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Evaluation of medicinal uses, phytochemistry and biological activities of *Ehretia cymosa* Thonn. (Ehretiaceae)

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Abstract

Ehretia cymosa Thonn. is a deciduous medium-sized to large tree which occurs naturally from Sierra Leone in West Africa to Eritrea and Kenya in East Africa, and Zimbabwe in southern Africa. This study aims to provide a comprehensive review of medicinal uses, phytochemistry and biological activities of *E. cymosa*. This review examines the existing literature on the medicinal uses, phytochemistry and biological activities of *E. cymosa*. This study revealed that the bark, leaf juice, leaves, roots, seeds, stems, twigs and whole plant parts of *E. cymosa* are mainly used as aphrodisiac, laxative and ethnoveterinary medicines and as traditional medicines for gastro-intestinal problems, wounds, malaria, fever, typhoid, convulsions, epilepsy, toothache and respiratory infections. Phytochemical research revealed that the species is characterized by alkaloids, anthraquinones, essential oils, fatty acids, flavonoids, glycosides, phenolics, proanthocyanidins, pseudotannins, reducing sugars, saponins, steroids, tannins and terpenes. Ethnopharmacological research revealed that the extracts of *E. cymosa* and phytochemical compounds isolated from the species showed antibacterial, antidiabetic, antihyperglycaemic and antioxidant activities. *Ehretia cymosa* should be subjected to detailed phytochemical, pharmacological and toxicological evaluations aimed at correlating its medicinal uses with its phytochemistry and pharmacological properties.

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INTRODUCTION

The genus *Ehretia* P.Browne was described by Browne in 1756 as a taxon within the Boraginaceae family consisting of approximately 40 species (Gottschling *et al.*, 2016). Recent molecular and phylogenetic studies based on nuclear (ITS) and plastid loci (rps16, trnL-trnF and trnS-trnG) supported the segregation of the family Ehretiaceae from Boraginaceae *sensu lato* (Gottschling *et al.*, 2016). The plant species belonging to the genus *Ehretia* have been recorded in the Old and New World tropics with a few species in tropical America and the West Indies, with centres of diversity in tropical Africa and East Asia (Gottschling *et al.*, 2016). *Ehretia cymosa* Thonn. occurs naturally from Sierra Leone in West Africa to Eritrea and Kenya in East Africa, and Zimbabwe in southern Africa (Martins *et al.*, 1990; Miller, 2002). *Ehretia cymosa* is divided into three varieties distinguished by flower size, hairiness of the inflorescence and geographical distribution. *Ehretia cymosa* var. *cymosa* is confined to the evergreen forests of Uganda (Verdcourt *et al.*, 1991). *Ehretia cymosa* var. *divaricata* (Bak.) Brenan is widespread, recorded in evergreen forest, grassland and bushland in DRC, Ethiopia, Kenya, Malawi, Mozambique, Tanzania, Uganda, Zambia

and Zimbabwe (Verdcourt *et al.*, 1991). *Ehretia cymosa* var. *silvatica* (Gürke) Brenan has been recorded in the rain forest, riverine forest, bushland and grassland in Ethiopia, Kenya, Tanzania and Uganda (Verdcourt *et al.*, 1991). The genus name *Ehretia* is in honour of a German botanical artist and entomologist of the 18^{th} century known as Georg Dionysius Ehret (1708-1770). The species name *cymosa* is derived from the Latin word "*cymosus*", meaning "flowers in a cyme", that is, flowers forming clusters with flowers opening from the centre first, then in succession outward towards the periphery. Synonyms of *E. cymosa* include *E. abyssinica* R.Br. ex Fresen., *E. breviflora* De Wild., *E. corymbosa* Bojer ex A.DC., *E. diffusa* Vahl ex A.DC., *E. divaricata* Baker, *E. inamoena* Standley, *E. laevis* Sieber ex A.DC., *E. silvatica* Gürke and *E. thonningiana* Exell (Verdcourt *et al.*, 1991; Miller, 2002).

Ehretia cymosa is a deciduous medium-sized to large tree growing up to a height of 20 metres. *Ehretia cymosa* has been recorded in the understory or at edges of evergreen forest, riverine forest, forest margins, wooded savanna and bushland on steep mountain slopes. The bark of *E. cymosa* grey to dark grey in colour, ranging from smooth to rough and scaly. The leaves are simple and entire, arranged spirally, broadly ovate to elliptic in shape, papery to leathery, glossy dark green above and paler dull green below. Flowers of *E. cymosa* are white in colour, sweetly scented, occurring in large terminal heads. The fruit is a drupe, ovoid to globose in shape, fleshy, orange to red and turning black when ripe.

The fruits of *E. cymosa* are edible and the leaves are also consumed in Benin as leafy vegetables (Achigan-Dako *et al.*, 2010). The fresh leaves of *E. cymosa* are sold in local markets in Benin as leafy vegetables (Achigan-Dako *et al.*, 2010). But the fruits of *E. cymosa* are known to cause gastrointestinal disorders and the leaves and roots are also known to be poisonous (Wickens and Burkill, 1986; Dharani, 2019). It is, therefore, within this context that the current study was undertaken aimed at documenting the medicinal uses, phytochemistry and biological activities of *E. cymosa*.

MATERIALS AND METHODS

Results of the current study are based on a literature search on the ecological, biological and medicinal properties of *E. cymosa* throughout its distributional range using information from internet databases. The databases used included Scopus, Google Scholar, PubMed and Science Direct. Other sources of information used included pre-electronic sources such as journal articles, theses, books, book chapters and other scientific articles obtained from the university library.

RESULTS AND DISCUSSION

Medicinal uses of *Ehretia cymosa*

The herbal concoctions prepared from the bark, leaf juice, leaves, roots, seeds, stems, twigs and whole plant parts of *E. cymosa* are used to treat and manage at least 38 human and animal diseases and ailments (Table 1). The major diseases and ailments treated by *E. cymosa* extracts include gastro-intestinal problems recorded in five countries based on eight literature records (Figure 1), followed by wounds (four countries, eight literature records), malaria (three countries, five literature records), fever and typhoid (three countries, four literature records), convulsions and epilepsy (three countries, four literature records), ethnoveterinary medicine (three countries, three literature records), aphrodisiac (two countries, five literature records), toothache (two countries, four literature records), respiratory infections (two countries, four literature records) and laxative (two countries, two literature records).

Phytochemical composition of *Ehretia cymosa*

Researchers identified several phytochemical compounds from the leaves, roots and whole plant parts of *E. cymosa* (Table 2). The phytochemical compounds identified from the species include alkaloids, anthraquinones, essential oils, fatty acids, flavonoids, glycosides, phenolics, proanthocyanidins, pseudotannins, reducing sugars, saponins, steroids, tannins and terpenes (Table 2). Some of these phytochemical compounds may be responsible for the biological activities exhibited by the species.

Biological activities of *Ehretia cymosa*

The following biological activities have been documented from the leaf and whole plant parts of *E. cymosa* as well as phytochemical compounds isolated from the species, antibacterial, antidiabetic, antihyperglycaemic and antioxidant activities.

Antibacterial activities

Sarkodie *et al.* (2015) evaluated the antibacterial activities of 70% ethanolic extract of the whole plant of *E. cymosa* against *Bacillus subtilis, Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Escherichia coli* using agar diffusion assay with gentamicin (10.0 μg/mL) as a positive control. The extract exhibited activities against tested pathogens. Bagaje *et al.* (2017) evaluated the antibacterial activities of the

Table 1: Medicinal applications of *Ehretia cymosa*

Medicinal use	Parts used	Country	References
Anthelmintic	Bark and seeds	Ethiopia	Tamene (2020)
Aphrodisiac	Bark, leaves and roots	Kenya and Tanzania	Jeruto *et al.* (2008); Dharani (2019)
Bleeding	Leaves	Ethiopia	Jima and Megersa (2018)
Brucellosis	Roots	Kenya	Dharani (2019)
Boils	Whole plant	Kenya	Odongo *et al.* (2018)
Cancer	Bark and leaves	Ethiopia	Tefera and Kim (2019)
Candidiasis	Twigs	Benin	Fanou *et al.* (2020)
Chew sticks	Stems	Ghana	Wickens and Burkill (1986)
Convulsions and epilepsy	Leaves and roots	Kenya, Nigeria and Uganda	Wickens and Burkill (1986); Anywar *et al.* (2020)
Diabetes	Leaves	Ghana	Sarkodie *et al.* (2015)
Febril illness	Leaves	Ethiopia	Jima and Megersa (2018)
Febrifuge	Leaves	Gabon	Wickens and Burkill (1986)
Fever and typhoid	Leaves and roots	Kenya, Nigeria and Uganda	Wickens and Burkill (1986); Jeruto *et al.* (2008)
Fractured bones	Leaves	Ghana	Lewis and Avioli (1991)
Gastric ulcers	Leaves	Nigeria	Kayode *et al.* (2019)
Gastro-intestinal problems (diarrhoea, dysentery and stomach ache)	Bark, leaves, roots and whole plant	Benin, Ethiopia, Ghana, Kenya and Tanzania	Wickens and Burkill (1986); Odongo *et al.* (2018)
Headache	Leaves	Uganda	Anywar *et al.* (2020)
Infantile tetanus	Leaves and roots	Ghana	Wickens and Burkill (1986)
Laxative	Leaves	Gabon and Nigeria	Wickens and Burkill (1986); Odugbemi (2008)
Malaria	Leaves, roots and twigs	Benin, Kenya and Yemen	Jeruto *et al.* (2008); Hussein and Dhabe (2018)
Measles	Leaves	Nigeria	Wickens and Burkill (1986)
Menstrual problems	Bark	Ivory Coast	Wickens and Burkill (1986)
Mental problems	Leaves and roots	Kenya	Jeruto *et al.* (2008)
Pain	Leaves	Ethiopia	Jima and Megersa (2018)
Respiratory infections (asthma, chest pains, dry cough and pneumonia)	Bark, leaves, roots and whole plant	Kenya and Yemen	Hussein and Dhabe (2018); Odongo *et al.* (2018)
Tonsillitis	Leaves and roots	Kenya	Jeruto *et al.* (2008)
Toothache	Bark, leaves and stems	Benin and Ethiopia	Hounnankpon *et al.* (2017); Tefera and Kim (2019)
Venereal diseases	Leaves and roots	Kenya	Jeruto *et al.* (2008)
Wounds	Bark, leaf juice, leaves and roots	Ethiopia, Eritrea, Kenya and Tanzania	Dharani (2019); Tefera and Kim (2019)
Ethnoveterinary medicine (anaplasmosis, diarrhoea, dysentery and mange)	Leaves and roots	Ghana, Kenya and Nigeria	Wickens and Burkill (1986)

Table 2: Phytochemical composition of *Ehretia cymosa*

Phytochemical compound	Value	Plant part	Reference
Alkaloids	-	Leaves, roots and whole plant	Borokini and Omotayo (2012); Ogundajo and Ashafa (2017a)
α and β-amyrin	-	Leaves	Bagaje *et al.* (2017); Sori *et al.* (2018)
Anthraquinone	-	Leaves and roots	Jeruto *et al.* (2011)
Bauerenol	-	Leaves	Sori *et al.* (2018)
Benzamide (%)	0.06	Leaves	Ogundajo and Ashafa (2017b)
trans-α-Bergamotene (%)	15.2	Leaves	Ogundajo *et al.* (2016)
2,2-Bis (4-nitrobenzyl)-1-phenylbutane-1,3-dione (%)	0.06	Leaves	Ogundajo and Ashafa (2017b)
β-Bisabolene (%)	7.1	Leaves	Ogundajo *et al.* (2016)
o-tert-Butylphenol (%)	3.0	Leaves	Ogundajo *et al.* (2016)
β-Caryophyllene (%)	4.9	Leaves	Ogundajo *et al.* (2016)
Isocaryophyllene (%)	7.5	Leaves	Ogundajo *et al.* (2016)
β-Cedrene (%)	14.0	Leaves	Ogundajo *et al.* (2016)
Citronellyl propionate (%)	0.3	Leaves	Ogundajo and Ashafa (2017b)
Crude protein (%)	21.3	Leaves	Wolde *et al.* (2019)
ar-Curcumene (%)	14.5	Leaves	Ogundajo *et al.* (2016)
β-Damascenone (%)	9.3	Leaves	Ogundajo *et al.* (2016)
Diglycidyl ether (%)	0.04	Leaves	Ogundajo and Ashafa (2017b)
2-Dodecenyl acetate (%)	0.9	Leaves	Ogundajo and Ashafa (2017b)
n-Docosane (%)	0.4	Leaves	Ogundajo and Ashafa (2017b)
Flavonoids (mg quercetin/g)	235.3	Leaves, roots and whole plant	Sarkodie *et al.* (2015); Sori *et al.* (2018)
Glycosides	-	Leaves, roots and whole plant	Jeruto *et al.* (2011); Sarkodie *et al.* (2015)
6-hepten-3-one (%)	0.1	Leaves	Ogundajo and Ashafa (2017b)
n-Hexadecane (%)	0.2	Leaves	Ogundajo and Ashafa (2017b)
2-hexadecyloxirane (%)	34.2	Leaves	Ogundajo and Ashafa (2017a,b)
Lavandulyl acetate (%)	0.8	Leaves	Ogundajo and Ashafa (2017b)
Linalool (%)	2.7	Leaves	Ogundajo *et al.* (2016)
Methyl heptanoate (%)	0.08	Leaves	Ogundajo and Ashafa (2017b)
Methyl hexadecanoate (%)	17.5	Leaves	Ogundajo and Ashafa (2017b)
Methyl linolelaidate (%)	5.0	Leaves	Ogundajo and Ashafa (2017b)

Continued on next page

Table 2 continued

Phytochemical compound	Value	Plant part	Reference
Methyl linolenate (%)	28.9	Leaves	Ogundajo and Ashafa (2017b)
Methyl octadecanoate (%)	4.5	Leaves	Ogundajo and Ashafa (2017b)
Methyl salicylate (%)	8.9	Leaves	Ogundajo *et al.* (2016)
4-Methylvaleric acid (%)	0.04	Leaves	Ogundajo and Ashafa (2017b)
1-Oxacyclopropyl-3,4-epoxycyclohexane (%)	2.2	Leaves	Ogundajo and Ashafa (2017b)
n-Pentadecane (%)	0.5	Leaves	Ogundajo and Ashafa (2017b)
Phenethyl alcohol (%)	0.7	Leaves	Ogundajo and Ashafa (2017b)
Phenolic (mg gallic acid/g)	27.4	Leaves and whole plant	Sarkodie *et al.* (2015); Sori *et al.* (2018)
S-Phenyl (2S,1'S)-2-(2-Nitro-1-phenylethyl)-1-(1-phenylethyl) aziridine-2-carbothioate (%)	0.06	Leaves	Ogundajo and Ashafa (2017b)
Phytol (%)	1.8	Leaves	Ogundajo and Ashafa (2017a,b)
Phytosterols	-	Leaves	Sori *et al.* (2018)
Proanthocyanidins (mg catechin/g)	28.3	Leaves	Ogundajo and Ashafa (2017a,b)
Pseudotannins	-	Whole plant	Sarkodie *et al.* (2015)
Reducing sugars	-	Whole plant	Sarkodie *et al.* (2015)
Saponins	-	Leaves and roots	Borokini and Omotayo (2012); Bagaje *et al.* (2017)
trans-Sesquisabinene hydrate (%)	3.4	Leaves	Ogundajo *et al.* (2016)
Stearic acid (%)	1.0	Leaves	Ogundajo and Ashafa (2017a,b)
Steroids	-	Leaves	Ogundajo and Ashafa (2017a,b)
Tannins	-	Leaves and whole plant	Borokini and Omotayo (2012); Sarkodie *et al.* (2015)
Terpenes	-	Leaves and roots	Borokini and Omotayo (2012); Sori *et al.* (2018)
2,2,6,6-Tetramethyl-4-(4-nitrobenzyl) heptane-3,5-dione (%)	0.04	Leaves	Ogundajo and Ashafa (2017b)
n-Undecane (%)	0.7	Leaves	Ogundajo and Ashafa (2017b)
β-Ylangene (%)	9.5	Leaves	Ogundajo *et al.* (2016)

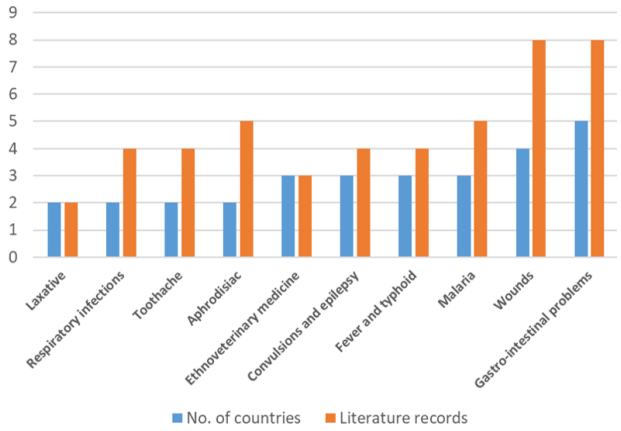

Figure 1: Main diseases and ailments treated and managed by *Ehretiacymosa*

methanol extract of *E. cymosa* leaves against *seudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus aureus* and *Proteus mirabilis* using well diffusion method with gentamicin and vancomycin as positive controls. The extract exhibited activities against *Escherichia coli* and *Staphylococcus aureus* with a zone of inhibition of 12.0 mm and 9 mm, respectively (Bagaje *et al.*, 2017). Similarly, Sori *et al.* (2018) evaluated the antibacterial activities of n-hexane, methanol and ethyl acetate extracts and the triterpenoid compound isolated from *E. cymosa* leaves against *Pseudomonas aeruginosa* and Staphylococcus aureus using disc diffusion assay with gentamicin as a positive control. The extracts and the compound exhibited activities with inhibition zones ranging from 9.0 mm to 30.0 mm in comparison to the inhibition zone of 22.0 exhibited by the positive control (Sori *et al.*, 2018).

Antidiabetic activities

Ogundajo and Ashafa (2017a,b) evaluated the antidiabetic activities of ethanol, methanol and ethyl acetate extracts of *E. cymosa* leaves using α-amylase and α-glucosidase inhibitory assays. The extracts exhibited activities against α-glucosidase (0.6 mg/mL) and α-amylase (2.1 mg/mL), respectively (Ogundajo and Ashafa, 2017a,b).

Antihyperglycaemic activities

Sarkodie *et al.* (2015) evaluated the *in vivo* antihyperglycaemic activities of 70% ethanolic extract of the whole plant of *E. cymosa* using Sprague Dawley rats. The extract exhibited dose independent decrease of blood glucose (Sarkodie *et al.*, 2015).

Antioxidant activities

Sarkodie *et al.* (2015) evaluated the antioxidant activities of 70% ethanolic extract of the whole plant of *E. cymosa* using 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging assay with ascorbic acid and butylated hydroxytoluene (BHT) as positive controls. The extract exhibited activities with a half maximal inhibitory concentration (IC_{50}) value of 0.5 μg/ml, comparable to IC_{50} values of 03 μg/ml and 0.4 μg/ml exhibited by ascorbic acid and BHT, respectively (Sarkodie *et al.*, 2015). Bagaje *et al.* (2017) evaluated the antioxidant activities of the methanol extract of *E. cymosa* leaves using DPPH free radical scavenging assay with ascorbic acid as a positive control. The extract exhibited low inhibition of DPPH in comparison to high activities exhibited by the positive control (Bagaje *et al.*, 2017). Ogundajo and Ashafa (2017a,b) evaluated the antioxidant activities of methanol, ethanol and ethyl acetate extracts of *E. cymosa* leaves using DPPH, 2,2-azino-bis (3-ethylbenzothiazoline)-6-sulfonic (ABTS), hydroxyl radical, metal chelating and superoxide anion scavenging assays. The extracts showed activities exhibiting IC_{50} values ranging from 0.5 mg/mL to 1.7 mg/mL Ogundajo and Ashafa (2017a,b).

CONCLUSIONS

Ehretia cymosa is known to be poisonous and there is a need for detailed clinical and toxicological evaluations of crude extracts and compounds isolated from the species. Therefore, the widespread use of *E. cymosa* as a food plant and source of traditional medicines throughout its distributional range suggest that the species is not taken at toxic dosages. But the use of *E. cymosa* as food and the treatment of human diseases and ailments should be treated with caution and rigorous toxicological and clinical studies of the bark, fruits, leaves, roots, seeds, tubers and compounds isolated from the species are necessary.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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