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Review Article

Pharmacognostical and Pharmacological Properties of *Sauropus Androgynus* : An Updated Review

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Abstract

Background: *Sauropus androgynus* (L.) Merr., a perennial shrub mainly found in the regions of South and Southeast asia. It serves dual roles as a traditional medicine for fever, ulcers, diabetes, and lactation disorders and nutritious vegetable. Despite documented pharmacological benefits, over consumption can cause bronchiolitis obliterans, necessitating rigorous safety evaluation. Objective: This review examines the pharmacognosy, phytochemistry, ethnopharmacology, and pharmacology of *S. androgynus*, .It also summarizes the chemical constituents and pathogenic mechanisms underlying *Sauropus*-induced bronchiolitis obliterans. Methods: Systematic literature were searched in Google Scholar, Wiley, Springer, CNKI, Web of Science, and Science Direct. Peer-reviewed articles, theses, and texts were prepared regarding botanical characteristics, traditional uses, phytochemical profiles, pharmacological activities, and toxicological data. Results: *S. androgynus* contains high nutritional value with increased proteins, vitamins, minerals, and bioactive compounds including polyphenols, flavonoids, lignans, and fatty acids. Experimental studies proved the properties of *S. androgynus* which includes anti-inflammatory, antioxidant, immunomodulatory, anti-obesity, anti-ulcer, and anti-diabetic activities. One of the major constituents in this plant is papaverine. The recent studies conducted on papaverine indicates additional aqueous constituents may trigger pulmonary toxicity through macrophage activation, endothelial inhibition, and TGF-β/eNOS-mediated fibroproliferation. Conclusion: *S. androgynus* possesses great therapeutic potential supported by traditional use and experimental pharmacology, yet its clinical application may develop bronchiolitis obliterans. Future researches including phytochemical characterization, toxicological mechanism elucidation, and safe dosage establishment are required to enable evidence-based therapeutic utilization.

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Introduction

Sauropus androgynus (L.) Merr., known as star gooseberry or katuk, is a perennial shrub mainly found in the tropical and subtropical regions of South and Southeast Asia. The species has dual role one as nutritious leafy vegetable and as a botanical therapeutic across diverse traditional medical systems(1). Nutritional characterization reveals higher content of proteins, vitamins, minerals, and bioactive phytochemicals that exceed concentrations typical of conventional green vegetables (1).Traditional medicine systems across its native range have employed *S. androgynus* for pathological conditions spanning infectious, metabolic, gastrointestinal, and reproductive domains. Various studies had reported about the medicinal value of *S. androgynus* include fever, mucosal ulceration, diabetes mellitus, obesity, visual impairment, and insufficient lactation (1).

This plant is widely used in traditional medicine and also as nutritional vegetable as part of the daily diet, which makes it very necessary for systemic pharmacological activity(2). Pharmacognosy is the study of medicinal plants and their chemical constituents, which is very helpful in such pharmacological research. Application of pharmacognostic principles to *S. androgynus* comprises botanical authentication, phytochemical profiling, and biological activity evaluation. (3). Pharmacognosy is the study of plants which includes identifying the plant correctly, understanding its chemical components, and testing its biological effects. Research on *S. androgynus* has found many chemical constituents such as flavonoids, polyphenols, healthy fatty acids, and nitrogen-containing substances. These

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constituents may work together to produce different health benefits (3).

Scientific studies using plant extracts—and sometimes pure compounds—have shown various beneficial health activities. These include antiinflammatory, helping with weight and metabolism, improving insulin sensitivity, and protecting the stomach lining from ulcers. These results support traditional knowledge, but more research is still required to understand the therapeutic potential of the plant.Although *S. androgynus* has various health benefits, its safety is complicated and it cannot be fully recommended as a medicine because of a serious lung disease. A disease outbreak in Taiwan in 1995 showed that drinking raw *S. androgynus* juice caused a serious lung disease called bronchiolitis obliterans, were the smaller air passages are getting damaged permanently. Bronchiolitis obliterans is a severe and frequently progressive obstructive lung disease characterized by irreversible small airway fibrosis (4). Later researchers confirmed this risk and showed that some people may be more vulnerable, possibly due to inflammation and scarring in the lungs. Because of these risks, it is important to carefully compare the pharmacological activity and toxicity of using this plant. Until this is clear, its use in medicine and diet should be done with caution.

This review aims to combine current knowledge about the plant's properties, benefits, and risks required for future research and safe medical use. Without such knowledge, the transition of *S. androgynus* from traditional remedy to evidence-based therapeutic agent remains limited, and public health recommendations regarding dietary consumption of this plant requires precautionary limitations (5). The present review summarizes current understanding of *S. androgynus* across pharmacognostic, phytochemical, pharmacological, and toxicological dimensions, with particular attention to mechanisms underlying both therapeutic efficacy and adverse pulmonary effects, in order to inform future research directions and clinical application strategies.

Objectives

1. To study the pharmacological, ethnopharmacological, phytochemical, and botanical activities of *S androgynus*.
2. To study the chemical components of bronchiolitis obliterans caused by *S. androgynus* and talk about the toxicity or harmful effects for further study.

Methodology

Research on *S androgynus* was conducted using a variety of electronic resources. Data were collected from a variety of unpublished academic sources, including books, theses, dissertations, and peer-reviewed journal papers(6). Botany, ethnopharmacology, phytochemistry, pharmacological actions, and toxicological consequences of *S. androgynus* were the primary topics of the gathered literature. The therapeutic uses and toxicological considerations of *S. androgynus*, such as the risk of bronchiolitis obliterans, were carefully chosen to fill gaps in our knowledge(7).

Botany

S androgynus (L.) Merr or Balakr. is found in the regions of tropical and subtropical Southeast Asia (Vietnam, Laos, Cambodia, Philippines, Malaysia, Indonesia, Thailand), South Asia (India, Sri Lanka), and China. *Breynia androgyna* (L.) Chakrab. & N.P. It thrives in hot & humid regions with stable temperatures and heavy precipitation also tolerate partial shade. Soils between 5.5 to 8.0 pH are best for this plant's root development; acidic or dry soils impairs the growth (8). The plant is adaptive to different environmental conditions and robust. The shrub grows upright to a height of one to three meters and flowers between April to July (Fig. 1). Its flower clusters may be monoecious or heterophytic usually having one or two petals. The male flowers are disk-shaped or virtually disk-shaped, with slender stalks 5-12 mm width and 5.0-7.5 mm thickness(9). The ripe fruit are bright yellow round capsule with a red calyx. It may exceed 1.5 cm in circumference and ranging from depressed globose to globose. The dried seeds are dark, ribbed, and inactive.

Ethnopharmacology

Medicinal plants play a key role in major alternative and complementary medical system such as Ayurveda, Siddha, Jamu, Unani, and traditional Chinese medicine.In these system medicinal plants are widely used to treat various diseases. *S androgynus* is commonly used in herbal mixtures especially in Indonesian Jamu. In Indonesia, fresh leaves and roots are known to have uterotonic effect ie they are used after parturition to help expel the placenta. The other properties of leaves are for treating respiratory problems like cough, hoarseness, chest congestion, and fever. Other than treating respiratory problem it also includes anti-inflammatory and antipyretic properties(10).

One of the most common traditional uses of *S androgynus* across Southeast Asia—including Indonesia, Malaysia, Thailand, Vietnam, and the Philippines—is to increase the production of breast milk in nursing mothers. This widespread use highlights its importance as a galactagogue and various studies reported its effects on hormones like prolactin and oxytocin. ethnobotanical databases like Duke's Phytochemical and Ethnobotanical Databases recorded other traditional applications of *S androgynus* mainly spanning hepatic, ocular, dermatological, and infectious disease indications. They also include treatment of cholestasis, fever, ophthalmia, coryza, cutaneous soreness, and erythrasma, reflecting the broad therapeutic repertoire attributed to this species across diverse cultural contexts (11).

Taiwanese ethnobotanical surveys have reported various applications in management of chronic metabolic and cardiovascular conditions. Traditional practitioners use *S. androgynus* for weight management and respiratory problems ,BP regulation, gynecological disorders, hyperlipidemia, hyperuricemia, urolithiasis, and cholelithiasis, as well as for gastrointestinal complaints including constipation (12). In the southern Chinese provinces traditional healers have historically relied upon leaf decoctions for hemoptysis, xerostomia, and productive cough, while rural communities extend the uses to hepatitis, laryngitis, enteritis, and visual disturbances. Root decoctions of *S. androgynus* are used in Indonesia and Malaysia for treating scabies, diarrhea, tuberculosis, and urinary disorders(13).

In India, the plant is used for treating eye disorders like myopia, tonsillitis, wound healing, and diabetes, while in Vietnam and Thailand it is used as a diuretic, antipyretic, antiseptic, and for treating gastrointestinal issues. Some of the studies reported its use in cancer treatment, though details are limited.

Overall, *S. androgynus* is both a medicinal plant and a nutritional food source, sometimes used as a natural food colorant and preservative. Its widespread use in daily diets increases exposure to its active chemical constituents , which may provide health benefits but also raises concerns about potential risks.

Table 1 provides systematic documentation of local names and ethnobotanical applications across the major regions of traditional use (10-13).

Figure 1. Leaf, plant, flower, and fruit characteristics of S. androgynus(14)**.**

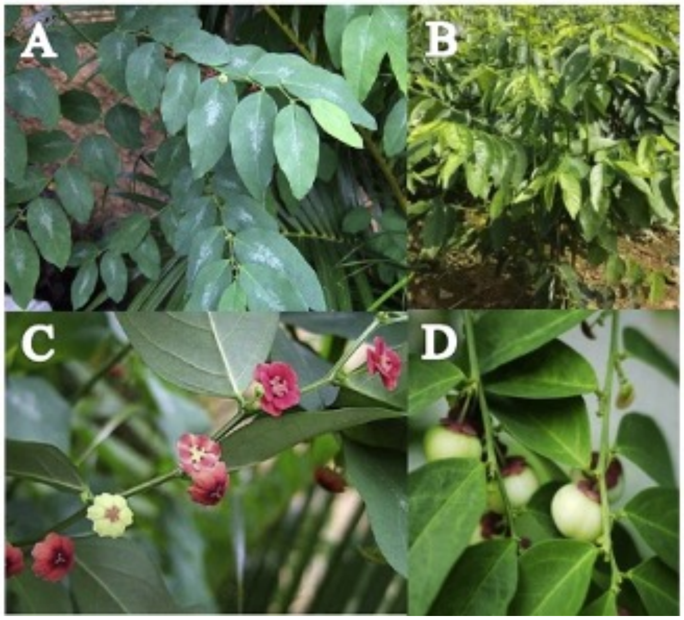

Table 1: Local names and ethnobotanical applications of S. androgynus (15)

Place	Regional Names	Uses of Ethnobotany	Reference
Indonesia	Daun Katuk, Babin, Simani	Increase lactation, treat cough, fever, uterotonic	Andarwulan et al., 2012; Runi, 2000
India	Star gooseberry, Chakrani beru	Treat eye problems, diabetes, fever, diarrhea, earache	Sai and Srividya, 2002; Singh et al., 2011
Malaysia	Katuk, Cekurmanis	Increase lactation, treat cough, diabetes, hypertension	Arifin, 2005; Ong et al., 2011
Thailand	Phak wan ban, Pak waan	Anti-fever, food poisoning antidote, gastrointestinal	Benjapak et al., 2008; Manosroi et al., 2006
China	Tiao lv xiang, Shou gong mu	Slimming agent, treat cough, hepatitis, hypertension	Lai et al., 1996; Wu et al., 1997
Vietnam	Rau ngot, bu ngot	Diuretic, relieve fever, fungal infections	Ogle et al., 2003

Phytochemistry

Seeds and roots have been studied less than leaves in phytochemical investigations. The aerial parts of *S. androgynus* contain bioactive chemicals with therapeutic properties. This study isolated and identified two terpenoids (9-10), four nucleosides (5-8), four lignans (1-4), three flavonoids (11-13), and two steroids (14-15). Table 4 contains these compounds' names, molecular formulae, CAS numbers, precise masses, and sources, whereas Fig. 2 displays their structures(16). Researchers have only utilized GC-MS and GC to identify most of the plant's components; many phytochemical compounds need to be extracted and described. *S. androgynus* leaves and seeds contain fatty acids and volatile oils.

Table 2: *S. androgynus* micronutrient content and composition in India

Component	Value (mg/100 g dry weight)—India
Moisture (%)	85.42 ± 1.90
Ash (%)	5.25 ± 1.10
Crude protein (%)	5.25 ± 0.87
Crude fibre (%)	1.75 ± 0.56
Crude fat (%)	0.58 ± 0.17
Vitamin C	314.30 ± 1.84
K (Potassium)	45.70 ± 1.45
P (Phosphorus)	61.20 ± 3.46
Co (Cobalt)	1.62 ± 0.10
Mn (Manganese)	25.60 ± 5.80
Cu (Copper)	768.70 ± 11.40
Na (Sodium)	306.31 ± 52.8
Zn (Zinc)	15.93 ± 6.61
Ca (Calcium)	84.44 ± 8.14
Fe (Iron)	212.50 ± 2.82
Mg (Magnesium)	664.90 ± 38.14

The number of milligrams per hundred grams, measured on a fresh weight basis, is based on the first chemical composition study that was conducted by Padmavathi and Rao (1990) and Yang and Guo (2002).

Table 3: Indian *S. androgynus* phytochemicals

Component	Value (mg/100 g dry weight)—India
Quercetin	—
Kaempferol	—
Sum of flavonoids	—
Phenolic acids	—
Total phenols	1150.95 ± 2.86
Total anthocyanin	82.94 ± 1.12
Total carotenoids	19.40 ± 0.56
β-Carotene	—
Chlorophyll	45.60 ± 0.66

Gas chromatography–mass spectrometry detected sixteen volatile oils in steam-distilled S. androgynus leaves. Key volatile oil components included carvacrol methyl ether, thymol, and butylated hydroxytoluene. Essential oils should be researched for their antibacterial properties since they combat viral, bacterial, and fungal infections (17). The main ingredients of seeds of S. androgynus are fatty acids, including lauric, myristic, palmitic, stearic, oleic, linoleic, and α-linolenic acids. Of the fatty acids, 51.4% are α-linolenic acid, and more than 80% are unsaturated. Here is what another study discovered. The primary components of *S. androgynus* seeds extract by GC-MS were linoleic, oleic, palmitic, and linolenic acids Fatty acids and their derivatives and metabolites may alter ROS signaling and intracellular synthesis, making ROS proapoptotic in many cell types (18).This plant has antioxidant qualities due to its abundance of polyphenols, flavonoids, and fatty acids. Twenty compounds, including L-(+)-ascorbic acid 2,6-dihexadecanoate, were isolated from an ethanol extract of *S. androgynus* leaves recently. The fact that *S. androgynus* was the most abundant element in the plant proved that it was multivitamin. Three types of antioxidants, anti-inflammatory, and anti-nociceptive actions were discovered. Table 5 lists *S. androgynus* leaf and seed GCMS chemicals from numerous studies(19).

Pharmacological Activity

The pharmacological profile of *S androgynus* explains a range of biological activities studied through various experimental models. Most research has relied on crude extracts—aqueous, ethanolic, or methanolic—rather than isolated compounds, which preserves potential synergistic effects. In vitro chemical assays, such as the DPPH radical scavenging test are used to assess antioxidant and melanogenesis-inhibitory activities. During initial screening, these tests do not reflect complex physiological processes such as absorption, metabolism, and cellular uptake, so the relevance of these findings to in vivo antioxidant effects remains uncertain. Table 4 provides documentation of experimental substances, controls, effective dosage ranges, assessment methodologies, and primary pharmacological outcomes observed in animal studies. This document reveals consistent evidence for antioxidant, anti-inflammatory, and anti-obesity properties across multiple investigations (20).

Despite these limitations, more studies have reported regarding the anti-inflammatory, immunomodulatory, anti-ulcer, and anti-nematodal activities. However, melanogenesis inhibition remains unsupported in vivo, limiting its application in cosmetics. The major concern in the studies is the imbalance between pharmacological and toxicological research: pharmacological studies are numerous but often methodologically weak, whereas toxicological studies, though fewer, are crucial due to documented risks such as bronchiolitis obliterans in humans. Major drawback from the studies are small sample sizes, single-dose designs, lack of dose-response evaluation, and insufficient mechanistic endpoints, limiting both biological interpretation and clinical translation (20).

Current evidence indicates that *S. androgynus* cannot be considered safe for unrestricted consumption. Its pharmacological potential is promising but preliminary, and the documented toxic effects outweigh unverified benefits when considering regulatory or clinical use. As such, the plant may be better positioned as an adjunctive herbal therapy under professional supervision rather than a primary treatment. Advancing pharmacological research will require rigorous in vitro studies using physiologically relevant models, followed by carefully designed in vivo experiments, dosage optimization, and toxicity profiling (21).

Anti-inflammatory Activity

Among its pharmacological activities, the anti-inflammatory effects of *S. androgynus* have been studied. Inflammation involves the key regulatory check point which includes activation of cellular and humoral systems, with lysosomal membrane integrity. Stabilization of these membranes prevents release of various destructive enzymes from neutrophils, tissue repair or reduces damage and attenuating inflammatory signaling. Recent studies reported that *S. androgynus* leaves demonstrated protective effects in vitro: in hypotonicity-induced hemolysis assays, 100 µg/mL of protein extract provided 74.17% protection, while protein denaturation assays showed 83.60% stabilization. These results suggest that constituents of *S. androgynus* may limit inflammatory cascades through membrane stabilization (22).

Invitro studies were conducted on *S. androgynus* to determine nitric oxide modulation in activated macrophages. The methanolic leaf extracts suppressed nitric oxide production in a concentration-dependent manner, achieving 68.28 ± 7.05% inhibition at 100 µg/mL without any cell toxicity. Since nitric oxide contributes to vasodilation, tissue damage, and increased vascular permeability during inflammation indicates that these results have therapeutic relevance in conditions marked by heightened inflammatory mediator activity. However, its effects in complex biological systems can be confirmed only through in vivo studies (22).

Invitro studies on *S. androgynus* have provided more robust support for anti-inflammatory activity. The two main animal models to study the inflammation are carrageenan-induced paw edema and formaldehyde-induced chronic inflammation models. Methanolic leaf extracts of *S. androgynus* were tested in Swiss albino mice inflammation models . At a dose of 500 mg/kg body weight, the extract showed significant effect by reducing the edema by 58.33 ± 0.40% in acute and 63.15 ± 0.04% in chronic models, but the efficacy of our extract is slightly lower than the standard marketed drug diclofenac. These findings highlight the potential of *S. androgynus* as an anti-inflammatory agent.

In summary, *S. androgynus* exhibits diverse pharmacological activities, particularly anti-inflammatory effects, supported by both in vitro and in vivo studies. However, widespread reliance on crude extracts, incomplete phytochemical characterization, and insufficient toxicological data limit the clinical use of these findings. Systematic, standardized, and mechanistically detailed research is essential to validate therapeutic potential .

Evaluation of 250 mg/kg and 500 mg/kg doses—representing approximately 10% and 15% of the determined maximum safe dose of 2500 mg/kg—yielded statistically indistinguishable anti-inflammatory effects (23). Although the extract shows anti-inflammatory activity, the exact molecular mechanism behind this is still unknown. It may inhibit the key inflammatory enzymes such as cyclooxygenase or lipoxygenase, thereby blocking pro-inflammatory signaling molecules like cytokines, regulating pathways such as NF-κB, or stabilizing cell membranes. However, these are only proposed mechanisms and require confirmation through various studies including gene expression profiling, enzyme assays, and receptor binding experiments. Additionally, the specific chemical constituents responsible for the anti-inflammatory activity—whether proteins, flavonoids, terpenoids, or a combination of these—have not yet been identified. Determining these active constituents is very important for ensuring consistent quality, standardization of preparations, quality control in manufacturing, and rational formulation design for clinical development (22,23).

Table 4. Chemical components of S. androgynus

No.	Compound Name	Molecular Formula	Precise Mass (g/mol)	CAS Number	Reference
1	(+)-3α-O-β-glucosyl-isolariciresinol	$C_{26}H_{34}O_{11}$	522.54	63358-11-2	Kanchanapoom et al. (2003)
2	(−)-3α-O-β-glucosyl-isolariciresinol	$C_{26}H_{34}O_{11}$	522.54	143236-04-8	Kanchanapoom et al. (2003)
3	(−)-3α-O-β-apiofuranosyl-(1→2)-O-β-glucosyl-isolariciresinol	$C_{31}H_{42}O_{15}$	654.66	610754-91-1	Kanchanapoom et al. (2003)
4	(+)-di-O-β-glucosyl-syringaresinol	$C_{34}H_{46}O_{18}$	742.72	573-44-4	Kanchanapoom et al. (2003)
5	Guanosine	$C_{10}H_{13}N_5O_5$	283.24	118-00-3	Wang and Lee (1997)
6	Adenosine	$C_{10}H_{13}N_5O_4$	267.24	58-61-7	Wang and Lee (1997)
7	5′-deoxy-5′-methylsulphinyl-adenosine	$C_{11}H_{15}N_5O_4S$	313.33	3387-65-3	Wang and Lee (1997)
8	Uridine	$C_9H_{12}N_2O_6$	244.20	58-96-8	Wang and Lee (1997)
9	Corchoionoside C	$C_{19}H_{30}O_8$	386.44	185414-25-9	Zhang et al. (2018)
10	Sauroposide	$C_{19}H_{30}O_9$	402.44	610783-40-9	Kanchanapoom et al. (2003)
11	3-O-β-D-glucosyl-7-O-α-L-rhamnosyl-kaempferol	$C_{27}H_{30}O_{15}$	594.52	2392-95-2	Wang and Lee (1997)
12	3-O-β-D-glucosyl-(1→6)-β-D-glucosyl-kaempferol	$C_{27}H_{30}O_{16}$	610.52	22149-35-5	Wang and Lee (1997)
13	3-O-β-D-glucosyl-(1→6)-β-D-glucosyl-7-O-α-L-rhamnosyl-kaempferol	$C_{33}H_{40}O_{20}$	756.66	173740-43-7	Wang and Lee (1997)
14	5-ene-3β,20β-diol-stigmast	$C_{29}H_{50}O_2$	430.71	610272-36-1	Zhang et al. (2018)
15	5,24(28)-diene-3β,20β-diol-stigmasta	$C_{29}H_{48}O_2$	428.69	2102536-94-5	Zhang et al. (2018)

Antioxidant Activity

Sauropus androgynus leaves are a rich reservoir of antioxidant phytochemicals, including chlorophyll, flavonoids, polyphenols, and bioactive proteins. These phytochemicals have the ability to neutralize free radicals and reduce oxidative stress. These compounds may act through various complementary mechanisms to maintain cellular redox balance, although their chemical complexity of their preparations makes detailed pharmacological characterization challenging.

Initial evidence of antioxidant activity comes from in vitro studies, particularly by various assays including the2,2-diphenyl-1-picrylhydrazyl(DPPH)radical scavenging assay, FRAP assay and ABTS assay which demonstrated strong free radical neutralizing capacity. Notably, a recent study reported that aqueous leaf leaves showed greater antioxidant activity than standard compounds such as curcumin and vitamin E under similar conditions. However, such in vitro methods provide only limited insight, as they do not account for pharmacokinetic studies.

Together, these findings indicate that *S. androgynus* possesses significant antioxidant potential and can exert biologically relevant effects in living systems. This supports its traditional medicinal use in conditions associated with oxidative stress and highlights the need for further research to isolate active compounds and develop standardized therapeutic formulations (24).

The rising problem of antimicrobial resistance and the risk of birth defects from some modern medicines have increased interest in herbal based therapies like *Sauropus androgynus*, especially for use during pregnancy. Studies in pregnant mice with *Salmonella* infection showed that when *S. androgynus* was used (along with *Elephantopus scaber*), it improved immune function by increasing immune cells (CD4+ T-cells) and enhanced interferon-gamma and interleukin-2 production, and reciprocal reduction in interleukin-4 and B220+ lymphocyte expression . These alterations in the cytokine, T-helper-1 polarization, coincided with significant reduction of fever However, the effect of *S. androgynus* alone is still unknown (24).

Researchers reported that flavonoids in the plants activate certain cell signalling pathways and boost immune responses, but this has not yet been fully proven. Other studies using leaf extracts showed that the plant extracts significantly improve white blood cell count, improving antibody response, and fight against foreign substances. Along with reduced excessive immune reactions (like hypersensitivity) it is also improving overall immunity, suggesting it helps balance the immune system rather than just stimulate it. *S. androgynus* increases phagocytosis (the ability to destroy harmful particles) thereby improving innate immunity (the body's first line of defense) ,improving organ function, and enhancing neutrophil activity. However, these effects are not strongly dose-dependent, which makes it difficult to establish the optimal dosage (25).In addition, studies performed in animals and fish models using *S. androgynus* to the diet can improve growth, boost immunity, and increase resistance to infections. Overall, *S. androgynus* are showing strong potential as an immune stimulating agent for both humans and animals. However, more research requires to identify the active compounds, mechanism of action, determine optimal doses, and confirm their therapeutic potential(25). Table 5 summaries the pharmacological activity of *S. androgynus.*

Table 5: *S. androgynus* pharmacology

Pharmacological Activity	Testing Plant Parts	Models	Effective Dose	Positive Controls	Effect	Reference
Anti-inflammatory activity	Dialyzed protein extract	Inhibition of protein denaturation and membrane stabilization in vitro	100 µg/mL	Acetylsalicylic acid, Diclofenac	Max. protection (74.17%) & protein denaturation max. protection (83.60%)	Madhu et al. (2014)
	Methanol extract	Mice model with acute and chronic inflammation (carrageenan, formaldehyde)	500 mg/kg, i.g., 5 d	Diclofenac	Significant edema suppression: 58.33 ± 0.40% and 63.15 ± 0.04%	Kumar and George (2016)
	Methanol extract	IFN-γ/LPS-treated macrophages in vitro	100 µg/mL	L-NAME	NO production inhibition 68.28 ± 7.05% without cytotoxicity	Lee et al. (2011)
Antioxidant activity	Dialyzed protein extract	Hydroxyl radical scavenging, reducing power, etc. in vitro	50 µg/mL	Curcumin, Tannic acid, Vitamin E	Hydroxyl radical (55.62%), reducing power (0.286 Abs), DMSO (72.51%), phosphomolybdenum (0.198 Abs)	Madhu et al. (2014)
	Chlorophyll	Subacute $NaNO_2$-induced female Wistar rats in vivo	0.016 mg/mL, p.o., 14 d	Cu-chlorophyllin	Increased Hb, transferrin, ferritin, RBC; decreased MDA and fragmentocyte %	Suparmi et al. (2016)
Immunomodulatory activity	Ethanol extract (E. scaber & S. androgynus leaves)	Pregnant mice with typhoid fever (S. typhi) in vivo	200 mg/kg & 150 mg/kg, p.o., 18 d	Pregnant & healthy mice controls	Increased CD4+ T, IFN-γ & IL-2; reduced IL-4+, B220+ lymphocytes	Djati et al. (2016)
	Methanol extract	DTH, neutrophil adhesion, carbon clearance, HA titer assays	500 mg/kg, p.o., 14 d, daily	Septilin	↑ leukocytes, HA titer, organ weight, neutrophil adhesion; ↓ footpad thickness	Kumar and George (2016)
Anti-obesity activity	GGK	Wistar rats	60 mg/kg, i.g., 28 d, daily	Pioglitazone	Food intake ↓ 15%, serum free triglycerides ↓ without histopathology	Yu et al. (2006)
	96% Ethanol extract (Z. ottensii & S. androgynus)	Obese rats (high-fat + carbohydrate diet)	100 mg/kg (1:1), p.o., 42 d, daily	Metformin, Orlistat, Curcumin	Significant reduction in AST, ALT, perirenal and testicular fat weight	Warditiani et al. (2016)
Anti-ulcer activity	Ethanol extract	Aspirin-induced peptic ulcers in rats	24.3 mg/100 g, i.g., 14 d, daily	Aspirin-induced peptic ulcers	Decreased TNF-α in duodenum; improved duodenal histopathology	Roosdiana et al. (2018)
Anti-diabetes activity	Aqueous leaves digestion	Non-insulin dependent diabetic subjects	10 g/200 mL, p.o., once	–	Significantly lower GI scores compared to control group	Sai and Srividya (2002)

Anti-obesity Activity

S androgynus is traditionally used in Southeast Asia as a "nutritional vegetable" because it helps to control weight. Recent studies supported this use and suggested that certain active compounds in the plant may reduce appetite, fat metabolism, and energy balance. Phytochemical investigation of *S androgynus* identified of 3-O-β-D-glucosyl-(1→6)-β-D-glucosyl-kaempferol (GGK) as a principal flavonoid glycoside with potential anti-obesity properties. animal studies, it reduced 15% food intake and led to steady weight loss without causing organ damage. It also improved lipid levels by reducing triglycerides and fat metabolism.

However, the exact mechanism of how GGK works is still unknown. It may reduce food intake, increase energy use, or act through multiple mechanisms. Studies using whole leaf powder also showed weight loss over prolonged use. In addition, combination of *S. androgynus* with other plants like *Zingiber ottensii* further improved results by reducing body fat and protecting fat tissue from damage caused by obesity. Overall, both isolated compounds and whole plant preparations show promising anti-obesity effects (26).

Anti-ulcer Activity

The gastroprotective potential of *S androgynus* has been identified within Thai traditional medicine, where leaf extracts have been used for the treatment of aphthous ulcers and other mucosal lesions (27). This ethnopharmacological application provided the rationale for experimental investigation of *S. androgynus* efficacy in controlled models of gastric mucosal injury, with its anti-inflammatory modulation mechanism and tissue repair.

In vivo studies was performed with ethanolic leaf extracts in a rat model of aspirin-induced peptic ulceration. This study reported that animals received *S. androgynus* extract at a dosage of 24.3 mg per 100 grams over a fourteen-day treatment period revealed substantially reduced tumor necrosis factor-alpha (TNF-α) concentrations in duodenal tissues of treated animals compared to ulcerated controls. Additionally histopathological examination showed improved architectural restoration of duodenal tissues, with reduced inflammatory infiltrate, enhanced epithelial reconstitution, and diminished necrotic areas (27).

These findings prove *S. androgynus* as a promising candidate for development of herbal therapeutics targeting gastric ulcer disease. The observed reduction in inflammatory mediators like TNF-α levels is particularly significant in reducing gastric inflammation, chemotaxis, and promoting mucosal barrier dysfunction. By suppressing TNF-α production or signaling, *S. androgynus* constituents may interrupt the inflammation cycle and reduce tissue destruction characteristic of peptic ulcer pathophysiology (27).

Antimicrobial Activity

The antimicrobial properties of *S androgynus* have been investigated across multiple solvent extracts . Early studies demonstrated that methanolic and ethanolic leaf extracts effectively suppressed the growth of clinically significant bacterial species or bacteriostatic including *Staphylococcus aureus*, *Bacillus cereus*, *Proteus vulgaris*, and *Escherichia coli* (28). These findings revealed the antibacterial property of *S androgynus.*

Comparative evaluation of aqueous versus organic solvent extracts has yielded important insights regarding the chemical nature of active constituents. Ariharan and colleagues reported that aqueous preparations exhibited less bacteriostatic activity against Gram-positive bacteria when compared to that of methanolic extracts. This suggests that lipophilic or moderately polar compounds contribute disproportionately to antibacterial effects (28). This polarity-dependent activity pattern was further assessed through direct comparison of water-based and ethanolic extracts against *Klebsiella pneumoniae* and *Staphylococcus aureus*. Reports revealed that ethanol preparations showed significant bacteriostatic activity(28). The increased antimicrobial activity of organic solvent extracts indicates that active principles may include flavonoid aglycones, terpenoids, or phenolic compounds with limited aqueous solubility.

In contrast to the relatively modest antibacterial activity of aqueous preparations, *S. androgynus* extracts show significant stronger antifungal activity when compared to antibacterial activity. They effectively inhibit pathogens like *Aspergillus flavus* and *Candida albicans*. This suggests that through various specific mechanisms they destroy fungi, such as disrupting cell walls or membranes (28).

The phytochemical basis for antimicrobial activity has been attributed primarily to secondary metabolite classes abundant in *S. androgynus* tissues. Flavonoids and tannins, present in substantial concentrations throughout leaf and stem materials, plays a major role in in growth inhibition of pathogenic microorganisms (28). These polyphenolic compounds exert antimicrobial effects through multiple mechanisms . The mechanisms include inhibition of enzymes, interference with cell wall synthesis, disruption of cell membrane and inhibition of protein synthesis essential for microbial metabolism.

Essential oil derived from the plant contains high concentrations of lipophilic compounds like carvacrol methyl ether, thymol, and butylated hydroxytoluene. They exert antimicrobial effects through membrane disruption and protein denaturation, with the non-polar nature of essential oil components facilitating penetration of microbial cell envelopes.

The transition from in vitro observation to clinical application requires systematic evaluation of bioavailability, pharmacokinetics, and toxicity in relevant biological systems(28).

Anti-diabetic Activity

The hypoglycemic potential of *S androgynus* has attracted considerable attention within traditional medicine systems, particularly in the southern Indian states of Tamil Nadu and Kerala. In Tamil Nadu and Kerala local populations commonly refer to this plant as "diabetic greens" (29). Clinical studies suggest that *S. androgynus* leaves may reduce postprandial blood glucose in humans. They moderate the carbohydrate absorption or increase glucose utilization . In a study it is reported that an aqueous preparation of 5 g leaves per 100 mL water lowered glycemic indices when compared to controls. However, limitations—including single-dose testing, lack of pharmacokinetic data, and unidentified active compounds makes it difficult to draw conclusions about efficacy, dosage, or safety. The mechanisms behind the antidiabetic effect remain unclear, but possible pathways include inhibition of carbohydrate-digesting enzymes, improved insulin secretion, or enhanced insulin sensitivity. Future research should focus on isolating active compounds, establishing dose-response relationships, and conducting invitro, in vivo and clinical studies to confirm safety and therapeutic potential in diabetes management (29).

Toxicology

One of the major toxicities observed with *S androgynus* is Bronchiolitis obliterans (BO) represents a severe, irreversible obstructive lung disease characterized by inflammatory fibrosis of the small airways, leading to progressive airflow limitation and debilitating dyspnea [30]. BO mostly complicates hematopoietic stem cell transplantation, lung transplantation, or heart-lung transplantation. In Taiwan 1995 outbreak of respiratory illness a watershed moment in understanding BO, as epidemiological investigation revealed the excess consumption of *S androgynus* and the development of this otherwise uncommon condition (30).

Patients diagnosed with *S androgynus*-associated bronchiolitis obliterans (SABO) were predominantly 40-year-old middle-aged women . The quantitative exposure assessment indicated that affected individuals consumed daily approximately 82grams of raw *S. androgynus* leaves over a ten-week period. However, assessment in Malaysian populations showed that a weekly intake of 150–200 grams of cooked leaves did not cause any BO (30). This assessment implicates that the thermal processing potentially degrades or modify putative toxic constituents.

The development of bronchiolitis obliterans (BO) involves complex interactions between innate and adaptive immune responses. BO begins with inflammation of lungs, recruitment of immune cells, and damage to airway tissues, which can progress to irreversible fibrosis and chronic obstructive pulmonary disease if left untreated. Although early immunosuppressive or immunomodulatory therapy may slow the disease progression, chronic BO is largely untreatable. The only remedy for the chronic BO is lung transplantation. The etiology of the BO is the release of various inflammatory mediators like TNF-α and T-cell responses, while later research identified the toxic chemical component papaverine, in *S androgynus* .Experimental studies showed that certain extract fractions, especially lipophilic ones, cause significant cell damage, and papaverine exposure can induce BO-like changes by increasing factors such as TGF-β and eNOS that promote fibrosis and tissue injury (31,32,33).

However, recent studies suggest that papaverine alone may not fully explain the toxicity, as papaverine-free extracts also triggered inflammation, immune activation, and lung damage through various mechanistic pathways. Multiple compounds can also result in BO development , including water-soluble substances and possibly heavy metals like cadmium, may contribute to the disease. The plant's ability to accumulate cadmium, which can damage the DNA and result in oxidative stress (34).

Overall, the toxicity of *S. androgynus* appears to result from the combination of multiple constituents rather than one compound. Therefore, in vivo and invitro studies are needed to identify the toxic agents, understand their interactions.

Discussion

The present review summarizes the current understanding of *S androgynus,* a medicinal plant within traditional medicine systems and contemporary pharmacological research. The accumulated evidence indicates that *S androgynus* offers substantial nutritional and therapeutic value, its clinical utility is constrained by significant safety concerns (35).

The pharmacological profile of *S. androgynus* consist of bioactive constituents that have been partially identified through modern analytical techniques. The identification of flavonoid glycosides, particularly 3-O-β-D-glucosyl-(1→6)-β-D-glucosyl-kaempferol (GGK), along with lignans, nucleosides, and terpenoids, provides multiple pharmacological activity(36-39). The major activity exhibited by the plant extract is anti-inflammatory effect which is demonstrated in both in vitro and in vivo models. Here protein extracts and methanol fractions have shown reduced protein denaturation and membrane stabilization comparable to reference non-steroidal agents (39,40). The suppression of nitric oxide production in lipopolysaccharide-stimulated macrophages further supports the immune modulation (41).

The antioxidant effects of *S androgynus* are mainly due to it's the active polyphenols and chlorophyll. Studies in rats have shown that chlorophyll from the leaves can ameliorated sodium nitrite-induced oxidative stress in rats. This was revealed by reduced malondialdehyde levels and improved hematological parameters. These findings support its traditional use for treating conditions related to oxidativestress. However, antioxidant assays like the DPPH assay only give limited information, so their results should not be directly assumed to reflect real effects in clinical studies(42,43).

The plant extract also exhibits immune-boosting properties. In in vivo, it elevated CD4+ T-cells and interleukin-2, which are important for immune defense, especially against infections like typhoid. This suggests it may help in controlling infectious diseases.

Traditional claims regarding galactagogue activity, is the most widespread ethnopharmacological use of this plant across Indonesia, Malaysia, and the Philippines. This plant has received preliminary experimental support through studies demonstrating prolactin and oxytocin gene expression in lactating mice (44,45). Similarly, the anti-obesity effects observed in Wistar rats treated with flavonoid called GGK—manifesting as reduced food intake and serum triglycerides without histopathological abnormalities (46).The anti-ulcer activity demonstrated in aspirin-induced peptic ulcer models, where ethanolic extracts reduced tumor necrosis factor-alpha levels and improved duodenal tissue architecture, (47).

The 1995 Taiwanese outbreak of bronchiolitis obliterans associated with raw vegetable juice consumption marked aa a major adverse reaction in the scientific assessment of this plant (48). The observed demographic pattern—where middle-aged women consumed about 82 grams of raw *Sauropus androgynus* leaves daily over ten weeks—indicates two major possibilities. First, women in this group may be more prone (susceptible) to the harmful effects. Second, the toxicity may be dose-dependent (49). Similarly papaverine in leaf extracts at concentrations of 580 mg per 100 grams fresh weight when administered to animal revealed constrictive bronchiolitis development (50,51).

Chang et al. reported that aqueous fractions without papaverine induced bronchiolar injury in murine models through macrophage activation, endothelial cell inhibition, and upregulation of transforming growth factor-beta and endothelial nitric oxide synthase (52). These findings suggest that *S androgynus*-induced bronchiolitis obliterans likely involves multiple toxicological pathways (52).

Lung damage caused by *S androgynus* differs from chronic obstructive pulmonary disease (COPD) in its progression. Patients typically show an initial decline in lung function, followed by long-term stability. The condition mainly affects the small airways, as confirmed by tissue examinations. This also indicates that these airways have limited ability to regenerate after injury (48,51).

Future research on *S androgynus* should focus on identifying all its active compounds through advanced metabolomic studies, followed by in vivo and invitro studies. It is also important to determine safedose. Clinical trials evaluating its traditional uses, especially for improving breastmilk production and blood sugar control monitoring for possible side effects, particularly on the lungs. Overall, *S. androgynus* highlights the challenge of balancing traditional knowledge with scientific evidence, as it offers nutritional and medicinal benefits but also carries potential health risks. Therefore, continued interdisciplinary research is essential to ensure its safe and effective use in modern healthcare

Conclusion

S androgynus, a medicinal plant rich in active compounds like chlorophyll, fatty acids, polyphenols, flavonoids, and other bioactive compounds. It is well known for its pharmacognostical and pharmacological properties. In vitro and in vivo studies show that this plant has various pharmacological property including anti-inflammatory, antioxidant, immunomodulatory, anti-diabetic, anti-obesity, anti-ulcer, and melanogenesis-inhibitory properties. *S. androgynus* phytochemistry is still unclear. Many physiologically active compounds in the plant's roots and leaves remain unknown, limiting its therapeutic use. Early data supports several traditional claims, such as enhancing breast milk in nursing mothers and curing metabolic illnesses, but more pre-clinical and clinical data are required to support this claim. Pharmacovigilance is concerned because excessive usage of S. androgynus has been related to bronchiolitis obliterans (BO), a serious and irreversible respiratory disorder. This adverse effect also limits its therapeutic use. More toxicological study is needed to identify the optimal dose, cytotoxic and genotoxic effects. S. androgynus has nutritional and medicinal potential. Once its safety profile is known and scientifically proved, pharmaceutical formulations and natural health remedies may benefit. To ensure its safe and effective use in modern medicine, future researchs should mainly focus on phytochemical characterization and mechanistic pharmacological studies.

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