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Review Article

The phytochemical and pharmacological actions of *Entada africana* Guill. & Perr.

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ABSTRACT

Entada africana (*Ea*, Asteraceae) has been widely used traditionally to treat different ailments, as food, insecticides, source of gums, in some small carpentry works. Studies on the pharmacognostic characterization, nutritional, elemental and physicochemical contents has been reported. *In vivo* and *in vitro* studies on the plant validated some ethnomedicinal claims of the use of the plant as an anti-inflammatory, analgesic, antibacterial, antioxidant, anti-viral, anti-angiogenic, cytotoxic agents among others. Triterpenes, saponins, flavonoids and sugars were reported as bioactive constituents which might be responsible for the aforementioned pharmacological actions of the plant.

However, more researches are required in order to isolate bioactive compounds from the different parts of *Ea* and evaluate their effects on different ailments.

1. Introduction

Entada africana Guill. & Perr. (*Ea*) is a small tree which is mostly found in tropical and subtropical regions (Nielsen, 1992). It is commonly known as "*Tawatsa*" in Hausa Language, "*Ogurobe*" in Yoruba (Burkill, 1995). It can be used as food, medicine and fibre. Extensive literature search revealed the paucity of researches on the different parts of the plant. However, no review was conducted on the phytochemical, toxicological and pharmacological properties of *Ea*. This review will therefore focus not only on the phytochemistry and pharmacological properties of *Ea* but also on botanical aspects of the plant, its scientific applications and translational research.

2. Main text

2.1. Botanical description

The genus Entada (Leguminosae; Mimosoideae) comprises of about 30 species of lianas and scandent shrubs or subshrubs (Diniz, 1991; Nielsen, 1992). Plants in the leguminosae family have characteristic leaves and pods that help identify them as legumes and many species in the Mimosoideae and Caesalpinoideae subfamilies (Table 1) provide valuable dyes, tannins, resins, gums, insecticides, medicines and fibres (Allen and Allen, 1982).

2.1.1. Morphology

The plant *Ea* belongs to the family Fabaceae which is popularly known as Legumes and it is the third largest order of seed-plants containing about 600 genera with 12000 species (Sharma and Kumar, 2013). It is a small tree that grows up to 4–10 m in height and 90 cm in girth and it has branches low down with a crown (Figs. 1 and 2). The bark of the plant is brown-grey to black with a very rough, transversely stripped, scaly, with a peeling in long fibrous strips which has a red or yellow-brown slash fibrous. They have 3–9 pairs of bioinnate and alternate leaves with about 8–24 pairs of leaflets with a 15–45 cm glabrous common stalk and rachis of 25–30 cm long with 2–9 pairs of pinnae (Fig. 2); they also have 2–3 × 0.5–1.5 cm leaflets which has an elongated elliptic and rounded apex and occasionally minutely notched, with the base asymmetrical and the lower edge is more rounded than the upper. The flowers of the plant are creamy-white or reddish yellow and are about 6 mm long; they are also slightly scented and densely clustered in a spike-like racemes 5–15 cm long including the short central stalk in small cluster in the leaf axills or arranged in panicles at the end of shoots. The fruit (Fig. 1) is a pod (15 cm) and it is very persistent which is untidily hanged down for many months and it breaks up on the tree eventually; it is very flat and fragile with slightly curved seeds with thick wavy margins and are usually reddish-brown on the outside. The fruit has segments on the dry interior part of the pod, which contains about

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Table 1
Fabaceae subfamilies and their estimated number of species.

Subfamily	Estimated number of species
Mimosoideae	550
Caesalpinoideae	650
Papilionoideae	7000
Total	8200

Source: (Allen and Allen, 1982)

Fig. 1. Pods of *Entada africana* in its natural habitat (Photograph by Macro Schmidt). Source: www.westafricanplants.senckenberg.de.

Fig. 2. *E. africana* branch with leaves (Photograph by Adjima Thiombiano). Source: www.westafricanplants.senckenberg.de.

10–15 broad elliptic flat seeds about 12 mm long; when broken, the outer coat of each segment of the pod peels off and the straw-coloured inner coat remain attached to the seed which in turn act as a wig (Orwa et al., 2009).

2.1.2. Biology and ecology

Ea grows in high rainfall savannah areas; thus in Nigeria, the flowers of the plant tend to grow or appear with new fresh leaves from the month of February–April; the trees are mostly found in Sudan zone, southern Sahel, in Burkina Faso, Senegal, Cameroon, Uganda, Republic of Congo, Nigeria and Zaire. It is mostly found on ground water sites especially on lower slopes or banks of swamps and it is very sensitive to bush fires (Sornay, 1916; Orwa et al., 2009).

Scientific classification

Kingdom:	Plantae
Phylum:	Tracheophyta
Class:	Magnoliopsida
Order:	Fabales
Family:	Fabaceae
Subfamily:	Mimosoideae
Genus:	Entada
Species:	*Entada africana*

Source: (Roskov et al., 2019)

Common names

Arabic:	Dorot
Hausa:	Tawatsa
Yoruba:	Ogurobe
Nupe:	Locigaga
Gwari:	Bwadaraye

2.2. Uses

2.2.1. Ethnomedicinal uses

Ea is used as decoction to cure malaria fever, dysentery and stomach ache and it has been used as tonic. The plant antidote has effects against various toxic agents due to its emetic properties (Orwa et al., 2009); the plant is used in northern part of Nigeria to treat snakebite victims [Personal Communication].

The stem bark of *Ea* is said to have abortive effects and the root decoction is used as a stimulating agent (Orwa et al., 2009). Healing and fever-reducing beverages are prepared from the leaves, stem bark, roots and shoots of the plant and in northern Nigeria and northern part of Ghana, an infusion of the leaves or stem bark is used as tonic and in the treatment of stomach ache; the leaves constitutes a good wound dressing effect and it also prevents suppuration (Keay, 1989; Orwa et al., 2009). The stem bark and roots have been reportedly used to treat chronic wounds and female infertility. *Ea* is also used in traditional medicine to treat respiratory track disorders (Occhiuto et al., 1999). In Burkina Faso, it is used to treat diabetes, hypertension and diarrheoa (Nacoulma-Ouedraogo, 1996). The leaves of the plant is commonly known for their pharmacological properties including haemostatic, antiseptic on wounds, sore and skin infections; it is also used as an emetic which is administrated in case of food poisoning, it has also been used as tonic, stomachic, as an abortificient, antipyretic and for rheumatism (Berhaut, 1975; Burkill, 1995). The leaves also has piscicidal property (Kerharo and Adam, 1974).

In Senegal, decoctions from the roots and trunk bark of *Ea* is used as an anti-poison remedy while the macerated stem bark is used to treat bronchitis and cough (Kerharo and Adam, 1974). In addition, the roots of the plant are known for their fortifier, diuretic, anti-gonococci and anti-syphilitic action (Oliver-Bever, 1986; Tibiri et al., 2007a). In African traditional medicine, *Ea* is used for the treatment of dysentery, cataract, wound healing, stomach ache, fever and liver related diseases (Owona et al., 2013a). In Mali, the plant is used to treat different ailment such as fever (malaria), inflammation (hepato-protective and wound healing) (Maiga et al., 2005). A decoction of the root and bark is also used to wash wounds while that of the root alone is used in the treatment of hepatitis.

The juice of the fresh root or bark is used for its hemostatic properties. In Guinea-Bissau, the roots are used for the treatment of wounds while the seeds are used to treat wounds, sores, skin-eruptions, rheumatism, cataract, fevers and dysentery as reported by Orwa et al. (2009).

In West and Central Africa, *Ea* is used to treat liver diseases (Borris et al., 2014). Northern region of the Republic of Benin used medicinal plants such as *Ea* to treat patients with pain-associated diseases like musculoskeletal disorders (Codo-Toafode et al., 2017). A cold infusion of the *Ea* root has been similarly utilized as a lotion for sore eyes (Watt and Breyer-Brandwijk, 1962). The species has been widely used for treating fevers (including malaria), infectious disorders (cough, cold, tuberculosis); herpes infections, diabetes, candidiasis, gonorrhea, diarrhea and hepatitis (Mbatchou et al., 2011). Other traditional uses of *Ea* include; healing potential, arthritis, rheumatism, pulmonary troubles, stomach ache, emetics, diarrhea, dysentery, cutaneous and subcutaneous parasitic infection, venereal diseases, fabrifuges, paralysis, epilepsy, convulsions spasm among others (Burkill, 1985; Diallo et al., 2001).

2.2.2. Other uses

The bark of *Ea* contains fibre which is used mainly in making ropes, bands, storage bins among others and it is also a source of tannins, which have been shown to possess antiseptic, astringent, haemostatic and anti-parasitic properties and thus, this may partly explain the basis for the use of the gum for wound-dressing on sores and psoriasis; the leaf of the plant serve as a source of food such as sauces, condiments, spices and flavorings (Burkill, 1985). A low quality gum is obtained from the tree and the bark contains low level of rotenone, which has been reportedly use as insecticide, and it is effective against a range of horticultural pests such as aphids, caterpillars and external body parasites like tick, lice, fleas and flies. It has also been reported to be ineffective against bedbugs, cockroaches, scale insects and red spiders. The rotenone can be widely found in various parts of the plant, however, it is found in abundance, in the root bark. The wood is soft and very easy to work with which is why it found application in small carpentry and the tree yields gum with different content depending on the origin; reports revealed that it may consist of 10 % tragacanth and 90 % water-soluble polymers of the Arabic type (Oliver-Bever, 1986; Von Maydell, 1986; Keay, 1989; Orwa et al., 2009).

2.3. Pharmacognostic characterization

Microcopy of the whole leaf of *Ea* revealed wavy and straight walled epidermal cells, and the presence of hypostomatic paracytic stomata with an arch-shaped collaterally closed vascular bundle, collenchyma, sclerenchyma and palisade cells was reported. Microscopy of the powdered samples also revealed prismatic calcium oxalate crystals with stone cells, fibres, pitted and scalar form xylem vessels (Baidoo et al., 2018).

2.4. Nutritional, elemental and physicochemical contents

Nutritional composition of the seeds of *Ea* revealed 39.81 % of the crude protein content and the content of dry matter was 80.00 %; other contents reported include, crude fibre (15.50 %), ether extract (17.50 %), metabolized energy (4.88 kcal/kg), acid detergent fibre (39.00 %) and neutral detergent fibre (53.00 %) (Belewu et al., 2008).

Mineral analysis of the seeds revealed the presence of calcium (7.66 %), sodium (0.20 %), magnesium (45.42 %), potassium (44.92 %), iron (0.17 %) (Belewu et al., 2008).

The leaves has moisture content of 4.2 % and ash content of 13.3 %. It also has an adequate crude lipid of 10 %, the content of crude fibre and crude protein were 18.56 and 14.60 %, respectively while the carbohydrate value was 38.44 % (Olanrewaju and Ahmed, 2014).

Physicochemical parameters such as the moisture content, ash content, mineral content, solvent soluble extractives and pH of edible extracts were also reported by Baidoo et al. (2018).

2.5. Phytochemical constituents

Hassan et al. (2018) conducted preliminary phytochemical investigation on the *n*-hexane, ethylacetate (EtOAc) and methanol (MeOH) stem bark extracts of *Ea* and the results revealed that the *n*-hexane extract contained steroids/triterpenes and cardiac glycosides while the EtOAc and MeOH extracts contained tannins, flavonoids, steroids/triterpenes, carbohydrates, saponins and cardiac glycosides. The aforementioned extracts were obtained using successive extraction by maceration.

Similar phytochemical screening of the leaf and stem bark extract of *Ea* revealed the presence of glycosides, saponins, tannins, flavonoids, coumarins, triterpenes and sterols (Baidoo et al., 2018).

Qualitative phytochemical analysis conducted on the acetone and MeOH stem bark extracts of *Ea* obtained via successive maceration revealed total polyphenol and flavonoids contents of (0.528 ± 0.02 and 0.650 ± 0.09) and (0.500 ± 0.02 and 0.253 ± 0.00), respectively (Kwaji et al., 2017).

Of the five fractions of the stem bark of *Ea* including methylene chloride (F0), methylene chloride-MeOH (95/5: v/v) (F5), methylene chloride-MeOH (90/10: v/v) (F10), methylene chloride-MeOH (75/25: v/v) (F25) and MeOH (F100), F10, F25 and F100 were found to have the highest polyphenol content which ranges from 29.013 ± 0.714–41.372 ± 0.201 mgCAE/g of extract (Njayou et al., 2015). Phytochemical screening of the five fractions above revealed the presence of sterols, terpenes, polyphenols, flavonoids, sugars and saponins (Njayou et al., 2015).

Another study by Njayou et al. (2013) reported similar phytochemicals using *n*-hexane, methylenechloride-MeOH mixture and distilled water extracts obtained from sohxlet apparatus. The *n*-hexane extract revealed the presence of only steroids/triterpenes while methylenechloride-MeOH and water extracts contained similar constituents such as reducing sugars, flavonoids, polyphenols, tannins and leucoanthocyanins.

Qualitative phytochemical studies conducted on the seeds of the plant revealed high concentration of saponins and condensed tannins while the quantitative analysis indicated 6.00 and 0.17 % of saponins and tannins, respectively (Belewu et al., 2008).

Qualitative phytochemical content of the different solvents extracts of the stem bark of *Ea* obtained via maceration method have been adequately documented (Mbatchou et al., 2011). The ethanol extract revealed the presence of alkaloids, amino acids, anthraquinones, cardiac glycosides, saponins, tannins, steroids and triterpenes; diethyl ether fraction contained alkaloids, amino acids, anthraquinones, flavonoids, glycosides, saponins, tannins, steroids and triterpenes; chloroform fraction revealed the presence of cardiac glycosides, flavonoids, glycosides, tannins, steroids and triterpenes and lastly the methanol soluble and insoluble portions contained constituents including, alkaloids, amino acids, anthraquinones, cardiac glycosides, flavonoids, glycosides, saponins, steroids and triterpenes (Mbatchou et al., 2011).

Similarly, a study using *n*-hexane, MeOH and aqueous leaf extracts of *Ea* was conducted (Olanrewaju and Ahmed, 2014); carbohydrates, alkaloids, tannins, steroids, saponins, glycosides, cardiac glycosides and resins were found in the *n*-hexane extract; and all the aforementioned constituents were also found in the methanol extract except cardiac glycosides, resins and terpenoids while the aqueous extract contained only alkaloids, steroids, saponins and terpenoids (Olanrewaju and Ahmed, 2014).

Ifemeje et al. (2014) indicated that the ethanol stem bark extract of *Ea* obtained from maceration method contained tannins, alkaloids, anthraquinones, terpenes, sterols, phenols, resins and saponins.

Another study reported by Tibiri et al. (2007b) determined the phenolic content of *Ea* leaf and bark; different solvent extracts including MeOH, chloroform, EtOAc and residual aqueous fractions. Total phenolic content of the bark and leaf of the plant are summarized as crude MeOH extracts (4.91 and 4.09 μg/mL), chloroform (5.18 and 9.60 μg/mL), EtOAc (6.55 and 9.64 μg/mL) and water (10.44 and 10.49 μg/mL) fractions, respectively. Non-tannic phenolics (4.33 and 6.47 μg/mL) for the crude MeOH extract, chloroform (1.43 and 1.95 μg/mL), EtOAc (2.60 and 8.33 μg/mL), water (2.13 and 3.05 μg/mL) fractions, respectively. Non-flavonoidic phenolics for crude MeOH extracts were (0.87 and 1.37 μg/mL),

chloroform (1.64 and 1.39 μg/mL), EtOAc (3.95 and 6.25 μg/mL) and water (1.27 and 2.18 μg/mL) fractions, respectively (Tibiri et al., 2007b).

The differences observed in the phytochemical constituents might be due the use of different extraction methods, solvents, part of the plant used, location or environment (geographical, regional and seasonal variations), ecology and harvest conditions of the plant.

2.6. Bioactive constituents

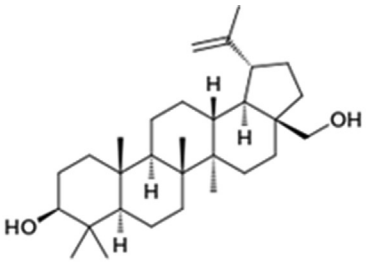
The main bioactive constituents of *Ea* (so far isolated) that contributes to its biological/pharmacological properties are triterpenes, saponins, flavonoids, sugars.

2.6.1. Triterpenes and saponins

Ea have been reported to contain high percentage of triterpenes; Betulin (1) was isolated from the dichloromethane soluble portion of the stem bark of the plant (Kwaji et al., 2018). Nine new triterpenes saponins (2–3) were isolated form the roots of *E. africana* (Cioffi et al., 2006).

2.6.2. Flavonoids

Bioactivity-guided fractionation of the antigiogenic principles of the chloroform/MeOH extract of the roots of *Ea* yielded two flavonoids; apigenin (4) and robinetin (5) as the active constituents (Maria et al., 2014). Naringenin-7-*O*-glucoside (6) was also isolated from the MeOH leaf extract of *Ea* (Marquardt et al., 2017). Three myricetin-derived



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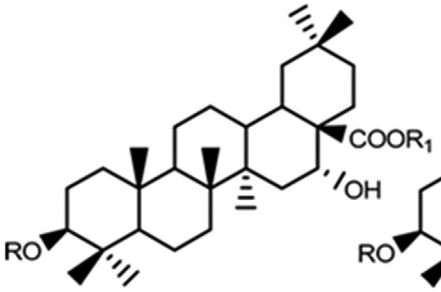

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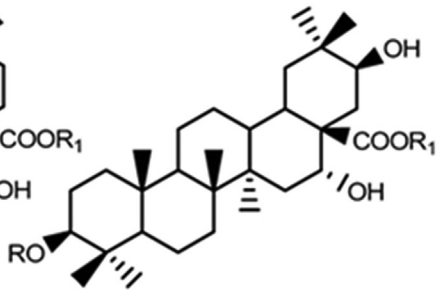

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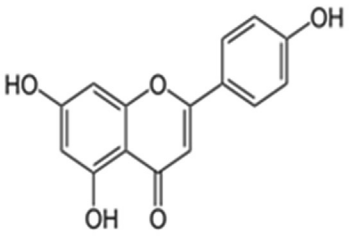

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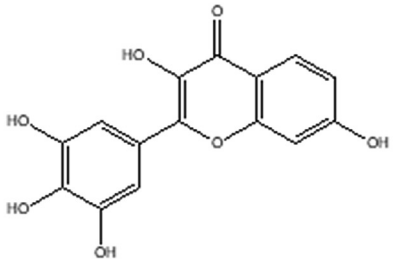

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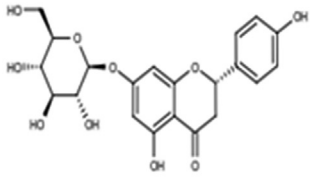

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flavonols were isolated from the roots of *Ea* (Montoro et al., 2005).

2.6.3. Sugars

Arabinogalactan type II polysaccharide and rhamnogalacturonan type I pectic type were found in abundance in the root of *Ea* (Diallo et al., 2001).

2.7. Fluorescence and UV analysis

Fluorescence characteristics of various solvents extracts of the leaf and stem bark of *Ea* upon treatment with acidic and basic chemical reagents in visible short (254 nm) and long (365 nm) wavelength have been documented (Baidoo et al., 2018).

For quality control purposes, a characteristic UV spectra of the leaf or stem bark extract of *Ea* was evaluated; the study indicated that, the leaf and stem bark extracts contained the same class of constituents with extensive conjugated systems in their chemical structures (Baidoo et al., 2018).

2.8. Biological and pharmacological activities

Ea has been subjected to numerous scientific investigations including analgesic, anti-inflammatory, antioxidant, antibacterial among others;

2.8.1. Toxicity studies

Acute toxicity studies of the MeOH stem bark and leaf extracts of *Ea* was evaluated in mice revealed an LD_{50} value of 146.7 and 249.9 mg/kg, respectively. The extracts did not show cytotoxicity against KB and Vero cells (Tibiri et al., 2007a). Sub-chronic toxicity was also assessed in rabbits and there was no significant ($p < 0.05$) modification of haematological and biochemical parameters, total cholesterol, urea, creatine and aspartate amino-transferase (AST). The methanol extracts significantly ($p < 0.05$) lowered serum glucose by 52 % within two weeks of treatment; and there was a temporary decrease ($p < 0.05$) of Alanine amino transferase (ALT) by 26.1 and 39.1 % for the stem bark and leaf extracts, respectively. Also, the stem bark extract significantly ($p < 0.05$) increased triglycerides by 108 % at the last week of treatment; the study indicated the safety of sub-chronic oral administration of the MeOH stem bark and leaf extracts of *Ea* in rabbits up to 146.7 and 249.0 mg/kg (Tibiri et al., 2007a).

Oral acute toxicity of the ethylacetate stem bark extract of *Ea* indicated that the extract is relatively safe up to a dose of 3.8 g/kg body weight (Hassan et al., 2017). The ethanol leaf extract of *Ea* was non-cytotoxic at 100 μg/mL (Ezenyi et al., 2013).

2.8.2. Anti-inflammatory

A fraction, CH_2Cl_2/MeOH (1:1 v/v) of the stem bark of *Ea* suppresses lipopolysaccharide-induced inflammation in RAW 264.7 cells. The fractions exhibited no significant effect on the viability of macrophages at 100 μg/mL after 24 h incubation; of all the fractions, the CH_2Cl_2/MeOH 5 % (Ea5) was the most potent in inhibiting the production of NO with IC_{50} = 18.36 μg/mL and had 89.068 % inhibition (Owona et al., 2013a). Ea5 also inhibited the expression of inducible NO synthase in a concentration-dependent manner; it also stimulated the expression of anti-inflammatory cytokines (IL10 and IL13) and indicated 30 % inhibition of the activity of p38 MAPK kinase (Owona et al., 2013a; Ayissi et al., 2013). Ethanol leaf extract of *Ea* exhibited significant ($p < 0.05$) anti-inflammatory effect at 200 mg/kg (Ezenyi et al., 2013).

CH_2Cl_2/MeOH 5% (Ea5 fraction) of the bark of *Ea* inhibited LPS-induced NO protection in a dose dependent manner with 87.07 %; it was more active than Baicalin in terms of NO production. The expression of TNFα, IL-1β, IL-6 and NOs was strongly suppressed by Ea5 in microglia; the fraction also inhibited the activity of p38MAPk kinase (Owona et al., 2013b).

2.8.3. Analgesic activity

The EtOAc extract of the stem bark of *Ea* significantly ($p < 0.05$) and dose-dependently inhibited the abdominal constrictions induced by acetic acid by 56.6, 49.2 and 40 % at 500, 250 and 125 mg/kg (Hassan et al., 2017).

The aqueous root extract of *Ea* reduced endometriosis related writhing frequency following three days treatment periods, writhing frequency decreased by 42, 72 and 67 % at 127.5, 255.0 and 510.0 mg/kg, respectively (Marie et al., 2017).

Ezenyi et al. (2013) reported that, the ethanol leaf extract of *Ea* significantly ($p < 0.01$, 0.05) reduced the number of abdominal constrictions induced by acetic acid by a range of 58.62–65.51 % which was higher than that observed by the standard drug, diclofenac.

2.8.4. Antibacterial activity

The ethanol stem bark extract of *Ea* significantly inhibited the growth of *S. typhi* and *B. subtilis* with zone of inhibition of 12.00 ± 0.02 and 0.80 ± 0.00 mm, respectively; the MIC and MBC for the organisms were 5 and 10 mg/mL (Ifemeje et al., 2014).

The ethanol stem bark extract *Ea* and its diethyl ether, chloroform, MeOH soluble and insoluble fractions were evaluated against *S. typhi*. The MeOH soluble fraction showed highest activity with mean zone of inhibition of range of 9.2 ± 0.3–26.7 ± 2.0 mm; however, the chloroform fraction did not show any inhibition (Mbatchou et al., 2011).

The *n*-hexane, dichloromethane, acetone and MeOH stem bark extracts of *Ea* has demonstrated good antibacterial effect; the acetone extract exhibited the highest effect against *E. feacalis*, *E. coli* and *S. aureus* with inhibition zone ranging from 14.00 ± 1.00–17.00 ± 1.73 mm. Moderate activity was observed against *E. feacalis* and *E. coli* from the MIC values of 0.39 and 0.20 mg/mL, respectively while *S. aureus* had an MIC value of 13.88 mg/mL indicating weak activity (Kwaji et al., 2017).

Antibacterial activity of Betulin (1) from the dichloromethane soluble portion of the mmethanol/acetone (1:1 v/v) stem bark extract of *Ea* was conducted against *E. coli*, *K. pneumonia*, *S. typhi* and *S. aureus*; the study revealed an MIC range between 62.50 – 250 μg/mL for betulin (Kwaji et al., 2018).

Marthe et al. (2014) reported the effect of the CH_2Cl_2/MeOH stem bark extract of *Ea* against multi-drug resistant Gram-negative bacteria in Cameroon; the extract exhibited selective antibacterial effect with an MIC of 64 μg/mL and MBC of 250 μg/mL against *E. coli* AG100A.

Antimicrobial (Kisangau et al., 2007; Karou et al., 2011), fungistatic and fungicidal (Fabry et al., 1996) effects of *Ea* have been also documented.

Scientific investigation conducted in Nigeria revealed the antimicrobial effect of *Ea* against the causative agent for cholera (i.e. *Vibrio cholerae*) (Akinsinde and Olukoya, 1995).

2.8.5. Antioxidant activity

Antioxidant activity of the *n*-hexane, dichloromethane, acetone and MeOH stem bark extracts of *Ea* using 1,1-diphenyl-2-picrylhydrazyl (DPPH) revealed similar activity which was comparable to that of the standard drug, ascorbic acid and the effect was concentration dependent (Kwaji et al., 2017).

MeOH and EtOAc extracts of the leaf, stem bark and roots of *Ea* showed good antioxidant activity using DPPH assay (Marquardt et al., 2017).

The antioxidant potential of the *n*-hexane, methylene chloride-methanol (MCME) and water (WE) extracts of *Ea* stem bark was assessed using DPPH, β-carotene-linoleic acid system (β-CLAMS) and microsomal lipid peroxidation (MLP) assays; there was maximum inhibition of MLP assay by the MCME and WE extracts with IC_{50} values of 0.50 ± 0.07 and 3.50 ± 0.11 μg/mL, respectively (Njayou et al., 2013).

Lyophilized extracts of *Ea* were evaluated for their radical scavenging activity (Tibiri *et al.*, 2007a,b). The aqueous and MeOH extracts were found to have the maximum effect with EC_{50} values of 5.7 and 5.3 μg/mL, respectively. Other extracts were moderately active with EC_{50} values ranging from 6.90 – 20.0 μg/mL (Tibiri *et al.*, 2007a,b).

The aqueous roots extract of *Ea* possessed significant radical scavenging activity similar to those of the standard drugs used (quercetin and

ascorbic acid) (Tibiri et al., 2010).

Fractions F10, F25 and F100 from the stem bark of *Ea* showed high antioxidant activity which was strongly correlated with the total polyphenolic content of the plant (Njayou et al., 2015). Antioxidant activity of three myricetin-derived flavonols isolated from the roots of *Ea* was also documented (Montoro et al., 2005).

In vitro antioxidant potential of the leaf of *Ea* has been confirmed by Atawodi (2004).

Antioxidant property of *Ea* was also reported by (Karou et al., 2011). Another study by Guissou et al. (2010) reported the antioxidant activity of *Ea*. Antioxidant property of triterpenes saponins from *Ea* was reported by Nzowo *et al.* (2010).

2.8.6. Antimycobacterial activity

Ea used in the treatment of tuberculosis and other respiratory diseases was evaluated for activity against *Mycobacterium tuberculosis* and a strain of *Mycobacterium bovis* (BCG); *Ea* did not exhibit any inhibitory effect even at a higher concentration (1250 μg/mL) (Mann et al., 2008).

2.8.7. Cytotoxic activity

Cytotoxicity studies of Betulin form the stem bark of *Ea* evaluated using brine shrimp nauplii revealed an LC_{50} value of 10.00 μg/mL indicating significant cytotoxic effect (Kwaji et al., 2018).

The crude MeOH and aqueous bark extracts of *Ea* were cytotoxic on KB or vero cells (Tibiri et al., 2007b). Cytotoxic potential of triterpenes saponins from *Ea* was also reported (Nzowo, 2010).

2.8.8. Anti-angiogenic activity

Anti-angiogenic activity of the root extracts (*n*-hexane, chloroform, chloroform/MeOH and MeOH) of *Ea* was evaluated by determination of endogenous alkaline phosphatase in zebrafish embryos. The study revealed a marked reduction on capillary formation which was evidenced in chick chlorioallantoic membrane after treatment with the active fractions or isolated compounds (Maria et al., 2014).

2.8.9. Molluscicidal activity

The tannin-containing bark of *Ea* has also demonstrated molluscicidal activity (Ayoub Hussein and Yakov, 1986).

2.8.10. Anti-ulcerogenic activity

Anti-ulcerogenic effect of *Ea* have been reported (Obidike and Emeje, 2011).

2.8.11. Endometriosis

The effect of the aqueous root extract of *Ea* on endometriosis related dysmenorrhea and ovarian dynamic in an experimental rat model was evaluated; the findings indicated the ability of the extract to prevent the progress of endometriosis, reduced dysmenorrhea, promoted ovarian follicle growth, prevented anovulation and stimulated the special period of rat sexual desire, hence an alternative for the treatment of endometriosis (Marie et al., 2017).

2.8.12. Anti-hepatitis C virus activity

The stem bark extracts (methylenechloride-MeOH i.e. MCM and its fractions) of *Ea* have demonstrated antiviral activities against Hepatitis *C virus* (HCV); LucUbiNeo-ET and Huh5.15 cell lines were used as genotype Ib (GT1b) replicon systems; the crude extract (MCM) dose-dependently inhibited the replication of HCV while some fractions (EaF10) exhibited strong anti-HCV activity with an $IC_{50} = 0.453 \pm 0.00117$ μg/mL. Hence, *Ea* was able to indirectly regulate the HCV regulation (Borris *et al.*, 2014).

2.8.13. Antiproliferative activity

Cioffi et al. (2006) reported the antiproliferative effect of some triterpenes esters that were isolated form the roots of *Ea*; the compounds demonstrated moderate to high cytotoxic activity against J774. AI, HEK-293 and WEHI-164 cell lines.

2.8.14. Complement fixing effect

Diallo et al. (2001) reported that the root of *Ea* contains different types of polysaccharides which interfere with the complement system. The study indicated that the most active fraction contained an arabinogalactan type II polysaccharide while other fractions consisting of rhamnogalacturonan type I pectic type were less active.

2.8.15. Hepatoprotective and cytoprotective activity

Hepatoprotective activity of *n*-hexane, methylene chloride-methanol (MCME) and water extracts of *Ea* stem bark evaluated using acetomophen-induced damage in rat liver slices in measuring lactate dehydrogenase (LDH) leakage as toxicity maker indicated that the MCME extract efficiently decreased LDH leakage from liver slices with 80.44 %; the water extract also inhibited the leakage of LDH enzyme from acetaminophen intoxicated rat liver in a concentration dependent manner (Njayou et al., 2013).

Synergistic Hepatoprotective effect of the active fractions of the stem bark of *Ea* was evaluated against paracetamol-induced toxicity in primary cultures of rat hepatocytes (Njayou et al., 2016). The MCM fraction was very effective with EC_{50} value of 13.47 ± 2.06 μg/mL; the fractions and their combination significantly ($p < 0.05$) improved cell viability, inhibit ALT leakage and MDA formation and there was restoration of cellular CAT, SOD activities and GSH content. The active fractions exhibited synergistic action in the protection of rat hepatocytes against paracetamol-induced damage (Njayou et al., 2016).

Cytoprotective activity of fraction F25 from the stem bark of *Ea* was comparable to that of quercetin which inhibited LDH leakage with low half inhibition concentration (IC_{50}) of 3.8 ± 0.02 μg/mL and the fraction significantly ($p < 0.05$) induced nuclear Nrf2 translocation by two fold in a human hepatocyte cell lines (Njayou et al., 2015).

Njayou et al. (2004) also reported the anti-hepatotoxic effect of *Ea*. The root extract of the plant have been reported to protect rat liver against CCl_4-induced damage (Sanogo et al., 1998).

2.8.16. Antiplasmodial activity

The ethanol leaf extract of *Ea* showed moderate antiplasmodial activity against HB3 and FcM29 ($IC_{50} = 26.36$ & 28.86 μg/mL, respectively) and it exhibited a concentration-dependent inhibition of synthetic heme (IC_{50}) (Ezenyi et al., 2013).

Karou et al. (2011) also reported the antiplasmodial effect of *Ea*. Owona et al. (2013b) also confirmed the antiplasmodial potential of *Ea*.

3. Conclusion

This paper shows information about *Ea* including the variety of traditional and ethnomedicinal uses, pharmacological and/or biological studies; however, limited data is available on the isolation and characterization of the bioactive constituents. Further screening by targeting and isolating the bioactive principles is needed. In addition, optimization of activity through molecular docking studies of the active compound(s) would be required and more robust toxicity and biochemical studies in order to ascertain the safety of the plant should be conducted. The efficacy and therapeutic index of the lead compound should as well be determined by comparing with standard agent.

Declarations

Author contribution statement

Amina Yusuf Jega: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Musa Ismail Abdullahi: Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or

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The authors declare no conflict of interest.

Additional information

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