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ARTOCARPUS LAKOOCHA ROXB: AN OVERVIEW

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ABSTRACT

Artocarpus lakoocha (Moraceae) is a widely used medicinal plant by tribals of Jharkhand, India for the treatment of many diseases. *Artocarpus lakoocha* Roxb. (Hindi: Dahu, Barhal, Beng. Dahu, Sans. Lokoocha, Eng.: Monkey Jack) is a large deciduous tree reaching 15-18 m in height with a spreading head. Reviews of the records in both, traditional and scientific literature. Using DPPH and Ferric Ion Reducing properties investigated the antioxidant activity of the plant. *Artocarpus lakoocha* Roxb. contains a crude protein, crude fiber and mineral contents.

INTRODUCTION

Artocarpus lakoocha Roxb trees of the Moraceae familyThe edible fruit pulp is believed to act as a tonic for the liver. *Artocarpus lakoocha* Roxb. belongs to family of Moraceae. It is commonly called as Monkey jack. *Artocarpus lakoocha* Roxb. is a perennial tree found on west coast from Kokan southwards to Kerala and Tamil Nadu. A large deciduous tree reaching 15-18m in height with a spreading head bark roughy , grayn, young shoot thin densely clothed with a soft grey , tawny and rusty tomentum. Leaves coriaceous, 10-30 by 5-15 cm., oblong elliptic or subovate. The unripe fruit is hot, sour, sweet, causes tridosa impotency, loss of apetite, blood complaint. The ripe fruit is sour sweet, tonic to liver. The seed are good purgative for childrens (Yunani) [1]. It has many pharmacological activities such as anti-inflammatory, antiviral, anticancer and anti-HIV [2].

BOTANICAL CLASSIFICATION OF *ARTOCARPUS LAKOOCHA*.

Kingdom	Plantae
Division	Tracheophyta
Class	Magnoliophyta
Order	Rosales
Family	Moraceae
Genus	Artocarpus
Species	lakoocha [3]

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ETHANOPHARMACOLOGICAL USES

Artocarpus lakoocha Roxb (Syn: *A. lacucha* Buch.-Ham.) is a member of the family Moraceae and is cultivated in Uttar Pradesh, Bengal, Khasi Hills and Western Ghats. It is called Monkey Jack in English and in Ayurveda it is called Lakuch, Kshudra Panas, Granthiphala and Pitanaasha. Bark when applied externally, draws out purulent matter; heals boils, cracked skin and pimples. Seeds are purgative, haemagglutinating. Antibacterial *A. lakoocha* possessed several similar properties such as blood type agglutination [4]. Oxyresveratrol, isolated from heartwood of *A. lakoocha* has shown moderate anti-herpes simplex virus activity and anti-HIV activity against a wild-type human immunodeficiency virus type 1 [5].

MORPHOLOGY

Artocarpus lakoocha is a large deciduous tree reaching 15-18 m in height with a spreading head.

Leaves: Leaves alternate, 10-25 cm long, elliptical, pointed and leathery.

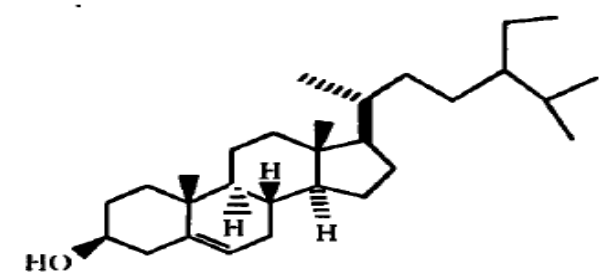
Flower: Flowers unisexual-male and female flowers in separate spherical heads but on the same tree. Male flowers are yellow-orange while the female are reddish.

Fruit: Fruit is a syncarp (the entire female inflorescence forms a fruit), irregularly rounded, green when young, turning yellow at the time of maturity, later brown. The

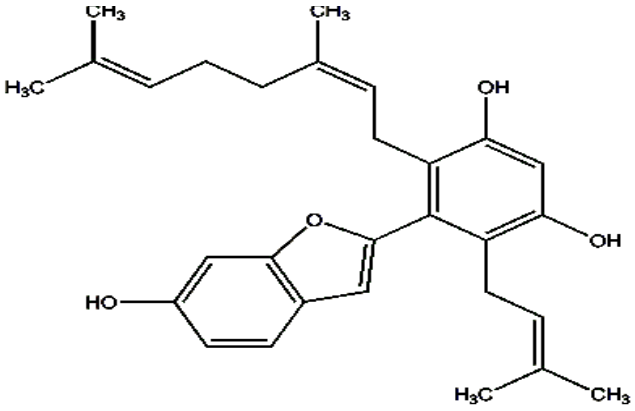
size differs but the diameter is typically 5-10 cm while fruit weights 200-350 g. The number of seeds/fruit varies accordingly, but typically there are 10-30 per fruit.

Seed: Seeds irregular and vary in size like the fruits. At maturity, most seeds are about one cm long, more or less flattened and pointed at the embryo end, the seed-coat is thin and white. The seeds contain sticky white latex.

Chemical Constituents: The heartwood contains artocarpin, norartocarpin, norcycloartocarpin, cycloartocarpin, resorcinol, and oxyresveratrol. β-sitosterol [6].



β-Sitosterol



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PHARMACOLOGICAL PROPERTIES OF *ARTOCARPUS LAKOOCHA*

Antiviral activity

Artocarpus lakoocha Roxburgh was investigated for its ability to inhibit the growth of herpes simplex virus (HSV). It is a DNA virus divided with two types HSV-1 and HSV-2. The HSV-1 is responsible for facial infections, visceral infections in immune compromised hosts, and HSV encephalitis in adults. HSV-2 is associated with infections of the genital tract and HSV related neonatal diseases. The stilbene oxyresveratrol (2,4,3,5-tetrahydroxystilbene) was also studied for its anti-HIV activity. The stilbene oxyresveratrol possessed moderate activity against both types of HSV. In addition, oxyresveratrol was evaluated for potential anti-HIV activity against a wild-type human immunodeficiency virus type 1 (HIV-1/LAI) isolate and was found to be a modest inhibitor of HIV (EC50 28.2 mM), showing no toxicity in PBM, CEM and Vero cells at 100mM. The heartwood of *Artocarpus lakoocha*, which contains a large amount of oxyresveratrol, could be considered as a source of starting material for the development of a new natural product as anti-HSV and anti-HIV agents [7].

Inhibitors of tyrosinase activity

The heartwood extract of *Artocarpus lakoocha* Roxb. was evaluated for the in vitro tyrosinase-inhibitory activity and the in vivo melanin-reducing efficacy in human volunteers. The IC50 of the extract and oxyresveratrol, its major active ingredient, against mushroom tyrosinase was 0.76 and 0.83_g/ml, respectively. The extract dissolved in propylene glycol was subsequently tested in female volunteers using a parallel clinical trial with self-control (n = 20 per group). The first group received the 0.25% (w/v) *Artocarpus lakoocha* solution as the test solution, whereas the second and the third group, respectively, received 0.25% licorice extract and 3% kojic acid as the reference solutions in the same solvent. Then each group were applied twice daily and the test (or reference) solution in one of upper arm, whereas the remaining arm was treated with only propylene glycol (self-control) for 12 weeks.

Anthelmintic activity

The effect of the crude extract of *Artocarpus lakoocha* (70%compositionis 2,4,30,50-tetrahydroxystilbene -THS) on adult *Fasciola gigantica* was evaluated after incubating the parasites in M-199 medium containing 250, 500, 750 and 1000 lg/ml of the crude extract, or triclabendazole (TCZ) at the concentrations of 80 and 175 lg/ml as the positive control, for 3, 6, 12 and 24 h, using relative motility (RM) assay and observation by scanning electron microscope (SEM). Decreased contraction and motility were first observed after 3 h incubation with TCZ at the concentration 80 and 175 lg/ml. TCZ markedly reduced the parasite's motility at the concentration of 175 lg/ml at 6 h, and killed the worms after 12 h exposure. The crude extract of A. lakoocha at all concentrations reduced the parasite's motility similar to TCZ at 3 h incubation. In 250 and 500 lg/ml of the crude extract, the values were decreased from 3 to 12 h, then they were stable between 12 and 24 h and reduced to the level approximately 30–40% of the control. At 750 and 1000 lg/ml concentrations the crude extract rapidly reduced the RM values from the start to 12 h and killed the parasites between 12 and 24 h incubation. The crude extract also inhibited the larval migration by 75% and 100% at the concentrations of 250–500 and 750–1000 lg/ml, respectively [8].

Antioxidants and antiglycation activity

From the heartwood of *Artocarpus lakoocha*, oxyresveratrol was isolated with a yield of 10%. The isolated oxyresveratrol showed strong antiglycation and antioxidant activities. The IC50 value for antiglycation was 2.0±0.03 μg/ml (five times higher than that of aminoguanidine), and the IC50 values for antioxidation

were 0.1±0.01 mg/ml (DPPH method) and 0.43±0.03 mg/ml (TBARS method), which were nearly twice as strong as those of resveratrol [9].

Antimicrobial activity

Two new stilbene derivatives, lakoochins A (**1**) and B (**2**), were isolated from the roots of *Artocarpus lakoocha*. The structures of **1** and **2** were elucidated by analysis of their spectral data. Lakoochins A (**1**) and B (**2**) exhibited antimycobacterial activity with the respective MIC values of 12.5 and 50 *í*g/mL. While **1** was cytotoxic against the BC (breast cancer) cell line (IC50 6.1 *í*g/mL) but inactive (at 20 *í*g/mL) toward KB (nasopharyngeal carcinoma) cells, compound **2** possessed cytotoxicity against the BC and KB cell lines with IC50 values of 3.1 and 6.1 *í*g/mL, respectively [10].

Activities of other species of Artocarpus

Antimalarial activity

Antimalarial activity-guided study of the aerial parts of Artocarpus integer led to the isolation of the prenylated stilbene, trans-4-(3-methyl-E-but-1-enyl)-3,5,2',4'-tetrahydroxystilbene with an EC50 of 1.7 micrograms/ml against Plasmodium falciparum in culture. The known stilbenes, trans-4-isopentenyl-3,5,2',4' tetrahydroxy stilbene and 4-methoxy-2,2-dimethyl-6-(2-(2,4-dihydroxy)phenyl-trans ethenyl) chromene , were also isolated. Structures of these compounds were deduced on the basis of their spectral data [11]

Antimalarial activity in vitro

Two new prenylated flavones, artocarpones A and B (1 and 2), and seven known isoprenylated flavonoids, artonin A (3), cycloheterophyllin (4), artoindonesianin E (5), artoindonesianin R (6), heterophyllin (7), heteroflavanone C (8), and artoindonesianin A-2 (9), have been isolated from the stem bark of Artocarpus champeden. Their structures were determined by spectroscopic analysis. Among the compounds isolated,8 had the most potent inhibitory activity against the growth of Plasmodium falciparum 3D7 clone, with an IC50 value of 1 nmol L−1 [12]

Antitubercular and Antiplasmodial activity

Antitubercular and antimalarial activity-guided study of the roots of *Artocarpus altilis* led to the isolation of nine prenylated flavones. Cycloartocarpin, artocarpin, and chaplashin, were isolated from the dichloromethane extract of the root stems, whereas morusin, cudraflavone B, cycloartobiloxanthone, artonin E, cudraflavone C and artobiloxanthone were found in the root barks. The isolated compounds exhibited antitubercular and antiplasmodial activities, and also showed moderate cytotoxicity against KB (human oral epidermoid carcinoma) and BC (human breast cancer) cell lines [13].

Anti-herpes simplex virus (HSV-1) activity

Oxyresveratrol, a major compound purified from *Artocarpus lakoocha*, a Thai traditional medicinal plant, was evaluated for its mechanism of action and therapeutic efficacy on cutaneous herpes simplex virus (HSV) infection in mice. The inhibitory concentrations for 50% HSV-1 plaque formation of oxyresveratrol, three clinical isolates, thymidine kinase (TK)-deficient and phosphonoacetic acid (PAA)-resistant HSV-1 were 19.8, 23.3, 23.5, 24.8, 25.5 and 21.7microg/ml, respectively. Oxyresveratrol exhibited the inhibitory activity at the early and late phase of viral replication and inhibited the viral replication with pretreatment in one-step growth assay of HSV-1 and HSV-2. Oxyresveratrol inhibited late protein synthesis at 30microg/ml. The combination of oxyresveratrol and acyclovir (ACV) produced synergistic anti-HSV-1 effect, as characterized by the isobologram of plaque inhibition. Mice orally treated with oxyresveratrol (500mg/kg/dose) dose at 8 h before and three times daily had significant delay in herpetic skin lesion development ($P<0.05$). Topical application of 30% oxyresveratrol ointment five times daily significantly delayed the development of skin lesions and protected mice from death ($P<0.0001$) [14].

Antiatherosclerotic activity

The cytoprotective effects of various solvent extracts of *Artocarpus altilis* (Parkinson) Fosberg were evaluated. The cytoprotective effects were determined in human U937 cells incubated with oxidized LDL (OxLDL) using the 4-[3-(4-iodophenyl)-2-(4-nitrophenyl)-2H-5-tetrazolio]-1, 3-benzene disulfonate (WST-1) assay. The results demonstrated that the ethyl acetate extract showed cytoprotective activities. To identify the main cytoprotective components, a bioassay guided isolation of the ethyl acetate extract afforded b-sitosterol (1) and six flavonoids (2-7). Their chemical structures were established on the basis of spectroscopic evidence and comparison with literature data. Of these compounds, compound 6 was obtained from A. altilis for the first time. The cytoprotective effect offers good prospects for the medicinal applications of *A. altilis* [15].

Antifungal activity

Antifungal activity guided fractionation of the *n*-butanol extract from the methanol extract of the leaves of *Artocarpus nobilis* furnished 2′, 4′, 4-trihydroxy-3′-geranylchalcone, 2′, 4′, 4-trihydroxy-3′- [6-hydroxy-3,7-dimethyl-2(*E*), 7-octadienyl]chalcone, 2′,4′,4-trihydroxy-3′-[2- hydroxy- 7 -methyl-3-methylene- 6- octaenyl]chalcone, 2′,3,4,4′-tetrahydroxy- 3′- geranylchalcone, 2′, 3, 4, 4′ tetrahydroxy-3′-[6-hydroxy-3,7-dimethyl-2(*E*), 7-octadienyl] chalcone. The chalcones 3 and 5 are new natural products whereas 1 and 2 are reported first time from the family Moraceae. All these compounds showed good fungicidal activity against *Cladosporium cladosporioides* and high radical scavenging activity towards the 2,2′-diphenyl-1-picrylhydrazyl (DPPH) radical

in TLC bio-autography method [16].

Anti-rotavirus and Antidiarrhoeal activity

Acute diarrhea, especially in children, is a very common disease with worldwide distribution and with a significant public health impact. Rotaviruses have been recognized as the major agents of diarrhea in infants and young children in developed as well as developing countries. In Brazil, diarrhea is one of the principal causes of death, mainly in the infant population. To fight diarrhea, traditional Brazilian medicine uses a great variety of plants. In this work, 12 medicinal plant species were screened for simian (SA-11) and human (HCR3) rotaviruses inhibition in vitro. At non-cytotoxic concentrations, the extracts from *Artocarpus integrifolia* L. (Moraceae) bark (480 µg/ml) Our results indicate that the extracts of *Artocarpus integrifolia*, *Myristica fragrans* and *Spongias lutea* can be useful in the treatment of human diarrhea if the etiologic agent is a rotavirus [17].

Antidiabetic activity

Investigations were carried out to evaluate the effects of hot-water extracts of *Artocarpus heterophyllus* leaves and *Asteracanthus longifolia* whole plant material on the glucose tolerance of normal human subjects and maturity-onset diabetic patients. The extracts of both *Artocarpus heterophyllus* and *Asteracanthus longifolia* significantly improved glucose tolerance in the normal subjects and the diabetic patients when investigated at oral doses equivalent to 20 g/kg of starting material [18].

Wound healing activity

Neutrophil influx is essential for corneal regeneration (Gan et al. 1999). KM+, a lectin from *Artocarpus integrifolia*, induces neutrophil migration (Santos-de-Oliveira et al. 1994). This study aims at investigating a possible effect of KM+ on corneal regeneration in rabbits. A 6.0-mm diameter area of debridement was created on the cornea of both eyes by mechanical scraping. The experimental eyes received drops of KM+ (2.5 microg/ml) every 2 h. The control eyes received buffer. The epithelial wounded areas of the lectin-treated and untreated eyes were stained with fluorescein, photographed and measured. The animals were killed 12 h (group 1, n = 5), 24 h (group 2, n = 10) and 48 h (group 3, n = 5) after the scraping. The corneas were analysed histologically (haematoxylin and eosin and immunostaining for proliferation cell nuclear antigen, p63, vascular endothelial growth factor, c-Met and laminin) [19].

Inhibitory activity

A new prenylated chalcone,3' ',3'dimethylpyrano[3',4']2,4,2'trihydroxychacone (1), was isolated from the heartwood of *Artocarpus communis*. Two flavonoid derivatives, (-)-cycloartocarpin (9) and (-)-cudraflavone A (10), were isolated as new isomers. In addition, eight known flavonoids, isobacachalcone (2), morachalcone A (3), gemichalcones B (4) and C (5), artocarpin (6), cudraflavone C (7), licoflavone C (8), and (2S)-euchrenone a (7) (11), were isolated and identified from this plant for the first time. Compounds 1-4, 6, and 11 exhibited potent inhibitory activity on nitric oxide production in RAW264.7 LPS-activated mouse macrophage cells with IC (50) values of 18.8, 6.4, 16.4, 9.3, 18.7, and 12.3 microM, respectively. The structure of compound 1 was elucidated by spectroscopic data analysis, including 1D and 2D NMR experiments [20].

CONCLUSION

Artocarpus lakoocha is an easily available plant. The plant belongs to family Moraceae, Family Moraceae which has given us many important medicinal plants like *A. camansi. A. hirsutus A. gomezianus.A. rigida A. altilis*. etc. Apart from this, old traditional texts like Yunani, Ayurveda, mention the protective role of *Artocarpus lakoocha* on important body organ like liver, blood, digestive etc, many of which are scientifically proven. Clinical investigation on peptic ulcer with aqueous extract. It contains almost all the properties of pharmaceutical care designed like antioxidant property, antidiabetic property, cholesterol lowering and potent antimicrobial property etc. The antioxidant constituents present in the fruits play important role in scavenging free radicals and reactive oxygen species which are responsible for number of human disorders. Another traditional use of *Artocarpus lakoocha* has been in the treatment of tapeworm infection. Seventy percent of the crude aqueous extract of *Artocarpus lakoocha* composed of phenolic compound, 2,4,3_,5_ tetrahydroxystilbene (THS). The chemical structure of THS is similar to that of halogenated phenolicfasciolocides. Hence, it is possible that THS could acts as a drug for the treatment of liver fluke infection in cattle and human.

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