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Traditional uses, phytochemical and pharmacological profiles, and toxicity of *Enantia chlorantha* (Oliver): An overview

Olivier Tene Tcheghebe, Francis Ngouafong Tatong, Armel Jackson Seukep

ABSTRACT

This article aims to provide a comprehensive review on the traditional uses, phytochemical and pharmacological profiles as well as the toxicity of *Enantia chlorantha* (Oliver) We have examined most of the publications on this plant and focused our attention on the active metabolites of its extracts which support its traditional uses. *Enantia chlorantha* is reported to be used in folkloric medicine for the treatment of many diseases, such as malaria, aches, wounds, boils, vomiting, yellow bitter, fever, chills, sore, spleen in children, hepatitis, worms, intestinal spasms, sexual asthenia, jaundice, urinary tract infections, typhoid fever, leprosy spots, tuberculosis, gastric and duodenal ulcers. It can also serve as a haemostatic agent, and as an uterine stimulant. *Enantia chlorantha* stem bark has been scientifically studied for its several pharmacological activities. These include: antimalarial, antimicrobial and antibacterial, antioxidant, anti-*Helicobacter pylori*, anticonvusion and anti-inflammatory, analgesic and antipyretic, antiviral, gastro protective and enhancing male fertility. Some bioactive constituents such as saponins, flavonoids, alkaloids, phenols, reducing sugar and cardiac glycoside significantly present in the plant extracts, support its multiple properties and uses in traditional medicine. Moreover, it is demonstrated that this plant extract can be safely taken until a dose of 500 mg/kg body weight. We sincerely hope that we have provided a data base for proper evaluation of *Enantia chlorantha* extracts which could lead to the discovery of new and more effective drugs.

Keywords: *Enantia chlorantha*, Pharmacology, Toxicity

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INTRODUCTION

The African rainforest encompasses approximately 10 countries in west and central Africa, and is home to one of the greatest global diversity of fauna and flora in the world [1]. This flora comprises many plants of medicinal value among them, there is *Enantia chlorantha* Oliver (or *Annickia chlorantha*). Belonging to annonaceae

family, this plant is commonly known as African yellow wood and is also called Awopa, Osu pupa or Dokitaigbo (Yoruba), Osomolu (Ikale), Erumeru (Nigeria), Kakerim (Boki), Erenba-vbogo (Benin) [2], yellow moambi (English) and moambi jaune (French). It is an ornamental tree which may grow up to 30 m high with dense foliage and spreading crown [3]. The outer bark which is thin and dark brown is fissured geometrically, while the inner bark is brown above and pale cream beneath [4]. The stem is fluted and aromatic while the elliptic leaves are about 0.14–0.15 m long and 0.05–0.14 m broad [5]. The leaves display up to 20 pairs of prominent lateral vein and parallel secondary nerves. It is a dense forest tree found in the east and south forest of Cameroon, south part of Nigeria, Gabon, Angola and DRC. *Enantia chlorantha* is common in Cameroon and is a medicinal tree mostly used for the treatment of malaria and typhoid fever, but also used against other ailments of the human body. The bark, and in rare cases the leaves or the roots, are the main parts used for medicinal purposes.

Traditional uses

In the traditional medicine, this plant has been used for a long time in many parts of the African continent to treat various ailments of the human body. Many ethnobotanical studies support this. According to Tsabang et al. [6], a decoction of 500 g of stem bark in three liters of water for 20 min is used to treat malaria symptoms, aches, wounds, boils, vomiting, yellow bitter, fever, chills, sore, spleen in children and hepatitis (take 250 mL of this decoction orally, 3 times daily for 15 consecutives days), or make a decoction of a mixture of 300 g of stem bark of each of *Enantia chlorantha*, *Rauvolfia vomitaria* and *Fagara macrophylla* and /or Nauclea latifolia in four liters of water for 20 min (take 250 mL of this decoction orally, three times daily for 10 consecutives days). The stem bark decoction, taken orally, has also been reported to treat intestinal worms, intestinal spasms, malaria and sexual asthenia [7]. The same decoction is effective against hepatitis, jaundice, urinary tract infections and typhoid fever [8]. Root decoction is used for malaria, jaundice and as antipyretic [9]. Dried stem bark is used to treat malaria, hepatic disorders, tuberculosis and ulcers [10]. Gill and Akinwunmi noted the use of infusion of bark for the treatment of cough and wounds in Nigeria [11]. JL Vennerstrom [12] reported the use of the bark of this plant against malaria. In the southern forest zone of Cameroon, *Enantia chlorantha* is also used for the management of stomach problems, as well as for the treatment of jaundice, tuberculosis, urinary tract infections, malaria, hepatitis and some forms of ulcer. In the western Cameroon, a mixture of *Enantia chlorantha* bark, cut into small pieces, Citrus limonum fruit also cut into small pieces with its peels and Allium sativum bulb crushed is macerated in water for two days and the resulting liquid taken twice daily to cure malaria.

The stem bark of this plant has also been reported for treating leprosy spots, as hemostatic agent, and as uterine stimulant [13]. The bark of *Enantia chlorantha* has several medicinal properties and has been used by traditional medical practitioners in Nigeria for the treatment of skin, gastric and duodenal ulcers, and as an antimalarial [14]. The scientific classification of *Enantia chlorantha* is given in (Table 1).

Table 1: Scientific Classification

Kingdom: Plantae	Order: Magnoliales	Family: Annonaceae
Genus: *Enantia*	Species: *Chlorantha*	Scientific name: Enantia chlorantha Oliver
Stem bark images		

Reported phytoconstituents

Enantia chlorantha contains many bioactive compounds which justify its numerous medicinal virtues. Dawodu et al. conducted a study aimed at ascertaining the nutritive potential of this plant material and its solvent extracts potential, with the objectives to determine the proximate component and the phytochemical constituents of *Enantia chlorantha* stem bark in aqueous and ethanol extract [15]. The proximate analysis revealed a high content of crude fibre (72.25%) and a low ash content (2.48%) with other four compounds present (crude protein 10.78%, carbohydrate 6.29%, moisture 3.85% and crude fad 3.78%). Phytochemical screening showed the presence of saponins, flavonoids, alkaloids, phenols, reducing sugar and cardiac glycoside. Alkaloids (146.22%) quantitatively were revealed higher than the other constituents and flavonoids (7.63%) least. Gbadamosi et al. [16] found the same six active constituents in it proximate analysis and concluded that this plant bark can be used as food supplement in weaning food, due to its nutritive potential. The phytochemical active constituents have been said to be alkaloids-berberine, saponins and tannins. On a phytochemical analysis of aqueous and ethanol extracts of this plants stem bark, Adesokan et al. also showed the presence of phenolics, flavonoids, alkaloids, glycosides and saponins constituents [17].

Pharmacological activities

The research data indicate that *Enantia chlorantha* possesses enormous pharmacological values which

support its various traditional uses for the management of health problems. The following are most important.

Antimalarial activity

There are several reports on the antimalarial potential of *Enantia chlorantha*. Antimalaria activities of *Enantia chlorantha* and *Rauwolfia vomitoria* extracts were carried out by Agbaje et al. in rodent's malaria [18]. The antimalarial activities of the aqueous extracts of *Rauwolfia vomitoria* and *Enantia chlorantha*, employed separately and in combination in *Plasmodium berghei* infected male albino mice were investigated. Results showed that the prophylactic group, which received the extract prior to challenge with malaria parasite, recorded a suppression of infection compared with the control but no total protection was offered in all the case investigated. *Enantia chlorantha* extract like *Rauwolfia vomitoria* extract was found to be efficient against *Plasmodium berghei* as compared to the control group were they recorded deaths from day-7, but combination therapy produced a better result than either extract used alone. Another study of three plants traditionally used in the treatment of malaria in the south-eastern part of Nigeria was investigated by Ogbanna et al. to determine their efficacies as antimalarial compounds [19]. Ethanolic extracts from the roots of *Salacia nitida*, *Nauclea latifolia* and stem bark of *Enantia chlorantha* (Oliv.) were assessed for antimalarial activity against chloroquine sensitive *Plasmodium berghei* in mice using a 4-day suppressive test procedure. The extracts had intrinsic antimalarial properties that were dose dependent. The comparison analysis indicated that 250 mg/kg body weight of the root of *S. nitida* produced 71.15% suppression of parasitemia and the 500 mg/kg body weight of the stem bark of *E. chlorantha*, roots of *S. nitida*, *N. latifolia* and the three herbs combined, produced 75.23, 73.28, 71.15 and 77.46%, respectively, compared with chloroquine with 71.15% suppression. The results were significant at $p < 0.05$ when compared to a placebo and support the traditional use of these plants for the treatment of malaria. Two other studies, conducted by Kimbi et al. [20] and Vennrstrom et al. [20] respectively, also revealed the presence of two alkaloids [12] in this plant, possessing antimalarial properties.

Anticonvulsion and anti-inflammatory activity

Agbaje et al. investigated the effect of boiled and evaporated extracts of *Enantia chlorantha* in reversing bicucculine-induced convulsions and carrageenan-induced inflammation in rodents [21]. The results showed that, while the evaporated aqueous herbal drug increased the latency of convulsion in all the treated animals, the aqueous extract did not, behaving rather similar to the control mice given distilled water. *Enantia chlorantha* did not compare well with phenobarbitone (2.0–6.0 mg/kg) which protected all the animals from seizure. On the other hand, a dose dependent anti-inflammatory action of evaporated extract of *Enantia chlorantha* (50.0–250.0 mg/kg) in carrageenan induced inflammation was obtained showing a better efficacy than the boiled aqueous preparation and compared favorably with aspirin. *Enantia chlorantha* showed statistically significant activity at doses of 100 and 250 mg/kg, exhibiting 67% and 90% inhibition respectively post six hours induction of inflammation. No inhibition was observed in the control group. They concluded that *Enantia chlorantha*, especially the evaporated extract, exhibited significant anti-inflammatory effect on carrageenan-induced inflammatory edema in rats. They added that this effect is more gradual and more sustained than a similar effect of aspirin.

Antiviral activity

Taiye et al. [22] conducted a study designed to evaluate the antiviral effects of bark extract of *Enantia chlorantha* on yellow fever virus (YFV) in vitro, using Vero cell line, to determine the minimum tolerance dose of these plants extract on Vero cells, and to justify in this regard, the administration of this medicinal plant by the traditional practitioners. This study showed that aqueous extracts exhibit antiviral activities against yellow fever virus. *Enantia chlorantha* resulted in inhibition of YFV at MICs of 0.025 mg/mL. The result of the study revealed that the water extract of this plant showed significant antiviral activity. Based on this experimental evidence, the authors suggested that the extracts were considered effective against YFV as they completely inhibited the infectivity of YFV as evident in complete absence of cytopathic effects. These researchers added that, the broad-spectrum antiviral activity of the plant extracts is possible due to the identified alkaloids. Wafo et al. also noted the antiviral activity of extracts from dried stem bark of *Enantia chlorantha* [23].

Antioxidant activity

Olanlokun et al. [24] conducted a study in order to determine the in vitro antioxidant activity of the solvents (methanol, n-hexane, chloroform, ethyl acetate and water) extracted material from stem bark of *Enantia chlorantha*, using models of DPPH(2,2-diphenyl-1-picrylhydrazyl) radical scavenging activity, nitric oxide scavenging property, ferric reducing property (FRAP) and hydroxyl radical scavenging property. Methanol extract revealed the highest flavonoids and phenolic contents followed by aqueous, ethyl acetate, chloroform, n-hexane respectively. As the phenolic and flavonoid contents rose, free radical scavenging potential of the extracts was high. From this result, we can suggest that this plant's antioxidant property justify its uses in the traditional medicine for the management of malaria, cough and wounds which are all stress related diseases.

Antimicrobial and antibacterial activity

Nyong et al. [25] conducted a research work aimed to determine the in vitro and in vivo antimicrobial activity of an ointment formulated with a purified alkaloid isolated from *Enantia chlorantha*, on rats infected with fungi. The result showed the effectiveness of this ointment against *Trichophyton tonsurans* and *Candida glabrata*, while *Trichophyton interdigitali* and *Candida albicans* was less sensitive. 50 mg/mL ointment had even a better percentage inhibition than Tioconazole cream 1%, used as reference drug. They concluded that the alkaloid fraction of *Enantia chlorantha* stem bark as well as the formulated ointment exhibited significant in vitro and in vivo antifungal activities against different species of candida, dermatophytes and plants fungi. Another study conducted by Atukpawu and Ozoh [26] on antimicrobial effects of *Enantia chlorantha* extracts revealed that, the ethanolic one showed antimicrobial activity on all the seven isolates tested (*Staphylococcus aureus*, *Escherichia coli*, *Salmonella typhi*, *Enterococcus faecalis*, *Shigella sonnei*, *Proteus vulgaris* and *Candida albicans*), with zones of inhibition in the range of 5 mm to 33 mm, and a minimum inhibitory concentration (MIC) between 1.56 and 12.5 mg/mL. The antibacterial activity of aqueous extracts of *Enantia chlorantha* stem bark was also investigated by Adesokan et al. [27]. The zones of inhibition on bacterial isolates (*Staphylococcus aureus* and *Bacillus* substilis, *Escherichia coli*, *Salmonella typhymurium* and *Pseudomonas aeruginosa*) were proportional to the concentration of the plant extract. Gram-positive bacteria were more sensitive to the extract than gram-negative one. They suggested that the identified alkaloid might be responsible of the antibacterial activities. Atata et al. [28] and Moody et al. [29] had also noted the antibacterial activity of this plant extracts. Palmatine chloride and jatrorrhizine chloride have also been identified as the major antimicrobial constituent of the plant extracts [29].

Anti-helicobacter pylori activity

Tan et al. [30] studied the in vitro and in vivo anti-Helicobacter/Campylobacter activity of aqueous extract of *Enantia chlorantha* stem bark. The in vitro activity was dose-dependent, and they recorded the same antimicrobial parameters (MAQ = 0.63 mg; MIC = 0.39 mg/mL; MBC = 1.56 mg/mL; ET (100) = 8 h) for both *H. pylori* and *C. jejuni or C. coli*. Antral mucus sample cultures from mice treated with *Enantia chlorantha* extract (500 and 1000 mg/kg for three days) did not yield any growth. The results finally revealed that, apart from its in vitro effects, *Enantia chlorantha* aqueous extract also possesses in vivo antibiotic activity against *H. pylori*.

Analgesic and antipyretic activity

Aqueous extract of the bark of *Enantia chlorantha* administered intraperitoneally into healthy adult albino mice at doses of 1.0 and 5.0 g/kg resulted in elevation of pain threshold. *Enantia chlorantha* extract was about 20 times less potent than morphine, a reference drug. However, a dose of 15.0 g/kg given orally to rabbits infected with Klebsiella sp was capable to relieve the pyrogenic induced fever whereas no such effect was mentioned in the control group that was given simple water [4].

Gastroprotective activity

Siminialayi and Agbaje conducted a scientific study to determine the gastroprotective effects of *Enantia chlorantha* against induced- gastric ulcers in rats [14]. First of all gastric ulcers were induced by administering 1 ml of absolute ethanol and 30 mg/kg of indomethacin, separately to two groups of rats. On the other side, two other groups of rats were pretreated with the ethanol extract (300 mg/kg) of *Enantia chlorantha* 30 minutes before the ulcerogenic agents. After this, the ulcer indices were compared. The results showed that rats pretreated with extract before the administration of the ulcerogenic agents were well protected. The inhibition effect of extract against ethanol-induced ulcers was most effective than indomethacin-induced ulcers. These researchers suggested that the extract acts particularly as a cytoprotective agent, but also by inhibiting the secretion of gastric acid.

Enhance male fertility

Oyewopo et al. conducted a work aimed at evaluating the effect of aqueous extract of stem bark of *Enantia chlorantha* on the sperm parameters and the histoarchitecture of the testicles of rats [31]. Some of this rats (Group 1, 2 and 3) were successively treated with lead (IV) oxide and *Enantia chlorantha* extract, while negative control rats (group 4) received lead IV only. Testicles histoarchitecture showed the spermatogonia as well as the spermatids and spermatocytes that were quite obvious in the rats treated with extract as compared with those of group 4. The interstitial spaces were abnormally widened and the leydig cells were destroyed in group 4 rats. The sperm quality (sperm count, mobility, viability and progressivity) of group 1, 2 and 3 rats were very good, while those of rats in group 4 were weak. They finally suggested that in addition to enhance fertility, this plant's extract can play a protective and a regenerative role against destroying agents when used as prophylactic. Salman et al. [32] also showed that the extract of *Enantia chlorantha* significantly increases sperm mobility and viability in a dose-dependent manner, but they did not notice any important increase in the sperm accounts. Following the results obtained in these studies, we can say that, low doses of this plant extracts could improve sperm quality, hence male fertility.

Reported toxicity

Enantia chlorantha is widely used in herbal medicine for the treatment of several ailments of the human body. However, its toxicity profiles are not well documented [33]. Like other therapeutic agents, *Enantia chlorantha* may not be devoid of side effects or toxicity in both human and animal's studies [34]. In order to verify this, Olamide et al. conducted a study [35]. Ethanolic extract of stem bark from this plant was then administered to rats and some parameters (body weight changes, biochemical and hematological parameters as well as histology of vital organs like heart, kidneys and liver) measured. The results showed that the therapeutic application of the extract of *Enantia chlorantha* was quite safe at doses below 1000 mg/kg body weight. The obtained results suggest that oral application of *Enantia chlorantha* may not produce severe toxic effects at doses lower than 500 mg extract/kg body weight. Tan et al. conducted a similar study aimed to evaluate the acute and sub-acute toxicity profiles of the aqueous stem bark extract of *Enantia chlorantha* using mice and rats [35]. The results showed that, the extract of *Enantia chlorantha* is not toxic in acute intake up to 5000 mg/kg, but can cause lungs, hepatic and kidneys disorders following medium to long-term use at doses greater than 500 mg/kg. Given the wide ethno pharmacological applications of *Enantia chlorantha*, the present toxicity results constitute safety information that can be used in obtaining regulatory approval for its commercialization [31].

CONCLUSION

It is well known, nowadays, that more than 80% of the world population depends on traditional system of health care, mostly in the rural area. Whole plants or their individual parts can be used for the treatment of various disorders of the human body. It is quite evident from this study that *Enantia chlorantha* possesses a number of phytoconstituents which justify it traditional uses for the management of various ailments, and prove its pharmacological activities. More interesting yet, it has been reported that its extracts can be safely taken to cure diseases till doses as greater as 500 mg/kg.

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Author Contributions

Olivier Tene Tcheghebe – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Francis Ngouafong Tatong – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Armel Jackson Seukep – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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