

## The Utilization and bioactivity of *Scrollura ferruginea* (Roxb. Ex Jack) Danser

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### Abstract

*Scurrula ferruginea* (Roxb. Ex Jack) Danser, synonymous *Loranthus ferrugineus* Roxb. Ex Jack is a type of parasite that is easy to find in Indonesia. This study aims to explain the botany, benefits and bioactivity of *S. ferruginea*. The method used in this research is a literature review obtained online, especially from Google Scholar, using the keywords *S. ferruginea* and *Loranthus ferrugineus*. The analysis data was carried out qualitatively by synthesizing all the information obtained so that the research objectives could be explained well. The *S. ferruginea* is easily recognized by its parasitic habit, young branches, dark reddish brown and "mealy" leaves with the main hosts being *Coffea*, *Melastoma*, *Pithecellobium*, and *Saurauia*. In traditional medicine, *S. ferruginea* is used to treat various diseases such as hypertension, digestive tract disorders, anti-cancer, anti-viral, antimicrobial, anti-asthmatic, anti-hyperglycemic, and analgesic. The bioactivity of *S. ferruginea* as anti-oxidant, anti-cancer, anti-microbial, anti-aging, anti-inflammatory, anti-hypertension and anti-wound. Compounds that support the antioxidant activity of *S. ferruginea* are phenolics, polyphenols and flavonoids. The use of *S. ferruginea* as an anti-cancer which is associated with its bioactivity as an antioxidant and bioactive compounds needs to be researched further so that it can be developed in the pharmaceutical industry.

**Keywords:** *Scurrula ferruginea*; Anti-cancer; Antioxidant; Phenolic

### 1. Introduction

*Benalu* is the general name used by local Indonesian people for plants that are parasitic on other plants. One type of parasite that is easy to find in Indonesia is *Scurrula ferruginea* (Roxb. Ex Jack) Danser with the name synonymous with *Loranthus ferrugineus* Roxb. ex Jack. By local people Indonesian, this species has been long used as a traditional medicine to treat various diseases. To facilitate understanding, the scientific name used in this study will be *S. ferruginea*. The discovery of new therapeutic agents from nature, especially plants, is a promising approach for the treatment of various diseases [1], making it a topic of much interest in drug discovery [2].

In taxonomy, *S. ferruginea* is one species of 900-1076 species found in the *Loranthaceae* family [3,4]. This plant is easily recognized by its parasitic habit, young branches, dark reddish brown and "mealy" leaves. The host of *S. ferruginea* such as *Coffea*, *Melastoma*, *Pithecellobium*, *Saurauia* [5], although empirically parasites in Indonesia, it appears that parasites from coffee are considered to have better properties compared to others.

*S. ferruginea* is a species of parasite belonging to the *Loranthaceae*, which grows on the branches of many deciduous trees in tropical countries [6] including Indonesia [8]. In traditional medicine *S. ferruginea* is used to treat various diseases such as hypertension [1,8,9], digestive tract disorders [1,8], anti-cancer, anti-viral, anti-microbial, anti-asthmatic, anti-hyperglycemic, and analgesics [9].

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The use of *S. ferruginea* as a traditional medicine and its bioactivity are related to its secondary metabolite content. Bioactivity of *S. ferruginea* as many studies show antioxidant activity related to phenolic compounds, flavonoids, and ascorbic acid [11]. Until now, in-depth studies on *S. ferruginea* are still very limited even though this plant has been widely used empirically. An understanding of botany, benefits and bioactivity can be used as a data base for developing *S. ferruginea* as a traditional or herbal medicine.

## 2. Methodology

The method used in this research is a literature review obtained online, especially from Google Scholar and exploration in the surrounding environment. Some of the keywords used in document searches are *Scurrula ferruginea* and *Loranthus ferrugineus*. The information obtained was synthesized to explain the botany, benefits and bioactivity of *Scurrula ferruginea*. To complete the botanical information, exploration was carried out in the surrounding environment to obtain photographs including habitus, leaves, flowers and fruit.

## 3. Results and discussion

### 3.1. Botany of *Scrullura ferruginea* (Roxb. ex Jack) Danser

*Loranthaceae* contains about 73-76 genera and about 900-1076 species. Only 3 genera out of 76 genera of *Loranthaceae* have parasitic roots and aerial branches [3,4]. The www.theplantslist records 90 scientific plant names at species level for the genus *Scurrula*, but only 10 species have been accepted [10]. In the Malesian region, this family consists of 21-23 genera and more than 200 species. The genus *Scurrula* is represented in the region by 8 species in the Malesia region [5].

Description: Shrub ca. Height 1 m, young branches and leaves with dark reddish-brown color, vertical hairs are longer and shorter, soon mealy. Branches grey, glabrous, lenticellate. The indumentum is usually long dendritic hairs visible above the shorter hairs but these sometimes disappear with age quite in groups in the young, ocher to reddish brown or very rarely darker. Leaf lamina (3-) 5-10 cm long, (1.5-) 2-5.5 cm wide; Leaf stalks are 2-6 (-10) mm long. The flower axis is usually short but up to 15 mm long; Peduncle 0.5-2.5(-4) mm long. Corolla on mature shoots (6-)8-14(-23) mm, usually strong but sometimes relatively slender and weakly club-shaped, usually straight but sometimes slightly curved, mostly obtuse to rounded or truncated at apex but sometimes very sharp.

Common and widespread in areas ranging from India, southern China and mainland Southeast Asia (Thailand, Cambodia, Laos, Vietnam, Malaya) to Singapore, Sumatra, Java, Kalimantan, the Philippines (Palawan, doubtless Luzon), Sulawesi and the Archipelago Lesser Sunda (Flores), mostly recorded at low altitudes from sea level to 1000 m. Host specificity may be very low and hosts are noted (*Coffea*, *Melastoma*, *Pithecellobium*, *Saurauia*). This species can be recognized by the combination of a relatively dark indumentum (ochre to reddish brown), with long dendritic hairs. Usually seen on shorter ones; and a crown of short to medium length (mostly 8-18 mm), usually strong, straight and blunt at the top. The color of the corolla is obscured by the indumentum externally, but the internal color varies characterized by greenish, yellowish, orange and red colors [5].



**Figure 1** *Scrullura ferruginea* (Roxb. Ex Jack) Danser parasite. A. habitus; B. Stems that support the fruit

### 3.2. Uses and Bioactivities of *Scrullura ferruginea* (Roxb. ex Jack) Danser

In traditional medicine *S. ferruginea* is used to treat various diseases such as hypertension [1,8,9], digestive tract disorders [1,8], anticancer, antiviral, antimicrobial, antiasthmatic, anti-hyperglycemic, and analgesics [9]. The use of *S. ferruginea* as a traditional medicine is related to its bioactivity. Below, the bioactivity will be further studied as anti-oxidant, anti-cancer, anti-microbial, anti-aging, anti-inflammatory, anti-hypertension and anti-wound.

### 3.3. Antioxidants

Antioxidants are compounds that can inhibit or slow down the oxidation process [12,13] which in treatment can reduce the risk of degenerative diseases [14]. In the laboratory, biological activity as an antioxidant can be tested using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) method with the standard compound ascorbic acid [1,15-17] and the test Folin Ciocalteu [1]. Compounds that support the antioxidant activity of *S. ferruginea* are phenolics [11,16], polyphenols [16], flavonoids, and ascorbic acid [11]. The phenolic content of *S. ferruginea* varies in the order stem (309,069 µg/mL) > leaves (144,217 µg/mL) > flowers (126,379 µg/mL) [1].

The use of *S. ferruginea* as an antioxidant is more prominent than other uses and is thought to be related to its use as an anti-cancer. Various experts have reported *S. ferruginea* activity as an anti-oxidant as reported by Marvibaigi et al [1], Kristiningrum et al [14], Yulian & Safrijal [17], Pratama et al [12], Juwitaningsih et al [18], Efdi et al [15], Kristiani & Kasmiyati [11], and Telaumbanua [16]. The extract of *S. ferruginea* has very strong activity as an antioxidant [1,12,17,18].

The acetone extract from *S. ferruginea* has very strong antioxidant activity with an IC<sub>50</sub> value = 48.7122 µg/mL [18], while the ethanol extract has an IC<sub>50</sub> value of 6.063 ppm [17]. Differences in the bioactivity of *S. ferruginea* extracts are related to differences in compounds extracted from various solvents. The *S. ferruginea* ethanol extract dissolved in various fractions has different contents, namely the ethyl acetate fraction (polyphenols, tannins, flavonoids, monoterpenoids, steroids, triterpenoids, quinones), fractions (polyphenols, flavonoids, monoterpenoids, sesquiterpenoids, steroids, triterpenoids) while the n fraction -hexane (steroid, triterpenoid). The ethanol extract, water fraction, ethyl acetate fraction, and n-hexane fraction showed antioxidant activity [16]. The all *S. ferruginea* organ extracts have antioxidant activity, but the activity depends on the dose of phenolic content. The highest total phenolic content was found in stem extract (309,069 µg/mL) [1].

### 3.4. Anti-Cancer

The discovery of new therapeutic agents from nature, especially plants, is one of the promising approaches for treating various diseases such as cancer [1]. The main principle in treatment is to control cancer cell division without disturbing normal cells. The methanol extract of *S. ferruginea* mediates growth inhibition of MDA-MB-231 cells through induction of apoptosis [6].

The anticancer activity test of acetone extract from *S. ferruginea* showed cytotoxic activity against HeLa cells with an IC<sub>50</sub> value = 47.62 µg/mL and for A549 cells with an IC<sub>50</sub> value = 192.83 µg/mL [18]. The cytotoxic activity on human breast cancer cell lines (MDA-MB-231) and non-cancerous human skin fibroblast cells (HSF-1184) of *S. ferruginea* extract is directly proportional to the strong antioxidant activity, as well as the high phenolic and flavonoid content [6]. Methanol extract induced increased reactive oxygen species (ROS) generation and mitochondrial depolarization in MDA-MB-231 cells, indicating strong apoptotic activity [6]. Of the three natural flavanol compounds that have been isolated from the *S. ferruginea* ethyl acetate fraction, namely quercetin and quercitrin, the flavanol glycoside 4-O-acetyl-quercitrin. Cytotoxicity evaluation on four human cancer cell lines showed quercetin to be the most active with an IC<sub>50</sub> of 35µm on U251 (human glioblastoma cells) [19].

### 3.5. Anti-Microbial

Pathogenic microbes are the cause of various infectious diseases in humans, so to control them or inhibit their growth, anti-microbial compounds are needed. On the other hand, microbial resistance to antibiotics is increasing so that the search for natural ingredients as anti-microbials continues to be carried out, including *S. ferruginea*. In research, the effectiveness of natural ingredients as anti-microbials can be compared with various standard compounds such as gentamycin, ampicillin (positive control) for *Staphylococcus aureus* and Sulphamethoxazole (positive control) for *Escherichia coli*, while for negative control Dimethyl sulfoxide can be used [2].

The acetone extract of *S. ferruginea* inhibits the growth of various types of bacteria such as *Bacillus cereus*, *Salmonella enterica*, *Propionibacterium acnes* and *Streptococcus mutans* with an inhibition zone diameter ranging from 6.2 mm - 11.1 mm [18] although this is still lower than the positive control. There was an increase in the zone of inhibition in

*Staphylococcus aureus* strains with increasing concentrations of *S. ferruginea* extract [2] (David et al 2017). The bioactivity of *S. ferruginea* as an anti-microbial is related to the content of alkaloids, flavonoid compounds, triterpenoids and tannins [18]. Further studies need to be carried out to obtain a single compound so that it can be isolated and developed in the pharmaceutical industry as an antimicrobial.

### 3.6. Anti-Aging

Various factors cause premature aging, including genetic factors, lifestyle, environment, gene mutations, damage to the immune system and free radicals [13]. Skin is an easily visible indicator of the aging process. Exposure to ultraviolet light is the main negative impact on human skin such as aging, sunburn, pigmentation, wrinkles and skin cancer [20]. One of the best ways to protect the skin from UV rays is to use sunscreen [20].

Lotion containing *S. ferruginea* extract subfractions has a sun protection factor (SPF) value of  $32.270 \pm 0.227$  to  $38.171 \pm 0.440$  at a concentration of 2% - 12% [20]. Providing a gel preparation containing *S. ferruginea* ethanol extract from coffee mistletoe at 4% can result in the best skin recovery and is able to increase water content from dry to normal, reduce skin hardness from normal to smooth, shrink pores from large to small, reduce blemishes from many blemishes become few blemishes, reducing wrinkles [13].

### 3.7. Anti-Inflammatory

The *S. ferruginea* is widely used as a herbal medicine to treat inflammation, rheumatism and stroke [21]. Anti-inflammatory activity can be tested assessed through inhibition of nitric oxide (NO) production in lipopolysaccharide (LPS) and interferon- $\gamma$  (IFN- $\gamma$ )-induced RAW 264.7 macrophage cells [21,22]. Aqueous extract of freeze-dried *S. ferruginea* stem samples inhibited IL-1 $\beta$  protein production along with down-regulation of iNOS and IL-1 $\beta$  mRNA expression. In addition, the extract significantly suppressed the release of IL-6 and IL-10 proteins in a concentration-dependent manner. Bioactivity of *S. ferruginea* as anti-inflammatory associated with inhibition of iNOS and IL-1 $\beta$  mRNA expression, creation of NO, IL-1 $\beta$ , IL-6, IL-10, and production of TNF- $\alpha$  protein [21]. Anti-inflammatory bioactivity may be related to the presence of choline, isoleucine, catechin, leucine, and chlorogenic acid [22].

### 3.8. Anti-Hypertension

Traditionally, *S. ferruginea* herb is used to treat high blood pressure [8,23,24]. The vasodilation is one mechanism that may explain its use in the management of hypertension [25]. The methanol extract of *S. ferruginea* antagonized and modulated norepinephrine-induced vasoconstriction investigated in rat aortic rings [26].

The butanol fraction of *S. ferruginea* methanol extract (SFME) was found to be the most active in blood pressure lowering activity in experimental animals (rats, pigs, guinea pigs) [25]. The butanol fraction of *S. ferruginea* methanol extract ( $1.0 \times 10^{-5}$  to 3.0 mg/ml) to be the most potent for relaxing previously contracted endothelium intact phenylephrine (1  $\mu$ M) and high K<sup>+</sup> (80 mM) ring rat aorta [24]. The butanol fraction of *S. ferruginea* methanol extract induces vascular relaxation by stimulating muscarinic receptors, activating the endothelium-derived nitric oxide-cGMP relaxant pathway, promoting prostacyclin release and/or possibly through its ability to prolong the half-life of released nitric oxide [24].

The SFME has a marked hypotensive effect that can be attributed to stimulation of muscarinic receptors and/or stimulation of NO release [23]. The SFME contains several biologically active substances that produce a dose-dependent blood pressure lowering effect [25]. Similar to verapamil and papaverine, *S. ferruginea* extract produced a rightward shift in the log norepinephrine concentration response curve and a significant decrease in the maximum response. The methanol extract of *S. ferruginea* exerts its vascular effects by reversible noncompetitive antagonism of norepinephrine-induced vasoconstriction [26].

### 3.9. Anti-Wound

Wounds are one of the entry points for pathogenic microorganisms into the body. In general, wounds are divided into cuts and burns. Burns are damage or loss that can be caused by heat (fire, hot liquid/fat, hot steam), radiation, electricity, chemistry [27], while cuts are a form of damage to the skin epithelium or disruption of the normal anatomical structure. in tissue due to trauma caused by sharp objects [28].

The leaf extract of *S. ferruginea* has an effect as a medicine for cuts with the best concentration, namely at a concentration of 10%, but does not exceed the effectiveness of the positive control (betadine ointment) [28]. The effect of mistletoe ethanol extract as a medicine for burns with the best concentration is at a concentration of 15% but does not exceed the effectiveness of the positive control (Bioplacenton gel) [27]. The *S. ferruginea* contains flavonoids,

tannins, saponins, alkaloids, phenols which have benefits as medicine for cut wounds [28]. Almost the same thing was stated by Syahrial [27] that mistletoe coffee leaves have secondary metabolite compounds such as flavonoids, tannins, saponins, alkaloids, phenolics which play a role in producing burn healing effects.

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#### 4. Conclusion

- The characteristics of *S. ferruginea* are easily recognized from its parasitic habit, young branches, leaves with a dark reddish brown and "mealy".
- The *S. ferruginea* is used to treat various diseases such as hypertension, digestive tract disorders, anticancer, antiviral, antimicrobial, antiasthmatic, anti-hyperglycemic, and analgesic.
- Bioactivity of *S. ferruginea* is anti-oxidant, anti-cancer, anti-microbial, anti-aging, anti-inflammatory, anti-hypertension and anti-wound

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#### Compliance with ethical standards

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##### *Disclosure of conflict of interest*

There is no conflict of interest in this manuscript.

##### *Statement of ethical approval*

There is no animal/human subject involvement in this manuscript.

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