Pharmacology and Phytochemistry Overview on Sauropus androgynous

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ABSTRACT
Active compounds of natural ingredients need to be extensively explored to get their properties. Sauropus androgynous is widely grown in southern Asia and Southeast Asia. The aim of this study was to provide an overview of S. androgynous profiles, pharmacological compound and their phytopharmacological activity. The method used to collect literature is the Science Direct, PubMed and Google Scholar search engines with keywords. The active compounds of S. androgynous which can be detected i.e.sauropside and some secondary metabolites i.e. alkaloids, flavonoids, phenols, terpenoids, glycosides, and some vitamins i.e. carotene, ascorbic acid and α-tocopherol. Many studies showed that S. androgynous has efficacy as an antioxidant, analgesic, anti-inflammatory, antimicrobial, antibacterial, cytotoxicity, aphrodisiac, lactation enhancer, antidiabetic and hypoglycaemic, anti-cholesterol, and wound healing activity. Further research needs to be done to make pharmaceutical preparations in the form of patent drugs with appropriate therapeutic doses.

Keywords: Katuk leaf, Pharmacology, Phytochemistry, Sauropus androgynous

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INTRODUCTION
Natural materials are alternative products to increase productivity, prevent and treat diseases worldwide. Natural materials developed into various drugs and multifunctional forms of therapy, especially for people who are not familiar with modern medicine.1 Potential natural materials have three main criteria, namely having new entities to be synthesized into alternative products, types of diseases that can be treated, and frequency of treatment.2

Katuk leaves (Sauropus androgynous) are found to be very abundant in Indonesia. Some people use S. androgynous as traditional herbal medicine and animal feed. S. androgynous can be a supplement to increase breastmilk production. Some kinds of beauty products also use S. androgynous as raw material. S. androgynous are known by the Javanese people as vegetables and food coloring. S. androgynous are only planted as home decorations on fences and courtyards, but extensification methods can be developed on special plantations.3 The aim of this study was to provide an overview of the profiles of S. androgynous, chemical compounds and their phytopharmacological actions.

HABITAT AND DISTRIBUTION
S. androgynous can grow in a humid atmosphere. It is widely found in the tropics of Southern Asia. According to the United States Department of Agriculture (USDA), released data on S. androgynous plants spread in the countries of South Asia i.e. China, India, Sri Lanka and Southeast Asia i.e. Vietnam, Indonesia, Malaysia, Papua New Guinea and Philippines.4 It is commonly known as Katuk (Indonesia), Mani Cai (China), Cekur Manis (Malaysia), Pak-Wanban (Thailand), Raungot (Vietnam), and Simani (M inangkabau). In Indonesia, it can grow with enough water and a house fence. It can grow with the ideal environment, i.e. an air temperature of 21-32°C, a relative humidity rate (RH) of 50-80% and rainfall between 750-2500 mm/year. It can decreases in the dry season more than six consecutive months. S. androgynous grows in lowlands up to 120 m above sea level and in forests as wild plants. In West Java, this plant can be found in fields with an altitude of 1300 m. Stem cuttings can be used to improve the vegetative process.5

MORPHOLOGY
S. androgynous includes clumped shrub plants with a height of 3-5 m. (Figure 1) The stem – grows tall and has a strong cambium. Can grow new branches quickly. Leaves – are small like Moringa leaves, green, have a width of 5-10 cm. Flowers – are small, dark red to yellowish, with red spots. The flower will produce white fruit in which there are black seeds.5

TAXONOMICAL CLASSIFICATION
Kingdom: Plantae  
Division: Magnoliophyta  
Class: Magnoliopsida  
Order: Malpighiales  
Family: Phyllanthaceae  
Genus: Sauropus  
Species: androgynous  
Binomial name: Sauropus androgynous.6

PHYTOCHEMICAL STUDIES
According to the Ministry of Health of the Republic of Indonesia and research on Free Radical Scavenging activity of Multivitamins, S. androgynous contains many nutrients that can be used as the human diet (Table 1).7 Based on physical analysis and spectroscopic data, S. androgynous contains a lignan diglycoside, (−)-isolariciresinol 3α,6-O-β-apiofuranosyl-(1→2)-O-β-glucopyranoside and a megastigmaene glucoside. Sauroposide (Figure 2) were isolated from the aerial part of S. androgynous.
together with (+)-isoricirsinol 3α-O-β-glucopyranoside, (-)-isoricirsinol 3α-O-β-glucopyranoside, (+)-syringaresinol di-O-β-glucopyranoside, guanosine and corchoinoside C.8

The active compound of S. androgynus has been characterized with several compounds i.e. 9, 12, 15-octadecatrienoic acid, ethyl ester, (Z, Z, Z)- (14.48%), Phytol (13.08%), Glycerin (2.52%), 1-methyl-2-pyrrolidinedinenanol (2.27%), Acetic acid (1.81%), Pent-1-en-3-one, 1-(2-furyl)-5-dimeth-yalamino (1.69%), Benzofuran, 2, 3-dihydro- (1.65%), 2-Acetylpiperydine (1.51%), 4-O-methylmannose (1.46%), N-Ethyl-2-carboxymethoxazetidine (1.43%), 9-Ethyloxy-10-oxatricyclo [7.2.1.0 (1, 6)] dodocan-1-one (1.36%), 1H-Indole, 5-fluoro- (1.30%), Hexadecanoic acid (1.18%), Oleic acid (1.18%), Heptaethylene glycol monododecyl ether (1.12%), N, N-Dimethyl-2-aminoethanol (1.05%), 2-Methoxy-4-vinylphenol (0.97%), L-Phenylalanine (0.95%), Pentaethylene glycol (0.95%), 4, 6-Di-O-methyl-α-d-galactose (0.94%), Octadecanoic acid (0.85%), Thiophene, tetrahydro-2-methyl (0.82%), 3-Hexanol, 2, 5-dimethyl (0.79%), Phenol (0.76%), Tetraacidoic acid (0.75%), Benzophenone, 3-methoxy-4′-methyl (0.75%), Ethylidenecycloheptane (0.75%), β-sitosterol (0.68%), 9, 12-Octadecadienoic acid, methyl ester, (E, E)- (0.63%), 2-pyrrolidine (0.50%), Morpholine (0.48%), N-Chloroacetyl-d-phenylalanine (0.47%), 1-butanol, 2-ethyl (0.44%), 4, 6-Di-O-methyl-α-d-galactose (0.40%).

Unidentified compounds (38.03%).9 α-Tocopherol content was evaluated used high-performance liquid chromatography (HPLC) method in S. androgynus leaves for 426.8 mg/kg edible portion.10 Secondary metabolite content i.e. alkaloids, flavonoids, phenols, terpenoids and glycosides have been evaluated contained in S. androgynus leaves.11

**PHYTOPHARMACOLOGICAL STUDIES**

**Antioxidant activity**

Antioxidants have several functions i.e. neutralize free radicals, prevent inflammatory reactions in infectious diseases, aging and degenerative diseases. Leaves function as antioxidants because the vitamin C content was relatively high around 239 mg.7 Polyphenols and flavonoids in S. androgynus extract have potential antioxidant properties and are able to treat free radical-mediated diseases. Antioxidant activity was found in 20 µg/ml flavonoid doses of S. androgynus.12 Total phenol of S. androgynus of 1.52 mg GAE/100 g was used as an alternative antioxidant. Antioxidant activity measured by ferric cyanide reducing power, DPPH (2,2-diphenyl-1-picrylhydrazyl) and ABTS (2,2′-azino-bis-(3-ethylbenzthiazoline-6-sulfonic acid) scavenging, and inhibition of linoic acid oxidation.13

**Analgesic and antipyretic and anti-inflammatory activity**

Administration of S. androgynus ethanol extract 400 mg/kg/body weight showed an anti-inflammatory effect on rat hind edema.14 Protein denaturation is the cause of the increasing rat body temperature. Increased body temperature causes fever due to inflammation and infiltration of neutrophils. These neutrophils have lysosome and anti-inflammatory activity which are found in many plants. Other lysosome derivatives including bacterial enzymes and extracellular released proteinases cause significant inflammation and tissue damage. The S. androgynus extract showed the efficacy of flavonoids and the related inhibits the release of lysosomal content from polyphenolic neutrophils and contributes significantly as an anti-inflammatory at the site of inflammation.15

S. androgynus is beneficial during the inflammatory response, pain and fever. The presence of alkaloids, steroids and terpenoids is alleged to be a counter-response to pain and fever.16 Phytoconstituent derivatives were found in S. androgynus i.e. saponins, tannins, triterpenoids and coumarin associated with Non-steroidal anti-inflammatory drugs (NSAIDs) properties. The presence of secondary metabolites from constituent derivatives can be antinociceptive and analgesic in traditional medicine.17

**Antimicrobial and antibacterial activity**

The antibacterial activity of S. androgynus leaf extract in methanol and ethanol can inhibit the growth of Bacillus cereus, Bacillus subtilis, Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae and Salmonella typhimurium. Whereas, aqueous Extract showed moderate activity against Salmonella typhimurium and Klebsiella pneumoniae.18 Methanol leaf extract S. androgynus showed a more significant inhibitory effect on gram-positive bacteria when compared with ethanol extract. Methanol leaf extract also showed a more significant inhibitory effect on gram negative bacteria when compared with ethanol and aqueous extracts.19 Antibacterial activity is supported by multivitamins and peptides, glycosides, alkaloids, saponins, terpenoids, and flavonoids.20

**Cytotoxicity**

S. androgynus was evaluated for toxic effects on the culture of human mesenchymal stem cells originating from the bone marrow (hMSCs-BM). Cell cultures were incubated for 72 hours with extract concentrations of 250-2500 mg L⁻¹. S. androgynus extract is less cytotoxic to hMSCs-BM with a dose of IC₅₀ 2450 mg L⁻¹. The mechanism of inhibiting cell viability is done through the apoptotic pathway. S. androgynus extract was shown to have a percentage of viability in hMSCs-BM cell cultures 37% to 75%.21 Cytotoxicity and genotoxicity reactions were also evaluated in studies using Chinese hamster lung (CHL) cells for 24, 48 and 72 hours. The extract dose used i.e. 250; 2500; 5000; 10000; 20000; 40000 µg/ml, respectively. Observations were made on chromosome aberration. The results showed that the lower the dose showed the higher the effect of cytotoxicity. Conversely, the higher the dose shows the lower the cytotoxic effect.22

**Aphrodisiac activity**

The effusion effect of S. androgynus leaves on libido in male rats as an aphrodisiac was measured by a libido meter. The results were obtained that orally administration effusion for 14 days was effective in increasing male libido.23
androgynous leaves contain steroid biosynthesis. These compounds were androstane-3,7-one and 3-ethyl-3-hydroxy-5-alpha, which can increase the concentration of androgen-binding protein (ABP) through increased concentrations of steroid hormones, especially testosterone in plasma.24

Lactation enhancer
S. androgynus leaf extract traditionally used by Indonesians to increase breast milk production.25 The lactation process is stimulated by increasing levels of the hormone prolactin and oxytocin.26 Vitamin A is sourced from carotenoids from S. androgynus extract. Vitamin A synthesizes retinol which reacts with fatty acids to trigger the release of the hormone prolactin. The presence of the hormone prolactin stimulates the development of secretory glands in the intralobular duct. Increased activity of secretory glands with lipids and unilocular fat tissue can prepare mammary glands before the time of let down milk.27

Antidiabetic and hypoglycaemic activity
Aqueous S. androgynus extract of 10g/200ml water used in animal models showed a decrease in blood glucose. Measurements using the glycemic index (GI) score showed a 50% decrease in activity compared to normal blood glucose.28 In another study used a dose of 250 mg/kg Body weight of ethanol S. androgynus extract can reduce blood glucose and liver glycogen in mice induced by alloxan. Decreased total cholesterol and triglycerides showed the same dose. Decreased levels of ALT, AST and ALP enzymes showed a decrease in oxidative activity in the liver.29 Alloxan acts as an insulin inhibitor secreting pancreatic cells and increases the α-glucosidase enzyme during metabolism of polysaccharides. The hypoglycemia activity of S. androgynus ethanol extract can inhibit the release of the α-glucosidase enzyme during the regeneration of pancreatic β cells.30

Anti-cholesterol activity
Administration of S. androgynous feed in a 10% diet of broiler chicken body weight can reduce carcass cholesterol levels by 58.48 mg/100 g.31 In another study used administration of S. androgynous supplementation of 90 mg/kg of diet can reduce HDL, LDL, VLDL cholesterol and atherogenic index. The alkaloid and non-alkaloid effects of S. androgynous leaves have dose dependence. Alkaloid and non-alkaloid supplementation reduces the risk of atherosclerosis indicated by a lower atherogenic index.32

Wound healing activity
Topical administration of S. androgynous 5% in incision and excision wounds can increase wound closure in albino rats. Carotenoids, thiamine, ascorbic acid, toluene and thymol are promoters of the wound healing process. Carotenoids play a role in maintaining epithelial integrity. Thiamine acts as a co-factor for collagen synthesis and the main cross-linking for wound closure. Ascorbic acid as an antioxidant is very important for collagen synthesis and prevents vitamin C deficiency. Thymol is a stimulant for wound healing and the re-epithelialization process.33

CONCLUSION
The study of literature has widely explained the efficacy of S. androgynous as traditional herbal medicine, breast milk inducer, wound healing, and antioxidants. The content of sauroposide and some secondary metabolites i.e. alkaloids, flavonoids, phenols, terpenoids, glycosides, and some vitamins i.e. carotenoids, thiamine, ascorbic acid and α-tocopherol are useful in many traditional treatments of S. androgynous extract. The simplest application of extracting simplicia was aqueous extract by boiling the leaves, flowers and seeds. Although many studies have been conducted to evaluate the efficacy of S. androgynous, further studies still need to be done to make pharmaceutical preparations in the form of patent drugs that can be used as therapy.

REFERENCES


ABBREVIATIONS
ABP: Androgen-binding protein; ABTS: 2,2′-azino-bis-(3-ethylbenzthiazoline-6-sulfonic acid; ALP: Alkaline phosphatase; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; CHL: Chinese hamster lung; DPPH: 2,2-diphenyl-1-picrylhydrazyl; GAE: Gallic acid equivalent; GI: Glycemic index; HDL: High-density lipoprotein; hMSCs-BM: Human mesenchymal stem cells originating from the bone marrow; HPLC: High-performance liquid chromatography; LDL: Low-density lipoprotein; NSAIDs: Non-steroidal anti-inflammatory drugs; RH: Relative humidity; USDA: United States department of agriculture; VLDL: Very low-density lipoprotein.
Figure 1: *S. androgynous* with leaves and flowers in the rainy season

![Image of *S. androgynous* with leaves and flowers in the rainy season]

Figure 2: Structure of Sauroposide present in *S. androgynous*

![Image of Sauroposide structure]

Table 1: Nutrition of *S. androgynous* in 100 grams of fresh ingredients

<table>
<thead>
<tr>
<th>Types of nutrients</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calories (cal)</td>
<td>59.00</td>
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<tr>
<td>Protein (g)</td>
<td>4.80</td>
</tr>
<tr>
<td>Fat (g)</td>
<td>1.00</td>
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<tr>
<td>Carbohydrate (g)</td>
<td>11.00</td>
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<tr>
<td>Calcium (mg)</td>
<td>204.00</td>
</tr>
<tr>
<td>Phosphor (mg)</td>
<td>83.00</td>
</tr>
<tr>
<td>Iron (mg)</td>
<td>2.70</td>
</tr>
<tr>
<td>Vitamin A (IU)</td>
<td>10370.00</td>
</tr>
<tr>
<td>Vitamin B1 (mg)</td>
<td>0.10</td>
</tr>
<tr>
<td>Vitamin C (mg)</td>
<td>239.00</td>
</tr>
<tr>
<td>Water (g)</td>
<td>81.00</td>
</tr>
<tr>
<td>Edible parts (%)</td>
<td>40.00</td>
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</tbody>
</table>