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Caesalpinia sappan L: REVIEW ARTICLE

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ABSTRACT

Background: *Caesalpinia sappan L*, synonym *Biancaea sappan L.*, is a medicinal plant used in Asia, especially India, China, and Southeast Asia. In Indonesia, Sappanwood (Secang) is traditionally consumed as herbal drink to boost immune system, kill bacteria, treat diarrhea, and tumor. *Caesalpinia sappan L.* contains homoisoflavonoids and phenols such as brazilin, brazilein, and other active ingredients.

Aim: The aim of this study is to report phytochemical contents and benefits of *Caesalpinia sappan L* for medicinal use.

Methods: The method used in finding articles was a literature review, using the keywords. Search was conducted electronically using several databases, including Science Direct and Google Scholar.

Results: Medicinal benefits from *Caesalpinia sappan L* have been proved by several studies. These medicinal effects are caused by the presence of *Caesalpinia sappan*'s active ingredients such as brazilin, brazilein, 3-deoxysappanchalcone, sappanchalcone, Caesalsappanins A, G, H, and I.

Conclusion: *Caesalpinia sappan L* has medicinal benefits and could be applied to treat several diseases.

Keyword: *Caesalpinia sappan L*, traditional use, medicinal use

INTRODUCTION

Caesalpinia sappan L, synonym *Biancaea sappan L.*, is a medicinal plant used in Asia, especially India, China, and Southeast Asia. In Indonesia, Sappanwood (Secang) is traditionally consumed as herbal drink and has different local names for examples seupeng (Aceh); sebang (Gayo); sopang (Batak); cacang (Minangkabau); secang (Sunda); kayu secang, soga Jawa (Jawa); kaju secang (Madura); cang (Bali); sebang (Sasak); supa, suang (Bima); sepel (Timor); ; hong (Alor); kayu sema (Manado); dolo ; sapang (Makassar); seppang (Bugis); sefen (Halmahera Selatan); sawala, hiniaga, sinyiang, singiang (Halmahera Utara); sunyiha (Ternate); and roro (Tidore) [1]. *Caesalpinia sappan L* heartwood flakes poured with boiling water would alter water color into redness and ready to be consumed or applied as immunomodulator, antibacterial, astringent, and antitumor.

Table 1. *Caesalpinia sappan L* classification. United States Department of Agriculture [2]

Kingdom	Plantae – Plants
Subkingdom	Tracheobionta – Vascular plants
Superdivision	Spermatophyta – Seed plants
Division	Magnoliophyta – Flowering plants
Class	Magnoliopsida - Dicotyledons
Subclass	Rosidae
Order	Fabales
Family	Fabaceae / Leguminosae – Pea family
Genus	<i>Caesalpinia L</i> – nicker
Species	<i>Caesalpinia sappan L</i> – sappanwood



Figure 1, 2. *Caesalpinia sappan* L [3]

Caesalpinia sappan is a small to medium-sized, shrubby tree, 4-8(-10) m tall; trunk up to 14 cm in diameter; bark with distinct ridges and many prickles, greyish brown; young twigs and buds hairy, brownish. Flowering can occur after 1 year of growth and usually during the rainy season, fruiting about 6 months later. In Myanmar, the tree flowers in August, and in Indonesia pods are produced 13 months after planting [4].

METHODS

The method used was a literature review, using keywords *Caesalpinia sappan*, traditional use, medicinal use. The research was conducted digitally using several databases, including 159 publications of *Caesalpinia sappan* medicinal use from Science Direct, 4,660 publications of *Caesalpinia sappan* medicinal and traditional use from Google scholar.

After the initial screening of titles and abstracts and elimination of duplicates, 60 studies were selected for retrieval of full text and 4,759 were excluded. These were excluded if they were irrelevant to the research question. The 60 articles selected for retrieval of full texts were subjected to inclusion and exclusion criteria. After review and consensus, 30 studies were excluded and 30 studies were included for this review. The inclusion criteria were clinical, preclinical, and experimental studies of *Caesalpinia sappan*, including its active constituents and or reported dosage. The study design were Systematic review, Meta-analysis, and Quasi-experimental studies. The outcome were medicinal uses of *Caesalpinia sappan*. This research was conducted from books and academic papers published within 1998 until 2019.

RESULTS

Caesalpinia sappan L, is a medicinal plant used in Asia, especially India, China, and Southeast Asia. Heartwood of *Caesalpinia sappan* L. indicated the presence of homoisoflavonoids and phenolic such as 4-O-methylsappanol, protosappanin A, protosappanin B, protosappanin E, brazilin, brazilein, caesalpin, brazilide A, neosappanone A, caesalpin P, sappanchalcone, 3-deoxysappanone, 10 7,3',4'-trihydroxy-3-benzyl-2H-chromene, and others [5,6,7] caesalsappanins A–L, two new cassane diterpenes, designated caesalsappanin R and caesalsappanin S [8,9], 3-deoxysappanchalcone, rhamnnetin [10].

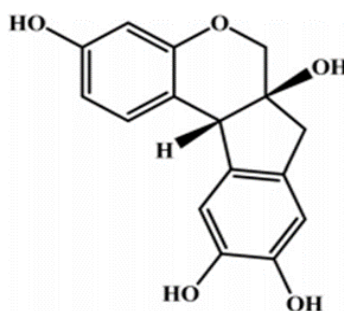


Figure 3. Chemical structure of brazilin

[(6aS,11bR)-7,11b-dihydro-6H-indeno[2,1-c] chromene-3,6a,9,10-tetrol] [11]

Caesalpinia sappan L boiled with 70°C water for 20 minutes yielded finest quality of Brazilin [12]

Redness produce by brazilin was correlated with pH level [13]

Table 2. pH level and *Caesalpinia sappan* wood appearance

pH	Color
2-5	Yellowish Orange
6-7	Light red
>7	Dark red

Based on those active constituents, *Caesalpinia sappan* L extract represents a potential treatment for oxidative stress-induced skin photoaging [14] possesses gastroprotective activity [15], kills fungus, virus, and bacteria [6,9,10,16,17,18,19], protects cardiovascular system [20,21], reduces inflammation [22,23] and blood glucose [24], inhibits human breast cancer [25,26,27,28], cures miliaria [29] and diarrhea [30].

DISCUSSION

Medicinal Use

20 studies were conducted to review medicinal uses of *Caesalpinia sappan* L. The inclusion criteria were clinical, preclinical, and experimental studies of *Caesalpinia sappan* L, including its active constituents and or reported dosage.

Antioxidant

20 µg/mL of the *Caesalpinia sappan* L extract contained 1.74–4.4 µg/mL of brazilin. Brazilin showed a DPPH free radical scavenging effect in a dose-dependent manner. Compared to L-ascorbic acid, which was used as a positive control, *Caesalpinia sappan* L extracts showed similar radical scavenging activity. *Caesalpinia sappan* L and its major compound, brazilin, scavenged UVA-induced secretions of H₂O₂ and enhanced antioxidant enzyme expression (especially that of GPX7). Moreover, *Caesalpinia sappan* L extract and brazilin exhibited protective effects against oxidative stress, as the result, this natural compound isolated from *Caesalpinia sappan* L represented a potential treatment for oxidative stress-induced skin photoaging [14].

Gastroprotective

In vitro studies showed that the hydroalcoholic extract of *Caesalpinia sappan* heartwood showed a dose-dependent cytoprotective effect against indomethacin-induced cytotoxicity and exhibited maximal cytoprotective effect with 76.82% reduction against indomethacin-induced cytotoxicity at 25 µg/ml of dose. *Caesalpinia sappan* showed 63.91% inhibition in H⁺/K⁺ ATPase inhibitory assay at the concentration 500 µg/ml.

In vivo studies using Wistar albino model was also reported. Before induced by necrotizing agents, the hydroalcoholic extract of *Caesalpinia sappan* heartwood at the dose level 250 and 500 mg/kg body weight was selected and administered orally to fasting overnight Wistar albino model. Rats that received treatment with *Caesalpinia sappan* at the dose level 500 mg/kg showed better mucosal architecture and this observation is supported by a reduction in ulcer area and no signs of hemorrhage were also observed.

Caesalpinia sappan heartwood possesses gastroprotective activity, possibly mediated through cytoprotection and antioxidant mechanisms [15].

Antibacterial

The fractionated extract from ethanol (F-EtOH) presented the strongest activities with the minimum bactericidal concentration (MBC) of 125-250 µg/mL. Killing kinetics of F-EtOH was depended on the

bacterial species and the concentration of F-EtOH. Two-fold MBC of F-EtOH could kill all tested pathogenic bacteria causing dental caries and gingivitis (*Streptococcus mutans* DMST9567, *Streptococcus mutans* DMST41283, and *Streptococcus intermedius* DMST42700). Within 12 h whereas its 4-fold MBC showed killing effect against *Streptococcus intermedius* DMST42700 within 6 h [16].

F-EtOH and brazilin were compared for inhibitory potential on the biofilms of three strains of *S. mutans*. F-EtOH showed higher effective than brazilin. The antibacterial activity of F-EtOH is according to the synergistic effects of the existing compounds including brazilin in F-EtOH [17].

Caesalsappanins R exhibited active antiplasmodial activity in vitro with IC₅₀ at 3.60 μ M. Caesalsappanins A, G, H, and I displayed antiplasmodial activities with IC₅₀ values of 7.4, 0.78, 0.52, and 2.5 μ M, respectively [9,10].

The extracted 3-deoxysappanchalcone possessed activity against both drug-susceptible and drug-resistant strains of *M. tuberculosis* at MIC₅₀ s of 3.125-12.5 μ g/mL in culture broth and MIC₅₀ s of 6.25-12.5 μ g/mL inside macrophages and pneumocytes. 3-Deoxysappanchalcone was also found to act in partial synergy with streptomycin/ethambutol against *M. tuberculosis* H37Rv. 3-Deoxysappanchalcone had no cytotoxicity against the A549 cell line up to a concentration of 100 μ g/mL (selectivity index > 8-32) [18].

Antimicrobial activity of *Caesalpinia sappan* against clinical isolates of methicillin-resistant *Staphylococcus aureus* (MRSA) and effect of *Caesalpinia sappan* extract on the invasion of MRSA to human mucosal fibroblasts (HMFs) was investigated. The MIC₉₀ and MIC range of methanol extract against MRSA are 312.5g/ml and 312.5–156.25 g/ml, respectively. MRSA invasion were notably decreased in the presence of 20–80g/ml of methanol extract of *Caesalpinia sappan* extract compared to the control group. Results reported here showed that the methanol extract of *Caesalpinia sappan* possesses antimicrobial activity, lowers the MICs of β -lactam antibiotics against MRSA, and inhibits the MRSA invasion to HMFs [19].

Antiviral

3-deoxysappanchalcone and sappanchalcone exhibited the highest activity against influenza virus (H3N2) with IC₅₀ values of 1.06 and 2.06 mg/mL, respectively, in comparison to the positive control oseltamivir acid and ribavirin with IC₅₀ values of 0.065 and 9.17 mg/mL, respectively [10].

Antifungal

B. bassiana is a harmful fungal pathogen which grows on silkworm, *Bombyx mori*. 4-O-Methylsappanol showed good activity against *B. bassiana* at a concentration of 100 mg/ml comparable to that of standard drug Dithane M-45 [6].

Cardiovascular System Protection

Application of brazilin (10–100 μ mol/L) dose-dependently relaxed the NE- or high K⁺ -induced sustained contraction of endothelium-intact aortic rings (the EC₅₀ was 83.51 \pm 5.6 and 79.79 \pm 4.57 μ mol/L, respectively). Brazilin induces relaxation in rat aortic rings via both endothelium-dependent and -independent ways as well as inhibiting NE-stimulated phosphorylation of ERK1/2 and MLC. Brazilin also attenuates vasoconstriction via blocking voltage- and receptoroperated Ca²⁺ channels [20].

0.01g of a 70% ethanol extract of *Caesalpinia sappan* L. per 20g of body weight can modulate unfavorable lipoprotein composition in hypercholesterolemic patients. Found an elevated antioxidative capacity to suppress lipid peroxidation and protein oxidation in mice fed with hypercholesterolemic diet supplemented with ethanol extract of *Caesalpinia sappan* L. This supports of ethanol extract of *Caesalpinia sappan* L. supplementation had beneficial effects in preventing human cardiovascular diseases, especially atherosclerosis, by attenuating intracellular oxidative stress and inflammation [21].

Anti-inflammation

Purified brazilin (10 mg/kg body weight) isolated from *C. sappan* reduced the arthritis index score and the extent of acute inflammatory paw edema in CIA-mice model administered intraperitoneally daily or every three days for 21 days [22].

124 mg sappanchalcone from the dried heartwood of *C. sappan* regulates the level of pro-inflammatory cytokines such as TNF- α , IL-1 β , and IL-6 in a CIA mouse model. Sappanchalcone showed anti-inflammatory effects in collagen-sensitized mice by down-regulating the pro-inflammatory serum cytokines and decreasing subsequent bone loss. Sappanchalcone can be used as an anti-inflammatory and bone protective agent for the treatment of Rheumatoid Arthritis [23].

Anti diabetic

Traditional drink made from 0,22 g of *Caesalpinia sappan* boiled with 200 ml water for 20 minutes was consumed for 28 day. Fasting blood glucose level reduction was $14,36 \pm 19,19$ mg/dl [24].

Anticancer

Brazilein induced cells death and growth inhibition of human breast cancer MCF-7 cells by downregulation of CD1 protein and mRNA expression, and which was mediated through the Akt/GSK-3b/bCatenin pathway [25]. the suppressed effect of brazilein on expression and activity of MMP-2 might be correlated with the inactivation of p38 MAPK, PI3K/Akt and NF- κ B pathway. [26] MMPs are a family of zinc-containing endopeptidases, and of these, MMP-2 and MMP-9 are highly expressed in aggressive breast tumors and are associated with poor clinical outcome.[27,28] The suppressive effect on MMP-2 expression contributes to anti-migration and invasion activity of brazilein on MDA-MB-231 cells [26].

Miliaria Therapy

In vivo study involving 40 babies with miliaria were divided into two groups: bathed with *Caesalpinia sappan* boiled water and without *Caesalpinia sappan*. The result reported that the mean curing time of babies bathed with *Caesalpinia sappan* boiled water (intervention group) was 5.75 days. However, in control group, the mean curing time was 9.80 days [29].

Astringent Agent

Tannin is an astringent agent used to treat diarrhea. *Caesalpinia sappan* boiled with water for 20 minutes yielded tannin with concentration level 0.137% [30].

Based on those medicinal uses, pharmacies could conduct further study and technology to formulate drug with active ingredients made from *Caesalpinia sappan* or its active constituents such as brazilin, brazilein, 3-deoxysappanchalcone, sappanchalcone, Caesalsappanins A, G, H, and I.

CONCLUSION

Advantage of *Caesalpinia sappan* as traditional medicine has been proved by studies mentioned above. These medicinal effects are caused by the presence of *Caesalpinia sappan*'s active ingredients such as brazilin, brazilein, 3-deoxysappanchalcone, sappanchalcone, Caesalsappanins A, G, H, and I. Further studies should be conducted to determine other active ingredients and benefits from *Caesalpinia sappan*, including formulations to be administered as modern drug.

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