Review

Artocarpus Camansi Blanco: A Review on Its Traditional Use, Nutritional Value, Phytochemistry, and Pharmacology

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Abstract

Artocarpus camansi Blanco or breadnut (Family: Moraceae) is primarily found in tropical regions of the world. Different parts of the plant provide potential use in medicine, nutraceutical development, and livelihood. The present review attempts to document literature on the traditional use, nutritional value, phytochemistry, and pharmacological investigation carried out with breadnuts. The included literatures of the plant were collected from various sources and databases like Google scholar, PubMed, ScienceDirect, Crossref, and Scopus. Breadnuts are rich in secondary metabolites. Studies have reported the isolation of several triterpenoid compounds and the broad spectrum of its pharmacological activities such as antidiabetic, antimalarial, antioxidant, anti-tumor, antibacterial, and immunomodulatory properties. The approximate composition of the seed and the fruit also highlights the nutritional importance of this plant. *A. camansi* Blanco is an underutilized tree that holds significant potential if further research and sustainable conservation is applied. Efforts to mainstream its use as functional food and increase awareness among the locals should also be given attention.

Keywords: *Artocarpus*; *Artocarpus camansi*; kamansi; phytochemistry; pharmacology; secondary metabolites

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Introduction

The use of plants and other natural products have been used as medicine since ancient times [1]. The World Health Organization reported that around 75% of the world's population uses herbs as part of their healthcare needs [2]. Current advances in drug discovery and development utilizes natural products as direct source of therapeutic agents, used as starting material to develop semi-synthetic drugs, and as chemical basis to design novel molecules [3]. Example of recent breakthroughs in natural products was the discovery of avermectins from microbes and artemisinin from *Artemisia annua*. These compounds are used to eradicate parasitic worms and treat malaria, respectively, and led to the awarding of the 2015 Nobel Prize in Physiology or Medicine to William C. Campbell, Satoshi Omura, and Youyou Tu [4]. From 1981 - 2019, approximately 41% or 75 of the 185 small molecules were considered to be naturally inspired sources of antitumor agents [5]. Filipinos have been harnessing the use of natural products since pre-colonial times. This is evident as herbs and other medicinal plants were used as aid to rituals and alternative to medicines in places where resources and access to primary health care are restricted [6].

The Philippines is one of the world's mega-biodiverse countries. A huge number of thriving flora and fauna can be found in the archipelago [7]. This covers around 5% of the world's flora and an astounding 25 genera known to be endemic in the country. However, the country is also one of the world's biodiversity hotspots. Climate-induced disasters and human activities have been contributing to its destruction [8]. For years, there have been efforts in promoting and domesticating forests using native trees. It is reported that promotion of native trees is beneficial to maintain a healthy ecosystem and boost economic function [9]. Trees are also reservoirs of important chemicals that may be exploited for medicinal use [10]. In Iloilo, Philippines, an ethnobotanical documentation of medicinal plants used by indigenous *Panay Bukidnon* showed that 31% of the medicinal plants used by the people came from trees [11]. Some of these trees include: *Spondias pinnata* (L.f.) Kurz, *Alstonia scholaris* (L.) R.Br., *Antidesma bunius* (L.) Spreng, and *Sandoricum koetjape* (Burm.f.) Merr.

Artocarpus camansi Blanco. is a native fruit-bearing tree found in the Philippines and several countries in southeast asia. This species belongs to the mulberry family or the Moraceae family and one of the 50 species belonging to the genus *Artocarpus*. This review highlights the historical, nutritional, and pharmacological perspective of *Artocarpus camansi* Blanco.

Methodology

Online literatures pertaining to *Artocarpus camansi* Blanco were considered. The species name was confirmed using an online plant database, World Flora Online (https://wfoplantlist.org/plant-list/taxon/wfo-0000550450-2021-12) which was formerly known as The Plant List. All online literature published until June 2022 and discusses medicinal uses, phytochemistry, toxicity, pharmacological use, or nutritional value were considered using various databases such as Google scholar, PubMed, ScienceDirect, and Scopus. Only articles published in the English language were included from the database carried out using the keywords *Artocarpus camansi* and *A. camansi*. Double apostrophes were used to limit articles referring to *Artocarpus camansi*. In this paper, the included literatures were only taken from published work. Thesis, conference proceedings, and other unpublished works were not included. Articles that cannot be accessed even with prior requests to the author were not also included. Chemical structures were illustrated using ChemDraw Ultra 12.0 (PerkinElmer Informatics, USA).

Botanical description

A. camansi Blanco from the family Moraceae have numerous synonyms including: dulugian, kamansi, kolo, pakau, ugod (various Philippine dialect), kelur, kulur (Malaya, Java), kapiak (New Guinea), castaña (spanish), and breadnut (english).

The tree towers at approximately 15 m in height and its trunk measures about 1 m in diameter. Its leaves are alternate, 40 - 60 cm long, with 4-6 pairs of lobes and sinuses while the fruit is fleshy, large, oval in shape that measures about 13-20 cm long and 7-12 cm round, and weighing around 800 g. The fruit is also known to produce a number of seeds depending on the size of the fruits. This characteristic distinguishes the difference between *A. camansi* Blanco and *A. altilis* (Parkinson ex F.A. Zorn) Fosberg, which the latter doesn't produce seeds. Additionally, *A. camansi* Blanco have a spiny skin while *A. altilis* lacks this characteristic allowing identification relatively faster. The tree is usually found between 0 - 1550 m elevation range with 1300 - 3800 of mean annual rainfall. The tree also thrives in an environment with mean annual temperature of

15 - 40 °C, fertile and well drained soils, and prefers full exposure to the sun. Its ability to tolerate flooding and withstand strong winds makes it an ideal crop [12]. The taxonomic classification is shown in Table 1.

Table 1. Taxonomical classification

Kingdom	Plantae
Class	Magnoliopsida
Order	Rosales
Family	Moraceae
Genus	*Artocarpus* J.R. Forst & G. Forst.
Species	*Artocarpus camansi* Blanco

Distribution

A. camansi Blanco is a tall evergreen tree that can be found in places in the pacific and the tropics. Specifically, this tree is indigenous to Moluccas, New Guinea, and the Philippines. While its presence in the island of New Caledonia, Tahiti, and Hawai'i among others, were reported to be introduced by immigrants of the Philippines [13]. Furthermore, its presence in the Caribbean was introduced by the French in the 1700s [14]. This tree has now been an important source of commodities of Caribbean countries like Trinidad and Tobago [15]. Historical records have claimed that *A. camansi* is the progenitor of the seedless-fruit producing tree *A. altilis* [16].

Traditional uses

Various parts of the tree offer beneficial uses. The trunk and branches of the tree are often used as timber and fuelwood while dried male flowers were used as mosquito repellent [12]. The fruit contains highly nutritious seeds which are compared to nuts such as almond and macadamia. The seeds are either roasted or boiled while the fruit pulp is often prepared in stews or soups. The seed is also a good raw material in making flour and oil that could be a good product alternative as well as a source of livelihood [13]. Yellowing or deteriorating leaves are boiled and used to relieve hypertension and control diabetes while tree sap is used as plaster in aiding dislocated joints [14].

Nutritional value and proximate composition

Fruit-bearing trees are a highly valued source of nutrition as well as a form of livelihood of the general population. However, crops that are neither commercially grown nor traded widely may be considered as underutilized crops [17]. The fruit and the seeds of *A. camansi* contain valuable micromolecules, macromolecules, and vitamins. Various studies reported its proximate composition. Extracted starch from the seed in presence or absence of alkaline solution yielded 2.44% and 1.82%, respectively. Breadnut seed immersed in alkaline solution showed 79.26%, 25.63%, and 53.63% of starch, amylose, and amylopectin content, respectively, while the seed that was not immersed in alkaline solution showed 75.13%, 31.46%, and 43.67% of starch, amylose, and amylopectin content, respectively. This was compared to avocado seed which showed less values than breadnut seed [18]. Table 2 presents the proximate composition, mineral, amino acid, and organic acid composition of the seed while the fatty acid content was determined from the oil obtained [19,20]. Similarly, the proximate composition, mineral, and vitamin composition in various ways of preparing flour seed were reported to have substantial implication [21,22]. Table 3 presents the values for the raw breadnut seed flour.

Phytochemistry

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The leaves, fruit peels, and the seed of *A. camansi* Blanco. contains a number of known compounds. Friedelinol, squalene, β-sitosterol, stigmasterol, and phytol were isolated from the leaves. Polyprenol, cycloartenol, cycloartenol acetate were isolated from the stems. The seeds found in the fruit are also a source of lectin while the triterpenoid, lupeol acetate were isolated from the fruit peels [23-26]. The identified chemical constitutes is shown in Figure 1. The compounds mentioned have known activities and are briefly discussed in this paper.

Friedelinol is a pentacyclic triterpene found mainly in plants and commonly examined for its cytotoxic activity. The compound 3β-friedelinol is a major constituent of *Euphorbia vajravelui* where it reported no toxic effect on human cardiac cell line and no cytotoxic towards a cervical cancer cell line [27]. The non-toxic effects of this compound were also observed when evaluated using ARPE-19 or human retinal pigmented epithelium cell line and CRL2120 or human skin fibroblast [28,29].

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Table 2. Nutritional composition of breadnut seeds

		[19]	[20]	[57]
Chemical composition (%)	Moisture	60.96 ± 0.41	45.00	66.3 ± 0.04
	Protein	4.87 ± 0.50	12.6	1.12 ± 0.02
	Fat	3.48 ± 0.13	16.10	1.85 ± 0.28
	Crude Fiber	1.20 ± 0.26	1.38	2.72 ± 0.34
	Ash	3.43 ± 0.52	2.00	1.24 ± 0.03
	Carbohydrates	26.11 ± 0.14	21.5	26.8 ± 0.01
	Dry matter	39.04 ± 0.33	-	-
Mineral Content	Potassium (K)	325 ± 0.14 mg/100 g	5.85 g/100g	-
	Calcium (Ca)	185 ± 0.39 mg/100 g	0.03 g/100g	126 ± 0.31 mg/100 g
	Phosphorus (P)	363 ± 0.67 mg/100 g	0.46 g/100g	-
	Iron (Fe)	0.05 ± 0.21 mg/100 g	0.01 g/100g	15.8 ± 0.56 mg/100 g
	Copper (Cu)	0.12 ± 0.33 mg/100 g	-	1.57 ± 0.05 mg/100 g
	Manganese (Mn)	1.20 ± 0.49 mg/100 g	<0.01 g/100g	1.60 ± 0.14 mg/100 g
	Sodium (Na)	248 ± 0.50 mg/100 g	0.71 g/100g	4.50 ± 0.42 mg/100 g
	Magnesium (Mg)	1.48 ± 0.38 mg/100 g	0.03 g/100g	-
	Zinc (Zn)	-	0.07 g/100g	28.5 ± 0.71 mg/100 g
Amino acid composition	Arginine	293 mg/g N	-	-
	Histidine	167 mg/g N	-	-
	Isoleucine	245 mg/g N	-	-
	Leucine	392 mg/g N	-	-
	Lysine	275 mg/g N	-	-
	Phenylalanine	312 mg/g N	-	-
	Tyrosine	185 mg/g N	-	-
	Cysteine	112 mg/g N	-	-
	Tryptophan	24 mg/g N	-	-
	Methionine	95 mg/g N	-	-
Fatty acid composition (%)	Oleic	12.4	14.7	-
	Stearic	2.0	9.29	-
	Lauric	1.7	-	-
	Palmitic	21.4	19.4	-
	Linolenic	14.8	12.4	-
	Linoleic	-	43.6	-
	Arachidic	-	0.01	-
	Behenic	-	0.01	-
	Arachidonic	1.9	-	-
	Myristic	-	0.00	-

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	Palmitoleic	-	0.54	-
Organic acid (mg/kg)	Butyric acid	0.012 ± 0.12 mg/kg	-	-
	Citric acid	0.185 ± 0.32 mg/kg	-	-
	Acetic acid	0.050 ± 0.48 mg/kg	-	-
	Malic acid	0.012 ± 0.17 mg/kg	-	-
	Lactic acid	0.317 ± 0.51 mg/kg	-	-

Table 3. Proximate composition, mineral, and vitamin composition of Breadnut seed flour

		[21]	[22]
Proximate composition (%)	Moisture content	11.05 ± 0.24	2.59
	Protein	5.10 ± 0.03	6.16
	Fat	3.92 ± 0.12	9.07
	Crude fiber	2.02 ± 0.45	1.78
	Ash	2.10 ± 0.04	5.01
	Carbohydrates	75.88 ± 0.21	75.39
Mineral composition (%)	Calcium	0.44 ± 0.01	-
	Magnesium	0.05 ± 0.01	-
	Iron (mg/100g)	22.25 ± 0.35	-
	Zinc (mg/100g)	8.70 ± 0.68	-
	Phosphorus (mg/100g)	0.23 ± 0.01	-
Vitamin composition (%)	Vitamin A	0.26 ± 0.01	-
	Vitamin C	0.85 ± 0.01	-

Squalene is a triterpene hydrocarbon that is ubiquitously found in nature. Animals, humans, plants, and microorganisms in some sort harbors or produces this compound. This is due to it being a precursor of numerous compounds such as cholesterol and hundreds of triterpenes. In humans, squalene can act as an antioxidant and be used as an adjunct dietary supplement. Squalene is also studied for its use in oxidative stress, hypercholesterolemia, and hypertension [30,31].

Stigmasterol and ***β-sitosterol*** are phytosterols that are structurally similar to animal cholesterol and present mainly on plant cell membranes. Structural resemblance lies on the common cyclopenta[α]phenanthrene ring with modification in the long side chain at carbon-17 [32]. The abundance of these compounds and its relative ubiquity in the human diet allowed its exploitation. For decades, both plant sterols have been extensively studied, offering numerous potential pharmacologic uses. Several of its biological activities are: immunomodulatory [33], antibacterial [34], anti-cancer [35,36], antidiabetic [37,38], lipid-lowering [39], and hepatoprotective activity [40].

Phytol or 3,7,11,15-tetramethylhexadec-2-en-1-ol is a diterpene compound which is structurally observed with four isoprene units. It is abundantly present in all organisms which undergo photosynthesis. Its relation to humans has been attributed to it being a precursor of phytanic acid after a plant material containing phytol is consumed and digested. Additionally, this plant constituent reported several pharmacologic activity: antibacterial, anxiolytic, anticonvulsant, anti-inflammatory, anti-angiogenic, and immune-modulating activity [41,42]

Lupeol acetate is a pentacyclic triterpene or a lupeol molecule having the oxygen at carbon-3 acetylated. This compound offers various pharmacologic activities: antifungal, antifertility, anti-inflammatory, enzyme inhibition activities (**α**-amylase and tyrosine phosphatase 1B), and antimalarial activities [43-47].

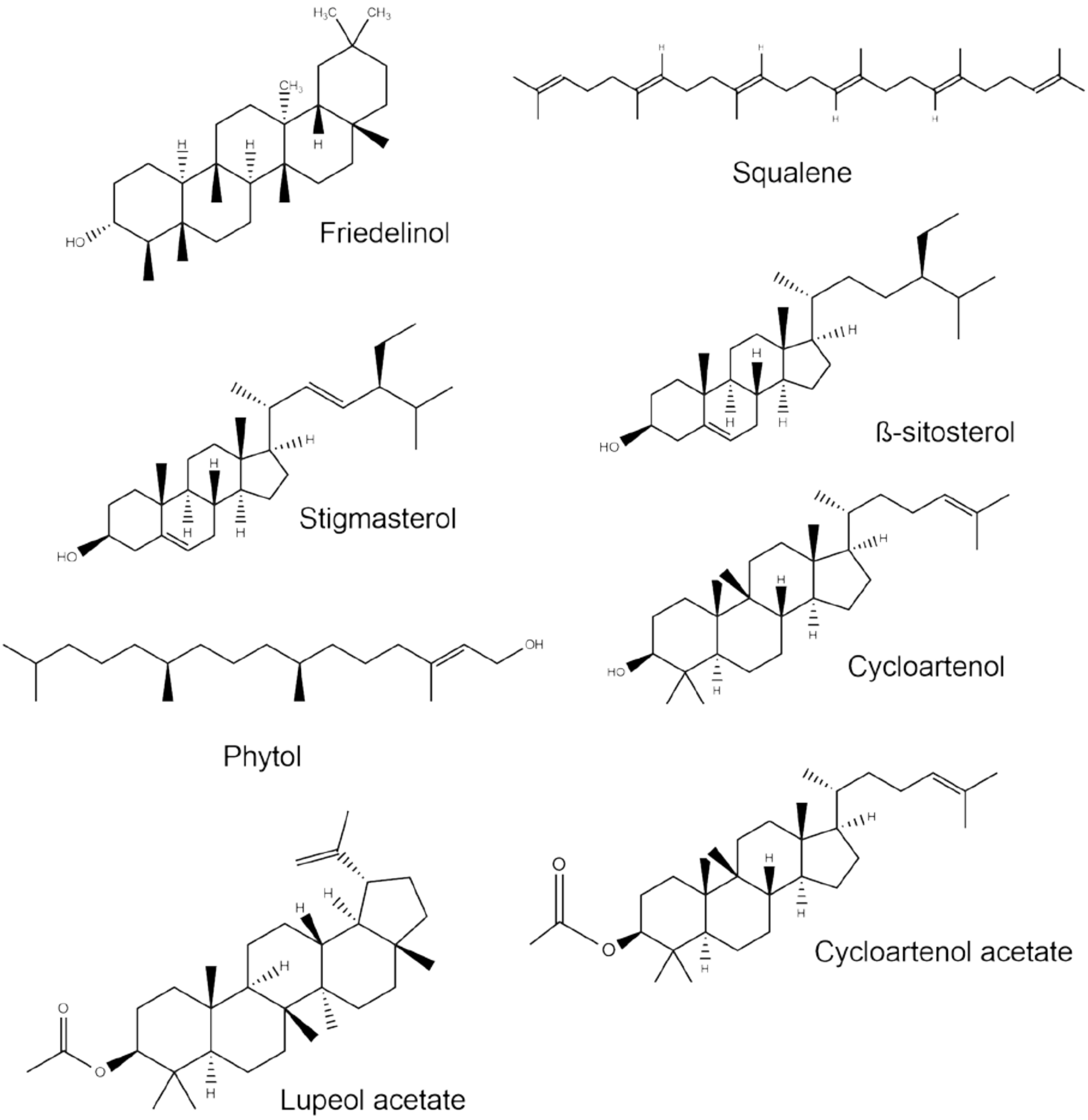

Figure 1. Structures of phytochemical constituents determined from *A. camansi* Blanco.

Pharmacological activities

Literature discussing the folkloric use of *A. camansi* Blanco is relatively limited. However, studies conducted on this tree show results that are note-worthy.

Antidiabetic activity

The fruit peel of *A. camansi* Blanco was macerated using *n*-Hexane. The obtained extract was used to investigate the antidiabetic activity of the extract using male Swiss webster mice as animal model. Following the glucose-tolerance test, the crude n-Hexane extract showed an activity of 65.59% compared to glibenclamide as positive control [48]. The effects of *A. camansi* macerated dried fruit extract were also investigated using sucrose-induced diabetes mellitus in *Drosophilia melanogaster*. In this study, the downregulation of insulin-like receptors and ILP2 or insulin-like peptides indicates improvement of glucose balance in the system [49].

Antimalarial activity

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Crude extracts obtained from the leaves and bark of three *Artocarpus* species were investigated to determine its antimalarial activity using *Plasmodium falciparum* and *Plasmodium berghei* as model organisms. Both in-vitro and in-vivo models were utilized. In-vitro model was used to determine the percentage inhibition of *P. falciparum* growth and Peter's test was used to determine the in-vivo antimalarial activity. Maceration using 80% ethanol was primarily used to obtain the extract. The leaves of *Artocarpus altilis* got the highest activity on in-vivo models showing an ED_{50} of 0.82 mg/kg body weight. However, the inhibitory activity of *A. camansi* leaves in-vitro shows note-worthy results of IC_{50} of 5.31 ug/ml which is relatively close to *A. altilis* leaves with 1.32 ug/ml [50].

Antioxidant activity

The fruit peels and the leaves of *A. camansi* and *A. altilis* were macerated in distilled water. The extracts obtained were used in various antioxidant activity assays such as: total phenolic content, total flavonoid content, total antioxidant capacity, DPPH scavenging activity, reducing power assay, and lipid peroxidation assay. Among the various test samples, it was breadnut leaf, breadnut seed, and breadfruit leaves that exhibited remarkable results (Vianney et al., 2020). In another study, in-vivo mice models were also utilized to determine the antioxidant activity of the leaves extracted using 96% ethanol. The measurement of superoxide dismutase (SOD) in mice putatively indicates the enzymatic activity of the endogenous antioxidant. The ethanolic extract obtained from *A. camansi* leaves was able to improve SOD enzyme level in dose-dependent trend [51].

Cytotoxic activity

Crude and fractionated extracts of the leaves and bark of *Gliricidia sepium*, *Premna odorata*, and *Artocarpus camansi* were assessed in various cancer cell lines, namely: human colon cancer cell line (HCT116), breast cancer cell line (MCF-7), and lung adenocarcinoma cell line (A549). A non-cancer cell line, Chinese hamster ovary or AA8 cell line, was utilized to determine the selectivity of the extract's cytotoxicity. Despite that *A. camansi* leaf extract did not show toxicity in HCT116 and A549, it showed high cytotoxicity against breast cancer cell lines [52].

Immunomodulatory activity

Allergic dermatitis is a delayed-type hypersensitivity reaction after prior exposure to allergens. This is mediated by T lymphocytes that are part of the immune system [53]. Mature leaves of *A. camansi* were assessed on the activity of the sample in mediating contact hypersensitivity induced in mice. The extracts were obtained after the sample was heated in distilled water and fractionated using ethyl acetate. The model made use of 4,6-trinitrochlorobenzene in acetone that would induce the hypersensitivity reaction in mice. Using various doses of the extract (100 - 1000 mg/kg body weight) and prednisolone (20 mg/kg body weight) as the positive control, the extract and the control were able to inhibit ear swelling after 24 hrs. Furthermore, the 1000 mg/kg BW was still able to inhibit ear swelling at 48 hrs. This showed the potential of the hot water extract to contain phytochemicals that may modulate immune response [54].

Antibacterial activity

Essential oils extracted from the leaves, stem bark, and seed were reported to potentially elicit antibacterial activity. Microplate alamar blue assay were conducted using various organisms: *Escherichia coli*, *Shigella flexneri*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Salmonella typhi*. Various parts of the plant exhibited varying inhibition at 20 ug/ml [55]. Another study also reported the antibacterial activity of *A. camansi* leaves that was macerated using various organic solvent with different polarity. Well diffusion assay and broth microdilution assay were used to determine the zone of inhibition as well as the minimum concentration that would inhibit bacterial growth. The ethanol extract was able to effectively inhibit *S. aureus* growth with 1.150 ± 0.086 cm and *E.coli* with 1.03 ± 0.153 cm against cefotaxime that was able to inhibit growth of *S. aureus* with 1.633 ± 0.416 cm and *E.coli* with 2.467 ± 0.351 cm [56].

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Future perspective

Despite the huge progress and new advancement in science in recent decades, plants remain an integral part of research. This is especially true since until now, there are undiscovered species of plants and others remain to be underutilized. *Artocarpus camansi* Blanco is native to tropical countries such as the Moluccas, New Guinea, and the Philippines. It is related to other fruit-bearing trees such as Jackfruit (*A. heterophyllus*), Marang (*A. odoratissimus*), and Breadfruit (*A. altilis).* Available literature indicated the importance of its fruits, seed, and leaves which could be a source of nutraceuticals and novel compounds that can be used in drug development. Breadnut is known to be a backyard crop. The fruit is usually used in soups and stews and contains highly nutritious seeds which could be developed into marketable goods. Hence, mainstreaming of its importance and use should be done locally. Further research on its possible economic impact could help bring new types of commodities in the market. At the same time, focusing on native plants could lead to a positive impact on the environment. Phytochemical and pharmacological studies conducted on the plant also exhibited remarkable potential to be exploited for novel compounds. A more comprehensive methodology could be implemented to maximize the available literatures on this species. The leaves were used for the isolation and identification of several compounds. Using powerful analytical instruments such as LC/MS and NMR in combination with robust methodology to obtain various extracts could help in profiling secondary metabolites. Other parts of the tree also remain unexplored for potentially useful phytochemical constituents.

Conclusion

The present review gathered relevant literature related to *Artocarpus camansi* Blanco. It revealed that the plant contains valuable phytochemicals and has various pharmacological activities. Its fruits and seeds are highly nutritious and could be considered a functional food. Several gaps can also be elucidated that warrants further research. The relative scarcity of phytochemical and pharmacological studies in this species despite the presented evidence for its bioactivities further highlights its importance.

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