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Therapeutic potential and traditional uses of *Sauropus androgynous:* A review

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Abstract
Plants have been well documented for their medicinal uses for thousands of years and traditional medicines are still major part of habitual treatments of different maladies. Until recently, a large number of medicinal plants have been subjected to chemical investigations and this has led to isolation of pure bioactive molecules which have been pharmacologically evaluated. As a result, new drugs have been discovered. Interestingly *Sauropus androgynous* herb is highly valued due to its high nutritive value and inexpensive source of dietary protein which is also used in traditional medicine. The present review provides updated information about its traditional and pharmacological uses.

Keywords: Therapeutic potential, traditional use, pharmacological use

Introduction
In the recent past, focus on food-plant research has increased many folds all over the world and experts are of the opinion that nutrition will become the primary treatment modality in the 21st century [1]. A significant amount of such studies to date has demonstrated the protective potentials of plant-based diets against a number of modern ailments. These include the leading clinical and public health issues in the developed countries and perhaps in the rest of the world too, namely, cardiovascular and neurodegenerative diseases, carcinogenesis and diabetes, which may be attributed predominantly to their antioxidant property. In recent years, there has been growing interest in alternative therapies and the therapeutic use of natural products; especially those derived from plants.Plants have developed survival and defense mechanisms in response to environmental stressors, pathogen-attack, competing-plants and herbivores [2]. This protection may be either mechanical or chemical in nature and the later is the result of the synthesis of the non-nutritive/antinutritive plant secondary metabolites.
The dietary antioxidant micronutrients accumulated in fresh fruits and vegetables, particularly the leafy-vegetables, promote good-health by assisting in preventing cancer and high blood pressure, stimulating the immune system, improving drug metabolism and tissue regeneration. There are approximately 40 vitamins and minerals, which are considered essential for physical and mental development, immune system and metabolic processes. These are essentially acquired only through diet. It is estimated that up to 70 000 plant species are used in folk medicine and a vast majority of these species are found in the Asia-Pacific region [3]. One of the most popular functional leafy-vegetables of South and Southeast Asia is *Sauropus androgynus* [4], which has, in addition, gained popularity as a commodity of commerce [5]. The leaves and succulent young tips of the plant reportedly possess a pleasant taste, similar to fresh garden peas and slightly nutty. They are normally eaten like tropical asparagus, raw in the form of either salads or steamed, or alternatively added to stir-fry, rice and egg dishes, soups or casseroles.

Systematic position of Sauropus androgynous
Kingdom: Plantae
Division: Magnoliophyta
Class: Magnoliopsida
Order: Malpighiales/Euphorbiales.
Family: Phyllanthaceae/Euphorbiaceae
Genus: Sauropus
Species: androgynous.

Parts used
Whole plant including, tender leaves, shoot tips, flowers, immature fruits and roots.

Table 1: Vernacular names of *S. androgynous*

Language/Country	Local name (Ethnic group/Location)
English	Star gooseberry, sweet-leaf bush, sweet-leaf sauropus, sweet shoot, Chinese malunggay, Japanese Malungay, multivitamin green, multivitamin plant
Khmer (Cambodian)	Dom nghob, ngub
Chinese	Mani cai, Shou gong mu (Guangdong), Shu zai cai (Haina), yue nan cai (Guangxi)
Indonesia	Daun katuk (Sundanese), babing (Javanese), simani (Minangkabau)
Japanese	Ruridama-no-ki
Laos	Hvaan baanz
Malaysia	Katuk, sayur manis, asin-asin, cekur manis, chekup manis, cekok manis, pucuk manis, changkok manis (Peninsular), cangkok manis (Iban, Malay, Melanau)
Myanmar	Yo-ma-hin-yo
Philippines (Tagalog)	Binahian
Sri Lanka	Mella-dum-kola, Japan batu, Japanbatu kola
Spanish	Katuk
Thailand	Phak waan baan (General), pak waan (pak-wanban), kaan tong (Northern), ma yom paa (Prachuap Khiri Khan)
Vietnamese	Rau ngot, bu ngot (bo ngot), rau tuot, hum ngot, phac ot (Thai)
Indian States	–
Andaman & Nicobar Islands	Chakrmani
Assamese (Assam)	Bari sundari
Bengali (W. Bengal)	Chakurmani
Khasi (Meghalaya)	Dieng soh pit
Kannada (Karnataka)	Chakrani beru, Chinese soppu Lepcha (Sikkim) Sengtungrung
Malayalam (Kerala)	Malay cheera, elacheera (Muthuvan tribes of Idukki district)
Tamil (Tamil Nadu)	Thavasai murungai (thavasimurungai)

***Sauropus androgynous* (SA), also called star gooseberry**, is a tropical shrub grown as a leafy vegetable. It is from Euphorbiaceae family. In Malaysia, it is named as cekormanis or katuk. The Indian, Indonesian, and Thai names of SA are Chakrmani, Katu, and Phak Wan Ban, respectively. The plant is known to be introduced from Malaya to India [6]. The tree of SA can grow up to 3 m in height, and the leaves are oblong in shape. The leaves are typically 2-6 cm long and 1-3 cm wide, the top and bottom of the leaves are dark green and lighter green, respectively. SA leaves are commonly known as sweet leaves due to the sweet taste of the leaves after cooking. The leaves are a typical Indian vegetable dish. The physicochemical properties of SA leaves have been reported [7]. The leaves contained 4.28% total ash, 0.81% acid insoluble ash, 1.24% water insoluble ash, and 3.42% sulphated ash; the solvent extractable yields were 24.1% for methanol, 9.67% for chloroform, 17.4% for benzene, 13.3% for petroleum ether, and 20.6% for water. Besides that, the swelling factor of the leaf powder was 9 ml.

Vitamin composition of leaves of *Sauropus androgynus*

Vitamin Quantity	(mg/100 g)
Vitamin C (Ascorbic acid)	298.32±0.34
Vitamin B2 (Riboflavin)	0.25±0.22
Vitamin B1 (Thiamine)	0.43±0.25

(Values are Means±SD calculated as mg/100 g dry weight (DW) for *Sauropus androgynus* analyzed individually in triplicate)

Phytochemical investigation of the leaves of *S.androgynus* reveals they contained sterols, resins, tannins, saponins, alkaloids, flavonoids, terpenoids, glycosides, phenols, catechol, cardiac glycosides, and acidic compounds [8]. Previously, preliminary phytochemical screening on the leaves of *S. androgynus*, showed polyphenols, anthocyanins, carotenoids, ascorbic acids, and tannins [9]. Further phytochemical studies [10] suggested that the leaf ethanol and aqueous extracts of *S.androgynus* contain tannins, saponins, flavonoids, terpenoids, phenolics, steroids, and alkaloids. These preliminary phytochemical studies suggested that *S. androgynus* contains a wide range of biomolecules constituents that might contribute to its medicinal, toxic, and antioxidant properties. Six compounds were isolated (three nucleosides, two flavonol diosides, and one compound flavonol trioside) based on spectral analysis from butanol extract of *S. androgynus* leaves [11]. One of the novel isolated compounds, known as 3-O-β-D-glucosyl-(1-6)-β-D-glucosyl-kaempferol (GGK), was reported to have a high potential as an antiobesity agent [12]. A study elucidated and identified seven bioactive compounds from the methanolic extract of the aerial part of *S.androgynus*, including three lignan glycosides, a lignin diglycoside, a megastigmane glucoside, and a megastigmane glucoside compound [13]. *S. androgynus* leaves were found to have highest content of flavonoids and bioactive compounds among 11 vegetables from Indonesia with 142.64mg per 100 gram of freshweight with quercetin, myricetin, luteolin, apigenin, and kaempferol which were detected by HPLC analysis [14, 15]. Further, phenolic acids such as chlorogenic acid, caffeic acid, and ferulic acid were also identified in their study. occurrences of phytol and squalene in ethanolic extract of *S.androgynus* using gas chromatography-mass spectrometry (GC-MS) analysis were also found [16]. Further analysis on ethanolic *S. androgynus* leaves extract by GCMS discovered nine compounds withmedicinal functionality such as antimicrobial, anti-inflammatory, antioxidant, and anticancer properties [8].

Table 2: Nutritional composition of *Sauropus androgynus* (SA) leaves.

Composition	India [18]	India [19]	India* [17]	Thailand* [20]	Thailand* [22]	Indonesia [21]	Indonesia* [27, 23]	Vietnam [24]	Malaysia [25]
Energy (kcal)	-	28.0	-	40.4	317	401.4	-	-	100.5
Moisture (%)	69.9	88.0	85.4	88.5	89.9	-	82.9g	86.9	79.4
Protein (%)	7.4	3.4	5.3	4.2	15.8	29.2	8.31h	-	7.6

Carbohydrate (%)	-	0.5	-	3.9	54.5	-	-	-	6.9
Fat (%)	1.1	1.4	0.6	0.9	4.0	4.6	-	-	1.8
Fiber (%)	1.8	1.7	1.8	1.2	36.0	8.2	-	-	1.9
Ash (%)	-	-	5.3	1.4	12.9	12.1	-	1.4	2.0

Footnote: * indicates the data have been reported in the review article by Petrus [26]. For the samples obtained from Thailand [22] and Indonesia [21]; the compositions are expressed as % dry weight (DW) excluding the moisture content.

Uses

Traditional uses for the treatment of diseases:

Genito-urinary diseases: The roots of *Sauropus androgynous*, have diuretic properties which is being taken advantage of by some traditional practitioners to treat various urinary complaints. Amongst the diseases treated include, symptomatic relieve of dysuria.

Cardiovascular diseases: Again the roots are used in the treatment of cardiovascular disease or symptoms of this group of diseases including vertigo, dizziness, fainting spells. It is also being recommended to those with hypertension.

Antiobesity: The leaf extract of *Sauropus androgynous* was used for body weight reduction. Its popularity as a "Slimming agent" was high in Asian countries specifically in Taiwan, Malaysia, etc., in mid 90's. In America, since 1995, Sauropus androgynous leaves fries, salads and beverages were consumed by many people as drug antiobesitas (body slimming).

Other uses

- The leaves are given to women after delivery to allow post partum recovery and to enhance lactation in feeding mothers. The enhancement in the breast milk production probably derived from the hormonal effects of chemical compounds that are estrogenic sterols.
- The leaf juice is used to treat cholecystosis, diorrhea and other forms of fever, rhinosis.
- Decoction of the leaves and roots is remedy for epitaxis and oriental sores.
- Another application of the leaves is for oral thrush in infants. Paste of the leaves is applied over nasal ulcers and yaws, erythrema and measles.
- Juice extracted from the leaves is used as an eye lotion for eye complaints.
- Leaves are used as cattle and poultry feed.
- Planted as a live fence in home gardens.

Pharmacological uses

Antioxidant Activity

The effect of antioxidants on DPPH radical scavenging is thought to be due to their hydrogen-donating ability. DPPH is a stable free radical and accepts an electron or hydrogen radical to become a stable diamagnetic molecule [28] study revealed that *S. androgynus* leaves possess a high total phenolic content and antioxidant activities. Based on the electron transfer reaction assays, *S.androgynus* leaves contained higher antioxidant activities than many other leafy vegetables of Indonesian origin [29]. A previous study on antioxidant activities on aqueous extracts of 25 tropical plants showed that *S. androgynus* has a high polyphenol content, cupric ion chelating activities, free radical scavenging and reducing ferric ion antioxidant properties [30]. The leaves have containing bioactive antioxidants, such as carotenoids, flavonoids and other phytochemicals. These phytochemicals can reduce oxidative stress, thus reduce the risk of some chronic diseases [29].

Several studies reported positive antioxidant activity of *S. androgynus* [31, 32, 33]. A study conducted [32] implies potential of this herb to become a strong antioxidant agent. This plant was found to have highest flavonoid content among 11 vegetables of Indonesian origin. Another experiment done [33] used methanol extracts of this herb using several *in vitro* free radical-scavenging assays. The study found that *S. androgynus* has IC50 value of 341 μg/mL, 12.58 μg/mL, and 228.75 μg/mL using DPPH radicals, ABTS cation radicals, and inhibition of lipid peroxidation, respectively.

A previous study on antioxidant activities on aqueous extracts of 25 tropical plants showed that *S. androgynus* has a high polyphenol content, cupric ion chelating activities, free radical scavenging, and reducing ferric ion antioxidant properties [34].

The results obtained from SA leaf extract were also compared with the other vegetables (curry leaves, celeries, sweet potato leaves, winged beans, and garlic chives). Moreover, the EC_{50} values (95, 135, and 63 µg/ml) of SA leaf extract for ferricyanide reducing power, DPPH, and hydrogen peroxide scavenging assays, respectively, were higher than the EC_{50} values of typical antioxidants, ascorbic acid, and epicatechin [35]. Also, the antiradical activity ($1/EC_{50}$) of SA leaves was 0.7 [36]. The $1/EC_{50}$ value is higher than many other Thai plants. Based on all the reported data, therefore, SA leaves are considered as the vegetable with moderately high antioxidant activities.

Weight Loss

A flavonoid isolated from SA plant has been shown to prevent weight gain in laboratory rats fed with a high-fat diet. The rats supplemented with 60 mg/kg body weight (BW) of the flavonoid [3-O-β-D-glucosyl-(1→6)-Dglucosyl- kaempferol] isolated from SA plant significantly reduces food intake by 15%, and significantly reduced serum free triglyceride level without obvious histopathological changes [37]. Previously, the fresh leaves of SA or juice from the leaves have been used by young and middle-aged women for the perceived weight loss effect. On the contrary, there are cases reported in some countries in Asia regarding the adverse effect of consuming SA leaves [38]. The cases were related to "bronchiolitis interstitial pneumonitis". Based on a study [39], ten healthy women who have confirmed lung distress self-reported that they consumed SA leaves (juice, extract, or cooked dishes) for weight loss. The respiratory distress could probably due to the ingestion of fresh SA leaves. Alkaloids, glycosides, and saponin have been detected in fresh leaves of most plants. These compounds are somehow toxic [40]. Although papaverine is one of the main bioactives in SA leaves, some researchers hypothesized that it can cause bronchiolitis. However, an animal study in Taiwan proven that ingestion of SA leaves and papaverine do not cause bronchiolitis [41]. In fact, papaverine is an antispasmodic drug. For that reason, consumption of fresh SA leaves or freshly blended juice of SA leaves is not recommended for weight loss. Cooking or blanching of SA leaves for consumption as vegetable dishes will somehow work better.

Antimicrobial activity

Studies on antimicrobial screening using extracts of Sauropus

androgynous against various bacterial pathogens were carried out by a few workers. Gothandam *et al*., (2010) conducted antibacterial screening against ten bacterial pathogens using crude methanol extracts of ten medicinal plants including Sauropus androgynous. According to their study, S. androgynous exhibited antibacterial activity against grampositive bacteria Bacillus megaterium and gram-negative bacteria Enterobacter aerogens and Salmonella typhimurium. A year later in 2011, a study reported the antibacterial effect of *Sauropus androgynous* against Klebsiella pneumoniae and Staphylococcus aureus using aqueous and ethanolic extraction. The study revealed that the ethanolic extract with having the higher inhibitory effect than the aqueous extract for both type of bacteria

SA leaves can inhibit the growth of both gram positive and gram negative bacteria. Scientists [42] reported that the ethanolic extract of SA leaves showed higher inhibitory effects against *Klebsiella pneumonia* (gram negative) and *Staphylococcus aureus* (gram positive) than the aqueous extract. Besides the inhibitory effects of these bacteria, the methanolic extract of SA leaves has the highest inhibitory effect against *Pseudomonas aeruginosa*, *S. aureus*, *Proteus vulgaris*, and *Bacillus subtilis* compared with the methanolic extracts of SA stems and roots, except for *Eschelicia coli* [43].

Conversely, the aqueous extract of SA leaves has weaker microbial inhibition than the methanolic extract. The methanol, ethanol, and aqueous extracts of SA were also tested for antimicrobial activities. Based on the results obtained from agar diffusion assays, the methanolic extract has higher inhibition activity than the aqueous extract of SA leaves against six bacterial strains (gram positive and gram negative bacteria) [44]. However, the inhibition zones of all the extracts were lesser than the standard streptomycin used. The results also showed that the SA leaf extracts have 41% to 79% of inhibition in relation to streptomycin.

Anti-Inflammatory Activity

Anti-inflammatory activity of *S. androgynus* was also reported [45]. The study evaluated the effect of ethanolic and aqueous leaf extracts of this herb on Wister rats using carrageenan induced rat paw edema. The ethanolic extract showed a higher anti-inflammatory effect than aqueous extract. This was supported by another study on *in vitro* anti-inflammatory properties of the methanolic extract of this plant, showing significant nitric oxide inhibitory activity using Griess assay [46].

Lung Injury

An *in vitro* study shows that the aqueous fraction of SA dried powder significantly elevated the inflammatory cytokine and chemokine production in monocytic lineage cells, significantly induced apoptosis of endothelial cells, and enhanced intraluminal obstructive fibrosis in allogeneic trachea allograft in the murine bronchiolitis obliterans syndrome's model [47]. The study also reported that consumption of SA leaves stimulated production of TNF-α in monocytes of healthy controls and induced a high-level production of TNF-α from monocytes of patients who consumed SA leaves.

Besides the *in vitro* studies, the outbreak of lung diseases or bronchiolitis obliterans is known to be associated with intake of SA leaves [48]. Several cases of obstructive ventilatory impairment and bronchiolitis obliterans have been found to associate with the consumption of SA leaves in Taiwan [49] and Japan [50]. The outbreak of obstructive ventilatory defect among 44 Taiwanese was reported [49]. They suffered from typical symptoms, including temporary insomnia, poor appetite, and breathing difficulty after intake of SA leaves for four weeks or more. Out of the 44 patients, 93.2% of them were women who consumed SA leaves as a vegetable.

Antidiabetes Activity

An experiment was presented [51] which focused on the evaluation of the effects of aqueous leaf digest of *S. androgynus* on the postprandial glucose levels in human blood. The results show that glycemic index (GI) scores for patients that were administered the *S. androgynus* leaf digest were significantly lower compared to the control group. This result suggests that this plant possesses a high potential for lowering glucose levels in human blood, which would likely assist in the global battle to reduce diabetes.

Lactation inducing activity

Consumption of SA leaves could benefit lactating women. A study reported that lactating mice supplemented with SA leaf extracts have 2 to 26-fold increased expression of prolactin and oxytocin genes in the pituitary glands of the mice [52]. It shows that SA leaf extracts helped to increase the milk production. In a humanbased study, the leaf extract of SA has been proven to increase production of mother's breast milk. Besides, a study in Indonesia reported that SA leaf extract has increased breast milk production of lactating mothers up to 50.7% compared to placebo [53]. Another similar study proved the benefit of consuming SA leaves for increasing production of human breast-milk [54]. Moreover, increased consumption of SA leaves has significantly increased the level of vitamin A in the breast milk of breastfed mothers in a few districts of Indonesia [55]. In addition, milk production in mammals resulting from the consumption of SA leaves has also been determined using several animal models.

Other Health Benefits

Although no previous literature has reported the potential cardioprotective effect of SA leaves using *in vivo* model, a study has demonstrated that fermented SA leaves were effectively reduced 19.32% cholesterol content in chicken meat compared to control (ration without addition of fermented SA leaves) [56]. The experimental chicken were fed with fermented SA leaves for eight weeks before slaughtered. The study hypothesized that the cholesterol reducing effect in the chicken was mainly contributed by the β-carotene content in SA leaves. The effect could be due to the inhibition of enzyme HMG-CoA reductase activity by β- carotene in the leaves.

Consumption of average cumulative dosage of SA leaves (2.67±1.89 kg, range 0.4-8.0 kg) was shown to significantly lower Tiffeneau-Pinelli index (FEV1/FVC ratio) of the patients with respiratory symptoms than the patients without the symptoms. The result showed some improvement in the severe impairment of alveolar permeability for the patient with obstructive and restrictive lung disease that treated with SA leaves [57]. Besides, the antioxidants in SA leaves could prevent several chronic diseases, such as cancer and coronary heart disease [58]. A previous study on the determination of alpha-tocopherol contents in 62 edible tropical plants reported the leaves of SA have the highest concentration (426.8 mg/kg edible portion) of alphatocopherol [59]. The high alpha-tocopherol content of SA leaves signifies a potential protective effect of SA against several chronic diseases.

Antiobesity Effect

High consumption of young leaves of *S. androgynus* over a long period in the belief that the plant helps to maintain weight resulted in a sudden increase of bronchiolitis obliterans in Taiwan, which is normally rare life-threatening lung disease. The believe that *S. androgynus* had values as an antiobesity agent was confirmed in a study by Yu *et al*. [60], which focused on effects of *S. androgynus* isolated GGK compound in combination with EtOAc and n- BuOH fractions for body weight reduction in Wistar male rats. The results show that 60mg per kg dose of GGK led to a decrease of food intake of rats by 15% and this led to a reduction in body weight of these rats. This loss of food intake directly corresponded to doses of GGK administered to different groups of rats. Further, no histopathological changes were observed. It was concluded that GGK has a potential to become an antiobesity agent and is unlikely to result in similar side effects as observed when consuming the entire plant.

Conclusions

Sauropus androgynus is a traditional medicinal plant used in Southeast Asia, especially in Malaysia known as a green multivitamin herb. Previous studies have reported the prospective of this plant as antioxidant, antimicrobial, wound-healing, anti-inflammatory, antidiabetic, and antiobesity agent aswell as its potential to increase breast milk production. Despite these pharmacological properties, consumption of its raw leaf juice for weight reduction resulted in outbreak of bronchiolitis obliterans. It seems that papaverine is the chemical compound responsible for occurrence of this pulmonary failure. Further studies should be made in order to fully understand the cytotoxicity of this plant, mechanism of toxicity, dosages and ways of consumption, and effects on human health.

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