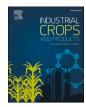


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The Vietnamese medicinal and food plant *Abelmoschus sagittifolius* (Kurz.) Merr., an underestimated resource



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ABSTRACT

In Vietnam, "Sam Bo Chinh" [Abelmoschus sagittifolius (Kurz.) Merr., Malvaceae] market has rapidly expanded following the COVID-19 pandemic due to its health benefits. Since the 19th century, its root has been utilized in Traditional Vietnamese Medicine with properties similar to fresh Ginseng, particularly for treating fatigue, neurasthenia, sore throat, and stomach ache. Similar applications of its root are documented in Traditional Chinese Medicine, but leaf and fruit are also employed for detoxification, phlegm expulsion, liver softening, and kidney nourishment. However, further evidence is required to assess its medicinal value and explore additional avenues for development. Articles were searched on PubMed, CNKI, Google Scholar, ResearchGate, and VISTA using the four commonly used synonyms as keywords. Duplications and articles on other species were then screened out. Related books, articles, and websites were also discussed. The species has unique characteristics that are distinctive from other Malvaceae species. Traditional Vietnamese and Chinese medicine practitioners describe similar properties of A. sagittifolius root as qi and yin tonifying material. Various traditional Vietnamese formulas and Chinese patents illustrate the values of the root, leaf, or fruit to treat digestive, respiratory, neuropsychological, and genitourinary disorders. Pharmacological research and phytochemical profiles also highlight the ability of A. sagittifolius root to be an adjuvant treatment for post-COVID-19 symptoms with gastric protection, stamina enhancement, antioxidant, anti-inflammatory, and anti-cancer activities, and simultaneously, they suggest more potential such as neuroprotection, immunomodulatory and anti-hypertention. Moreover, cultivating and processing techniques are simple. So, A. sagittifolius production can be industrialized and developed into medicines or functional foods. However, the plant is not used in other countries and is not well-studied, so a more rigorous assessment of its phytochemical and pharmacological properties is needed. Its leaf and fruit also have different uses and can be developed and more medicinal potential.

1. Introduction

"Sam Bo Chinh" or "Sam Bao" [Abelmoschus sagittifolius (Kurz.) Merr., Malvaceae] was first mentioned in Traditional Vietnamese Medicine in the 19th century as a substitution for *fresh Ginseng* (Le, 2005). Nowadays, it is still consumed as a health-benefiting food. In China, this species is named *Jian ye qiu kui* (Medicinal Plant Name Services, 2023), while its root is called *Wu zhi shan shen* (Guangzhou Military, 1969). The leaf (*Wu zhi shan shen ye*) is used as a toxin-resolving and pus-expelling drug, and the fruit (*Huo pao cao guo*) has been used as a *liver* softening and *kidney* nourishing agent in Traditional Chinese Medicine (TCM) (Song, 1999).

In Vietnam, "Sam Bo Chinh" has been considered a valuable plant as there is a specific monograph in the Vietnamese Pharmacopoeia (VPC, 2018) and a standard agricultural procedure was developed (Pham et al., 2013). Interestingly, since 2020, many new *A. sagittifolius*

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Abbreviation: ASW, *Abelmoschus sagittifolius* root water extract; ASE, *A. sagittifolius* root ethanol extract; BAP or BA, Benzyl aminopurine; GA3, Gibberellin A3; IBA, indole-3-butyric acid; KT, Kinetin; NAA, α-Naphthaleneacetic acid; 2,4-D, 2,4-Dichlorophenoxyacetic acid; MPNS, Medicinal Plant Name Services, RBG Kew.

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cultivating farms started to operate B., (2023); D., (2021); D., (2022); L., (2022); P., (2023); P.N., (2022); Phan, (2023); Phan, (2022); T., (2023); V. and G., (2023) with broadened marketing on online newspapers and social networks. This trend may not directly relate to the introduction of a new organic cultivating procedure in December 2020 (CESTI, 2020) or to the latest National Program for the Development of Pharmaceutical and Medicinal Material Industry in 2021 (Prime Minister, 2021) but to the concurrent expansion of interest in natural health-benefiting products for treating post-COVID-19 symptoms, such as dyspnea, fatigue, dry cough, and neuropsychiatric dysfunction (Nalbandian et al., 2021; Ng et al., 2023).

It is unfair that *A. sagittifolius* root is used only because its appearance, flavors, properties, and tonifying effect are similar to *fresh Ginseng* (Do, 2004; Le, 2005). Hence, to express that the potential of *A. sagittifolius* is underestimated, this study aimed to review what we know about the species, how it can be characterized, cultivated, and developed into herbal drugs and functional foods, clarify the nutritional, medicinal, and economic potential of the species, offer numerous scientific opportunities and poses a range of challenges.

2. Methods

Review or original research was retrieved from PubMed (Kim et al., 2023), CNKI (CNKI, 2023), Vietnam Information of Science and Technology Agency (VISTA) (Science and Technology Information System, 2023), Google Scholar (Google Scholar, 2023), and Research Gate (ResearchGate, 2023) databases regardless of language, including Indian, Thai, Arabian, and Dutch but none was found. The searches were done up to September 2023, using the keywords Abelmoschus sagittifolius, Abelmoschus moschatus subsp. tuberosus, or Hibiscus sagittifolius in all fields. Article titles and abstracts were skimmed to filter out articles on other species, like Abelmoschus esculatus and A. moschatus. Then, full texts were scanned for mentions of the species' scientific names, synonyms, or common names; if the mentions were in the introduction sections or reference lists only, the articles were also removed. Articles with the same name but from different databases, have the name translated into other languages, or have different names but similar content were considered duplicates and removed. During the document overview, articles without information on research methods are also counted [Appendix 1] but not referenced in the paper.

For global ecological distribution, the Global Biodiversity Information Facility (Secretariat) was referred to, using an occurrence search filtered by scientific names of "Abelmoschus rhodopetalus F. Muell.", "Abelmoschus sagittifolius (Kurz.) Merr.", "Abelmoschus moschatus subsp. tuberosus (Span.) Borss. Waalk.", "Hibiscus sagittifolius Kurz.", "Hibiscus sagittifolius var. quinquelobus Gagnep", basis of record of "human observation" and occurrence status of "present". Ethnomedicine usages of the species in other countries were searched on ResearchGate and Web of Science using the keywords "(ethnomedicine OR ethnopharmacy OR ethnopharmacology OR ethnobotanical) AND (country name)". All of the retrieved articles were scanned for mentions of the species.

To review the bioactivities of commercially available isolated compounds, PubChem (Kim et al., 2023), Drugbank (Wishart et al., 2017), ChemBL (Zdrazil et al., 2024), HIT (Yan et al., 2022), and TCMSP (Ru et al., 2014) databases were referred to. Bioactivities that were concluded to be "Active" were recorded; "Unspecified" or "Inactive" ones were left over.

3. Results

3.1. Recognition of Abelmoschus sagittifolius (Kurz.) Merr

The plant's names varied in well-known botanical and pharmacognosic documents, such as *Abelmoschus sagittifolius* (Kurz.) Merr. (Guangzhou Military, 1969), *Abelmoschus moschatus* ssp. *tuberosus* (Span.) Borss. (Pham, 1999), *Hibiscus sagittifolius* Kurz. (Do, 2004) and Hibiscus sagittifolius Kurz var. quinquelobus Gagnep. (Do et al., 2009). This indicates no fixed species name in documents. Therefore, at the beginning of this review, a quick screening for articles on Google Scholar and ResearchGate was done to select suitable search keywords. According to RBG Kew's Medicinal Plant Name Services (MNPS), the accepted name of the species is *Abelmoschus rhodopentalus* F. Muell, with 33 scientific synonyms (Medicinal Plant Name Services, 2023). However, related articles were barely found using synonyms other than "A. sagittifolius", "A. moschatus subsp. tuberosus" and "Hibiscus sagittifolius", so they were accepted as search keywords.

The plant can be recognized as a perennial herb, 30–100 cm high or higher; it grows upright, weakly, or leaning on surrounding plants. The stem is cylindric, slightly red, hispid, and has stiff hair. The root is swollen, radish-shaped, or humanoid-shaped, resembling *Ginseng*. Leaf shape varies. Basal leaves are oval, cordate, or sagittate with dull tips. Upper leaves are palmately 5-lobed or sagittate 3-lobed and indumentum. The stipule is filiform. The flower grows single at the leaf axil, 8 cm in diameter. Pedicel is 5–8 cm long and hispid. 7–10 epicalyx are linear, 10–14 mm long. Five calyx are succiform, notched, and deciduous. The petal is red, pink, or reddish-brown with a white or slightly yellow base. Stamen is tubular and red with anthers inserted along the length. Style is 5-branched at the top, containing stigma. Capsule ovate, acute, 3 cm in height, consisted of 5 carpels. Seed kidney-shaped, brown, pubescent with fine, slightly yellow ridges (Do, 2004; Pham, 1999; Vo, 2019).

Although the Flora of China (Wu et al., 2007) and the Flora of Vietnam (Pham, 1999) take different approaches to the key to genera of Malvaceae and the key to species of *Abelmoschus*, they agree that *Hibiscus* is the closest genus to *Abelmoschus* and *A. moschatus* Medik. is the closest species to *A. sagittifolius* (Kurz.) Merr.; this result is consistent with phylogenetic analysis (Li et al., 2020). Their similar and distinctive features are presented in Table 1 and Table 2.

The species can be characterized by the combination of indumentum hispid herbs, sagittate or palmately lobed leaf blades, red or pink petals with white or pink bases, filament tubes with anthers inserted along the length, 5-branched apex, and radish-shaped swollen roots.

There are wide varieties of *A. sagittifolius* in Vietnam, with variable leaf blade shapes and petal colors. Leaf blades can be sagittate, palmately lobed, or heart-shaped. Petals can be pink with a white base, yellow with a red base, or pink with a red base, obovate-oblong, obovate, or subrounded (Nguyen et al., 2020).

The variety from Quang Binh province was considered the best, providing the highest yields and mucilage contents (Nguyen et al., 2020). Interestingly, this variety is also the one documented in Vietnamese Traditional medicine literature (Le, 2005) and monographs (Do et al., 2009; Do, 2004; Pham, 1999; Vo, 2019). Thus, it is the most common cultivar and can be considered the morphological standard for cultivated plants. (Pham T.H. et al., 2021)

When this review was started, the accepted name in MPNS was *A. sagittifolius* (Kurz.) Merr., but in December 2023, it was changed into *A. rhodopentalus* F. Muell. Nevertheless, articles were not found using the new name, so the change does not affect the collected data. "Rhodopetalus" means Rhododendron-like petals and is first mentioned in the name *Hibiscus rhodopetalus* (F.Muell.) F.Muell. ex Benth. According to Flora of Vietnam (Pham, 1999), together with Flora of China (Wu et al.,

Table 1

Similar and distinctive features between genera of Abelmoschus and Hibiscus.

	Abelmoschus	Hibiscus	
Similarities	Loculicidal capsule fruit grown from 3 to 5 fused carpels ovary;		
	5-12-lobed epicalyx, growing together with flowers; filament tube		
	with anthers inserted along the length, 5-toothed or truncate apex;		
	Reniform but rarely globose seed with parietal or pendent placentation		
Differences	Spathe-like calyx, split down one	Symmetrical calyx, regularly	
	side and deciduous	lobed and persistent	

Table 2

Similar and distinctive features between A. sagittifolius and A. moschatus.

	A. sagittifolius	A. moschatus
Similarities	Indumentum herb, hispid with yellow hairs Ovate-hastate, sagittate, or palmately lobed leaf blade	
	2–7 cm long pedicel; 6–12-lobed 2–6 cm long epicalyx; subglobose or ellipsoid 4–8 cm long capsule.	
Differences	0,3–0,5(0,7) m tall herb; Often-swollen root;	1–2 (3.5) m tall herb; Never-swollen root;
	Red or pink but rarely yellow petals with white or pink bases	Light yellow petals with brown or violet bases
	4–5 cm long capsule, pubescent seed.	5–8 cm long capsule, smooth seed

2007) and others from eFlora, *A. sagittifolius* is the only *Abelmoschus* species with red or pink petals, but white and yellow are also mentioned. Therefore, "rhododendron-like" may represent the particular shape of obovate-oblong petals instead of obovate ones of other species. The new name may describe the specific features mentioned above better because petals are the feature that distinguishes standard variety from others.

3.2. Distribution and cultivation

It is cultivated in various areas in Vietnam, from the Middle Vietnam and Tay Nguyen highlands to the Northern and Southern Vietnam plains (Do et al., 2009; Do, 2004; Nguyen et al., 2020; Pham, 1999; Pham T.H. et al., 2021; Vo, 2019). In Hainan, the species is found in Yinggeling Mountain (Zheng and Xing, 2009). It is also found in Luocheng, Guangxi (Hu et al., 2020), in Rongjiang, Guizhou (Chen et al., 2019), and Qianjiang, Chongqing, China (Zhang and Li, 2018).

Based on the Global Biodiversity Information Facility (GBIF), its distribution center is Northern Australia, but it can also be found in India, French Polynesia, the USA, the Dominican Republic, Thailand, and Vuanatu (User, 2024).

This is a significant finding because *A. sagittifolius* is not unique to Vietnam and China, letting researchers and cultivators from other countries research their local plants.

3.3. Traditional uses

In Vietnam, A. sagittifolius root was first used as a substitution for fresh Ginseng in the 19th century, in the famous book "Hai Thuong Y Tong Tam Linh". It was described as a blood-in-qi drug combined with other materials in formulas tonifying yang and yin or qi and blood (Le, 2005). Later, researchers collected many other formulas from communities and documented them in books on Medicinal Materials (Do et al., 2009; Do, 2004; Vo, 2019). It was an ingredient in medicinal formulas to treat cough, fever, thirst, and leanness related to heat and dryness or as a diuretic or menstruation regulator (Do et al., 2009; Do, 2004; Vo, 2019). The Vietnamese Pharmacopoeia describes that 'Sam Bo Chinh' has a sweet and mild flavor, neutral properties, and toward spleen and lung meridian tropism. It is used to tonify qi, benefit blood, promote the secretion of bodily fluids, alleviate thirst, arrest cough, and eliminate phlegm; for patients with a weakened body, fatigue, lack of appetite and sleeping, neurasthenia, dizziness, stomach ache, diarrhea, cough, sore throat, bronchitis, in forms of aqueous decoctions, powders or alcoholic beverages (VPC, 2018) [Appendix 4]. Most formulas were tonifying and used to nourish yang, yin, qi, or blood; this confirms the neutral properties of A. sagittifolius root and the various possibilities of using the material with different ingredients for diverse purposes. However, it is most commonly used in tonifying qi or nourishing patients with weakness, malnutrition, or neurasthenia.

In China, *A. sagittifolius* root is described as having a sweet and mild flavor, slightly warm properties, and action through the *spleen* and *kidney* meridian. It has nourishing and tonifying health effects and is used for neurasthenia, dizziness, low back pain, stomach ache, and diarrhea (Guangzhou Military, 1969). The fruit has a sweet and mild flavor and neutral properties. It is used to soften *liver* and nourish *kidney*, regulate

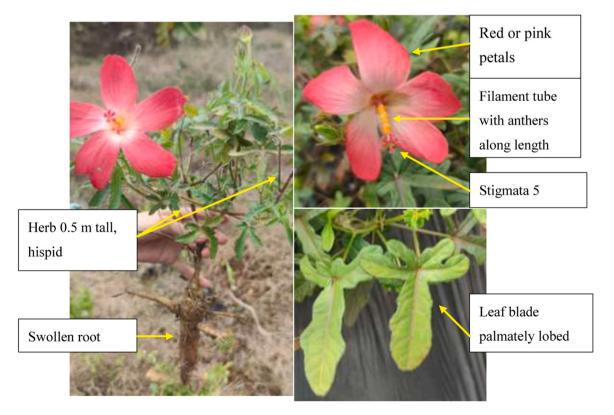


Fig. 1. Abelmoschus sagittifolius (Kurz.) Merr. and its features. Source: taken in Quang Nam province



Fig. 2. Different leaf blades and petals among A. sagittifolius varieties (Nguyen et al., 2020).

stomach, and relieve pain for kidney deficiency, hearing loss, stomach pain, malnutrition, and juvenile poliosis. (Song, 1999) The leaf has a slightly sweet flavor, neutral properties, and toxin-resolving and phlegm-expelling effects. It could be used externally for swelling and toxic sores (Song, 1999). Besides, root and leaf can be used as mashed and applied in massage therapy to treat rheumatoid arthritis and sore (Zheng and Xing, 2009). According to Patentscope by the World Intellectual Property Organization (WIPO), 23 patents applying *A. sagittifolius* were published, all from China (WIPO, 2024). Most patents describe complex preparations, including *A. sagittifolius*. From *A. sagittifolius*, root, leave, and fruit were used. The products were either drug formulas or foods. [**Appendix 5**]. This demonstrates the various potentials of *A. sagittifolius* in developing health-benefiting products.

Besides, no medicinal uses of the species were found in the other countries, as no record of local/traditional uses was found in the relevant databases (Hussain et al., 2021; Kiewhuo et al., 2023; PFAF, 2010-2023; Samal, 2022; USDA, 1992-2016) and ethnopharmacy reports (Chassagne et al., 2023, 2022; Clarke, 2015; Girardi et al., 2015; Hughes et al., 2019; Inta et al., 2008, 2013; Jost et al., 2016; Junsongduang et al., 2013, 2020; Kantasrila et al., 2020; Locher et al., 1995; Maneenoon et al., 2015; McClatchey, 1996; Neamsuvan et al., 2015; Nguanchoo et al., 2023, 2019; Panyadee et al., 2018, 2019; Srithi et al., 2009, 2012; Tangjitman et al., 2015; Whistler, 1991). As a result, A. sagittifolius is underestimated because its medicinal value is only acknowledged in Hainan and Vietnam. Even though the Vietnamese and the Hainanese describe the tropism of A. sagittifolius root differently, it contributes to Vietnamese formulas for neural, menstrual, or urinary disorders related to kidney functions and Chinese patents for respiratory diseases. This indicates that Vietnamese and Chinese practitioners have similar underlying theories for applications of A. sagittifolius root. Tonifying qi and yin and acting through the spleen, lung, and kidney meridians are essential commonalities between both systems. Moreover, substituting usage between the leaf and the fruit suggests similarities in phytochemical and pharmacological properties among the used parts.

3.4. Medicinal value of A. sagittifolius (Kurz.) Merr

3.4.1. From traditional chinese medicine perspective

Although only 10-30% of patients may experience post-COVID-19

disorders (Ng et al., 2023), any respiratory, digestive, cardiovascular, or neuropsychiatric disorder will intervene in life quality, especially dyspnea, dry cough, chronic fatigue disorders, neurasthenia, and reduced gastrointestinal function (Nalbandian et al., 2021; Ng et al., 2023). In those cases, the integration of Traditional Chinese Medicine and Modern Medicine shows an impactive role similar to acute conditions. According to Traditional Chinese Medicine, primary conditions relate to qi and yin depletion or deficiency, liver *qi* or *blood* stagnation, dampness, heat-dampness, or phlegm accumulation (Jiang, 2021; Thede, 2021). As a result, *A. sagittifolius* root became a proper choice for those conditions as it can tonify *lung qi* and spleen qi and nourish *yin* and detoxify.

The tonifying effect of *A. sagittifolius* root is more than just theoretical. Nutritionally, it is rich in total protein, total sugar, reducing sugars, fatty acids, fiber, and minerals (Do et al., 2009). Eighteen amino acids, including nine essential ones, were determined through HPLC analysis (Tran and Nguyen, 2021). According to the investigation of Dao Thi Vui *et al.* (2007), its aqueous extract enhanced mice's performance in Brekhman's swimming test by 85.3% (p < 0.01) with added 5% of weight and pool temperature of 29 \pm 1°C while ethanol extract enhanced 35.1% (p < 0.05) of performance (Dao, 2007). In Castiella et al.'s hexobarbital-induced sleep test, *A. sagittifolius* root ethanol and aqueous extract expressed sedative effects as they prolonged sleep time by 164.6% (p < 0.01) and 79.4% (p <0.01), respectively, (Dao, 2007). This suggests the extract can be used for patients with exhausted, weakened, or malnourished bodies or with dysregulation of *qi*.

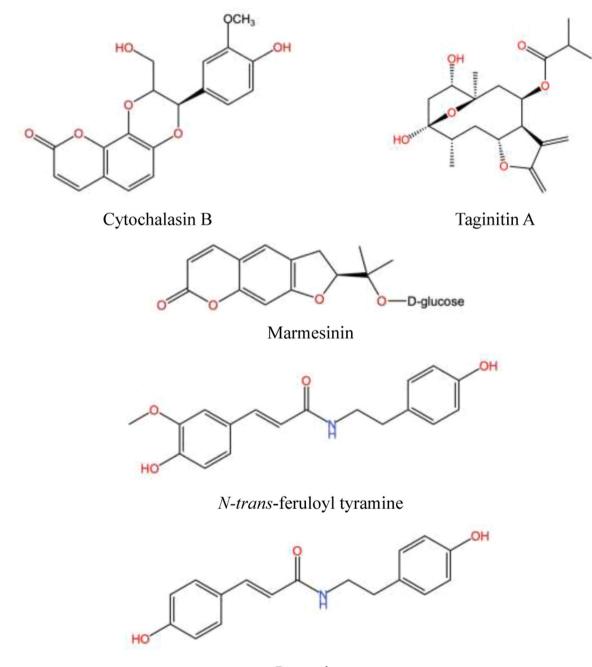
Simultaneously, in white rats, the aqueous extract and total mucilage also reduced total acid content in gastric juice by 79.5% and 69.5%, respectively (p <0.01, 2.67 g/kg dosage) (Dao, 2007), as well as successfully inhibited *Helicobacter pylori* of 76.7% and 82.5%, respectively (p < 0.001, *in-vitro*, 24 hours of contact) (Dao, 2007). The aqueous extract effectively reduced ulcers in pyloric ligation and ethanol-related acute gastric ulcer models at 10 g/kg (Dao, 2007). In the indomethacin-related acute ulcer model, it effectively protected the stomach from ulcers (73.6%, p < 0.01, at the dosage of 10 g/kg, taken 30 minutes before indomethacin) and promoted restoration after 48 hours of treatment (74.3%, p < 0.01) (Dao, Nguyen, and Nguyen, 2007). However, in acetic acid-induced chronic ulcers, it did not significantly prevent ulcer formation but effectively promoted restoration after 15 days of treatment (70.7%, p <0.01) (Dao, 2007). As a result, *A. sagittifolius* root aqueous extract can be used in gastrointestinal disorders, especially ones relating to dysregulation of *liver* and *stomach*.

A. sagiitifolius root water extract is devoid of acute toxicity and chronic damage to liver and kidney functions (Dao, 2007). Even using a 100–180 g/kg dosage, the extract did not cause death in white rats 72 hours after administration (Dao, 2007). Similarly, after 15 and 30 days of administration, the water extract at 3 g/kg and 9 g/kg did not affect rabbits' body weight and normal activities. No significant changes in blood formula, plasma AST, ALT, protein, cholesterol, bilirubin, and creatinine content; similar results were found in liver and kidney histology (Dao, 2007). As a result, it is a safe material that can be used for a long time, fitting the potential of a tonifying drug.

Hence, according to the Traditional Chinese Medicine perspective and partial support from pharmacological reports, it is reasonable for *A. sagittifolius* root to become a complementary treatment for post-COVID-19 fatigue, digestive disorders, and neuropsychiatric imbalances.

3.4.2. From pharmacognosy perspective

Through phytochemical screening, flavonoids, coumarins, phytosterols, sesquiterpenoids, amino acids, organic acids, reduced sugar, and mucilage were tentatively reported as metabolites in *A. sagittifolius* root (Dao, 2007; Le et al., 2022). Mucilage is the most abundant constituent of *A. sagittifolius* root with about 30–40% yield (Le et al., 2022). Besides, 31 compounds were also isolated, mainly from the root (Chen et al., 2019, 2016; Dinh, Vu, Le, et al., 2022) and some from aerial parts (Dinh,



Paprazine

Fig. 3. Potential compounds isolated from A. sagittifolius.

Vu, Vu, et al., 2022), including 11 sesquiterpenoids, three steroids, one triterpenoid, and 12 phenols [**Appendix 2**]. Among them, 14 are commercially available, 12 of which can be considered distinctive to *Abelmoschus moschatus* Medik. (Pawar, 2017), including: **3**. Taginitin A, **8**. Vomifoliol, **12**. Friedeline, **13**. Cleomiscosin A, **14**. Marmesinin, **16**. Paprazine, **17**. (*R*)-lasiodiplidin, **18**. (*R*)-de-*O*-methyl lasiodiplodin, **21**. Cytochalasin B and **22**. Dibutyl phthalate (Fig. 3).

Generally, its mucilage and polysaccharides need to be assessed for anti-inflammatory and immuno-modulatory effects (Ng et al., 2023), similar to mucilages of Hibiscus sabdariffa L., Abelmoschus esculentus (L.) Moench, and other species (Hussein et al., 2019; Seo and Shin, 2012; Shang et al., 2007; Tieobut et al., 2020; Tosif et al., 2021). Otherwise, its terpenoids and polyphenols may have anti-inflammatory, antioxidant, and anti-tumor activities, while its amides can provide neurological effects. Abelsaginol from the ethyl acetate fraction of A. sagittifolius root expressed a significant ABTS++ scavenging activity with IC_{50} = 41.04 \pm 6.07 mM, twice as high as of Trolox (IC_{50} = 25.16 \pm 1.64 mM) (Dinh, Vu, Le, et al., 2022). Moreover, N-trans-feruloyl tyramine and Hibiscone B was found to have α -glucosidase inhibitory activity with IC₅₀ values of $4.3 \pm 0.5 \,\mu\text{g/mL}$ and $121.7 \pm 3.9 \,\mu\text{g/mL}$, respectively (Hoang et al., 2021). Finally, eight compounds from A. sagittifolius root acetone extract performed cytotoxicity effect, including Acylhibiscone B, 2β , 7, 3-trihydroxycalamenene 3-O-β-D-glucoside, N-(p-trans-coumaroyl)-N-methyl tyramine, Cleomiscosin A, 9,12,13-trihydroxy-10,15-heptadeca-dienoic acid, Cytochalasin B, Marmesinin and N-(p-trans-coumaroyl) tyramine (Chen et al., 2019).

To explore the pharmacological potential further, commercially available compounds were assessed for bioactivities using Pubchem, Drugbank, ChemBL, HIT, and TCMSP databases [Appendix 3]. No compounds except Dibutyl phthalate are recorded in the Drugbank database; only Cytochalasin B and Dibutyl phthalate were recorded in ChemBL and HIT 2.0. Cytochalasin B was noted by HIT 2.0 to directly inhibit Solute carrier family 2, facilitated glucose transporter member 1 (SLC2A1) (Yan et al., 2022), while it was reported by PubChem to have acute toxicity and inhibit plenty of enzymes and proteins, including D3 Dopamine Receptor, cystic fibrosis induced NFkB, TDP1, PRPC, etc., together with significant anti-tumor activities such as inhibiting Peg3 Promoter, APP translation, Mdm2/MdmX interaction, inducing DNA re-replication in SW480, mitochondrial apoptosis in HeLa cells, inhibiting cell growth against HOP-18, SNB-75, SN12K1, CAKI-1, UO-31, IEC-6 and cytotoxicity against A549, XF498, HeLa, SKOV3, HCT15, SK-MEL-2 cells... (Kim et al., 2023). It thus seems to be the most critical bioactive and toxic compound. Dibutyl phthalate is a common anti-parasitic agent in many medicinal plants (Kim et al., 2023; Wishart et al., 2017; Yan et al., 2022; Zdrazil et al., 2024). N-trans-feruloyl tyramine is predicted to interact with several targets, such as Neuronal

acetylcholine receptor; $\alpha 3/\beta 4$, Adenosine A1, A2a, A3 receptor, Muscarinic acetylcholine receptor M1, Nitric oxide synthase, Matrix metalloproteinase 9, Sodium/hydrogen exchanger 1, Monoglyceride lipase... (Zdrazil et al., 2024) and it is indicated to have anti-inflammatory activity by inhibiting sodium nitroprusside induced nitrite accumulation, LPS-induced iNOS protein expression, LPS-induced PGE2 production and porcine pancreatic lipase (Kim et al., 2023). Although *Friedeline* is predicted to interact with several targets similarly to N-trans-feruloyl tyramine (Zdrazil et al., 2024), it is indicated to have antifungal activity against Phytophthora cactorum (Kim et al., 2023). Paprazine is also a potential anti-inflammation and anti-melanogenic agent (Kim et al., 2023). It is noted to inhibit phorbol-12-myristate-13-acetate-induced ROS production, LPS-induced NO production, porcine pancreatic lipase, monophenolase activity of tyrosinase, baker's yeast α -glucosidase, Saccharomyces cerevisiae α-MSH-stimulated mouse B16F10 cells α -glucosidase, and CD3/CD28/mAbs-stimulated human T-cell proliferation (Kim et al., 2023).

The bioactive potentials of *A. sagittifolius* fit Chester Yan Jie Ng et al. (2023) summary of potential medicinal foods in managing post-COVID-19 disorders (Ng et al., 2023). They also indicate that *A. sagittifolius* can be an effective antioxidant, anti-inflammatory, hep-atoprotective, and neuroprotective agent. Again, this strengthens the value of *A. sagittifolius* as an adjuvant treatment against post-COVID-19 symptoms. However, it needs to be noted that many of the effects reported are based on early-stage experimental or *in-silico* approaches.

3.5. Potential for industrial crops and products

3.5.1. Plant physiological properties

Nowadays, A. sagittifolius is cultivated in several provinces throughout Vietnam (Nguyen et al., 2020; Pham T.H. et al., 2021), which indicates that it can adapt to various conditions. However, it prefers loamy, friable soil with a deep topsoil layer, good drainage, and abundant sunlight (Do et al., 2009; Pham et al., 2013), so it tends to grow better on lightly wooded low mountains. The basis for A. sagittifolius cultivating is its strong photoautotrophy. Clonal plants from node cuttings grew better within 16 hours per day in 150 µmol·m² $\cdot s^{-1}$ light intensity and photo-/dark period temperature of 28/25°C in a light exposure-dependent manner (Nguyen T.P.D. et al., 2017). Moreover, glucose and vitamins are not essential for A. sagittifolius under high photosynthetic photon flux density. Still, minerals help increase plant fresh weight significantly and the dried weight to a limited degree (Nguyen L.T.M. et al., 2017). However, excessive nitrogen supply can reduce root size, highlighting that fertilizers must not be abused (Nguyen et al., 2021).



Fig. 4. An A. sagittifolius field with black covers to prevent weeds and retain moisture. Source: taken in Quang Nam province

Like other species, growth regulators help in shoot and root induction and growth. It was found that the most and the highest shoots grew in a medium with 0.5 mg/L of Benzylaminopurine (BAP or BA) and 0.1 mg/L of indole-3-butyric acid (IBA); then, nodes from in-vitro shoots rooted best within 0.75 mg/L IBA (Mai and Trinh, 2022). For callus propagation, 2,4-Dichlorophenoxyacetic acid (2,4-D), Kinetin (KT) (Hu and He, 2012), BA (Duong et al., 2020) and α -Naphthaleneacetic acid (NAA) (Ngo et al., 2018) helped in callus induction and proliferation from cotyledon and hypocotyl. Callus induction was better from hypocotyl within 1.5 mg/L of BA and 0.5 mg/L of NAA (Duong et al., 2020) but better from cotyledon within 1.0 mg/L of 2,4-D and 0.1 mg/L of KT (Hu and He, 2012). Roots could grow better from callus than from cotyledon and hypocotyl within 0.3 mg/L of Indole-3-acetic acid (IAA) (Duong et al., 2020) or within 2 mg/L of BA and 1.0 mg/L of NAA (Hu and He, 2012). In in-vitro models, mediums for cultivating can be Schenk and Hildebrandt (SH) medium (Nguyen T.P.D. et al., 2017) or Murashige and Skoog (MS) medium (Mai and Trinh, 2022; Nguyen L.T.M. et al., 2017; Phan et al., 2014) carried in agar. MS medium can be modified by reducing nitrogen content (Nguyen L.T.M. et al., 2017), adding sucrose (Phan et al., 2014), or adding coconut juice (Mai and Trinh, 2022).

A study applied simulated microgravity on *A. sagittifolius* seeds and gained better germination ratios and aerial part growth rates; however, roots grown in microgravity were shorter and more branched (Duong et al., 2017). Although total coumarin and saponin content slightly increased when growing in microgravity (Duong et al., 2017), significant changes in the biological behavior of seedlings might be an issue.

These physiological properties explain the strong adaptability and wide occurrence of *A. sagittifolius*. The usual strong photoautotrophic behavior, with no need for complex techniques and excessive fertilization, allows it to be cultivated in various conditions that provide good drainage and abundant sunlight.

3.5.2. Cultivating techniques

Based on the aforementioned biological properties, areas for cultivating *A. sagittifolius* must be slightly gradient with a thick loamy layer (30–40 cm), well-drained, and not prone to flooding (Pham et al., 2013). Soil must be prepared carefully, with 25–30 cm high beds carrying 2–3 furrows 7–10 cm in depth (Do et al., 2009; Pham et al., 2013). Plants are propagated around February 15 (Pham et al., 2013) or from February to March (Do et al., 2009) from seeds, then are collected in December-January (Do et al., 2009; Pham et al., 2013). Seeds can be planted commonly at 2 cm depth in soiled furrow (Do et al., 2009) or be treated by quick sun-drying and soaking in warm water to germinate before planting (Pham et al., 2013).

There are no specific requirements during cultivation, but regular watering, weeding, shallow plowing, and scheduled fertilizing to provide enough nitrogen and other nutrients (Do et al., 2009; Pham et al., 2013). Planting density and fertilizer dosages help enhance growth indicators, fresh root weight, and dried root weight (Nguyen et al., 2021); plant spacing should be $25-30 \times 25-30$ (cm) (Do et al., 2009) or 20×15 (cm) (Pham et al., 2013) or 30×30 (cm) (Nguyen et al., 2021). Pests and diseases such as aphids (Do et al., 2009; Nguyen et al., 2021; Pham et al., 2013), caterpillars (Do et al., 2009; Nguyen et al., 2021; Pham et al., 2013), fruit decay (Do et al., 2009), spiders, *Rhizoctonia* root rot, stem base rot and root-knot nematode (Nguyen et al., 2021) can occur during cultivating. It was suggested that leaves and flowers could be trimmed so roots could receive a good nutrient supply (Do et al., 2009), but people tend to collect whole plants, even seeds.

Some authors suggested disinfecting seeds before germination by soaking them in a 0.10% solution of $HgCl_2$ for 10 minutes (Ngo et al., 2018), in a 25% solution of NaClO for 5 minutes, followed by an $HgCl_2$ 0.10% solution for 3 minutes (Duong et al., 2020) or in a 5% solution for 15 minutes (Pham T. et al., 2021). Gibberellin A₃ (GA₃) was also used to enhance germination (Duong et al., 2020; Phan et al., 2014).

The most critical preparation for *A. sagittifolius* cultivation is bed formation, especially in plains or rainy areas. According to farmers, root

rot can significantly damage crop yields, but it is common among tuberous plants. An annual crop also has advantages compared to *Ginseng*.

3.5.3. Harvesting and processing techniques

A. sagittifolius root is harvested on sunny days from December to January (Do et al., 2009; Do, 2004; Pham et al., 2013) when the plant turns yellow (Pham et al., 2013), then aerial parts and rootlets are removed. This harvesting period also fits the common high demand during the Lunar New Year. Although the quality and yield of *A. sagittifolius* root typically improve until the 12th month of cultivation (Pham et al., 2022), the 10–11-month period is more effective for market supply. Roots are usually sold fresh or made into liquors. They can be processed into dried pieces or powders, alone or mixed with aerial parts and other ingredients. Besides, it can be steamed (Do et al., 2009; Do, 2004), soaked in alum solution or ginger decoction, or soaked in rice water and steamed before drying (Do, 2004) for particular purposes.

There is no uniform drying method for A. sagittifolius root. It can be sun-dried or dried in an oven, whole, or in 3-5 mm thick pieces until reaching 12% humidity (Do et al., 2009; Do, 2004; Pham et al., 2013). While the Vietnamese Pharmacopoeia indicated that they could be sun-dried or dried in ovens (VPC, 2018), it was suggested to be dried at no more than 40°C (Do, 2004). The challenge is that monoterpenoids, sesquiterpenoids, and polyphenols are sensitive to high temperatures and UV lights. At the same time, insects, rodents, yeast, or other enzymatic damages can occur during long-period shade-drying or drying. Using total extract, mucilage, total saponin, and total polyphenol contents as criteria, Pham T.H.V. et al. (2022) suggested that drying at 55°C was acceptable while drying at 65°C and higher could damage appearance and phytochemical qualities (Pham et al., 2022). Similarly, steaming should not take longer than 5 minutes (Pham et al., 2022). They also suggested using modified atmosphere packaging (MAP) to store dried A. sagittifolius roots instead of vacuum packages, which might not be as effective as predicted (Pham et al., 2022).

These findings provide fundamentals to explain the agriculture and harvest routine. *A. sagittifolius* does not require cultivation for years like the *Panax* species; the best crop is annual. It is unreasonable to treat *A. sagittifolius* root like Ginseng, either. The material is better dried at 45–55°C, which will take up to 2 days. Steaming is acceptable within 5 minutes but contributes little to the products' stability.

3.6. Recent quality control strategies

Recently, only a monograph for *A. sagittifolius* root has been published in the Vietnamese Pharmacopoeia, which regulates description, microscopic identity, chemical identification tests, total mucilage extract, and other requirements of loss of drying, total ash, hydrochloride and insoluble ash, and impurities (VPC, 2018). Based on it, microscopic features of cultivated *A. sagittifolius* (Ho and Tran, 2023; Pham T.H. et al., 2021) were described and similar to those documented (VPC, 2018).

There is no monograph for *A. sagittifolius* or products from it in the Chinese Pharmacopoeia, but based on the regulated General Rules, a quality control strategy for *A. sagittifolius* root was introduced, including material description, microscopic indentification, TLC identification, moisture content, acid-insoluble components, ash content, and 70% ethanol extract content (Ou et al., 2023). TLC identification is a better perspective than chemical identification in the Sam Bo Chinh monograph in the Vietnamese Pharmacopoeia. However, 70% ethanol extract contributes better to heat-clearing and sedative activities, while total mucilage extract relates better to tonifying activities. Combining them seems to be a good strategy, but finding more precise assay methods would be better.

Besides, starch properties were studied by Pan Hao et al. (2022) (Pan et al., 2022), and a complete chloroplast genome of *A. sagittifolius* from Guangzhou, China was reported (Li et al., 2020). They can applied in

further identification or genomics studies.

3.7. Needs for further studies

Searching for *Abelmoschus sagittifolius* and three common synonyms, 23 articles were found from ResearchGate, 22 from Google Scholar, and nine from VISTA. After filtering duplication, 33 articles were identified [**Appendix 1**]. Such a limited number of studies suggests that the medicinal values of *A. sagittifolius* parts are mainly accepted based on Traditional Medicine perspectives, and we have yet to gain significant insights into its phytochemistry, pharmacokinetics, and pharmacodynamics properties.

Because *A. sagittifolius* can be found in many countries (Secretariat) and cultivated in various conditions (Do et al., 2009; Do, 2004; Nguyen et al., 2020; Pham T.H. et al., 2021; Pham et al., 2013), together with nonuniform drying methods (Do et al., 2009; Do, 2004; Pham et al., 2013), it is necessary to develop fingerprinting techniques that give insights into differences among cultivating conditions, processing methods, main active components and provide the basis for quality control and assurance strategies.

In another aspect, there are differences between the ethanol extract and the aqueous extract in terms of the pharmacological effects (Dao, 2007), and this partially explains doubts about which solvent is the best to prepare extracts: water, strong alcohol, or diluted ones. However, 33 hydrophobic compounds have been identified from *A. sagittifolius* methanol and acetone extracts but with low yields (Chen et al., 2019; Dao, Nguyen, Nguyen, et al., 2007; Dinh, Vu, Le, et al., 2022; Hoang et al., 2021). It doubts their significance, and mucilage is still considered the dominant constituent. The Vietnamese Pharmacopoeia regulates mucilage content as a quantification criterion; however, ethanol extract and isolated compounds provide relevant effects and are worth exploring their particular roles (Dao, 2007).

Interestingly, according to Dr. Duke's database summary, commonly used Abelmoschus and Hibiscus species, such as A. esculentus (L.) Moench, A. manihot (L.) Medik., A. moschatus Medik., H. cannabicus L., H. mutabilis L., H. rosa-sinensis, H. sabdariffa, and H. tiliaceus share the same general phytochemical profile, containing polyphenols, flavonoids, sterols, monoterpenoids, sesquiterpenoids, amides, amines, organic acids, and mucilages. They are also similarly used for treating inflammations, infections, fever, digestive, respiratory, cardiovascular, neuropsychiatric, and rheumatic disorders and as diuretics, aphrodisiacs, or antidotes (USDA, 1992-2016). Because A. sagittifolius parts are used for similar purposes, there is a strong potential that they have the same various phytochemical profiles, and more research is needed. On the other hand, mucilages and polysaccharides from different species have been found to have immuno-regulating activities (Hussein et al., 2019; Seo and Shin, 2012; Shang et al., 2007; Tieobut et al., 2020; Tosif et al., 2021); A. sagittifolius root mucilage may contribute to tonifying properties of the material.

Other extraction methods were also expected to yield better extraction results. The optimized parameters for ultrasonic-assisted extraction using aqueous ethanol 70% (v/v) were determined as 57.2 W/g of power, 11.4 minutes of ultrasonication time, and 17.3 minutes of following extraction (Pham T.M.T. et al., 2021). Vo T.P. *et al.* (2023) applied ultrasonic and microwave-assisted extraction procedures of phenolics and terpenoids using natural deep eutectic solvents (NADESs) and gained positive results (Vo et al., 2023).

Still, other aspects need to be controlled when establishing practical businesses. Quality assurance for cultivars, environmental impacts, crop cycling, heavy metal content control, and different approaches between food and medicine productions are essential for establishing sustainable cultivation. In market regulation, growth trends, downturns, consumer needs regarding flavors, appearance, benefits, and estimated value compared to *Ginseng* and other commonly used *Abelmoschus* and *Hibiscus* species must also be assessed. Correlations between phylogenetics and morphological characteristics, metabolism, and metabolomics, as well

as between phytochemical profile and pharmacokinetic and pharmacodynamic properties, require vigorous effort and provide abundant research opportunities.

In the future, more industrial production ideas can be developed, such as instant herbal drugs, foods, food bases, complementaries, or medicines, novelly designed or based on traditional medicinal formulas [**Appendix 4**]. The products can be developed not only from *A. sagittifolius* but also from other used parts or a mixture of them. Then, research on optimizing formulas and production procedures, assessing pharmacokinetics and pharmacological effectiveness, and the stability and safety of new products will also be needed. Therefore, the industrial application of *A. sagittifolius* can be considered a vast blue ocean where supplies are convenient and outcome products are variable.

3.8. Limitations of the evidence

Few reports about *A. sagittifolius* were found, but they are on different objectives and samples (**Appendix 1**); therefore, the results were not repeatedly confirmed. Moreover, reports from Vietnam and China were primarily published in national scientific journals and had limited contacts.

4. Conclusion

The expansion of *Abelmoschus sagittifolius* cultivation started in 2020, which relates to the need for health-befitting materials for post-COVID-19 symptoms. However, social belief in its potential is primarily based on the Traditional Medicine perspective, and it casts doubt. On the other hand, expanding species use requires a much more rigorous assessment. In modern conditions, health-benefitting product suppliers cannot rely on simple marketing. Still, they must provide a better scientific evidence base for the product's safety and effectiveness and commit to sustainable quality. Therefore, this review summarized all reports on the species in Vietnamese, Chinese, and English and highlighted that *A. sagittifolius* has more potential than expected.

Besides, this review clarified some cultivating and processing routines in the community. Firstly, *A. sagittifolius* leaf and fruit have different medicinal properties; combining the root with aerial parts is acceptable. Secondly, pharmacological and phytochemical findings partially explain traditional medicinal uses of *A. sagittifolius* root, but more work is needed to comprehend better and establish suitable policies for developing it. Thirdly, *A. sagittifolius* can be found in many countries but is not commonly used and needs to be studied better, so there is vast potential for conducting scientific research and developing industrial products.

CRediT authorship contribution statement

Yuan Shiun CHANG: Writing – review & editing, Supervision, Methodology, Conceptualization. Phu Loc Nguyen: Writing – original draft, Resources, Investigation. Yu-Ling Ho: Writing – original draft, Validation, Funding acquisition, Data curation. Van Minh Le: Writing – review & editing, Writing – original draft, Validation, Resources, Data curation. Michael Heinrich: Writing – review & editing, Validation, Methodology, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Supplementary data

Supplementary data associated with this article include Appendix 1, Articles collected from PubMed, CNKI, Google Scholar, ResearchGate, and VISTA databases; Appendix 2, Compounds isolated from *A. sagittifolius* root; and Appendix 3, Availability of information for commercially available isolated compounds on databases.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.indcrop.2024.118690.

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