblonga* Müll. Arg.) which well various ecosystems over all the continents, with a special pantropical distribution. Numerous reports of ethnopharmacological uses of species belonging this genus exist mainly in Africa and Brazil, to treat different inflammatory and infectious diseases: arthritis, dysentery, infectious diseases, inflammation, intestinal disorders, fractures, leprosy, malaria, management of ringworm affections, muscle pain, rheumatism and ulcer. The genus *Alchornea*, contains different secondary metabolites and they have been reported such as: Alkaloids, terpenes and steroids, phenolic acid, saponins, principaly. The aim of the present review is to provide gathered and organized information with pharmacological, toxicological, traditional and phytochemical traits of plants from the *Alchornea* genus in order to define the biological potential of the genus and to define a state-of-art-platform stating the perspectives for further pharmacological/chemotaxonomical studies.

Keywords: *Alchornea*, biological activities, Euphorbiaceae, phytochemistry, traditional use.

Resumen: El género *Alchornea* comprende 55 especies aceptadas y otras dos especies por confirmar (*Alchornea acerifera* Croizat y *Alchornea oblonga* Müll. Arg.) qué habitan en diversos ecosistemas en todos los continentes, con una distribución pantropical especial. Existen numerosos reportes de usos ethnofarmacologicos de especies que pertenecen a este género en Africa y Brasil, en el tratamiento de diferentes enfermedades inflamatorias e infecciosas: la artritis, la disentería, los desórdenes intestinales, las fracturas, la lepra, la malaria, dolor del músculo, reumatismo y úlcera. En el género *Alchornea*, se han reportado diversos tipos de metabolitos secundarios tales como: alcaloides, terpenos y esteroides, ácidos fenolicos, saponinas, principalmente. El objetivo de esta revisión fue de compendiar y organizar la información farmacológica, toxicológica, de usos tradicionales y de fitocompuestos de plantas del género de *Alchornea* en el orden de definir el potencial biológico del género y establecer la plataforma del estado-de-arte con las perspectivas de los futuros estudios farmacológico/quimiotaxonómicos que se podrían realizar.

Palabras clave: *Alchornes*, actividades biológicas, Euphorbiaceae, fitoquimica, uso tyradicional.

ABBREVIATIONS

Acetylcholinesterase (AChE), alanine aminotransferase (ALT), alkalinephosphatase (ALP), aspartate aminotransferase (AST), 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid) (ABTS$^{.+}$), cyclooxygenase (COX), di-(2-ethylhexyl) phthalate (DEHP), dichloromethane (DCM), 2,2-diphenyl-picrylhydrazyl (DPPH$^{.}$), ethyl acetate (EtOAc), ethyl ether (Et$_2$O), ferric reducing antioxidant power (FRAP), glutathione S-transferase (GSTs), half inhibitory concentration (IC$_{50}$), hemoglobin (Hb), high performance liquid chromatography (HPLC), human umbilical vein endothelial cells (HUVEC), lactate dehydrogenase (LDH), lipopolysaccharides (LPS), median lethal dose (LD$_{50}$), methanol (MeOH), methicillin resistant *Staphylococcus aureus* (MRSA), methicillin susceptible *Staphylococcus aureus* (MSSA), minimal amoebicidal concentration (MAC), minimum inhibitory concentration (MIC), nitric oxide (NO), nonsteroidal anti-inflammatory drug (NSAID), packed cell volume (PCV), peripheral blood mononuclear cells (PBMCs), red blood cell (RBC), serum glutamate pyruvate transaminase (SGTP/ALT), thin layer chromatography (TLC).

INTRODUCTION

The Euphorbiaceae family is one of the most representative group of the Magnoliophyta division which is reported to include approximately 299 genera and 8000 species in a cosmopolitan distribution (Webster, 2014), with a great architecture diversity predominating trees and shrubs, but also herbs in five of its subfamilies (Hallé, 1971; Webster, 1994). This family also possess some noticeable applications with diverse economic benefits, considering rubber exploitaition (*Hevea brasiliensis*), yucca or mandioca crops (*Manihot esculenta*) or castor oil obtention (*Ricinus communis*), among others. The *Alchornea* genus exhibit a marked pantropical distribution (Murillo, 2004) compromising, to date, 55 accepted names, based on the Plant List (**http://www.theplantlist.org**). This genera dwell in different types of ecosystems with a strong tendency to tropical rainy forests in America (Gillespie, 1993), continent which contain the major number of native and endemic species (Webster, 1994), in that sense, Table 3 gather information of botanically described species with their respective geographical localization, being reported in tropical countries of America (Brazil, Colombia and Peru), tropical countries of Africa (Congo and Nigeria), and

Asia (China and Vietnam), but also the entire quantity of articles summarized in this review demonstrate the presence (Sites of collection) of *Alchornea* species in Australia, Cameroon, Costa Rica, Democratic Republic of Congo, Gabon, Ghana, Ivory Coast, Mexico, Sierra Leone and South Africa, highlighting the noticeable fact that Nigeria and Brazil were the countries with highest number of reports considering traditional uses and plant occurrence.

The leaves of *Alchornea* species are entire to dentate sometimes stipulate. Axillary spiciform inflorescences. Staminate calyx closed in bud flowers, splitting into 2-5 valvate segments, filaments basally slightly connate. Pollen grains spheroidal, angulaperturate. Pistillate flowers sessile, sepals 3-6, disk obsolete, usually pubescent. Ovary 2-5 locular, ovules with outer integument vascularized. Fruits capsular, smooth or tuberculate. Elliptic ecarunculate seeds with smooth testa and vascularized mesotesta (n = 9,18) (Webster, 2014).

The *Alchornea* species exhibit a great variety of biological activities, in this sense, several studies have validated the ethnopharmacological uses of species belonging to this genus around the world, especially in tropical regions of Africa (Nigeria, Congo and Ivory Coast) and also have characterized pharmacologically active molecules present in different plant tissues (leave, bark or root). As a consequence, the number of academic papers published in this area have been raising through the years with 1 document per year (average) to the 70 decade to 28 documents in 2011 as maximum (Search performed on Scopus with *Alchornea* as unique search word). The aim of this review is to summarize biological, pharmacological, phyto-chemical and ethnobotanical aspects of *Alchornea*.

REVIEW METHODOLOGY

The most relevant published literature regarding to the different pharmacology (biological activities) and phytochemistry (reported compounds) aspects of *Alchornea* species were collected through electronic data bases searches (EBSCO, Google Books, Google Scholar, PubMed, Reaxys, Scopus and Science Direct). Literature searches and data mining were mainly performed along the time during this review was written, between 2013 and February of 2016. In order to avoid ambiguity in scientific plant names and thus, reporting invalid information (Bennett & Balick, 2014), every plant name was compared and

confirmed based on valid botanical databases (Rivera *et al.,* 2014) such as The Plant List (http://www.theplantlist.org/) and The Missouri Botanical Garden (http://www.tropicos.org/). Documents used to construct the present manuscript have a very diverse origin, in that sense, information herein discussed and displayed were individually reported in Spanish, English, Portuguese, French and Chinese.

Collected information was organized in three major tables and five figures with structural features of most commonly isolated compounds. In this sense, Table 3 provides information regarding ethnopharmacological (Folk) uses and common names of *Alchornea* species in different countries around the world. Otherwise, Table 2 summarizes all the reported biological activities and the techniques by which they were assessed and finally Table 1 gather the phytochemical aspects of studied species belonging to *Alchornea* genus. Previous reviews over other plant species belonging to *Acalypha* genus (Euphorbiaceae) or *Betula* genus (Betulaceae), published by Seebaluck *et al.* (2015) and Rastogi *et al.* (2015), respectively, were used as model for the design and construction of this work.

RESULTS AND DISCUSSION
Botanical databases searches employing *Alchornea* as unique keyword yield 195 matching record names using The Plant List platform, besides, IPNI generate a 228 *Alchornea* species list. Result from which 55 represents accepted names, 138 correspond to synonyms and 2 species remain still unresolved (The Plant List, 2013).

Representative reports of *Alchornea* species found in academic databases and other web sources just mention seventeen species, which are documented in this review. To date, there is any available paper with different ethnobotanical, pharmacological and phytochemical aspects of plants of the genus *Alchornea.* Amongst all the reviewed species, *Alchornea cordifolia* gained more attention by the scientific community and were studied by different authors (Adewunmi *et al.,* 2001; Adebayo & Krettli, 2011; Ezuruike & Prieto, 2013; Agyare *et al.,* 2014; Fomogne-Fodjo *et al.,* 2014; McGaw *et al.,* 2014) because of its diverse biological activities like antimalarial, trypanocidal, anthelmintic, antidiabetic, antibacterial and cytotoxic, among others. In this review, uses of *Alchornea* plants from people of South America (Brazil, Colombia and Peru), Asia

(China and Vietnam) and Africa (Congo and Nigeria) are documented. From 12 reviewed plant species (71% of reviewed species) 29 biological activities have been assessed through 15 *in vivo* and 35 *in vitro* assays. Additionally, from 15 species (88% of reviewed species) have been mostly reported the presence of alkaloids, flavonoids, lignans, saponins, steroids, sterols, tannins and terpenoids. Besides, 160 compounds have been isolated and identified from the same plant species from which the most commonly reported molecules were depicted in Figures 1 to 5, which separately shows structures of isolated phenolic compounds, flavonoids, quercetin derivatives, alkaloids and stigmastane steroids, respectively.

Alchornea aquifolium (Js. Sm.) Domin
This specie belongs to the Australian flora, being found in the Victoria state in the locality of Melbourne. Leaf extract showed medium alkaloids content when tested with the Mayer's reagent (Bick, 1996).

Alchornea bogotensis Pax & K. Hoffm.
This specie is reported in natural forests belonging to Colombian biodiversity. *A. bogotensis* dwells in ecosystems located between 1350-1600 meters above sea level (Orrego *et al.,* 2008). Usage of this plant is documented only as wood source or fuel (Cenicafé, 2010).

Alchornea castaneifolia (Humb. & Bonpl. ex Willd.) A. Juss.
Alchornea castaneifolia is distributed in sites with high sedimentation rates and pioneer forests in central Amazonian regions (Wittmann *et al.,* 2011). Traditional healers from the Cerrado region of Brazil and the indigenous Shipibo-Conibo tribe from the Peruvian-Amazonian basin use plant decoctions to treat inflammatory diseases and ulcer (Dunstan *et al.,* 1997; Costa *et al.,* 2008). Additionally, ethanolic extract of the whole plant was only mildly active against *Staphylococcus epidermis* with an inhibition zone of 12 mm (Chloramphenicol: 16 mm) at 500 µg/mL. Its TLC profiling showed the presence of phenolic compounds, flavonoids (catechin and isoquercitrin), saponins, steroids, tannins and triterpenes (Costa *et al.,* 2008). Also 70% hydroethanolic extract inhibited at 66% the prostaglandin COX-1-mediated biosynthesis *in vitro* over bovine seminal vesicle microsomes and rat ear

ethyl phenylpropiolate (EPP)-induced oedema with a maximum of 55% after 2 hours (Dunstan *et al.,* 1997). Hiruma-Lima *et al.* (2006) showed that the same hydroethanolic extract and a further flavonoid enriched fraction ameliorate the healing process of induced ulcers (acetic acid; pylorus ligature and stress) and stimulated synthesis of defensive agents as prostaglandin and somatostatin and inhibited gastrin secretion.

Alchornea coelophylla Pax & K.Hoffm.

Gaviria *et al.* (2015) reported the presence of flavonoids, phenolic compounds, saponins, sterols and triterpenoids in dichloromethane and methanolic extracts of the aerial parts of this specie; additionally, antioxidant activity was assessed through both colorimetric methods $ABTS^{.+}$ and $DPPH^{.}$ and expressed as Trolox equivalents, showing the highest values for the methanolic extract at 837.42 and 41.65 µmol of Trolox/g of extract, respectively, and also the phenolic content in the same extract was found to be 0.314 µg Gallic Acid/mg of extract. Niño *et al.* (2012) also reported the presence of alkaloids and tannins in dichloromethane and methanolic extracts and the existence of antibacterial activity from the hexane extract with a MIC value of 4 mg/mL against *Pseudomonas aeruginosa* and from the methanolic extract against *Bacillus subtilis, Staphylococcus aureus, P. aeruginosa* and *Escherichia coli* with MICs values of 4 mg/mL for the first strain and 1 mg/mL for the three missing. The IC_{50} of the methanolic extract for $DPPH^{.}$ assay was 41.14 µg/mL (Mosquera *et al.,* 2007).

Alchornea cordifolia (Schumach. & Thonn.) Müll.Arg.

This specie is by great difference the most studied specie among the *Alchornea* genus. This plant occurs mainly in west to central Africa in countries as Congo, Ivory Coast, Nigeria and Ghana. Amongst the tens of reports regarding the isolation of phytocompounds from *A. cordifolia*, Kleiman *et al.* (1977) reported the isolation of a new C_{20}-epoxide fatty acid which constitute approximately the 50% of the seed oil of this specie. Traditional use of plant decoctions to treat diarrhea, could be supported with the antiamoebic and spasmolytic activities found in polyphenol, crude saponin and total alkaloid fractions from aqueous leaf extract, which showed MAC values ranging 5 to >50 µg/mL against *Entamoeba histolytica* and also inhibited contraction of Guinea-

pig's ileum when stimulated with acetylcholine and KCl (Tona *et al.,* 2000). Alkaloids, steroidal glycosides and tannins were found in polar (acetone, ethanol and methanol) stem bark extracts, but also flavonoids, saponins and terpenoids were found in both polar and petroleum ether stem bark extract (Ajali, 2000). Likewise, cyanogenic and cardiac glycosides were found to be present in aqueous leaf extract (Mohammed *et al.,* 2013).

Aqueous leaf extracts showed moderate to low antibacterial activities with MIC values of 3.1, 1.6, 0.4, 6.3, 6.3, 12.5 and 1.6 mg/mL, against methicillin resistant *Staphylococcus aureus* (MRSA I), UELSHB 102; MRSA II, UELSHB 103; methicillin susceptible *Staphylococcus aureus* (MSSA), NCTC 6571; *Streptococcus pyogenes*, UELSHB 333; *Escherichia coli*, ATCC 25922; *Pseudomonas aeruginosa,* ATCC 27853; *Proteus vulgaris*, UELSHB 241, respectively; additionally, such aqueous (Stomacher) extract (50 mg/mL) were further tested with 15 MRSA strains isolated from nose, leg ulcer, wound swab, stomach, penis, vagina and eyes showing inhibition zones with diameters varying between 15 and 31 mm, showing some cases similar values to control antibiotics allicin (100 µL of 500 µg/mL), gentamicin 10 µg and vancomycin 30 µg (Pesewu *et al.,* 2008). Otherwise, Lamikanra *et al.* (1990) reported the isolation of gallic acid and triisopentenyl guanidine which exhibited inhibition zones similar or even higher than antibiotic controls (chloramphenicol and chlorocresol) against *S. aureus* and *E. coli* at concentrations of 50 mg/mL. Also quercetin and quercetin arabinosyl and galactosyl derivatives were isolated. On the other hand, Ebi (2001) compared the antimicrobial activities of methanolic leaf, stem bark and root bark extracts and further fractions through agar-diffusion method, obtaining the highest responses from the leaf extract (inhibition diameters ranging 12 to 21 mm at 10 mg/mL). He also reported activity against bacterial strains *B. subtilis* and *Klebsiella pneumoniae*, and against fungal isolates *Aspergillus niger* and *Candida albicans*. Further fractionation methods conclude that the highest antibacterial activity observed, could exist due to the presence of alkaloids, phenolics, saponins and terpenes.

The anti-stress activity of aqueous leaf and root extracts reported by (Ishola *et al.,* 2008; Umukoro & Aladeokin, 2010) together with the antidepressant effect of hydroethanolic leaf extract observed in male Swiss albino mice, were mediated

through interactions with dopamine (D_1 and D_2), noradrenergic (α_1 and α_2 adrenoreceptors) and serotonergic ($5HT_{1B}$) receptors (Ishola *et al.,* 2014). Leaf and root extracts, together with isolated compounds (β-sitosterol, daucosterol, di-(2-ethylhexyl) phthalate (DEHP), acetyl aleuritolic acid, diisopentenyl guanidine and triisopentenyl guanidine) showed noteworthy anti-inflammatory activity values, exhibiting greater inhibitions than the anti-inflammatory indomethacin-control at doses of 90 $\mu g/cm^2$ in mouse ear oedema models (Mavar-Manga *et al.,* 2008). Those results agree with previous investigations, which concluded that the lowest polar (hexane) fraction of the methanolic-soxhlet leaf extract showed the highest anti-inflammatory activity with a 42.1% of inhibition of ear oedema formation in Swiss albino mice at a dosage of 0.7 $\mu g/cm^2$ (Manga *et al.,* 2004). Osadebe & Okoye (2003), also tested the anti-inflammatory activity of methanolic and hexane leaf extracts and further fractions in egg-albumin-induced rat hind paw oedema model, obtaining the highest percentages of inhibition for the terpenoid and polyphenolic fractions with 66.67% and 60%, respectively, at dosages of 100 mg/Kg; moreover, the phytochemical screening of *A. cordifolia* extracts showed the presence of alkaloids, carbohydrates, glycosides, flavonoids, phenolics, saponins, tannins and triterpenoids.

Antioxidant properties of *A. cordifolia* have been also reported. Ethanolic leaf extract protected Wistar albino rats against acetaminophen-induced liver damage, when administered 2 g/Kg, at dosages raging 200-300 mg/Kg of extract (Olaleye *et al.,* 2006), through a glutathione S-transferases (GSTs) inhibition in both liver and serum at optimum dosages of 200 mg/Kg and 400-500 mg/Kg, respectively (Olaleye *et al.,* 2007). Additionally, a stock solution at 5 mg/mL showed 92% of inhibition of the DPPH˙ radical, even higher than the vitamin E control at the same concentration. Moreover, antioxidant activity of ethyl acetate and aqueous leaf extracts against superoxide anion radical is reported by Kouakou-Siransy *et al.* (2010) with IC_{50} values ranging 4.1 and 13.4 $\mu g/mL$ in cellular and acellular-*in vitro* systems. Otherwise, Osadebe *et al.* (2012) showed another hepatoprotective mechanism with a serum glutamate pyruvate transaminase (SGTP/ALT) level decrease in CCl_4-induced hepatic damage Wistar albino rats, when treated with ethyl acetate fraction of methanolic leaf extract at a 300 mg/Kg dose.

Aqueous, ethanolic and pentane extracts of aerial parts (leaf and stem) of *A. cordifolia* showed significant antiplasmodial activity against two chloroquine-resistant strains of *Plasmodium falciparum* (FcB1-Colombia and FcM29-Cameroon) and a Nigerian chloroquine-sensitive strain, showing IC_{50} values ranging 3.06-4.56, 2.30-3.51 and 2.43-3.15 $\mu g/mL$, respectively for the three strains (Mustofa *et al.,* 2000). Banzouzi *et al.* (2002) also reported strong activity of aqueous fraction from ethanolic extract and isolated ellagic acid against FcM29 (IC_{50}: 0.21 and 0.11 $\mu g/mL$) and Nigerian (IC_{50}: 0.21 and 0.17 $\mu g/mL$) strains at 24 hours of exposition. Likewise, aqueous leaf extract showed an IC_{50} value of 4.64 $\mu g/mL$ against a chloroquine and pyrimethamine-resistant K1 *P. falciparum* strain (Musuyu Muganza *et al.,* 2012).

Mesia *et al.* (2008) reported the strong antiprotozoal activity of hydroethanolic leaf extract against *Trypanosoma brucei brucei* (*Tbb*) with an IC_{50} of 0.7 $\mu g/mL$. Also medium activity was observed against *Trypanosoma cruzi* (IC_{50}: 34 $\mu g/mL$). Additionally, toxicity towards a drug-sensitive and a multiresistant clones of *Trypanosoma congolense* was evaluated with a LD_{50} of 68.06 and 68.9 $\mu g/mL$, respectively by the ethanolic leaf extract (Adewunmi *et al.,* 2001). Aqueous leaf extract exerted similar toxicity against *Tbb, T. cruzi* and *Leishmania infantum* with IC_{50} values of 6.67, 36.27 and 32.46 $\mu g/mL$, respectively (Musuyu Muganza *et al.,* 2012). Also toxicity test were carried out using HeLa cells with ethanolic and pentane extracts of aerial parts of the plant, revealing medium activity with LD_{50} values of 54.97 and 144.43 $\mu g/mL$, respectively (Mustofa *et al.,* 2000). Hydroethanolic leaf extract when evaluated against MRC-5 cells showed an IC_{50} value about >64 $\mu g/mL$ (Mesia *et al.,* 2008). Cytotoxicity assay of ethanolic leaf extract against bovine aorta endothelial cells revealed moderate activity with LD_{50} of 220.72 $\mu g/mL$ (Adewunmi *et al.,* 2001).

Enzyme inhibition was observed against elastase, produced by human polymorphonuclear neutrophils, by ethyl acetate and aqueous leaf extract with IC_{50} values 2.2 and 4.7 $\mu g/mL$, respectively (Kouakou-Siransy *et al.,* 2010). Additionally, immunomodulatory properties were observed when polysaccharides-containing fractions from ethanolic leaf extract exerted a stimulation of NO production over murine J774.A1 macrophages and an increased production of tumor necrosis factor- α (TNF-α),

interleukines (IL) IL-6 and granulocyte macrophage-colony stimulation factor (GM-CSF) cytokines by Mono Mac 6 cells, murine J774.A1 macrophages and human peripheral blood mononuclear cells (PBMCs) (Kouakou *et al.,* 2013).

Mohammed *et al.* (2013) evaluated antidiabetic activity and haematological properties of *n*-butanol fraction from aqueous leaf extract in streptozotocin-induced diabetes Wistar albino rats. They observed that treated group suffered concentration-dependent significant decrease in blood glucose levels, with higher values at dosages of 400-800 mg/Kg, but after day 14 treatment, all treated groups reduced their glucose levels. Additionally, extract treatment exerted a significant packed cell volume (PCV), red blood cells count (RBC), hemoglobin concentration (Hb) and the total protein level increase, compared with the diabetic control group. It also elevated total leucocyte and lymphocyte count. Antidrepanocytary activity reported by Mpiana *et al.* (2007) consisted in a 93.3% normalization rate of sickled blood cells at a concentration of 0.097 µg/mL when treated with an anthocyanin-containing leaf extract. Aqueous extract also helped with SS erythrocytes normalization of 73.3% at 48.8 µg/mL.

Alchornea davidii Franch.
This specie is distributed in Asia and is mainly found in China. A phytochemical investigation conducted by Cui and Tan (2004) reported the isolation of pinoresinol, monomethylpinoresinol, (+)-syringaresinol, graminone A, boehmenan, gallic acid, methyl gallate, 3,3'-di-*O*-methylellagic acid 4-*O*-α-L-arabinofuranoside and 3,3'-di-*O*-methylellagic acid 4-*O*-(5'-*O*-acetyl)- α-L-arabinofuranoside from ethyl acetate fraction of petroleum ether-Et$_2$O-MeOH (1:1:1), which constituted the first report of lignans isolation from species belonging the *Alchornea* genus. Furthermore, a new flavonol glycose, isorhamnetin-3-*O*-β-D-xyloside isolated from aerial part (leaves and twigs) of *A. davidii* showed moderate antimicrobial activity with MICs of 50 µg/mL against *S. aureus, B. subtilis, Pseudomonas fluorescens, C. albicans, A. niger* and *Trichophyton rubrum (*Cui *et al.,* 2003).

Alchornea floribunda Müll.Arg.
This specie is widely used in traditional medicine in Africa. (Okoye & Osadebe, 2010) isolated 3,5,7,3'-tetrahydroxyflavone-3-*O*-α-L-rhamnoside from leaf

methanolic extract. This new anti-inflammatory flavonol glycoside showed a 51.4% inhibition in egg-albumin-induced paw oedema in rats after a 3 hours treatment at a dosage of 50 mg/Kg and also protected the 90.9% of human-blood erythrocytes against heat-induced haemolysis at 50 µg/mL. Likewise, three stigmastane-type steroids (3β-hydroxy-5α-stigmastane-24-ene; 5α-stigmastane-3,6-dione; 5α-stigmastane-23-ene-3,6-dione) isolated from hexane leaf extract were associated to anti-inflammatory and membrane stabilizing properties. The three steroidal isolated compounds showed moderate activity against xylene-induced ear oedema formation with inhibition percentages of 32.3, 50.9 and 34.4, respectively, once passed 3 hours at a dose of 20 mg/Kg. Higher values were obtained through egg-abumin-induced paw oedema assay with inhibitions of 58.16%, 67.50% and 81.45% at dosages of 100 mg/Kg and 2 hours of treatment. Also inhibitions ranging 70.70% to 85.30% were obtained for the two first steroidal compounds in heat-induced erythrocytes hemolysis, at doses of 100 µg/mL, and an inhibition of 76.86% was observed at 50 µg/mL for the latter (Okoye *et al.,* 2010). Furthermore, a highly lipophilic fraction from hexane leaf extract, by which were isolated 1,1-bis(dodecyloxy)-hexadecane; E-2-methyl-3-tetradecene-1-ol-acetate; 3-ethyl-5-(2-ethylbutyl)-octadecane; 9-hexadecenoic acid; 7-methyl-Z-tetradecen-1-ol-acetate; 3-(octadecyloxy)propyl oleate; 3-octyl-*cis*-oxiraneoctanoic acid; 17-pentatriacotene 2,6,10,14-tetramethylpentadecane; 2,6,10-trimethyldodecane; 2,6,10-trimethyltetra-decane, showed significant topical anti-inflamatory activity when applied (5 mg) in xylene-induced inflammation in albino mice ears *(Okoye et al.,* 2011).

Also, the presence of three alkaloids (alchorneine, alchorneinone and isoalchorneine) in leaves, stem barks and roots (Khuong-Huu *et al.,* 1972) was associated with the traditional stimulating properties of the plant (Raymond-Hamet, 1952; De Smet, 1996).

Other investigations based on traditional uses of the plant are reported. Thus, Fomogne-Fodjo *et al.* (2014) found antibacterial potential in MeOH-dichloromethane (DCM) (1:1) leaf extract with MIC values of 50 and 65 µg/mL against *Mycobacterium smegmatis* and a *Morexella cattarhalis*. Also moderate to low activity was observed against *Mycobacterium aurum* (MIC: 500 µg/mL). Furthermore, different solvent extracts (hexane,

chloroform, ethyl acetate, methanol and ethanol) from diverse plant tissues (root, stem bark and leaves) showed moderate activity against *Bacillus cereus*, *Enterococcus faecalis*, *E. coli*, *S. aureus*, *K. pneumoniae*, *Moraxella catarrhalis*, *Proteus mirabilis* and *Staphylococcus saprophyticus* with MICs values ranging 50 to 500 μg/mL (Noundou *et al.,* 2014).

Root and leaf aqueous extracts showed a noteworthy antiprotozoal and antiplasmodial activity against *T. brucei brucei*, *T. cruzi*, *L. infantum* and a chloroquine and pyrimethamine-resistant K1 strain of *P. falciparum*, with IC_{50} values of 19.65, 37.26, >64 and 20.80 μg/mL, respectively (Musuyu Muganza *et al.,* 2012).

Alchornea glandulosa **Poepp.**
This specie is mainly distributed in Brazil, where is widely used in folk medicine, but also is present in pluvial forest of Colombia. Ethyl acetate fraction (EAF) of methanolic leaf extract induced an endothelial cell proliferation decrease and drastically diminished the formation of cord-like structures of human umbilical vein endothelial cells (HUVEC) to approximately 0.4% of control values, this activity was probably supported upon the 43.33% reduction in NF-κβ transcriptional factor observed in EAF-treated HUVEC cells (Lopes *et al.,* 2011). In addition, corilagin, isoquercitrin, isovitexin, methyl gallate, protocatechuic acid and rutin were isolated from the antiangiogenic-EAF. Similarly, a previous study reported the isolation of a pterogynidine alkaloid with the same NF-κβ inhibition-mediated antiangiogenic activity (Lopes *et al.,* 2009). Moreover, Conegero *et al.* (2003) reported antiproliferative (cytostatic) activities of methanolic leaf extract in a concentration-dependent manner against lung (NCI460), melanoma (UACC62), breast (MCF7) and resistant breast (NCIADR) tumoral human cell lines. Also further moderate antimicrobial activities were observed for alkaloidal fraction against *Bacillus subtilis* and *Candida tropicalis* with MIC values of 62.5 and 31.2 μg/mL and the isolation of β-sitosterol, stigmasterol, loliolida, N_1,N_2,N_3-triisopentenyl guanidine and corilagin.

Lopes *et al.* (2005) found modulatory properties when lipopolysaccharides (LPS) or phorbol myristate acetate (PAM)-activated peritoneal macrophages were treated with ethyl acetate fraction of methanolic leaf extract. Thus, H_2O_2 production of PMA-activated macrophages suffered a 68.38%

reduction at 62.50 μg/mL, also moderate to low inhibition in NO and TNF-α production was observed in LPS-activated macrophages, with values of 38.73% and 15.16%, respectively.

Methanolic leaf extract also showed DNA intercalation (21.13% at 125 μg/mL) through HPLC technique, further phytochemical screening revealed the presence of triterpenes, lactones and mainly saponins (Correa *et al.,* 2007). Moreover, ethanolic leaf extract, further fractions and six isolated compounds showed moderate toxicity against brine shrimp with LD_{50} values ≤ 228.3 μg/mL, also significant antifeedant activity was observed against *Spodoptera frugiperda* neonate larvae with a larval weight loss of 95, 92 and 76%, respectively, to aqueous fraction, quercetin and quercetin-3-*O*-L-rhamnoside. The missing isolated compounds correspond to gallic acid, kaempferol-3-*O*-L-rhamnoside and myricetin-3-*O*-L-rhamnoside (Urrea-Bulla *et al.,* 2004).

Studies conducted by Calvo *et al.* (2007) reinforced traditional usage of *A. glandulosa*, which showed positive effects over gastrointestinal system. Methanol leaf extract prevented the formation of 85%, 64% and 78% of gastric lesions in ethanol-induced ulcer in rats model, HCl/Ethanol and NSAID induced ulcers in mice at doses of 1000 mg/Kg and 250 mg/Kg for the two latter. Further experiments with blocker of SH compounds and NO synthase inhibitor revealed the role of endogenous SH and NO in gatroprotection. Additionally, treated mice showed a total acid (μEq/mL/4 h) reduction in gastric production when the extract was administered orally or intraduodenal at dosage of 1000 mg/Kg.

Alchornea hirtella **Benth.**
The presence of alchorneine in dichloromethane stem bark extract was reported by Khuong-Huu *et al.* (1972). After that, the results obtained by Koroma and Ita (2009) confirmed the presence of alkaloidal nucleus in a whole-plant (leaves, stem and root barks) polar extracts (ethanol and water), together with flavonoids, saponins, sterols, tannins and terpenoids. Also flavonoids and saponins were found in less amount in petroleum ether extract. Additionally, low to moderate antibacterial activity was obtained from the aqueous whole-plant extract with inhibition percentages (relative to the standard drug: ciprofloxacin) of 27%, 28%, 33% and 56%, against *S. pyogenes*, *S. aureus*, *E. coli* and *P. vulgaris*, respectively when evaluated through disc diffusion

method at 1 mg/mL. The ethanolic leaf extract showed a MIC value of 1.9 mg/mL against *S. pyogenes*.

Traditional uses of the plant is reported in the Democratic Republic of Congo where aqueous decoction of leaves are used for the treatment of fractures (Chifundera, 2001), and leaves and fruits extracts are used in the treatment of dysentery in Sierra Leone (Jusu & Sanchez, 2013).

Alchornea rugosa (Lour.) Müll.Arg.
Isolation of alkaloids from leaf and bark tissues from *A. rugose* (*A. javanensis*) reports the presence of two different class of alkaloidal compounds. Two guanidine alkaloids (N_1,N_1-diisopentenylguanidine and N_1,N_2,N_3-triisopentenylguanidine) and two hexahydroimidazo[1,2-α]pyrimidines alkaloids (alchornine and alchornidine) (Hart *et al.*, 1970a; Hart *et al.*, 1969).

These guanidine alkaloidal compounds were also later discovered in other *Alchornea* species such *A. cordifolia* and *A. glandulosa* with antibacterial and anti-inflammatory activities (Lamikanra *et al.*, 1990; Mavar-Manga *et al.*, 2008).

Alchornea latifolia Sw.
Studies over the chloroform leaf extract revealed the rich presence of triterpenoids, which were epifriedelinol, friedelin, taraxerol, taraxerone and two new compounds, *seco*-3,4-friedelin and *seco*-3,4-taraxerone. These two latter compounds showed cytotoxic activities against two human carcinoma cell lines, exhibiting IC_{50} values of 35.5 and 11.7 μM against Hep-G2 and 29.7 and 38.2 μM against A-431; and topoisomerase II inhibition with MIC values of 7 μM (Setzer *et al.*, 2000).

Alchornea laxiflora (Benth.) Pax & K.Hoffm.
Literature report a wide traditional usage of this plant specie in Cameroon and Nigeria. An ethnobotany an phytomedicine inventory published by Jiofack *et al.* (2009) reports therapeutic indication of leaves to treat dysentery, hemorrhoids and urinary infections.

In vitro anti-inflammatory activity was observed when acetone leaf extract inhibited the 70% oxidation of xylenol orange by 15-lypoxygenase at 100 μg/mL and a IC_{50} of 46.03 μg/mL and when the same extract exerted a marked inhibition of NO production by LPS-RAW 264.7 activated macrophages at rates raging 93.81% to 86.38% of

inhibition at 50 and 6.25 μg/mL, respectively (Dzoyem & Eloff, 2015).

Acetone leaf extract also showed acetylcholinesterase inhibitory properties diminishing about the 70% of AChE activity through the Ellman's colorimetric method at 500 μg/mL and an IC_{50} value of 364.12 μg/mL. Otherwise, high values of antioxidant activity were obtained through DPPH·, ABTS·+ and Ferric reducing antioxidant power (FRAP) colorimetric methods with IC_{50} values of 17.19, 18.53 and 438.42 μg/mL, respectively, being explained by the total phenolic and flavonoid contents in the extract with 147.95 mg gallic acid/mg and 13.84 mg quercetin/mg (Dzoyem & Eloff, 2015). Additionally, different plant extracts (hexane root, methanol root, hexane leaf and methanol leaf) showed medium to high radical scavenging activities, which were assessed through different methods including the above mentioned colorimetric assays and the linoleate-thiocyanate model, in which the hexane root extract exerted the greatest protection against the oxidation mediated by the thiocyanate assay with an inhibition percentage of 76.4% comparable to the BHA. Further fractions of such extract were then evaluated through β-carotene-linoleate and Fe^{+2}/ascorbate/H_2O_2-induced rat liver microsomal lipid peroxidation models revealing inhibition rates ranging 69% to 5% for the latter activity. Moreover, the presence of terpenoids in the hexane root extract was noticed and linked to the high lipid peroxidation-protective activity (Farombi *et al.*, 2003). Adeloye *et al.* (2005) reported the antioxidant activity of 50% ethanolic leaf extract with IC_{50} values of 106.74 μg/mL, 12.97% and 24.34% for the crude extract, and ethyl acetate and butanol fractions, respectively, together with the isolation of a taxifolin glycoside.

However, different phytochemical types have been reported such as saponins, alkaloids, tannins, phlobatannins, flavonoids, cardiac glycosides, steroids, phenolics and reducing sugars (Ogundipe *et al.*, 1999; Schmelzer, 2007; Oloyede *et al.*, 2010; Borokini & Omotayo, 2012).

Ogundipe *et al.* (2001a) and Ogundipe *et al.* (2001b) reported the isolation of several flavonoids from the ethyl acetate fraction of the methanol leaf extract completing the identification of quercetin-3',4'-disulphate, quercetin-7,4'-disulphate, quercetin, quercetin-3,4'-diacetate, rutin and quercetrin which then showed high antimicrobial activities with MIC values ranging >200 to 3.13 μg/mL against *C.*

albicans, *P. aeruginosa*, *S. aureus*, *B. cereus* and inhibition zones comparable to controls were observed against *E.coli*, *B. subtilis* and *Aspergillus flavus* at 1 mg/mL. Hydromethanolic leaf extract also exerted medium to low antibacterial activity against *Micrococcus luteus*, *P. fluorescens*, *Clostridium sporogenes*, *K. pneumoniae*, *B. subtilis*, *Bacillus polymyxa*, *Clostridium pyogenes*, *E. faecalis*, *P. vulgaris* and *B. anthracis* with IC_{50} values ranging 0.78 to 25 mg/mL; also low antifungal activity against *A. niger*, *Aspergillus fumigatus*, *Aspergillus glaucus*, *Penicillium expansum*, *Trichophyton tonsurans*, *Trichophyton interdigitale*, *Penicillium camemberti*, *Trichophyton mentagrophytes*, *A. flavus*, *Scopulariopsis brevicaulis*, *Penicillium italicum*, *Trichophyton rubrum* and *Candida pseudotropicalis* with IC_{50} values ranging 2.19 to 35 mg/mL (Akinpelu *et al.,* 2015). Oloyede *et al.* (2011) also report the isolation of quercetin-3-*O*-β-D-glucopyranoside and quercetin-3,7,3',4'-tetrasulphate from the butanol soluble fraction of ethanol leaf extract.

Additionally, two new compounds (10*Z*)-tetradec-10-enoic acid-(2*S*)-2-carboxy-2-hydroxyethyl ester and 3-*O*-β-D-glucopyranoside of β-sitosterol, together with (2*R*)-2-hydroxy-*N*-[(2*S*,3*S*,4*R*,15*Z*)-1,3,4-trihydroxy-15-triaconten-2-yl] octacosamide, 3-*O*-acetyl oleanolic acid, 3-*O*-acetyl ursolic acid, ellagic acid, 3-*O*-methylellagic acid and 3-*O*-methyl-3'-*O*-α-rhamnopyranosyl ellagic acid were isolated from methylene chloride/methanol (1:4) stem bark extract, from which the first, the fifth and sixth compounds exhibited cytotoxic activity against human promyelocytic leukaemia HL60 with IC_{50} values of 58.7, 6.6 and 6.8 µM (Sandjo *et al.,* 2011).

Aqueous leaf extract of *A. laxiflora* showed positive effects in gastric pH and the activity of disaccharidases in small intestine of iron-deficient treated albino rats, enhancing the activity of maltase, lactase and sucrase to levels higher than the control group (iron-sufficient rats) at dosage of 300 mg/Kg and increasing the gastric pH to 3.58 from 2.59 (the control iron-deficient group) to similar levels of the control animals at a dosage of 200 mg/Kg (Olatunde *et al.,* 2014).

Hepatoprotective activity was observed when administration of ethyl acetate fraction (EAF) of ethanol leaf extract exerted significant protection against CCl_4-induced hepatotoxicity, reducing the levels of serum marker hepatocellular damage enzymes: aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkalinephosphatase (ALP) and lactate dehydrogenase (LDH) from 35.712, 12.513, 27.509 and 480.312 U/L to 18.872, 7.054, 22.864 and 180.321 U/L, for the EAF-treated group and CCl_4 control, respectively. Also histological studies confirmed the hepatoprotection, showing the presence of normal hepatic cords, the absence of necrosis an lesser fatty infiltration in EAF-treated group, contrary to the observed in CCl_4 controls (Oloyede *et al.,* 2011).

Bum et al. (2009) assessed the anticonvulsant activity of aqueous leaf extract over different convulsive-induced models in *Mus musculus* Swiss mice. Treated groups were only protected against *N*-methyl-D-aspartate and strychnine-induced convulsions with inhibition percentages of 100% and 75% at dosages of 60 mg/Kg and 120 mg/Kg, respectively. No sedative activity was observed.

Traditional use of *A. laxiflora* to treat snakebite was supported by the study published by Molander *et al.* (2014), which demonstrated that ethanolic leaf extract exerted considerable inhibition in hyaluronidase, phospholipase A2 and protease enzymes. The inhibition values were 64%, 111% and 51%, respectively, for the three enzymes coming from *Bitis arietans* venom. Also 102% and 119% inhibition of hyaluronidase were obtained by the aqueous and ethanol leaf extract against *Naja nigricollis* venom.

Alchornea sidifolia **Müll.Arg.**
Barbo *et al.* (2002) reported the isolation of pentatronol and β-sitosterol from methanolic leaf extract, together with the crude extract antifungal activity (data not shown). Also the isolation of triterpenoids from *A. sidifolia* is reported by Leone (2005) which identified corimbol from chloroform leaf extract, aside of the isolation of diphenilsulfide and α-amorphene from further fractions with marked antifungal activity against *Cladosporium sphaerospermum* through TLC bioautography. Furthermore, α-humulene and β-caryophyllene was identified in an active fraction from the chloroform root bark extract with antifungal activity through the same bioautography determination.

Finally, Leone (2005) also reported the presence of quercetrin from the ethyl acetate leaf extract.

Alchornea tiliifolia (Benth.) Müll.Arg.

This specie is widely distributed in Asia, where a study conducted by Dũng *et al.* (2009) identified in great extent the volatile constituents of the leaf oil of this specie, in which allo-aromadendrene, bicyclogermacrene, (E)-γ-bisabolene, bisabolol oxide B, (Z)-γ-bisabolene, borneol, δ-cadinene, α-calacorene, camphene, β-caryophyllene, caryophyllene oxide, α-cedrene, 1,8-cineole, α-copaene, β-cubebene, γ-curcumene, p-cymene, γ-eudesmol, (E,E)-α-farnesene, (Z,E)-α-farnesene, (E)-β-farnesene, farnesol, α-fenchol, germacrene D, β-gurjunene, α-humulene, limonene, linalool, α-muurolene, myrcene, myrtenol, nerolidol, neryl formate, nonanal, (E)-β-ocimene, (Z)-β-ocimene, α-pinene, β-pinene, sabinene, α-terpinene, terpinen-4-ol, α-terpineol, γ-terpinene, terpinolene and α-thujene were characterized.

Alchornea trewioides (Benth.) Müll.Arg.

The traditional Chinese medicines encyclopedia published by Zhou *et al.* (2011) mentions diverse folk uses varying from the treatment of itching, scabs and bedsores to dysentery and hematuria. Additionally, hepatoprotective activity of root extract was reported by Lü *et al.* (2007), in which treated rat groups were protected in the alcohol-induced hepatic fibrosis.

Antiviral activity was also observed by the ethyl acetate extract of *A. trewioides* when exposure inhibited the replication of hepatitis C virus and NS3 proteins expressions in the CBRH7919 cell lines model of study with an IC_{50} of 14.60 µg/mL (Wang *et al.,* 2013).

Moreover, the isolation of 1-*O*-galloyl-6-*O*-vanilloyl-β-glucose, a new phenolic acid from 95% ethanol roof bark extract, was reported together with the identification of gallic acid, ethyl gallate, syringic acid, glucosyringic acid, erigeside C, 3,4-dimethoxyphenyl-(6'-*O*-α-L-rhamnosyl)-β-D-gluco-pyranoside and 3,4,5-trimethoxyphenyl-(6'-*O*-galloyl)-*O*-β-D-glucopyranoside (Qin *et al.,* 2012).

Alchornea triplinervia (Spreng.) Müll.Arg.

This tree specie is mainly distributed in Colombian Amazonian rainforest and the Cerrado region of Brazil. Macrae *et al.* (1988) reported a diverse group of biological activities from the ethyl acetate (organic phase, O.P.) and water (aqueous phase, A.P.) soluble fractions of the methanolic stem bark extract, which includes considerable antifungal activity (both phases) against dermatophytic fungi *Microsporum*

canis, M. fulvum, M. gypseum and *Trichophyton gallinae* with concentrations producing > 75% of inhibition, ranging from 0.25 to 1.0 µg/mL; strong antiviral activity in infected 3T3 mouse cells were detected against Sindbis virus with a $LC_{50} < 1$ µg/mL through pre-infection treatment and LC_{50} values of 17 and 35 µg/mL in post-infection model for A.P. and O.P., respectively, and against Murine cytomegalovirus with LC_{50} of 0.22 and < 1 µg/mL in preventive treatments for A.P. and O.P., respectively, and none response in the curative (post-infection) model was observed; antitumoral activity was also observed by the O.P. with an EC_{50} of 0.62 µg/mL inhibiting the formation of tumors induced by *Agrobacterium tumefaciens* over potato disks; moderate activity was observed in toxicity assay using *Artemia salina* model with LC_{50} values of 92 and 110 µg/mL, respectively to A.P. and O.P.

Additionally, methanol leaf extract exerted protection against HCl/ethanol and Piroxicam-induced ulcer models in mice and ethanol-induced ulcer in rats with inhibition percentages of 90%, 77% and 89%, respectively at dosages of 1000 mg/Kg. Further ethyl acetate fraction also showed 50% of inhibition in ethanol-induced ulcer in rats at a dose of 100 mg/Kg (Lima *et al.,* 2008). Further determinations using a SH blocker (*N*-ethylmaleimide), a nitric oxide synthase inhibitor (L-arginine methyl ester) and prostaglandin determination in gastric mucosa helped to elucidate the biological pathway through which gastroprocetion was favored by methanolic extract, showing a PGE_2 increase-mediated response.

Antibacterial activity of *A. triplinervia* includes mild antibacterial activity (O.P.) extract against *S. aureus* (Macrae *et al.*, 1988), and moderate anti-*Helicobacter pylori* activity with a MIC value of 0.25 mg/mL (Lima *et al.,* 2008).

Further investigations over detected gastro protective properties of ethyl acetate fraction from methanol leaf extract, showed that treatment with such fraction at dosages of 100 mg/Kg accelerated the healing process of acetic acid-induced gastric ulcers in rats through epithelial cell proliferation mediated by the enhanced COX-2 and proliferation cell nuclear antigen expression and increase in both neutrophils count and number of vessel in ulcer margin (Lima *et al.,* 2011).

Finally, Braca *et al.* (2002) reported the isolation of amentoflavones, gallic acid, β-D-glucogallin, isocorilagin and methyl gallate from

CHCl₃-MeOH (9:1) and MeOH extracts.

CONCLUSION
The present document represents the first compilation of biological, pharmacological, phytochemical and traditional information regarding species belonging to *Alchornea* genus. This paper gather in systematically ordered way information regarding 18 species of the genus, compromising the 33% of accepted species listed within this taxa. From the exposed data it is noticeable that, despite the presence of some species in tropical America, the strongest presence of this

genus takes place in tropical Africa in countries including Ivory Coast, Ghana, Nigeria and Congo where their traditional uses were the most prominent source of information for scientific studies, but also that the most studied specie with the greatest number of different biological activities reported is *Alchornea cordifolia*.

It is important to state that the great diversity observed within reported biological activities and isolated phytochemicals sets important perspectives in order to study other *Alchornea* species.
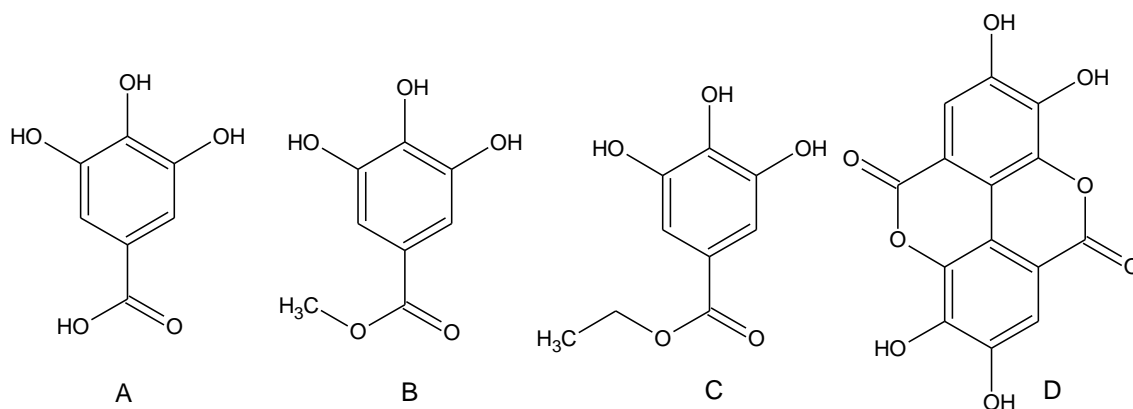

Figure 1
Most common phenolic compounds isolated from *Alchornea* species. A) Gallic acid, B) methyl gallate, C) ethyl gallate and D) ellagic acid.
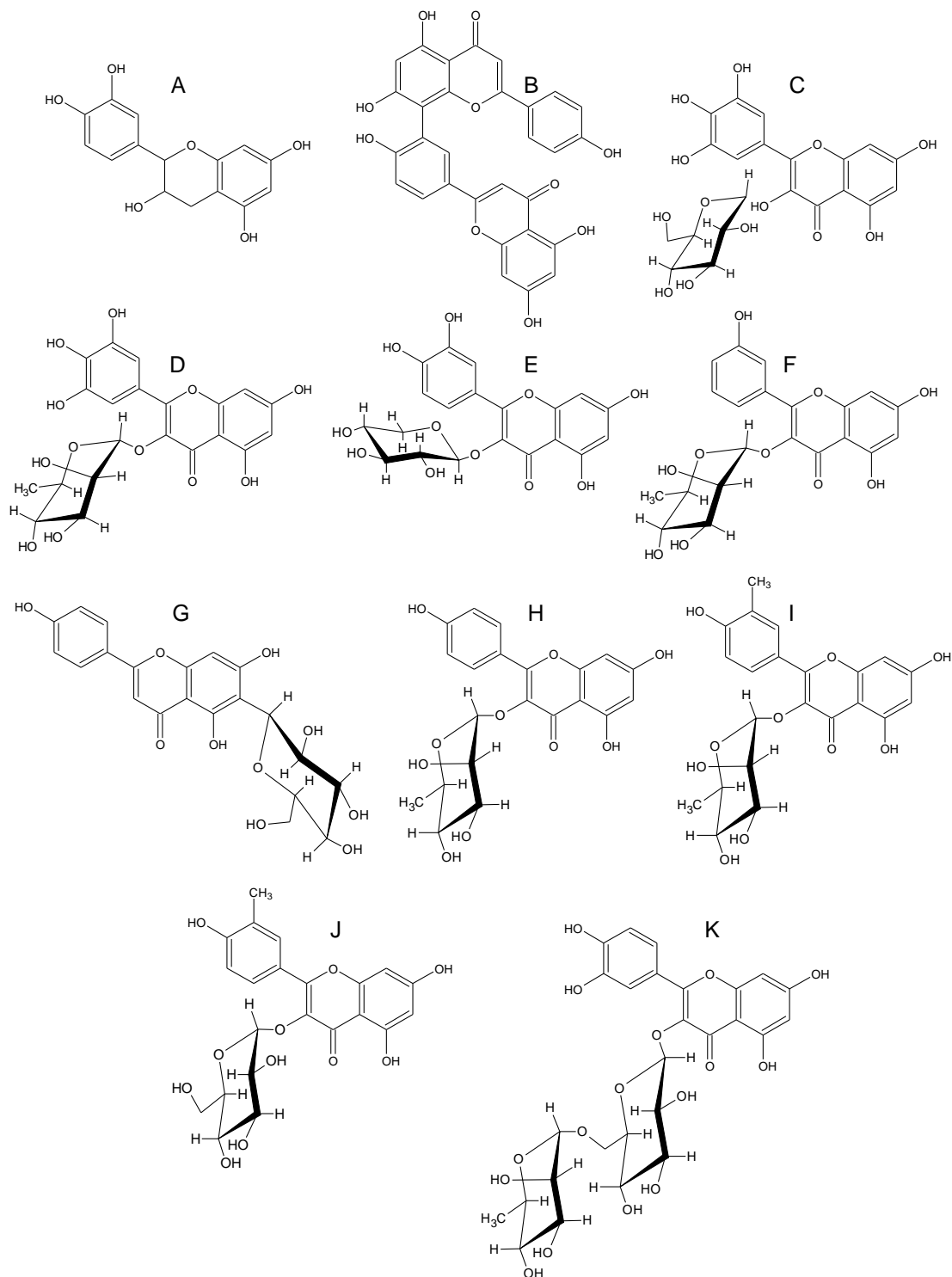
Figure 2
Most common isolated flavonoids from *Alchornea* species. A) Amentoflavone, B) catechin, C) myricetin-3-glucopyranoside, D) myricetin-3-rhamnopyranoside, E) isorhamnetin-3-O-β-*D*-xyloside, F) 3,5,7,3'-tetrahydroxyflavone-3-O-α-*L*-rhamnoside, G) isovitexin, H) Kaempferol-3-O-α-*L*-rhamnoside, I) quercetrin, J) isoquercetrin and K) rutin.
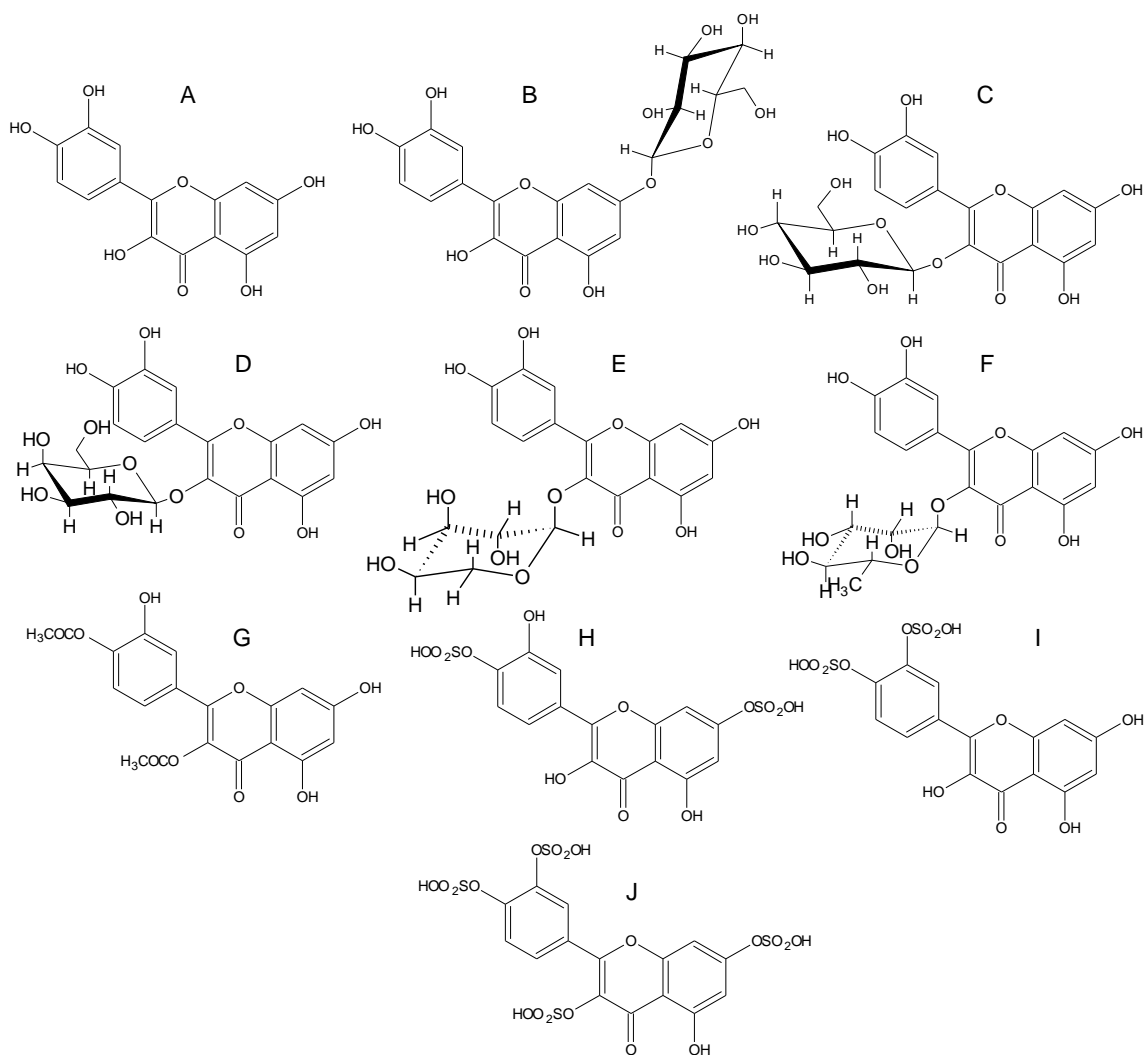
Figure 3

Quercetin derivatives isolated from *Alchornea* species. A) Quercetin, B) quercetin-7-O-glucopyranoside, C) quercetin-3-O-β-*D*-glucopyranoside, D) quercetin-3-O-β-*D*-galactopyranoside, E) quercetin-3-O-α-*D*-arabinopyranoside, F) quercetin-3-O-*L*-rhamnopyranoside, G) quercetin-3,4'-diacetate, H) quercetin-7,4'-disulphate, I) quercetin-3',4'-disulphate and J) quercetin-3,7,3',4'-tetrasulphate.
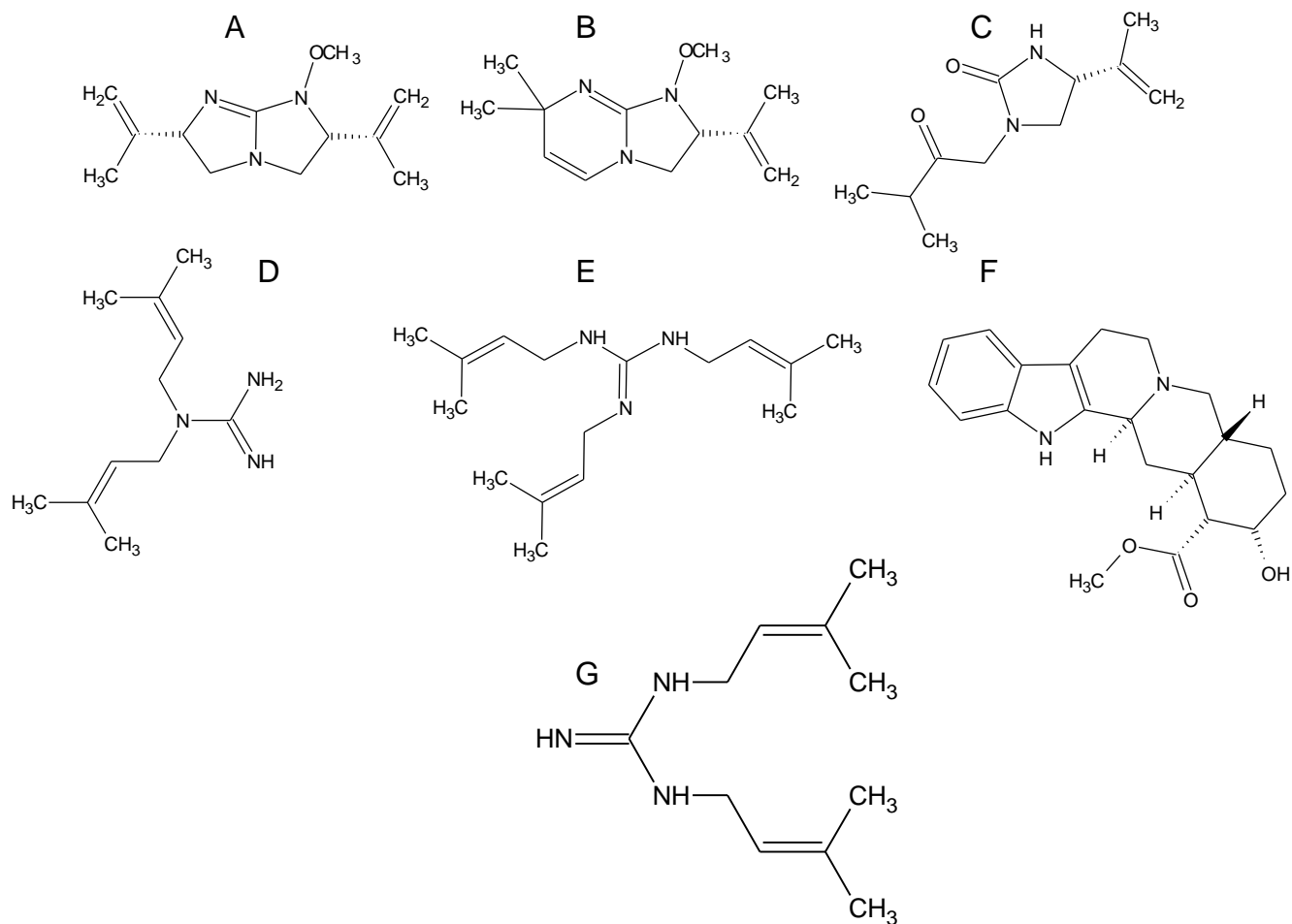
Figure 4
Alcaloids isolated from *Alchornea* species. A) Isoalchorneine, B) Alchorneine, C) Alchorneinone, D) N₁,N₂-diisopentenyl guanidine, E) N₁,N₂,N₃-triisopentenyl guanidine, F) yohimbine and G) pterogynidine.
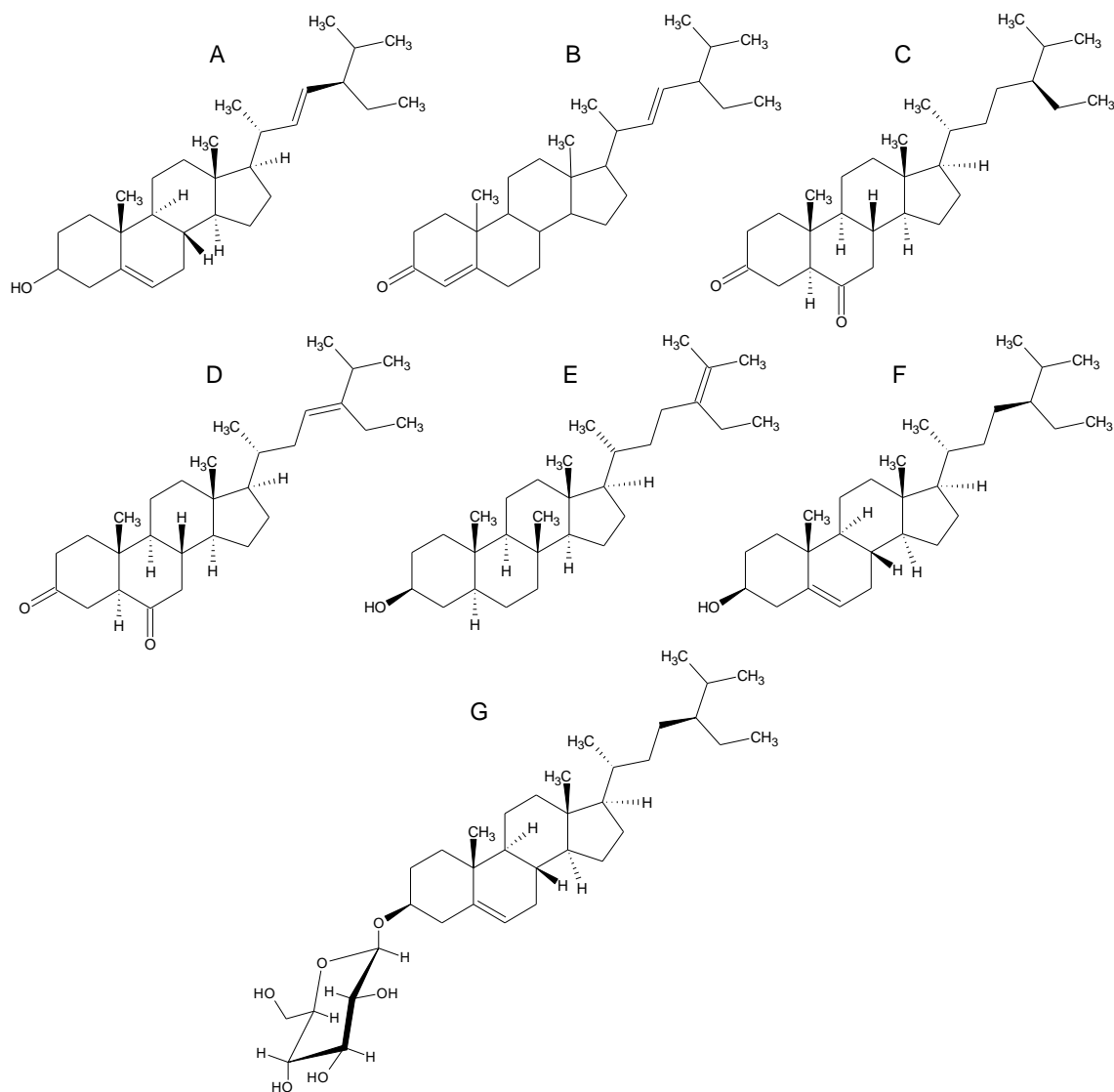
Figure 5
Stigmastane steroids isolated from *Alchornea* species. A) Stigmasterol, B) stigmasta-4,22-dien-3-one, C) 5α-stigmastane-3,6-dione, D) 5α-stigmastane-23-ene-3,6-dione, E) 3-β-hydroxy-5α-stigmastane-24-ene, F) β-sitosterol and G) 3-O-β-*D*-glucopyranosyl-β-sitosterol.

Table 1
Reported phytochemicals for species belonging to *Alchornea* genus.

Species	Part of Plant Used	Phytochemicals	Reported Compounds	Reference
Alchornea aquifolium (Js. Sm.) Domin	Leaf	Alkaloids	Not reported	(Bick, 1996)
Alchornea castaneifolia (Humb. & Bonpl. ex Willd.) A. Juss.	Whole plant	flavonoids, phenolics, saponins, steroids, tannins, triterpenoids	Amentoflavone; catechin; gallic acid; gallic acid methyl ester; isoquercitrin; methyl gallate; myricetin-3-*O*-α-L-arabinopyranoside; quercetin; quercetin-3-*O*-α-L-arabinopyranoside; quercetin-3-*O*-β-D-galactopyranoside.	(Hiruma-Lima *et al.*, 2006; Costa *et al.*, 2008)
Alchornea coelophylla Pax & K. Hoffm	Leaf	Alkaloids, flavonoids, phenolics, saponins, sterols, tannins, terpenoids	Not reported	(Niño *et al.*, 2012; Gaviria *et al.*, 2015)
Alchornea cordifolia (Schumach. & Thonn.) Müll. Arg	Seed	Epoxy fatty acids	(+)-*cis*-14,15-epoxy-*cis*-11 eicosenoic acid; alchornoic acid; methyl vernolate; vernolic acid.	(Kleiman *et al.*, 1977)
	Leaf	Alkaloids, cyanogenic glycosides, flavonoids, saponins, steroidal glycosides, tannins and terpenoids	3-Acetoxy-7,8-epoxylanostan-1-ol; acetyl aleuritolic acid; (*E*)-α-bergamotene; borneol; cadinol; caryophylene; cubenol; daucosterol; di-(2-ethylhexyl)- phthalate; diisopentenylguanidine; ellagic acid; ethyl iso-allocholate; eucalyptol; eugenol; *L*-fenchone; gallic acid; 1-heptatriacontanol; 1-isopropyl-4-methyl-(R)-3-cyclohexen-1-ol; *D*-limonene; linalool; 5'-methyl-4'-propenoxy anthocynidine 7-*O*-β-glucopyranoside; myricetin-3-glucopyranoside; myricetin-3-rhamnopyranoside; nonacosane; 3-(octadecyloxy)propyl	(Lamikanra *et al.*, 1990; Ogungbamila & Samuelsson, 1999; Ajali, 2000; Tona *et al.*, 2000; Banzouzi *et al.*, 2002; Ayisi & Nyadedzor, 2003; Mavar-Manga *et al.*, 2008; Okwu & Ukanwa, 2010; Okoye *et al.*, 2011; Mohammed *et al.*, 2013)

			oleate; 1-octen-3-ol; proanthocyanidin A2; protocatechuic acid; quercetin; quercetin-3-*O*-arabinopyranoside; quercetin-3-*O*-galactopyranoside; β-sitosterol; triisopentenylguanidine; 3,7,11-trimethyldodecanol and yohimbine.	
	Stem bark	Phenolic compounds, steroids and terpenoids	3-*O*-Acetyl-aleuritolic acid; 3-*O*-acetyl-erythrodiol; friedelane-3-one-28-al; friedelin; methyl-3,4,5-trihydroxybenzoate; stigmasta-4,22-dien-3-one; stigmasterol.	(Noundou, 2014)
	Root	Alkaloids and phenolic compounds	Anthranilic acid; gentisic acid and yohimbine.	(Ajali, 2000)
Alchornea davidii Franch.	Leaf and Stem bark	Lignans and tannins	Boehmenan; gallic acid; graminone A; isorhamnetin-3-*O*-β-*D*-xyloside; methyl gallate; 3,3'-di-*O*-methylellagic acid-4-*O*-α-*L*-arabinofuranoside; 3,3'-di-*O*-methylellagic acid 4-*O*-(5'-*O*-acetyl)-α-*L*-arabinofuranoside; monomethylpinoresinol; pinoresinol; (+)-syringaresinol.	(Cui *et al.*, 2003; Cui & Tan, 2004)

Alchornea floribunda Müll.Arg.	Leaf	Alkaloids, fatty acids, flavonoids and steroids	Alchorneinone; 1,1-bis(dodecyloxy)-hexadecane; *E*-2-methyl-3-tetradecene-1-ol-acetate; 3-ethyl-5-(2-ethylbutyl)-octadecane; 9-hexadecenoic acid; 9-hexylheptadecane; 3-β-hydroxy-5-α-stigmastane-24-ene; isoalchorneine; 7-methyl-*Z*-tetradecen-1-ol-acetate; 3-(octadecyloxy)propyl oleate; 3-octyl-*cis*-oxiraneoctanoic acid; oleate; 17-pentatriacotene; 5α-stigmastane-3,6-dione; 5α-stigmastane-23-ene-3,6-dione; 3,5,7,3'-tetrahydroxyflavone-3-*O*-α-*L*-rhamnoside (AFF1); 2,6,10,14-tetramethylpentadecane; 2,6,10-trimethyldodecane; 2,6,10-trimethyltetradecane.	(Khuong-Huu *et al.,* 1972; Okoye *et al.,* 2010; Okoye & Osadebe, 2010; Okoye *et al.,* 2011; Lifongo *et al.,* 2014)
	Stem bark	Alkaloids	Alchorneine	(Khuong-Huu *et al.,* 1972)
	Root	Alkaloids	Alchorneine and isoalchorneine	(Khuong-Huu *et al.,* 1972)
Alchornea glandulosa Poepp.	Leaf	Alkaloids, gallic acid derivatives, glycoside flavonoids, lactones, saponins, sterols, tannins	Amentoflavone; corilagin; ethyl gallate; gallic acid; isoquercetrin; isovitexin; kaempferol-3-*O*-*L*-rhamnoside; loliolide; methyl gallate; myricetin-3-*O*-*L*-rhamnoside; protocatechuic acid; pterogynidine; quercetin; quercetin-3-*O*-α-*L*-arabinopyranoside; quercetin-3-*O*-β-*D*-galactopyranoside; quercetin-3-*O*-*L*-rhamnoside; β-sitosterol; stigmasterol and	(Conegero *et al.,* 2003; Urrea-Bulla *et al.,* 2004; Calvo *et al.,* 2007; Correa *et al.,* 2007; Lopes *et al.,* 2005; Lopes *et al.,* 2009; Lopes *et al.,* 2011)

			N_1,N_2,N_3-triisopentenylguanidine	
Alchornea hirtella Benth.	Leaf	Alkaloids, flavonoids, saponins, sterols, terpenoids, tannins	Not reported	(Koroma & Ita, 2009)
	Stem bark	Akaloids	Alchorneine	(Khuong-Huu *et al.,* 1972)
*Alchornea latifolia*Sw.	Leaf	Phenolic compounds and terpenoids	Epifriedelinol; friedelin; pyrocatechol; *seco*-3,4-friedelin (dihydroputranjivic acid); *seco*-3,4-taraxerone; taraxerol; taraxerone;	(Setzer *et al.,* 2000)
Alchornea laxiflora (Benth.) Pax & K. Hoffm	Leaf	Alkaloids, carbohydrates, cardiac glycosides, flavonoids, phenols, phlobatannin, saponins, steroids, tannins, terpenoids.	Ellagic acid; 3-*O*-methylellagic acid; 3-*O*-methyl-3'-*O*-α-rhamnopyranosil-ellagic acid; (2*R*)-2-hydroxy-*N*-[(2*S*,3*S*,4*R*,15*Z*)-1,3,4-trihydroxy-15-triaconten-2-yl]octacosamide; 3-*O*-acetyl-oleanolic acid; quercetin; quercetin-3,4'-diacetate; quercetin-3',4'-disulphate; quercetin-3-*O*-β-*D*-glucopyranoside; quercetin-3-*O*-rhamnoside; quercetin-7,4'-disulphate; quercetin-3,7,3',4'-tetrasulphate; quercetrin; rutin; 3-*O*-β-*D*-glucopyranosyl-β-sitosterol; taxifolin glycoside; (10*Z*)-tetradec-10-enoic acid-(2*S*)-2-carboxy-2-hydroxyethyl ester; 3-*O*-acetyl-ursolic acid.	(Ogundipe *et al.,* 2001; Farombi *et al.,* 2003; Adeloye *et al.,* 2005; Oloyede *et al.,* 2010; Oloyede *et al.,* 2011; Sandjo *et al.,* 2011; Borokini & Omotayo, 2012; Noundou, 2014)

Alchornea rugosa (Lour.) Müll.Arg	Stem bark	Alkaloids	Alchornine; alchornidine; N_1,N_1-diisopentenylguanidine; N_1,N_2,N_3-triisopentenylguanidine; 2,2-dimethylacrylamide.	(Hart *et al.*, 1969; Hart *et al.,* 1970b; Collins *et al.,* 1990; Bick, 1996)
Alchornea sidifolia Müll.Arg.	Leaf	Flavonoids, terpenoids	α-Amorphene; corymbol; diphenylsulfide; pentatronol; quercetrin; β-sitosterol.	(Barbo *et al.,* 2002; Leone, 2005)
	Root	Terpenoids	β-caryophyllene; α-humulene.	(Leone, 2005)
Alchornea tiliifolia (Benth.) Müll. Arg.	Leaf	Terpenoids	Allo-aromadendrene; bicyclogermacrene; (*E*)-γ-bisabolene; bisabolol oxide B; (*Z*)-γ-bisabolene; borneol; δ-cadinene; α-calacorene; camphene; β-caryophyllene; caryophyllene oxide; α-cedrene; 1,8-cineole; α-copaene; β-cubebene; γ-curcumene; *p*-cymene; γ-eudesmol; (*E,E*)-α-farnesene; (*Z,E*)-α-farnesene; (*E*)-β-farnesene; farnesol; α-fenchol; germacrene D; β-gurjunene; α-humulene; limonene; linalool; α-muurolene; myrcene; myrtenol; nerolidol; neryl formate; nonanal; (*E*)-β-ocimene; (*Z*)-β-ocimene; α-pinene; β-pinene; sabinene; α-terpinene; terpinen-4-ol; α-terpineol; γ-terpinene; terpinolene; α-thujene.	(Dũng *et al.,* 2009)
Alchornea trewioides (Benth.) Müll. Arg.	Root	Phenolic compounds	3,4-dimethoxyphenyl-(6'-*O*-α-L-rhamnosyl)-β-D-glucopyranoside; 3,4,5-trimethoxyphenyl-(6'-*O*-galloyl)-*O*-β-D-glucopyranoside; erigeside C; ethyl gallate; gallic acid; 1-*O*-galloyl-6-*O*-vanilloyl-β-glucose; glucosyringic acid; syringic acid.	(Qin *et al.,* 2012)

Species			
Alchornea triplinervia (Spreng.) Müll.Arg.	Leaf	Flavonoids and phenolic compounds	Amentoflavone; ellagic acid; gallic acid; β-*D*-glucogallin; isocorilagin; methyl gallate; quercetin-3-*O*-arabinopyranoside; quercetin-3-*O*-galactopyranoside; quercetin-3-*O*-glucopyranoside; quercetin-7-*O*-glucopyranoside.	(Braca *et al.,* 2002; Lima *et al.,* 2008)

Table 2
Biological activities reported for species belonging to *Alchornea* genus.

Species	Reported Activity	Description	Reference
Alchornea castaneifolia (Humb. & Bonpl. ex Willd.) A. Juss.	Antibacterial	Mild inhibition was observed against *Staphylococcus epidermis* with an inhibition zone of 12 mm at 500 µg/mL.	(Costa *et al.,* 2008)
	Antiulcerogenic	In an *in vivo* model of mice, hydroalcoholic leaf extract and flavonoid enriched fraction at doses of 500 and 100 mg/Kg, ameliorate the healing process of induced ulcers and stimulated synthesis of defensive agents as prostaglandin and somastatin and inhibited gastrin secretion	(Hiruma-Lima *et al.,* 2006)
	Anti-inflammatory	*In vitro* and *in vivo* models of bovine seminal vesicle microsomes and mice, showed that ethanolic extract exhibited moderate inhibition of COX-1 prostaglandin biosynthesis and a 55% of inhibition of oedema in ear's mice after 2 h.	(Dunstan *et al.,* 1997)

Alchornea coelophylla Pax & K. Hoffm	Antibacterial	*In vitro:* MICs against *Bacillus subtilis, Staphylococcus aureus, Pseudomonas aeruginosa and Escherichia coli* were 4 mg/mL to the first and 1 mg/mL for the three latter to the methanolic leaf extract. The hexane extract also displayed activity against *P. aeruginosa* (MIC: 4 mg/mL).	(Niño *et al.,* 2012)
	Antioxidant	Dichloromethane and methanol extracts displayed an IC$_{50}$ of 126.38 and 41.14 µg/mL (TEAC 40.61 and 41.65 µmol Trolox/g extract, respectively) through *in vitro* DPPH$^{.}$ assay. Additionally, through *in vitro* ABTS$^{.+}$ assay, TEAC values for the same extracts were 149.06 and 837.42 µmol Trolox/g extract, respectively.	(Mosquera *et al.,* 2007; Gaviria *et al.*, 2015;)
Alchornea cordifolia (Schumach. & Thonn.) Müll. Arg	Antiamoebic	*In vitro* assay against *Entamoeba histolytica* with *n*-butanol (polyphenol extract), crude saponin and total alkaloid extracts found minimal amoebicidal concentrations (MAC) of 5, >50 and 16.7 µg/mL, respectively. Otherwise, leaf aqueous decoction crude extract exhibited a MAC of 125 µg/mL.	(Tona *et al.,* 2000)

	Antibacterial	Acetone, ethanol and methanol extracts of leaves where active against *Staphylococcus aureus* (MIC 2.8, 2.6 and 1.5 mg/mL, respectively), *Bacillus subtilis*(3.0, 2.8 and 2.4 mg/mL), *Escherichia coli* (3.8, 4.2 and 2.8 mg/mL), *Klebsiella pneumoniae* (5.0, 4.4 and 3.2 mg/mL) and *Pseudomonas aeruginosa* (4.4, 3.3 and 2.2 mg/mL), when evaluated *in vitro* by agar dilution method. Also inhibition zones (>10 mm) were detected when ethanolic and aqueous extracts were evaluated against *Proteus vulgaris*, *Streptococcus pyogene*, methicillin susceptible *Staphylococcus aureus* and Multi-Resistent *Staphylococcus aureus*bacterial isolates (MIC ranging from 0.4 to 12.5 mg/mL for the aqueous extracts). Moderate antibacterial activity were observed when leaf aqueous decoctions where tested against *Escherichia paracoli, Citrobacter diversus, Salmonella enteritidis* and *Shigella flexneri*. Similarly, moderate activity were observed by MeOH-DCM (1:1) leaf extract against *Mycobacterium smegmatis* (MIC 65 µg/mL) and a stem bark extract from the same solvent mixture showed a MIC of 250 µg/mL against *Mycobacterium aurum.*	(Tona *et al.,* 1999; Ajali, 2000; Pesewu *et al.,* 2008; Fomogne-Fodjo *et al.*, 2014;)

	Antidepressant	Evidence indicated that the hydroethanolic leaf extract of *Alchornea cordifolia* possesses antidepressant-like effect mediated through interaction with dopamine (D1 and D2), noradrenergic ($\alpha 1$ and $\alpha 2$ adrenoceptors), and serotonergic ($5HT_{1B}$ receptors) systems in mice.	(Ishola *et al.,* 2014)
	Anti-diabetic	*n*-Butanol fraction of aqueous leaf extract reduced glucose blood level in streptozotocin-induced diabetic Wistar rats at dosages of 200, 400 and 800 mg/Kg. It also exerts other haematological effects.	(Mohammed *et al.*, 2013)
	Antidiarrhoeal	Ethanolic leaf extract significantly stimulated a net absorption of water and a reduction in electrolytes secretions, showing an inhibition of 64.6% on intestinal transit at a dosage of 800 mg/Kg in mice.	(Agbor *et al.,* 2004)
	Antidrepanocytary/ Antisickling	Alkaloids and anthocyanins containing fractions from aqueous leaf extracts were able to normalize erythrocytes of SS blood samples.	(Mpiana *et al.,* 2007)
	Anti-HIV	Aqueous decoction of plant were effective inhibitors of HIV-1 and HIV-2, when inhibited viral cytopathicity when treatment was delayed for 2 hours, and in a early-stage fusion of chronically HIV infected cells with uninfected cells.	(Ayisi & Nyadedzor, 2003)

Anti-inflammatory	Lipophilic and polar fractions obtained from leaf methanolic extract and some isolated compounds, revealed significant cutaneous inhibition in some cases even higher than positive control, indomethacin. Otherwise, terpenoid and tannin-containing fraction were found to be partially responsible for the mentioned activity.	(Osadebe & Okoye, 2003; Manga *et al.*, 2004; Mavar-Manga *et al.,* 2008)
Antioxidant	Hydroethanolic leaf extract showed significant protection against paracetamol-induced hepatotoxicity inhibiting glutathione *S*-transferases. Additionally, aqueous and ethyl acetate extracts were able to inhibit and scavenge human ROS (HOCl and H_2O_2) and neutrophil elastase and superoxide anion in acellular and cellular systems.	(Olaleye *et al.,* 2007; Kouakou-Siransy *et al.,* 2010a; Kouakou-Siransy *et al.,* 2010b)
Antiplasmodial	*In vitro* assays using aqueous, ethanolic and pentane extracts against two chloroquine-resistant and a Nigerian chloroquine-sensitive strain of *Plasmodium falciparum*, showed IC_{50} values ranging 2.43-4.56 µg/mL, 2.30-3.95 µg/mL and 15.50-43.40 µg/mL, respectively, in 24 and 72 hours assays. Aqueous leaf extract was also active against a chloroquine and pyrimethamine resistant K1 *Plasmodium falciparum* strain with an IC_{50} of 4.84 µg/mL.	(Mustofa *et al*., 2000; Banzouzi *et al.,* 2002; Mesia *et al.*, 2008; Musuyu Muganza *et al.,* 2012)

	Antitrypanosomal	Hydromethanolic (80%) extract when evaluated *in vitro* against *Trypanosoma brucei brucei* and *Trypanosoma cruzi* displayed IC_{50} values of 0.7 and 34 µg/mL, respectively. Ethanol extract showed moderate activity against *T. congolense* strains with IC_{50} values of 68.06 and 68.9 µg/mL, the latter was a resistant strain. Also aqueous leaf extracts showed moderate activity against *Leishmania infantum* with an IC_{50} value of 32.46 µg/mL and moderate activity with the above mentioned *Trypanosoma* strains.	(Adewunmi *et al.,* 2001; Mesia *et al.,* 2008)
	Hepatoprotective	Acetone, chloroform and ethyl acetate fractions from methanol leaf extract reduced levels of some biochemical parameters (serum glutamate oxalate transaminase, serum glutamate pyruvate transaminase, alkaline phosphatase and total bilirubin) on CCl_4 induced damage in rats. Also aqueous decoctions of this plant were able to inhibit the negative consequences after hepatotocity-induced damage not only by paracetamol intoxication through an antioxidant mechanism, but also reduced the production of thiobarbituric acid reactive substances (TBARS) induced by pro-oxidant agents.	(Olaleye & Rocha, 2007; Olaleye & Rocha, 2007; Osadebe *et al.,* 2012)

	Immunomodulatory	Isolated polysaccharides from ethanol leaf extract activate human monocyte/macrophages modulating NO and cytokines (IL-1β, IL-6, TNF-α, GM-CSF and IL-10) productions.	(Kouakou *et al.,* 2013)
	Spasmolytic	*n*-Butanol and crude saponin extracts inhibited contraction of Guinea-pig's ileum when stimulated with acetylcholine (Ach) and KCl.	(Tona *et al.,* 2000)
	Toxicity tests	The hydroethanolic leave extract up to 4000 mg/Kg did not induce mortality but behavioral toxic symptoms were observed in albino mice. Methanolic extract displayed a LD_{50} of 1131.4 mg/Kg when administered intraperitoneally in mice. Also toxicity assays were carried out with bovine aorta endothelial, HeLa and MRC-5 cells with LD_{50} of 220.72, 54.97-62.75 and > 64 µg/mL, respectively, by leaf ethanol extract.	(Mustofa *et al.,* 2000; Adewunmi *et al.,* 2001; Osadebe & Okoye, 2003; Okoye & Osadebe, 2010; Musuyu Muganza *et al.,* 2012; Isholae *et al.,* 2014)
Alchornea davidii Franch.	Antibacterial	*In vitro* assays of isolated compound from ethyl acetate fraction from the methanol plant extract revealed MICs of 50 µg/mL against *Bacillus subtilis, Staphylococcus aureus* and *Pseudomonas fluorescens.*	(Cui *et al.,* 2003)
	Antifungal	An isolated flavonol from methanol extract was evaluated against *Candida albicans, Aspergilus niger* and *Trichophyton rubrum* showing antimicrobial activity with MICs of 50 µg/mL.	(Cui *et al.,* 2003)

Alchornea floribunda Müll. Arg.	Antibacterial	Medium polar leaf extracts (DCM-MeOH (1:1)) showed strong antibacterial activities with MIC values of 65 and 50 μg/mL against *Morexella cattarhalis* and *Mycobacterium smegmati*, respectively. Additionally, moderate activity was observed for both leaf and stem bark extracts, with a MIC value of 500 μg/mL against *Mycobacterium aurum*. Also strong antibacterial activity for medium polar extracts (EtOH, MeOH, EtOAc, CHCl$_3$) against *Staphylococcus aureus* (MIC ≥ 50 μg/mL) and *Klebsiella pneumoniae* (MIC ≥ 64 μg/mL) was reported. In addition, aqueous, EtOH, MeOH, EtOAc, CHCl$_3$ and hexane extracts displayed moderate antibacterial activity (MIC ≥ 250 μg/mL) but also strong activity were observed with MIC values ranging amongst 50 and 70 μg/mL against *Bacillus cereus*, *Enterococcus faecalis*, *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Morexella cattarhalis*, *Proteus mirabilis* and *Staphylococcus saprophyticus.*	(Fomogne-Fodjo *et al.,* 2014; Noundou *et al.,* 2014)
	Anti-inflammatory	Ethyl acetate fractions from methanol leaf extract and further isolated compound were able to inhibit oedema induced in rats by sub-plantar injections with inhibition percetages varying amongst 78.4 and	(Okoye & Osadebe, 2010)

		40.5 once 3 hours passed. Further more, lipophilic leaf hexane extract was active against xylene-induced ear oedema with a 64% of inhibition.	
	Antiprotozoal	Moderate antiprotozoal activities were observed when strains of *Trypanosoma brucei brucei*, *Trypanosoma cruzi*, *Leishmania infantum* and a K1 strain of *Plasmodium falciparum*(chloroquine and pyrimethamine-resistant) were tested against plant decoctions showing IC_{50} values of 19.65, 37.26, >64 and 20.80 μg/mL, respectively.	(Musuyu Muganza *et al.,* 2012)
Alchornea glandulosa Poepp.	Antiangiogenic	Ethyl acetate fraction from methanol leaf extract exerted inhibitory effects on angiogenesis acting on endothelial cells and preventing angiogenic steps such proliferation, invasion and capillary-like structures formations on human umbilical vein enothelial cells (HUVEC). Further investigations identified the mechanism of action, through NFκβ inhibition.	(Lopes *et al.,* 2009; Lopes *et al.,* 2011)
	Antifeedant	Ethanol leaf extract and further petroleum ether, toluene, isopropanol and water fractions showed moderate activity against neonate larvae of *Spodoptera frugiperda* with IC_{50} values of 23, 48, 43, 25 and 95 μg/mL, respectively.	(Urrea-Bulla *et al.*, 2004)

	Antiulcerogenic	Methanolic leaf extract showed antisecretory and gastroprotective activites when administered for 14 days to male Swiss albino mice, accelerating the healing process of gastric ulcers by promoting epithelial cell proliferation in different acute models of gastric ulceration.	(Calvo *et al.,* 2007)
	DNA interaction	Mild inhibition percentage (21.13%) was obtained when methanolic extract (250 mg/L) was mixed with a herring sperm DNA aqueous solution (100 mg/L) through RP-HPLC technique.	(Correa *et al.,* 2007)
	Immunomodulatory	Ethyl acetate fraction from methanol leaf extract showed some inhibition on H_2O_2 and NO production in lipopolysaccharide (LPS) and phorbol myristate acetate (PMA) activated peritoneal macrophages, possibly through a transcriptional mechanism because a moderate inhibition in TNF-α production was also observed.	(Lopes *et al.,* 2005)
Alchornea grandiflora Müll.Arg.	DNA interaction	Low interaction was observed when dichloromethane and methanolic extracts were tested through DNA HPLC-interaction assay with 5.46% and 28.95% of inhibition, respectively, at 250 mg/L.	(Correa *et al.,* 2007)

Alchornea hirtella Benth.	Antibacterial	Leaf aqueous extract showed moderate to low antibacterial activity through the diffusion method against *Streptococcus pyogenes*, *Staphylococcus aureus*, *Escherichia coli* and *Proteus mirabilis* with inhibition percentages of 27%, 28%, 33% and 56%. Additionally, ethanolic leaf extract displayed mild activity with 56%, 27%, 14% and 33% inhibition percentages against the respective above mentioned strains.	(Koroma & Ita, 2009)
*Alchornea latifolia*Sw.	Antibacterial	Crude chloroform leaf extract showed activity against *Staphylococcus aureus* and *Streptococcus pneumoniae.*	(Setzer *et al.,* 2000)
	Cytotoxic	Crude chloroform leaf extract was active against A-431 and Hep-G2 cells using the cell viability MTT assay. The displayed activity was apparently due to the inhibition of topoisomerase II. The crude extract killed the 92.7% and 94.8% of the respective cells tested at a concentration of 250 μg/mL. Otherwise two isolated compounds (*seco*-3,4-friedelin and *seco*-3,4-taraxerone) showed IC_{50} values ranging 11.7 to 38.2 μg/mL.	
	Topoisomerase II inhibition	Two seco-3,4-triterpenoids isolated from the chloroform crude leaf extract inhibited the topoisomerase activity using pBR322 plasmid DNA with comercially	

		available topoisomerase II. Such compounds showed MIC values of 7 µM.	
Alchornea laxiflora (Benth.) Pax & K.Hoffm	Antibacterial	Some isolated flavonoids from the ethyl acetate soluble fraction from the methanol leaf extract exerted significant activity through diffusion method when evaluated at 1 mg/mL against *Aspergillus flavus, Bacillus cereus, Bacillus subtilis, Candida albicans, Escherichia coli, Pseudomonas aeruginosa* and *Staphylococcus aureus.*	(Ogundipe *et al.,* 1999)
	Anticholinesterase	Acetone leaf extract inhibited the activity of acetylcholinesterase with a IC$_{50}$ value of 364.12 µg/mL.	(Dzoyem & Eloff, 2015)
	Anticonvulsant and sedative	Leaves decoction protected 100% of *Mus musculus* Swiss mice against *N*-methyl-D-aspartate (NMDA)-induced turning behavior at a dose of 60 mg/Kg. Additionally, 75% of mice were protected against strychnine (STR)-induced convultions at a dosage of 120 mg/Kg. Extracts were administrated orally for both determinations.	(Bum *et al.,* 2009)
	Anti-inflammatory	Acetone leaf extract exert strong inhibition to 15-lipoxygenase and the production of iNOS in LPS-activated RAW 2647 macrophages with an IC$_{50}$ value of 46.03 µg/mL and percentage inhibitions ranging 93.81% to 86.38% related to concentrations amongst 50 and 6.25	(Dzoyem & Eloff, 2015)

		μg/mL, respectively.	
	Antioxidant	Acetone leaf extract showed strong antioxidant activity through DPPH· and ABTS·+ scavenging assays with IC$_{50}$ values of 17.19 and 18.53 μg/mL, respectively. Additionally, an IC$_{50}$ of 438.42 μg/mL was reported in the FRAP assay. Moreover, ethyl acetate and butanol fractions from water-ethanol (1:1) showed strong activity through the DPPH· bleaching test with IC$_{50}$ values of 12.97 and 24.34 μg/mL, respectively. Butanol leaf extract displayed an antioxidant activity of 78% at 500 μg/mL; similar behavior was the observed for α-tocopherol (82% at 500 μg/mL) when evaluated through the ferric thiocynate method.	(Adeloye *et al.,* 2005; Oloyede *et al.*, 2010; Dzoyem & Eloff, 2015)
	Cytotoxic	Two isolated compounds (3-*O*-acetyloleanoic acid and 3-*O*-acetoxyursolic acid) from CH$_2$Cl$_2$-MeOH (1:4) leaf extract showed an IC$_{50}$ value of 6.6 and 6.8 μM, respectively, when tested against human promyelocytic leukaemia (HL60) cell line.	(Sandjo *et al.,* 2011)

Enzyme modulatory	Aqueous leaf extracts considerably increased the activity of lactase, maltase and sucrase in gut when administered to mice at dosages of 100, 200 and 300 mg/Kg. In addition, aqueous extract inhibited hyaluronidase activity in *Naja nigricollis* venom-induced tissue necrosis assay with an IC_{50} value of 150 μg/mL. Moreover, moderate to high inhibition percentages were reported for ethanolic and aqueous extracts against hyaluronidase, phospholipase A_2 and proteolytic activities in *Bitis arietans* venom-induced tissue necrosis assay at concentrations of 5 mg/mL and 2.5 mg/mL for the latter determination.	(Molander *et al.,* 2014; Olatunde *et al.,* 2014)
Gastric modulatory	Treatments with aqueous leaf extract to iron deficient albino rats (*Rattus norvegicus*) at dosages of 100, 200 and 300 mg/Kg significantly increased levels of gastric pH to 3.26, 3.58 and 3.53; pH values comparable to the iron sufficient and reference drug groups.	(Olatunde *et al.,* 2014)
Hepatoprotective	Ethyl acetate leaf extract decreased the levels of biochemical parameters related to CCl_4-induced hepatotoxicity at the point that there where no significant difference with control (non-treated) group. Such marker enzymes were aspartate aminotransferase (AST), alanine aminotransferase	(Oloyede *et al.,* 2011)

		(ALT), alkalinephostatase (ALP) and lactate dehydrogenase (LDH). The dosage administered to adults Wistar rats were 200 mg/Kg. Results were also supported with further histopathological studies.	
Alchornea sidifolia Müll.Arg.	Antifungal	Root and bark chlorofom extracts showed activity against *Cladosporium sphaerospermum*	(Leone, 2005)
Alchornea trewioides (Benth.) Müll.Arg.	Antiviral	The ethyl acetate extract inhibited the hepatitis C virus replication and NS3 proteins expression in CBRH7919 cell culture model with an IC_{50} of 14.60 µg/mL.	(Wang *et al.,* 2013)
	Hepatoprotective	Root extract protected rats against alcohol-induced hepatic fibrosis, reducing levels of transforming growth factor β1 (TGFβ1), tissue inhibitor of metalloproteinase-1 (TIMP-1), hyaluronic acid (HA), laminin (LN), procolagen type III (PC III), collagen type IV (C IV) glutamic-pyruvic transaminase (ALT) and glutamic-oxalacetic transaminase (AST) in serum.	(Lü *et al.,* 2007)
Alchornea triplinervia (Spreng.) Arg.	Antibacterial	Ethyl acetate fraction of methanolic bark extract exerted some inhibition through paper disc method against *Staphylococcus aureus.* Moreover, methanolic leaf extract showed activity against *Helicobacter pylori* with a MIC value of 0.25 mg/mL.	(Macrae *et al.*, 1988; Lima *et al.,* 2008)

Antifungal	Aqueous fraction of methanol bark extract produced a >75% of inhibition at 1 μg/mL against *Microsporum canis, Microsporum fulvum, Microsporum gypseum* and *Trichophyton gallinae*. However, lesser concentrations of ethyl acetate fraction of the same extract were needed to obtain the same response, with 0.25 μg/mL against *M. canis* and *M. gypseum*, 0.5 μg/mL against *T. gallinae* and 1.0 μg/mL for *M. fulvum* inhibition.	(Macrae *et al.,* 1988)
Antitumoral	Ethyl acetate fraction of methanol bark extract inhibited the tumor formation induced by *Agrobacterium tumefaciens* over *Solanum tuberosum* disks with a EC_{50} of 0.62 μg/mL.	
Antiulcerogenic	Methanolic leaf extract exerted some inhibition ranging from 77% to 90% on the formation of gastric lesions in mice when induced by HCl/Ethanol and Piroxicam models at dosages amongst 250 and 1000 mg/Kg. Additionally, inhibition of ethanol-induced lesions on rats were observed with methanol extract (85-89% at 500-1000 mg/Kg) and ethyl acetate fraction (50% at 100 mg/Kg), further determinatios showed that the gastroprotective action is due to the increase in PGE_2 levels.	(Lima *et al.,* 2008)

	Antiviral	Both aqueous and ethyl acetate fractions inhibited 100% of the plaque forming ability with a LC_{50} <1 μg/mL at the pre-infection treatment, otherwise LC_{50} values of 35 and 17 μg/mL were obtained for ethyl acetate and aqueous extracts, respectively, at the post infection treatment against Sindbis virus on infected 3T3 mice cells. Additionally, with the same pre/post treatment against murine cytomegalovirus (MCMV) only LC_{50} values of 0.22 and <1 μg/mL were reported for the ethyl acetate and aqueous extracts, respectively, for the pre-infection treament over the same infected cell lines.	(Macrae *et al.,* 1988)
	Toxicity tests	Ethyl acetate and aqueous fractions were assayed against Artemia salina brine shrimp test and they exhibited LC_{50} values of 110 and 92 μg/mL, respectively.	(Macrae *et al.,* 1988)

Table 3
Reported common names and folk usages of species belonging to *Alchornea* genus.

Species	Common Name	Country	Use/ Folk Use	Reference
Alchornea bogotensis Pax & Hoffm	Carcomo	Colombia	Food, fuel and wood	(Orrego *et al.,* 2008; Cenicafé, 2010)
Alchornea castaneifolia (Humb. & Bonpl. ex Willd.) A. Juss.	Sarã, sarão and gurupiá	Brazil	Inflammation, rheumatism and ulcer	(Duke & Martinez, 1994; Costa *et al.,* 2008)

Alchornea cordifolia (Schumach. & Thonn.) Müll. Arg	Ewe eepa, esinsin and eepa	Southest Nigeria	Dermatitis, diarrhea, fever, hemorrhoids, *Herpes zoster*, inflammatory-related diseases, malaria, prevention of abortion, purgative, reuhmatic pains, ringworm, snakebites and treatment of leprosy	(Houghton & Osibogun, 1993; Tona *et al.,* 1999; Ajali, 2000; Osadebe & Okoye, 2003; Tor-anyiin *et al.,* 2003; Pesewu *et al.,* 2008; Jusu & Sanchez, 2013; Ishola *et al.,* 2014;)
Alchornea davidii Franch.	Shanmagan	China	Infectious or inflammatory diseases	(Cui *et al.,* 2003; Cui & Tan, 2004)
Alchornea discolor Poepp	Palometa huayo	Peru	Fish bait, also fishermen like to fish in the shade of this three	(Duke & Martinez, 1994; Wittmann & Wittmann, 2011; Grandtner & Chevrette, 2013)
Alchornea floribunda Müll. Arg.	Ononn, ngombo	Democratic Republic of Congo	Aphrodisiac, arthritis, inflammatory, intestinal, muscle pain, respiratory and urinay disorders	(Mesia *et al.,* 2008; Okoye & Osadebe, 2010; Musuyu Muganza *et al.,* 2012; Lifongo *et al.,* 2014)
Alchornea glandulosa Poepp.	Tapiá	Brazil	Anti-inflammatory	(Lopes *et al.,* 2011)
Alchornea hirtella Benth	Not Reported	Not Reported	Dysentery, fractures	(Chifundera, 2001; Jusu & Sanchez, 2013)
Alchornea latifolia Sw	Escobo	Colombia	Not Reported	(Orrego *et al.,* 2008; Grandtner & Chevrette, 2013)
Alchornea laxiflora (Benth.) Pax & K. Hoffm	Iya/pépé	Nigeria	Disentery, food preservation, infectious and inflammatory disorders	(Adewole, 1993; Farombi *et al.*, 2003; Kayode & Omotoyinbo, 2008; Jiofack *et al.,* 2009)
Alchornea sidifolia Müll. Arg.	Tapiá-guaçu	Brazil	Not Reported	(Secco & Giulietti, 2004; Grandtner & Chevrette, 2013)
Alchornea tiliifolia (Benth.) Müll. Arg.	Dom dom la day	Vietnam	Not Reported	(Dũng *et al.,* 2009)
Alchornea trewioides (Benth.) Müll. Arg.	Hongbeiyegen	China	Not Reported	(Lü *et al.,* 2007)
Alchornea triplinervia (Spreng.) Müll. Arg.	Not Reported	Not Reported	Gastric disturbances	(Silva *et al.,* 2000)

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