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Utilization and bioactivity of *Ketepeng cina* (*Senna alata* (L.) Roxb.)

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Abstract

Senna alata (Fabaceae) has been long used by local people in Indonesia and other countries to treat various skin infections. This study aims to explain the relationship between the benefits and bioactivity of *S. alata*. The method used is library research on various research results published online at Google Scholar using the keywords *Senna alata* , uses of *S. alata* and *S. alata* bioactivity. The results obtained were synthesized to provide comprehensive information on the botanical, benefits and bioactivity of *S. alata*. Traditionally, *S. alata* is used to cure typhoid, diabetes, malaria, asthma, ringworm, skin infections, scabies, blotches, herpes, and eczema. The *S. alata* has bioactivity as anti-microbial, anti-cancer, antidiabetic mellitus and abortion, but its use as an antimicrobial is more prominent, so it has the potential to be developed as a drug to treat skin disease. The bioactivity of *S. alata* as an antimicrobial is related to the content of its secondary metabolites, especially anthraquinones, which be used as a compound to standardize the quality of *S. alata* raw materials.

Keywords: *Senna alata*; Antimicrobial; Atraquinone; Timur

1. Introduction

Ketepeng cina or *Senna alata* is a species of the Fabaceae family that has long been used as traditional medicine, especially for skin [1]. This plant is easily found in various landscapes in Indonesia such as yards, roadsides, and neglected land. The flower of *S. alata* have beautiful characteristics so they are often used as ornamental plants. In 2021, several mass media in Indonesia reported that *S. alata* leaves have good prospects as an economic commodity and have been exported abroad as medicinal ingredients.

Empirically, it can be seen that the use of plants as traditional medicine is often doubted due to the lack of scientific information about *S. alata* in a comprehensive manner, especially in Indonesian. From various scientific reports, it was found that *S. alata* has long been used to treat various skin disorders in various Asian and African countries and has been registered as herbal medicine in Thailand [2] and has been developed as an agent to treat topical fungal skin infections [2,3]. Oladeji et al [4] also reported that it is also used for the treatment of typhoid, diabetes, malaria, asthma, ringworm, tinea infections, scabies, blotch, herpes, and eczema.

The use of *S. alata* in traditional medicine is related to its bioactivity, including antibacterial, antioxidant, antifungal [4,5] dermatophyte, anticancer, hepatoprotective, anti-lipogenic, anti-convulsant, anti-diabetic, anti-hyperlipidemic, anti-malarial, anti-helmintic, and anti-viral [4] and anti-inflammatory [5]. If further traced the bioactivity of *S. alata* as an antimicrobial (bacteria and fungi) is more prominent than the others, this is a very good potential to overcome various infections. Ehiowemwenguan et al [6] stated that drug-resistant microorganisms are a threat to public health, therefore the exploration of natural ingredients as antimicrobials needs to be continued.

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Plant bioactivity is related to the content of its secondary metabolites. The kaempferol of *S. alata* showed strong activity anti bacteria [7], while anthraquinone has activity as antifungal [3]. On the other hand, various secondary metabolites of *S. alata* can be toxic so that their use needs to be careful. The *S. alata* contains anti-nutrients such as oxalate, cyanide and phytate in the leaves and root bark, but its toxicity is low [8]. Alkaloids of *S. alata* can cause abortion [9, 10] while conanine and coniceine toxic so that it can cause death in animals and humans [11]. Therefore, it is necessary to conduct an in-depth study of the bioactivity and utilization of *S. alata*.

2. Methods

The method used in writing this study is a research library obtained online on the results of research on *S. alata*. The main source of information comes from Google scholar using several keywords, namely *S. alata*, uses of *S. alata* and bioactivity of *S. alata*. The information obtained was synthesized so as to explain the botany, benefits and bioactivity of *S. alata* in a comprehensive manner. To complete the data, especially the botanical description and exploration of the surrounding environment.

3. Results and discussion

3.1. Botany of *Senna alata* (L.) Roxb.

Senna Mill. is a genus which widespread has diversity of habits such as herbs, shrubs, small trees, tall trees and lianas. This genus consists of 350 species and about 80% of its species inhabit in the America, tropical Africa, Madagascar and Australia, and only a few species live in Southeast Asia and the Pacific Islands [12,13]. The type Senna were formerly included in *Cassia* L. s.l. [14]. The taxonomic treatments are further divided: *Cassia* s.l. into three distinct genera, namely, *Cassia* s. str., *Chamaecrista* Moench and *Senna* Mill. [12].

Description: *S. alata* is a shrub with a height of up to 3 m. The stem is spherical in shape and has a sympodial branching system. The leaves are even pinnate compound leaves (Figure 1A) which are oblong to breech oval in shape. The size of the leaflets are stiff with a length of 5-15 cm, a width of 2.5-9 cm, the tip of the leaf is blunt with a pointed leaf base and the leaf edge is flat. The leaf veins are pinnate with short leaf stalks ± 2 cm long and green. Flowers are compound flowers arranged in long and upright stems located at the ends of the branches with bright yellow flower crowns (Figure 1C). The fruit is in the form of flat, rectangular pods with a length of ± 18 cm and a width of ± 2.5 cm and is black. The fruit has wings on both sides with a length of 10 – 20 mm and a width of 12 – 15 mm (Figure 1C). The fruit is ripe, then on both sides it will open or break so that the seeds contained in the pod will be thrown out. Seeds owned are triangular in shape and flattened, totaling 50-70 seeds in each pod [12,14].

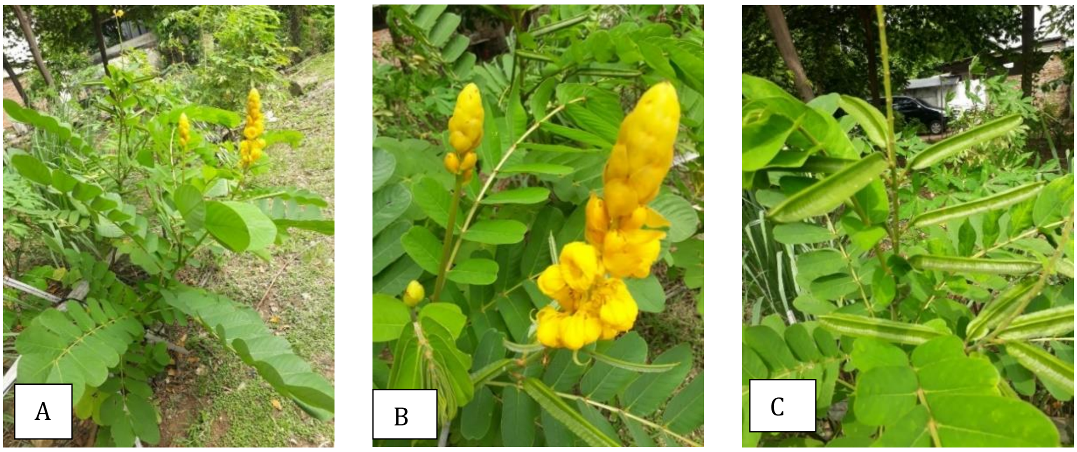

Figure 1 *Senna alata*. A. Habitus with compound leaves, B. Flower bunches with yellow crowns, C. Winged pods

3.2. Uses and Bioactivities

Senna alata has long been used as a traditional medicine, especially to treat skin disorders. In traditional medicine, *S. alata* has long been used in traditional medicine to treat typhoid, diabetes, malaria, asthma, ringworm, tinea infections, scabies, blotch, herpes, eczema [4], skin disease, arthritis, high blood pressure, and laxatives or laxatives [8]. The use of *S. alata* as a traditional medicine is related to its bioactivity. The following will explain in more detail the bioactivities of *S. alata* as an anti-microbial, anti-cancer, anti-obesity, anti-diabetes mellitus and abortion.

3.3. Anti-Microbial

The bioactivity of *S. alata* as an antimicrobial is more prominent than other bioactivities, in line with its use to treat various skin disorders such as ringworm and rash, eczema, and itching. When explored further, it turns out that the use of *S. alata* leaves to treat skin disorders has long been embedded in various local wisdoms in various countries in Asia and Africa. *Senna alata* has been used for a long time for the treatment of tinea versicolor and ringworm infections in Thailand [2]. In the Philippines, clinical trials have also confirmed the usefulness of *S. alata* as a topical agent in treating fungal skin infections [3]. In Cameroon, *S. alata* is used for the treatment of several infections including: gonorrhea, gastro-intestinal and skin diseases [15]. *Senna alata* is used to treat ringworm, scabies, and boils, swelling and inflammatory conditions, skin parasites [16].

Saidina et al [17] stated that *S. alata* extract has the potential to be developed as an ointment to protect skin infections. Purified *S. alata* flower extract was almost as potent as standard antibiotics, showing zones of bacterial growth against multiple antibiotic-resistant local isolates that were not susceptible to methicillin, penicillin, and streptomycin [18]. Oyedele et al [19] reported that *S. alata* leaf extract exhibits antimicrobial properties that promise to be useful for the treatment of topical infections. Antiseptic herbal soap containing a combination of methanolic dry leaf extract of *S. alata* and *Eugenia uniflora* showed antimicrobial activity against *Staphylococcus aureus* and *Candida albicans* comparable to a comparison commercial antiseptic soap containing 0.30% triclosan [19].

Thw fungi was inhibited by *S. alata*, such as: *C. albicans*, *Aspergillus niger* [2,6], *Microsporum canslaslomyces, Trichophyton verrucosum, T. mentagrophytes, Epidermophyton floccosum* [19], *Penicillium spp., Trichophyton spp., Rhizopus spp.* [20], *Geotricum candidum, C. utilis, Aspergillus brevipes, Penicillium sp.* [21] *A. flavus and Cryptococcus neoformans* [6]. *Various types of bacteria were reported to be stunted by the addition of various extracts of S. alata, namely S. aureus* [22], *Vibrio cholerae, Shigella flexneri* [15], *Escherichia coli, Proteus mirabilis, Pseudomonas aeruginosa, Stretococcus pyogenes and S. aureus, Salmonella typhi* [6], *S. aureus, Bacillus subtilis, Micrococcus luteus, and Pseudomonas putida* [23].

The antimicrobial activity of *S. alata* was influenced by various factors including the organ used, the extraction compound, and the concentration. The mechanism of antibacterial activity of *S. alata* involves leakage of potassium ions and proteins [23]. Crude bark extract of *S. alata* showed higher inhibition of *T. verrucosum* and *E. floccosum* compared to *M. canslaslomyces* [19]. Ethanol extract of *S. alata* leaves inhibited the growth of *S. aureus*, but did not inhibit *E. coli* [22].

The antimicrobial bioactivity is related to its secondary metabolites. The compound anthraquinones [3], tannins, steroids, alkaloids, anthraquinones, terpenes and saponins [20,24] is the main compound responsible for the antifungal activity [3]. Anthraquinone aglycans are compounds that inhibit the growth of *C. albicans* [2]. Kaempferol inhibited the growth of *P. aeruginosa* [7], luteolin and aloeemodin showed the highest antibacterial activity against drug-resistant *V. cholerae* and *S. flexneri* [15]. The bioactivity of *S. alata* leaves as a natural antibacterial source is due to the presence of flavonoid and anthraquinone compounds [15]. Aqueous, acetone and methanol extracts of the roots and leaves of *S. alata* were most susceptible to *Streptococcus pyogenes* and *S. aureus*, followed by *S. typhi* and *E. coli*. The fungi that were most susceptible to *S. alata* leaf extract were *Cryptococcus neoformans* and *C. albicans* while the most susceptible is *A. flavus* [6].

3.4. Anti-Cancer

Cancer is one of the leading causes of human death due to uncontrolled cell growth. Plants used by humans as anti-cancer are plants that produce compounds that can inhibit the growth of cancer cells but do not interfere with normal cell growth. The *S. alata* leaf extract showed antitumor activity on various cancer cell lines. The use of *S. alata* as anti-cancer has been reported by various researchers including: Kittiwattanokhun et al [5] and Chahardehi et al [1]. Reports on the potential of *S. alata* as an anti-cancer will add alternative types for the development of cancer drugs. Chahardehi et al [1] reported that 80% ethanol extract and *S. alata* and their fractions had a cytotoxic effect on breast cancer (MCF-7).

The addition of *S. alata* extract in cancer cells showed a decrease in the expression of matrix metalloproteinases (MMP-2) and MMP-9 and an increase in the expression of metalloproteinase inhibitors (TIMP-1) and TIMP-2. The extract of *S. alata* also suppressed phosphorylation of ERK1/2, p38 and Akt and decreased expression of the transcription factor NF-B in SW1353 cells. The *S. alata* extract could reduce MMP-2 and MMP-9 expression by downregulating NF-B downstream of MAPKs and the PI3K/Akt signaling pathway in SW1353 cells resulting in reduced migration and invasion of cancer cells [5].

3.5. Anti-Diabetes Mellitus

Diabetes mellitus (DM) is a metabolic disorder that causes glucose levels to be above normal. Diabetes mellitus is a chronic disease that affects the normal metabolic pathways in several organs [25]. Until now, the management of oxidative stress is a big challenge because it is associated with various types of diseases, including diabetes mellitus. Sugumar et al [26] stated that tissue damage due to oxidative stress is thought to be the main cause of diabetes mellitus and its complications. Glibenclamide is one of the trademarks of synthetic drugs used to treat DM. Although there are many trademarks for DM drugs, the use of natural ingredients is considered to have lower side effects, therefore the use of exploration continues to be carried out, including *S. alata*.

The potential and utilization of *S. alata* for DM have been reported by Sugumar et al [26], Mohanasundaram et al [25], Kazeem et al [27]. Diabetic rats induced with alloxan were then given the ethanolic extract of the leaves of *S. alata*, which had anti-diabetes mellitus activity with no significant difference with insulin [28]. Liver and kidney-based antioxidant enzyme activity was significantly responsive to treatment in diabetic rats [26]. One of the antidiabetic action mechanisms of *S. alata* leaves is the inhibition of intestinal α-glucosidase [27]. Administration of *S. alata* also in diabetic rats showed a change in typical biochemical parameters associated with DM such as protein, urea, uric acid, and creatinine levels from abnormal to normal in control rats and diabetic induced rats [26]. It was further reported that administration of *S. alata* leaves to DM rats increased vitamin E, catalase, glutathione peroxidase and glutathione-s-transferase and decreased vitamin C and glutathione levels [26]. The same thing was also reported by Mohanasundaram et al [25] that oral administration of *S. alata* extract (400 mg/kg body weight) in DM rats decreased the level of glycogenolytic factors including: glycogen phosphorylase, glucose 6 phosphatase, glycosylated hemoglobin, and lactate. dehydrogenase, and a significant increase in the levels of glycogenic factors such as plasma insulin, glycogen synthase, liver glycogen, hexokinase, pyruvate kinase returned to near-normal levels. In addition, *S. alata* extract increased muscle and liver glycogen levels, exhibiting anti-diabetic properties.

The bioactivity of the extract of *S. alata* as a DM drug varies greatly depending on the solvent. The acetone extract of *S. alata* showed the highest inhibitory activity against α-amylase (IC50 = 6.41 mg/mL) while the hexane extract showed the highest inhibitory effect on α-glucosidase (IC50 = 0.85 mg/mL) in hyperglycemic rats. Both acetone and hexane extracts of *S. alata* inhibited α-amylase and α-glucosidase competitively and uncompetitively, respectively [27]. The bioactivity of *S. alata* to treat DM is related to the content of its secondary metabolites such as kaempferol, 3-oegentiobioside, phytol, stigmasterol, sitosterol, and octanoic acid derivatives [25].

3.6. Anti-Obesity

Obesity is excess weight that directly or indirectly affects health. Male mice fed a high-fat diet (45 kcal% fat) for 12 weeks, then at 7 week the diet was fed with aqueous extract of *S. alata* leaves (concentrations 250 and 500 mg/kg/day) showed a significant decrease in levels of high blood glucose and decreased serum insulin and leptin levels [29]. The administration of *S. alata* water extract also reduced total serum cholesterol, triglycerides, non-esterified fatty acids, and triglyceride levels. Hepatic lipogenic gene expression showed that *S. alata* decreased the binding activity of the sterol regulatory element protein 1c, fatty acid synthase, and acetyl-CoA carboxylase [29].

The *S. alata* has an anti-lipogenic effect on high-fat diet-induced obesity (HFD) mice [30]. Treatment with *S. alata* (250 and 500 mg/kg) significantly reduced hyperglycemia, hyperinsulinemia, and hyperleptinemia. Glucose intolerance corrected by *S. alata*. Elevated monocyte chemoattractant protein-1 (MCP-1) and tumor necrosis factor-α (TNF-α) levels in obese mice were reduced in the treatment of *S. alata*. Compared with obese control mice, mice treated with *S. alata* showed significantly increased reductions in hepatic glucose-6-phosphatase (G6Pase) and protein phosphoenolpyruvate carboxykinase (PEPCK). The *S. alata* regulates phosphorylated hepatic and muscle adenosine monophosphate-activated protein kinase (pAMPK) and muscle glucose transporter 4 (GLUT4). The results suggest that the restoration of impaired glucose metabolism of *S. alata* may be associated with decreased hepatic gluconeogenesis and increased glucose uptake through AMPK activation [29].

3.7. Abortion

Abortion is a procedure performed to intentionally terminate a pregnancy before the fetus can live outside the womb. The bioactivity of *S. alata* as an abortion has been reported by Yakubu and Musa [9] and Yakubu et al [10], therefore its use, especially in pregnant people, must be careful. The *S. alata* extract administered to pregnant rats (250, 500 and 1,000 mg/kg body weight) significantly reduced the number of live fetuses, body weight and fetal survival ratio [10]. Twenty-four pregnant rats given the alkaloids extracted from *S. alata* orally (250, 500 and 1000 mg/kg bw) showed fetal death. Alkaloids from the leaves of *S. alata* showed anti-implantation, anti-gonadotropic activity, anti-progesterone, embryonic resorptive, feto-maternal toxic [12] (Yakubu and Musa 2012). The *S. alata* leaves in "washing the uterus". The abortifacient properties were most pronounced at 500 and 1,000 mg/kg bw extract and were similar to animals treated with 2.85 mg/kg body weight mifepristone. The extract of *S. alata* showed positive results for saponins, flavonoids, cardiac glycosides, cardenolides and dienolides, phenolics and alkaloids [9].

4. Conclusion

Traditionally, *Senna alata* is used in the treatment of typhoid, diabetes, malaria, asthma, ringworm, tinea infections, scabies, blotch, herpes, and eczema. The *S. alata* has bioactivity as anti-microbial, anti-cancer, antidiabetic mellitus and abortion, but its use as an antimicrobial is more prominent than others, so it has the potential to be developed as a drug to treat various skin disorders.

Compliance with ethical standards

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