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Phytochemical and Pharmacological Properties of *Opilia amentacea* Roxb (Previously *Opilia celtidifolia* (Opiliaceae) Guill. Perr.): A Review

Ollo Youl [1,2,*], Gérard Josias Yaméogo [2,5], Ernest N. Sombié [1], Sibidou Yougbaré[3], Rainatou Boly [4], Adama Hilou [1], Maminata Traoré/Coulibaly [3]

1 Laboratoire de Biochimie et de Chimie Appliquée (LABIOCA) / Université de Ouagadougou, 09 BP 24 Ouagadougou 09, Burkina Faso; hiloudio@gmail.com (A.H.); ernestsombie@yahoo.fr (S.N.E.);
2 Agence Nationale pour la Sécurité Sanitaire de l'Environnement, de l'Alimentation, du Travail et des Produits de Santé (ANSSEAT), 03 BP 848 Ouagadougou 03, Burkina Faso; youl.ollo@yahoo.com;
3 Institut de Recherche en Sciences de la Santé (IRSS-CNRST), Unité de Recherche Clinique de Nanoro, Burkina Faso; ysibidou@gmail.com (S.Y) ; traore_maminata@yahoo.fr (M.T.C.);
4 Institut de Recherche en Sciences de la Santé, MEPHATRA-PH, 03 BP 7192 Ouagadougou 03, Burkina Faso; rainatoub@gmail.com (R.B.);
5 Laboratoire du Développement du Médicament (LADME), Centre de Formation de Recherche et d'Expertises en Sciences du Médicament (CEA-CFOREM), Université Joseph KI-ZERBO, 03 BP 7021 Ouaga, Burkina Faso; josiasbyg@yahoo.fr (G.J.Y);
* Correspondence: youl.ollo@yahoo.com;

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Abstract: The genus Opilia (*Opiliaceae*) includes only two species: amentacea and campestris. Opilia amentacea Roxb. (*O. amentacea*), also called Opilia celtidifolia Guill. & Perr) is a West African woody climber plant, a heavily-branched shrub or tree up to 10 m. *O. amentacea* grows in fringing forests and savannah, often on anthills. It is widespread from Senegal to Nigeria and dispersed over the drier parts of tropical Africa. The plant is commonly used in traditional medicine to treat dermatoses, malaria, wounds, abdominal pain, internal worms, jaundice, headaches, and fever. Many phytochemical and pharmacological investigations have already been done on the Opilia genus. Opilia species were found to have anti-inflammatory, antimicrobial, antioxidant, wound healing, and anticancer activities. This review summarizes previous chemical and pharmacological studies conducted on Opilia amentacea.

Keywords: Opilia amentacea; phytochemistry; pharmacological properties; review.

1. Introduction

Opiliaceae are a pantropical family of the Santalales with approximately 36 species [1]. All species of *Opiliaceae* are root parasites, and the family has a pantropical distribution in Africa, Asia, and Australia, with only one genus in the neotropics [1–3].

The genus *Opilia* (*Opiliaceae*) contains two species, amentacea and campestris. *Opilia amentacea* Roxb. (*O. amentacea*) or *Opilia celtidifolia* Guill. & Perr grows in scrub and savannah, often on anthills [3]. It is widespread from Senegal to Nigeria and scattered throughout the drier parts of tropical Africa [4,5].

O. amentacea is well known for its traditional uses and through ethnobotanical, chemical, and pharmacological studies. From ethnopharmacological surveys, it appears that *O. amentacea* is commonly used by West African traditional healers to cure a wide variety of

ailments such as malaria, dermatitis, lack of appetite, constipation, abdominal pains, intestinal worms, and many other diseases [6,7]. Phytochemical analyses of *O. amentacea* extracts revealed the presence of saponosides, coumarins, steroids, tannins, polyphenols, flavonoids, alkaloids, and active polysaccharides, which prove its many uses [7–10]. In addition, various extracts and fractions of the plant have demonstrated biological activities that include hypotensive and coronary blood flow depressant effects, antispasmodic, antiparasitic (*Taenia pisiformis* and *Toxoscaris leonani* in dogs), and uterine stimulation effects. The polysaccharides from Leaf have been shown to possess healing properties, including protection of the gastric mucosa activation of several immune system components (complement, macrophages, B and T lymphocytes). [4,5,9,11–13]. For an overview of *O. amentacea*, this narrative review aims to summarize the results of ethnopharmacological investigations, chemical constituents, and pharmacological effects of this medicinal plant.

2. Materials and Methods

Google Scholar, PubMed, Science Direct, and Scopus were used to retrieve publications related to the study with key terms including *Opilia amentacea*, ethnobotanical use, phytochemical compounds, anti-inflammatory, antioxidant, antimicrobial activities, and toxicity.

3. Results and Discussion

The search results in a list of fifteen publications on the ethnobotanical use of *O. amentacea*, twenty papers on the phytochemical studies on *O. amentacea*, twenty-three studies treating the biological activity of *O. amentacea* including antimicrobial, antiparasitic, antioxidant, anti-inflammatory, hepatoprotective, heart and circulatory and abortificient effects and only, three publications referred to side effects and toxicity.

3.1. Botanical description of Opilia celtidifolia (Guill. & Perr.).

3.1.1. Taxonomic classification.

Kingdom: *Plantae*
Subkingdom: *Eukaryotes*
Phylum: *Tracheophyta*
Subphylum: *Angiosperms*
Class: *Magnoliopsida*
Order: *Santalales*
Family: *Opiliaceae*
Genus: *Opilia*
Species: *Opilia amentacae* Roxb
Synonyms: *Opilia celtidifolia* (Guill. & Perr.) Endl. ex Walp.
Local name: ***Dioula***: *Nembossi* ; ***Moore***: *Waagsalga* ; ***Senoufo***: *kagbogo, kamugi* ; ***Bobo-fing:*** *nyèso*

3.1.2. Description.

The family *Opiliaceae* in *Santalales* is divided into four tribes (*Agonandreae, Anthoboleae, Champereieae,* and *Opilieae*) according to the latest classification, comprising 12 genera and 38 species [3]. The life forms of this family include trees, shrubs, and lianas;

some species occur in evergreen primary or secondary forests, while others are found in a more seasonal climate [14].

Members of *Opiliaceae* are usually monoecious with bisexual flowers, although some dioecious variants have been reported with unisexual flowers. The ovary is superior with a single locule that bears one ovule, developing into a drupe [1]. Flowers are small, fragrant, or odorless, aggregated in inflorescence in axillary clusters, panicles, spikes, or umbels. Fertile flowers hermaphrodite, or functionally male, or functionally female. Fruits look like drupes with large seeds [15].

O. amentacea is a liana reaching 8-10 m high or a sarmentose shrub of 2- 4 m with a short and twisted stem. The branches are flexible and drooping. The plant is widespread in the region from Senegal to Nigeria (West Africa) and scattered in the dry part of tropical Africa like Burkina Faso [16].

3.2. Medicinal uses.

The plant is commonly used in traditional medicine, and all parts (Whole plant, roots, stem barks, leaves, and fruits) are concerned. Ethnobotanical surveys of the literature clearly demonstrate that the leaves and roots of *O. amentacea* are the main treatment traditional healers in West Africa recommended for dermatoses, malaria, wounds, abdominal pain, internal worms, headaches, and fever [4,6]. The root powder is indicated for constipation, jaundice, liver cirrhosis, and anorexia. The root decoction has purgative and diuretic properties. A decoction of leaves and roots is employed in treating edema, leprosy, and meningitis [17]. It is also used in traditional medicine as a healer of wounds and ulcers [9,13]. In Mali, the leaves are used against jaundice [18] and hepatitis [19].

In Benin, the stem barks of *O. amentacea* are a traditional remedy commonly used to treat hepatitis B and C [20].

In Kenya, the charred roots mixed with crushed snake teeth are used as an antivenom when applied to the bite site [21].

In Burkina Faso, *O. amentacea* is used in the west of the country to treat malaria and in the center for skin diseases. The designation "waagsalga" (makes the skin smooth) refers to skin conditions in the local Moore language [22,23]. The decoction of *O. amentacea* leaves mixed with *Combretum fragrance* is taken as a bath and drink for treating severe malaria by traditional practitioners in Niangologo [24].

The fruits of *O. amentacea* are used mystically against cattle theft or to prevent their loss. The leaves are used as a fishing poison [15].

3.3. Chemical constituents.

A preliminary screening performed on the methanolic stem bark extract of *O. amentacea* revealed many sterols and saponin products and, more or less, the presence of alkaloids [25]. Therefore, the liquid-liquid fractionation allowed the isolation of fraction F1 composed of four saponins with Rt of 0.85 (G_1), 0.60 (G_2), 0.42 (G_3), and 0.24 (G_4), whose identification was performed by thin layer chromatography. Three polar saponins (GI-G3) were isolated in pure form. The sugar part of all isolated saponins consists of arabinose and mannose, while the aglycone content differs between saponins. G_1 and G_3 were identified as oleanolic acid, while the aglycone composition of G_2 was found to be hederagenin [25].

Druet *et al*. (1986) also identified several triterpene aglycones from an acid hydrolyzate of glycosides extracted from the root bark of *O. amentacea* [26,27].

The analysis of the chemical structure of these aglycones allowed the identification of major compounds such as oleanolic acid hederagenin and pentacyclic triterpenes, including apigenin as minor compounds; 3β-acetoxy-28α, 20β-ursanolide, glycogenic acid, 3β-acetoxygypsogenic acid [27] and a new triterpene with a chemical structure close to 3P-hydroxy lupane were identified.

Crespin *et al*. 1993 have isolated, by liquid chromatography coupled with a UV detector, six triterpene saponins, namely 3-O-[α-L-rhamnopyranosyl-(1→3)-β-D-glucopyranosyl-(1→2)-β-D-glucuronopyranosyl]-28-O-β-D-glucopyranosyl-oleanate **(1)**, 3-O-[α-L-rhamnopyranosyl-(1→3)-β-D-glucuronopyranosyl]-28-O-β-D-glucopyranosyl-oleanate **(2),** 3-O-[α-L-rhamnopyranosyl-(1→3)-β-D-glucuronopyranosyl]-28-O-β-D-glucopyranosyl-hederagenin (**3**), 3-O-α-L-rhamnopyranosyl-(1→3)-β-D-glucuronopyranosyl-oleanate **(4),** 3-O-β-D-glucuronopyranosyl-28-O-β-D-glucopyranosyl-oleanate **(5)** 3-O-[α-L-rhamnopyranosyl-(1→3)-β-D-xylopyranosyl-(1→2)-β-D-glucuronopyranosyl]-28-O-β-D-glucopyranosyl-oleanate (**6**) in the leaves and stems hydromethanolic extracts of the plant, collected in Burkina Faso and Ivory Coast [28].

Saponosides, cardiotonic heterosides, sterols and triterpenes, coumarins, reducing compounds, oses, holosides, and mucilages were significantly found in the leaves [29].

Another study revealed the presence of saponosides, oses, and coumarins in the leaves of the aqueous extract of *O. amentacea* [9]. Chemical groups such as tannins, flavonoids, alkaloids, carotenoids, anthracenosides, reducing compounds, cardiotonic heterosides, cyanogenetic heterosides, anthocyanins, and leucoanthocyanins were not detected [9].

The studies carried out by Sangaré (2003) on *O. amentacea* showed the presence of saponosides, cardiotonic heterosides, sterols and triterpenes, coumarins, reducing compounds, oses and holosides and mucilages in the leaves. In *O. amentacea* stem bark, saponosides, tannins, cardiotonic heterosides, sterols and triterpenes, coumarins, reducing compounds, oses and holosides, mucilages and anthocyanins have been characterized [8].

The carbohydrate composition of the leaves of *O. amentacea* was particularly studied for its biological properties.

Polysaccharides isolated from aqueous extracts of the leaves by gel filtration and anion exchange chromatography gave fractions Oc50A1 and Oc50A2 [4,5,12].

Arabinose (26.7 and 13.2%), galactose (31.5 and 28%), and galacturonic acid (5.3 and 7.8%) were the monosaccharides found in Oc50A1 and Oc50A2, respectively. The Yariv test confirmed the presence of arabinogalactan type II in both fractions [5].

Gel filtration on Sephacryl S-400 of fraction Oc50A1 gave two purr fractions (Oc50A1.I and Oc50A1.II), which were further purified on a Superdex 200 column. In minor amounts, the polysaccharides identified were heavily branched type II arabinogalactans and rhamnogalacturonan I regions.

The arabinogalactan type II consists of galactose as both β-D-(1→3)-galactose and β-D-(1→6)-galactose units as the main core with β-D-(1→3,6)-galactose as branching points [4].

Šutovská *et al*. (2009) have also reported that the water- and ethanol-soluble polysaccharides isolated from the leaves of *O. amentacea* contained residues of galactose (~32%) and arabinose (~27%). In the same study, low rhamnose and GalA residues content indicates the presence of an arabinogalactan (~60%) and a rhamnogalacturonan (~14%) or

their complex. In addition, the presence of partially methylated glucuronoxylans (~14%) and a relatively high glucose content were revealed [11].

A phytochemical screening of the aqueous extract of the leafy stems of the plant, carried out in Benin, revealed the presence of flavonoids (flavones), reducing compounds, anthocyanins, leucoanthocyanins, saponosides, triterpenoids and mucilages [30]. The total polyphenols and flavonoids were quantified at 89.712 mg GAE/g extract and 37.040 mg QAE/g extract, respectively [30].

Elsewhere, in Mali, from two studies of phytochemistry, the decoction of leaves *of O. amentacea* was found to contain saponosides, flavonoids, saccharides and mucilage holosides, sterols and triterpenes, leucoanthocyanins and cardiotonic glycosides[31]. The aqueous extracts of the leafy stem of *O. amentacea* from Togo were reported to contain abundant saponosides, tannins in minor proportion, alkaloids, and flavonoids [32].

The richness of the plant in anthocyanins, leucoanthocyanins, saponosides, triterpenes, steroids, mucilages, coumarins, and reducing compounds [10] has been confirmed from a Beninese species.

The chloroform extract of leaves of *O. amentacea* from Nigeria showed the presence of alkaloids, phlobitannins, terpenoids, and anthraquinones [7,33].

Phytochemical screening conducted by Bhuvaneswari *et al*. [34] using organic and aqueous leaf extracts of Indian species found almost all chemical groups, namely tannins, saponins, flavonoids, catechins and sugar in ethanol extract; however, the acetone extract tested negative for all phytochemical groups while the water extract tested positive for tannins, saponins, flavonoids, and catechins.

Quantitative evaluation of total alkaloids gave a content of 43.30 ± 0.4 mg/100g [7,33]. A bioguided fractionation of the mixture of ethyl acetate and dichloromethane extracts of *O. amentacea* [35] led to the isolation of a pure fraction identified as (E)-7-octadecen-9-ynoic), an acetylenic fatty acid [35]. The quantitative evaluation demonstrated that the ethyl acetate fraction of the leaves of *O. amentacea* exhibited the highest polyphenol content (62.01 ±0.62 milligrams of gallic acid equivalent per gram (mg GAE/g)) in comparison to the leafy stems (53.23±0.18 mg GAE/g) and roots (39.45±0.01 mg GAE/g). Similarly, the total flavonoid content of the ethyl acetate fraction of the leaves, leafy stems, and roots was found to be 28.32 ± 0.01, 23.62 ± 0.68, and 5.31 ± 0.54 mg-rutin equivalent per gram (mg RE/g), respectively[36].

Elsewhere, the fruit polysaccharides of the plant (OAFP) were estimated to be 864 ± 1 mg glucose equivalent/g of sugar content in the pre-digested OAFP. The gastric digested sample (880 ± 1 mg glucose equivalents/g of the sample) revealed a higher sugar content than *the* pancreatic (101 ± 2 mg glucose equivalents/g of the sample) and pre-digested sample [37].

3.4. Pharmacological effects.

During the study period, several studies investigated the biological activities of *O. amentacea*, which has antimicrobial, antioxidant, anti-inflammatory, hepatoprotective, antitussive, and anti-diabetic effects etc.

3.4.1. Antimicrobial effects.

3.4.1.1. Antibacterial and antifungal activity.

Three studies based on the antimicrobial activity of *O. amentacea* were reviewed. The crude chloroform extract of the leaves of *O. amentacea* was screened against a panel of Gram-positive and Gram-negative bacteria. *Escherichia coli* (*E. coli*) was susceptible to the extract with a minimal inhibitory concentration (MIC) = 78 µg/mL. The MIC on *Bacillus Cereus* and *Pseudomonas aeruginosa* (*P. Aeruginosa*) was around to 156 µg/mL. A very weak antibacterial activity was obtained against *Staphylococcus* (MIC= 625 µg/mL), while *Staphylococcus epidermidis* (*S. epidermidis*) and *Serratia marcescens* were particularly not susceptible to the extract [7,33].

The pectic polysaccharides of Oc50A1.I.A induced protective activity against *S. pneumoniae* serotype 6B infection in mice. Pectins did not show direct antibacterial effects on *S. pneumonia*; however, they produced a range of cytokines and chemokines, ensuring protection against the bacteria [12].

The aqueous and organic extracts (96° ethanol, 80° hydro-ethanol, n-hexane) of *O. amentacea* leaves, stems, and root barks were tested on American-type culture collection (ATCC) reference strains. The results exhibited a range of inhibitory effects on bacterial growth. The inhibitory effects were variable depending on the part of the plant and the type of extract. Ethanolic extracts (96° and 80°) of the root barks with MICs ranging from 30 to 240 µg/mL were more active on Gram-positive cocci such as *Streptococcus pyogenes* and *Streptococcus agalactiae*. Aqueous extracts of the leaves and stem barks were more active on *S. aureus* with inhibition zone diameters of 10.33 and 13.67 mm, respectively [38].

In another study, the antimicrobial activity of dichloromethane fractions (FDFe, FDET, and FDER) derived from ethanolic extracts was found to exhibit the highest inhibitory effect against Gram-positive cocci (*S. aureus; S. pyogenes S. agalactiae*), with inhibition diameters ranging from 12 to 15 mm on a standardized inoculum (10^8 CFU/mL) by the disc diffusion method and MIC values of 0.96 to 4.64 mg/mL.

The same study revealed that both the hexane fractions of leaves (FHFe) and root barks (FHER) demonstrated notable antifungal efficacy against *Candida tropicalis* at minimum inhibitory concentrations (MIC) of 0.23 mg/mL and 0.43 mg/mL, respectively [39].

Antibacterial potency of the ethanolic extract of the leaves of the plant on diarrheal pathogens, *Escherichia coli* ATCC 25922, *Salmonella typhimurium*, and *Shigella dysenteriae* has also been reported in India [34]. At 0.2 mg/mL, the extract inhibited the growth of *Escherichia coli* and *Shigella dysenteriae* (respectively 5 and 6 mm in diameter of the zone of inhibition). *S.typhi* was inhibited at 0.15 mg/ml.

Moses Owolabi *et al*. during their study showed the antifungal activity of the chloroform extract of the leaves of *O. amentacea* on *Botrytis cinerea (B. Cinerea)* and *Aspergillus niger* (*A. Niger)* with MIC of 156 µg/mL and 1250 µg/mL, respectively [7].

4.2.1.2. Antiparasitic effects.

The F1 saponin fraction of the methanolic extract of *O. amentacea* has been tested for its *in vitro* anthelmintic effect on canine intestinal worms (*Tacnia pisiformis* and *Toxascaris leonina*). The fraction produced stimulated the motility of these parasites, as it has antispasmodic action on the intestinal muscles. *Toxascaris leonina* is stimulated only slightly

at high doses (bath of 100 and 150 mg/50 mL), whereas *Taenia pisiformis* is easily stimulated at all the doses tested (50-150 mg/50 mL bath) [25]. Methanolic, aqueous, and dichloromethane extracts of leaves of *O. amentacea* have also been tested for their antimalarial properties. Methanolic and aqueous extracts of the aerial parts of the plant displayed weak antiplasmodial activity *in vitro* against clinical strains of *Plasmodium falciparum* [32]. The chemical characterization of the extracts revealed that the major components are the saponins, which are much better known as tensioactive than antimalarial agents.

Sangaré, who investigated medicinal plants used in the management of malaria by traditional healers in Mali, reported different effects depending on the type of extract.

Elsewhere, the dichloromethane extract of the leaves of *O. amentacea* effectively inhibited 50% of chloroquine-resistant *P. falciparum* strains with an IC50 of 4.01 µg/mL in vitro assay compared to the control chloroquine (IC_{50} of 0.05 µg/mL) [8,40].

Aqueous and dichloromethane macerates and the decoctate after digesting *O. amentacea* stem bark inhibited the growth of chloroquine-resistant *Plasmodium falciparum* strains with an IC_{50} of 6.60, 7.64, and 9.07 µg/mL respectively. Eight other extracts showed moderate antiplasmodial activity with an IC50 greater than 10 µg/mL; these were: ethanolic extracts of leaves (IC_{50} = 10.92 µg/mL) and stem barks (IC_{50} = 11.16 µg/mL), aqueous macerated of leaves (IC_{50} = 11. 01 µg/mL), methanolic extracts of stem barks and leaves (IC50 =13. 38 µg/mL and 14.23 µg/mL, respectively), digested leaves and stem barks (IC_{50} = 12.28 µg/mL and 13.46 µg/mL respectively) and the decocted after digesting leaves (IC_{50} = 15.09 µg/mL) [8].

A study in Guinea has also demonstrated the moderate antiplasmodial activity *in vitro* (IC50 = 12.7 µg/mL) [41] of the dichloromethane extract of the stem barks of *O. amentacea.*

The antiplasmodial effect of ethyl acetate and dichloromethane extracts of the root bark of the plant has been studied in Burkina Faso [35]. The two extracts showed a moderate effect against *P. falciparum* (IC50 =11µg/ml), while the ((E)-7-octadecen-9-ynoic) isolated from these extracts had a very weak activity on the parasite (IC_{50} >100 µg/mL [35].

Sanon *et al.* also reported good antiplasmodial activity (IC_{50} =2.8µg/mL) of the dichloromethane extract of the leaves of *O. amentacea* on a chloroquine-resistant strain of *P. falciparum* K1. The crude alkaloid extract showed moderate antiplasmodial activity on the same strain (IC_{50} = 6.9µg/mL) [42].

Secondary metabolites such as terpenoids, alkaloids, and phenolic compounds are known to be responsible for the antiparasitic properties of plants. The most illustrative of alkaloid is quinine, isolated from the genus Cinchona [43,44]. Artemisin, a sesquiterpene compound, is a highly successful new antiplasmodial drug [45,46]. The presence of these chemical groups in *O. amentacea* may justify its biological and pharmacological effects.

3.4.2. Antioxidant activity.

The antioxidant activity of the flavonoid-rich fractions of the extracts of *O. amentacea* was studied using different essays. The fraction showed antioxidant capacity with an IC_{50} of 70 µg/mL with the β-carotene-linoleate test, 10 µg/mL with DPPH radical scavenging assay, 25 µg/mL with chelation of iron (II) assay, and 55 µg/mL with lipid peroxidation assay [47]. However, the fraction could not chelate ferrous ions compared to the control [47].

Konaté *et al*. [36] investigated antioxidant activities of the bioactive ethyl acetate fraction of the leaves, leafy stems, and roots from *O. amentacea* using three separated methods, namely hydroxyl radical scavenging assay, hydrogen peroxide scavenging assay, and

phosphomolybdate assay for the total antioxidant capacity of the fraction. The hydroxyl radical scavenging activity was determined by measuring the rate of inhibition of the degradation of deoxyribose by the free radicals generated by the Fenton reaction. The ethyl acetate fraction of leaves showed an IC_{50} (0.35±0.96 mg/mL) similar to that of quercetin (0.30±0.01 mg/mL) with the hydroxyl radical scavenging assay. The IC_{50} was 0.17±0.01 mg/mL with the hydrogen peroxide scavenging assay. The IC_{50} values of fractions from the leafy stems and roots were 0.33±0.48 and 0.37±0.54 mg/mL in hydroxyl radical scavenging assay, and 0.36±0.01 mg/mL and 0.50±0.01 mg/mL with the hydrogen peroxide scavenging assay, respectively [36].

The total antioxidant capacity assessed by the phosphomolybdenum method gave interesting antioxidant activity: leaves fractions (47,12±0.01 mg GAE/g), leafy stems fraction (42, 23±0.02 mg GAE/g) and roots fraction (23, 33±0.03 mg GAE/g).

In vitro evaluation of the antioxidant activity of aqueous leaf extracts in Benin, using the DPPH test, revealed a free radical scavenging activity with an IC_{50} value of 0.29 mg/ml [30].

Recently, Boly *et al*. [48] reported weak radical scavenging and lipid peroxidation inhibitory effects of *O. amentacea* leaves decoction. In contrast, the macerate of the same part showed a high ability (664.90 ± 0.71 mol Ascorbic Acid Equivalent/g dry extract) to reduce the ferric ions.

In vitro antioxidant performance of *O. amentacea* fruit polysaccharides (OAFP) was evaluated by DPPH, ABTS+, FRAP, phosphomolybdenum, and superoxide reduction radical scavenging methods [37].

The pre-digested OAFP efficiently inhibited DPPH-radical (IC_{50} = 100.95 ± 1.20 µg/mL). However, samples digested in the stomach (IC_{50}=150.12 ± 3.71 µg/mL) and pancreas (IC_{50} = 196.52 ± 2.10 µg/mL) showed reduced activity compared to the previous ones.

In $ABTS^+$ radical scavenging activity, pre-digested OAFP showed remarkable scavenging activity (3.28 ± 0.21 mmol Trolox equivalent/g sample). OAFP digested in the stomach and pancreas showed significantly lower ABTS (2, 2′-Azino-bis (3-ethylbenzthiazoline-6-sulfonic acid) scavenging activity (2.01 ± 0.52 and 1.05 ± 0.16 mmol Trolox equivalent/g sample) respectively.

With the iron-reducing assay, pre-digested OAFPs showed greater reduction of 2,4,6-Tri(2-pyridyl)-s-triazine iron 3^+ (TPTZ- Fe (III)) complex to TPTZ- Fe (II) (3.21 ± 0.10 mmoL Fe (II) E/g than digested gastric and pancreatic OAFPs (2.20 ± 0.42 and 0.72 ± 0.29 mmoL Fe (II) E/g. Pre-digested OAFP revealed better total antioxidant activity (287.58 mg ascorbic acid equivalents/g sample) with the phophomolybdenum reduction assay. Gastric and pancreatic digested OAFP (130.56 and 86.21 mg ascorbic acid equivalents/g sample) exhibited lower total antioxidant activity [37].

Antioxidant activities of ethanol 70% extract of the leaves of *O. amentacea* and six fractions (A1-A6) characterized by liquid chromatography were investigated using DPPH scavenging radical assay, and their anti-tyrosinase effects evaluated according to *in vitro* mushroom tyrosinase assay [49].

Compounds **1-11** include two news flavonol tetraglycosides, namely isorhamnetin-3-O-α-L-rhamnopyranosyl-(1→6)-β-D-galactopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→6)-β-D-glucopyranoside (**1**) and isorhamnetin-3-O-α-L-rhamnopyranosyl-(1→6)-β-D-galactopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→6)-β-D-galactopyranoside (**2**) isolated from fraction A3 were also evaluated for their antioxidant capacity.

The ethanol 70% extract exhibited a moderate to low scavenging effect on DPPH radicals (IC_{50}=250 µg/mL) and fungal tyrosinase inhibitory activity (IC_{50} = 509 µg/mL).

A3 revealed moderate DPPH scavenging (IC_{50} = 200 µg/mL) and fungal tyrosinase inhibitory activities (IC_{50} =326 µg/mL) [49].

Only compounds **10** (5,5-dimethoxylariciresinol-4-O-β-D-glucopyranoside) and **11** (eleutheroside E1) exhibited significant tyrosinase inhibitory effect (IC_{50} = 42.1 µM and 28 µM, respectively), compared to the reference kojic acid (IC_{50} = 45.98 µM). Compounds **10** and **11** shown also good inhibitory effect on DPPH assay (IC_{50} = 85.1 µM and 42.1 µM respectively), compared to ascorbic acid (IC_{50} = 56.8 µM) [49].

3.4.3. Anti-inflammatory effects.

Several extracts from the plant have shown significant anti-inflammatory activities. The ethyl acetate fraction from the leaves at 300 µg/mL showed significant anti-inflammatory activity with 80.18% protection of Human Red Blood Cell (HRBC) in hypotonic solution compared to standard diclofenac, which showed 81.45% protection. HRBC protection by other fractions were 79.03±1.00% for the leafty stems fraction and 62.01±0.00% for the roots fraction. The RBC stabilization implies that the extract may as well stabilize lysosomal membranes and then could limit the inflammatory response by preventing the release of lysosomal constituents from activated neutrophils, including bactericidal enzymes and proteases [36]. In addition, the three fractions (ethyl acetate fraction of leaves, leafy stems, and roots) effectively inhibited the heat-induced hemolysis (73.61±1.00, 66.61±0.00% and 61.90±0.58% respectively) at 300 µg/mL. The ethyl acetate fraction also displayed proteinase inhibitory activity, and the best inhibition was observed at 300µg/mL (67.45%).

However, experiments have shown that the ethyl acetate fractions of leaves, leafy stems, and roots of *O. amentacea* at 300 µg/mL have good activity on the inhibition of soy 15-lipoxygenase enzyme (81.35 ±1.65 µg/mL, 79.15±0.31 and 80.6 ±0.31 µg/mL), respectively [36].

Another anti-inflammatory study using carrageenan-induced mouse paw edema showed that the decoction leaf extracts of the plant significantly reduced the mouse paw's thickness at 600 mg/kg bw [48].

3.4.4. Hepatoprotective activity.

The plant has also been shown to have hepatoprotective activity. The aqueous extracts of the leaves of *O. amentacea* were tested against ethanol-induced liver injury in rats at 100, 200, and 400 mg/kg bw [50]. The extracts at 200 and 400 mg/kg bw showed pronounced hepatoprotective effects by decreasing the levels of aspartate aminotransferase (ASAT), alanine aminotransferase (ALAT), alkaline phosphatase (ALP), bilirubin, triglycerides, and total cholesterol compared to the negative control.

The water extract has also been shown to prevent histopathological changes in the liver, kidneys, and lungs due to ethanol toxicity [50].

At 200 and 400 mg/kg, the water extract from the leaves inhibited hepatocellular injury, expressed by a significant decrease in ALAT and ASAT levels. The extract also significantly reduced bilirubin levels at 100, 200, and 400 mg/kg bw ALP at 400 mg/kg; that could be a clinical indication of the inhibition of cholestasis. It also lowered total cholesterol and

triglyceride levels in rats at 400 mg/kg. The administration of the extract restored serum total protein levels around the normal values after the decrease observed in negative controls.

At 200 mg/kg, *O. amentacea* water extract from the leaves protects hepatocytes from the toxic effects of ethanol efficiently.

3.4.5. Abortificient effect.

The antispasmodic effect of the saponin fraction of stem bark methanolic extracts from *O. amentacea* was evaluated on several smooth muscles using the glass Jar bath apparatus of a 50 mL capacity organ bath [25].

The results indicated stimulation of the uterine musculature and inhibition of intestine musculature. In addition, no fraction stimulation was observed on the muscles of the pregnant woman' uterus at a 40 mg/50 mL bath, and slight stimulation was observed at a 100 mg/50mL bath [25].

The effect of a saponin-rich fraction was studied on blood pressure and respiratory movements *in vivo* in anesthetized Mongrel dogs with a body weight between 10 and 20 kg using a kymograph and a sphygmograph [25]. The fraction was also administrated via an intravenous route in an isolated rabbit's heart. At 20 mg/kg, there was an increase in respiratory rate and a drop in blood pressure, which started to increase slightly after 30 minutes but did not reach its normal level; no effect on renal circulation was observed.

A dose of 2 mg/rabbit's heart did not affect heart rate and coronary circulation. Effective doses (5 to 25 mg) induced inhibition of the amplitude and frequency of cardiac contractions followed by relaxation; these doses showed a severe reduction in coronary outflow [25].

3.4.6. Anti-diabetic and hypolipidemic effects.

The anti-diabetic effect was studied on *in vitro* gastrointestinal digestion of free radicals, α-glucosidase, and α-amylase inhibitory activities of OAFP [37]. OAFP effectively inhibited the enzymatic activity of α-glucosidase and α-amylase, key enzymes in the transformation of polysaccharides into glucose that the body can absorb

OAFP effectively inhibited the enzymatic activity of α-glucosidase and α-amylase, key enzymes in the transformation of polysaccharides into glucose that the body can absorb. The α-glucosidase inhibition of pre-digested, gastric-digested, and pancreatic-digested OAFP was 65%, 70%, and 45%, respectively, at 50µg/mL, while the α-amylase activity gave 69%, 72%, and 49%, respectively at the same concentration. The α-glucosidase repressive activity of pregastric and gastric digested OAFP was comparable to the acarbose inhibitory activity (80%). More interesting, the pre-digested OAFP revealed a non-competitive inhibition of α-glucosidase enzyme because the Michaelis constant (Km) remains the same (22.8 and 21.2 mM) and subordinates Vmax (4.8 and 3.6 mM/min) at 0.050 and 0.100 mg/mL than the control group. Furthermore, at 0.050 mg/mL, the gastric and pancreatic digested samples were non-competitively inhibited α-glucosidase with Km=23, 23.1mM and Vmax = to 5.1, 4.2 mM/min correspondingly. Likewise, the OAFP non-competitively inhibited α-amylase. A Km = 26 mM and a Vmax = 4.9 mM/min at 0.050 mg/mL OAFP were obtained with the pre-digested sample [37].

Another study has shown that the flavonoid-rich fractions of *O. amentacea* have inhibitory properties on a key enzyme linked to type 2 diabetes, such as α-amylase and α – glucosidase. In the amylase assay, the positive control acarbose showed an IC_{50} of 5.70 µg/mL,

and flavonoid-rich fractions exerted an IC_{50} of 6.12 µg/mL for amylase inhibitory activity comparatively to the amylase inhibition assay by quantitative starch hydrolysis where flavonoid-rich fractions exerted an IC_{50} of 6.23 for glucose inhibition activity ($p < 0.001$). The flavonoid-rich fraction showed an IC_{50} of 4.70 µg/mL on the glucose inhibitory activity and an IC_{50} of 4.61 µg/mL on glucosidase enzyme inhibition.

The flavonoid-rich fraction of *O. amentacea* also had significant hypoglycaemic and hypolipidaemic activities *in vitro* in alloxan-induced diabetic mice. The extract normalizes the concentration of glucose, cholesterol, and triglycerides. Oral administrations of flavonoid-rich fractions from *O. amentacea* at 300 mg/kg of body weight decreased serum glucose level from 186.1 ± 2.10 to 146.6 ± 2.71 mg/dL ($p < 0.0001$ versus diabetic control) for single-day administration and from 203.2 ± 2.04 to 118.7 ± 1.51 mg/dL after 7 days ($p < 0.0001$ versus diabetic control) for subacute study. In addition, a dose-dependent effect of flavonoid-rich fractions on cholesterol and total lipids was observed. In this order, oral administration of flavonoid-rich fractions of *O. amentacea* at 500 mg/kg for 28 days returned serum lipid levels (triglycerides, total cholesterol, and phospholipids) to near normal levels in diabetic rats and another re-administration of flavonoids for a period of 28 days restored levels. Total cholesterol, triglycerides, and phospholipids in hepatic tissue of diabetic rats decreased from 60.17 ± 2.31, 2.17 ± 0.32, and 10.01 ± 0.33, respectively, to 53.01 ± 1.10, 1.71 ± 1.10, and 9.02 ± 0.1 after treatment with bioactive fractions [47].

3.4.7. Antitussive activity.

Water and ethanol-soluble polysaccharides isolated from the leaves of *O. amentacea* were tested on citric acid-induced cough reflex and airway smooth muscle reactivity *in vivo* in guinea pigs. The results showed that oral administration of *O. amentacea* polysaccharide significantly decreased the number of cough reflexes in guinea pigs. Indeed, oral administration of polysaccharides from *O. amentacea* at 50 mg/kg body weight resulted in a reduction in the number of citric acid-induced coughing efforts. A significant reduction in the number of coughing efforts was observed 1h after the administration of polysaccharides was tested, and their effects were comparable to those of narcotic codeine. The highest reduction in the number of coughing efforts by the polysaccharides was observed after 5 h and is still comparable to that of the narcotic codeine. The antitussive effect of *O. amentacea* polysaccharides was accompanied by a bronchodilator property by the induction of a decrease in specific airway resistance [11].

3.4.8. Anti-convulsant activity.

The decoction of leafy stems of *O. amentacea* has been studied for its anticonvulsant potency. Oral administration of the extract in a pharmacological model of epilepsy induced by intraperitoneal (IP) injection of pilocarpine in Wistar rats demonstrated that the extract was able to delay the onset of convulsions significantly. The same extract, at the same dose, significantly reduced the intensity of the convulsions, thus protecting the rats from a death precipitated by the violence of the convulsions [30].

3.4.9. Antiulcer effects and wound healing properties.

Crude and depleted decoctions from leaves of *O. amentacea* have been tested *in vivo* in rats for their healing and antiulcer properties [9,31].

Oral administration of depleted decocted extract at 100 mg/kg induced 75% protection of gastric mucosa against ethanol-induced ulceration versus 31% protection for crude decocted extract at the same dose (100 mg/kg).

O. amentacea is also known for its healing properties. According to a study carried out in Mali, 10% of ointments based on the polysaccharide fractions FI, FII (arabinogalactans and rhamnogalacturonan's type), and crude aqueous extracts of the leaves of *O. amentacea*, showed healing activity on superficial incision- type wounds (16 cm^2) induced on the depilated skin of rabbits. The polysaccharide fraction FII induced complete healing in 12 days and was the most effective compared to the other extracts (17 days for FII and 20 days for the crude extract) [31].

3.4.10. Anticancer effects.

The anticancer properties of methanolic and chloroform extracts have been evaluated in vitro on cancer cell lines. The methanolic extract of the plant showed moderate cytotoxic activity on HeLa and A431 cells (50-75% cell proliferation at the 100 µg/mL) [51].

The chloroform leaf extract of *O. amentacea* showed selective *in vitro* cytotoxicity to Hep-G2 cells (IC50 = 24.7 µg/mL) [7].

Sanon *et al*., after evaluating the antiplasmodial effect of extracts of *O. amentacea*, reported the risk of cytotoxicity to Human hepatoma cells ATCC # HB-8065 (HepG2) [42]. High cytotoxicity has been recorded with water-methanol extracts from *O. amentacea* leaves (SI: 0.4), whereas low cytotoxicity was recorded with dichloromethane, methanol, aqueous and alkaloid extracts with a SI ranging from 3.1 to 17.4.

3.4.11. Immunomodulatory effect.

The Oc50A1 and Oc50A2 polysaccharide fractions isolated from leaves of *O. amentacea* were evaluated for their immunomodulatory effect using inhibition of sheep red blood cell hemolysis SRBC) and measurement of nitric oxide released from stimulated macrophage cell line R2 [5].

The polysaccharide fractions isolated from the leaves of *O. amentacea* demonstrated a strong human complement-fixing activity and a dose-dependent induction of nitric oxide release by macrophages. The concentration of fractions giving 50% of hemolysis (ICH_{50}) were 0.5 and 0.9 µg/mL, respectively, in the complement fixation test, and they induced the release of 7.2 and 7.3 µM of nitrite oxide of macrophages, respectively, at 100 µg/mL.

3.4.12. Appetizing properties.

O. amentacea appears to be a plant that stimulates appetite and weight gain. The decoction of the plant tested in rats stimulated appetite, inducing weight gain [29]. Moreover, at high doses (> 100 mg/kg), the extract induces a decrease in the enzyme Alanine aminotransferase (ALAT), leading to a reduction in blood glucose level and, therefore, could have an effect on diabetes[18].

3.4.13. Side effects and toxicity.

Few references mention the toxicity of the plant extracts. The acute toxicity of water-acetone extracts of *O. amentacea* was evaluated *in vivo* on mice, and the lethal dose *(*LD50) was 636.2 mg/kg body weight. Signs of reversible toxicity were also observed during the 14-day acute toxicity test, and the extract was found to be moderately toxic [47]. The acute toxicity

of water-acetone extracts of *O. amentacea* was evaluated *in vivo* in mice, and the lethal dose (LD50) was 636.2 mg/kg body weight.

In Benin, another study demonstrated the non-toxicity of the decoction of leafy stems of *O. amentacea* on *Artemia salina* shrimp larvae (IC_{50} > 0.1 mg/mL) [30].

A study conducted in Mali revealed that the ethanolic extract of the leaves of *Opilia amentacea* did not show significant toxic effects on the liver, kidneys, and blood tissues when administered at a dose of 2000 mg/kg body weight [52]. Similarly, administration of the extract at the same dose to Wistar rats did not result in significant alterations after 14 days of observation. No mortality, only a general state of sleep was observed in the animals of the control and treated groups; biochemical parameters, including transaminase (AST, ALT), bilirubin (free and conjugated), alkaline phosphatases, uric acid, urea, and creatinine, demonstrated no statistically significant difference ($p > 0.05$) between the two groups. Similarly, hematological parameters showed a non-statistical difference ($p>0.05$) between the two groups of animals [52].

A similar result was recorded in Burkina, where the decoction of *O. amentacea* leaves demonstrated low acute toxicity with a lethal dose estimated to be higher than 2000 mg/kg bw [48].

4. Conclusions

This review provides an overview of previous scientific work on the plant. *O. amentacea* is well-known in traditional medicine in Africa and elsewhere. It is a species with many medical virtues and which, through scientific studies, has proven to be antimicrobial, anticonvulsant, healing, appetite stimulant, and immune. The plant has also been shown to have selective toxicity on liver cancer cells. Ointments have been offered from Mali for the treatment of wounds. These multiple biological properties make it a plant of medical interest, requiring further exploration for its better valorization.

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Conflicts of Interest

The authors declare no conflict of interest.

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