Minireview Article

Review on *Artocarpusnobilis* Thw. (*Moraceae*): An endemic plant of Sri Lanka

ABSTRACT

The genus *Artocarpus* consists of about 50 species of large evergreen trees with various medicinal and economical uses. *Artocarpus nobilis* (Family: Moraceae) is commonly referred to as Ceylon breadfruit and it is endemic to Sri Lanka. Synonyms of *A. nobilis* are *Artocarpusimperialis* André, *Artocarpus pubescens* Moon and *Saccus nobilis* (Thwaites) Kuntze. Extracts from leaves, bark, fruits and latex are rich in phytochemical compounds such as flavanones, flavonoids, triterpenoids, xanthones, stilbenes and chalcones. These bioactive compounds contribute to various pharmacological properties of Ceylon breadfruit (*Artocarpusnobilis*).It is used in Ayurvedic and folk medicine to treat asthma, diarrhea, worm infestations and wound healing. It also used in traditional ayurvedic formulations like *Chandana guli wattoruwa*. Several research that has been carried out on this plant include the evaluation of antibacterial activity, anti-inflammatory activity, antioxidant, antifungal, biosorption and Glutathione-S transferase inhibitory activities. Apart from these it is a productive source of edible fruit and yield good timber. A combination of traditional and new technologies will be important in the future to develop therapeutic products from *Artocarpusnobilis*. In this present review,attempts on providing comprehensive information on research conducted on *A. nobilis.*

Keywords: Artocarpus nobilis, Ceylon breadfruit, Endemic plant, Sri Lanka

1. INTRODUCTION

The family Moraceae consists of about 37 genera of plants and *Artocarpus* is one of the important genera, which consists of about 55 species[1,2]. In Sri Lanka, mainly *Artocarpus heterophyllus* and *Artocarpus nobilis* can be found[3,4]. This review mainly focused on reviewing *Artocarpus nobilis,* also known as Ceylon breadfruit, which is endemic to Sri Lanka. It is a plant that possesses a wide range of uses, practical applications, and used in folk and ayurvedic medicine.*A. nobilis* is a large evergreen tree containing medicinally important secondary metabolites like phenols, alkaloids, flavonoids and terpenes. Due to the presence of thesemetabolites, it has received a great level of scientific interest on phytochemistry. Several studies have been done on the phytochemistry of *A. nobilis* and have identified many novel compounds and their structures using high end instruments like NMR spectroscopy and Mass spectrometry. It serves as a productive multipurpose crop for making timber and fruits. Extracts of different parts of the plant (Bark, leaves, fruit, latex and roots) have been applied in the folk and ayurvedic medicine for the treatment of diarrhea, worm infestations, asthma, abscesses and soft tissue infections[3,5]. This review focuses on the morphology and distribution, bioactivity, pharmacological properties, ethnomedicinal properties, and phytochemistry of *Artocarpus nobilis*.However, future efforts should focus more on *in vitro* and *in vivo* studies, as well as clinical trials, in order to validate traditional knowledge.

1.1 Synonyms and other names

The synonyms of ***Artocarpus nobilis Thwaites*** are *Artocarpus imperialis* André, *Artocarpus pubescens* Moon, *Saccus nobilis* (Thwaites) Kuntze
English name: Breadfruit, Ceylon Breadfruit
(Most *Artocarpus* species have edible bread-like fruits, which give them the names breadfruit or Ceylon breadfruit)
Sinhala name: Bedi del, Wal del ,Hingala del
Tamil name: Arsini Pla Irappala, Aresini-pilaka, Asiri-pillakai [6]

1.2 Taxonomic classification

Kingdom: Plantae, Sub kingdom: Tracheophytes, Division: Angiosperms, Class: Eudicotyledons, Subclass: Rosids, Order: Rosales, Family: Moraceae, Genus: *Artocarpus*, Species: *nobilis* [7].

2. GEOGRAPHICAL DISTRIBUTION

Artocarpus genera includes *Artocarpus heterophyllus, Artocarpus altilis, Artocarpus nobilis, Artocarpus anisophyllus, Artocarpus camansi, Artocarpus hirsutus,* etc. These species are spread throughout the East, South, Southeast Asia, New Guinea, and South Pacific areas. It is abundant, up to an elevation of 2,500 ft in wet zones in low country. It is commonly found in the mid-country homesteads and the wet zone forests in Sri Lanka [8].

3. MORPHOLOGY OF *ARTOCARPUS NOBILIS*

Artocarpus nobilis is a large evergreen tree, to 25 m high with immense crown, stem, stout, boughs and wide spreading roots. All parts contain white latex. Bark is thick, dull brown irregularly furrowed and exfoliating. Leaves alternate, large, dark green above and paler below.They are entire to pinnatifid or pinnate, spirally arranged or alternate and distichous, coriaceous, glabrous to pubescent. Stipules 3-12 cm long; leaf lamina 14-32 x 8-23 cm; lateral veins 10-13 pairs; petiole 2-3 cm long; Sapling leaves pinnately lobed. Inflorescence is unisexual, Male head 7-13 x 1.5 cm, cylindricto globose, covered by flowers and bracts; peduncle 3-7 cm long. Female head covered by peltate bracts. Syncarp up to 20 x 10 cm, cylindric, covered with persistent peltate bracts; peduncle 10-15 cm long, formed by the enlargement of the entire female head. Flowers Monoecious, male spikes, female dense, on a terminal or axillary club like in a receptacle.Seeds 8 x 7 mm in size, cylindric, pale chestnut brown [6,9].

4. ETHNOMEDICINAL INFORMATION

When considering the medicinal properties of the *Artocarpus nobilis*, according to Compendium of medicinal plants: a Sri Lankan study, 2004, crushed stem bark extract is used for fracture healing and muscle strains, for the treatment of dysentery. Both latex and steamed bark parts with herbal leaves are used for the treatment of abscesses and blisters. Latex mixed with ginger extract, castor oil used for vermifuge, worm infestations in children. Latex is also used for “Krimi dosha” and “Muha kassa”. Seeds are good for Asthma patients. Roasted seeds are used to improve the sexual ability of males, latex of the young shoots is used for skin diseases and also roots are used in folk medicinal recipes “Chandana guli wattoruwa”. Edible fruits and seeds possess good nutritional value and are mainly used for worm infections (e.g., Ascariasis) [6, 9,10].

Figure 1: Artocarpus nobilis Leaves [10]

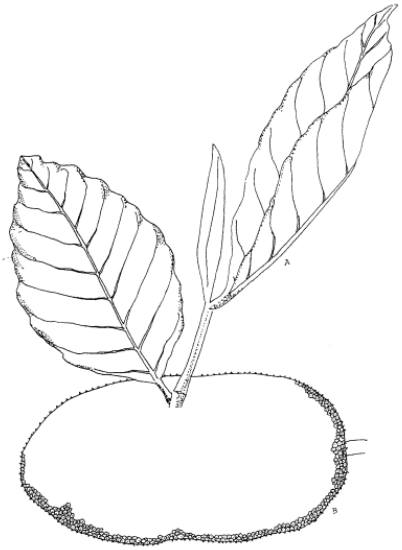

Figure 2: Artocarpus nobilis leaves and fruit [9]

5. PHYTOCHEMISTRY

The chemistry of Moraceae has been reviewed and some of the triterpenoid bark constituents of several species of the genus *Artocarpus* have been reported (refere to the supplementary data provided at the end of this review).

5.1 Stem Bark

Six chromeno flavonoids were identified in benzene and methanol extracts from the bark of *Artocarpus nobilis*. Five flavonoid compounds present in the benzene extract were shown in thin layer chromatography (TLC). These were isolated and purified over silica gel followed by fractional precipitation. Arto-bilochromen (0.8%) was the main compound in the extract[11]. A study conducted on the bark of *A. nobilis* identified two new pyranodihydrobenzo xanthones. This finding was significant because it was the first report of the occurrence of dihydrobenzo xanthones in plants[12]. In another recent study two new cycloartane-type triterpenoids, Artocarpuate A and Artocarpuate B were identified. With the help of extensive NMR

spectroscopic studies, the structures of these new compounds have been identified[13].

Antifungal activity-guided fractionation of n-butanol extract from *Artocarpus nobilis* stem bark methanol extract contained two derivatives of stilbene. In the TLC bioautography method, both compounds showed strong antifungal activity against Cladosporium cladosporioides and high radical scavenging activity against the 2,2-Diphenyl-1-picrylhydrazyl (DPPH) radical[14].Two novel compounds were isolated from the sequential ethyl acetate and ethanol extracts of stem bark of *A. nobilis*. Compounds were Di carbonyl ester and Artolankanin A. Artonin E and artobiloxanthone also isolated which were known compounds from previous studies. Bioassay-guided fractionation using a combination of normal phase and size exclusion column chromatography were used to isolate and structural details were obtained using NMR, Mass, IR, and UV spectroscopy. The identified compounds were evaluated for DPPH (2,2-diphenyl-1-picrylhydrazyl) free radical scavenging activity, tyrosinase, elastase, hyaluronidase, and A5-lipoxygenase enzyme inhibitory activities lipopolysaccharide-induced nitric oxide (NO) production inhibitory activity in SIM-A9 microglial cells. In LPS-stimulated microglia cells, artonin E showed prominent tyrosinase and A5-lipoxygenase enzyme inhibitory activities as well as NO inhibition activity.Both artobiloxanthone and artolankanin A showed strong A5-lipoxygenase enzyme inhibitory activity. In conclusion of the results, it was suggested that *A. nobilis* has the potential to develop anti inflammatory and depigmenting agents using these bioactive compounds [15].

5.2 Root bark

Chemical examination of the n-butanol extract from the *Artocarpus nobilis* root bark methanol extract contained four new prenylated flavonoids together with artonin E 2'-methylether, isoartonin E 2'-methylether, dihydroisoartonin E 2'-methylether, artonin V 2'-methylether, artobiloxanthone, artonin E, and cycloartobiloxanthone. All these compounds were shown to have good radical scavenging properties towards DPPH radical[16].

5.3 Leaves

Several antifungal activities and radical scavenging activity investigations were carried out on *Artocarpus nobilis*. In such a study, antifungal activity directed fractionation of the extract of n-butanol from the methanol extract of the leaves of *Artocarpus nobilis* contained five chalcones. In the TLC bio-autography method, all of these compounds showed good fungicidal activity against Cladosporium cladosporioides and high radical scavenging property against the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical[17].

5.4 Fruits

Dichloromethane and ethyl acetate extracts of fruit produced four new geranylated phenolic constituents together with six known chalcones and flavanones. Spectrophotometric methods demonstrated good antioxidant activity against DPPH radical[18].

6. BIOACTIVITY

6.1 Antioxidant activity

The methanol extract and the n-butanol extract from the methanol extract of the stem bark of *A. nobilis* showed high radical scavenging activity towards the 2,2-diphenyl-1-picrylhydrazyl radical (DPPH) in TLC bio-autography method [14].Sequential ethyl acetate and ethanol extracts of stem bark of *A. nobilis* (Compound Artonin E) showed

prominent tyrosinase and A5-lipoxygenase enzyme inhibitory activities as well as NO inhibition activity In LPS-stimulated microglia cells. Both artobiloxanthone and artolankanin A compounds showed strong A5-lipoxygenase enzyme inhibitory activity [15].N-butanol extract from the methanol extract of the leaves of *A. nobilis* showed high radical scavenging activity towards the DPPH radical in TLC bio-autography method[17]. Generylated phenolic constituents from the fruits of *A. nobilis* showed strong antioxidant activity against DPPH radicals by the spectrometric method[18].

6.2 Antibacterial Activity

Only few research has been reported on anti-bacterial activity of *A. Nobilis*. A study done by Senadeera *et al*, 2021 have used eight extracts of leaves and bark (aqueous, methanol, dichloromethane, hexane extracts from each plant part) of *A. nobilis* and tested those against *Escherichia coli* (ATCC® 25922TM) *and Staphylococcus aureus* (ATCC® 25923TM)using agar well diffusion method.The aqueous bark extract showed the highest antibacterial activity against *Escherichia coli* and methanol bark extract showed marked antibacterial activity against *Staphylococcus aureus* determined by agar well diffusion methodwith the positive control Gentamicin[3].

6.3 Antifungal activity

The n-butanol extract of stem bark of *A. nobilis* showed antifungal activity against *Cladosporium cladosporioides*[14]. Guided fractionation of the n-butanol extract from the methanol extract of the leaves of *A. nobilis* showed antifungal activity against *Cladosporium cladosporioides*[17].

6.4 Anti-inflammatory activity

Methanol extract of stem bark and aqueous extract of leaves of *A. nobilis* showed anti-inflammatory activity by in vitro protein (egg albumin) denaturation method[5].

6.5 Acetylcholinesterase inhibitory activity

New cycloartane type terpenoids isolated from ethanolic extract of *A. nobilis* showed weak acetylcholinesterase activity determined by using modified Ellman's assay[13].

6.6 Biosorption of metal ions

The peel of *A. nobilis* showed remarkable Biosorption capabilities toward Ni(II) heavy metal ions and Cr(III) and Cr(VI) ions. that the peel of *Artocarpus nobilis* fruit can be used as an effective bio-sorbent for the removal of Ni(II) from wastewater[19].

6.7 Glutathione-S transferase (GST) inhibitory activity

Ethanolic extract of *A. nobilis* resulted in GST inhibitory activity. It was found that this activity was mainly due to the presence of flavonoids[20].

7. OTHER USES OF *A. NOBILIS*

Bothfruit (tender portions) and seeds are edible. Excavations in the Kitulgala area have revealed that 12,500 years ago, prehistoric men ate roasted seeds of wild breadfruit.

Fruit and seeds are boiled and eaten. Seeds contain a high percentage of oil and can be roasted and eaten as a snack.[9] Aside from the edible fruit, the timber of the *Artocarpus* species is used for long lasting construction and furniture making.

8. CONCLUSION

Thisreview highlights the ethnomedicinal, pharmacological and phytochemical properties of *A.nobilis* endemic to Sri Lanka. Although there are many articles on the *Artocarpus* genus, only a few research has been done on *A.nobilis* Thw. Based on the literature review, *A. nobilis* contains various phytochemicals including flavanones, flavonoids, triterpenoids, xanthones, stilbenes and chalcones and currently more than 25 novel phytochemical compounds have been isolated and identified.

Table 1 : Supplementary Data

Plant part	Extraction method/solvent used	Isolated and identified chemical	Identification method
Stem Bark [11]	Benzene and Methanol extracts	Six chromenoflavinoids 1. Artobilochromen 2. chromanoartobilochromen b 3. dihydrofuranoartobilochromen a 4. dihydrofuranoartobilochromen b 5. dihydrofuranoartobilochromen b2 6. Artobilochromen with formic acid gave chromanoartobilochromens a and b with dichlorodicyanobenzoquinonegave dihydrofuranoartobilochromen *a*	Thin Layer Chromatography - five flavonoid compounds in the benzene extract. Further purified by column chromatography over silica gel followed by fractional precipitation. Further analysis by Nuclear Magnetic Resonance (NMR) spectroscopy.
Stem Bark [12]	Extraction method: Sequential extraction Hot petrol Hot C_6H_6 Hot Methanol	Two pyranodihydrobenzoxanthones 1. 5,6,1 l-trihydro-1,3,4,8-tetrahydroxy-5-isopropenyl-l1,1 1-dimethylbenzo[1,2:u]pyrano [2',3':j]xanthene-7-one (artobiloxanthone) 2. 5,5a, 6,11-tetrahydro-1,3,8-trihydroxy-5,5, 11, 1l-tetramethylbenzofuro [3,3a,4:ab] pyrano [2',3'q]xanthen-7-one (cycloartobiloxanthone)	Mass spectrometry NMR spectroscopy IR spectroscopy UV spectroscopy
Stem Bark [13]	95% ethanol Filteration and Evaporation	two new cycloartane-type triterpenoids 1. Artocarpuate A 2. Artocarpuate B	Thin Layer Chromatography NMR spectroscopy
Stem Bark [14]	Methanol extract	two stilbene derivatives 1. (E)-4-isopentenyl-3,5,20,40-tetrahydroxystilbene 2. (E)-4-(3-methyl-E-but-1-enyl)-	Mass spectrometry (Electrospray Ionization-MS) NMR spectroscopy HPLC analysis UV spectroscopy

		3,5,20,40-tetrahydroxystilbene	
Stem Bark [15]	Sequential ethyl acetate and ethanol extracts	Two new compounds, 1. Dicarbonyl ester 2. Artolankanin A Other: artonin E and artobiloxanthone	Mass spectrometry, NMR, IR and UV spectroscopy. Normal phase and size exclusion column chromatography
Root Bark [16]	*n*-butanol extract from the methanol extract	Four new prenylated flavonoids 1. Artonin E 2′-methylether 2. Isoartonin E 2′-methylether 3. Dihydroisoartonin E 2′-methylether 4. Artonin V 2′-methylether Other: Artobiloxanthone Artonin E Cycloartobiloxanthone	HPLC analysis UV spectroscopy NMR spectroscopy Mass spectrometry
Leaves [17]	Guided fractionation of the *n*-butanol extract from the methanol extract	Five chalcones were identified. The chalcones 3 and 5 are new natural products whereas 1 and 2 are reported first time from the family Moraceae. 1. 2’,4’,4-trihydroxy-3’-geranylchalcone 2. 2’,4’,4-trihydroxy-3’-[6-hydroxy-3,7-dimethyl-2(E),7 octa dienyl]chalcone 3. 2’,4’,4-trihydroxy-3’-[2-hydroxy-7-methyl-3-methylene-6-octaenyl]chalcone 4. 2’,3,4,4’-tetrahydroxy-3’-geranylchalcone 5. 2’,3,4,4’-tetrahydroxy-3’-[6-hydroxy-3,7-dimethyl-2(E),7-octadienyl]chalcone	UV spectroscopy NMR spectroscopy Mass spectrometry
Fruits [18]	Sequential extraction with dichloromethane, ethyl acetate and methanol	Four new geranylated phenolic constituents 1. 2,4,4’-trihydroxy-3-[(2E)-5-methoxy-3,7-dimethylocta-2,6-dienyl]chalcone 2. 1-(3,4-dihydro-3,5-dihydroxy-2-methyl-2-(3-methyl-2-butenyl)-2H-1-benzopyran-6-yl-3-(4-hydroxyphenyl)-2(E)-propen-1-one 3. 8-geranyl-3’,4’,7-trihydroxyflavone 4. 3’-geranyl-4’,5,7-trihydroxyflavanone	HPLC analysis UV spectroscopy NMR spectroscopy Mass spectrometry

		together with known related compounds xanthoangelol xanthoangelol B, 3-geranyl-2,3',4,4'-tetrahydroxychalcone, lespeol, 8-geranyl-40,7-dihydroxyflavanone, and isonymphaeol-B.	

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