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# Ethnopharmacological Relevance of *Eusideroxylon Zwageri* Teijsm. et Binnend: A Review

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**ABSTRACT**

*Eusideroxylon zwageri* is found in several areas in Indonesia, such as Borneo and Sumatra. The limited reports on its ethno medical use, phytochemical constituents, and pharmacological activities indicated the needs to search its bioactive compounds. This review is aiming to collect data or information from the previous studies on *Eusideroxylon zwageri,* especially regarding its ethno medical use, phytoconstituents and pharmacological activities. Literature search is carried out with the help of three searching engines: PubMed, Science Direct and Google Scholar. The searching was carried out with keyword: *Eusideroxylon zwageri*. From PubMed, Science direct and Google Scholar we got 4, 52 and 15 results. Twelve articles were excluded due to duplication. Thirty-four articles were excluded due to irrelevant information. There were 25 full text articles that meet the criteria of systematic review. Ethnologically, it can be used as diabetes remedial, anti-inflammatory agents, antimicrobial agents, and grey hair, and whitening agents. The main phytochemical constituents are condensed tannin and lignin, and mainly eusideron. The most used parts are stem bark. Limited information is available on the seed and leave.

**Keywords:** Borneo, *Eusideroxylon zwageri*, Kalimantan, kayu ulin, kayu besi, iron wood, ulin wood

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## INTRODUCTION

*Eusideroxylon zwageri* (Lauraceae) is an endemic tropical tree known as kaju ulin, kaju besi, Borneo iron wood, or bulian.[1, 2] The wood of this tree has important economic value and should be conserved properly. Its barks, leaves and seeds are often used for local needs, especially for the medical uses. Any effort related with the use of all parts of this tree should be cover two aspects, both in benefitting people and in protecting their environment.[3]

Beside the use of its wood for house construction, other parts of the tree (*E. zwageri*) have been locally used as traditional medicine. Reports are more available on the studies of the use of the wood as furniture or household, roof and wooden house. Not much scientific articles are available on the medicinal use of other parts of the tree, such as leave, bark, seed. Many people live within or adjacent to forested areas and derive at least some part of their livelihood inputs from environmental resources.[4] Complex customary Dayak rules exist that control the use and inheritance of these forests that help to avoid over-exploitation of resources.[5]

Objectives of this literature study were to collect information of the ethnomedical use, phytochemical components and pharmacological activities from previous scientific reports on *E. zwageri.*

## METHODS

Search activities were done with the use of PubMed, Science Direct, and Google Scholar. The Keyword was *Eusideroxylon zwageri*. The searching was done on 2 March 2020. From PubMed, Science direct and Google Scholar we got 4, 52 and 15 results. Twelve articles were excluded due to duplication. Thirtyfour articles were excluded due to irrelevant information. Total results were 25. A complete literature review focused on the traditional medicinal use in Borneo, Indonesia was conducted.

## ETHNOMEDICINAL USE OF *E. ZWAGERI*

Stem bark, leave and seed are used to treat several diseases. Stem bark is used as tooth ache agent, jaundice, after birth herbal treatment, to make hair black. Cognation of Leave and root is used for after birth treatment of the mothers. Seed oil is sold in the market for the hair growth and black coloring. Ethanol extract of *E. zwageri* is traditionally used for the treatment of diabetes in the Ethnic of Kutai, Borneo. The plant extract of the stem bark has antioxidant capacity, inhibitory activity on α-glucosidase and α-amylase, thus has pot ential as antidiabetic agent. But , the limited reports of *E. zwageri* indicated the needs to search the active compounds from plant as potential antidiabetic agents by considering plant conservation status.[6]

Aqueous extract of ironwood is used traditionally to treat a toothache. It inhibits the growth of Staphylococcus aureus in vitro. The literature on the use as Aphrodisiac is limited.[7]

### *Phytochemical profile of E.zwageri*

As the other member of family Lauraceae, many phytochemical constituents of various plant parts belongs to arylpropanoids, alkaloids, flavanoids and terpene (Table 1).[8] The defensive strategy of E. zwageri is depend on its net production of plant secondary metabolites, especially condensed tannins and lignins. By employing this extreme defensive strategy, its wood is extremely durable and has a high specific gravity with a very slow growth rate. The concentrations of condensed tannins and lignins are very high in the leaves and stems, at about 20% and 30%, respectively.[9]

### *Simple phenolic and flavonoid compounds*

Limited information is available concerning the simple and flavonoid compounds in plant parts of *E. zwageri*. The total phenolic, total flavonoid and totap proanthocyanidin of the extract has 31.28 GAE/g extract (mg), 30.48 CE/g extract (mg) and 183.3 PE/g extract (mg) repectively.[6] These phenolic and flavonoid compounds are building materials of the complex structure of condensed tannins.

### *Alkaloid compounds*

Plant parts of *E.zwageri* is a rich source of alkaloids that are derived from the benzyl tetrahydroisoquinoline nucleus.[10] The occurrence of alkaloids in leave and bark

Table 1. List of major phytochemicals of *Eusideroxylon zwageri*

| Compounds | Part | Solvent | Extraction | Ref. |
|---|---|---|---|---|
| **Phenolic compounds** | | | | |
| Total phenolic | Stem bark | Ethanol | 31.28 mg GAE/g extract | (6) |
| **Flavonoids** | | | | |
| Total Flavonoids | Stem bark | Ethanol | 30.48 mg CE/g extract | (6) |
| **Proanthocyanidin** | | | | |
| total proanthocyanidin contents | Stem bark Bark | Ethanol | 183.3 mg PE/g extract | (6) |
| **Alkaloids** | | | | |
| benzyl tetrahydroisoquinoline nucleus | Leave, Bark | | | (10, 11) (12) |
| **Condensed tannins** | | | | |
| Condensed Tannins | Stem bark, Leave | Acetone:water | 20% | (9) |
| **Neolignans characterized by a phenylpropanoid core** | | | | |
| Eusiderin A | Wood | n-hexane fraction of acetone | n.d. | (14) |
| Eusiderin I | Wood | n-hexane fraction of acetone | n.d. | (14) |
| (2R,3R,4S)-2,3-dimethyl-6,7-dimethoxy-4-ethoxy (3′,4′,5′-trimethoxybenzene)-1,5-dihydroxytetralin | Wood | n-hexane fraction of acetone | n.d. | (14) |
| (2R,3S,4S)-2,3-dimethyl-6,7-dimethoxy-4-ethoxy(3′,4′,5′-trimethoxybenzene)-1,5-dihydroxytetralin. | Wood | n-hexane fraction of acetone | n.d. | (14) |
| **Lignin** | | | | |
| lignins | Stem, Bark, Leave | Acetone:water | 30% | (9) |
| **Lignan or Neolignan are monomer of lignin** | | | | |
| p-hydroxyphenyl (4-hydroxyphenyl, P) | Stem, Bark, Leave | Acetone:water | | (9) |
| guaiacyl (4-hydroxy-3-methoxyphenyl, G) | Stem, Bark, Leave | Acetone:water | | (9) |
| syringyl (4-hydroxy-3,5-dimethoxyphenyl, S) | Stem, Bark, Leave | Acetone:water | | (9) |
| N-cis-Feruloyl typamine | Seed | Ethanol | 148.787 (51.76%) | (23) |
| 3′-O-Methylviolanone | Seed | Aqueous | 58.178 (74.87% | (23) |
| 3′-O-Methylviolanone | Seed | Ethyl Acetate | 55.730 (60.78%) | (23) |
| 3-(4'-Hydroxy-benzyl)-5,7-dihydroxy-6-methyl-8-methoxy-chroman-4-one | Seed | Ethyl Acetate | 31.132 (33.95%) | (23) |
| 6-Hydroxy-2-[2-(4'-methoxyphenyl)ethyl] chromone | Seed | Ethanol | 94.652 (32.93%) | (23) |
| β-Asarone | Seed | Ethanol | 73.05 -82.44 % | (23) |
| **Others** | | | | |
| 4,11,11-trimethyl-8-methylene-bicyclo[7.2.0] undec-4-ene | Wood | Dichlormethane | 17.60 % | (21) |
| Cadina-3,9-diene | Wood | Dichlormethane | 11.90 % | (21) |
| α Panasinsen (sesquiterpenoids) | Wood | Dichlormethane | 7.10 % | (21) |
| 1,2,3-Trimethoxy-5-(1E)-1-propenyl] benzene | Wood | Dichlormethane | 16.80 % | (21) |
| 4-methoxy-6-(2-propenyl)-1,3-Benzofioxole (Myristicin) | Wood | Dichlormethane | 10.20 % | (21) |
| 1,3-Bis(1,1-dimethylethyl)-1,1,3,3-tetramethyldisiloxane | Wood | Methanol | 43.50 % | (21) |
| Tetratetraacontane | Wood | Methanol | 8.30 % | (21) |
| Methyl octacosanoate | Wood | Methanol | 10.00 % | (21) |

from *E.zwageri* are reported qualitatively. The type of alkaloids is not yet confirmed, but probably exhibit unique structures. A contribution for the scientific community is needed to enable the search for alkaloids in species belonging to the *E.zwageri*.[10-12]

***Tannins***

Tannins (tannic acid) are water-soluble complex plant polyphenols [13] that divided into condensed and hydrolyzable tannins. The condensed tannins contain the benzene nuclei. The hydrolyzable tannins contain ester or glucoside bonds that are readily decomposed by acids. Tannins are reported fot their anticarcinogenic and antimutagenic potentials, antioxidative property, which is important in protecting cellular oxidative damage, including lipid peroxidation, antimicrobial activities (fungi, yeasts, bacteria, and viruses). Tannic acid and propyl gallate, but not gallic acid, are inhibitory to foodborne bacteria, aquatic bacteria, and off-flavor-

producing microorganisms. Tannins have also been reported to exert other physiological effects, such as to accelerate blood clotting, reduce blood pressure, decrease the serum lipid level, produce liver necrosis, and modulate immunoresponses.[13]

Condensed Tannins are found in wood, stem bark and leave of *E. zwageri*. Together with lignin, condensed tannins has a significant role in defense mechanisms of ironwood tree which seemed to employ an extreme defensive strategy. The wood of *E. zwageri* is extremely durable and has a high specific gravity with a very slow growth rate. The concentrations of condensed tannins and lignins were very high in the leaves and stems of this species, at about 20 and 30%, respectively. Its net production to defensive substances (condensed tannin + lignin) of *E.zwageri* is about 35%. The condensed tannins in *E. zwageri* help to prolong the lifespan of the leaves, and the lignins in the stems enhance the durability of the wood. Condensed tannins can inhibit several digestive enzymes, such as trypsin, α-amylase, and lipase. The inhibitory effect on trypsin activity is more marked with condensed tannins than with hydrolyzable tannins.[9]

Hydrolysable tannins usually result from binding to sugar fragments (mainly to the d-glucose moiety) of gallic, meta-digallic, or hexahydroxydiphenic acid residues. Literature on hydrolysable tannins of *E.zwageri* is not yet available.

***Neolignans and lignin***

Lignans are natural products that occur plant kingdom including iron wood. They contain the same monomers as lignins but are dimeric instead of polymeric. They are characterized by a phenylpropanoid core. Lignans is a dimeric C6C3 coupled motifs linked at carbons 8 and 8′ . Compounds with the coupling of the two C6C3 units at positions different from C8–C8′ as neolignans (Figure 1). Several neolignans can be detected in *E.zwageri*. Four lignans can be isolated from wood *E.zwageri*, viz. eusiderin A, eusiderin I, (2R,3R,4S)-2,3-dimethyl-6,7-dimethoxy-4-ethoxy (3′,4′,5′-trimethoxybenzene)-1,5-dihydroxytetralin and (2R,3S,4S)-2,3-dimethyl-6,7-dimethoxy-4-ethoxy(3′,4′,5′-trimethoxybenzene)-1,5-dihydroxytetralin (Figure 2).

Eusiderin A is a neolignan derivate, which makes up the majority of the secondary metabolite of *E. Zwageri.* [14] Eusiderin is identified as a major component of the n-hexane soluble fraction of the *E. zwageri* acetone extract, which was the most effective fraction in reducing the mycelial growth.[15] Eusiderin A has been reported as a potent antifungal agent. The oxidation of terminal methylene of the allylic chain in Eusiderin A produces primary alcohol, pinacol, an aldehyde which demonstrated strong activity against dermal fungi The hydrophilicity of Eusiderin A can be improved via oxidation of the allylic chain in order to derive a potent antifungal property. Transformation of Eusiderin A has been achieved to produce 7,3'-epoxy-8,4'-oxyneolignane-1'-carboxylic acid.[16]

Lignans have been attributed with a range of biological activities including anticancer, antioxidant, antihypertensive, antiviral, estrogenic, and insecticidal properties. But bioactivity researches on lignans, especially from *E. zwageri* have not yet developed. Therefore, it opens window for further interesting research topics. Eusiderin which was the most effective fraction in reducing the mycelial growth.[15]

Many types of lignan or neolignan are monomer of lignin, as building materials of lignin. Lignin is a crosslinked phenolic polymer mainly comprised of three constituent monomers, p-hydroxyphenyl (4-hydroxyphenyl, P), guaiacyl (4-hydroxy-3-methoxyphenyl, G), and syringyl (4-hydroxy-3,5-dimethoxyphenyl, S), arranged in a hyper branched topology with no regular repeating structure. Lignin is the most important aromatic polymer from renewable resources due to its natural abundance, robust material properties, and the fact that its use does not directly compete with the food supply. Lignin is any of a class of propyl phenolic dimers including many found in plants and noted for having antioxidant and estrogenic activity.

Lignin, a major polymer component of plant cell walls, provides the strength, water resistance, and rigidity of cell walls, thereby providing the mechanical support that allows vascular plants to stand upright. The amount and chemical structure of lignin vary among woody species, with the variations particularly occurring within the reaction wood (RW) of stems or branches. Lignin distribution is thought to play an important role in the adaption of trees to their environment. Regardless of the RW type, the lignin content is relatively higher on the lower side (lsW) of the leaning woody stem than on the upper side (usW).

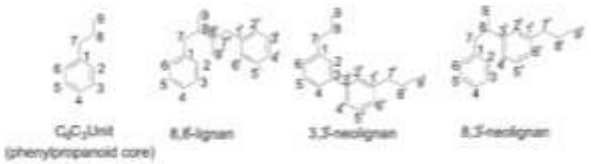


Figure 1. Lignan and neolignan core structures

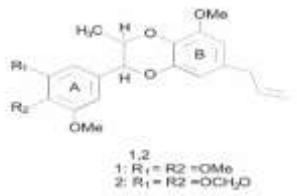


Figure 2. Chemical structure of Eusiderin A (1) and Eusiderin I (2)

***Bioactivities and Pharmacological activities***

***Antioxidant activity***

The ethanolic extract of the stem bark has antioxidant activity. The IC50 values of antioxidant activity of the extract in DPPH and superoxide radical scavenging mechanisms were 44.90 µg/ml and 30.47 µg/ml.[6] It is reported also that the methanol seed extracts of E. zwageri showed DPPH radical-scavenging activity of more than 70% at 100 microg/ml.[17]

***Inhibitory activity on α-glucosidase, α-amylase and tyrosinase***

The *E. zwageri* stem bark ethanol extract show inhibitory activities against α-glucosidase, and α-amylase. Therefore, this extract has antidiabetic potential. The limited reports of *E. zwageri* indicated the needs to search the active compounds from plant as potential antidiabetic agents. This ability is determined by its flavonoid content.[6]

Methanol seed extract of E.zwageri show inhibitory activities on tyrosinase inhibitor.[17] Therefore, seed extract of *E. zwageri* (seed extract/oil) has anti-melanogenesis potential, due to its strongly inhibition on the melanin production. These findings indicate that *E. zwageri* are potential ingredients for skin-whitening cosmetics if their safety can be confirmed.[17]

***Antibacterial and antifungal activity***

Stem, ethanol stem bark extract of *E. zwageri* show antibacterial and antifungal activities. Gram positive and Gram negative bacteria are inhibited. Gram positive bacteria, *Staphylococcus aureus* is inhibited Gram negative bacteria, such as *Escherichia coli* and *Salmonella typhi* are inhibited.[18] These extracts are containing antibacterial compounds alkaloids, flavonoids, triterpenoids, tannins and saponins.[19] Therefore, *E. zwageri* extract has potential to the treatment of diarrhea and typhoid fever.[20] Its methanol leaf extract shows antibacterial activity against *Enterococcus faecalis, Staphylococcus aureus, Salmonella typhi and Escherichia Coli*.[24] Its Eusiderin A has a potent antifungal activity against *Trichophyton mentagrophytes*.[16] DCM crude wood extract and Methanol crude wood extract are reported for their inhibitory against *Trametes versicolor*, *Gloeophylum trabeum*, and *Chaetomium globosum*.[21]

***Anti-inflammatory agent***

The methanol leaf extract of *E. zwageri* has an anti-eosinophilia activity and an ability to down-regulate the inflammatory cytokines such as IL-5 or eotaxin. It inhibits eosinophils proliferation in bone marrow and spleens. The down regulation of eotaxin is related to the inhibition of eosinophils recruitment to the inflammation site.[25]

## CONCLUSIONS AND FUTURE RECOMMENDATIONS

Limited literatures are available on ethno medical use, phytochemical profile, and the pharmacological potential of various plant part of *E. zwageri*.

- An ethnobotanical survey needs to be conducted in the Sumatra and Borneo. The knowledge and the attitude towards traditional medicine of the local population in those islands may be useful in developing novel medicine.
- Phytochemical constituents of various plants part need to be investigated. Alkaloid of *E.zwageri* is needed to investigate.
- Pharmacological activities of *E.zwageri* are also not yet intensively investigated. The need for further studies is necessary because of a greater urgency in recent times in the wake of the threat posed by rapid development and with the growing concern that valuable plant substances which may present useful lead compounds for drug discovery may be lost.[22]

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