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Medicinal Plants Used in Mali for the Treatment of Malaria and Liver Diseases

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Today, ethno-pharmacology is a very important resource in order to discover new therapies for the current diseases. Moreover, another good justification for the ethno-pharmacological approach is to obtain new, effective, less expensive and simple therapies, limiting at the same time the cost of pharmaceutical research. Two major anti-malarial drugs widely used today, i.e. quinine and artemisinin, came respectively from Peruvian and Chinese ancestral treatments reported in the traditional medicines. In this contest, there is an urgent need for the discovery of new drugs, due to the critical epidemiological situation of this disease and to the growth of resistances. In Mali, malaria and liver diseases remain one of the leading public health problems. Many medicinal plants are often used, in local traditional medicine, for the treatment at the same time of malaria and liver diseases, including hepatic syndromes, jaundice, hepatitis and other hepatic disorders. Moreover, in the local language Bamanan, the word “*Sumaya*” is used both for malaria and some liver diseases. In addition, we noted that some of the improved traditional phytomedicines produced by the Department of Traditional Medicine are prescribed by modern doctors both for malaria and liver diseases. In this review, pharmacological, toxicological and phytochemical data on *Argemone mexicana* L. (Papaveraceae), *Cochlospermum tinctorium* Perr. ex A. Rich (Cochlospermaceae), *Combretum micranthum* G.Don (Combretaceae), *Entada africana* Guillet Perr. (Mimosaceae), *Erythrina senegalensis* A. DC (Fabaceae), *Mitragyna inermis* (Willd) Kuntze (Rubiaceae), *Nauclea latifolia* Smith syn. *Sarcocephalus latifolius* (Smith) Bruce (Rubiaceae), *Securidaca longepedunculata* Fresen (Polygalaceae), *Trichilia emetica* Vahl. (Meliaceae), and *Vernonia colorata* (Willd) Drake (Asteraceae) are reported. Some of the collected data could be used to improve the actual herbal drugs and to propose new phytomedicines for the management of malaria and liver diseases.

Keywords: Mali, Malaria, Liver diseases, Medicinal plants, Phytomedicines.

Malaria is a serious parasitic disease of tropical regions caused by species of *Plasmodium* and transmitted by *Anopheles* mosquitoes. It is prevalent in many developing countries in Africa, Asia, and South America, with about 250 million malaria cases per year. According to the World Malaria Report, approximately one million people die from malaria each year [1]. The emergence and rapid spread of multidrug-resistant strains of *Plasmodium falciparum* represent a major problem for the disease treatment, which becomes more difficult and limits the choice of drugs to be used.

Today, ethno-pharmacology is a very important resource in order to discover new therapies for the current diseases. Moreover, another good justification for the ethno-pharmacological approach is to obtain new, effective, less expensive and simple therapies, limiting at the same time the cost of pharmaceutical research. In Mali, the sanitary situation is characterised by a predominance of many endemic and epidemic diseases, together with a lack of qualified health workers, medicines and equipment. Traditional medicine, being a significant element in the cultural patrimony, still remains the main recourse for a large majority of people for treating health problems. A high level of Malian government commitment supported the research and development of traditional medicines, with the creation in 1968 of the first institute for medicinal plants study. Today, this institute is the Department of Traditional Medicine (DMT) within the National Institute for Research on

Public Health (INRSP) of the Ministry of Health. The main activities of DMT are research and development on phytomedicines from local plants, named “Improved Traditional Medicines” (MTAs in French). The aim for promoting the local production of phytomedicines is to provide cost-effective medicines to populations, particularly those with limited access to quality healthcare. In malaria therapy, 11 drugs out of the anti-malarials included in the WHO therapeutic schemes for malaria treatment are either natural products or their analogues, or were design-based on the pharmacophores from natural products [2]. The great significance of plant-derived drugs for the treatment of the malaria is highlighted by the two major anti-malarial drugs widely used today, i.e. quinine and artemisinin, which came respectively from Peruvian and Chinese ancestral treatments reported in traditional medicines. In this contest, there is an urgent need for the discovery of new drugs, due to the critical epidemiological situation of this disease and to the growth of resistances to new drugs.

In Mali, malaria and liver diseases remain one of the leading public health problems. In the local language, Bamanan, the word “*Sumaya*” is used both for malaria and for some liver diseases. This is why many medicinal plants are often used at the same time, in local traditional medicine, for the treatment of malaria and liver diseases, including hepatic syndromes, jaundice, hepatitis and other hepatic disorders. Preclinical and clinical studies permitted to

confirm the safety, efficacy and quality of many of these medicinal plants and their effectiveness in the liver protection and in the treatment of malaria.

The aim of this review is to analyse experimental and literature data on ten medicinal plants frequently used in Malian traditional medicine for the management of malaria and liver diseases, selected through ethno-pharmacological and experimental studies: *Argemone mexicana* L. (Papaveraceae), *Cochlospermum tinctorium* Perr. ex A. Rich (Cochlospermaceae), *Combretum micranthum* G. Don (Combretaceae), *Entada africana* Guillet Perr. (Mimosaceae), *Erythrina senegalensis* A. DC (Papilionaceae), *Mitragyna inermis* (Willd) Kuntze (Rubiaceae), *Nauclea latifolia* Smith syn. *Sarcocephalus latifolius* (Smith) Bruce (Rubiaceae), *Securidaca longepedunculata* Fresen (Polygalaceae), *Trichilia emetica* Vahl. (Meliaceae), and *Vernonia colorata* (Willd) Drake (Asteraceae).

***Argemone mexicana* L. (Papaveraceae)**

Argemone mexicana (Papaveraceae), known as Mexican poppy or Mexican prickly poppy, is a species of poppy found in Mexico and now in the United States, India, Ethiopia and in other countries in Africa. The plant is pantropic in distribution and is a weed in waste places. A leaf decoction of *A. mexicana* is used by traditional healers in Mali to treat malaria and malarial fevers. So, it has been investigated in terms of modern pharmacology for anti-malarial activity [3-5]. After a long process, *A. mexicana* decoction was selected [6, 7], it has undergone clinical trials [3, 6, 8, 9], and will soon be approved as a new MTA for malaria. The new phytomedicine will be called SUMAFURA[®] Tiemoko BENGALY, in honour of the traditional healer who mainly used *A. mexicana* to treat malaria. It will be prepared from the plant aerial parts, without seeds. Other research is ongoing to prepare syrup with the decoction and hydro-ethanolic extract of the plant [10, 11]. This syrup can contribute to a better management of uncomplicated malaria in children.

A. mexicana is also traditionally used in the treatment of dropsy and jaundice [4], and has been investigated in terms of modern pharmacology for hepatoprotective activity [12]. Moreover, *A. mexicana* is extensively used as a traditional medicine for the treatment of ulcers, cataracts, as an antimicrobial, for wound healing, as a larvicidal agent, chemosterilant, and for its nematicidal, allelopathic, antibacterial, antifungal, molluscicidal, anticancer, anti-HIV and neuro-pharmacological activities [4, 13].

Chemical investigations of this plant revealed the presence of alkaloids [14, 15] and phenolics [16]. The aerial parts contain isoquinoline and benzyloisoquinoline alkaloids; other alkaloids like berberine, tetrahydroberberine, protopine, and benzo-phenanthridines have also been isolated from the plant [17], while sanguinarine is an alkaloid present in the seeds with potential liver toxicity [18].

***Cochlospermum tinctorium* Perr.ex A. Rich (Cochlospermaceae)**

Cochlospermum tinctorium is one of the plants used in rural areas of Mali for the management of malaria, abdominal pains and dermatitis [19]. Information collected from 106 traditional health practitioners (THPs), by an ethno-pharmacological survey demonstrated that the roots of the plant were the most frequently used for medicinal purposes in Mali. The main indications were to treat jaundice, gastro intestinal diseases or ailments, malaria, schistosomiasis and dysuria [20]. This species is also used to treat infectious diseases in Guinea Conakry [21] and in the West African sub-region for the management of various affections, including pain

and inflammation [22]. Various studies have been reported on different activities of extracts of *C. tinctorium*, but the main researches were focused on hepatoprotective and antiplasmodial properties.

Concerning malaria, fresh, frozen, and lyophilized extracts of *C. tinctorium* exhibited antiplasmodial activity against two strains of *P. falciparum* (chloroquine resistant and chloroquine sensitive) with IC₅₀ values of 1-2 µg/mL [22]. Crude extracts of the leaves tested *in vitro* showed the most antiplasmodial activity. The aqueous extract of rhizomes also demonstrated antiplasmodial activity *in vitro* and *in vivo* [23]. Recently, the essential oil of *C. tinctorium* was demonstrated to be active as an insecticide in the control of the malarial vectors in West Africa [24]. Fractionation of the ethanol extract of the roots afforded five compounds: 3-*O-E-p*-coumaroylaliphilic acid, cochloxanthin, dihydrocochloxanthin, aliphilic acid, and 1-hydroxytetradecan-3-one, of which the first demonstrated an antiplasmodial activity with an IC₅₀ value of 2.3 µM [25].

The methanol and ethanol extracts exhibited antihepatotoxic effects against cytotoxicity induced by CCl₄ and galactosamine in primary cultured rat hepatocytes [26]. Pretreatment of rats with different extracts of the plant (36 mg/kg), orally, resulted *in vitro* and *in vivo* in protection against hepatotoxicity induced by CCl₄, galactosamine and aflatoxin B1 [27]. Aqueous, hydro-ethanolic and ethanolic extracts showed significant dose-dependent hepatoprotective actions. The ethanolic and hydro-ethanolic extracts exhibited remarkable effects against the induction of lipid peroxidation and hepatocyte lysis [28]. The extracts and preparations with potent antihepatotoxic activity from *C. tinctorium* were selected for the treatment of various liver disorders [29]. The aqueous extracts (100-300 mg/kg) significantly and dose dependently demonstrated a hepatoprotective effect against CCl₄-induced liver damage in rats. This extract (5000 mg/kg) appeared to be safe when administered orally [30].

C. tinctorium demonstrated many other activities. Antimicrobial activities of some carotenoids from *C. tinctorium* were reported against *Candida albicans*, *Aspergillus fumigatus*, and *Escherichia coli* [31]. Arjunolic acid, an oleanene-type triterpene isolated from the rhizome of *C. tinctorium*, and its acetate and methyl ester derivatives, were tested using the short-term *in vitro* assay on Epstein-Barr virus early antigen activation in Raji cells induced by 12-*O*-tetradecanoylphorbol 13-acetate. Their inhibitory effects on skin tumor promoters were greater than those of previously studied natural products [32, 33]. Structures of two pectic arabinogalactans and their complement fixation and induction of B cell proliferation *in vitro* were also reported [34]. The cytotoxicity of the crude extract assessed on the K562 cell line, showed IC₅₀ values of 33-2000 µg/mL [35, 36]. Other reported activities are antifungal, antibacterial, radical scavenger, immunomodulating, anti-ulcer, analgesic and anti-inflammatory. The aqueous and methanol extracts of the rhizomes showed antibacterial and antifungal activities against *Staphylococcus aureus*, *Escherichia coli*, *Candida albicans*, *Salmonella typhi*, *Klebsiella pneumonia* and *Pseudomonas aeruginosa* [37]. The methanol extract of the roots demonstrated a potent antibacterial activity against *Shigella dysenteriae* [38]. Polysaccharides and polyphenols of the aqueous extract showed significant anti-ulcer activities against HCl/ethanol-induced gastric lesions in mice. The extract showed also DPPH-radical scavenging and immunomodulating activities *in vitro* [20]. The anti-ulcer activities of the crude water extracts and isolated polysaccharide fractions from the rhizome of *C. tinctorium* can be explained by the anti-adhesive properties of *Helicobacter pylori* [39]. Finally, the aqueous methanol extract of the leaves of *C. tinctorium* significantly and dose

dependently inhibited the acetic acid induced writhing in mice. The highest protection was produced by the aqueous methanol extract (80 mg/kg); the same extract significantly and dose-dependently inhibited carrageenan-induced hind paw edema in the rat [40].

Many phytochemical studies on the plant crude extracts are reported in the literature. Firstly, in 1987, polyphenolic compounds (gallic and ellagic acids) and carotenoids were detected in the antihepatotoxic active fractions [26]. Major carotenoids, identified as 6-hydroxy-8'-apo- ϵ -caroten-3-one-8'-oic acid (cochloxanthin) and 4,5-dihydro-6-hydroxy-8'-apo- ϵ -caroten-3-one-8'-oic acid (dihydrocochloxanthin), were later isolated from *C. tinctorium* by countercurrent chromatography and HPLC [41, 42]. Triacylbenzenes were isolated from a petrol extract of the rhizome of *C. tinctorium* [43], while phenolic and polyphenolic compounds (gallic and ellagic acids, ellagitannins, flavonoids), carotenoids, triterpenes, and flavonoids were identified in aqueous, hydro-ethanolic and ethanolic extracts of the plant roots [28, 23]. The aqueous extract of the plant roots contained polysaccharides (59.3%) and polyphenols (9.3%): the polysaccharides were purified and characterized as highly complex pectic arabinogalactans type II, while gallotannins and ferulic acids were identified as parts of the polyphenolic compounds [20]. Alkaloids, tannins, saponins, flavonoids, triterpenes, sterols, cardiac and cyanogenic glycosides, and volatile oils were identified from different plant extracts [30, 37]. Recently, pectin- and inulin-type polysaccharides, phenolic substances and proteins were isolated from the crude water extracts of *C. tinctorium* wild and cultivated roots [44].

***Combretum micranthum* G. Don (Combretaceae)**

Combretum micranthum, locally called “*N'golobé*”, is a small tree, common on the poor soil of the Sahel savannah. Like other *Combretum* species, it has characteristic four-winged fruit. Twigs with leaves are commonly sold in markets with the name of “*Kinkeliba*” and yield a drug having the same name, which has been listed in French, Spanish, and British Extra Pharmacopoeia under supplementary drugs with indication for black-water fever and bilious gastrointestinal conditions [45]. It was added to the French Pharmacopoeia in 1937 and to the African Pharmacopoeia in 1985 [45]. The plant is used in West Africa for the treatment of different diseases [46-49]. *C. micranthum* is also one of the most used plants in traditional medicine of Burkina Faso for the treatment of kidney symptoms [50], and is one of the common plants used in popular traditional herbal medicines from the Joolas [51].

Extracts obtained from *C. micranthum* and others plants, commonly used in Cote d'Ivoire by native healers for the treatment of malaria, tested on two strains of *Plasmodium falciparum*, FcB-Colombia (chloroquine-resistant) and F32-Tanzania (chloroquine-sensitive), had an apparent inhibitory effect on *P. falciparum* growth *in vitro*, while the other seemed to be less efficient [52]. In Mali, HEPATISANE[®] is an MTA produced with powder of *C. micranthum* leaves. The decoction is taken orally, and the operation is repeated twice daily for seven days. HEPATISANE[®] is used in the symptomatic treatment of hepatic insufficiency, in colds, hepatitis, dyspepsia and constipation. It is also used as diuretic remedy; it is not toxic and can be safely consumed when used appropriately. Patients with non-obstructive jaundice have been treated with HEPATISANE[®] and their bilirubin and transaminases returned to normal within 2-3 weeks of starting the treatment [53]. About 50 asymptomatic patients with chronic viral hepatitis B have been treated with HEPATISANE[®] in a clinical trial, but there was no clearance of the hepatitis B surface antigen. However, the herbal treatment was well-tolerated, there were no adverse effects, and the

compliance was good. Further clinical trials are needed to determine whether this treatment helps patients with symptomatic hepatitis, or whether it helps to prevent long-term consequences of chronic viral hepatitis.

The root extract of *C. micranthum* presented antibacterial activity against Gram-positive and Gram-negative organisms [54]. The methanolic extract of the leaves, prepared 7 days before the assay, demonstrated *in vitro* antiviral activity against HSV-1 and HSV-2. The freshly prepared extract contained inactive precursors which undergo spontaneous transformations into active compounds. The precursors have been identified as condensed catechin tannins, which, under alkaline conditions, suffer rapid cleavage, intramolecular rearrangement to catechinic acid and autooxidation. EC₅₀s of catechinic acid autooxidation products against HSV-1 and HSV-2 replication were 2 μ g/mL and 4 μ g/mL, respectively, when cell cultures were treated with the compound during virus infection [54]. Therefore, *C. micranthum* extracts are not only interesting sources for antimicrobial molecules, but also potential sources of phenolic antioxidants [55]. Methanol extract of *C. micranthum* leaves was studied for anti-inflammatory activity in rats and mice using the carrageenan-induced rat paw edema and the acetic acid-induced vascular permeability in mice. The extract (50, 100 mg/kg) significantly ($P < 0.05$) inhibited the edema production induced by carrageenan in rats. Increased vascular permeability caused by acetic acid injection was also inhibited by the extract, within the same dose range. *C. micranthum* extract (100 mg/kg) inhibited the granuloma formation in rats to a similar degree as indomethacin (5 mg/kg). These results provide evidence for the anti-inflammatory property of *C. micranthum* leaves [56]. An ethanol extract of *C. micranthum* leaves exhibited an anti-inflammatory activity. The extract was fractionated based upon polarity and subsequently assayed for antioxidant capacity. The most active fraction, ethylacetate, was then tested for anti-inflammatory activity and exhibited an inhibition of NO by 93.5% at only 60 μ g/mL and 100% at higher concentration [57]. The aqueous leaf extract of *C. micranthum*, at the dose of 100 mg/kg, produces a significant hypoglycemic and antidiabetic activity comparable with that of the standard drug (0.6 mg/kg glibenclamide) [58]. The ethanol and water extracts of leaves of *C. micranthum* demonstrated antioxidant properties, including scavenging of the 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical with IC values of 8.02 \pm 0.34 for the ethanol extract and 9.1 \pm 0.28 for the water extract; for the 2,2'-azinobis (3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) radical, the IC₅₀ values were 7.4 \pm 0.14 for the ethanol extract and 11.8 \pm 0.01 for the aqueous extract, and with the hydroxyl radical the ethanol extract had an IC₅₀ of 58.1%, and the aqueous extract 61.1%. At 20 mg/mL concentration, the water and ethanol extracts provided, respectively, 36.8%, and 75.1% inhibition of lipid peroxidation of linoleic acid emulsion. The IC₅₀ values of the ethanol extract in ABTS and DPPH tests were significantly lower than those of the water extract [59]. The aqueous extract of the fresh leaves of *C. micranthum* demonstrated antibacterial effects on both *S. aureus* and *E. coli* cultures [60]. In North-Western Nigeria, the leaves of the plant are used for treating diabetes [57]. A recent study, aimed to investigate how TPs in Mali treat common diseases and ailments during pregnancy, revealed that *C. micranthum* is one of the common plants most used [61].

Studies on chemical constituents reported the presence of salts (potassium nitrate), flavonoids (vitexin), organic acids, tannins, coumarins, sterols, terpenoids, carbohydrates (inositol, mannitol, sorbitol), and alkaloids (choline, stachydrine) [45, 51, 62-66]. Gallic acid, rutin trihydrate, (+)-catechin and benzoic acid are the main polyphenols identified in the 90% ethanol extract of the plant leaves

[67]. Some novel piperidine flavan alkaloids isolated from the aqueous extract of the plant were patented as anti-diabetic agents for the treatment of metabolic disorders [68].

***Entada africana* Guillet Perr. (Mimosaceae)**

Entada africana, called “*Samanéré*” in Mali, is a well known Leguminous tree used in traditional medicine throughout West-Africa in the treatment of many diseases such as fever, respiratory tract complaints, diabetes, hypertension, and diarrhea [69]: in particular, the plant is used in Mali for the treatment of malaria [70]; in Burkina Faso against diabetes, hypertension and diarrhea; in Cameroon, for wound dressing, liver related diseases, rheumatism, cataract, fevers and dysentery. Many studies reported the wound healing, hemostatic, anti-rheumatism, anti-inflammatory and hepatoprotective properties of extracts of this species [71]. The root bark is the part of the plant most used in traditional medicine; for this reason, the availability of the plant in Burkina Faso Plateau Central Region is endangered. Biological studies on *E. africana* extracts concerned antihepatotoxic, antimicrobial, antiplasmodial, antioxidant [72], fungistatic, fungicidal [73] and antiulcerogenic activities [74].

In a recent study, the antiplasmodial activity of the ethanolic leaf extract against chloroquine-sensitive (HB3) and chloroquine-resistant (FcM29) *P. falciparum* was investigated, as well as its peripheral antinociceptive and anti-inflammatory properties. At a concentration of 100 µg/mL, the extract was non-cytotoxic and demonstrated a moderate antiplasmodial activity against HB3 and FcM29 (IC₅₀ 26.36 and 28.86 µg/mL, respectively). It also exhibited concentration-dependent inhibition of synthetic heme (IC₅₀ 16 mg/mL). The extract at 200 mg/kg showed significant ($P < 0.05$) inhibition of paw inflammation, and significantly ($P < 0.01$, 0.05) reduced the number of abdominal writhes induced by acetic acid (58.62–65.51%), which was higher than that of diclofenac (50%, $P < 0.05$). These findings suggested that the antinociceptive effects and parasitocidal activity of the extract contribute to its antimalarial properties and it can be further explored as an effective therapy against malaria infection [75].

Extracts of *E. africana* protected the liver against CCl₄ intoxication by decreasing the level of transaminases and alkaline phosphatase [76]. The aqueous, hydroethanolic and ethanolic extracts of root and stem bark inhibited *in vitro* proliferation of hepatocarcinoma Hep3B cells with IC₅₀ values between 22.8 and 25.3 µg/mL. The extracts of stem bark are more active than those from the root. The aqueous ethanol extract of the root increased activity of caspase 7 and the number of apoptotic bodies. The extract induced disruption of α -tubulin diffusion in every sense of the α -tubulin during interphase. The ethanolic extract of the stem and root bark induced membrane defects, which appear jagged [77]. The extracts of *E. africana* stem bark inhibited, dose-dependently, the replication of hepatitis C virus (HCV) after 24 and 72 h of incubation. The dichloromethane fraction had the highest anti-HCV activity with an IC₅₀ of 0.453 ± 0.00117 mg/mL, but did not reduce cell viability to antiviral concentration [78]. The aqueous extracts of stem bark of *E. africana* at 100 and 500 µg/mL significantly presented a protective activity against hepatotoxicity induced *in vitro* by acetaminophen [79].

Extracts (ethyl acetate, methanol, and water) of the leaves and bark showed antiradical activity by inhibiting the DPPH radical in a colorimetric method with an EC₅₀ between 6.9 to 20 µg/mL [80]. A similar activity was demonstrated by Karou *et al.* for the methanolic extract with an IC₅₀ of 0.47 ± 0.01 µg/mL [81]. Recently, Owona Brice *et al.* investigated the capacity of *E. africana* stem bark to protect microglia from inflammatory insults by exploring the effect

of the CH₂Cl₂/MeOH 5% fraction on pro-inflammatory cytokine mRNA expression and found that this extract inhibited LPS-induced NO production in dose dependent manner, while the expression of TNF α , IL-1 β , IL-6 and iNOS was strongly suppressed in microglia. For this reason, *E. africana* may contain promising compounds useful for the treatment of diseases caused by over-activation of microglia, such as Alzheimer’s and other neurological diseases [81]. The same authors found also that the CH₂Cl₂/MeOH 5% extract suppressed lipopolysaccharide-induced inflammation in Raw 264.7 macrophages [82]. Finally, the extracts (*n*-hexane, chloroform, chloroform/methanol, and methanol) of *E. africana* roots demonstrated anti-angiogenic effects on zebrafish embryos [83].

Chemical constituents of *E. africana* are alkaloids, flavonoids, tannins, saponins, phlobotannins and anthraquinones [84, 85]. New saponins esters were isolated from the plant roots and were found to inhibit the proliferation of tumor cell lines J774.A1 (murine macrophage), HEK-293 (human kidney) and WEHI-164 (murine fibrosarcoma) [86]. The roots contained also arabinogalactan-protein type II polysaccharides [71]. Leaves of *E. africana* are rich in calcium, zinc and iron [87].

***Erythrina senegalensis* DC (Fabaceae)**

Erythrina senegalensis is frequently used in West Africa in the treatment of various diseases. In Benin and Togo, leaves and stem bark are used in the treatment of liver diseases and bronchus-pulmonary disorders. In Côte d’Ivoire, the root and stem bark are used in the treatment of fever, malaria, liver diseases and urogenital infections. In Nigeria and Senegal, the bark is used against fever and malaria. The root decoction is used in abdominal pain [88]. In Mali, the results of a survey on ethnopharmacological knowledge on the uses of *E. senegalensis* in traditional medicine in three different areas (Dioila, Kolokani and Koutiala) demonstrated that the plant is frequently used by the traditional healers in the treatment of various diseases, mainly amenorrhea, malaria, jaundice, infections, abortion, wound, and body pain [88].

Various studies were focused on the antiplasmodial and hepatoprotective activities of stem bark extracts of *E. senegalensis*. The ethanolic extract showed antiplasmodial activity *in vitro* on a strain of *P. falciparum* K1 with an IC₅₀ of 1.82 µg/mL. The aqueous extract at doses of 50-100 mg/kg orally reduced parasitaemia in mice infected with *P. berghei*, with inhibition percentages from 16.5 to 23.2% [89, 90]. The hydroethanolic extract of *E. senegalensis* exhibited antihepatotoxic effects against cytotoxicity induced by carbon tetrachloride in primary cultured rat hepatocytes, since the pretreatment of rats with different extracts of the plant (25 mg/kg), orally, resulted in an *in vivo* broad protection [91]. The hydroethanolic and ethanolic extracts of roots and stem bark of *E. senegalensis* inhibited *in vitro* proliferation of hepatocarcinoma Hep3B cells with IC₅₀ between 20.3 and 33.9 µg/mL for the roots extracts and 32.9 and 33.5 µg/mL for extracts of stem bark. The hydroethanolic extracts increased the activity of caspase 7 and the number of apoptotic bodies. The extract of stem bark, at two time its IC₅₀, induced an extension of cytoplasm and a destruction of α -tubulin, while the extract of roots induced a degradation of α -tubulin membrane to the nucleus, a deformation of the cells, and an abnormal co-localization of the Hep3B at the centrosomes of α/β -tubulin and γ -tubulin, with an increase of 5.6% compared with control cells treated only with DMSO [77].

Other reported activities of *E. senegalensis* are antibacterial and antioxidant. The ethanolic extract of the leaves and root bark

showed activity against *S. aureus* and *Proteus* spp. The extracts (*n*-hexane, ethyl acetate and ethanol) of leaves, stem and root bark showed antioxidant activity. The extracts of the stem and root bark showed improved activity with inhibition percentages of 82.8-91.5% and 78.9-94.6% at the concentrations of 0.05 mg/kg and 0.5 mg/kg, respectively.

The plant extracts resulted no toxic since it was found that the hydroethanolic extract of stem bark at a dose of 16 g/kg by gavage did not cause any change in behavior and mortality in mice; also the decoction of the plant, evaluated after acute and sub-chronic administration in rodents, resulted in no induced mortality or significant behavioral changes [92].

Phytochemical analysis of different parts of the plant revealed the presence of many active molecules, such as flavonoids, tannins, alkaloids, steroids, and cardiac glycosides [93]. The stem bark of the plant is the most studied from a chemical point of view: in 1995, two new prenylated isoflavonoids, erysenegalensein J and K, were isolated, in addition to five known pentacyclic triterpenes, β -amyrin, maniladiol, erythrodiol, oleanolic acid and cornulacic acid [94]. Later, two prenylated isoflavonoids named erysenegalensein N and O, together with six known isoflavonoids, erysenegalensein D, 8-prenylleutone, auriculatin, derrone, alpinumisoflavone and 6,8-diprenylgenistein were fully characterized [95]. The bioguided fractionation of the hydroethanolic extract permitted the isolation of two other diprenylated isoflavonoids, 2,3-dihydro-2'-hydroxyosajin, and osajin, together with 6,8-diprenylgenistein. All these compounds exhibited antihepatotoxic effects against cytotoxicity induced by CCl_4 in primary cultured rat hepatocytes with hepatoprotective percentages of 71.8 ± 1.45 , 67.54 ± 3.56 and 69.41 ± 2.56 , respectively [93]. Finally, in 2009, one new pterocarpan, named erybraedin F, along with 7 known prenylated flavonoids were isolated from the plant collected in Mali [96].

***Mitragyna inermis* (Willd) Kuntze (Rubiaceae)**

Mitragyna inermis is an exclusively African plant, occurring in West African countries from Cameroon to Sudan [97, 98]. It is found in wetlands and semi-arid tropics, in clay bottoms and temporarily flooded land, near ponds and streams, in rainforest as well as in savannah. The plant was selected by ethnobotanical survey as a species commonly used by traditional healers for the treatment of malaria, hepatic illness, stomach and intestinal disorders, hypertension, and HIV/AIDS [97, 99-101].

The alkaloids of leaves and roots of *M. inermis* have a strong antiplasmodial activity on *P. falciparum* standard and isolated from infected patients ($\text{IC}_{50} < 3 \mu\text{g/mL}$). At concentrations inhibiting 100% of parasite growth, the alkaloids are not toxic to human red blood cells [102]. The combination of extracts of *M. inermis* and *Guiera senegalensis* demonstrated a strong, synergistic inhibitory effect on *in vitro* plasmodial development and is devoid of cytotoxicity towards human cells [103]. This result justified the traditional use of this combination to treat malaria [104]. Antimalarial properties of the extract of *M. inermis* have been demonstrated by its ability to inhibit *P. falciparum* growth [105]. Decoctions of *M. inermis* and *M. ciliata*, prepared according to the recommendation of traditional healers, were tested on three strains of *P. falciparum*, FcB1-Colombia and FcM29-Cameroon (chloroquine-resistant strains) and a Nigerian chloroquine-sensitive strain. The extracts of the plants revealed either weak or very

low activities with IC_{50} values ranged from 2.34 to more than 500 mg/mL [105, 106]. Acute and chronic evaluation of the toxicity of the hydroethanolic leaf extract, administered orally at up to 3 g/kg/day, did not demonstrate toxic effects and can be used in traditional treatment of malaria [107]; the aqueous extracts traditionally used did not show high antimalarial activity [108], while alkaloids from the chloroform extract and ursolic acid from the hydromethanol extract of leaves, roots and stem barks of *M. inermis* induced a significant decrease in parasite proliferation [109].

Indole alkaloids such as rhynchophylline, rotundifoline, speciophylline and uncarine, triterpenoid saponins (inermiside I and inermiside II) and quinovic acid glycosides are the typical constituents of *M. inermis* [110-114]. Quinovic acid glycosides showed antitumor activity on Bel-7402 hepatic carcinoma. Alkaloids from aqueous extracts of *M. inermis* have been reported to increase biliary flow, and to decrease hepatic enzymes and total cholesterol in the rat [115].

According to bibliographic data, extracts of *M. inermis* exhibited antimalarial, antimicrobial, antihypertensive, antidiabetic, antioxidant, and anti-inflammatory activities. The decoction of fresh or dried leaves is used for wound healing [116]. The macerated leaves and bark are administered twice daily to treat sinusitis, stomach pain and dysentery [117]. The decoction of stem bark is used against amoebae worms [118]. The plant is also used in the treatment of leprosy [119] and diarrheal diseases such as dysentery and cholera [47]. Different preparations of the plant can be used in external and internal applications against arthritis, myalgia and intercostal pain [47]; in combination with other medicinal plants, it is also used in the treatment of rheumatic pains [120]. The decoction of stem and root barks is used in disorders of pregnancy and childbirth [47]. The leaves of the plant are used in retained placenta and as a sedative for uterine contractions. Alone or in combination with *Dialium guineense*, it is used for regulating the menstrual cycle in women [119, 121]. The macerated fruits and seeds are used in animal breeding to activate the estrous cycle [122]. The crude extract and the isolated compounds were tested *in vitro* for their preliminary cytotoxicity against *Artemia salina* [123]. Alkaloid rich extract derived from *M. inermis* induced a strong inhibition of protein synthesis in mammalian cells, but did not exhibit mutagenic or genotoxic activity [108]. Aqueous extracts of *M. inermis* produced a concentration-dependent *in vivo* increase in cardiac contractile response and coronary flow, but did not modify heart rate in the rat. This seemed to indicate that the extract possesses a cardiac inotropic effect and induces an increase in coronary flow without inducing tachycardia in isolated heart [124]. Sy *et al.* have reported the myorelaxant and antispasmodic activities of *M. inermis* extracts [125]. Some sequential *n*-hexane, acetone and 50% aqueous methanol extracts of the leaves, stem bark and roots of *M. inermis* and another three species were active against *Bacillus subtilis*, *Pseudomonas syringae* and *Cladosporium herbarum* [126]. Alkaloids from *M. inermis* are reported for their clinically useful anticonvulsant activity [127].

Bioactive compounds of the plant are mainly indole alkaloids [100]. In 2012, a new indole alkaloid, named naucleactonin D, together with fourteen known compounds, identified as nauclefine, nauclefine, nauclefidine, angustoline, angustine, barbinervic acid, quinovic acid, 3-*O*- α -L-rhamnopyranoside, betulinic acid, a mixture of ursolic and oleanolic acid, a mixture of stigmasterol and β -sitosterol, β -sitosterol, 3-*O*- β -D-glucopyranoside, and strictosamide were isolated from the roots and fruits of *M. inermis* [123].

***Nauclea latifolia* Smith syn. *Sarcocephalus latifolius* Smith (Rubiaceae)**

Nauclea latifolia (syn. *Sarcocephalus latifolius*) is a plant used in West Africa for the treatment of several diseases. In Mali, Ivory Coast, and East Africa, *N. latifolia* aqueous extracts are used for the treatment of fever and malaria [11, 128, 129]. In Burkina Faso, the plant is used against jaundice, malaria, infant gastroenteritis, and dysentery [130, 131]. Different extracts are used in the management of gastrointestinal tract disorders [132], sleeping sickness [133], prolonged menstrual flow [134], hypertension [129], and as a chewing stick [135]. The plant is also used as a tonic and fever medicine, and for toothache, dental caries, and septic mouth [136].

The aqueous extract of *N. latifolia* showed an antiplasmodial activity against the chloroquine-resistant FcB1 strain of *P. falciparum* with an IC₅₀ of 0.6 µg/mL. A similar IC₅₀ was obtained from a clinical strain from Nigeria. The IC₅₀ obtained by the ethanol extract of the plant was 8.9 µg/mL [97]. The root extract showed antiplasmodial activity *in vivo* in rats infected with *P. berghei berghei*. The prophylactic and curative ED₅₀ were 189.4 and 174.5 mg/kg, respectively.

Elevated transaminases and alkaline phosphatase induced intoxication in rats by CCl₄ were significantly attenuated by the ethanolic root bark extract. The ethanolic extract at a dose of 1 mg/mL remarkably reduced the leakage of lactate dehydrogenase (LDH) in isolated rat hepatocytes and had a significant effect on the peroxidation of lipids. Other fractions reduced leakage of LDH, but had no significant effect on lipid peroxidation [132]. The aqueous root extract (250 mg/kg) significantly reduced the activity of catalase ($P < 0.05$), but did not significantly reverse the activity of superoxide dismutase in the liver of alloxan-induced diabetic rats [137]. Extracts of the leaves and fruits showed antioxidant activity [138]. The ethanolic extract showed antimicrobial activity on Gram-positive bacteria at a concentration of 0.5 mg/mL and Gram-negative bacteria at a concentration of 1 mg/mL [100]. The root bark aqueous extract at doses of 50-200 mg/kg orally significantly ($P < 0.05$) attenuated torsions induced by acetic acid and increased the threshold of pain perception in the hot plate test in mice [139]. The aqueous and ethanol extracts of the plant leaves reduced significantly and dose-dependently the levels of glucose in fasting blood of STZ-diabetic rats without significantly lowering the level of glucose in the normo-glycaemic rats [140]. The decoction of root bark strongly increased total sleep time induced by diazepam. It also protected mice against induced seizures of electroshock maximum, pentamethylenetetrazole and strychnine [141].

Phytochemical analysis of the ethanol extract of the plant stem bark showed the presence of saponins, while tannins, flavonoids, and alkaloids were absent. Reducing sugars, flavonoids, steroids, saponins, alkaloids, terpenes and glycosides were revealed in the aqueous extract of the fruits [142]. The extract of the leaves contained tannins (0.37%) alkaloids (2.39%), flavonoids (0.37%), saponins (1.25%), phytate (0.38%) and 16.90 mg/kg of HCN [143]. In the leaves, various alkaloids such as naucleafoline, nauclechine, naufoline, nauclatine, nauclefine, naucleidinal, augustin, cardamine, naucleamide A-E, strictosamide, dihydrostrictosamide, tetrahydrodesoxycordfoline, naucleal, and epinaucleal were characterized [100]. A novel indole alkaloid, nauclefolinine and five known triterpenic compounds, rotundic acid, α -L-rhamnoquinovic acid, 3-O- β -D-glucopyranosyl- β -sitosterol, squalene, and sitosterol-3-O-6'-stearoyl- β -D-glucopyranoside were isolated from the roots of *N. latifolia* in 1991 [144]. Later, investigations of the roots extract led to the isolation of the new indole alkaloids 21-O-

methylstrictosamide aglycone and 21-O-ethylstrictosamide aglycone together with strictosamide, angustine, nauclefine, angustidine, angustoline, 19-O-ethylangustoline, naucleidinal, 19-*epi*-naucleidinal, quinovic acid-3-O- β -D-fucopyranoside, quinovic acid-3-O- α -L-rhamnopyranoside, scopoletin, and β -sitosterol [145, 146]. Derivatives of fructose (1,2,3,4,6-penta-O-benzoyl- α -D-fructofuranose, 1,2,3,4,6-penta-O-benzoyl- β -D-fructofuranose, 1,2,3,4,5-penta-O-benzoyl- β -D-fructopyranose, and 1,3,4,5-tetra-O-benzoyl- β -D-fructopyranose were isolated in the sugar fraction of the stem bark [147].

***Securidaca longepedunculata* Fres (Polygalaceae)**

Securidaca longepedunculata is a medicinal plant commonly used in different African countries. In Mali, the aqueous root extracts are used in trypanosomiasis and dysmenorrhea, while the decoction of the leaves and roots is used against fever and malaria. The powdered leaves or twigs are used against snakebites. In Benin and Togo, the bark is used alone or in combination with other plants in the treatment of fever and malaria. In Burkina Faso, the decoction of the roots is used as a purgative. In Senegal, the roots are used in bronchopulmonary, gastrointestinal and liver diseases, and both leaves and roots against fever and malaria [47, 48].

The light petroleum and dichloromethane extracts of *S. longepedunculata* roots inhibited the growth of a strain of *P. falciparum* K1 with IC₅₀ values of 7.34 and 8.26 µg/mL, respectively; on the contrary, the IC₅₀ could not be determined for either extract on the 3D7 strain of *P. falciparum* [148].

Other different activities were also reported. The aqueous, hydroethanolic and ethanolic extracts of the roots inhibited *in vitro* the proliferation of hepatocellular carcinoma Hep3B cells with IC₅₀ values between 16.3 and 19.9 µg/mL. The hydroethanolic extract increased the activity of caspase 7 and the number of apoptotic bodies, while the ethanolic extract induced abnormalities of membranes, which appeared jagged [77]. The aqueous extract of the roots showed cytotoxicity *in vitro* on certain cancer cell lines: it inhibited the proliferation of ascitic Ehrlich carcinoma cells (spontaneous mammary carcinoma in mice), with an IC₅₀ of 67 µg/mL and reduced *in vivo* in albino Swiss mice the growth of the same carcinoma cells after intraperitoneal administration of the extract at a dose of 10 mg/kg/day for 14 days [149]. The chloroform extract also showed strong cytotoxicity on human pancreatic cancer cell line PANC-1 with an IC₅₀ of 23.4 µg/mL [150].

Extracts of leaves and roots demonstrated an antibacterial activity against different microorganisms with an inhibition diameter between 15 to 20 mm and a minimum inhibitory concentration between 0.59 to 6.25 mg/mL [151]. The aqueous extract of the roots at doses of 200-400 mg/kg significantly reduced, in a dose-dependent manner, the pain induced by acetic acid and formalin in mice and also produced a significant ($P < 0.05$) naloxone reversible antidepressant like effect in the forced swimming test (an animal model of depression). These results suggested that the extract possesses antinociceptive and antidepressant like effects with possible involvement of opioidergic pathways [152]. The same extract administered intraperitoneally in mice at a dose of 50-800 mg/kg showed significant analgesic, anti-inflammatory and hypoglycemic dose dependent effects [153]. The aqueous extract of the roots at a dose of 100-400 mg/kg exhibited anticonvulsant, anxiolytic and sedative activities, using the strychnine and picrotoxin induced seizure models, justifying the use of the plant extract in traditional medicine for the management of convulsions and psychosis. The LD₅₀ in mice was 1.74 g/kg and 19.95 mg/kg for the oral and the intraperitoneal route, respectively. The aqueous extract

administered by gavage at a dose of 2000 mg/kg caused no mortality or signs of toxicity in mice [154]. Intraperitoneal administration of the aqueous extract of the roots produced a dose-dependent toxicity to kidneys, liver and lungs with an estimated LD₅₀ of 36.74 mg/kg in rats [155]. The oral LD₅₀ of the ethanolic extract was 547.72 mg/kg in mice. The same extract had no significant effect on hyperglycemia induced by streptozotocin [156].

Phytochemical analysis of the plant revealed the presence of alkaloids, flavonoids, saponins, tannins, cardiac glycosides, anthraquinones, steroids, essential oils and reducing sugars [151]. Investigation of the chloroform root extract led to the isolation of 28 compounds including five new polymethoxylated xanthenes and a new benzyl benzoate, namely benzyl 3-hydroxy-2-methoxybenzoate [149]; twelve diphenylmethyl-substituted xanthenes, named muchimangines A-L, were isolated from the roots and showed a characteristic phenylmethyl substituent at C-2 [158-161]. Also bidesmosidic saponins are typical secondary metabolites of the plant roots: in 2009, four triterpene saponins having presenegenin as aglycone were isolated by Mitaine-Offier and co-authors [162], while Stevenson and collaborators in the same year isolated two new medicagenic acid bidesmosidic saponins, which were named securidacaside A and B [163].

***Trichilia emetica* Vahl. (Meliaceae)**

Trichilia emetica, a tree native of Africa, and widely distributed in African tropical regions, is used in traditional medicine to treat various ailments such as abdominal pain, dermatitis, hemorrhoids, jaundice and chest pain. The plant is known also for its emetic, diuretic and purgative properties and for induction of labour [164, 165]. According to an ethno-pharmacological survey carried out to collect information on the use of seven medicinal plants in rural areas in the nearby regions of Bamako, the plant is used for the treatment of malaria, abdominal pain, and dermatitis [19]. Moreover, in Mali, the plant is used for the treatment of malaria during pregnancy by traditional healers [61]. In Benin and Madagascar, *T. emetica* is one of the plants used traditionally for the treatment of cognitive disorders [166].

The dichloromethane extract of *T. emetica* leaves demonstrated an antiplasmodial activity (IC₅₀ 12 µg/mL) and exhibited a good binding activity to the GABA(A)-benzodiazepine receptor. The water and methanol extracts of the same plant did not show any activity [148]. Different extracts of the plant presented antiplasmodial activity against different strains of *P. falciparum* 3D7 and Dd2 [89, 167, 168]. Kurubasch aldehyde, a sesquiterpenoid with a hydroxylated humulene skeleton, was isolated from *T. emetica* and found to be a modest inhibitor of the growth of *P. falciparum* (IC₅₀ 76 µM), and of slow-proliferating breast cancer cells MCF7 (78 µM), but a potent inhibitor of proliferation of S180 cancer cells (IC₅₀ 7.4 µM) [169].

The aqueous extract of *T. emetica*, rich in polyphenols and limonoids demonstrated a significant ($P < 0.05$) hepatoprotective effect at a dose of 1000 µg/mL, both on plasma membrane and mitochondrial function. This extract and its diethyl ether fraction did not show toxicity (LC₅₀ > 1000 µg/mL) in the brine shrimp bioassay [170]. The extracts submitted to alkaline hydrolysis showed high antioxidant properties in two *in vitro* assays: auto-oxidation of methyl linoleate (MeLo) and ascorbate/Fe²⁺-mediated lipid peroxidation in rat microsomes. An *in vivo* study was also performed to investigate the intestinal absorption of phenolic acids after oral administration of *T. emetica* extracts. Results showed high

levels of phenolic acids, free or conjugated to glucuronide, in the plasma of rats treated with the hydrolyzed extract [171].

Other biological activities were also investigated including anti-infective, anti-inflammatory, anti-schistosomal, anti-convulsant, anti-trypanosomal, anti-oxidant, anti-tussive, and anti-mutagenic properties. During a screening of some medicinal plants of Ethiopia for their anti-microbial properties and chemical profiles, different extracts of *T. emetica* demonstrated the most promising antifungal activity [172]. The anti-schistosomal and anti-trypanosomal activities of the plant extracts were also demonstrated [173-175]. Crude water-ethanol extract and polysaccharides from *T. emetica* showed antitussive activity against the citric acid-induced cough reflex and the reactivity of airways smooth muscle *in vivo* [176]. The *n*-hexane extract of the plant at non-toxic concentration demonstrated a β-amyloid peptide production activity that could be interesting for the treatment of Alzheimer's disease [166]. The ethyl acetate extract of *T. emetica*, without a detectable anticandidal activity, was detoxified by the multidrug transporter Cdr1p. In this extract, the presence of a non-toxic Cdr1p-mediated ketoconazole resistance modulator accompanying growth-inhibitory Cdr1p substrates was revealed by further fractionation experiments [177]. The dichloromethane extract of the seeds of *T. emetica* significantly inhibited the growth of *P. aeruginosa* [178]. Flavonoid-rich fractions of the plant leaf extracts showed the maximum radical scavenging activity and possessed marked anti-amylose activity *in vitro*. The same flavonoid-rich fractions presented anti-hyperglycemic, anti-lipidemic, and anti-hypertensive properties *in vivo*, demonstrating the antidiabetic potential of *T. emetica* as a therapeutic target for the management of type 2 diabetes [179]. *T. emetica* is also one of the most effective plants for the treatments of dysmenorrhea, with minimal side effects [180], and it is used in the treatment of dry-mouth syndrome induced as a side effect of antidepressant drugs.

A first phytochemical study on *T. emetica* showed the presence of limonoids as the main components of the ethylacetate extract. These isolates exhibited selective inhibitory activity towards DNA repair-deficient yeast mutants and showed antifungal, bactericidal, antiviral, antifeedant and growth regulating properties [181]. During a study of the chemical content of the leaves of the plant, used as wound healing remedy, pectin of the rhamnogalacturonan type I with side chains of the arabinogalactan type II has been isolated. Removal of terminal arabinofuranosides led to a drop in the activity, indicating that this structural unit may be involved in the bioactive site of the molecule [182].

A phytochemical analysis of the plant roots showed a high polyphenolic content in the aqueous extract and the presence of limonoids in the diethyl ether fraction [170]. Free phenolic acids were extracted with a mixture of methanol and 10% acetic acid. Bound phenolic acids were released using first alkaline and then acid hydrolysis. All fractions were quantified separately by HPLC. After alkaline hydrolysis, a remarkable increase in caffeic acid, ferulic acid, *p*-coumaric acid, syringic acid, vanillic acid, protocatechuic acid and gallic acid content was observed, showing that most of the phenolic acids in the drug are present as bound forms [171].

Steroids, terpenoids, alkaloids, flavanoids, coumarin and emodol were isolated from *T. emetica* used in Uganda [183]. Several limonoids have been isolated from the stem bark of the plant [184, 185], while four pregnanes, three androstanes, and three known pregnane derivatives were isolated from the root bark [186].

***Vernonia colorata* (Willd.) Drake (Asteraceae)**

Vernonia colorata is distributed through Benin, Cameroon, Senegal, Togo, and Mali. The leaves have a bitter taste that is said to resemble that of quinine. They are used against fever and stomach aches. Inhalation of a decoction from leaves is used in epileptic seizures. It is also combined with other plants in the treatment of schistosomiasis and sterility. Its leaves are commonly used by African traditional healers to treat diabetes. In Mali, the decoction of the leaves is used in liver diseases. In Ivory Coast, a decoction of the leaves is used against fever, malaria and liver diseases, while the stem bark is used in the treatment of digestive disorders. In Burkina Faso, a decoction of the leaves is a remedy to treat fever, malaria, bronchopulmonary diseases and diarrhea. In Senegal, the plant is used against malaria, intestinal worms, abdominal pain, dizziness and constipation [187].

The aerial parts of *V. colorata* extracts showed significant antiplasmodial activity with IC_{50} < than 5 $\mu\text{g/mL}$ [188]. The dichloromethane and methanol extracts demonstrated antiplasmodial activity against the W2 strains of *P. falciparum*, respectively of 6 $\mu\text{g/mL}$ and 15 $\mu\text{g/mL}$; the same extracts from the roots showed an activity of 3 $\mu\text{g/mL}$ and > 50 $\mu\text{g/mL}$, respectively [189]. The aqueous extracts of *V. colorata* were found to be significantly less active ($IC_{50} \geq 50$ $\mu\text{g/mL}$) as antimalarial agent against chloroquine susceptible (D10) and resistant (W2) strains of *P. falciparum* [187].

The effect of dietary incorporation of *V. amygdalina* and *V. colorata* on some biochemical and histopathological indices in liver of albino rats was studied: treatment of *V. colorata* fed animals with aflatoxin B1 resulted in a marked increase in alkaline phosphatase activity. Increase in aspartate amino transaminase (AST) activity was not significantly different from that of animals fed only with *V. colorata* without aflatoxin B1 [190].

The chloroform-methanol (9:1) extract of the plant leaves exhibited anti-inflammatory activity by using a carrageenan-induced rat paw. The bioassay-oriented fractionation of the extract permitted the isolation of compounds with and without anti-inflammatory activity [191]. The aqueous extract of the leaves presented both hypoglycemic and antidiabetic effects in normoglycemic and alloxan-induced diabetic rats [189]. The acetone extract (100 mg/kg *per os*) induced a significant decrease in blood glucose in normoglycemic rats. Blood glucose levels ranged from 4.72 ± 0.11 to 3.72 ± 0.22 mmol/L ($P < 0.05$, $n = 5$) 3 hours after oral administration. The *n*-hexane extract significantly increased the glucose levels in normoglycemic rats [192]. During a general screening of traditional Zulu medicinal plants used for the treatment of ailments of infectious nature, aqueous, methanol and ethyl acetate extracts of *V. colorata* demonstrated the highest antibacterial activity against Gram-positive bacteria [193]. The dichloromethane and butanol fractions demonstrated antibacterial activity with a minimum inhibitory concentration of 2.5 mg/mL [194]. The ethanol and aqueous extracts, at concentrations ranging between 2.00 to 5.00 mg/mL, demonstrated a good antibacterial activity against *S. aureus* and *P. aeruginosa*. The aqueous extract also showed the highest activity against *S. aureus* at a concentration of 5 mg/mL. The minimum inhibitory concentration of the aqueous extract ranged between 4.00 and 6.00 mg/mL, while that of the ethanolic extract ranged between 5.00 and 6.00 mg/mL [195]. All fractions from the aqueous extract at 10 mg/mL did not show a zone of inhibition against the tested bacteria. The chloroform fraction of

the ethanolic extract showed activity only against *S. aureus* at 10 mg/mL, with a zone of inhibition of 15.00 ± 0.20 mm. The antibacterial activity of the chloroform fraction of the ethanolic extract was significant in comparison with control ($P < 0.05$) [196].

Phytochemical analysis of both ethanolic and aqueous extracts of *V. colorata* led to the characterization of polyphenols, tannins, phlobatannins, saponins, sterols, triterpenes, coumarins, alkaloids, reducing sugars, and anthracenoids [195, 194]. Sesquiterpene lactones, vernolide, 11 β ,13-dihydroveranolide and vernodaline have been isolated and identified from spectroscopic data in the leaves of the plant [197]. Vernolide and vernodaline demonstrated antiplasmodial activity with IC_{50} values of 1.87 $\mu\text{g/mL}$ and 0.52 mg/mL, respectively [198]. Fractionation of the methanol extract of the leaves allowed the isolation of six new compounds, including two androstane and two stigmastane-type glycosides, and two stigmastane-type steroids [191]. The essential oils of the aerial parts of *V. colorata* and *V. nigritiana* grown wild in Mali, obtained by hydrodistillation, showed different qualitative-compositional; 115 components were identified [199].

Medicinal plants are a local heritage with a global importance; they are still the primary source of leads for pharmacologically active compounds. Medicinal plants also play an important role in the lives of rural people, particularly in remote parts of developing countries with a lack of health facilities. African medicinal plants, in addition to their traditional and cultural values, also hold great public health and medical interest worldwide as sources of standardized phytomedicines, extracts or novel lead compounds for drugs development

The present review montred the therapeutic value of different extracts of plants prepared according to the traditionally used forms. These plants have been studied for the different pharmacological activities, mainly antimalarial and hepatoprotective, of extracts, fractions and isolated compounds. Several bioactive compounds were elucidated in these plants, some of them having an interesting antiplasmodial and hepatoprotective activity. This review confirmed that these medicinal plants have both anti-plasmodial and hepatoprotective properties. *Argemone mexicana*, *Cochlospermum tinctorium*, *Combretum micranthum* and *Entada africana* from the Malian traditional pharmacopoeia present opportunities in the treatment of malaria and some liver diseases. The collected data will be useful to improve actual herbal drugs and to propose new phytomedicines for the management of these diseases. In Mali, phytodrugs prepared with these plants are important for the availability of essential medicines used by the majorly of the population. The successes of these herbal drugs open new opportunities for patients and stimulate research on medicinal plants with direct relevance to human health care.

Information was obtained from a literature search through electronic databases such as PubMed, SciFinder, Google Scholar and PROTA. Data collected were organised according to the plan: traditional uses, anti-plasmodial activity, liver disease care, other pharmacological activities, safety of use, and main phytochemical constituents. In Table 1 are reported the botanical names, traditional uses, biological activities and chemical constituents of the ten medicinal plants used in Malian traditional medicine for the treatment of malaria and liver diseases. Most of the authors have personally participated in experimental studies on different aspects of one or more of the ten plants, whose results were published and are among the articles cited in the reference.

Table 1: Botanical names, traditional uses, biological activities and chemical constituents of medicinal plants used in Malian traditional medicines for the treatment of malaria and liver diseases.

Botanical names (Families) (Local names Bamanan)	Traditional uses	Biological activities	Chemical constituents	References
<i>Argemone mexicana</i> (Papaveraceae) (Bozobo, Gnimmidiè)	Malarial, fever, jaundice, ulcers, dropsy	Antimalarial, antihepatotoxic, antimicrobial, wound healing, antibacterial, antifungal, molluscicidal, anticancer and anti-HIV	Isoquinoline and benzyloisoquinoline alkaloids, berberine, tetrahydroberberine, protopine, benzophenanthridines	[3-6, 15]
<i>Cochlospermum tinctorium</i> (Cochlospermaceae) (N'tiribara, N'dilibara)	Malaria, abdominal pain, dermatitis jaundice, gastro intestinal diseases, schistosomiasis	Antiplasmodial, antihepatotoxic	Gallic and ellagic acids, cochloxanthin, dihydrocochloxanthin, arjunolic acid, oleanene-type triterpene, 3-O-E-p-coumaroylalphitollic acid, alphitollic acid, 1-hydroxytetradecan-3-one	[19, 20, 30, 32]
<i>Combretum micranthum</i> (Combretaceae) (N'golobè)	Malaria, bilious fevers with hematuria, constipation, cholagogue, diuretic	Antiplasmodial, antihepatotoxic, anti-inflammatory, antiviral, antibacterial, antioxidant, hypoglycemic, antidiabetic	Vitexin, choline, stachydrine, gallic acid, rutin trihydrate, (+)-catechin and benzoic acid	[50, 52, 54-60, 62, 63, 65, 66]
<i>Entada africana</i> (Fabaceae) (Samanéré)	Malaria, fever, respiratory tract complaints, diabetes, hypertension, diarrheas, liver diseases, rheumatism, dysentery	Antihepatotoxic, antimicrobial, antiplasmodial, antioxidant, antiradical, anti-angiogenic, anti-hepatocellular carcinoma	Triterpene saponins	[69, 70, 76, 79-81, 84-87]
<i>Erythrina senegalensis</i> (Fabaceae) (N'den, Ntenbilin, Ntimini)	Malaria, jaundice, infections, liver diseases, fever, broncho-pulmonary disorders and urogenital infections	Antihepatotoxic, antiplasmodial, antibacterial, antioxidant, anti-hepatocellular carcinoma	2,3-Dihydro-2'-hydroxyosajin, osajin, 6,8-diprenylgenistein	[81, 88, 89, 93, 94]
<i>Mitragyna inermis</i> (Rubiaceae) (Jun, Djou)	Malaria, hepatic illness, stomach and intestinal disorders, hypertension, HIV/AIDS	Antimalarial, antimicrobial, antihypertension, antidiabetic, antioxidant, anti-inflammatory	Indole alkaloids	[97, 100, 101, 117, 118, 124, 125, 127]
<i>Nauclea latifolia</i> syn <i>Sarcocephalus latifolius</i> (Rubiaceae) (Baro)	Fever, malaria, jaundice, infant gastroenteritis and dysentery	Antiplasmodial, antioxidant, analgesic, antimicrobial, antidiabetic	Alkaloids, glycoalkaloids, saponins, nauclefine and nauclefine, indole-quinolizidine, indole alkaloids: nauclefolinine, triterpenic compounds	[93, 100, 128, 129, 130, 131, 139, 140, 141, 143, 145, 146]
<i>Securidaca longepedunculata</i> (Polygalaceae) (Joro)	Fever, malaria, trypanosomiasis, dysmenorrhea, bronchopulmonary diseases, gastrointestinal and liver diseases	Antiplasmodial, cytotoxicity, anti-hepatocellular carcinoma, antibacterial, analgesic, anti-inflammatory, hypoglycemic	Polymethoxylated xanthenes, benzyl 3-hydroxy-2-methoxybenzoate, diphenylmethyl-substituted xanthenes (muchimangines A-L), bidesmosidic saponins (securidacacides A and B), triterpene saponins, medicagenic acid	[81, 148-158, 160]
<i>Trichilia emetica</i> (Meliaceae) (Sulafinzan)	Malaria, abdominal pains, dermatitis, haemorrhoids, jaundice and chest pain	Antiplasmodial, hepatoprotective, anti-infective, anti-inflammatory, anticonvulsant, antitrypanosomal, anti-oxidant, antitussive, antimutagenic	Kurubasch aldehyde, limonoids, polysaccharides	[19, 93, 164, 165, 170, 172, 178, 179, 183, 185]
<i>Vernonia colorata</i> (Asteraceae) (Kosafunè)	Fever, malaria, liver disease, digestive disorders, bronchopulmonary diseases, diarrhea, intestinal worms and abdominal pain	Antiplasmodial, anti-inflammatory, hypoglycemic, antibacterial	Vernolide, vernodalin	[187, 189, 190, 193, 195]

References

- [1] WHO - World Health Organization (2009) World Malaria Report. Available from: who.int/malaria/publications/country-profiles/profile_moz_en.pdf
- [2] Bourdy G, Willcox ML, Ginsburg H, Rasoanaivo P, Graz B, Deharo E. (2008) Ethnopharmacology and malaria: new hypothetical leads or old efficient antimalarials? *International Journal of Parasitology*, **38**, 33-41.
- [3] Willcox ML, Graz B, Falquet J, Sidibe O, Forster M, Diallo D. (2007) *Argemone mexicana* decoction for the treatment of uncomplicated falciparum malaria. *Transactions of the Royal Society of Tropical Medicine & Hygiene*, **101**, 1190-1198.
- [4] Rekha S, Vidyasagar GM. (2014) Plant profile, phytochemistry and pharmacology of *Argemone mexicana* Linn. A review. *International Journal of Pharmacy and Pharmaceutical Sciences*, **6**, 45-53.
- [5] Adjobimey T, Edayè I, Lagnika L, Gbenou J, Moudachirou M, Sanni A. (2004) Activités antiplasmodiales *in vitro* de quelques plantes antipaludiques de la Pharmacopée béninoise. *CR Chimie*, **4**, 1023-1027.
- [6] Graz B, Willcox ML, Diakite C, Falquet J, Dakouo F, Sidibe O, Giani S, Diallo D. (2009) *Argemone mexicana* decoction versus Artesunate/Amodiaquine for the home-based management of malaria in Mali. Policy and public health implications. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **104**, 33-41.
- [7] Diallo D, Graz B, Falquet J, Traore AK, Giani S, Mounkoro PP, Berthé A, Sacko M, Diakite C. (2006) Malaria treatment in remote areas of Mali: use of modern and traditional medicines, patient outcome. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **100**, 515-520.
- [8] Willcox ML, Graz B, Diakite C, Falquet J, Dakouo F, Sidibe O, Giani S, Diallo D. (2011) Is parasite clearance clinically important after malaria treatment in a high transmission area? A 3-month follow-up of home-based management with herbal medicine or ACT. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **105**, 23-31.
- [9] Willcox ML, Graz B, Falquet J, Diakite C, Giani S, Diallo D. (2011) A new methodology for developing antimalarial phytomedicines. *Malaria Journal*, **10**, S8 <http://www.malariajournal.com/content/10/S1/S8>.
- [10] Sanogo R, Djimé A, Guirou C, Doumbia L, Maiga A, Doumbo O, Diallo D. (2008) Etude de la toxicité sub-chronique du décocté de *Argemone mexicana* L. *Pharmacopée et Médecine Traditionnelles Africaines*, **15**, 26-31.
- [11] Sanogo R, Traoré F, Djimé A, Doumbia L, Maiga A, Diallo D, Doumbo O. (2012) Formulation de sirops antipaludiques à base d'extraits de *Argemone mexicana*. *Pharmacopée et Médecine Traditionnelles Africaines*, <http://publication.lecames.org/index.php/pharm/article/view/22>.
- [12] Das PK, Sethi R, Panda P, Pani SR. (2009) Hepatoprotective activity of plant *Argemone mexicana* against carbon tetrachloride (CCl₄) induced hepatotoxicity in rats. *International Journal of Pharmaceutical Research and Development*, **8**, 1-20.
- [13] Sakthivadivel M, Thilagavathy D. (2003) Larvicidal and chemosterilant activity of the acetone fraction of petroleum ether extract from *Argemone mexicana* seed. *Journal of Bioresource Technology*, **89**, 213-216.
- [14] Hussain SF, Nakkady S, Khan L, Shamma M. (1983) Oxyhydrastinine, an isoquinoline alkaloid from the Papaveraceae. *Phytochemistry*, **22**, 319-320.
- [15] Nakkady S, Shamma M. (1988) Studies on the chemical constituents of *Argemone mexicana*. *Egypt Journal of Pharmaceutical Sciences*, **29**, 53-61.
- [16] Harborne JB, Williams CA. (1983) Flavonoids in the seeds of *Argemone mexicana*: a reappraisal. *Phytochemistry*, **22**, 1520-1521.
- [17] Kenneth WB. (2001) β -Phenylethylamines and the isoquinoline alkaloids. *Natural Product Reports*, **18**, 148-170.
- [18] Dalvi RR. (1985) Sanguinarine: its potential as a liver toxic alkaloid present in the seeds of *Argemone mexicana*. *Experientia*, **41**, 77-78.

- [19] Togola A, Diallo D, Dembele S, Barsett H, Paulsen BS. (2005) Ethnopharmacological survey of different uses of seven medicinal plants from Mali, (West Africa) in the regions Doila, Kolokani and Siby. *Journal of Ethnobiology and Ethnomedicine*, **1**, 7, [1-9] doi: 10.1186/1746-4269-1-7.
- [20] Nergard CS, Diallo D, Inngjerdigen K, Michaelsen TE, Matsumoto T, Kiyohara H, Yamada H, Paulsen BS. (2005) Medicinal use of *Cochlospermum tinctorium* in Mali anti-ulcer-, radical scavenging- and immunomodulating activities of polymers in the aqueous extract of the roots. *Journal of Ethnopharmacology*, **96**, 255-269.
- [21] Magassouba FB, Diallo A, Kouyate M, Mara F, Mara O, Bangoura O, Camara A, Traore S, Diallo AK, Zaoro M, Lamah K, Diallo S, Camara G, Traoré S, Kéita A, Camara MK, Barry R, Kéita S, Oularé K, Barry MS, Donzo M, Camara K, Totéc K, Vanden Berghech D, Tottéc J, Pieterse L, Vlietinck AJ, Baldé AM. (2007) Ethnobotanical survey and antibacterial activity of some plants used in Guinean traditional medicine. *Journal of Ethnopharmacology*, **114**, 44-53.
- [22] Benoit F, Valentin A, Pelissier Y, Marion C, Dakuyo Z, Mallie M, Bastide JM. (1995) Antimalarial activity *in vitro* of *Cochlospermum tinctorium* tubercle extracts. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **89**, 217-218.
- [23] Traore M, Guiguemde, A, Yago I, Nikiema JB, Tinto H, Dakuyo ZP, Ouedraogo JB, Guissou IP, Guiguemde TR. (2006) Investigation of antiplasmodial compounds from two plants, *Cochlospermum tinctorium* A. Rich and *Gardenia sokotensis* Hutch. *African Journal of Traditional, Complementary and Alternative Medicines*, **3**, 34-41.
- [24] Bossou AD, Mangelinckx S, Yedomonhan H, Boko PM, Akogbeto MC, De Kimpe N, Avlessi F, Sohounhloue DCK. (2013) Chemical composition and insecticidal activity of plant essential oils from Benin against *Anopheles gambiae* (Giles). *Parasites & Vectors*, **6**, 337/1-337/17.
- [25] Zederkopff BN, Traore M, Tinto H, Sittie A, Molgaard P, Olsen CE, Kharazmi A, Christensen SB. (2002) Antiplasmodial compounds from *Cochlospermum tinctorium*. *Journal of Natural Products*, **65**, 1325-1327.
- [26] Diallo B, Vanhaelen M, Kiso Y, Hikino H. (1987) Antihepatotoxic actions of *Cochlospermum tinctorium* rhizomes. *Journal of Ethnopharmacology*, **20**, 239-243.
- [27] Dalvi RR, Sere A. (1988) Protective effect of *Cochlospermum tinctorium* A. Rich extracts versus aflatoxin B-induced liver damage in rats. *International Journal of Crude Drug Research*, **26**, 117-120.
- [28] Diallo B, Vanhaelen-Fastre R, Vanhaelen M, Fiegel C, Joyeux M, Roland A, Fleurentin J. (1992) Further studies on the hepatoprotective effects of *Cochlospermum tinctorium* rhizomes. *Journal of Ethnopharmacology*, **36**, 137-142.
- [29] Ram VJ. (2001) Herbal preparations as a source of hepatoprotective agents. *Drug News & Perspectives*, **14**, 353-363.
- [30] Etuk EU, Agaie BM, Ladan MJ, Garba I. (2009) The modulatory effect of *Cochlospermum tinctorium* a rich aqueous root extract on liver damage induced by carbon tetrachloride in rats. *African Journal of Pharmacy and Pharmacology*, **3**, 151-157.
- [31] Diallo B, Vanhaelen-Fastre R, Vanhaelen M, Nkiani-Ibwala NY, Pelsener-Coremans J. (1991) Antimicrobial activity of two apocarotenoids isolated from *Cochlospermum tinctorium* rhizome. *Fitoterapia*, **62**, 144-145.
- [32] Diallo B, Vanhaelen M, Vanhaelen-Fastre R, Konoshima T, Kozuka M, Tokuda H. (1989) Studies on inhibitors of skin-tumor promotion. Inhibitory effects of triterpenes from *Cochlospermum tinctorium* on Epstein-Barr virus activation. *Journal of Natural Products*, **52**, 879-881.
- [33] Diallo B, Vanhaelen-Fastre R, Vanhaelen M, Konoshima T, Takasaki M, Tokuda H. (1995) *In vivo* inhibitory effects of arjunolic acid derivatives on two-stage carcinogenesis in mouse skin. *Phytotherapy Research*, **9**, 444-447.
- [34] Nergard CS, Kiyohara H, Reynolds JC, Thomas-Oates JE, Matsumoto T, Yamada H, Patel T, Petersen D, Michaelsen TE, Diallo D, Paulsen BS. (2006) Structures and structure-activity relationships of three mitogenic and complement fixing pectic arabinogalactans from the Malian antiulcer plants *Cochlospermum tinctorium* A. Rich and *Vernonia kotschyana* Sch. Bip. ex Walp. *Biomacromolecules*, **7**, 71-79.
- [35] Benoit-Vical F, Valentin A, Mallie M, Bastide J-M, Bessiere J-M. (1999) *In vitro* antimalarial activity and cytotoxicity of *Cochlospermum tinctorium* and *C. planchonii* leaf extracts and essential oils. *Planta Medica*, **65**, 378-381.
- [36] Benoit-Vical F, Valentin A, Mallie M, Bessiere J-M. (2001) Antiplasmodial activity of *Cochlospermum planchonii* and *C. tinctorium* tubercle essential oils. *Journal of Essential Oil Research*, **13**, 65-67.
- [37] Oyewale AO, Audu OT. (2007) The medicinal potentials of aqueous and methanol extracts of six flora of tropical Africa. *African Journal of Chemical Society of Nigeria*, **32**, 150-155.
- [38] Tijjani MB, Bello IA, Aliyu AB, Olurise T, Maidawa SM, Habila JD, Balogun EO. (2009) Phytochemical and antibacterial studies of root extract of *Cochlospermum tinctorium* A. Rich. (Cochlospermaceae). *Research Journal of Medicinal Plants*, **3**, 16-22.
- [39] Tvette Inngjerdigen K, Thole C, Diallo D, Paulsen BS, Hensel A. (2014) Inhibition of *Helicobacter pylori* adhesion to human gastric adenocarcinoma epithelial cells by aqueous extracts and pectic polysaccharides from the roots of *Cochlospermum tinctorium* A. Rich. And *Vernonia kotschyana* Sch. Bip. ex Walp. *Fitoterapia*, **95**, 127-132.
- [40] Ahmed T, Magaji M, Yaro A, Musa A, Adamu A. (2011) Aqueous methanol extracts of *Cochlospermum tinctorium* (A. Rich) possess analgesic and anti-inflammatory activities. *Journal of Young Pharmacists*, **3**, 237-242.
- [41] Diallo B, Vanhaelen M. (1987) Apocarotenoids from *Cochlospermum tinctorium*. *Phytochemistry*, **26**, 1491-1492.
- [42] Diallo B, Vanhaelen M. (1988) Large scale purification of apocarotenoids from *Cochlospermum tinctorium* by counter-current chromatography. *Journal of Liquid Chromatography*, **11**, 227-231.
- [43] Diallo B, Vanhaelen-Fastre R, Vanhaelen M. (1991) Triacylbenzenes and long-chain volatile ketones from *Cochlospermum tinctorium* rhizome. *Phytochemistry*, **30**, 4153-4156.
- [44] Tvette Inngjerdigen K, BalloN, Zhang B-Z, Malterud KE, Michaelsen TE, Diallo D, Paulsen SB. (2013) A comparison of bioactive aqueous extracts and polysaccharide fractions from roots of wild and cultivated *Cochlospermum tinctorium* A. Rich. *Phytochemistry*, **93**, 136-143.
- [45] Pousset J-L. (2004) *Plantes Médicinales d'Afrique*. Edisud, Aix-en-Provence, 287.
- [46] Irvine FR. (1961) *Woody Plants of Ghana with Special References to their Uses*. Oxford University Press, Oxford.
- [47] Kerharo J, Adam JG. (1974) *La Pharmacopée Sénégalaise Traditionnelle: Plantes Médicinales et Toxiques*. Vigot Frères, Paris.
- [48] Adjanohoun EJ, Ake Assi L, Floret JJ, Guindo S, Koumaré M, Ahyi AMR, Raynal J. (1985) *Médecine traditionnelle et pharmacopée contribution aux études ethnobotaniques et floristiques au Mali*. Edition Agence de Coopération Culturelle et Technique (ACCT), Paris.
- [49] Ake Assi L, Guinko S. (1991) *Plants used in Traditional Medicine in West Africa*. Editions Roche.
- [50] Lengani A, Lompo LF, Guissou IP, Nikiema JB. (2010) Traditional medicine in kidney diseases in Burkina Faso. *Nephrology Therapy*, **6**, 35-39.
- [51] Diatta W, Lo M, Fall AD, Bassene S, Sagna S, Badji K, Bassene E. (2009) Popular traditional herbal medicines from the Joolas of Essyl in the rural community of Enampor (Ziguinchor, Senegal): an ethnographic survey. *ACS Symposium Series*, **1021** (African Natural Plant Products), 111-133.
- [52] Malcolm SA, Sofowora EA. (1969) Antimicrobial activity of selected Nigerian folk remedies and their constituent plants. *Lloydia*, **32**, 512-517.
- [53] Diallo D, Paulsen BS, Hveem B. (2005) Les produits de la médecine traditionnelle. In *Les plantes sauvages du Sahel malien*. Berge G, Diallo D, Hveem B. (Eds) Editions Karthala, Paris, 135-141.
- [54] Ferrea G, Canessa A, Sampietro F, Cruciani M, Romussi G, Bassetti D. (1993) *In vitro* activity of a *Combretum micranthum* extract against herpes simplex virus types 1 and 2. *Antiviral Research*, **21**, 317-325.
- [55] Olajide OA, Makinde JM, Okpako DT. (2003) Evaluation of the anti-inflammatory property of the extract of *Combretum micranthum* G. Don (Combretaceae). *Inflammopharmacology*, **11**, 293-298.

- [56] Karou D, Dicko MH, Simpore J, Traore AS. (2005) Antioxidant and antibacterial activities of polyphenols from ethnomedicinal plants of Burkina Faso. *African Journal of Biotechnology*, **4**, 823-828.
- [57] Welch CR, Wu Q-L, Pan M-H, Ho C-T, Diatta M, Simon JE. (2008) Identification of the bioactive constituents of Kinkeliba (*Combretum micranthum*), a West African medicinal plant. Abstracts of Papers, 236th ACS National Meeting, Philadelphia, PA, USA, August 17-21 2008, AGFD-140.
- [58] Chika A, Bello SO. (2010) Antihyperglycaemic activity of aqueous leaf extract of *Combretum micranthum* (Combretaceae) in normal and alloxan-induced diabetic rats. *Journal of Ethnopharmacology*, **129**, 34-37.
- [59] Benoit F, Valentin A, Pelissier Y, Diafouka F, Marion C, Kone-Bamba D, Kone M, Mallie M, Yapo A, Bastide JM. (1996) *In vitro* antimalarial activity of vegetal extracts used in West African traditional medicine. *American Journal of Tropical Medicine and Hygiene*, **54**, 67-71.
- [60] Osonwa UE, Umeyor CE, Okon, UV, Uronnachi EM, Nwakile CD. (2012) Stability studies on the aqueous extract of the fresh leaves of *Combretum micranthum* G. Don used as antibacterial agent. *Journal of Chemistry and Chemical Engineering*, **6**, 417-424.
- [61] Nordeng H, Al-Zayadi W, Diallo D, Ballo N, Paulsen BS. (2013) Traditional medicine practitioners' knowledge and views on treatment of pregnant women in three regions of Mali. *Journal of Ethnobiology and Ethnomedicine*, **9**, <http://hdl.handle.net/11250/219439>
- [62] Paris R, Moysse-Mignon H. (1956) Paper chromatographic characterization of choline in some medicinal plants. *Annales Pharmaceutiques Francaises*, **4**, 464-469.
- [63] Ogan AU. (1962) The alkaloids in the leaves of *Combretum micranthum*. Studies on West African medicinal plants. *Planta Medica*, **10**, 210-217.
- [64] Spiegel K, Jentszsch P, Fuchs L. (1962) The constituents of the leaves of *Combretum micranthum*. *Planta Medica*, **10**, 1-8.
- [65] Bassene E, Olschwang D, Pousset JL. (1986). African medicinal plants. Alkaloids of *Combretum micranthum* G. Don (Kinkeliba). *Annales Pharmaceutiques Francaises*, **44**, 191-196.
- [66] Bassene E, Olschwang D, Pousset JL. (1981) African medicinal plants. I: Characterization of inositol and sorbitol, probable active principles of kinkeliba (*Combretum micranthum* G. Don). *Dakar Medicine*, **26**, 219-225.
- [67] Touré A, Xu X, Michel T, Bangoura M. (2011). *In vitro* antioxidant and radical scavenging of Guinean kinkeliba leaf (*Combretum micranthum* G. Don) extracts. *Natural Product Research*, **25**, 1025-1036.
- [68] Simon JE, Wu Q, Welch C. (2011) Novel piperidine-flavan alkaloid compounds derived from African herb tea kinkeliba as anti-diabetic agents. PCT Int. Appl. WO 2011140066 A1 20111110.
- [69] Occhiuto F, Sanogo R, Germano MP, Keita A, D'Angelo V, De Pasquale R. (1999) Effects of some Malian medicinal plants on the respiratory tract of Guinea-pigs. *Journal of Pharmacy and Pharmacology*, **51**, 1299-1303.
- [70] Maiga A, Diallo D, Fane S, Sanogo R, Paulsen BS, Cisse B. (2005) A survey of toxic plants on the market in the district of Bamako, Mali: traditional knowledge compared with a literature search of modern pharmacology and toxicology. *Journal of Ethnopharmacology*, **96**, 183-193.
- [71] Diallo D, Paulsen BS, Liljebäck TH, Michaelsen TE. (2001) Polysaccharides from the roots of *Entada africana* Guill. et Perr., Mimosaceae, with complement fixing activity. *Journal of Ethnopharmacology*, **74**, 159-171.
- [72] Sanogo R, Germano MP, D'Angelo V, Guglielmo M, De Pasquale R. (1998) Antihepatotoxic properties of *Entada africana* (Mimosaceae). *Phytotherapy Research*, **12** (Suppl. 1, Second International Symposium on Natural Drugs, 1997), S157-S159.
- [73] Fabry W, Okemo P, Ansorg R. (1996) Fungistatic and fungicidal activity of East African medicinal plants. *Mycoses*, **39**, 67-70.
- [74] Obidike IC, Emeje MO. (2011) Microencapsulation enhances the anti-ulcerogenic properties of *Entada africana* leaf extract. *Journal of Ethnopharmacology*, **137**, 553-561.
- [75] Ezenyi IC, Ranarivelo L, Oluwakanyinsola, SA, Emeje M. (2014) Analgesic, anti-inflammatory, and hemebiomineralization inhibitory properties of *Entada africana* ethanol leaf extract with antiplasmodial activity against *Plasmodium falciparum*. *Journal of Basic and Clinical Physiology and Pharmacology*, **25**, 217-223.
- [76] Karou SD, Tchacondo T, Ouattara L, Anani K, Savadogo A, Agbonon A, Attaia MB, de Souza C, Sakly M, Simpore J. (2011) Antimicrobial, antiplasmodial, haemolytic and antioxidant activities of crude extracts from three selected Togolese medicinal plants. *Asian Pacific Journal of Tropical Medicine*, **4**, 808-813.
- [77] Haïdara M. (2013), Caractérisation sur un modèle cellulaire d'hépatocarcinome humain de l'effet cytotoxique des extraits de *Entada africana* Guill et Perr, *Erythrina senegalensis* DC et *Securidaca longepedunculata* Fresen utilisés en médecine traditionnelle au Mali. Rapport de M2R. Université Paul Sabatier III de Toulouse, 21.
- [78] Galani Tietcheu BR, Sassi G, Njyou NF, Mkounga P, Tiegs G, Moundipa PF. (2014) Anti-hepatitis C virus activity of crude extract and fractions of *Entada africana* in genotype 1b replicon systems. *The American Journal of Chinese Medicine*, **42**, 853-868.
- [79] Njyou FN, Aboudi ECE, Tandjang MK, Tchana AK, Ngadjui BT, Moundipa PF. (2013) Hepatoprotective and antioxidant activities of stem bark extract of *Khaya grandifoliola* (Welw) CDC and *Entada africana* Guill. et Perr. *Journal of Natural Products*, **6**, 73-80.
- [80] Tibiri A, Rakotonandrasana O, Nacoulma GO, Banzouzi JT. (2007) Radical scavenging activity, phenolic content and cytotoxicity of bark and leaves extracts of *Entada africana* Guill. and Perr. (Mimosaceae). *Journal of Biological Sciences*, **7**, 959-963.
- [81] Owona Brice A, Njyou NF, Laufer SA, Schluesener HJ, Moundipa PF. (2013) *Entada africana* fraction CH₂Cl₂/MeOH 5% inhibits inducible nitric oxide synthase and pro-inflammatory cytokines gene expression induced by lipopolysaccharide in microglia. *BMC Complementary and Alternative Medicine*, **13**, 254 <http://www.biomedcentral.com/1472-6882/13/>
- [82] Germano MP, Certo G, D'Angelo V, Sanogo R, Malafrente N, De Tommasi N, Rapisarda A. (2015) Anti-angiogenic activity of *Entada africana* root. *Natural Product Research*, **29**, 1551-1556.
- [83] Ayissi OB, Njyou NF, Laufer SA, Moundipa PF, Schluesener HJ. (2013) A fraction of stem bark extract of *Entada africana* suppresses lipopolysaccharide-induced inflammation in RAW 264.7 cells. *Journal of Ethnopharmacology*, **149**, 162-168.
- [84] Bako SP, Bakfur MJ, John I, Bala EI. (2005) Ethnomedicinal and phytochemical profile of some savanna plant species in Nigeria. *International Journal of Botany*, **1**, 147-150.
- [85] Olajide OB, Fadimu OY, Osaguona PO, Saliman MI. (2013) Ethnobotanical and phytochemical studies of some selected species of leguminosae of northern Nigeria: a study of Borgu local government area, Niger state, Nigeria. *International Journal of Science and Nature*, **4**, 546-551.
- [86] Cioffi G, Dal Piazz F, De Caprariis P, Sanogo R, Marzocco S, Autore G, De Tommasi N. (2006) Antiproliferative triterpene saponins from *Entada africana*. *Journal of Natural Products*, **69**, 1323-1329.
- [87] Cook JA, Vander Jagt DJ, Pastuszyn A, Mounkaila G, Glew RS, Millson M, Glew RH. (2000) Nutrient and chemical composition of 13 wild plant foods of Niger. *Journal of Food Composition and Analysis*, **13**, 83-92.
- [88] Togola A, Austarheim I, Theis A, Diallo D, Paulsen BS. (2008) Ethnopharmacological uses of *Erythrina senegalensis*: a comparison of three areas in Mali, and a link between traditional knowledge and modern biological science. *Journal of Ethnobiology and Ethnomedicine*, **4:6**, 1-9 <http://www.ethnobiomed.com/content/4/1/6>.
- [89] Soh PN, Benoit-Vical F. (2007) Are West African plants a source of future antimalarial drugs? *Journal of Ethnopharmacology*, **114**, 130-140.
- [90] Saidu K, Onah J, Orisadipe A, Olusola A, Wambebe C, Gamaniel K. (2000) Antiplasmodial, analgesic, and anti-inflammatory activities of the aqueous extract of the stem bark of *Erythrina senegalensis*. *Journal of Ethnopharmacology*, **71**, 275-280.

- [91] Donfack JH, Njyou NF, Rodrigue TK, Chuisseu PD, Tchana NA, Vita Finzi P, Tchouanguep MF, Ngadjui BT, Moundipa PF. (2008) Study of a hepatoprotective and antioxidant fraction from *Erythrina senegalensis* stem bark extract: *in vitro* and *in vivo*. *Pharmacologyonline*, **1**, 120-130.
- [92] Atsamo AD, Nguelefack TB, Datte JY, Kamanyi A. (2011) Acute and subchronic oral toxicity assessment of the aqueous extract from the stem bark of *Erythrina senegalensis* DC (Fabaceae) in rodents. *Journal of Ethnopharmacology*, **134**, 697-702.
- [93] Donfack JH, Njyou NF, Ngameni B, Tchana A, Chuisseu PD, Vita Finzi P, Ngadjui BT, Moundipa PF. (2008) *In vitro* hepatoprotective and antioxidant activities of diprenylatedisoflavonoids from *Erythrina senegalensis* (Fabaceae). *Asian Journal of Traditional Medicines*, **3**, 172-178.
- [94] Wandji J, Awanchiri SS, Fomum ZT, Tillequin F, Michel-Daniwicz S. (1995) Prenylated isoflavonoids from *Erythrina senegalensis*. *Phytochemistry*, **38**, 1309-1313.
- [95] Oh WK, Lee HS, Ahn SC, Ahn JS, Mbafor JT, Wandji J, Fomum ZT, Chang HK, Kim YH. (1999) Prenylated isoflavonoids from *Erythrina senegalensis*. *Phytochemistry*, **51**, 1147-1150.
- [96] Togola A, Hedding B, Theis A, Wangenstein H, Rise F, Paulsen BS, Diallo D, Malterud KE. (2009) 15-Lipoxygenase inhibitory effects of prenylated flavonoids from *Erythrina senegalensis*. *Planta Medica*, **75**, 1168-1170.
- [97] Adjanahoun FJ, Ake A, Floret JJ, Guinko S, Kouame M, Ahyi AMR, Raynal J. (1985) *Contribution aux études ethnobotaniques et floristique du Mali. Médecine traditionnelle et pharmacopée*. ACCT, Paris, 64.
- [98] Malgras D. (1992) *Arbres et arbustes guérisseurs des savanes maliennes*. Edits Karthala et ACCT, Paris, 474.
- [99] Phillipson JD, Wright CW. (1991) Can ethnopharmacology contribute to the development of antimalarial agents? *Journal of Ethnopharmacology*, **32**, 155-165.
- [100] Karou SD, Tchacondo T, Ilboudo DP, Simporé J. (2011) Sub-Saharan Rubiaceae: a review of their traditional uses, phytochemistry and biological activities. *Pakistan Journal of Biological Sciences*, **14**, 149-169.
- [101] Nikiema JB, Djierro K, Simporé J, Guissou IP, Nacoulma OG, Bassene E. (2004) Contribution à la connaissance des plantes médicinales utilisées par les tradipraticiens de la ville de Ouagadougou (Burkina Faso), pour la prise en charge des personnes vivant avec le VIH/SIDA. *Le pharmacien d'Afrique*, **173**, 13-15.
- [102] Kumulungui S, Serges B, Alain O-A, Mints NA, Fumoux F, Traore A. (2012) *In vitro* antiplasmodial activity of seven plants commonly used against malaria in Burkina Faso. *Journal of Medicinal Plants Research*, **6**, 2284-2288.
- [103] Azas N, Laurencin N, Delmas F, Di Giorgio C, Gasquet M, Laget M, Timon-David P. (2002) Synergistic *in vitro* antimalarial activity of plant extracts used as traditional herbal remedies in Mali. *Parasitology Research*, **88**, 165-171.
- [104] Fiot J, Sanon S, Azas N, Mahiou V, Jansen O, Angenot L, Balansard G, Ollivier E. (2006) Phytochemical and pharmacological study of roots and leaves of *Guiera senegalensis* J.F. Gmel (Combretaceae). *Journal of Ethnopharmacology*, **106**, 173-178.
- [105] Mustafa VA, Benoit-Vical F, Pelissier Y, Kone-Bamba D, Mallié M. (2000) Antiplasmodial activity of plant extracts used in West African traditional medicine. *Journal of Ethnopharmacology*, **73**, 145-151.
- [106] Menan M, Banzouzi JT, Hocquette A, Pelissier P, Blache Y, Kon M, Malli M, Assi LA, Valentin A. (2006) Antiplasmodial activity and cytotoxicity of plants used in West African traditional medicine for the treatment of malaria. *Journal of Ethnopharmacology*, **105**, 131-136.
- [107] Monjanel-Mouterde S, Traoré F, Gasquet M, Doderó F, Delmas F, Ikoli JF, Lorec AM, Chamlian V, Portugal H, Balansard G, Pisano P. (2006) Lack of toxicity of hydroethanolic extract from *Mitragyna inermis* (Willd.) O. Kuntze by gavage in the rat. *Journal of Ethnopharmacology*, **103**, 319-326.
- [108] Traore-Keita F, Gasquet M, Di Giorgio C, Ollivier E, Delmas F, Keita A, Doumbo O, Balansard G, Timon-David P. (2000) Antimalarial activity of four plants used in traditional medicine in Mali. *Phytotherapy Research*, **14**, 45-47.
- [109] Fiot J, Baghdikian B, Boyer L, Mahiou V, Azas N, Gasquet M, Timon-David P, Balansard G, Ollivier E. (2005) HPLC quantification of uncarine D and the anti-plasmodial activity of alkaloids from leaves of *Mitragyna inermis* (Willd.) O. Kuntze. *Phytochemical Analysis*, **16**, 30-33.
- [110] Cheng ZH, Yu BY, Yang XW. (2002) 27-Nor-triterpenoid glucosides from *Mitragyna inermis*. *Phytochemistry*, **61**, 379-382.
- [111] Cheng ZH, Yu BY, Yang XW, Zhang J. (2002) Triterpenoid saponins from the bark of *Mitragyna inermis*. *Zhongguo Zhongyao Zazhi*, **27**, 274-277.
- [112] Shellard EJ, Sarpong K. (1969) The alkaloids of the leaves of *Mitragyna inermis* (Willd.) O. Kuntze. *Journal of Pharmacy and Pharmacology*, **21**, 113-117.
- [113] Shellard EJ, Sarpong K. (1970) The alkaloidal pattern in the leaves, stem-bark and root-bark of *Mitragyna* species from Ghana. *Journal of Pharmacy and Pharmacology*, **22**, 34-39.
- [114] Shellard EJ, Phillipson JD, Sarpong K. (1971) Rhynchophylline and isorhynchophylline N-oxides from species of *Mitragyna*. *Phytochemistry*, **10**, 2505-2511.
- [115] Touré H, Balansard G, Pauli AM, Scotto AM. (1996) Pharmacological investigation of alkaloids from leaves of *Mitragyna inermis* (Rubiaceae). *Journal of Ethnopharmacology*, **54**, 59-62.
- [116] Inngjerdingen K, Nergård CS, Diallo D, Mounkoro PP, Paulsen BS. (2004) An ethnopharmacological survey of plants used for wound healing in Dogonland, Mali, West Africa. *Journal of Ethnopharmacology*, **92**, 233-244.
- [117] Chifundera K. (2001) Contribution to the inventory of medicinal plants from the Bushi area, South Kivu Province, Democratic Republic of Congo. *Fitoterapia*, **72**, 351-368.
- [118] Keita SM, Arnason JT, Baum BR, Marles R, Camara F, Traore AK. (1995) Etude ethnopharmacologique traditionnelle de quelques plantes médicinales anthelminthiques de la République de Guinée. *Revue de Médecine et Pharmacie Africaine*, **9**, 119-134.
- [119] Bouquet A, Debray M. (1974) Plantes médicinales de la Côte d'Ivoire. *Travaux et Documents de l'ORSTOM*, **32**, Paris, 232.
- [120] Adjanahoun EJ, Ahyi AMR, Ake-Assi L, Dan Dicko L, Daouda H, Delmas M, De Souza S, Garba M, Guinko S, Kayonga A, Ngolo D, Raynal JL, Saadou M. (1981) *Contribution aux études ethnobotaniques et floristiques au Niger*. ACCT, Paris, 250.
- [121] Adjanahoun EJ, Adjakidjè V, Ahyi AMR, Aké Assi L, Akoègninou A, d'Almeida J, Apovo F, Boukef K, Chadare M, Cusset G, Dramane K, Eyme J, Gassita JN, Gbaguidi N, Goudote E, Guinko S, Hounnon P, Lo I, Keita A, Kiniffo HV, Kone-Bamba D, Musampa Nseyya A, Saadou M, Sodogandji T, De Souza S, Tchabi A, Zinsou Dossa C, Zohoun T. (1989) *Contribution aux études ethnobotaniques et floristiques en République populaire du Bénin*. ACCT, Paris, 895.
- [122] Ake-Assi YA. (1992) *Contribution au recensement des espèces végétales utilisées traditionnellement sur le plan zootechnique et vétérinaire en Afrique de l'Ouest*. Thèse de doctorat (Sc. Vétérinaires), Lyon, Université Claude Bernard, 220.
- [123] Donfack EV, Lenta BN, Kongue MDT, Fongang YF, Ngouela S, Tsamo E, Ditttrich B, Laatsch H. (2012) Naucleonin D, an indole alkaloid and other chemical constituents from roots and fruits of *Mitragyna inermis*. *Zeitschrift fuer Naturforschung B: A Journal of Chemical Sciences*, **67**, 1159-1165.
- [124] Ouédraogo S, Ranaivo HR, Ndiaye M, Kaboré ZI, Guissou IP, Bucher B, Andriantsitohaina R. (2004) Cardiovascular properties of aqueous extract from *Mitragyna inermis* (Willd.). *Journal of Ethnopharmacology*, **93**, 345-350.
- [125] Sy GY, Sarr A, Dièye AM, Faye B. (2004) Myorelaxant and antispasmodic effects of the aqueous extract of *Mitragyna inermis* barks on Wistar rat ileum. *Fitoterapia*, **75**, 447-450.
- [126] Asase A, Kokubun T, Grayer RJ, Kite G, Simmonds MSJ, Oteng-Yeboah AA, Odamtten GT. (2008) Chemical constituents and antimicrobial activity of medicinal plants from Ghana: *Cassia sieberiana*, *Haematostaphis barteri*, *Mitragyna inermis* and *Pseudocedrela kotschyii*. *Phytotherapy Research*, **22**, 1013-1016.

- [127] Muazu J, Kaita AH. (2008) A review of traditional plants used in the treatment of epilepsy amongst the Hausa/Fulani tribes of Northern Nigeria. *African Journal of Traditional, Complementary, and Alternative Medicines*, **5**, 387-390.
- [128] Kokwaro JO. (1976) Medicinal plants of East Africa. *East African Literature Bureau*, Nairobi.
- [129] Akabue P, Mittal GC. (1982) Clinical evaluation of a traditional herbal practice in Nigeria: a preliminary report. *Journal of Ethnopharmacology*, **6**, 355-359.
- [130] Fernandez de la Pradilla C. (1982) *Plantes Medicinales contre les hepatitis: 51 especes tropicales*. Ed. Librairie Jeunesse d'Afrique, Ouagadougou, 61.
- [131] Fernandez de la Pradilla C. (1982) *Plantes Medicinales vendue sur les marches de Ouagadougou*. Ed. Librairie Jeunesse d'Afrique, Ouagadougou, 22.
- [132] Maduabunyi W. (1995) Anti-hepatotoxic and trypanocidal activities of the ethanolic extract of *Nauclea latifolia* root bark. *Journal of Herbs Spices and Medicinal Plants*, **3**, 23-53.
- [133] Kerharo J. (1974) Historic and ethnopharmacognosic review on the belief and traditional practices in the treatment of sleeping sickness in West Africa. *Bulletin de la Societe medicale d'Afrique noire de langue francaise*, **19**, 217.
- [134] Elujoba AA. (1995) Female infertility in the hands of traditional birth attendants in South-West Nigeria. *Fitoterapia*, **66**, 239-248.
- [135] Asubiojo OI, Guinn VP, Okunuga A. (1982) Multi-element analysis of Nigerian chewing sticks by Instrumental Neuron Activation Analysis. *Journal of Radioanalytical Chemistry*, **74**, 149-156.
- [136] Lamidi ME, Oliver R, Faurel L, Debrauwer L, Nze E, Balandsard G. (1995) Quinovic acid glycosides from *Nauclea diderichii*. *Planta Medica*, **61**, 280-281.
- [137] Iwueke AV, Nwodo OFC, Ojiako OA, Okwu GN, Nwogu LA, Igwe CU. (2010) Modification of lipid peroxidation and oxidative stress in hepatocytes of diabetic rats treated with root extract of *Sarcocephalus latifolius* and *Daniella oliveri*. *Australian Journal of Basic and Applied Sciences*, **4**, 3578-3584.
- [138] Ayeleso AO, Oguntibeju OO, Brooks NL. (2014) *In vitro* study on the antioxidant potentials of the leaves and fruits of *Nauclea latifolia*. *Scientific World Journal*, 437081/1-437081/9.
- [139] Abbah J, Amos S, Chindo B, Ngazal I, Vongtau HO, Adzu B, Farida T, Odutola AA, Wambebe C, Gamaniel KS. (2010) Pharmacological evidence favouring the use of *Nauclea latifolia* in malaria ethnopharmacy: effects against nociception, inflammation, and pyrexia in rats and mice. *Journal of Ethnopharmacology*, **127**, 85-90.
- [140] Gidado A, Ameh DA, Atawodi SE, Ibrahim S. (2008) Hypoglycaemic activity of *Nauclea latifolia* Sm. (Rubiaceae) in experimental animals. *African Journal of Traditional, Complementary, and Alternative Medicines*, **5**, 201-208.
- [141] Ngo Bum E, Taiwe GS, Moto FCO, Ngoupaye GT, Nkantchoua GCN, Pelanken MM, Rakotonirina SV, Rakotonirina A. (2009) Anticonvulsant, anxiolytic, and sedative properties of the roots of *Nauclea latifolia* Smith in mice. *Epilepsy & Behavior*, **15**, 434-440.
- [142] Fadipe LA, Haruna K, Mohammed I, Ibikunle GF. (2013) Phytochemical and *in-vitro* antibacterial evaluation of the extracts, portions and sub-portions of the ripe and unripe fruits of *Nauclea latifolia*. *Journal of Medicinal Plants Research*, **7**, 629-636.
- [143] Eze O, Sunday EO. (2014) Phytochemical and nutrient evaluation of the leaves and fruits of *Nauclea latifolia* (Uvuru-ilu). *Communications in Applied Sciences*, **2**, 8-24.
- [144] Deeni Y, Hussain H. (1991) Screening for antimicrobial activity and for alkaloids of *Nauclea latifolia*. *Journal of Ethnopharmacology*, **35**, 91-96.
- [145] Abreu P, Pereira A. (1998) A new indole alkaloid from *Sarcocephalus latifolius*. *Heterocycles*, **48**, 885-891.
- [146] Abreu P, Pereira A. (2001) New indole alkaloids from *Sarcocephalus latifolius*. *Natural Product Letters*, **15**, 43-48.
- [147] Abreu P, Pereira A, Relva A. (2001) Characterisation of a sugar fraction from *Sarcocephalus latifolius* stem bark extract. *Carbohydrate Polymers*, **45**, 155-160.
- [148] Bah S, Jager AK, Adsersen A, Diallo D, Paulsen BS. (2007) Antiplasmodial and GABA(A)-benzodiazepine receptor binding activities of five plants used in traditional medicine in Mali, West Africa. *Journal of Ethnopharmacology*, **110**, 451-457.
- [149] Lawal RA, Ozaslan MD, Odesanmi OS, Karagoz ID, Kilic IH, Ebechi OAT. (2013) Cytotoxic and antiproliferative activity of *Securidaca longepedunculata* aqueous extract on Ehrlich ascites carcinoma cells in Swiss albino mice. *International Journal of Applied Research in Natural Products*, **5**, 19-27.
- [150] Dibwe DF, Awale S, Kadota S, Tezuka Y. (2012) Damnacanthal from the Congolese medicinal plant *Garcinia huillensis* has a potent preferential cytotoxicity against human pancreatic cancer PANC-1 Cells. *Phytotherapy Research*, **26**, 1920-1926.
- [151] Ndamitso MM, Mohammed A, Jimoh TO, Idris S, Oyeleke SB, Etsuyankpa MB. (2013) Phytochemical and antibacterial activity of *Securidaca longepedunculata* on selected pathogens. *African Journal of Microbiology Research*, **7**, 5652-5656.
- [152] Adebisi RA, Elsa AT, Agaie BM, Etuk EU. (2006) Antinociceptive and antidepressant like effects of *Securidaca longepedunculata* root extract in mice. *Journal of Ethnopharmacology*, **107**, 234-239.
- [153] Ojewole JAO. (2008) Analgesic, anti-inflammatory and hypoglycaemic effects of *Securidaca longepedunculata* (Fresen.) [Polygalaceae] root-bark aqueous extract. *Inflammopharmacology*, **16**, 174-181.
- [154] Adeyemi OO, Akindele AJ, Yemitan OK, Aigbe FR, Fagbo FI. (2010) Anticonvulsant, anxiolytic and sedative activities of the aqueous root extract of *Securidaca longepedunculata* Fresen. *Journal of Ethnopharmacology*, **130**, 191-195.
- [155] Dapar LP, Maxwell AJC, Wannang NN, Gyang SS, Tanko NM. (2007) The histopathologic effects of *Securidaca longepedunculata* on heart, liver, kidney, and lungs of rats. *African Journal of Biotechnology*, **6**, 591-595.
- [156] Keshebo DL, Choudhury MK, Dekebo AH. (2014) Investigation on toxicity, hypoglycemic effect of the root barks of *Securidaca longepedunculata* Fresen (Polygalaceae) and determination of heavy metals in it. *Annals of Biological Research*, **5**, 15-19.
- [157] Dibwe D, Awale S, Kadota S, Morita H, Tezuka Y. (2013) Hepta-oxygenated xanthenes as anti-austerity agents from *Securidaca longepedunculata*. *Bioorganic & Medicinal Chemistry*, **21**, 7663-7668.
- [158] Dibwe D, Awale S, Kadota S, Tezuka Y. (2012) Muchimangins A-D: novel diphenylmethyl-substituted xanthenes from *Securidaca longepedunculata*. *Tetrahedron Letters*, **53**, 6186-6190.
- [159] Dibwe D, Awale S, Kadota S, Morita H, Tezuka Y. (2014) Muchimangins E and F: novel diphenylmethyl-substituted xanthenes from *Securidaca longepedunculata*. *Tetrahedron Letters*, **55**, 1916-1919.
- [160] Dibwe D, Awale S, Kadota S, Morita H, Tezuka Y. (2014) Muchimangins G-J, fully substituted xanthenes with a diphenylmethyl substituent, from *Securidaca longepedunculata*. *Journal of Natural Products*, **77**, 1241-1244.
- [161] Dibwe D, Awale S, Kadota S, Morita H, Tezuka Y. (2014) Two new diphenylmethyl-substituted xanthenes from *Securidaca longepedunculata*. *Natural Product Communications*, **9**, 655-657.
- [162] Mitaine-Offier A-C, Penez N, Miyamoto T, Delaude C, Mirjolet J-F, Duchamp O, Lacaille-Dubois M-A. (2009) Acylated triterpene saponins from the roots of *Securidaca longepedunculata*. *Phytochemistry*, **71**, 90-94.
- [163] Stevenson PC, Dayarathna TK, Belmain SR, Veitch NC. (2009) Bisdesmosidic saponins from *Securidaca longepedunculata* roots: evaluation of detergency and toxicity to coleopteran storage pests. *Journal of Agricultural and Food Chemistry*, **57**, 8860-8867.
- [164] Komane BM, Olivier EI, Viljoen AM. (2011) *Trichilia emetica* (Meliaceae)-A review of traditional uses, biological activities and phytochemistry. *Phytochemistry Letters*, **4**, 1-9.

- [165] Tchacondo T, Karou SD, Agban A, Bako M, Batawila K, Bawa ML, Gbeassor M, de Souza C. (2012) Medicinal plants use in central Togo (Africa) with an emphasis on the timing. *Pharmacognosy Research*, **4**, 92-103.
- [166] Hage S, Kienlen-Campard P, Octave J-N, Quetin-Leclercq J. (2010) *In vitro* screening on β -amyloid peptide production of plants used in traditional medicine for cognitive disorders. *Journal of Ethnopharmacology*, **131**, 585-591.
- [167] El Tahir A, Satti GM, Khalid SA. (1999) Antiplasmodial activity of selected Sudanese medicinal plants with emphasis on *Maytenus senegalensis* (Lam.) Exell. *Journal of Ethnopharmacology*, **64**, 227-233.
- [168] Beroa J, Ganfona H, Jonville M-C, Frédéric M, Gbaguidi F, DeMold P, Moudachirouc M, Quetin-Leclercq J. (2009) *In vitro* antiplasmodial activity of plants used in Benin in traditional medicine to treat malaria. *Journal of Ethnopharmacology*, **122**, 439-444.
- [169] Traore M, Zhai L, Chen M, Olsen CE, Odile N, Pierre GI, Bosco OJ, Robert GT, Christensen SB. (2007) Cytotoxic kurubasch aldehyde from *Trichilia emetica*. *Natural Product Research*, **21**, 13-17.
- [170] Germano MP, D'Angelo V, Sanogo R, Catania S, Alma R, De Pasquale R, Bisignano G. (2005) Hepatoprotective and antibacterial effects of extracts from *Trichilia emetica* Vahl. (Meliaceae). *Journal of Ethnopharmacology*, **96**, 227-232.
- [171] Germano MP, D'Angelo V, Biasini T, Sanogo R, De Pasquale R, Catania S. (2006) Evaluation of the antioxidant properties and bioavailability of free and bound phenolic acids from *Trichilia emetica* Vahl. *Journal of Ethnopharmacology*, **105**, 368-373.
- [172] Geyid A, Abebe D, Debella A, Makonnen Z, Abera F, Tekla F, Kebede T, Urga K, Yersaw K, Biza T, Bisrat Haile M, Mulugeta G. (2005) Screening of some medicinal plants of Ethiopia for their anti-microbial properties and chemical profiles. *Journal of Ethnopharmacology*, **97**, 421-427.
- [173] Sparg SG, van Staden J, Jager AK. (2000) Efficiency of traditionally used South African plants against schistosomiasis. *Journal of Ethnopharmacology*, **73**, 209-214.
- [174] Hoet S, Opperdoes F, Brun R, Adjakidje V, Quetin-Leclercq J. (2004) *In vitro* antitrypanosomal activity of ethnopharmacologically selected Beninese plants. *Journal of Ethnopharmacology*, **91**, 37-42.
- [175] Kamanzi AK, Schmid C, Brun R, Kone MW, Traore D. (2004) Antitrypanosomal and antiplasmodial activity of medicinal plants from Cote d'Ivoire. *Journal of Ethnopharmacology*, **90**, 221-227.
- [176] Sutovska M, Franova S, Priseznakova L, Nosalova G, Togola A, Diallo D, Paulsen BS, Capek P. (2009) Antitussive activity of polysaccharides isolated from the Malian medicinal plants. *International Journal of Biological Macromolecules*, **44**, 236-239.
- [177] Kolaczowski M, Kolaczowska A, Sroda K, Ramallete C, Michalak K, Mulhovo S, Ferreira MJU. (2010) Substrates and modulators of the multidrug transporter Cdr1p of *Candida albicans* in antifungal extracts of medicinal plants. *Mycoses*, **53**, 305-310.
- [178] Madureira AM, Ramallete C, Mulhovo S, Duarte A, Ferreira MJU. (2012) Antibacterial activity of some African medicinal plants used traditionally against infectious diseases. *Pharmaceutical Biology*, **50**, 481-489.
- [179] Konate K, Yomalan K, Sytar O, Zerbo P, Brestic M, Van Damme P, Gagniac P, Barro N. (2014) Free radicals scavenging capacity, antidiabetic and antihypertensive activities of flavonoid-rich fractions from leaves of *Trichilia emetica* and *Opilia amentacea* in an animal model of type 2 diabetes mellitus. *Evidence-Based Complementary and Alternative Medicine*, Article ID 867075, <http://dx.doi.org/10.1155/2014/867075>.
- [180] Sanogo R. (2001) Medicinal plants traditionally used in Mali for dysmenorrhea. *African journal of traditional, complementary, and alternative medicines: AJTCAM/African Networks on Ethnomedicines*, **8**, 90-96.
- [181] Gunatilaka AAL, Bolzani V, Dagne E, Hofmann GA, Johnson RK, McCabe FL, Mattern MR, Kingston DGI. (1998) Limonoids showing selective toxicity to DNA repair-deficient yeast and other constituents of *Trichilia emetica*. *Journal of Natural Products*, **61**, 179-184.
- [182] Diallo D, Paulsen BS, Liljebäck THA, Michaelsen TE. (2003) The Malian medicinal plant *Trichilia emetica*, studies on polysaccharides with complement fixing ability. *Journal of Ethnopharmacology*, **84**, 279-287.
- [183] Oryema C, Ziraba RB, Odyek O, Omagor N, Opio A. (2011) Phytochemical properties and toxicity to brine shrimp of medicinal plants in Erute county, Lira district, Uganda. *Journal of Medicinal Plants Research*, **5**, 5450-5457.
- [184] Komane, BM, Olivier, EI, Viljoen, AM. (2011) *Trichilia emetica* (Meliaceae)—A review of traditional uses, biological activities and phytochemistry. *Phytochemistry Letters*, **4**, 1-9.
- [185] Dal Piaz F, Malafronte N, Romano A, Gallotta D, Belisario MA, Bifulco G, Gualtieri MJ, Sanogo R, De Tommasi N, Pisano C. (2012) Structural characterization of tetranortriterpenes from *Pseudocedrela kotschyi* and *Trichilia emetica* and study of their activity towards the chaperone Hsp90. *Phytochemistry*, **75**, 78-89.
- [186] Malafronte N, Sanogo R, Vassallo A, De Tommasi N, Bifulco G, Dal Piaz F. (2013) Androstanes and pregnanes from *Trichilia emetica* ssp. *suberosa* J.J. de Wilde. *Phytochemistry*, **96**, 437-442.
- [187] Iboudo DP, Basilico N, Parapini S, Corbett Y, D'Alessandro S, Dell'Agli M, Coghi P, Karou SD, Sawadogo R, Gnoula C, Simpore J, Nikiema JB, Monti D, Bosisio E, Taramelli D. (2013) Antiplasmodial and anti-inflammatory activities of *Canthium henriquesianum* (K. Schum), a plant used in traditional medicine in Burkina Faso. *Journal of Ethnopharmacology*, **148**, 763-769.
- [188] Kaou AM, Mahiou-Leddé V, Hutter S, Aïnouddine S, Hassani S, Yahaya I, Azas N, Ollivier E. (2008) Antimalarial activity of crude extracts from nine African medicinal plants. *Journal of Ethnopharmacology*, **116**, 74-83.
- [189] Sy GY, Nongonierma RB, Sarr M, Cisse A, Faye B. (2004) Antidiabetic activity of the leaves of *Vernonia colorata* (Willd.) Drake (Compositae) in alloxan-induced diabetic rats. *Dakar Medicine*, **49**, 36-39.
- [190] IjehII, Obidoa O. (2010) Biochemical and histopathological changes in liver of albino rats fed diets incorporated with *Vernonia amygdalina* and *Vernonia colorata* leaves. *International Journal of Medicine and Medical Sciences*, **2**, 285-289.
- [191] Cioffi G, Sanogo R, Diallo D, Romussi G, De Tommasi N. (2004) New compounds from an extract of *Vernonia colorata* leaves with anti-inflammatory activity. *Journal of Natural Products*, **67**, 389-394.
- [192] Sy GY, Cissé A, Nongonierma RB, Sarr M, Mbodj NA, Faye B. (2005) Hypoglycaemic and antidiabetic activity of acetonic extract of *Vernonia colorata* leaves in normoglycaemic and alloxan-induced diabetic rats. *Journal of Ethnopharmacology*, **8**, 171-175.
- [193] Kelmanson JE, Jäger AK, van Staden J. (2000) Zulu medicinal plants with antibacterial activity. *Journal of Ethnopharmacology*, **69**, 241-246.
- [194] Guenne S, Ouattara N, Hilou A, Millogo JF, Nacoulma OG. (2011) Antioxidant, enzyme inhibition activities and polyphenol contents of three Asteraceae species used in Burkina Faso traditional medicine. *International Journal of Pharmacy and Pharmaceutical Sciences*, **3**, 524-528.
- [195] Adebayo O, Berkoh L, Asamoah E, Mills-Robertson FC. (2012) *In vitro* evaluation of aqueous and ethanolic extracts of *Vernonia colorata* as an antibacterial agent. *International Journal of Current Research and Review*, **4**, 21-27.
- [196] Adebayo OL, Akwasi GS, Confidence A. (2013) *In vitro* antibacterial potential of solvent fractions of aqueous and ethanolic leaf extracts of *Vernonia colorata* against selected human pathogenic bacteria. *International Journal of Research Ayurveda Pharmacy*, **4**, 865-868.
- [197] Rabe T, Mullholland D, van Staden J. (2002) Isolation and identification of antibacterial compounds from *Vernonia colorata* leaves. *Journal of Ethnopharmacology*, **80**, 91-94.
- [198] Chukwujekwu JC, Lategan CA, Smith PJ, van Heerden FR, van Staden J. (2009) Antiplasmodial and cytotoxic activity of isolated sesquiterpene lactones from the acetone leaf extract of *Vernonia colorata*. *South African Journal of Botany*, **75**, 176-179.
- [199] Senatore F, Formisano C, Sanogo R. (2004) Essential oil from aerial parts of *Vernonia colorata* Drake and *Vernonia nigriflora* Oliver et Hiern. (Asteraceae) growing wild in Mali. *Journal of Essential Oil Bearing Plants*, **7**, 267-274.