

ARTOCARPUS HIRSUTUS: A REVIEW OF ITS TRADITIONAL USES, PHARMACOGNOSTICAL, PHYTOCHEMICAL, PHARMACOLOGICAL AND TOXICOLOGICAL ACTIVITIES.

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ABSTRACT

The term of medicinal plants include a various types of plants used in herbalism and some of these plants have a medicinal activities. These medicinal plants consider as a rich resources of ingredients which can be used in drug development and synthesis. *Artocarpus hirsutus*, belongs to the Moraceae family is a tall evergreen tree, generally 20-25 m in height and up to 5 m in girth, fruits are edible, bright yellow, ovoid or globose covered with spines, seeds ovoid and white. *Artocarpus hirsutus* has many medicinal uses. This species are known to possess potential phytochemicals and high nutritional value. This

review compiles traditional, phytochemical and pharmacological data on *Artocarpus hirsutus* species. *Artocarpus* species are rich in phenolic compounds including flavonoids, stilbenoids, arylbenzofurans and Jacalin, a lectin. The study was carried out to assess the Antioxidant, Antidiabetic, Hepatoprotective and Antiinflammatory activities of *Artocarpus Hirsutus*.

KEYWORDS: *Artocarpus hirsutus*, Wild jack, flavonoids, Antidiabetic, Hepatoprotective.

INTRODUCTION

Moracea is a large family comprising about sixty genera and nearly 1400 species, including important group such as *Artocarpus*, *Morus*, and *Ficus*. A number of *Artocarpus* species are used as food and for traditional folk medicines in South-East Asia, Indonesia, Western part of Java and India. *Artocarpus* species has long been recognized for their exceptional medicinal value and for their edible aggregate fruits. *Artocarpus* is a genus of approximately 60 trees and shrubs of Southeast Asian and Pacific origin, belonging to the mulberry family,

Moraceae. The name *Artocarpus* is derived from the Greek words artos ("bread") and karpos ("fruit"). *Artocarpus hirsutus* is an endemic tree species of southern Western Ghats of peninsular India, commonly called as 'wild jack'.

Taxonomy and Ethnobotany

Taxonomically *Artocarpus hirsutus* Lam. Belongs to angiosperms and the details are as follows:

- Kingdom –Plantae
- Division-Angiosperms (unranked)
- Phylum-Eudicots (unranked)
- Class-Rosids (unranked)
- Order-Rosales
- Family-Moraceae
- Tribe- Artocarpeae
- Genus-*Artocarpus*
- Species-*hirsutus*

Vernacular Names

Wild jack (English); Panasah (Sanskrit) Patphanas (Marathi); Petata (Telugu); Halasu, Hebbe-lasu, Hebhalasu, Hechchuva, Kaduhalasu, Pugguhalasu (Kannada); Akkini, Anjili, Anjuli, Pepla, Katupila, Tellai Kori mara (Tamil); Anjili, Ayani, Anniliayari (Malyalam)



MORPHOLOGY

Bark

The bark is grey colour, smooth when young and later becomes scaly and lenticellate. The branches of the tree are strigose with tawny hair and annular scars. The exudates called as latex will be milky white, sticky and profuse

Leaves: leaves are simple, alternate; stipules upto 4cm long, lateral, densely tawny bristly; leaf-stalk 1-3 cm long, stout, hairy; broadly ovate, obovate or elliptic, base pointed, blunt or round, tip somewhat pointed or very shortly tapering, margin entire, wavy, leathery, hairy velvet-hairy beneath; lateral nerves 6-12 pairs, pinnate, prominent.

Flowers: flowers are unisexual, minute, yellowish-green; male in leaf axils, drooping, in narrowly cylindrical spikes upto 15cm long; tepals 2, united below; stamen 1; anther protruding, ovate, bracteoles chaffy; female flowers in leaf-axils ovoid spikes; perianth tubular, ovary superior, straight, ovule drooping; style protruding; stigma undivided.

Fruits: fruits is a fleshy multiple fruit(like mulberry), 6-7.5cm across, spherical or ovoid, echinate, yellow when ripe, the spines cylindric, straight, bristly, perforate at the tip for thread like style. Seeds 16-18mm long, ovoid,

PHYTOCHEMISTRY

The *Artocarpus* species are rich in phenolic compounds including flavonoids, stilbenoids and arylbenzofurans. The phytochemical screening of various extracts of the plant such as ethanol, methanol, hydroalcoholic and Petroleum ether shows the presence of secondary metabolites such as tannins, carbohydrates, glycosides, alkaloids, flavonoids, triterpenoid, sterols, saponins, phenolic compounds, gum and mucilage. The analysis revealed the presence of alkaloids, flavonoids, saponins and terpenoids in the methanolic fruit extract of *Artocarpushirsutus*. Terpenoids was absent in the petroleum ether fruit extract. The various flavonoids present in *Artocarpus hirsutus* were found to be morin, cyanomaclurin, artocarpin, artocarpetin, dihydromorin, artocarpanone, norartocarpetin, artocarpesin, oxydihydroartocarpesin, cycloartocarpesin, cycloartocarpin. Three major flavonoids, cudraflavone A, cycloartocarpin and artocarpin were isolated from the stem wood extract. New prenyl ether and acetate derivatives of isolated flavonoids have been synthesized.

Traditional Use

Artocarpus hirsutus (wild jack) endogenous to Kerala has wide medicinal values which is well documented in the third volume of *Hortus Malabaricus*, the oldest comprehensive printed book on the natural plant wealth of Asia.^[1]

Roots

The decoction of roots and bark are supposed to cure diarrhoea. The juice from the cooked fruits are believed to induce appetite and also when applied to the anus, relieve the pains of haemorrhage.

Bark

Ash of the plant bark mixed with coconut oil is used against 'dhobi's itch' and ringworm externally. Bark paste mixed in coconut oil can also applied for snake bite.

Leaves

Used to treat joint pain and rigidity. The leaves when used with white camphor and root of curcuma are believed to treat venereal bubones and chronic haemorrhage respectively. (A folk medicine in northern Kerala)

Seeds

Roasted with crushed onion fried in yogurt and inserted rectally to treat constipation. It is also used as laxative.

Seed Oil

Appetite stimulant.

Wood

Used as a substitute for making 'oil massagecot' popularly known as ennathoni (wooden vessel for Ayurvedic oil massage) for the 'panchakrma' treatment. (Ayurvedic system practiced in Kerala). The bark infusion is applied to cure small pimples and cracks of the skin. Powered bark is used to heal sores. Dry leaves are used to treat burbose and hydrocele.^[2]

Medicinal Uses

Wild jack in Ayurvedic medicine pacifies vitiated *vata* (the air quality present within the human body) and *pitta* (bile present within the body), anorexia, burning sensation of extremities and sexual weakness. Unripened fruit cause vitiation of *tridosha* (three types of substances that are important in balancing the human body and health according to Ayurveda).^[3]

Pharmacognostical Studies

The study includes Pharmacognostical studies of the bark of *Artocarpus hirsutus* Lam. Secondary phloem is wider than the periderm. In between the periderm and secondary phloem is a narrow zone of cortex where the cells compressed and tangentially elongate. The secondary phloem can be differentiated into outer or collapsed phloem, and inner is non collapsed phloem. The collapsed phloem consists of crushed dark thick irregular lines of phloem elements and isolated scattered sclerenchyma elements. **Dibinlal D et al.**,^[4]

The study includes Pharmacognostical studies of the leaf and stemwood of *Artocarpus hirsutus* Lam. The leaf shows the distinct network of mesophyll cells with the pearl glands and the palaside parenchyma cells possessing 2 to 4 cells thick with several chloroplasts. The axial parenchyma cells of stem wood are paratracheal and vessels are filled with tylose and vessels elements show the pits with simple perforation plates. **Ananthanarayanan Nagarajan et al.**,^[5]

The study includes histology of *Artocarpus hirsutus* Lam. seeds including seed coat, testa and cotyledon was recorded. TS of the seed shows an outer Arillus consisting of a layer of broken, tubular cells of epidermis, 3-4 layer of lignified cells of parenchymatous cells lying underneath it and inner zone of compactly arranged 4-5 rows of sclereids and stone cells of various sizes. TS of cotyledon shows an outer and inner epidermis enclosing the wide parenchymatous zone of mesophyll **Ankita, et al.**,^[6]

The study includes Pharmacognostical studies of the seeds of *Artocarpus hirsutus* Lam. TS passing through the centre of the seed is circular, shows thin layer of Arillus encircling the narrow brown coloured testa and centrally located unequal sized horizontally placed cotyledon. The crystals are prisamate type. Starch grains are abundant in the powder The starch grains have centric hilum. **Suma.v.k et al.**,^[7]

Phytochemical Studies

The Phytochemical examination of *Artocarpus hirsuta* roots, on conventional extraction and various chromatographic methods yielded five compounds: stigmasterol, lupeol, cyclomorusin, cycloartomunin and betulinic acid. All the compounds were isolated for the first time from this species *Artocarpus hirsuta* and the Isolation of cyclomorusin is the first time report from the genus *Artocarpus*. **Lakshmi Pethakamsetty et al.**,^[8]

The *Artocarpus hirsutus* fruit contain an appreciable amount of bioactive compounds. Fruit is a good source of carbohydrate, protein, phenol, and alkaloid. The presence of phenolic acids was confirmed by HPTLC analysis. Medically the presence of these phytochemicals especially the phenols and flavonoids. The methanol fruit extract has high carbohydrate content (267±0.02 mg/g FW). And good amount of protein, phenol, flavanoid were also found. The results of mineral studies show that elements such as potassium (1.601%) and nitrogen (1.4%) were present in higher quantity. **Neha C. P et al.**,^[9]

PHARMACOLOGICAL ACTIVITIES

Antioxidant Activity

The methanolic fruit extract of *Artocarpus hirsutus* showed potent antioxidant activity compared to reference standard BHA and ascorbic acid. The methanolic fruit extract of *Artocarpus hirsutus* was found to be effective in DPPH radical scavenging activity. The DPPH radical scavenging activity of the extract was increased with the increased concentration of crude plant methanolic fruit extract. The reducing power of the extract was carried out with ascorbic acid as a standard reducing agent. The methanolic fruit extract was potentially exhibited concentration dependent DPPH radical scavenging and reducing power is an increased quest to obtain natural antioxidants with broad-spectrum actions. **Vinay Suvarna M N et al.,**^[10]

The ethanolic extracts of leaf, bark and wood of *A.hirsutus* showed strong antioxidant and tyrosinase inhibitory activity *in vitro*. Although all the extracts significantly scavenged DPPH radicals with similar IC₅₀ values, the ORAC value and tyrosinase inhibitory activity were much higher in wood extract compared to the leaf and bark extracts. To recognize the specific active molecule responsible for these activities, water was added into the ethanolic extract of wood to separate the water soluble and water insoluble portions. It was observed that the ORAC value of water soluble portion was notably higher than the insoluble portion. Oxyresveratrol was isolated from the water soluble portion, which showed excellent ORAC value. **Nagarajan et al.,**^[11]

Anti Microbial Activity

The *in vitro* antimicrobial activity was performed by agar well diffusion method against the clinically important bacterial strains viz., *Staphylococcus aureus*, *Bacillus subtilis*, and *Klebsiella pneumoniae* with the concentration of different extracts. It has shown the concentration dependent antimicrobial activity. The study shows the effective antimicrobial activity against *Staphylococcus aureus* and *Klebsiella pneumoniae* bacterial strains with maximum zone of inhibition compared with standard drug tetracycline. **Makari hanumanthappa k et al.,**^[12]

Antimicrobial activity of *A. hirsutus* leaf and fruit were tested against the following bacterial strains such as *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella spp.*, *Enterobacter sp.*, and fungal strains such as *Aspergillus tamarisii*, *Aspergillus fumigates*, *Aspergillus flavus*, and *Aspergillus niger*. Antibacterial activity was carried out by standard disc diffusion method.

Antimicrobial activity of fruit and leaf extract of *A. hirsutus* were tested against fungal and bacterial strains. Acetone extract isolated from both leaf and fruit of *A. hirsutus* have good active antibacterial activity. It exhibited good inhibition activity against *S. aureus*, *Klebsiella* spp., *Enterobacter* sp. Acetone extract showed the maximum zone of inhibition against *S. aureus*. Ethanolic extract showed low inhibition activity against bacterial strains, respectively. Ethanolic extract isolated from both leaf and fruit of *A. hirsutus* have good active antifungal activity. It exhibited good inhibition activity against *A. tamarii*, *A. fumigates*, *A. flavus*, and *A. niger*. Ethanolic extract showed the maximum zone of inhibition against *A. tamarii*. **Shanmugapriya k et al.**,^[13]

The aqueous extract of bark of *Artocarpus hirsutus* is a suitable antimicrobial agent against *E. coli*, *Pseudomonas* and *Bacillus* sp. The antimicrobial efficacy of the aqueous extract of bark of *Artocarpus hirsutus* against *E. coli*, *Pseudomonas aeruginosa* and *Bacillus subtilis*. The aqueous extract was found very significantly inhibiting the *E. coli* and *Pseudomonas* even at low concentrations. **Jim Thomas et al.**,^[14]

Anti Inflammatory Activity

The ethanol extract of *Artocarpus hirsutus* was screened for its anti-inflammatory activity *in vivo*. From the results, it may be concluded that tender leaves of *Artocarpus hirsutus* possess significant anti-inflammatory activity. **Anupriya Thomas et al.**,^[15]

Hepatoprotective Activity

The *in vivo* hepatoprotective activity showed that the methanol extract of exhibit significant hepatoprotective activity. This might be flavonoids and tanins present in the plant extract. Antioxidant protections of MEAH might be due to presence of Flavonoids and tannins that regenerate liver cells and fix the membrane. The study shows that the MEAH at higher dose (500mg/kg p.o.) is close to standard. The histopathological study shows that constituents like tannins and flavonoids in extract showed superb protection to liver architecture almost to the level of the Silymarin treated group. The extracts also show the significant liver protection activity in dose dependent mode by reducing enzymes. Thus 70% MEAH proven hepatoprotective activity may be due to flavonoids and tannins. **Jithendra Patel et al.**,^[16]

Anti Diabetic Activity

The ethyl acetate seed extract of *Artocarpus hirsutus* at different doses was selected and administered orally. The blood glucose levels were estimated by the glucose oxidase method,

and insulin levels were measured by chemiluminescence assay method. The study has shown that different doses of *A. hirsutus* exhibited a significant antihyperglycemic activity in diabetic animals. **Sireesha.K et al.**,^[17]

The histopathological evaluation of ethanolic *Artocarpus hirsutus* extract (200 mg/kg, 400 mg/kg) shows the regeneration of the beta cells of islets cells of pancreas. This shows the protective action of the extract of *Artocarpus hirsutus* on beta cells of the pancreas. **R.Rajeswari et al.**,^[18]

Synthesis of Silver Nano Particles

Nanoparticle synthesis and the study of their size and properties are of fundamental importance in the advancement of recent research in the field of medicinal search. The leaves of *Artocarpushirsutus* were used to synthesize silver nanoparticles. Silver nitrate is used as reducing agent as silver has distinctive properties such as good silver conductivity, catalytic and chemical stability. The aqueous silver ions when exposed to plant extracts were reduced in solution, there by leading to the formation of silver hydrosol. The time duration of change in color varies from plant to plant. The synthesis of SNPs had been confirmed by measuring the UV-Vis spectrum of the reaction media. The preliminary analysis of the extracts was performed to determine the presence or absence of the primary or secondary metabolites. The phytochemical analysis showed the presence of Carbohydrate, Flavonoids, Alkaloids and Proteins in aqueous, boiled, methanolic and dried extract of *Artocarpus hirsutus*. **Anu.V et al.**,^[19]

Antiulcer Activity

The antiulcer activity was conducted with ethanolic extract of the plant bark using rat. The effect of the extract and the standard on gastric acid secretion volume, pH, total acidity and gastric ulcer were noted. **D. Dibin Lal et al.**,^[20]

Diuretic Activity

The aqueous extract of *Artocarpus hirsutus* fruits were evaluated for diuretic activity using modified Lipchitz method. The parameters like urine volume, concentration of excreted sodium and potassium ions, ratio of sodium to potassium ions excreted were noted. Significant diuretic activity was found to present in the *Artocarpus hirsutus* fruit extract. **Azeem.a.k et al.**,^[21]

Alzheimer's Disease

Based on both the insilico and invitro studies, it is concluded that the edible fleshy part of the fruit of *Artocarpus hirsutus* can be used as food supplement which, may reduce the progress or severity of Alzheimer's disease. The study showed that the compounds in *Artocarpus hirsutus* fruit pulp have better binding affinity against Acetylcholine Esterase and is an efficient free radical scavenger. **M.Jeyam et al.**,^[22]

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